



Clinical trial results:

A Phase 1/2a Open Label, Multicenter Study to Assess the Safety, Tolerability, Pharmacokinetics and Preliminary Efficacy of AFM24 in Patients with Advanced Solid Cancers

Summary

EudraCT number	2019-003296-19
Trial protocol	ES GB DE
Global end of trial date	24 June 2024

Results information

Result version number	v1
This version publication date	27 July 2024
First version publication date	27 July 2024

Trial information

Trial identification

Sponsor protocol code	AFM24-101
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04259450
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Affimed GmbH
Sponsor organisation address	Gottlieb-Daimler-Straße 2, Mannheim, Germany, 68165
Public contact	Clinical Operations, Affimed GmbH, +49 621 560030, trials@affimed.com
Scientific contact	Clinical Operations, Affimed GmbH, +49 621 560030, trials@affimed.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	Interim
Date of interim/final analysis	30 September 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	24 June 2024
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

PHASE 1:

Determine the maximum tolerated dose (MTD), select a recommended phase 2 dose (RP2D), and investigate the safety and tolerability of AFM24 in patients with advanced solid malignancies.

PHASE 2a:

Assess the preliminary anti-tumor efficacy of AFM24, using tumor response criteria as defined by local Response Evaluation Criteria in Solid Tumors (RECIST) v1.1

Protection of trial subjects:

Only eligible subjects that met all the study inclusion and none of the exclusion criteria could enter the study. Subjects could withdraw from the study at any time without stating a reason and without prejudice to further treatment. The investigator may have withdrawn a subject from the study and discontinued study drug and assessments at any time. The sponsor reserved the right to request withdrawal of a subject because of protocol violation or any other significant reason.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	20 January 2020
Long term follow-up planned	Yes
Long term follow-up rationale	Safety, Efficacy
Long term follow-up duration	3 Months
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Spain: 25
Country: Number of subjects enrolled	United Kingdom: 9
Country: Number of subjects enrolled	Germany: 1
Country: Number of subjects enrolled	Korea, Republic of: 27
Country: Number of subjects enrolled	United States: 23
Worldwide total number of subjects	85
EEA total number of subjects	26

Notes:

Subjects enrolled per age group

In utero	0
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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)	50
From 65 to 84 years	35
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

AFM24-101 was a first in human Phase 1/2a open-label, non-randomized, multi-center, multiple ascending dose escalation/expansion study evaluating AFM24 as monotherapy in patients with advanced solid malignancies whose disease has progressed after treatment with previous anticancer therapies.

Pre-assignment

Screening details:

Phase 1 subjects enrolled if they had a tumor known to express Epidermal Growth Factor Receptor (EGFR), Phase 2 subjects were screened for positive EGFR from tumor site.

Specialists assessed the subjects, and they were enrolled in the study if they met all inclusion criteria and none of the exclusion criteria.

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	Phase 1- 14 mg Cohort 1

Arm description:

Subjects, with tumors known to express EGFR, who received 14 milligram (mg) AFM24 on Day 1, Day 8, Day 15, and Day 22 of a 28-day cycle.

Arm type	Experimental
Investigational medicinal product name	AFM24
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Intravenous AFM24 administrated 14 milligram weekly until disease progression, unacceptable toxicity, investigator discretion or withdrawal of consent.

Arm title	Phase 1- 40 mg Cohort 2
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Arm description:

Subjects, with tumors known to express EGFR, who received 40 milligram (mg) AFM24 on Day 1, Day 8, Day 15, and Day 22 of a 28-day cycle.

Arm type	Experimental
Investigational medicinal product name	AFM24
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Intravenous AFM24 administrated 14 milligram weekly until disease progression, unacceptable toxicity, investigator discretion or withdrawal of consent.

Arm title	Phase 1- 80 mg Cohort 3
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Arm description:

Subjects, with tumors known to express EGFR, who received 80 milligram (mg) AFM24 on Day 1, Day 8, Day 15, and Day 22 of a 28-day cycle.

Arm type	Experimental
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Investigational medicinal product name	AFM24
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for solution for infusion
Routes of administration	Intravenous use
Dosage and administration details:	
Intravenous AFM24 administrated 14 milligram weekly until disease progression, unacceptable toxicity, investigator discretion or withdrawal of consent.	
Arm title	Phase 1- 160 mg Cohort 4
Arm description:	
Subjects, with tumors known to express EGFR, who received 160 milligram (mg) AFM24 on Day 1, Day 8, Day 15, and Day 22 of a 28-day cycle.	
Arm type	Experimental
Investigational medicinal product name	AFM24
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for solution for infusion
Routes of administration	Intravenous use
Dosage and administration details:	
Intravenous AFM24 administrated 14 milligram weekly until disease progression, unacceptable toxicity, investigator discretion or withdrawal of consent.	
Arm title	Phase 1- 320 mg Cohort 5
Arm description:	
Subjects, with tumors known to express EGFR, who received 320 milligram (mg) AFM24 on Day 1, Day 8, Day 15, and Day 22 of a 28-day cycle.	
Arm type	Experimental
Investigational medicinal product name	AFM24
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for solution for infusion
Routes of administration	Intravenous use
Dosage and administration details:	
Intravenous AFM24 administrated 14 milligram weekly until disease progression, unacceptable toxicity, investigator discretion or withdrawal of consent.	
Arm title	Phase 1- 480 mg Cohort 6
Arm description:	
Subjects, with tumors known to express EGFR, who received 480 milligram (mg) AFM24 on Day 1, Day 8, Day 15, and Day 22 of a 28-day cycle.	
Arm type	Experimental
Investigational medicinal product name	AFM24
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for solution for infusion
Routes of administration	Intravenous use
Dosage and administration details:	
Intravenous AFM24 administrated 14 milligram weekly until disease progression, unacceptable toxicity, investigator discretion or withdrawal of consent.	
Arm title	Phase 1- 720 mg Cohort 7
Arm description:	
Subjects, with tumors known to express EGFR, who received 720 milligram (mg) AFM24 on Day 1, Day 8, Day 15, and Day 22 of a 28-day cycle. A dose could be given over two days (split day dosing).	
Arm type	Experimental

Investigational medicinal product name	AFM24
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Intravenous AFM24 administrated 14 milligram weekly until disease progression, unacceptable toxicity, investigator discretion or withdrawal of consent.

Arm title	Phase 2- CRC 480 mg Cohort A
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Arm description:

Subjects with microsatellite stable (MSS) colorectal cancer (CRC) with rat sarcoma gene (RAS) wild-type tumor expressing EGFR who received who received 480 milligram (mg) AFM24 weekly on Day 1, Day 8, Day 15, and Day 22 of a 28-day cycle. A dose could be given over two days (split day dosing).

Arm type	Experimental
Investigational medicinal product name	AFM24
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Intravenous AFM24 administrated 14 milligram weekly until disease progression, unacceptable toxicity, investigator discretion or withdrawal of consent.

Arm title	Phase 2- ccRCC 480 mg Cohort B
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Arm description:

Subjects with clear cell renal cell carcinoma (ccRCC) expressing EGFR who recieved 480 milligram (mg) AFM24 weekly on Day 1, Day 8, Day 15, and Day 22 of a 28-day cycle. A dose could be given over two days (split day dosing).

Arm type	Experimental
Investigational medicinal product name	AFM24
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Intravenous AFM24 administrated 14 milligram weekly until disease progression, unacceptable toxicity, investigator discretion or withdrawal of consent.

Arm title	Phase 2- NSCLC 480 mg Cohort C
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Arm description:

Subjects with advanced or metastatic (non-small cell lung cancer) NSCLC with an epidermal growth factor receptor (EGFR) mutation who received 480 milligram (mg) AFM24 weekly on Day 1, Day 8, Day 15, and Day 22 of a 28-day cycle. A dose could be given over two days (split day dosing).

Arm type	Experimental
Investigational medicinal product name	AFM24
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Intravenous AFM24 administrated 14 milligram weekly until disease progression, unacceptable toxicity, investigator discretion or withdrawal of consent.

Number of subjects in period 1	Phase 1- 14 mg Cohort 1	Phase 1- 40 mg Cohort 2	Phase 1- 80 mg Cohort 3
Started	2	6	4
Completed	0	0	0
Not completed	2	6	4
Adverse event, serious fatal	-	-	-
on treatment	-	-	-
Consent withdrawn by subject	-	-	-
Disease progression	2	3	4
Adverse event, non-fatal	-	3	-
Other than listed	-	-	-

Number of subjects in period 1	Phase 1- 160 mg Cohort 4	Phase 1- 320 mg Cohort 5	Phase 1- 480 mg Cohort 6
Started	5	6	6
Completed	0	0	0
Not completed	5	6	6
Adverse event, serious fatal	-	-	-
on treatment	-	-	-
Consent withdrawn by subject	-	-	-
Disease progression	4	6	6
Adverse event, non-fatal	1	-	-
Other than listed	-	-	-

Number of subjects in period 1	Phase 1- 720 mg Cohort 7	Phase 2- CRC 480 mg Cohort A	Phase 2- ccRCC 480 mg Cohort B
Started	6	19	8
Completed	0	0	0
Not completed	6	19	8
Adverse event, serious fatal	-	1	1
on treatment	-	1	1
Consent withdrawn by subject	-	1	-
Disease progression	6	15	6
Adverse event, non-fatal	-	1	-
Other than listed	-	-	-

Number of subjects in period 1	Phase 2- NSCLC 480 mg Cohort C
Started	23
Completed	0
Not completed	23
Adverse event, serious fatal	-
on treatment	2
Consent withdrawn by subject	-
Disease progression	17

Adverse event, non-fatal	3
Other than listed	1

Baseline characteristics

Reporting groups

Reporting group title	Phase 1- 14 mg Cohort 1
Reporting group description: Subjects, with tumors known to express EGFR, who received 14 milligram (mg) AFM24 on Day 1, Day 8, Day 15, and Day 22 of a 28-day cycle.	
Reporting group title	Phase 1- 40 mg Cohort 2
Reporting group description: Subjects, with tumors known to express EGFR, who received 40 milligram (mg) AFM24 on Day 1, Day 8, Day 15, and Day 22 of a 28-day cycle.	
Reporting group title	Phase 1- 80 mg Cohort 3
Reporting group description: Subjects, with tumors known to express EGFR, who received 80 milligram (mg) AFM24 on Day 1, Day 8, Day 15, and Day 22 of a 28-day cycle.	
Reporting group title	Phase 1- 160 mg Cohort 4
Reporting group description: Subjects, with tumors known to express EGFR, who received 160 milligram (mg) AFM24 on Day 1, Day 8, Day 15, and Day 22 of a 28-day cycle.	
Reporting group title	Phase 1- 320 mg Cohort 5
Reporting group description: Subjects, with tumors known to express EGFR, who received 320 milligram (mg) AFM24 on Day 1, Day 8, Day 15, and Day 22 of a 28-day cycle.	
Reporting group title	Phase 1- 480 mg Cohort 6
Reporting group description: Subjects, with tumors known to express EGFR, who received 480 milligram (mg) AFM24 on Day 1, Day 8, Day 15, and Day 22 of a 28-day cycle.	
Reporting group title	Phase 1- 720 mg Cohort 7
Reporting group description: Subjects, with tumors known to express EGFR, who received 720 milligram (mg) AFM24 on Day 1, Day 8, Day 15, and Day 22 of a 28-day cycle. A dose could be given over two days (split day dosing).	
Reporting group title	Phase 2- CRC 480 mg Cohort A
Reporting group description: Subjects with microsatellite stable (MSS) colorectal cancer (CRC) with rat sarcoma gene (RAS) wild-type tumor expressing EGFR who received who received 480 milligram (mg) AFM24 weekly on Day 1, Day 8, Day 15, and Day 22 of a 28-day cycle. A dose could be given over two days (split day dosing).	
Reporting group title	Phase 2- ccRCC 480 mg Cohort B
Reporting group description: Subjects with clear cell renal cell carcinoma (ccRCC) expressing EGFR who recieved 480 milligram (mg) AFM24 weekly on Day 1, Day 8, Day 15, and Day 22 of a 28-day cycle. A dose could be given over two days (split day dosing).	
Reporting group title	Phase 2- NSCLC 480 mg Cohort C
Reporting group description: Subjects with advanced or metastatic (non-small cell lung cancer) NSCLC with an epidermal growth factor receptor (EGFR) mutation who received 480 milligram (mg) AFM24 weekly on Day 1, Day 8, Day 15, and Day 22 of a 28-day cycle. A dose could be given over two days (split day dosing).	

Reporting group values	Phase 1- 14 mg Cohort 1	Phase 1- 40 mg Cohort 2	Phase 1- 80 mg Cohort 3
Number of subjects	2	6	4
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)	0	4	3
From 65-84 years	2	2	1
85 years and over	0	0	0
Age continuous Units: years			
arithmetic mean	73.0	54.7	47.2
standard deviation	± 0.0	± 14.12	± 20.89
Gender categorical Units: Subjects			
Female	1	1	0
Male	1	5	4
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	0	2	1
Not Hispanic or Latino	2	2	3
Unknown or Not Reported	0	2	0
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	1	0	0
White	1	4	4
More than one race	0	0	0
Unknown or Not Reported	0	2	0

Reporting group values	Phase 1- 160 mg Cohort 4	Phase 1- 320 mg Cohort 5	Phase 1- 480 mg Cohort 6
Number of subjects	5	6	6
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)	4	3	4
From 65-84 years	1	3	2
85 years and over	0	0	0
Age continuous Units: years			
arithmetic mean	58.4	57.7	59.7
standard deviation	± 11.35	± 16.99	± 12.08

Gender categorical Units: Subjects			
Female	4	3	2
Male	1	3	4
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	2	1	0
Not Hispanic or Latino	3	5	6
Unknown or Not Reported	0	0	0
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	1	1	0
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	0	1	0
White	4	4	5
More than one race	0	0	0
Unknown or Not Reported	0	0	1

Reporting group values	Phase 1- 720 mg Cohort 7	Phase 2- CRC 480 mg Cohort A	Phase 2- ccRCC 480 mg Cohort B
Number of subjects	6	19	8
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)	6	10	3
From 65-84 years	0	9	5
85 years and over	0	0	0
Age continuous Units: years			
arithmetic mean	53.8	62.7	67.1
standard deviation	± 10.57	± 9.32	± 15.0
Gender categorical Units: Subjects			
Female	1	5	2
Male	5	14	6
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	0	1	1
Not Hispanic or Latino	6	18	7
Unknown or Not Reported	0	0	0
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	1	10	1

Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	0	0	0
White	5	9	7
More than one race	0	0	0
Unknown or Not Reported	0	0	0

Reporting group values	Phase 2- NSCLC 480 mg Cohort C	Total	
Number of subjects	23	85	
Age categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	13	50	
From 65-84 years	10	35	
85 years and over	0	0	
Age continuous Units: years			
arithmetic mean	61.1		
standard deviation	± 11.83	-	
Gender categorical Units: Subjects			
Female	10	29	
Male	13	56	
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	1	9	
Not Hispanic or Latino	21	73	
Unknown or Not Reported	1	3	
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	
Asian	18	32	
Native Hawaiian or Other Pacific Islander	0	0	
Black or African American	0	2	
White	5	48	
More than one race	0	0	
Unknown or Not Reported	0	3	

End points

End points reporting groups

Reporting group title	Phase 1- 14 mg Cohort 1
Reporting group description: Subjects, with tumors known to express EGFR, who received 14 milligram (mg) AFM24 on Day 1, Day 8, Day 15, and Day 22 of a 28-day cycle.	
Reporting group title	Phase 1- 40 mg Cohort 2
Reporting group description: Subjects, with tumors known to express EGFR, who received 40 milligram (mg) AFM24 on Day 1, Day 8, Day 15, and Day 22 of a 28-day cycle.	
Reporting group title	Phase 1- 80 mg Cohort 3
Reporting group description: Subjects, with tumors known to express EGFR, who received 80 milligram (mg) AFM24 on Day 1, Day 8, Day 15, and Day 22 of a 28-day cycle.	
Reporting group title	Phase 1- 160 mg Cohort 4
Reporting group description: Subjects, with tumors known to express EGFR, who received 160 milligram (mg) AFM24 on Day 1, Day 8, Day 15, and Day 22 of a 28-day cycle.	
Reporting group title	Phase 1- 320 mg Cohort 5
Reporting group description: Subjects, with tumors known to express EGFR, who received 320 milligram (mg) AFM24 on Day 1, Day 8, Day 15, and Day 22 of a 28-day cycle.	
Reporting group title	Phase 1- 480 mg Cohort 6
Reporting group description: Subjects, with tumors known to express EGFR, who received 480 milligram (mg) AFM24 on Day 1, Day 8, Day 15, and Day 22 of a 28-day cycle.	
Reporting group title	Phase 1- 720 mg Cohort 7
Reporting group description: Subjects, with tumors known to express EGFR, who received 720 milligram (mg) AFM24 on Day 1, Day 8, Day 15, and Day 22 of a 28-day cycle. A dose could be given over two days (split day dosing).	
Reporting group title	Phase 2- CRC 480 mg Cohort A
Reporting group description: Subjects with microsatellite stable (MSS) colorectal cancer (CRC) with rat sarcoma gene (RAS) wild-type tumor expressing EGFR who received who received 480 milligram (mg) AFM24 weekly on Day 1, Day 8, Day 15, and Day 22 of a 28-day cycle. A dose could be given over two days (split day dosing).	
Reporting group title	Phase 2- ccRCC 480 mg Cohort B
Reporting group description: Subjects with clear cell renal cell carcinoma (ccRCC) expressing EGFR who recieved 480 milligram (mg) AFM24 weekly on Day 1, Day 8, Day 15, and Day 22 of a 28-day cycle. A dose could be given over two days (split day dosing).	
Reporting group title	Phase 2- NSCLC 480 mg Cohort C
Reporting group description: Subjects with advanced or metastatic (non-small cell lung cancer) NSCLC with an epidermal growth factor receptor (EGFR) mutation who received 480 milligram (mg) AFM24 weekly on Day 1, Day 8, Day 15, and Day 22 of a 28-day cycle. A dose could be given over two days (split day dosing).	

Primary: Phase 1: The Number of Subjects With Dose Limiting Toxicities (DLTs) During Cycle 1

End point title	Phase 1: The Number of Subjects With Dose Limiting Toxicities (DLTs) During Cycle 1 ^{[1][2]}
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End point description:

The number of patients with dose limiting toxicities (DLTs) in the first cycle, as assessed by the National Cancer Institute Common Terminology Criteria for Adverse Events (CTCAE) v5.0. DLT is defined as an adverse event (AE) or abnormal laboratory value assessed as unrelated to underlying disease, disease progression, inter-current illness, or concomitant medications, that occurs ≤ 28 days following the first dose of AFM24 (Cycle 1).

The Dose-Determining Set (DDS): All patients in the safety set (all patients who received at least one dose of AFM24), who had either (a) experienced DLT at any time during Cycle 1, or (b) met the minimum safety evaluation requirements without experiencing DLT within Cycle 1.

End point type	Primary
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End point timeframe:

During Cycle 1 (up to 28 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: As per protocol, endpoint was only analyzed descriptively.

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: According to the Protocol, the endpoint only considers subjects in the Phase 1 cohort.

End point values	Phase 1- 14 mg Cohort 1	Phase 1- 40 mg Cohort 2	Phase 1- 80 mg Cohort 3	Phase 1- 160 mg Cohort 4
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	2	4	4	4
Units: Participants	0	1	0	0

End point values	Phase 1- 320 mg Cohort 5	Phase 1- 480 mg Cohort 6	Phase 1- 720 mg Cohort 7	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	5	6	6	
Units: Participants	0	0	0	

Statistical analyses

No statistical analyses for this end point

Primary: Phase 2a: Overall Response Rate (Complete Response [CR] + Partial Response [PR])

End point title	Phase 2a: Overall Response Rate (Complete Response [CR] + Partial Response [PR]) ^{[3][4]}
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End point description:

Overall response as defined by achieving confirmed CR and/or PR assessed by Response Evaluation Criteria in Solid Tumors (RECIST) v1.1. Partial or complete response needs to be confirmed with repeated assessment at least 4 weeks after the initial assessment.

The safety set: All patients who received at least one dose of AFM24.

End point type	Primary
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End point timeframe:

Up to approximately 16 weeks.

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: According to the Protocol, the endpoint only considers subjects in the Phase 2 cohort.

[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: According to the Protocol, the endpoint only considers subjects in the Phase 2 cohort.

End point values	Phase 2- CRC 480 mg Cohort A	Phase 2- ccRCC 480 mg Cohort B	Phase 2- NSCLC 480 mg Cohort C	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	19	8	23	
Units: Participants	0	0	2	

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 1: The Number of Subjects With Treatment-emergent Adverse Events (TEAEs)

End point title	Phase 1: The Number of Subjects With Treatment-emergent Adverse Events (TEAEs) ^[5]
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End point description:

Adverse Events (AEs) will be summarized with patient counts by Medical Dictionary for Regulatory Activities (MedDRA) System Organ Classes (SOCs) and Preferred Terms (PTs).

The safety set: All patients who received at least one dose of AFM24.

End point type	Secondary
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End point timeframe:

From the start of first infusion till the last infusion + 30 days, up to approximately 43 weeks.

Notes:

[5] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: According to the Protocol, the endpoint only considers subjects in the Phase 1 cohort.

End point values	Phase 1- 14 mg Cohort 1	Phase 1- 40 mg Cohort 2	Phase 1- 80 mg Cohort 3	Phase 1- 160 mg Cohort 4
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	2	6	4	5
Units: Participants	2	6	4	5

End point values	Phase 1- 320 mg Cohort 5	Phase 1- 480 mg Cohort 6	Phase 1- 720 mg Cohort 7	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	6	6	6	
Units: Participants	6	6	6	

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 1: The Number of Subjects With Serious Adverse Events (SAEs)

End point title	Phase 1: The Number of Subjects With Serious Adverse Events (SAEs) ^[6]
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End point description:

Serious adverse Events (SAEs) will be summarized with patient counts by Medical Dictionary for Regulatory Activities (MedDRA) System Organ Classes (SOCs) and Preferred Terms (PTs).
The safety set: All patients who received at least one dose of AFM24.

End point type	Secondary
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End point timeframe:

From the start of first infusion till the last infusion + 30 days, up to approximately 43 weeks.

Notes:

[6] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: According to the Protocol, the endpoint only considers subjects in the Phase 1 cohort.

End point values	Phase 1- 14 mg Cohort 1	Phase 1- 40 mg Cohort 2	Phase 1- 80 mg Cohort 3	Phase 1- 160 mg Cohort 4
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	2	6	4	5
Units: Participants	2	3	2	2

End point values	Phase 1- 320 mg Cohort 5	Phase 1- 480 mg Cohort 6	Phase 1- 720 mg Cohort 7	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	6	6	6	
Units: Participants	4	3	2	

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 1: Area Under the Concentration-time Curve From Time 0 to Time Tau (7 Days) of AFM24 in Serum

End point title	Phase 1: Area Under the Concentration-time Curve From Time 0 to Time Tau (7 Days) of AFM24 in Serum ^[7]
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End point description:

Area under the concentration-time curve from time 0 to time tau (7 days) of AFM24 in serum(AUC0-

168).

The Pharmacokinetic set: all subjects who received at least one adequately documented dose of study drug and had at least one adequately documented post dose PK measurement. Subjects were excluded if they did not have at least two quantifiable concentration values, two of which must have occurred after T_{max}, this was the case for one subject in Cohort 6.

End point type	Secondary
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End point timeframe:

Pre-dose (2 hours maximum) and 15, 30, 45 min after start of infusion (SOI) and end of infusion (EOI) and 1, 4, 18, 24, 48, 144 hours after EOI on Cycle 1 Day 22.

Notes:

[7] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: According to the Protocol, the endpoint only considers subjects in the Phase 1 cohort.

End point values	Phase 1- 14 mg Cohort 1	Phase 1- 40 mg Cohort 2	Phase 1- 80 mg Cohort 3	Phase 1- 160 mg Cohort 4
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	2	3	4	4
Units: hours*nanogram /milliLiter				
arithmetic mean (standard deviation)	53400 (± 61700)	549000 (± 254000)	1290000 (± 395000)	4940000 (± 1370000)

End point values	Phase 1- 320 mg Cohort 5	Phase 1- 480 mg Cohort 6	Phase 1- 720 mg Cohort 7	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	6	5	6	
Units: hours*nanogram /milliLiter				
arithmetic mean (standard deviation)	18100000 (± 6120000)	28700000 (± 7620000)	40200000 (± 12000000)	

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 1: Maximum Plasma Concentration (C_{max}) of AFM24

End point title	Phase 1: Maximum Plasma Concentration (C _{max}) of AFM24 ^[8]
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End point description:

Maximum measured concentration (C_{max}) of AFM24 in serum.

The Pharmacokinetic set: all subjects who received at least one adequately documented dose of study drug and had at least one adequately documented post dose PK measurement.

End point type	Secondary
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End point timeframe:

Pre-dose (2 hours maximum) and 15, 30, 45 min after start of infusion (SOI) and end of infusion (EOI) and 1, 4, 18, 24, 48, 144 hours after EOI on Cycle 1 Day 22.

Notes:

[8] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: According to the Protocol, the endpoint only considers subjects in the Phase 1 cohort.

End point values	Phase 1- 14 mg Cohort 1	Phase 1- 40 mg Cohort 2	Phase 1- 80 mg Cohort 3	Phase 1- 160 mg Cohort 4
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	2	3	4	4
Units: nanogram /milliLiter				
arithmetic mean (standard deviation)	3290 (± 2860)	13200 (± 3100)	29200 (± 6620)	60900 (± 17600)

End point values	Phase 1- 320 mg Cohort 5	Phase 1- 480 mg Cohort 6	Phase 1- 720 mg Cohort 7	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	6	6	6	
Units: nanogram /milliLiter				
arithmetic mean (standard deviation)	204000 (± 55600)	298000 (± 71100)	354000 (± 104000)	

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 1: Time of Maximum Observed Concentration (Tmax) of AFM24

End point title	Phase 1: Time of Maximum Observed Concentration (Tmax) of AFM24 ^[9]
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End point description:

First time to maximum observed concentration of AFM24 sampled during a dosing interval.
The Pharmacokinetic set: all subjects who received at least one adequately documented dose of study drug and had at least one adequately documented post dose PK measurement.

End point type	Secondary
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End point timeframe:

Pre-dose (2 hours maximum) and 15, 30, 45 min after start of infusion (SOI) and end of infusion (EOI) and 1, 4, 18, 24, 48, 144 hours after EOI on Cycle 1 Day 22.

Notes:

[9] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: According to the Protocol, the endpoint only considers subjects in the Phase 1 cohort.

End point values	Phase 1- 14 mg Cohort 1	Phase 1- 40 mg Cohort 2	Phase 1- 80 mg Cohort 3	Phase 1- 160 mg Cohort 4
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	2	3	4	4
Units: hours				
arithmetic mean (standard deviation)	1.84 (± 1.19)	3.43 (± 1.97)	5.63 (± 1.71)	5.64 (± 1.30)

End point values	Phase 1- 320 mg Cohort 5	Phase 1- 480 mg Cohort 6	Phase 1- 720 mg Cohort 7	
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Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	6	6	6	
Units: hours				
arithmetic mean (standard deviation)	7.18 (\pm 0.564)	7.52 (\pm 1.38)	5.21 (\pm 0.280)	

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 1: Minimum Plasma Concentration (Cmin) of AFM24

End point title	Phase 1: Minimum Plasma Concentration (Cmin) of AFM24 ^[10]
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End point description:

Minimum measured concentration (Cmin) of AFM24 in serum.

The Pharmacokinetic set: all subjects who received at least one adequately documented dose of study drug and had at least one adequately documented post dose PK measurement.

End point type	Secondary
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End point timeframe:

Pre-dose (2 hours maximum) and 15, 30, 45 min after start of infusion (SOI) and end of infusion (EOI) and 1, 4, 18, 24, 48, 144 hours after EOI on Cycle 1 Day 22.

Notes:

[10] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: According to the Protocol, the endpoint only considers subjects in the Phase 1 cohort.

End point values	Phase 1- 14 mg Cohort 1	Phase 1- 40 mg Cohort 2	Phase 1- 80 mg Cohort 3	Phase 1- 160 mg Cohort 4
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	2	3	4	4
Units: ng/mL				
arithmetic mean (standard deviation)	32.7 (\pm 46.2)	311 (\pm 281)	810 (\pm 482)	12000 (\pm 3540)

End point values	Phase 1- 320 mg Cohort 5	Phase 1- 480 mg Cohort 6	Phase 1- 720 mg Cohort 7	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	6	6	6	
Units: ng/mL				
arithmetic mean (standard deviation)	73800 (\pm 40600)	117000 (\pm 49600)	233000 (\pm 113000)	

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 1: The number of subjects who developed anti-drug antibodies (ADAs) and neutralizing ADAs during treatment with AFM24

End point title	Phase 1: The number of subjects who developed anti-drug antibodies (ADAs) and neutralizing ADAs during treatment with AFM24 ^[11]
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End point description:

The number of subjects who developed anti-drug antibodies (ADAs) at any time during the study.
The safety set: All patients who received at least one dose of AFM24.

End point type	Secondary
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End point timeframe:

Pre-dose cycle 1 Day 1 and end of treatment, up to approximately 39 weeks.

Notes:

[11] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: According to the Protocol, the endpoint only considers subjects in the Phase 1 cohort.

End point values	Phase 1- 14 mg Cohort 1	Phase 1- 40 mg Cohort 2	Phase 1- 80 mg Cohort 3	Phase 1- 160 mg Cohort 4
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0 ^[12]	0 ^[13]	0 ^[14]	0 ^[15]
Units: Participants				

Notes:

[12] - Analysis is ongoing

[13] - Analysis is ongoing

[14] - Analysis is ongoing

[15] - Analysis is ongoing

End point values	Phase 1- 320 mg Cohort 5	Phase 1- 480 mg Cohort 6	Phase 1- 720 mg Cohort 7	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0 ^[16]	0 ^[17]	0 ^[18]	
Units: Participants				

Notes:

[16] - Analysis is ongoing

[17] - Analysis is ongoing

[18] - Analysis is ongoing

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 1: Overall Response Rate (Complete Response (CR) + Partial Response (PR))

End point title	Phase 1: Overall Response Rate (Complete Response (CR) + Partial Response (PR)) ^[19]
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End point description:

Overall response as defined by achieving confirmed CR and/or PR assessed by Response Evaluation Criteria in Solid Tumors (RECIST) v1.1. Partial or complete response needs to be confirmed with repeated assessment at least 4 weeks after the initial assessment by local reader.

The safety set: All patients who received at least one dose of AFM24.

End point type	Secondary
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End point timeframe:

From the start of first infusion till the last infusion + 30 days, up to approximately 43 weeks.

Notes:

[19] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: According to the Protocol, the endpoint only considers subjects in the Phase 1 cohort.

End point values	Phase 1- 14 mg Cohort 1	Phase 1- 40 mg Cohort 2	Phase 1- 80 mg Cohort 3	Phase 1- 160 mg Cohort 4
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	2	6	4	5
Units: Participants	0	0	0	0

End point values	Phase 1- 320 mg Cohort 5	Phase 1- 480 mg Cohort 6	Phase 1- 720 mg Cohort 7	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	6	6	6	
Units: Participants	0	0	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 1: Disease Control Rate (Complete Response (CR) + Partial Response (PR) +Stable Disease (SD))

End point title	Phase 1: Disease Control Rate (Complete Response (CR) + Partial Response (PR) +Stable Disease (SD)) ^[20]
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End point description:

Disease control at months 3, 6, and 9, as defined by achieving CR and/or PR and/or SD assessed by Response Evaluation Criteria in Solid Tumors (RECIST) v1.1.

The safety set: All patients who received at least one dose of AFM24.

End point type	Secondary
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End point timeframe:

From the start of first infusion till the last infusion + 30 days, up to approximately 43 weeks.

Notes:

[20] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: According to the Protocol, the endpoint only considers subjects in the Phase 1 cohort.

End point values	Phase 1- 14 mg Cohort 1	Phase 1- 40 mg Cohort 2	Phase 1- 80 mg Cohort 3	Phase 1- 160 mg Cohort 4
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	2	6	4	5
Units: Participants	0	1	0	0

End point values	Phase 1- 320 mg Cohort 5	Phase 1- 480 mg Cohort 6	Phase 1- 720 mg Cohort 7	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	6	6	6	
Units: Participants	0	2	1	

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Phase 1: Duration of Response Rate (DOR)

End point title	Phase 1: Duration of Response Rate (DOR) ^[21]
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End point description:

The DOR defined as time from first assessment of partial response (PR) or complete response (CR) to follow-on first assessment of progressive disease will be summarized by descriptive statistics including median DOR and where appropriate the respective 95% CIs.

No subjects had a response.

End point type	Other pre-specified
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End point timeframe:

through study completion (estimated up to 24 weeks)

Notes:

[21] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: According to the Protocol, the endpoint only considers subjects in the Phase 1 cohort.

End point values	Phase 1- 14 mg Cohort 1	Phase 1- 40 mg Cohort 2	Phase 1- 80 mg Cohort 3	Phase 1- 160 mg Cohort 4
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0 ^[22]	0 ^[23]	0 ^[24]	0 ^[25]
Units: Participants				

Notes:

[22] - No data displayed because Outcome Measure has zero total participants analyzed.

[23] - No data displayed because Outcome Measure has zero total participants analyzed.

[24] - No data displayed because Outcome Measure has zero total participants analyzed.

[25] - No data displayed because Outcome Measure has zero total participants analyzed.

End point values	Phase 1- 320 mg Cohort 5	Phase 1- 480 mg Cohort 6	Phase 1- 720 mg Cohort 7	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0 ^[26]	0 ^[27]	0 ^[28]	
Units: Participants				

Notes:

[26] - No data displayed because Outcome Measure has zero total participants analyzed.

[27] - No data displayed because Outcome Measure has zero total participants analyzed.

[28] - No data displayed because Outcome Measure has zero total participants analyzed.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From the start of first infusion till the last infusion + 30 days, up to approximately 68 weeks

Adverse event reporting additional description:

The safety set consisted of all subjects who received at least one dose of AFM24.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	26.0
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Reporting groups

Reporting group title	Phase 1- 14 mg Cohort 1
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Reporting group description:

Subjects, with tumors known to express EGFR, who received 14 milligram (mg) AFM24 on Day 1, Day 8, Day 15, and Day 22 of a 28-day cycle.

Reporting group title	Phase 1- 40 mg Cohort 2
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Reporting group description:

Subjects, with tumors known to express EGFR, who received 40 milligram (mg) AFM24 on Day 1, Day 8, Day 15, and Day 22 of a 28-day cycle.

Reporting group title	Phase 1- 80 mg Cohort 3
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Reporting group description:

Subjects, with tumors known to express EGFR, who received 80 milligram (mg) AFM24 on Day 1, Day 8, Day 15, and Day 22 of a 28-day cycle.

Reporting group title	Phase 1- 160 mg Cohort 4
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Reporting group description:

Subjects, with tumors known to express EGFR, who received 160 milligram (mg) AFM24 on Day 1, Day 8, Day 15, and Day 22 of a 28-day cycle.

Reporting group title	Phase 1- 320 mg Cohort 5
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Reporting group description:

Subjects, with tumors known to express EGFR, who received 320 milligram (mg) AFM24 on Day 1, Day 8, Day 15, and Day 22 of a 28-day cycle.

Reporting group title	Phase 1- 480 mg Cohort 6
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Reporting group description:

Subjects, with tumors known to express EGFR, who received 480 milligram (mg) AFM24 on Day 1, Day 8, Day 15, and Day 22 of a 28-day cycle.

Reporting group title	Phase 1- 720 mg Cohort 7
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Reporting group description:

Subjects, with tumors known to express EGFR, who received 720 milligram (mg) AFM24 on Day 1, Day 8, Day 15, and Day 22 of a 28-day cycle. A dose could be given over two days (split day dosing).

Reporting group title	Phase 2- CRC Cohort 1
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Reporting group description:

Subjects with microsatellite stable (MSS) colorectal cancer (CRC) with rat sarcoma gene (RAS) wild-type tumor expressing EGFR who received who received 480 milligram (mg) AFM24 weekly on Day 1, Day 8, Day 15, and Day 22 of a 28-day cycle. A dose could be given over two days (split day dosing).

Reporting group title	Phase 2- ccRCC Cohort 2
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Reporting group description:

Subjects with clear cell renal cell carcinoma (ccRCC) expressing EGFR who received 480 milligram (mg) AFM24 weekly on Day 1, Day 8, Day 15, and Day 22 of a 28-day cycle. A dose could be given over two days (split day dosing).

Reporting group title	Phase 2- NSCLC Cohort 3
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Reporting group description:

Subjects with advanced or metastatic (non-small cell lung cancer) NSCLC with an epidermal growth factor receptor (EGFR) mutation who received 480 milligram (mg) AFM24 weekly on Day 1, Day 8, Day 15, and Day 22 of a 28-day cycle. A dose could be given over two days (split day dosing).

Serious adverse events	Phase 1- 14 mg Cohort 1	Phase 1- 40 mg Cohort 2	Phase 1- 80 mg Cohort 3
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 2 (100.00%)	3 / 6 (50.00%)	2 / 4 (50.00%)
number of deaths (all causes)	1	6	4
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Metastatic neoplasm			
subjects affected / exposed	0 / 2 (0.00%)	0 / 6 (0.00%)	1 / 4 (25.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cancer pain			
subjects affected / exposed	0 / 2 (0.00%)	0 / 6 (0.00%)	0 / 4 (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			
Fatigue			
subjects affected / exposed	0 / 2 (0.00%)	0 / 6 (0.00%)	0 / 4 (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
Non-cardiac chest pain			
subjects affected / exposed	0 / 2 (0.00%)	0 / 6 (0.00%)	0 / 4 (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
Pain			
subjects affected / exposed	1 / 2 (50.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Asthenia			

subjects affected / exposed	0 / 2 (0.00%)	0 / 6 (0.00%)	0 / 4 (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
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	0 / 2 (0.00%)	0 / 6 (0.00%)	0 / 4 (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
Hypoxia			
subjects affected / exposed	0 / 2 (0.00%)	0 / 6 (0.00%)	0 / 4 (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
Pleural effusion			
subjects affected / exposed	0 / 2 (0.00%)	0 / 6 (0.00%)	0 / 4 (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
Productive cough			
subjects affected / exposed	0 / 2 (0.00%)	0 / 6 (0.00%)	0 / 4 (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
Tachypnoea			
subjects affected / exposed	1 / 2 (50.00%)	0 / 6 (0.00%)	0 / 4 (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
Pneumonitis			
subjects affected / exposed	0 / 2 (0.00%)	0 / 6 (0.00%)	0 / 4 (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
Pulmonary haemorrhage			
subjects affected / exposed	0 / 2 (0.00%)	0 / 6 (0.00%)	0 / 4 (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
Injury, poisoning and procedural complications			

Hip fracture			
subjects affected / exposed	0 / 2 (0.00%)	0 / 6 (0.00%)	0 / 4 (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
Infusion related reaction			
subjects affected / exposed	0 / 2 (0.00%)	1 / 6 (16.67%)	0 / 4 (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
Cardiac disorders			
Myocardial infarction			
subjects affected / exposed	0 / 2 (0.00%)	1 / 6 (16.67%)	0 / 4 (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
Sinus tachycardia			
subjects affected / exposed	0 / 2 (0.00%)	0 / 6 (0.00%)	0 / 4 (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
Sinus bradycardia			
subjects affected / exposed	0 / 2 (0.00%)	0 / 6 (0.00%)	0 / 4 (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
Nervous system disorders			
Cerebral haemorrhage			
subjects affected / exposed	0 / 2 (0.00%)	0 / 6 (0.00%)	0 / 4 (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
Epilepsy			
subjects affected / exposed	0 / 2 (0.00%)	0 / 6 (0.00%)	0 / 4 (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
Seizure			
subjects affected / exposed	0 / 2 (0.00%)	0 / 6 (0.00%)	0 / 4 (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

Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 2 (0.00%)	0 / 6 (0.00%)	0 / 4 (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
Eye disorders			
Blindness			
subjects affected / exposed	0 / 2 (0.00%)	0 / 6 (0.00%)	0 / 4 (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
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 2 (0.00%)	1 / 6 (16.67%)	0 / 4 (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
Small intestinal obstruction			
subjects affected / exposed	0 / 2 (0.00%)	0 / 6 (0.00%)	0 / 4 (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
Gastrointestinal haemorrhage			
subjects affected / exposed	0 / 2 (0.00%)	0 / 6 (0.00%)	0 / 4 (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
Hepatobiliary disorders			
Cholangitis			
subjects affected / exposed	0 / 2 (0.00%)	0 / 6 (0.00%)	0 / 4 (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
Bile duct stenosis			
subjects affected / exposed	0 / 2 (0.00%)	0 / 6 (0.00%)	0 / 4 (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
Dilatation intrahepatic duct acquired			

subjects affected / exposed	0 / 2 (0.00%)	0 / 6 (0.00%)	0 / 4 (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
Jaundice cholestatic			
subjects affected / exposed	0 / 2 (0.00%)	0 / 6 (0.00%)	0 / 4 (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
Renal and urinary disorders			
Haematuria			
subjects affected / exposed	0 / 2 (0.00%)	0 / 6 (0.00%)	0 / 4 (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
Urinary tract obstruction			
subjects affected / exposed	0 / 2 (0.00%)	0 / 6 (0.00%)	0 / 4 (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
Musculoskeletal and connective tissue disorders			
Failure to thrive			
subjects affected / exposed	1 / 2 (50.00%)	0 / 6 (0.00%)	0 / 4 (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
Bone pain			
subjects affected / exposed	0 / 2 (0.00%)	0 / 6 (0.00%)	0 / 4 (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
Infections and infestations			
COVID-19			
subjects affected / exposed	0 / 2 (0.00%)	0 / 6 (0.00%)	1 / 4 (25.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
COVID-19 pneumonia			
subjects affected / exposed	0 / 2 (0.00%)	0 / 6 (0.00%)	0 / 4 (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 / 2 (0.00%)	1 / 6 (16.67%)	0 / 4 (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	
Cholangitis infective				
subjects affected / exposed	0 / 2 (0.00%)	1 / 6 (16.67%)	0 / 4 (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	
Anorectal infection				
subjects affected / exposed	0 / 2 (0.00%)	0 / 6 (0.00%)	0 / 4 (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	
Bacterial abscess central nervous system				
subjects affected / exposed	0 / 2 (0.00%)	0 / 6 (0.00%)	0 / 4 (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	
Influenza				
subjects affected / exposed	0 / 2 (0.00%)	0 / 6 (0.00%)	0 / 4 (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	
Oesophageal candidiasis				
subjects affected / exposed	0 / 2 (0.00%)	0 / 6 (0.00%)	0 / 4 (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	
Sepsis				
subjects affected / exposed	0 / 2 (0.00%)	0 / 6 (0.00%)	0 / 4 (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	
Urinary tract infection				
subjects affected / exposed	0 / 2 (0.00%)	0 / 6 (0.00%)	0 / 4 (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	
Vascular device infection				

subjects affected / exposed	0 / 2 (0.00%)	0 / 6 (0.00%)	0 / 4 (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

Serious adverse events	Phase 1- 160 mg Cohort 4	Phase 1- 320 mg Cohort 5	Phase 1- 480 mg Cohort 6
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 5 (40.00%)	4 / 6 (66.67%)	3 / 6 (50.00%)
number of deaths (all causes)	3	4	4
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Metastatic neoplasm			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 6 (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
Cancer pain			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 6 (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			
Fatigue			
subjects affected / exposed	0 / 5 (0.00%)	1 / 6 (16.67%)	0 / 6 (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
Non-cardiac chest pain			
subjects affected / exposed	0 / 5 (0.00%)	1 / 6 (16.67%)	0 / 6 (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
Pain			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 6 (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
Asthenia			

subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 6 (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
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	0 / 5 (0.00%)	1 / 6 (16.67%)	0 / 6 (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
Hypoxia			
subjects affected / exposed	1 / 5 (20.00%)	0 / 6 (0.00%)	0 / 6 (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
Pleural effusion			
subjects affected / exposed	1 / 5 (20.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Productive cough			
subjects affected / exposed	0 / 5 (0.00%)	1 / 6 (16.67%)	0 / 6 (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
Tachypnoea			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 6 (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
Pneumonitis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 6 (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
Pulmonary haemorrhage			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 6 (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
Injury, poisoning and procedural complications			

Hip fracture			
subjects affected / exposed	0 / 5 (0.00%)	1 / 6 (16.67%)	0 / 6 (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
Infusion related reaction			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 6 (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
Cardiac disorders			
Myocardial infarction			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 6 (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
Sinus tachycardia			
subjects affected / exposed	0 / 5 (0.00%)	1 / 6 (16.67%)	0 / 6 (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
Sinus bradycardia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 6 (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
Nervous system disorders			
Cerebral haemorrhage			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 6 (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
Epilepsy			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 6 (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
Seizure			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 6 (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

Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 6 (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
Eye disorders			
Blindness			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 6 (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
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 6 (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
Small intestinal obstruction			
subjects affected / exposed	0 / 5 (0.00%)	1 / 6 (16.67%)	0 / 6 (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 haemorrhage			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 6 (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
Hepatobiliary disorders			
Cholangitis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bile duct stenosis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 6 (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
Dilatation intrahepatic duct acquired			

subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 6 (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
Jaundice cholestatic			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 6 (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
Renal and urinary disorders			
Haematuria			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 6 (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
Urinary tract obstruction			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 6 (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
Musculoskeletal and connective tissue disorders			
Failure to thrive			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 6 (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
Bone pain			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 6 (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
Infections and infestations			
COVID-19			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 6 (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
COVID-19 pneumonia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 6 (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 / 5 (0.00%)	0 / 6 (0.00%)	0 / 6 (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
Cholangitis infective			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 6 (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
Anorectal infection			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 6 (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
Bacterial abscess central nervous system			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 6 (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
Influenza			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 6 (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
Oesophageal candidiasis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 6 (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
Sepsis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 6 (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
Urinary tract infection			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 6 (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
Vascular device infection			

subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 6 (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

Serious adverse events	Phase 1- 720 mg Cohort 7	Phase 2- CRC Cohort 1	Phase 2- ccRCC Cohort 2
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 6 (33.33%)	8 / 19 (42.11%)	6 / 8 (75.00%)
number of deaths (all causes)	5	14	6
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Metastatic neoplasm			
subjects affected / exposed	0 / 6 (0.00%)	0 / 19 (0.00%)	0 / 8 (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
Cancer pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 19 (0.00%)	0 / 8 (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			
Fatigue			
subjects affected / exposed	0 / 6 (0.00%)	0 / 19 (0.00%)	0 / 8 (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
Non-cardiac chest pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 19 (0.00%)	0 / 8 (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
Pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 19 (0.00%)	0 / 8 (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
Asthenia			

subjects affected / exposed	0 / 6 (0.00%)	1 / 19 (5.26%)	0 / 8 (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			
Dyspnoea			
subjects affected / exposed	1 / 6 (16.67%)	0 / 19 (0.00%)	0 / 8 (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
Hypoxia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 19 (0.00%)	0 / 8 (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
Pleural effusion			
subjects affected / exposed	0 / 6 (0.00%)	0 / 19 (0.00%)	0 / 8 (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
Productive cough			
subjects affected / exposed	0 / 6 (0.00%)	0 / 19 (0.00%)	0 / 8 (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
Tachypnoea			
subjects affected / exposed	0 / 6 (0.00%)	0 / 19 (0.00%)	0 / 8 (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
Pneumonitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 19 (0.00%)	0 / 8 (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
Pulmonary haemorrhage			
subjects affected / exposed	0 / 6 (0.00%)	0 / 19 (0.00%)	1 / 8 (12.50%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Injury, poisoning and procedural complications			

Hip fracture			
subjects affected / exposed	0 / 6 (0.00%)	0 / 19 (0.00%)	0 / 8 (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
Infusion related reaction			
subjects affected / exposed	0 / 6 (0.00%)	0 / 19 (0.00%)	0 / 8 (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
Cardiac disorders			
Myocardial infarction			
subjects affected / exposed	0 / 6 (0.00%)	0 / 19 (0.00%)	0 / 8 (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
Sinus tachycardia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 19 (0.00%)	0 / 8 (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
Sinus bradycardia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 19 (0.00%)	1 / 8 (12.50%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Cerebral haemorrhage			
subjects affected / exposed	0 / 6 (0.00%)	0 / 19 (0.00%)	0 / 8 (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
Epilepsy			
subjects affected / exposed	0 / 6 (0.00%)	0 / 19 (0.00%)	1 / 8 (12.50%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Seizure			
subjects affected / exposed	0 / 6 (0.00%)	0 / 19 (0.00%)	0 / 8 (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

Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 6 (0.00%)	1 / 19 (5.26%)	0 / 8 (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
Eye disorders			
Blindness			
subjects affected / exposed	0 / 6 (0.00%)	0 / 19 (0.00%)	1 / 8 (12.50%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 6 (0.00%)	2 / 19 (10.53%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Small intestinal obstruction			
subjects affected / exposed	0 / 6 (0.00%)	0 / 19 (0.00%)	0 / 8 (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
Gastrointestinal haemorrhage			
subjects affected / exposed	0 / 6 (0.00%)	1 / 19 (5.26%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Hepatobiliary disorders			
Cholangitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 19 (0.00%)	0 / 8 (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
Bile duct stenosis			
subjects affected / exposed	0 / 6 (0.00%)	1 / 19 (5.26%)	0 / 8 (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
Dilatation intrahepatic duct acquired			

subjects affected / exposed	0 / 6 (0.00%)	1 / 19 (5.26%)	0 / 8 (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
Jaundice cholestatic			
subjects affected / exposed	0 / 6 (0.00%)	1 / 19 (5.26%)	0 / 8 (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
Renal and urinary disorders			
Haematuria			
subjects affected / exposed	1 / 6 (16.67%)	0 / 19 (0.00%)	0 / 8 (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
Urinary tract obstruction			
subjects affected / exposed	0 / 6 (0.00%)	1 / 19 (5.26%)	0 / 8 (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
Musculoskeletal and connective tissue disorders			
Failure to thrive			
subjects affected / exposed	0 / 6 (0.00%)	0 / 19 (0.00%)	0 / 8 (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
Bone pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 19 (0.00%)	0 / 8 (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
Infections and infestations			
COVID-19			
subjects affected / exposed	0 / 6 (0.00%)	0 / 19 (0.00%)	1 / 8 (12.50%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
COVID-19 pneumonia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 19 (0.00%)	1 / 8 (12.50%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Pneumonia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 19 (0.00%)	0 / 8 (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
Cholangitis infective			
subjects affected / exposed	0 / 6 (0.00%)	0 / 19 (0.00%)	0 / 8 (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
Anorectal infection			
subjects affected / exposed	0 / 6 (0.00%)	1 / 19 (5.26%)	0 / 8 (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
Bacterial abscess central nervous system			
subjects affected / exposed	0 / 6 (0.00%)	0 / 19 (0.00%)	1 / 8 (12.50%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Influenza			
subjects affected / exposed	0 / 6 (0.00%)	0 / 19 (0.00%)	0 / 8 (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
Oesophageal candidiasis			
subjects affected / exposed	0 / 6 (0.00%)	1 / 19 (5.26%)	0 / 8 (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
Sepsis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 19 (0.00%)	1 / 8 (12.50%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 19 (0.00%)	1 / 8 (12.50%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular device infection			

subjects affected / exposed	0 / 6 (0.00%)	0 / 19 (0.00%)	1 / 8 (12.50%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Phase 2- NSCLC Cohort 3		
Total subjects affected by serious adverse events			
subjects affected / exposed	8 / 23 (34.78%)		
number of deaths (all causes)	5		
number of deaths resulting from adverse events	1		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Metastatic neoplasm			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cancer pain			
subjects affected / exposed	1 / 23 (4.35%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Non-cardiac chest pain			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pain			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Asthenia			

subjects affected / exposed	0 / 23 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hypoxia			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pleural effusion			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Productive cough			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Tachypnoea			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pneumonitis			
subjects affected / exposed	1 / 23 (4.35%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	1 / 1		
Pulmonary haemorrhage			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			

Hip fracture			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infusion related reaction			
subjects affected / exposed	2 / 23 (8.70%)		
occurrences causally related to treatment / all	2 / 2		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Myocardial infarction			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Sinus tachycardia			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Sinus bradycardia			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Cerebral haemorrhage			
subjects affected / exposed	1 / 23 (4.35%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Epilepsy			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Seizure			
subjects affected / exposed	1 / 23 (4.35%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Eye disorders			
Blindness			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Small intestinal obstruction			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal haemorrhage			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			
Cholangitis			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Bile duct stenosis			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Dilatation intrahepatic duct acquired			

subjects affected / exposed	0 / 23 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Jaundice cholestatic			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Haematuria			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Urinary tract obstruction			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Failure to thrive			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Bone pain			
subjects affected / exposed	1 / 23 (4.35%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
COVID-19			
subjects affected / exposed	1 / 23 (4.35%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
COVID-19 pneumonia			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Pneumonia				
subjects affected / exposed	1 / 23 (4.35%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Cholangitis infective				
subjects affected / exposed	0 / 23 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Anorectal infection				
subjects affected / exposed	0 / 23 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Bacterial abscess central nervous system				
subjects affected / exposed	0 / 23 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Influenza				
subjects affected / exposed	1 / 23 (4.35%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Oesophageal candidiasis				
subjects affected / exposed	0 / 23 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Sepsis				
subjects affected / exposed	0 / 23 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Urinary tract infection				
subjects affected / exposed	0 / 23 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Vascular device infection				

subjects affected / exposed	0 / 23 (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	Phase 1- 14 mg Cohort 1	Phase 1- 40 mg Cohort 2	Phase 1- 80 mg Cohort 3
Total subjects affected by non-serious adverse events			
subjects affected / exposed	2 / 2 (100.00%)	5 / 6 (83.33%)	4 / 4 (100.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Tumour pain			
subjects affected / exposed	0 / 2 (0.00%)	1 / 6 (16.67%)	1 / 4 (25.00%)
occurrences (all)	0	2	1
Acrochordon			
subjects affected / exposed	0 / 2 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Cancer pain			
subjects affected / exposed	0 / 2 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 2 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Hypotension			
subjects affected / exposed	0 / 2 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Flushing			
subjects affected / exposed	0 / 2 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Deep vein thrombosis			
subjects affected / exposed	0 / 2 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Hot flush			
subjects affected / exposed	0 / 2 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0

General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	0 / 2 (0.00%)	1 / 6 (16.67%)	1 / 4 (25.00%)
occurrences (all)	0	1	1
Pyrexia			
subjects affected / exposed	0 / 2 (0.00%)	1 / 6 (16.67%)	2 / 4 (50.00%)
occurrences (all)	0	5	3
Asthenia			
subjects affected / exposed	0 / 2 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Pain			
subjects affected / exposed	0 / 2 (0.00%)	0 / 6 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
Non-cardiac chest pain			
subjects affected / exposed	0 / 2 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Oedema peripheral			
subjects affected / exposed	1 / 2 (50.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Chills			
subjects affected / exposed	0 / 2 (0.00%)	1 / 6 (16.67%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Chest discomfort			
subjects affected / exposed	0 / 2 (0.00%)	0 / 6 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
Feeling of body temperature change			
subjects affected / exposed	0 / 2 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Influenza like illness			
subjects affected / exposed	0 / 2 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Infusion site extravasation			
subjects affected / exposed	0 / 2 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Temperature regulation disorder			

subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0	0 / 6 (0.00%) 0	0 / 4 (0.00%) 0
Immune system disorders Cytokine release syndrome subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0	2 / 6 (33.33%) 3	0 / 4 (0.00%) 0
Reproductive system and breast disorders Testicular pain subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0	0 / 6 (0.00%) 0	0 / 4 (0.00%) 0
Respiratory, thoracic and mediastinal disorders Dyspnoea subjects affected / exposed occurrences (all)	1 / 2 (50.00%) 1	0 / 6 (0.00%) 0	0 / 4 (0.00%) 0
Cough subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0	0 / 6 (0.00%) 0	0 / 4 (0.00%) 0
Epistaxis subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0	0 / 6 (0.00%) 0	0 / 4 (0.00%) 0
Haemoptysis subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0	0 / 6 (0.00%) 0	0 / 4 (0.00%) 0
Hiccups subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0	0 / 6 (0.00%) 0	0 / 4 (0.00%) 0
Pleural effusion subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0	0 / 6 (0.00%) 0	0 / 4 (0.00%) 0
Rhinorrhoea subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0	0 / 6 (0.00%) 0	0 / 4 (0.00%) 0
Tachypnoea subjects affected / exposed occurrences (all)	1 / 2 (50.00%) 2	0 / 6 (0.00%) 0	0 / 4 (0.00%) 0
Dysphonia			

subjects affected / exposed	0 / 2 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Dyspnoea exertional			
subjects affected / exposed	0 / 2 (0.00%)	1 / 6 (16.67%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Hypoxia			
subjects affected / exposed	0 / 2 (0.00%)	1 / 6 (16.67%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Oropharyngeal pain			
subjects affected / exposed	0 / 2 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Wheezing			
subjects affected / exposed	0 / 2 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
Insomnia			
subjects affected / exposed	1 / 2 (50.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Depression			
subjects affected / exposed	0 / 2 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Anxiety			
subjects affected / exposed	0 / 2 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Confusional state			
subjects affected / exposed	0 / 2 (0.00%)	0 / 6 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
Delirium			
subjects affected / exposed	0 / 2 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 2 (0.00%)	3 / 6 (50.00%)	0 / 4 (0.00%)
occurrences (all)	0	7	0
Aspartate aminotransferase increased			

subjects affected / exposed	0 / 2 (0.00%)	3 / 6 (50.00%)	1 / 4 (25.00%)
occurrences (all)	0	7	1
Blood pressure decreased			
subjects affected / exposed	0 / 2 (0.00%)	1 / 6 (16.67%)	0 / 4 (0.00%)
occurrences (all)	0	15	0
Blood bilirubin increased			
subjects affected / exposed	1 / 2 (50.00%)	1 / 6 (16.67%)	1 / 4 (25.00%)
occurrences (all)	1	3	1
Blood alkaline phosphatase increased			
subjects affected / exposed	0 / 2 (0.00%)	2 / 6 (33.33%)	0 / 4 (0.00%)
occurrences (all)	0	2	0
Neutrophil count decreased			
subjects affected / exposed	0 / 2 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Blood creatinine increased			
subjects affected / exposed	0 / 2 (0.00%)	0 / 6 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
Weight decreased			
subjects affected / exposed	0 / 2 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Platelet count decreased			
subjects affected / exposed	0 / 2 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
White blood cell count decreased			
subjects affected / exposed	0 / 2 (0.00%)	1 / 6 (16.67%)	0 / 4 (0.00%)
occurrences (all)	0	3	0
Activated partial thromboplastin time prolonged			
subjects affected / exposed	0 / 2 (0.00%)	0 / 6 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
Alpha tumour necrosis factor increased			
subjects affected / exposed	0 / 2 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Blood lactate dehydrogenase increased			

subjects affected / exposed	0 / 2 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
C-reactive protein increased			
subjects affected / exposed	0 / 2 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
International normalised ratio increased			
subjects affected / exposed	0 / 2 (0.00%)	0 / 6 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
Lipase increased			
subjects affected / exposed	0 / 2 (0.00%)	1 / 6 (16.67%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Lymphocyte count decreased			
subjects affected / exposed	0 / 2 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Serum ferritin increased			
subjects affected / exposed	0 / 2 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Urine output decreased			
subjects affected / exposed	0 / 2 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			
Infusion related reaction			
subjects affected / exposed	1 / 2 (50.00%)	5 / 6 (83.33%)	3 / 4 (75.00%)
occurrences (all)	4	42	4
Arthropod bite			
subjects affected / exposed	0 / 2 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Clavicle fracture			
subjects affected / exposed	1 / 2 (50.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Fall			
subjects affected / exposed	0 / 2 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Humerus fracture			

subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0	0 / 6 (0.00%) 0	0 / 4 (0.00%) 0
Radiation pneumonitis subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0	0 / 6 (0.00%) 0	0 / 4 (0.00%) 0
Sunburn subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0	0 / 6 (0.00%) 0	0 / 4 (0.00%) 0
Congenital, familial and genetic disorders Hydrocele subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0	0 / 6 (0.00%) 0	0 / 4 (0.00%) 0
Cardiac disorders Tachycardia subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0	0 / 6 (0.00%) 0	0 / 4 (0.00%) 0
Palpitations subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0	0 / 6 (0.00%) 0	0 / 4 (0.00%) 0
Nervous system disorders Headache subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0	0 / 6 (0.00%) 0	1 / 4 (25.00%) 1
Dizziness subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0	1 / 6 (16.67%) 1	0 / 4 (0.00%) 0
Peripheral sensory neuropathy subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0	0 / 6 (0.00%) 0	0 / 4 (0.00%) 0
Aphasia subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0	0 / 6 (0.00%) 0	0 / 4 (0.00%) 0
Bell's palsy subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0	0 / 6 (0.00%) 0	0 / 4 (0.00%) 0
Dysgeusia			

subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0	0 / 6 (0.00%) 0	0 / 4 (0.00%) 0
Presyncope subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0	0 / 6 (0.00%) 0	0 / 4 (0.00%) 0
Somnolence subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0	0 / 6 (0.00%) 0	0 / 4 (0.00%) 0
Tremor subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0	0 / 6 (0.00%) 0	0 / 4 (0.00%) 0
Blood and lymphatic system disorders Lymphopenia subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0	0 / 6 (0.00%) 0	0 / 4 (0.00%) 0
Anaemia subjects affected / exposed occurrences (all)	1 / 2 (50.00%) 1	2 / 6 (33.33%) 3	0 / 4 (0.00%) 0
Neutropenia subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0	0 / 6 (0.00%) 0	0 / 4 (0.00%) 0
Thrombocytopenia subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0	0 / 6 (0.00%) 0	0 / 4 (0.00%) 0
Eye disorders Chloropsia subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0	0 / 6 (0.00%) 0	0 / 4 (0.00%) 0
Vision blurred subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0	0 / 6 (0.00%) 0	0 / 4 (0.00%) 0
Conjunctival haemorrhage subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0	0 / 6 (0.00%) 0	0 / 4 (0.00%) 0
Diplopia			

subjects affected / exposed	0 / 2 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Eye pain			
subjects affected / exposed	0 / 2 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Halo vision			
subjects affected / exposed	0 / 2 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	2 / 2 (100.00%)	1 / 6 (16.67%)	1 / 4 (25.00%)
occurrences (all)	3	1	1
Constipation			
subjects affected / exposed	0 / 2 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Vomiting			
subjects affected / exposed	1 / 2 (50.00%)	2 / 6 (33.33%)	0 / 4 (0.00%)
occurrences (all)	1	2	0
Diarrhoea			
subjects affected / exposed	0 / 2 (0.00%)	0 / 6 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
Abdominal distension			
subjects affected / exposed	1 / 2 (50.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Abdominal pain			
subjects affected / exposed	0 / 2 (0.00%)	2 / 6 (33.33%)	0 / 4 (0.00%)
occurrences (all)	0	2	0
Abdominal discomfort			
subjects affected / exposed	0 / 2 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 2 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Ascites			
subjects affected / exposed	0 / 2 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0

Dry mouth			
subjects affected / exposed	0 / 2 (0.00%)	1 / 6 (16.67%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Proctalgia			
subjects affected / exposed	0 / 2 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Abdominal pain lower			
subjects affected / exposed	0 / 2 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Abdominal pain upper			
subjects affected / exposed	0 / 2 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Defaecation urgency			
subjects affected / exposed	0 / 2 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Dyspepsia			
subjects affected / exposed	0 / 2 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Fistula of small intestine			
subjects affected / exposed	0 / 2 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Inguinal hernia			
subjects affected / exposed	0 / 2 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Small intestinal obstruction			
subjects affected / exposed	0 / 2 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Stomatitis			
subjects affected / exposed	0 / 2 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Toothache			
subjects affected / exposed	0 / 2 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Hepatobiliary disorders			
Hepatic pain			

subjects affected / exposed	1 / 2 (50.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Jaundice			
subjects affected / exposed	0 / 2 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Dermatitis acneiform			
subjects affected / exposed	0 / 2 (0.00%)	0 / 6 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
Pruritus			
subjects affected / exposed	0 / 2 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Rash maculo-papular			
subjects affected / exposed	0 / 2 (0.00%)	1 / 6 (16.67%)	1 / 4 (25.00%)
occurrences (all)	0	1	2
Rash			
subjects affected / exposed	0 / 2 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Dry skin			
subjects affected / exposed	0 / 2 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Erythema			
subjects affected / exposed	0 / 2 (0.00%)	0 / 6 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
Night sweats			
subjects affected / exposed	0 / 2 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Rash macular			
subjects affected / exposed	0 / 2 (0.00%)	1 / 6 (16.67%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Renal and urinary disorders			
Proteinuria			
subjects affected / exposed	0 / 2 (0.00%)	1 / 6 (16.67%)	0 / 4 (0.00%)
occurrences (all)	0	3	0
Dysuria			

subjects affected / exposed	0 / 2 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Haematuria			
subjects affected / exposed	0 / 2 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 2 (0.00%)	3 / 6 (50.00%)	1 / 4 (25.00%)
occurrences (all)	0	3	3
Arthralgia			
subjects affected / exposed	0 / 2 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal chest pain			
subjects affected / exposed	0 / 2 (0.00%)	1 / 6 (16.67%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Myalgia			
subjects affected / exposed	0 / 2 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Muscle spasms			
subjects affected / exposed	0 / 2 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Pain in extremity			
subjects affected / exposed	0 / 2 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Axillary mass			
subjects affected / exposed	0 / 2 (0.00%)	0 / 6 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
Bone pain			
subjects affected / exposed	0 / 2 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Coccydynia			
subjects affected / exposed	0 / 2 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Flank pain			

subjects affected / exposed	0 / 2 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Groin pain			
subjects affected / exposed	0 / 2 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal discomfort			
subjects affected / exposed	0 / 2 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Neck pain			
subjects affected / exposed	0 / 2 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
COVID-19			
subjects affected / exposed	0 / 2 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Lower respiratory tract infection			
subjects affected / exposed	0 / 2 (0.00%)	1 / 6 (16.67%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Urinary tract infection			
subjects affected / exposed	0 / 2 (0.00%)	0 / 6 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
Oral candidiasis			
subjects affected / exposed	0 / 2 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Herpes zoster			
subjects affected / exposed	0 / 2 (0.00%)	1 / 6 (16.67%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Klebsiella urinary tract infection			
subjects affected / exposed	0 / 2 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Pneumonia			
subjects affected / exposed	0 / 2 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Rash pustular			
subjects affected / exposed	0 / 2 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0

Rhinitis			
subjects affected / exposed	0 / 2 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Skin infection			
subjects affected / exposed	0 / 2 (0.00%)	1 / 6 (16.67%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Staphylococcal bacteraemia			
subjects affected / exposed	0 / 2 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Tooth infection			
subjects affected / exposed	0 / 2 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Vascular device infection			
subjects affected / exposed	0 / 2 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	1 / 2 (50.00%)	1 / 6 (16.67%)	1 / 4 (25.00%)
occurrences (all)	4	2	1
Hyponatraemia			
subjects affected / exposed	0 / 2 (0.00%)	1 / 6 (16.67%)	1 / 4 (25.00%)
occurrences (all)	0	1	1
Hypoalbuminaemia			
subjects affected / exposed	0 / 2 (0.00%)	1 / 6 (16.67%)	0 / 4 (0.00%)
occurrences (all)	0	2	0
Dehydration			
subjects affected / exposed	0 / 2 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Hypocalcaemia			
subjects affected / exposed	0 / 2 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Hypophosphataemia			
subjects affected / exposed	0 / 2 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	Phase 1- 160 mg Cohort 4	Phase 1- 320 mg Cohort 5	Phase 1- 480 mg Cohort 6
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Total subjects affected by non-serious adverse events subjects affected / exposed	5 / 5 (100.00%)	6 / 6 (100.00%)	6 / 6 (100.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps) Tumour pain subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Acrochordon subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	1 / 6 (16.67%) 1	0 / 6 (0.00%) 0
Cancer pain subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Vascular disorders Hypertension subjects affected / exposed occurrences (all)	1 / 5 (20.00%) 2	0 / 6 (0.00%) 0	1 / 6 (16.67%) 1
Hypotension subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 6 (0.00%) 0	1 / 6 (16.67%) 1
Flushing subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Deep vein thrombosis subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Hot flush subjects affected / exposed occurrences (all)	1 / 5 (20.00%) 1	1 / 6 (16.67%) 1	0 / 6 (0.00%) 0
General disorders and administration site conditions Fatigue subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	4 / 6 (66.67%) 5	0 / 6 (0.00%) 0
Pyrexia subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 6 (0.00%) 0	1 / 6 (16.67%) 2
Asthenia			

subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Pain			
subjects affected / exposed	1 / 5 (20.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Non-cardiac chest pain			
subjects affected / exposed	0 / 5 (0.00%)	1 / 6 (16.67%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Oedema peripheral			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Chills			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Chest discomfort			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Feeling of body temperature change			
subjects affected / exposed	1 / 5 (20.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Influenza like illness			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Infusion site extravasation			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Temperature regulation disorder			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Immune system disorders			
Cytokine release syndrome			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Reproductive system and breast disorders			

Testicular pain			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	3 / 6 (50.00%)
occurrences (all)	0	0	5
Cough			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Epistaxis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Haemoptysis			
subjects affected / exposed	0 / 5 (0.00%)	1 / 6 (16.67%)	0 / 6 (0.00%)
occurrences (all)	0	2	0
Hiccups			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Pleural effusion			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Rhinorrhoea			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Tachypnoea			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Dysphonia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Dyspnoea exertional			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Hypoxia			

subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Oropharyngeal pain			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Wheezing			
subjects affected / exposed	0 / 5 (0.00%)	1 / 6 (16.67%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Psychiatric disorders			
Insomnia			
subjects affected / exposed	0 / 5 (0.00%)	1 / 6 (16.67%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Depression			
subjects affected / exposed	1 / 5 (20.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Anxiety			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Confusional state			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Delirium			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	2 / 5 (40.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	4	0	0
Aspartate aminotransferase increased			
subjects affected / exposed	2 / 5 (40.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	3	0	0
Blood pressure decreased			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Blood bilirubin increased			

subjects affected / exposed	1 / 5 (20.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	2	0	0
Blood alkaline phosphatase increased			
subjects affected / exposed	1 / 5 (20.00%)	1 / 6 (16.67%)	0 / 6 (0.00%)
occurrences (all)	2	2	0
Neutrophil count decreased			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Blood creatinine increased			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Weight decreased			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Platelet count decreased			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
White blood cell count decreased			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Activated partial thromboplastin time prolonged			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Alpha tumour necrosis factor increased			
subjects affected / exposed	1 / 5 (20.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Blood lactate dehydrogenase increased			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
C-reactive protein increased			
subjects affected / exposed	1 / 5 (20.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
International normalised ratio increased			

subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Lipase increased			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Lymphocyte count decreased			
subjects affected / exposed	1 / 5 (20.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Serum ferritin increased			
subjects affected / exposed	1 / 5 (20.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Urine output decreased			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			
Infusion related reaction			
subjects affected / exposed	4 / 5 (80.00%)	3 / 6 (50.00%)	6 / 6 (100.00%)
occurrences (all)	5	4	9
Arthropod bite			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Clavicle fracture			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Fall			
subjects affected / exposed	0 / 5 (0.00%)	1 / 6 (16.67%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Humerus fracture			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Radiation pneumonitis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Sunburn			

subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Congenital, familial and genetic disorders			
Hydrocele			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Cardiac disorders			
Tachycardia			
subjects affected / exposed	2 / 5 (40.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	3	0	1
Palpitations			
subjects affected / exposed	0 / 5 (0.00%)	1 / 6 (16.67%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Nervous system disorders			
Headache			
subjects affected / exposed	3 / 5 (60.00%)	1 / 6 (16.67%)	1 / 6 (16.67%)
occurrences (all)	3	2	1
Dizziness			
subjects affected / exposed	1 / 5 (20.00%)	0 / 6 (0.00%)	3 / 6 (50.00%)
occurrences (all)	1	0	3
Peripheral sensory neuropathy			
subjects affected / exposed	1 / 5 (20.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	3	0	0
Aphasia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Bell's palsy			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Dysgeusia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Presyncope			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Somnolence			

subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Tremor subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	1 / 6 (16.67%) 1	0 / 6 (0.00%) 0
Blood and lymphatic system disorders Lymphopenia subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	1 / 6 (16.67%) 7	2 / 6 (33.33%) 12
Anaemia subjects affected / exposed occurrences (all)	1 / 5 (20.00%) 2	1 / 6 (16.67%) 3	0 / 6 (0.00%) 0
Neutropenia subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Thrombocytopenia subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Eye disorders Chloropsia subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Vision blurred subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Conjunctival haemorrhage subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Diplopia subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	1 / 6 (16.67%) 1	0 / 6 (0.00%) 0
Eye pain subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Halo vision			

subjects affected / exposed occurrences (all)	1 / 5 (20.00%) 1	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	0 / 5 (0.00%)	3 / 6 (50.00%)	2 / 6 (33.33%)
occurrences (all)	0	3	2
Constipation			
subjects affected / exposed	0 / 5 (0.00%)	2 / 6 (33.33%)	1 / 6 (16.67%)
occurrences (all)	0	2	3
Vomiting			
subjects affected / exposed	0 / 5 (0.00%)	2 / 6 (33.33%)	0 / 6 (0.00%)
occurrences (all)	0	3	0
Diarrhoea			
subjects affected / exposed	1 / 5 (20.00%)	2 / 6 (33.33%)	1 / 6 (16.67%)
occurrences (all)	1	2	1
Abdominal distension			
subjects affected / exposed	1 / 5 (20.00%)	1 / 6 (16.67%)	1 / 6 (16.67%)
occurrences (all)	1	2	1
Abdominal pain			
subjects affected / exposed	0 / 5 (0.00%)	1 / 6 (16.67%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Abdominal discomfort			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Gastrooesophageal reflux disease			
subjects affected / exposed	1 / 5 (20.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Ascites			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Dry mouth			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Proctalgia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0

Abdominal pain lower subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Abdominal pain upper subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Defaecation urgency subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Dyspepsia subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Fistula of small intestine subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Inguinal hernia subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Small intestinal obstruction subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	1 / 6 (16.67%) 1	0 / 6 (0.00%) 0
Stomatitis subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Toothache subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Hepatobiliary disorders Hepatic pain subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Jaundice subjects affected / exposed occurrences (all)	1 / 5 (20.00%) 1	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Skin and subcutaneous tissue disorders			

Dermatitis acneiform subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	1 / 6 (16.67%) 1	4 / 6 (66.67%) 5
Pruritus subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	1 / 6 (16.67%) 1	1 / 6 (16.67%) 1
Rash maculo-papular subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 6 (0.00%) 0	1 / 6 (16.67%) 1
Rash subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Dry skin subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Erythema subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Night sweats subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Rash macular subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Renal and urinary disorders Proteinuria subjects affected / exposed occurrences (all)	1 / 5 (20.00%) 1	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Dysuria subjects affected / exposed occurrences (all)	1 / 5 (20.00%) 1	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Haematuria subjects affected / exposed occurrences (all)	1 / 5 (20.00%) 1	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Musculoskeletal and connective tissue disorders			

Back pain			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	2
Arthralgia			
subjects affected / exposed	0 / 5 (0.00%)	1 / 6 (16.67%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Musculoskeletal chest pain			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	2
Myalgia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Muscle spasms			
subjects affected / exposed	1 / 5 (20.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	1	0	1
Pain in extremity			
subjects affected / exposed	0 / 5 (0.00%)	1 / 6 (16.67%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Axillary mass			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Bone pain			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Coccydynia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Flank pain			
subjects affected / exposed	0 / 5 (0.00%)	1 / 6 (16.67%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Groin pain			
subjects affected / exposed	1 / 5 (20.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Musculoskeletal discomfort			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0

Neck pain subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Infections and infestations			
COVID-19 subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Lower respiratory tract infection subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	1 / 6 (16.67%) 1	0 / 6 (0.00%) 0
Urinary tract infection subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Oral candidiasis subjects affected / exposed occurrences (all)	1 / 5 (20.00%) 1	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Herpes zoster subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Klebsiella urinary tract infection subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Pneumonia subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Rash pustular subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Rhinitis subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Skin infection subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Staphylococcal bacteraemia			

subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Tooth infection subjects affected / exposed occurrences (all)	1 / 5 (20.00%) 1	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Vascular device infection subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Metabolism and nutrition disorders Decreased appetite subjects affected / exposed occurrences (all)	1 / 5 (20.00%) 1	1 / 6 (16.67%) 1	1 / 6 (16.67%) 1
Hyponatraemia subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	1 / 6 (16.67%) 2	0 / 6 (0.00%) 0
Hypoalbuminaemia subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	1 / 6 (16.67%) 3	0 / 6 (0.00%) 0
Dehydration subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 6 (0.00%) 0	1 / 6 (16.67%) 1
Hypocalcaemia subjects affected / exposed occurrences (all)	1 / 5 (20.00%) 1	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Hypophosphataemia subjects affected / exposed occurrences (all)	1 / 5 (20.00%) 1	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0

Non-serious adverse events	Phase 1- 720 mg Cohort 7	Phase 2- CRC Cohort 1	Phase 2- ccRCC Cohort 2
Total subjects affected by non-serious adverse events subjects affected / exposed	6 / 6 (100.00%)	19 / 19 (100.00%)	8 / 8 (100.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps) Tumour pain subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 19 (0.00%) 0	1 / 8 (12.50%) 1
Acrochordon			

subjects affected / exposed	0 / 6 (0.00%)	0 / 19 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Cancer pain			
subjects affected / exposed	0 / 6 (0.00%)	1 / 19 (5.26%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Vascular disorders			
Hypertension			
subjects affected / exposed	1 / 6 (16.67%)	0 / 19 (0.00%)	0 / 8 (0.00%)
occurrences (all)	3	0	0
Hypotension			
subjects affected / exposed	0 / 6 (0.00%)	1 / 19 (5.26%)	1 / 8 (12.50%)
occurrences (all)	0	3	1
Flushing			
subjects affected / exposed	1 / 6 (16.67%)	0 / 19 (0.00%)	0 / 8 (0.00%)
occurrences (all)	4	0	0
Deep vein thrombosis			
subjects affected / exposed	0 / 6 (0.00%)	1 / 19 (5.26%)	1 / 8 (12.50%)
occurrences (all)	0	1	1
Hot flush			
subjects affected / exposed	0 / 6 (0.00%)	0 / 19 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	3 / 6 (50.00%)	2 / 19 (10.53%)	3 / 8 (37.50%)
occurrences (all)	6	2	4
Pyrexia			
subjects affected / exposed	1 / 6 (16.67%)	4 / 19 (21.05%)	0 / 8 (0.00%)
occurrences (all)	1	4	0
Asthenia			
subjects affected / exposed	0 / 6 (0.00%)	4 / 19 (21.05%)	2 / 8 (25.00%)
occurrences (all)	0	4	5
Pain			
subjects affected / exposed	1 / 6 (16.67%)	1 / 19 (5.26%)	1 / 8 (12.50%)
occurrences (all)	1	1	1
Non-cardiac chest pain			

subjects affected / exposed	0 / 6 (0.00%)	1 / 19 (5.26%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Oedema peripheral			
subjects affected / exposed	0 / 6 (0.00%)	3 / 19 (15.79%)	0 / 8 (0.00%)
occurrences (all)	0	3	0
Chills			
subjects affected / exposed	1 / 6 (16.67%)	0 / 19 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Chest discomfort			
subjects affected / exposed	0 / 6 (0.00%)	0 / 19 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Feeling of body temperature change			
subjects affected / exposed	0 / 6 (0.00%)	0 / 19 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Influenza like illness			
subjects affected / exposed	0 / 6 (0.00%)	1 / 19 (5.26%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Infusion site extravasation			
subjects affected / exposed	0 / 6 (0.00%)	1 / 19 (5.26%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Temperature regulation disorder			
subjects affected / exposed	0 / 6 (0.00%)	0 / 19 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Immune system disorders			
Cytokine release syndrome			
subjects affected / exposed	0 / 6 (0.00%)	0 / 19 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Reproductive system and breast disorders			
Testicular pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 19 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	1 / 6 (16.67%)	2 / 19 (10.53%)	0 / 8 (0.00%)
occurrences (all)	1	2	0
Cough			

subjects affected / exposed	1 / 6 (16.67%)	0 / 19 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Epistaxis			
subjects affected / exposed	0 / 6 (0.00%)	1 / 19 (5.26%)	1 / 8 (12.50%)
occurrences (all)	0	1	3
Haemoptysis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 19 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Hiccups			
subjects affected / exposed	0 / 6 (0.00%)	1 / 19 (5.26%)	0 / 8 (0.00%)
occurrences (all)	0	2	0
Pleural effusion			
subjects affected / exposed	0 / 6 (0.00%)	0 / 19 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Rhinorrhoea			
subjects affected / exposed	1 / 6 (16.67%)	1 / 19 (5.26%)	0 / 8 (0.00%)
occurrences (all)	1	1	0
Tachypnoea			
subjects affected / exposed	0 / 6 (0.00%)	0 / 19 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Dysphonia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 19 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Dyspnoea exertional			
subjects affected / exposed	0 / 6 (0.00%)	0 / 19 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Hypoxia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 19 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Oropharyngeal pain			
subjects affected / exposed	1 / 6 (16.67%)	0 / 19 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Wheezing			
subjects affected / exposed	0 / 6 (0.00%)	0 / 19 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			

Insomnia			
subjects affected / exposed	1 / 6 (16.67%)	1 / 19 (5.26%)	1 / 8 (12.50%)
occurrences (all)	1	1	1
Depression			
subjects affected / exposed	1 / 6 (16.67%)	0 / 19 (0.00%)	1 / 8 (12.50%)
occurrences (all)	1	0	1
Anxiety			
subjects affected / exposed	0 / 6 (0.00%)	0 / 19 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Confusional state			
subjects affected / exposed	0 / 6 (0.00%)	0 / 19 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Delirium			
subjects affected / exposed	0 / 6 (0.00%)	1 / 19 (5.26%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	3 / 6 (50.00%)	2 / 19 (10.53%)	1 / 8 (12.50%)
occurrences (all)	5	4	1
Aspartate aminotransferase increased			
subjects affected / exposed	2 / 6 (33.33%)	3 / 19 (15.79%)	1 / 8 (12.50%)
occurrences (all)	5	4	1
Blood pressure decreased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 19 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Blood bilirubin increased			
subjects affected / exposed	0 / 6 (0.00%)	3 / 19 (15.79%)	0 / 8 (0.00%)
occurrences (all)	0	4	0
Blood alkaline phosphatase increased			
subjects affected / exposed	3 / 6 (50.00%)	0 / 19 (0.00%)	0 / 8 (0.00%)
occurrences (all)	3	0	0
Neutrophil count decreased			
subjects affected / exposed	0 / 6 (0.00%)	1 / 19 (5.26%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Blood creatinine increased			

subjects affected / exposed	0 / 6 (0.00%)	0 / 19 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	2
Weight decreased			
subjects affected / exposed	2 / 6 (33.33%)	0 / 19 (0.00%)	1 / 8 (12.50%)
occurrences (all)	3	0	1
Platelet count decreased			
subjects affected / exposed	1 / 6 (16.67%)	1 / 19 (5.26%)	0 / 8 (0.00%)
occurrences (all)	1	2	0
White blood cell count decreased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 19 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Activated partial thromboplastin time prolonged			
subjects affected / exposed	0 / 6 (0.00%)	0 / 19 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Alpha tumour necrosis factor increased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 19 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Blood lactate dehydrogenase increased			
subjects affected / exposed	1 / 6 (16.67%)	0 / 19 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
C-reactive protein increased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 19 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
International normalised ratio increased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 19 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Lipase increased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 19 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Lymphocyte count decreased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 19 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Serum ferritin increased			

subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 19 (0.00%) 0	0 / 8 (0.00%) 0
Urine output decreased subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	1 / 19 (5.26%) 1	0 / 8 (0.00%) 0
Injury, poisoning and procedural complications			
Infusion related reaction subjects affected / exposed occurrences (all)	4 / 6 (66.67%) 5	15 / 19 (78.95%) 19	5 / 8 (62.50%) 5
Arthropod bite subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 19 (0.00%) 0	1 / 8 (12.50%) 1
Clavicle fracture subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 19 (0.00%) 0	0 / 8 (0.00%) 0
Fall subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 19 (0.00%) 0	0 / 8 (0.00%) 0
Humerus fracture subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	1 / 19 (5.26%) 1	0 / 8 (0.00%) 0
Radiation pneumonitis subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 19 (0.00%) 0	1 / 8 (12.50%) 1
Sunburn subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 1	0 / 19 (0.00%) 0	0 / 8 (0.00%) 0
Congenital, familial and genetic disorders			
Hydrocele subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 19 (0.00%) 0	0 / 8 (0.00%) 0
Cardiac disorders			
Tachycardia subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 19 (0.00%) 0	0 / 8 (0.00%) 0
Palpitations			

subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 19 (0.00%) 0	0 / 8 (0.00%) 0
Nervous system disorders			
Headache			
subjects affected / exposed	1 / 6 (16.67%)	1 / 19 (5.26%)	2 / 8 (25.00%)
occurrences (all)	2	1	3
Dizziness			
subjects affected / exposed	0 / 6 (0.00%)	2 / 19 (10.53%)	0 / 8 (0.00%)
occurrences (all)	0	2	0
Peripheral sensory neuropathy			
subjects affected / exposed	0 / 6 (0.00%)	0 / 19 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Aphasia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 19 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Bell's palsy			
subjects affected / exposed	1 / 6 (16.67%)	0 / 19 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Dysgeusia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 19 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Presyncope			
subjects affected / exposed	0 / 6 (0.00%)	0 / 19 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Somnolence			
subjects affected / exposed	0 / 6 (0.00%)	0 / 19 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Tremor			
subjects affected / exposed	0 / 6 (0.00%)	0 / 19 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Blood and lymphatic system disorders			
Lymphopenia			
subjects affected / exposed	1 / 6 (16.67%)	3 / 19 (15.79%)	1 / 8 (12.50%)
occurrences (all)	3	5	3
Anaemia			

subjects affected / exposed	1 / 6 (16.67%)	4 / 19 (21.05%)	1 / 8 (12.50%)
occurrences (all)	1	9	1
Neutropenia			
subjects affected / exposed	0 / 6 (0.00%)	1 / 19 (5.26%)	0 / 8 (0.00%)
occurrences (all)	0	2	0
Thrombocytopenia			
subjects affected / exposed	1 / 6 (16.67%)	0 / 19 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Eye disorders			
Chloropsia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 19 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	2
Vision blurred			
subjects affected / exposed	2 / 6 (33.33%)	0 / 19 (0.00%)	0 / 8 (0.00%)
occurrences (all)	2	0	0
Conjunctival haemorrhage			
subjects affected / exposed	0 / 6 (0.00%)	1 / 19 (5.26%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Diplopia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 19 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Eye pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 19 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Halo vision			
subjects affected / exposed	0 / 6 (0.00%)	0 / 19 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	4 / 6 (66.67%)	1 / 19 (5.26%)	2 / 8 (25.00%)
occurrences (all)	7	1	2
Constipation			
subjects affected / exposed	3 / 6 (50.00%)	4 / 19 (21.05%)	3 / 8 (37.50%)
occurrences (all)	3	5	3
Vomiting			

subjects affected / exposed	3 / 6 (50.00%)	2 / 19 (10.53%)	1 / 8 (12.50%)
occurrences (all)	6	2	1
Diarrhoea			
subjects affected / exposed	0 / 6 (0.00%)	2 / 19 (10.53%)	0 / 8 (0.00%)
occurrences (all)	0	2	0
Abdominal distension			
subjects affected / exposed	1 / 6 (16.67%)	0 / 19 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Abdominal pain			
subjects affected / exposed	0 / 6 (0.00%)	3 / 19 (15.79%)	0 / 8 (0.00%)
occurrences (all)	0	3	0
Abdominal discomfort			
subjects affected / exposed	0 / 6 (0.00%)	3 / 19 (15.79%)	0 / 8 (0.00%)
occurrences (all)	0	3	0
Gastrooesophageal reflux disease			
subjects affected / exposed	1 / 6 (16.67%)	0 / 19 (0.00%)	1 / 8 (12.50%)
occurrences (all)	1	0	1
Ascites			
subjects affected / exposed	1 / 6 (16.67%)	1 / 19 (5.26%)	0 / 8 (0.00%)
occurrences (all)	1	1	0
Dry mouth			
subjects affected / exposed	0 / 6 (0.00%)	1 / 19 (5.26%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Proctalgia			
subjects affected / exposed	0 / 6 (0.00%)	2 / 19 (10.53%)	0 / 8 (0.00%)
occurrences (all)	0	2	0
Abdominal pain lower			
subjects affected / exposed	0 / 6 (0.00%)	1 / 19 (5.26%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Abdominal pain upper			
subjects affected / exposed	0 / 6 (0.00%)	1 / 19 (5.26%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Defaecation urgency			
subjects affected / exposed	0 / 6 (0.00%)	1 / 19 (5.26%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Dyspepsia			

subjects affected / exposed	0 / 6 (0.00%)	1 / 19 (5.26%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Fistula of small intestine			
subjects affected / exposed	0 / 6 (0.00%)	1 / 19 (5.26%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Inguinal hernia			
subjects affected / exposed	1 / 6 (16.67%)	0 / 19 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Small intestinal obstruction			
subjects affected / exposed	0 / 6 (0.00%)	0 / 19 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Stomatitis			
subjects affected / exposed	0 / 6 (0.00%)	1 / 19 (5.26%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Toothache			
subjects affected / exposed	0 / 6 (0.00%)	1 / 19 (5.26%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Hepatobiliary disorders			
Hepatic pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 19 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Jaundice			
subjects affected / exposed	0 / 6 (0.00%)	0 / 19 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Dermatitis acneiform			
subjects affected / exposed	3 / 6 (50.00%)	1 / 19 (5.26%)	0 / 8 (0.00%)
occurrences (all)	5	1	0
Pruritus			
subjects affected / exposed	2 / 6 (33.33%)	4 / 19 (21.05%)	2 / 8 (25.00%)
occurrences (all)	3	6	2
Rash maculo-papular			
subjects affected / exposed	1 / 6 (16.67%)	1 / 19 (5.26%)	1 / 8 (12.50%)
occurrences (all)	1	1	2
Rash			

subjects affected / exposed	1 / 6 (16.67%)	2 / 19 (10.53%)	0 / 8 (0.00%)
occurrences (all)	1	3	0
Dry skin			
subjects affected / exposed	1 / 6 (16.67%)	0 / 19 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Erythema			
subjects affected / exposed	0 / 6 (0.00%)	0 / 19 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Night sweats			
subjects affected / exposed	0 / 6 (0.00%)	1 / 19 (5.26%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Rash macular			
subjects affected / exposed	0 / 6 (0.00%)	0 / 19 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Renal and urinary disorders			
Proteinuria			
subjects affected / exposed	0 / 6 (0.00%)	0 / 19 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Dysuria			
subjects affected / exposed	1 / 6 (16.67%)	0 / 19 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Haematuria			
subjects affected / exposed	0 / 6 (0.00%)	0 / 19 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 6 (0.00%)	2 / 19 (10.53%)	1 / 8 (12.50%)
occurrences (all)	0	2	1
Arthralgia			
subjects affected / exposed	1 / 6 (16.67%)	1 / 19 (5.26%)	3 / 8 (37.50%)
occurrences (all)	1	1	3
Musculoskeletal chest pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 19 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Myalgia			

subjects affected / exposed	1 / 6 (16.67%)	0 / 19 (0.00%)	1 / 8 (12.50%)
occurrences (all)	1	0	1
Muscle spasms			
subjects affected / exposed	0 / 6 (0.00%)	0 / 19 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Pain in extremity			
subjects affected / exposed	0 / 6 (0.00%)	0 / 19 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Axillary mass			
subjects affected / exposed	0 / 6 (0.00%)	0 / 19 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Bone pain			
subjects affected / exposed	1 / 6 (16.67%)	0 / 19 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Coccydynia			
subjects affected / exposed	0 / 6 (0.00%)	1 / 19 (5.26%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Flank pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 19 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Groin pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 19 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal discomfort			
subjects affected / exposed	0 / 6 (0.00%)	1 / 19 (5.26%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Neck pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 19 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Infections and infestations			
COVID-19			
subjects affected / exposed	1 / 6 (16.67%)	2 / 19 (10.53%)	0 / 8 (0.00%)
occurrences (all)	1	2	0
Lower respiratory tract infection			
subjects affected / exposed	1 / 6 (16.67%)	0 / 19 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0

Urinary tract infection			
subjects affected / exposed	1 / 6 (16.67%)	0 / 19 (0.00%)	1 / 8 (12.50%)
occurrences (all)	1	0	1
Oral candidiasis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 19 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Herpes zoster			
subjects affected / exposed	0 / 6 (0.00%)	0 / 19 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Klebsiella urinary tract infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 19 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Pneumonia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 19 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Rash pustular			
subjects affected / exposed	0 / 6 (0.00%)	0 / 19 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Rhinitis			
subjects affected / exposed	1 / 6 (16.67%)	0 / 19 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Skin infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 19 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Staphylococcal bacteraemia			
subjects affected / exposed	0 / 6 (0.00%)	1 / 19 (5.26%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Tooth infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 19 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Vascular device infection			
subjects affected / exposed	0 / 6 (0.00%)	1 / 19 (5.26%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Metabolism and nutrition disorders			
Decreased appetite			

subjects affected / exposed	1 / 6 (16.67%)	0 / 19 (0.00%)	1 / 8 (12.50%)
occurrences (all)	1	2	0
Hyponatraemia			
subjects affected / exposed	2 / 6 (33.33%)	0 / 19 (0.00%)	0 / 8 (0.00%)
occurrences (all)	4	0	0
Hypoalbuminaemia			
subjects affected / exposed	1 / 6 (16.67%)	1 / 19 (5.26%)	0 / 8 (0.00%)
occurrences (all)	1	1	0
Dehydration			
subjects affected / exposed	1 / 6 (16.67%)	0 / 19 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Hypocalcaemia			
subjects affected / exposed	1 / 6 (16.67%)	0 / 19 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Hypophosphataemia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 19 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	Phase 2- NSCLC Cohort 3		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	23 / 23 (100.00%)		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Tumour pain			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Acrochordon			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Cancer pain			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Hypotension			

subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Flushing			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Deep vein thrombosis			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Hot flush			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	3 / 23 (13.04%)		
occurrences (all)	3		
Pyrexia			
subjects affected / exposed	2 / 23 (8.70%)		
occurrences (all)	2		
Asthenia			
subjects affected / exposed	3 / 23 (13.04%)		
occurrences (all)	4		
Pain			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Non-cardiac chest pain			
subjects affected / exposed	2 / 23 (8.70%)		
occurrences (all)	2		
Oedema peripheral			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Chills			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Chest discomfort			

subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Feeling of body temperature change			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Influenza like illness			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Infusion site extravasation			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Temperature regulation disorder			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Immune system disorders			
Cytokine release syndrome			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Reproductive system and breast disorders			
Testicular pain			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	3 / 23 (13.04%)		
occurrences (all)	3		
Cough			
subjects affected / exposed	5 / 23 (21.74%)		
occurrences (all)	6		
Epistaxis			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Haemoptysis			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Hiccups			

subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Pleural effusion			
subjects affected / exposed	2 / 23 (8.70%)		
occurrences (all)	2		
Rhinorrhoea			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Tachypnoea			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Dysphonia			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Dyspnoea exertional			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Hypoxia			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Oropharyngeal pain			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Wheezing			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Psychiatric disorders			
Insomnia			
subjects affected / exposed	2 / 23 (8.70%)		
occurrences (all)	2		
Depression			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Anxiety			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		

Confusional state			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Delirium			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Blood pressure decreased			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Blood bilirubin increased			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Blood alkaline phosphatase increased			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Neutrophil count decreased			
subjects affected / exposed	5 / 23 (21.74%)		
occurrences (all)	7		
Blood creatinine increased			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Weight decreased			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Platelet count decreased			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
White blood cell count decreased			

subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Activated partial thromboplastin time prolonged			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Alpha tumour necrosis factor increased			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Blood lactate dehydrogenase increased			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
C-reactive protein increased			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
International normalised ratio increased			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Lipase increased			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Lymphocyte count decreased			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Serum ferritin increased			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Urine output decreased			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Injury, poisoning and procedural complications			
Infusion related reaction			
subjects affected / exposed	19 / 23 (82.61%)		
occurrences (all)	19		
Arthropod bite			

subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Clavicle fracture			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Fall			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Humerus fracture			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Radiation pneumonitis			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Sunburn			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Congenital, familial and genetic disorders			
Hydrocele			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Cardiac disorders			
Tachycardia			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Palpitations			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Nervous system disorders			
Headache			
subjects affected / exposed	3 / 23 (13.04%)		
occurrences (all)	3		
Dizziness			
subjects affected / exposed	2 / 23 (8.70%)		
occurrences (all)	2		
Peripheral sensory neuropathy			

subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Aphasia			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Bell's palsy			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Dysgeusia			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Presyncope			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Somnolence			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Tremor			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Blood and lymphatic system disorders			
Lymphopenia			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Anaemia			
subjects affected / exposed	2 / 23 (8.70%)		
occurrences (all)	2		
Neutropenia			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Thrombocytopenia			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Eye disorders			
Chloropsia			

subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Vision blurred			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Conjunctival haemorrhage			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Diplopia			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Eye pain			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Halo vision			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	4 / 23 (17.39%)		
occurrences (all)	4		
Constipation			
subjects affected / exposed	2 / 23 (8.70%)		
occurrences (all)	2		
Vomiting			
subjects affected / exposed	2 / 23 (8.70%)		
occurrences (all)	2		
Diarrhoea			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Abdominal distension			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Abdominal pain			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		

Abdominal discomfort			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Ascites			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Dry mouth			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Proctalgia			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Abdominal pain lower			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Abdominal pain upper			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Defaecation urgency			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Dyspepsia			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Fistula of small intestine			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Inguinal hernia			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Small intestinal obstruction			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		

Stomatitis			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Toothache			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Hepatobiliary disorders			
Hepatic pain			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Jaundice			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Skin and subcutaneous tissue disorders			
Dermatitis acneiform			
subjects affected / exposed	3 / 23 (13.04%)		
occurrences (all)	4		
Pruritus			
subjects affected / exposed	3 / 23 (13.04%)		
occurrences (all)	3		
Rash maculo-papular			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Rash			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Dry skin			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Erythema			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Night sweats			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Rash macular			

subjects affected / exposed occurrences (all)	0 / 23 (0.00%) 0		
Renal and urinary disorders			
Proteinuria			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Dysuria			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Haematuria			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Arthralgia			
subjects affected / exposed	2 / 23 (8.70%)		
occurrences (all)	3		
Musculoskeletal chest pain			
subjects affected / exposed	2 / 23 (8.70%)		
occurrences (all)	2		
Myalgia			
subjects affected / exposed	2 / 23 (8.70%)		
occurrences (all)	2		
Muscle spasms			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Pain in extremity			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Axillary mass			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Bone pain			

subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Coccydynia			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Flank pain			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Groin pain			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Musculoskeletal discomfort			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Neck pain			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Infections and infestations			
COVID-19			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Lower respiratory tract infection			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Urinary tract infection			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Oral candidiasis			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Herpes zoster			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Klebsiella urinary tract infection			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		

Pneumonia			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Rash pustular			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Rhinitis			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Skin infection			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Staphylococcal bacteraemia			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Tooth infection			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Vascular device infection			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	4 / 23 (17.39%)		
occurrences (all)	3		
Hyponatraemia			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Hypoalbuminaemia			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Dehydration			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Hypocalcaemia			

subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Hypophosphataemia			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
04 November 2019	<p>A criterion to suspend further enrollment in study and performing safety analysis was added in case of occurrence of a Common Terminology Criteria for Adverse Events (CTCAE) Grade 5 event or a second CTCAE Grade 4 adverse event considered at least possibly related to AFM24 at any time during Phase 1 of the study. A criterion was added to permanently discontinue AFM24 in patients who experience dose-limiting toxicities (DLTs) during Cycle 1 treatment. a criterion was added to permanently discontinue AFM24 in patients who experience DLTs during Cycle 1 treatment.</p> <p>Some patients may experience cytokine release syndrome during or after the AFM24 infusion, and occurrence of such events (\geqCTCAE Grade 3) will be considered a DLT for this study. Observation time has been clarified for patients experiencing such an event.</p> <p>General additional clarification in text, tables and figures.</p>
26 March 2020	<p>the objectives of the trial were re-worded to define more precise endpoints and increase clarity. Additional rules were applied for cases where the AFM24 treatment is interrupted or delayed, which were not covered previously. More detailed guidelines were created for Infusion Related Reaction, as previous language did not cover all aspects. Additionally, the protocol's statistical section was updated to include more informative prior.</p>
16 September 2020	<p>The protocol was updated to introduce changes made to the premedication regimen for administration of AFM 24, as well as the guidance for the management of AFM 24 related infusion related reactions and other adverse events. In addition, the protocol was aligned with letter of amendment (LoA) submitted by the sponsor and guidance is added on infusion time to be followed during cycle 1 and subsequent cycles for management of IRRs. Also, additional safety follow-up visit was added after end-of treatment visit.</p>
16 December 2020	<p>The protocol was updated to for its patient populations to be included in the expansion cohorts of the Phase 2a of the study. The dose limiting toxicities (DLT) definitions are further clarified and the schedule/criteria are updated for collection of tumor biopsy samples. The statistical analysis for expansion phase (Phase 2a) are also revised per FDA guidelines on expansion cohorts for first-in-human (FIH) studies for expedited development on oncology drugs and biologics.</p>
03 May 2021	<p>The protocol was updated to add every-2-weeks (q2w) dosing for the dose expansion phase (Phase 2a) only. Additionally, split day dosing (infusion over 2 days) is also added for subjects who cannot tolerate the infusion over 4 hours. The protocol is also updated to include infusion related reactions (IRR) as an adverse event of special interest for AFM24, and to include more details on the monitoring and management of IRR including cytokine release syndrome (CRS).</p>
23 December 2021	<p>The protocol was updated to add clinical data available to date, justify the Recommended Phase II Dose (RP2D) and update of benefit risk section to reflect available clinical data. Furthermore, the inclusion criteria for phase 2 were aligned with regional requirements for standard of care.</p>

03 November 2022	The protocol was updated to revise several inclusion and exclusion criteria for clarifications and alignment. In addition, the language related to the safety review by independent data monitoring committee (IDMC) for the expansion phase was amended. To align assessment of Overall Survival (OS), updates to the observation period and End of Study were added. A clarification was added regarding Adverse Event (AE) evaluation and Serious AEs (SAE) and AE of Special Interest (AESI) reporting requirements.
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Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported