Clinical trial results:
A Phase I/II, Multicenter, Open-label, Clinical Trial of Intratumoral/Intralesional Administration of RGT100 in Subjects with Advanced or Recurrent Tumors

Summary

EudraCT number	2016-003028-22
Trial protocol	DE GB ES FR
Global end of trial date	18 May 2018

Results information

Result version number	v1 (current)
This version publication date	17 May 2019
First version publication date	17 May 2019

Trial information

Trial identification

Sponsor protocol code	4621-001

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03065023
WHO universal trial number (UTN)	-
Other trial identifiers	Rigontec GMBH Protocol Number: RGT100-001, Merck Protocol Number: MK-4621-001

Notes:

Sponsors

Sponsor organisation name	Merck Sharp & Dohme Corp.
Sponsor organisation address	2000 Galloping Hill Road, Kenilworth, NJ, United States, 07033
Public contact	Clinical Trials Disclosure, Merck Sharp & Dohme Corp., ClinicalTrialsDisclosure@merck.com
Scientific contact	Clinical Trials Disclosure, Merck Sharp & Dohme Corp., 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	18 May 2018
Is this the analysis of the primary completion data?	Yes
Primary completion date	18 May 2018
Global end of trial reached?	Yes
Global end of trial date	18 May 2018
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

This is a Phase I/II multicenter, first-in-human open-label, dose escalation study to evaluate the safety, tolerability, and anti-tumor activity of intratumoral (IT)/intralesional (IL) injections of MK-4621 (RGT100) in adult participants with selected advanced or recurrent tumors..

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	19 December 2016
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	Germany: 4
Country: Number of subjects enrolled	Spain: 5
Country: Number of subjects enrolled	United Kingdom: 6
Worldwide total number of subjects	15
EEA total number of subjects	15

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)	10
From 65 to 84 years	5

85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Fifteen (15) participants for this study were recruited from four (4) study sites in three (3) countries. Group B was not started.

Pre-assignment

Screening details:

Participants with transdermally/transmucosally injectable tumors or injectable liver tumors were screened for this study.

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	Group A: MK-4621 0.2 mg

Arm description:

Participants with transdermally/transmucosally injectable tumors including cutaneous, subcutaneous or lymph node injectable tumors received MK-4621 0.2.mg via intratumoral (IT)/intralesional (IL) injection twice each week over a period of 4 weeks during Cycle 1. Participants may have continued to receive study treatment beyond Cycle 1 for the remaining duration of the study as long as clinical benefit (no overt clinical progression or toxicity considered to be intolerable as per Investigator's assessment) was present (could have been up to approximately 2 years). Each cycle was 28 days.

Arm type	Experimental
Investigational medicinal product name	MK-4621
Investigational medicinal product code	
Other name	RGT100
Pharmaceutical forms	Dispersion for injection
Routes of administration	Intratumoral use, Intralesional use

Dosage and administration details:

MK-4621 0.2 mg via intratumoral (IT) or intralesional (IL) injection

Arm title	Group A: MK-4621 0.4 mg

Arm description:

Participants with transdermally/transmucosally injectable tumors including cutaneous, subcutaneous or lymph node injectable tumors received MK-4621 0.4 mg via IT/IL injection twice each week over a period of 4 weeks during Cycle 1. Participants may have continued to receive study treatment beyond Cycle 1 for the remaining duration of the study as long as clinical benefit (no overt clinical progression or toxicity considered to be intolerable as per Investigator's assessment) was present (could have been up to approximately 2 years). Each cycle was 28 days.

Arm type	Experimental
Investigational medicinal product name	MK-4621
Investigational medicinal product code	
Other name	RGT100
Pharmaceutical forms	Dispersion for injection
Routes of administration	Intratumoral use, Intralesional use

Dosage and administration details:

MK-4621 0.4 mg via intratumoral (IT) or intralesional (IL) injection

Arm title	Group A: MK-4621 0.6 mg

Arm description:

Participants with transdermally/transmucosally injectable tumors including cutaneous, subcutaneous or

lymph node injectable tumors received MK-4621 0.6 mg via IT/IL injection twice each week over a period of 4 weeks during Cycle 1. Participants may have continued to receive study treatment beyond Cycle 1 for the remaining duration of the study as long as clinical benefit (no overt clinical progression or toxicity considered to be intolerable as per Investigator's assessment) was present (could have been up to approximately 2 years). Each cycle was 28 days.

Arm type	Experimental
Investigational medicinal product name	MK-4621
Investigational medicinal product code	
Other name	RGT100
Pharmaceutical forms	Dispersion for injection
Routes of administration	Intratumoral use, Intralesional use

Dosage and administration details:

MK-4621 0.6 mg via intratumoral (IT) or intralesional (IL) injection

Arm title	Group A: MK-4621 0.8 mg

Arm description:

Participants with transdermally/transmucosally injectable tumors including cutaneous, subcutaneous or lymph node injectable tumors received MK-4621 0.8 mg via IT/IL injection twice each week over a period of 4 weeks during Cycle 1. Participants may have continued to receive study treatment beyond Cycle 1 for the remaining duration of the study as long as clinical benefit (no overt clinical progression or toxicity considered to be intolerable as per Investigator's assessment) was present (could have been up to approximately 2 years). Each cycle was 28 days.

Arm type	Experimental
Investigational medicinal product name	MK-4621
Investigational medicinal product code	
Other name	RGT100
Pharmaceutical forms	Dispersion for injection
Routes of administration	Intratumoral use, Intralesional use

Dosage and administration details:

MK-4621 0.8 mg via intratumoral (IT) or intralesional (IL) injection

Number of subjects in period 1	Group A: MK-4621 0.2 mg	Group A: MK-4621 0.4 mg	Group A: MK-4621 0.6 mg
Started	3	3	3
Completed	1	1	2
Not completed	2	2	1
Adverse event, serious fatal	2	-	1
Participant Decision	-	-	-
Consent withdrawn by subject	-	-	-
Progressive Disease	-	1	-
Lost to follow-up	-	1	-

Number of subjects in period 1	Group A: MK-4621 0.8 mg
Started	6
Completed	3
Not completed	3
Adverse event, serious fatal	1
Participant Decision	1
Consent withdrawn by subject	1

Progressive Disease	-
Lost to follow-up	-

Baseline characteristics

Reporting groups	
Reporting group title	Group A: MK-4621 0.2 mg
Reporting group description:	
Participants with transdermally/transmucosally injectable tumors including cutaneous, subcutaneous or lymph node injectable tumors received MK-4621 0.2.mg via intratumoral (IT)/intralesional (IL) injection twice each week over a period of 4 weeks during Cycle 1. Participants may have continued to receive study treatment beyond Cycle 1 for the remaining duration of the study as long as clinical benefit (no overt clinical progression or toxicity considered to be intolerable as per Investigator's assessment) was present (could have been up to approximately 2 years). Each cycle was 28 days.	
Reporting group title	Group A: MK-4621 0.4 mg
Reporting group description:	
Participants with transdermally/transmucosally injectable tumors including cutaneous, subcutaneous or lymph node injectable tumors received MK-4621 0.4 mg via IT/IL injection twice each week over a period of 4 weeks during Cycle 1. Participants may have continued to receive study treatment beyond Cycle 1 for the remaining duration of the study as long as clinical benefit (no overt clinical progression or toxicity considered to be intolerable as per Investigator's assessment) was present (could have been up to approximately 2 years). Each cycle was 28 days.	
Reporting group title	Group A: MK-4621 0.6 mg
Reporting group description:	
Participants with transdermally/transmucosally injectable tumors including cutaneous, subcutaneous or lymph node injectable tumors received MK-4621 0.6 mg via IT/IL injection twice each week over a period of 4 weeks during Cycle 1. Participants may have continued to receive study treatment beyond Cycle 1 for the remaining duration of the study as long as clinical benefit (no overt clinical progression or toxicity considered to be intolerable as per Investigator's assessment) was present (could have been up to approximately 2 years). Each cycle was 28 days.	
Reporting group title	Group A: MK-4621 0.8 mg
Reporting group description:	
Participants with transdermally/transmucosally injectable tumors including cutaneous, subcutaneous or lymph node injectable tumors received MK-4621 0.8 mg via IT/IL injection twice each week over a period of 4 weeks during Cycle 1. Participants may have continued to receive study treatment beyond Cycle 1 for the remaining duration of the study as long as clinical benefit (no overt clinical progression or toxicity considered to be intolerable as per Investigator's assessment) was present (could have been up to approximately 2 years). Each cycle was 28 days.	

Reporting group values	Group A: MK-4621 0.2 mg	Group A: MK-4621 0.4 mg	Group A: MK-4621 0.6 mg
Number of subjects	3	3	3
Age categorical Units: Subjects			
Adults (18-64 years)	2	2	2
From 65-84 years	1	1	1
Age Continuous Units: Years			
arithmetic mean	51.7	48.7	55.3
standard deviation	± 26.8	± 18.1	± 16.0
Sex: Female, Male Units: Subjects			
Female	2	1	2
Male	1	2	1
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	0	0	0

Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	0	0	0
White	3	3	3
More than one race	0	0	0
Unknown or Not Reported	0	0	0
Ethnicity (NIH/OMB)			
Units: Subjects			
Hispanic or Latino	0	0	0
Not Hispanic or Latino	3	3	3
Unknown or Not Reported	0	0	0
Plasma Cytokine Release: Interleukin-6			
Blood samples were collected at baseline for the analysis of cytokine release for Interleukin-6 (IL-6) in plasma.			
Units: ng/L			
median	9.3	9.3	10
full range (min-max)	9.3 to 9.3	9.3 to 31.5	7.5 to 12.9
Plasma Cytokine Release: Tumor Necrosis Factor-alpha (TNF-a)			
Blood samples were collected at baseline for the analysis of cytokine release for tumor necrosis factor-alpha [TNF-a]) in plasma.			
Units: ng/L			
median	8.3	8.3	24.2
full range (min-max)	8.3 to 8.3	8.3 to 8.3	9.7 to 24.4

Reporting group values	Group A: MK-4621 0.8 mg	Total	
Number of subjects	6	15	
Age categorical			
Units: Subjects			
Adults (18-64 years)	4	10	
From 65-84 years	2	5	
Age Continuous			
Units: Years			
arithmetic mean	64.2		
standard deviation	± 8.3	-	
Sex: Female, Male			
Units: Subjects			
Female	2	7	
Male	4	8	
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	6	15	
More than one race	0	0	
Unknown or Not Reported	0	0	
Ethnicity (NIH/OMB)			
Units: Subjects			
Hispanic or Latino	0	0	
Not Hispanic or Latino	6	15	

Unknown or Not Reported	0	0	

Plasma Cytokine Release: Interleukin-6			
Blood samples were collected at baseline for the analysis of cytokine release for Interleukin-6 (IL-6) in plasma.			
Units: ng/L median full range (min-max)	 7.5 7.5 to 15.6	 -	
Plasma Cytokine Release: Tumor Necrosis Factor-alpha (TNF-a)			
Blood samples were collected at baseline for the analysis of cytokine release for tumor necrosis factor-alpha [TNF-a]) in plasma.			
Units: ng/L median full range (min-max)	 9.7 9.7 to 30.4	 -	

End points

End points reporting groups

Reporting group title	Group A: MK-4621 0.2 mg

Reporting group description:

Participants with transdermally/transmucosally injectable tumors including cutaneous, subcutaneous or lymph node injectable tumors received MK-4621 0.2.mg via intratumoral (IT)/intralesional (IL) injection twice each week over a period of 4 weeks during Cycle 1. Participants may have continued to receive study treatment beyond Cycle 1 for the remaining duration of the study as long as clinical benefit (no overt clinical progression or toxicity considered to be intolerable as per Investigator's assessment) was present (could have been up to approximately 2 years). Each cycle was 28 days.

Reporting group title	Group A: MK-4621 0.4 mg

Reporting group description:

Participants with transdermally/transmucosally injectable tumors including cutaneous, subcutaneous or lymph node injectable tumors received MK-4621 0.4 mg via IT/IL injection twice each week over a period of 4 weeks during Cycle 1. Participants may have continued to receive study treatment beyond Cycle 1 for the remaining duration of the study as long as clinical benefit (no overt clinical progression or toxicity considered to be intolerable as per Investigator's assessment) was present (could have been up to approximately 2 years). Each cycle was 28 days.

Reporting group title	Group A: MK-4621 0.6 mg

Reporting group description:

Participants with transdermally/transmucosally injectable tumors including cutaneous, subcutaneous or lymph node injectable tumors received MK-4621 0.6 mg via IT/IL injection twice each week over a period of 4 weeks during Cycle 1. Participants may have continued to receive study treatment beyond Cycle 1 for the remaining duration of the study as long as clinical benefit (no overt clinical progression or toxicity considered to be intolerable as per Investigator's assessment) was present (could have been up to approximately 2 years). Each cycle was 28 days.

Reporting group title	Group A: MK-4621 0.8 mg

Reporting group description:

Participants with transdermally/transmucosally injectable tumors including cutaneous, subcutaneous or lymph node injectable tumors received MK-4621 0.8 mg via IT/IL injection twice each week over a period of 4 weeks during Cycle 1. Participants may have continued to receive study treatment beyond Cycle 1 for the remaining duration of the study as long as clinical benefit (no overt clinical progression or toxicity considered to be intolerable as per Investigator's assessment) was present (could have been up to approximately 2 years). Each cycle was 28 days.

Primary: Number of Participants Who Experienced a Treatment-related Adverse Event (AE) or Laboratory Abnormality by Severity Graded According to National Cancer Institute Common Terminology Criteria for Adverse Events (NCI CTCAE) Version 4.03 Criteria

End point title	Number of Participants Who Experienced a Treatment-related Adverse Event (AE) or Laboratory Abnormality by Severity Graded According to National Cancer Institute Common Terminology Criteria for Adverse Events (NCI CTCAE) Version 4.03 Criteria[1]

End point description:

An AE was defined as any untoward medical occurrence in a study participant administered study treatment which did not necessarily have a causal relationship with this treatment. Treatment-related was defined as having a "Possible" or "Related" relationship to study treatment, as assessed by the Investigator. Severity of AE referred to the extent to which an AE affected the participants daily activities as assessed by the Investigator and was based on NCI CTCAE grades: Grade 1 (Mild); Grade 2 (Moderate); Grade 3 (Severe or medically significant but not immediately life-threatening); Grade 4 (Life-threatening consequences); or Grade 5 (Death related to AE). The number of participants who experienced at least one treatment-related AE or laboratory abnormality are presented by severity. The safety population consisted of all participants who received ≥1 injection of MK-4621.

End point type	Primary

End point timeframe:

Up to 90 days post last injection (Up to approximately 192 days)

Notes:

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

End point values	Group A: MK-4621 0.2 mg	Group A: MK-4621 0.4 mg	Group A: MK-4621 0.6 mg	Group A: MK-4621 0.8 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	3	3	6
Units: Participants				
Grade 1	1	2	2	3
Grade 2	0	1	1	2
Grade 3	1	0	0	1
Grade 4	0	0	0	0
Grade 5	0	0	0	0

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants Who Experienced a Serious Adverse Event (SAE)

End point title	Number of Participants Who Experienced a Serious Adverse Event (SAE)[2]

End point description:

A SAE was defined as any AE, regardless of dose, causality or expectedness, that: • Resulted in death; • Was life-threatening; • Required inpatient hospitalization or prolonged existing inpatient hospitalization; • Resulted in persistent or significant incapacity or disability; • Was a congenital anomaly or birth defect; or • Was any other medically important event. The safety population consisted of all participants who received ≥1 injection of MK-4621.

End point type	Primary

End point timeframe:

Up to 90 days post last injection (Up to approximately 192 days)

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analysis was planned for or conducted for this end point.

End point values	Group A: MK-4621 0.2 mg	Group A: MK-4621 0.4 mg	Group A: MK-4621 0.6 mg	Group A: MK-4621 0.8 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	3	3	6
Units: Participants	2	2	1	3

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants Who Discontinued Study Treatment Due to a Treatment-related Adverse Event (AE)

End point title	Number of Participants Who Discontinued Study Treatment Due

	to a Treatment-related Adverse Event (AE)[3]

End point description:

An AE was defined as any untoward medical occurrence in a study participant administered a study treatment which did not necessarily have a causal relationship with this treatment. Treatment-related was defined as having a "Possible" or "Related" relationship to study treatment, as assessed by the Investigator. The number of participants who discontinued study treatment due to a treatment-related AE is presented. The safety population consisted of all participants who received ≥1 injection of MK-4621.

End point type	Primary

End point timeframe:

Up to last injection (Up to approximately 102 days)

Notes:

[3] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analysis was planned for or conducted for this end point.

End point values	Group A: MK-4621 0.2 mg	Group A: MK-4621 0.4 mg	Group A: MK-4621 0.6 mg	Group A: MK-4621 0.8 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	3	3	6
Units: Participants	0	0	0	0

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants Who Experienced a Dose-limiting Toxicity (DLT) by Severity Graded According to National Cancer Institute Common Terminology Criteria for Adverse Events (NCI CTCAE) Version 4.03 Criteria

End point title	Number of Participants Who Experienced a Dose-limiting Toxicity (DLT) by Severity Graded According to National Cancer Institute Common Terminology Criteria for Adverse Events (NCI CTCAE) Version 4.03 Criteria[4]

End point description:

DLTs were assessed during the 1st treatment cycle (28 days) & were defined as any drug-related toxicity that occurred during the 28-day DLT period & included:
• Non-hematologic toxicity Grade ≥3 (except diarrhea, nausea, & vomiting unless lasting >3 days despite optimal supportive care);
• Confirmed non-hematologic appropriately graded laboratory findings of Grade ≥3 that were ≤ Grade 1 at baseline;
• Hematologic toxicity: Grade 4 neutropenia ≥5 days, or Grade 3 neutropenia with fever (fever is >38.4ºC); Grade 4 thrombocytopenia, or Grade 3 thrombocytopenia lasting >7 days or with bleeding; and
• Any other toxicity assessed as related to MK-4621, & which, in the opinion of the Investigator & the Sponsor physician constituted a DLT.
The number of participants who experienced a DLT is presented by NCI CTCAE version 4.03 severity grade. The DLT evaluable population consisted of participants who completed Cycle 1 (Day 28) or

End point type	Primary

End point timeframe:

Cycle 1 (Up to approximately 28 days); Each cycle was 28 days.

Notes:

[4] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analysis was planned for or conducted for this end point.

End point values	Group A: MK-4621 0.2 mg	Group A: MK-4621 0.4 mg	Group A: MK-4621 0.6 mg	Group A: MK-4621 0.8 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	3	3	6
Units: Participants				
Grade 1	0	0	0	0
Grade 2	0	0	0	0
Grade 3	0	0	0	0
Grade 4	0	0	0	0
Grade 5	0	0	0	0

Statistical analyses

No statistical analyses for this end point

Secondary: Objective Response Rate as Evaluated Radiologically Using Immune-related Response Evaluation Criteria in Solid Tumors (irRECIST)

End point title	Objective Response Rate as Evaluated Radiologically Using Immune-related Response Evaluation Criteria in Solid Tumors (irRECIST)

End point description:

ORR was defined as the percentage of participants who had a Complete Response (CR) or a Partial Response. Per irRECIST, CR (irCR) was defined as the complete disappearance of all measurable and non-measurable lesions. Lymph nodes must also have decreased to <0 mm in short axis. And, per irRECIST, Partial Response (irPR) was defined as a decrease of ≥30% in total measured tumor burden (TMTB) relative to baseline. For this study, irRECIST was modified to follow a maximum of 10 target lesions and a maximum of 5 target lesions per organ. The percentage of participants who experienced an irCR or irPR based on irRECIST is presented. The efficacy population consisted of all allocated participants.

End point type	Secondary

End point timeframe:

Up to 60 days post last injection (Up to approximately 162 days)

End point values	Group A: MK-4621 0.2 mg	Group A: MK-4621 0.4 mg	Group A: MK-4621 0.6 mg	Group A: MK-4621 0.8 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	3	3	6
Units: Percentage of Participants				
number (confidence interval 95%)	0 (0.0 to 70.8)	0 (0.0 to 70.8)	0 (0.0 to 70.8)	0 (0.0 to 45.9)

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Mean Fold Change from Baseline in Plasma Cytokine Release by Cytokine Type: Day 1 (6 Hours Post Injection)

End point title	Mean Fold Change from Baseline in Plasma Cytokine Release by Cytokine Type: Day 1 (6 Hours Post Injection)

End point description:

Blood samples were collected at various time points for the analysis of mean fold change from baseline in cytokine release for selected cytokines (Interleukin-6 [IL-6] and tumor necrosis factor-alpha [TNF-a]) in plasma. The cytokine evaluable population consisted of all participants who received ≥1 injection of MK-4621 and had baseline and post treatment cytokine data for this end point.

End point type	Other pre-specified

End point timeframe:

Baseline and Cycle 1 Day 1 (6 hours post injection) (Up to 1 day); Each cycle was 28 days.

End point values	Group A: MK-4621 0.2 mg	Group A: MK-4621 0.4 mg	Group A: MK-4621 0.6 mg	Group A: MK-4621 0.8 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	3	3	6
Units: Fold change				
arithmetic mean (standard deviation)				
IL-6	1 (± 0)	1.95 (± 1.64)	2.71 (± 2.34)	2.52 (± 3.14)
TNF-a	1 (± 0)	1 (± 0)	1 (± 0.6)	0.89 (± 0.28)

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Mean Fold Change from Baseline in Plasma Cytokine Release by Cytokine Type: Day 1 (24 Hours Post Injection)

End point title	Mean Fold Change from Baseline in Plasma Cytokine Release by Cytokine Type: Day 1 (24 Hours Post Injection)

End point description:

Blood samples were collected at various time points for the analysis of mean fold change from baseline in cytokine release for selected cytokines (Interleukin-6 [IL-6] and tumor necrosis factor-alpha [TNF-a]) in plasma. The cytokine evaluable population consisted of all participants who received ≥1 injection of MK-4621 and had baseline and post treatment cytokine data for this end point.

End point type	Other pre-specified

End point timeframe:

Baseline and Cycle 1 Day 1 (24 hours post injection) (Up to 2 days); Each cycle was 28 days.

End point values	Group A: MK-4621 0.2 mg	Group A: MK-4621 0.4 mg	Group A: MK-4621 0.6 mg	Group A: MK-4621 0.8 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	2	3	3	6
Units: Fold change				
arithmetic mean (standard deviation)				
IL-6	1 (± 0)	1.27 (± 0.46)	1.14 (± 0.3)	1.68 (± 0.97)
TNF-a	1 (± 0)	1 (± 0)	1.48 (± 1.44)	0.89 (± 0.28)

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Mean Fold Change from Baseline in Plasma Cytokine Release by Cytokine Type: Day 25 (6 Hours Post Injection)

End point title	Mean Fold Change from Baseline in Plasma Cytokine Release by Cytokine Type: Day 25 (6 Hours Post Injection)

End point description:

Blood samples were collected at various time points for the analysis of mean fold change from baseline in cytokine release for selected cytokines (Interleukin-6 [IL-6] and tumor necrosis factor-alpha [TNF-a]) in plasma. The cytokine evaluable population consisted of all participants who received ≥1 injection of MK-4621 and had baseline and post treatment cytokine data for this end point.

End point type	Other pre-specified

End point timeframe:

Baseline and Cycle 1 Day 25 (6 hours post injection) (Up to 25 days); Each cycle was 28 days.

End point values	Group A: MK-4621 0.2 mg	Group A: MK-4621 0.4 mg	Group A: MK-4621 0.6 mg	Group A: MK-4621 0.8 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	3	3	5
Units: Fold change				
arithmetic mean (standard deviation)				
IL-6	0.95 (± 0.08)	2 (± 1.11)	1.02 (± 0.31)	1.5 (± 0.61)
TNF-a	1 (± 0)	1 (± 0)	0.77 (± 0.21)	0.77 (± 0.29)

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Mean Fold Change from Baseline in Plasma Cytokine Release by Cytokine Type: Day 25 (24 Hours Post Injection)

End point title	Mean Fold Change from Baseline in Plasma Cytokine Release by Cytokine Type: Day 25 (24 Hours Post Injection)

End point description:

Blood samples were collected at various time points for the analysis of mean fold change from baseline in cytokine release for selected cytokines (Interleukin-6 [IL-6] and tumor necrosis factor-alpha [TNF-a]) in plasma. The cytokine evaluable population consisted of all participants who received ≥1 injection of MK-4621 and had baseline and post treatment cytokine data for this end point.

End point type	Other pre-specified

End point timeframe:

Baseline and Cycle 1 Day 25 (24 hours post injection) (Up to 26 days); Each cycle was 28 days.

End point values	Group A: MK-4621 0.2 mg	Group A: MK-4621 0.4 mg	Group A: MK-4621 0.6 mg	Group A: MK-4621 0.8 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	3	3	5
Units: Fold change				
arithmetic mean (standard deviation)				
IL-6	1.52 (± 0.9)	1 (± 0)	0.99 (± 0.1)	0.89 (± 0.19)
TNF-a	1 (± 0)	1 (± 0)	1.02 (± 0.63)	0.88 (± 0.32)

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Area Under the Concentration-Time Curve From Start of Dosing to Last Observed Concentration Above Limit of Quantitation (AUC0-t) of MK-4621: Day 1

End point title	Area Under the Concentration-Time Curve From Start of Dosing to Last Observed Concentration Above Limit of Quantitation (AUC0-t) of MK-4621: Day 1

End point description:

Blood samples were collected at various time points during Cycle 1 for the determination of MK-4621 AUC0-t on Day 1, which was defined as the AUC from the start time of dosing to the time of the last observed concentration above the limit of quantitation (LOQ). The pharmacokinetic (PK) evaluable population consisted of all participants who received ≥1 injection of MK-4621 and had pre- and post-treatment PK data for this end point.

End point type	Other pre-specified

End point timeframe:

Cycle 1 Day 1: Predose, 5 and 30 minutes, 2, 4, 6 and 24 hours post dose (Up to 2 days); Each cycle was 28 days.

End point values	Group A: MK-4621 0.2 mg	Group A: MK-4621 0.4 mg	Group A: MK-4621 0.6 mg	Group A: MK-4621 0.8 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	3	3	6
Units: h*ng/mL				
arithmetic mean (standard deviation)	0.00 (± 0.00)	0.174 (± 0.157)	0.0360 (± 0.0623)	1.87 (± 4.55)

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Area Under the Concentration-Time Curve From Start of Dosing to Last Observed Concentration Above Limit of Quantitation (AUC0-t) of MK-4621: Day 25

End point title	Area Under the Concentration-Time Curve From Start of Dosing to Last Observed Concentration Above Limit of Quantitation (AUC0-t) of MK-4621: Day 25

End point description:

Blood samples were collected at various time points during Cycle 1 for the determination of MK-4621 AUC0-t on Day 25, which was defined as the AUC from the start time of dosing to the time of the last observed concentration above the limit of quantitation (LOQ). The PK evaluable population consisted of all participants who received ≥1 injection of MK-4621 and had pre- and post-treatment PK data for this end point.

End point type	Other pre-specified

End point timeframe:

Cycle 1 Day 25: Predose, 5 and 30 minutes, 2, 4, 6 and 24 hours post dose (Up to 26 days); Each cycle was 28 days.

End point values	Group A: MK-4621 0.2 mg	Group A: MK-4621 0.4 mg	Group A: MK-4621 0.6 mg	Group A: MK-4621 0.8 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	3	3	5
Units: h*ng/mL				
arithmetic mean (standard deviation)	0.00 (± 0.00)	1.07 (± 0.767)	0.099 (± 0.172)	0.156 (± 0.350)

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Maximum Plasma Concentration (Cmax) of MK-4621: Day 1

End point title	Maximum Plasma Concentration (Cmax) of MK-4621: Day 1

End point description:

Blood samples were collected at various time points during Cycle 1 for the determination of MK-4621 Cmax on Day 1. The PK evaluable population consisted of all participants who received ≥1 injection of MK-4621 and had pre- and post-treatment PK data for this end point.

End point type	Other pre-specified

End point timeframe:

Cycle 1 Day 1: Predose, 5 and 30 minutes, 2, 4, 6 and 24 hours post dose (Up to 2 days); Each cycle was 28 days.

End point values	Group A: MK-4621 0.2 mg	Group A: MK-4621 0.4 mg	Group A: MK-4621 0.6 mg	Group A: MK-4621 0.8 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	3	3	6
Units: ng/mL				
arithmetic mean (standard deviation)	0.00 (± 0.00)	4.18 (± 3.76)	0.863 (± 1.50)	9.24 (± 21.9)

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Maximum Plasma Concentration (Cmax) of MK-4621: Day 25

End point title	Maximum Plasma Concentration (Cmax) of MK-4621: Day 25

End point description:

Blood samples were collected at various time points during Cycle 1 for the determination of MK-4621 Cmax on Day 25. The PK evaluable population consisted of all participants who received ≥1 injection of MK-4621 and had pre- and post-treatment PK data for this end point.

End point type	Other pre-specified

End point timeframe:

Cycle 1 Day 25: Predose, 5 and 30 minutes, 2, 4, 6 and 24 hours post dose (Up to 26 days); Each cycle was 28 days.

End point values	Group A: MK-4621 0.2 mg	Group A: MK-4621 0.4 mg	Group A: MK-4621 0.6 mg	Group A: MK-4621 0.8 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	3	3	5
Units: ng/mL				
arithmetic mean (standard deviation)	0.00 (± 0.00)	7.43 (± 2.44)	1.703 (± 2.95)	3.75 (± 8.39)

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Immune Infiltration of Injected Tumors by CD3 T Cell Receptor and Ki-67 Nuclear Protein: Day 1

End point title	Immune Infiltration of Injected Tumors by CD3 T Cell Receptor and Ki-67 Nuclear Protein: Day 1

End point description:

Sequential participant tumor biopsies were assessed via immunohistochemistry for the presence of tumor infiltrating CD3 T cell co-receptor-marked cells and Ki-67 nuclear protein-marked cells in tumor biopsies. CD3 is a marker of T cells and Ki-67 is a cell marker of proliferation and activation. The percentage of positive CD3-marked cells and double-positive CD3 and Ki-67 nuclear protein-marked cells in tumor biopsies predose on Day 1 are presented. The immune infiltration evaluable population consisted of all participants who received ≥1 injection of MK-4621 and had pre- and post-treatment immune infiltration data for this end point.

End point type	Other pre-specified

End point timeframe:

Day 1 prior to injection (Up to 1 day)

End point values	Group A: MK-4621 0.2 mg	Group A: MK-4621 0.4 mg	Group A: MK-4621 0.6 mg	Group A: MK-4621 0.8 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	1	3	1	1
Units: Percentage Positive Cells				
median (full range (min-max))				
CD3 Cells	8.81 (8.81 to 8.81)	17.58 (7.03 to 20.81)	34.64 (34.64 to 34.64)	17.34 (17.34 to 17.34)

Ki-67 Positive CD3 Cells	25.44 (25.44 to 25.44)	25.19 (18.46 to 48.86)	39.23 (39.23 to 39.23)	32.19 (32.19 to 32.19)

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Immune Infiltration of Injected Tumors by CD3 T Cell Receptor and Ki-67 Nuclear Protein: Day 25

End point title	Immune Infiltration of Injected Tumors by CD3 T Cell Receptor and Ki-67 Nuclear Protein: Day 25

End point description:

Sequential participant tumor biopsies were assessed via immunohistochemistry for the presence of tumor infiltrating CD3 T cell co-receptor-marked cells and Ki-67 nuclear protein-marked cells in tumor biopsies. CD3 is a marker of T cells and Ki-67 is a cell marker of proliferation and activation. The percentage of positive CD3-marked cells and double-positive CD3 and Ki-67 nuclear protein-marked cells in tumor biopsies postdose on Day 25 are presented. The immune infiltration evaluable population consisted of all participants who received ≥1 injection of MK-4621 and had pre- and post-treatment immune infiltration data for this end point.

End point type	Other pre-specified

End point timeframe:

Day 25 post injection (Up to 25 days)

End point values	Group A: MK-4621 0.2 mg	Group A: MK-4621 0.4 mg	Group A: MK-4621 0.6 mg	Group A: MK-4621 0.8 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	1	3	1	1
Units: Percentage Positive Cells				
median (full range (min-max))				
CD3 Cells	12.72 (12.72 to 12.72)	8.43 (8.09 to 12.00)	11.77 (11.77 to 11.77)	32.19 (32.19 to 32.19)
Ki-67 Positive CD3 Cells	16.96 (16.96 to 16.96)	36.39 (35.81 to 48.32)	17.93 (17.93 to 17.93)	12.16 (12.16 to 12.16)

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From first dose through up to 90 days after last dose (Up to approximately 192 days)

Adverse event reporting additional description:

All participants who received ≥1 injection of MK-4621. Per protocol, disease progression of study cancer was not considered an AE unless considered related to study treatment. Therefore, MedDRA preferred terms "Neoplasm progression", "Malignant neoplasm progression" & "Disease progression" not related to study treatment are excluded as AEs.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	18.0

Reporting groups

Reporting group title	Group A: MK-4621 0.2 mg
Reporting group description: -	
Reporting group title	Group A: MK-4621 0.4 mg
Reporting group description: -	
Reporting group title	Group A: MK-4621 0.6 mg
Reporting group description: -	
Reporting group title	Group A: MK-4621 0.8 mg
Reporting group description: -	

Serious adverse events	Group A: MK-4621 0.2 mg	Group A: MK-4621 0.4 mg	Group A: MK-4621 0.6 mg
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 3 (66.67%)	2 / 3 (66.67%)	1 / 3 (33.33%)
number of deaths (all causes)	2	0	1
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Neoplasm progression			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Vascular disorders			
Haemorrhage			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			

Disease progression			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyrexia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
Breast swelling			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 3 (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
Respiratory, thoracic and mediastinal disorders			
Pleural effusion			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory failure			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (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
Infections and infestations			
Device related infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Soft tissue infection			

subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (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

Serious adverse events	Group A: MK-4621 0.8 mg		
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 6 (50.00%)		
number of deaths (all causes)	1		
number of deaths resulting from adverse events	0		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Neoplasm progression			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
Haemorrhage			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Disease progression			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Pyrexia			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Reproductive system and breast disorders			
Breast swelling			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			

Pleural effusion			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Respiratory failure			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Device related infection			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pneumonia			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Soft tissue infection			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Group A: MK-4621 0.2 mg	Group A: MK-4621 0.4 mg	Group A: MK-4621 0.6 mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	3 / 3 (100.00%)	3 / 3 (100.00%)	3 / 3 (100.00%)
Vascular disorders			
Hypotension			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
General disorders and administration site conditions			
Axillary pain			

subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Chest pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Chills			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Fatigue			
subjects affected / exposed	3 / 3 (100.00%)	0 / 3 (0.00%)	2 / 3 (66.67%)
occurrences (all)	3	0	2
Induration			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Inflammation			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Injection site bruising			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Injection site erythema			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Injection site haematoma			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Injection site inflammation			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Injection site pain			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Injection site reaction			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Localised oedema			

subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Oedema peripheral			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Pain			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	3	0	0
Pyrexia			
subjects affected / exposed	0 / 3 (0.00%)	3 / 3 (100.00%)	3 / 3 (100.00%)
occurrences (all)	0	4	4
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	1	0	1
Dyspnoea			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Nasal discomfort			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Pneumothorax			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Productive cough			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Sinus disorder			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Psychiatric disorders			
Anxiety			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Investigations			

Body temperature increased			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Procalcitonin increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Injury, poisoning and procedural complications			
Post procedural haemorrhage			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Wound			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Cardiac disorders			
Sinus tachycardia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Tachycardia			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Nervous system disorders			
Cognitive disorder			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Dysgeusia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Headache			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	2 / 3 (66.67%)
occurrences (all)	0	1	2
Presyncope			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Blood and lymphatic system disorders			
Anaemia			

subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Iron deficiency anaemia			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Lymphadenopathy			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Eye disorders			
Blindness			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Anal haemorrhage			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Constipation			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Diarrhoea			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Mouth ulceration			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Nausea			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	2 / 3 (66.67%)
occurrences (all)	0	1	2
Stomatitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Toothache			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Vomiting			

subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Night sweats			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Pruritus			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Skin mass			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Endocrine disorders			
Adrenal insufficiency			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Muscle contracture			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Myalgia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Infections and infestations			
Cellulitis			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	2	0	0
Lower respiratory tract infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1

Respiratory tract infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Hypophosphataemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Iron deficiency			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1

Non-serious adverse events	Group A: MK-4621 0.8 mg		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	6 / 6 (100.00%)		
Vascular disorders			
Hypotension			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
General disorders and administration site conditions			
Axillary pain			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Chest pain			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Chills			
subjects affected / exposed	3 / 6 (50.00%)		
occurrences (all)	3		
Fatigue			
subjects affected / exposed	5 / 6 (83.33%)		
occurrences (all)	6		
Induration			

subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Inflammation			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Injection site bruising			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Injection site erythema			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Injection site haematoma			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Injection site inflammation			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Injection site pain			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Injection site reaction			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Localised oedema			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Oedema peripheral			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Pain			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Pyrexia			
subjects affected / exposed	5 / 6 (83.33%)		
occurrences (all)	8		
Respiratory, thoracic and mediastinal			

disorders Cough subjects affected / exposed occurrences (all) Dyspnoea subjects affected / exposed occurrences (all) Nasal discomfort subjects affected / exposed occurrences (all) Pneumothorax subjects affected / exposed occurrences (all) Productive cough subjects affected / exposed occurrences (all) Sinus disorder subjects affected / exposed occurrences (all)	 0 / 6 (0.00%) 0 1 / 6 (16.67%) 1 0 / 6 (0.00%) 0 1 / 6 (16.67%) 1 0 / 6 (0.00%) 0 0 / 6 (0.00%) 0		
Psychiatric disorders Anxiety subjects affected / exposed occurrences (all)	 1 / 6 (16.67%) 2		
Investigations Body temperature increased subjects affected / exposed occurrences (all) Procalcitonin increased subjects affected / exposed occurrences (all)	 0 / 6 (0.00%) 0 0 / 6 (0.00%) 0		
Injury, poisoning and procedural complications Post procedural haemorrhage subjects affected / exposed occurrences (all) Wound	 0 / 6 (0.00%) 0		

subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Cardiac disorders			
Sinus tachycardia			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Tachycardia			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Nervous system disorders			
Cognitive disorder			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	3		
Dysgeusia			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Headache			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Presyncope			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	2		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Iron deficiency anaemia			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Lymphadenopathy			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Eye disorders			
Blindness			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Gastrointestinal disorders			

Anal haemorrhage			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Constipation			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Diarrhoea			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	2		
Mouth ulceration			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Nausea			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	2		
Stomatitis			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Toothache			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Vomiting			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Night sweats			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Pruritus			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Skin mass			

subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0		
Endocrine disorders Adrenal insufficiency subjects affected / exposed occurrences (all)	 0 / 6 (0.00%) 0		
Musculoskeletal and connective tissue disorders Back pain subjects affected / exposed occurrences (all) Muscle contracture subjects affected / exposed occurrences (all) Myalgia subjects affected / exposed occurrences (all)	 0 / 6 (0.00%) 0 0 / 6 (0.00%) 0 1 / 6 (16.67%) 1		
Infections and infestations Cellulitis subjects affected / exposed occurrences (all) Lower respiratory tract infection subjects affected / exposed occurrences (all) Respiratory tract infection subjects affected / exposed occurrences (all)	 0 / 6 (0.00%) 0 0 / 6 (0.00%) 0 1 / 6 (16.67%) 1		
Metabolism and nutrition disorders Decreased appetite subjects affected / exposed occurrences (all) Hypophosphataemia subjects affected / exposed occurrences (all) Iron deficiency subjects affected / exposed occurrences (all)	 1 / 6 (16.67%) 1 1 / 6 (16.67%) 1 0 / 6 (0.00%) 0		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
07 April 2017	Amendment 2.0: The purpose of this amendment was to provide clarifying information on the following topics: • Decision making between dose levels in dose escalation and initiation of dose expansion; • Dose volume intratumoral administration and lesion size; • Participant enrollment and slot allocation procedures; • Safety measures and observation period of participants; and • Role of Safety Review Committee (SRC).

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
18 May 2018	Group B not started for business reasons.	-

Notes:

Limitations and caveats

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

Group B not started for business reasons.

Notes: