Clinical trial results:
Phase 2, Parallel-Arm Study of MGCD265 in Patients with Locally Advanced or Metastatic Non-Small Cell Lung Cancer with Activating Genetic Alterations in Mesenchymal-Epithelial Transition Factor

Summary

EudraCT number	2015-002070-21
Trial protocol	HU GB ES PL IT
Global end of trial date	02 January 2019

Results information

Result version number	v1 (current)
This version publication date	18 January 2020
First version publication date	18 January 2020

Trial information

Trial identification

Sponsor protocol code	265-109

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02544633
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Mirati Therapeutics, Inc.
Sponsor organisation address	9393 Towne Centre Drive, San Diego, United States, 92121
Public contact	Vanessa Tassell, Mirati Therapeutics, Inc., tassellv@mirati.com
Scientific contact	Dr. Hirak Der-Torossian, Mirati Therapeutics, Inc., 001 858-332-3556,

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	06 September 2018
Is this the analysis of the primary completion data?	Yes
Primary completion date	06 September 2018
Global end of trial reached?	Yes
Global end of trial date	02 January 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To determine the tumor response to MGCD265 in patients with Locally Advanced or Metastatic Non-Small Cell Lung Cancer with Activating Genetic Alterations in Mesenchymal-Epithelial Transition Factor.

Protection of trial subjects:

This study was conducted in accordance with International Ethical Guidelines for Biomedical Research Involving Human Patients (Council for International Organizations of Medical Sciences 2002), Guidelines for Good Clinical Practice (GCP) (International Conference on Harmonization [ICH] 1996), and concepts that have their origin in the Declaration of Helsinki (World Medical Association 1996, 2008 & 2013).

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	28 October 2015
Long term follow-up planned	Yes
Long term follow-up rationale	Safety
Long term follow-up duration	2 Months
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Korea, Republic of: 10
Country: Number of subjects enrolled	Hungary: 1
Country: Number of subjects enrolled	United States: 45
Country: Number of subjects enrolled	Poland: 3
Country: Number of subjects enrolled	Italy: 2
Country: Number of subjects enrolled	United Kingdom: 3
Country: Number of subjects enrolled	Australia: 4
Worldwide total number of subjects	68
EEA total number of subjects	9

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0

Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	27
From 65 to 84 years	40
85 years and over	1

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Sponsor approval of each potential patient's genetic testing following pre-screening, whether performed by the study central lab or a Sponsor-approved local lab, was filed prior to proceeding to full clinical screening. All patients considered eligible for the study following clinical screening were submitted to Sponsor for registration approval.

Period 1

Period 1 title	Treatment Period
Is this the baseline period?	Yes
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	MET Activating Mutations in Tumor Tissue

Arm description:

MGCD265 (750 mg twice a day (BID) spray dried dispersion tablet or 1050 mg BID soft-gel capsule) in patients with mesenchymal-epithelial transition factor (MET) activating mutations in tumor tissue.

Arm type	Experimental
Investigational medicinal product name	MGCD265
Investigational medicinal product code	
Other name	Glesatinib
Pharmaceutical forms	Capsule, soft, Tablet
Routes of administration	Oral use

Dosage and administration details:

MGCD265 was administered twice-daily in 21-day cycles. MGCD265 could be taken as one of two formulations; softgel capsules (1050 mg) and spray dried dispersion (750 mg).

Arm title	MET Gene Amplifications in Tumor Tissue

Arm description:

MGCD265 (750 mg BID spray dried dispersion tablet or 1050 mg BID soft-gel capsule) in patients with mesenchymal-epithelial transition factor (MET) gene amplifications in tumor tissue.

Arm type	Experimental
Investigational medicinal product name	MGCD265
Investigational medicinal product code	
Other name	Glesatinib
Pharmaceutical forms	Capsule, soft, Tablet
Routes of administration	Oral use

Dosage and administration details:

MGCD265 was administered twice-daily in 21-day cycles. MGCD265 could be taken as one of two formulations; softgel capsules (1050 mg) and spray dried dispersion (750 mg).

Arm title	MET Activating Mutations in ctDNA

Arm description:

MGCD265 (750 mg BID spray dried dispersion tablet or 1050 mg BID soft-gel capsule) in patients with mesenchymal-epithelial transition factor (MET) activating mutations in the blood (circulating tumor DNA).

Arm type	Experimental

Investigational medicinal product name	MGCD265
Investigational medicinal product code	
Other name	Glesatinib
Pharmaceutical forms	Tablet, Capsule, soft
Routes of administration	Oral use

Dosage and administration details:

MGCD265 was administered twice-daily in 21-day cycles. MGCD265 could be taken as one of two formulations; softgel capsules (1050 mg) and spray dried dispersion (750 mg).

Arm title	MET Gene Amplifications in ctDNA

Arm description:

MGCD265 (750 mg BID spray dried dispersion tablet or 1050 mg BID soft-gel capsule) in patients with mesenchymal-epithelial transition factor (MET) gene amplifications in the blood (circulating tumor DNA).

Arm type	Experimental
Investigational medicinal product name	MGCD265
Investigational medicinal product code	
Other name	Glesatinib
Pharmaceutical forms	Capsule, soft, Tablet
Routes of administration	Oral use

Dosage and administration details:

MGCD265 was administered twice-daily in 21-day cycles. MGCD265 could be taken as one of two formulations; softgel capsules (1050 mg) and spray dried dispersion (750 mg).

Number of subjects in period 1	MET Activating Mutations in Tumor Tissue	MET Gene Amplifications in Tumor Tissue	MET Activating Mutations in ctDNA
Started	28	20	8
Completed	28	20	8

Number of subjects in period 1	MET Gene Amplifications in ctDNA
Started	12
Completed	12

Period 2

Period 2 title	Survival Follow-up Period
Is this the baseline period?	No
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes

Arm title	MET Activating Mutations in Tumor Tissue

Arm description:

MGCD265 (750 mg BID spray dried dispersion tablet or 1050 mg BID soft-gel capsule) in patients with mesenchymal-epithelial transition factor (MET) activating mutations in tumor tissue.

Arm type	Experimental
Investigational medicinal product name	MGCD265
Investigational medicinal product code	
Other name	Glesatinib
Pharmaceutical forms	Capsule, soft, Tablet
Routes of administration	Oral use

Dosage and administration details:

MGCD265 was administered twice-daily in 21-day cycles. MGCD265 could be taken as one of two formulations; softgel capsules (1050 mg) and spray dried dispersion (750 mg).

Arm title	MET Gene Amplifications in Tumor Tissue

Arm description:

MGCD265 (750 mg BID spray dried dispersion tablet or 1050 mg BID soft-gel capsule) in patients with mesenchymal-epithelial transition factor (MET) gene amplifications in tumor tissue.

Arm type	Experimental
Investigational medicinal product name	MGCD265
Investigational medicinal product code	
Other name	Glesatinib
Pharmaceutical forms	Capsule, soft, Tablet
Routes of administration	Oral use

Dosage and administration details:

MGCD265 was administered twice-daily in 21-day cycles. MGCD265 could be taken as one of two formulations; softgel capsules (1050 mg) and spray dried dispersion (750 mg).

Arm title	MET Activating Mutations in ctDNA

Arm description:

MGCD265 (750 mg BID spray dried dispersion tablet or 1050 mg BID soft-gel capsule) in patients with mesenchymal-epithelial transition factor (MET) activating mutations in the blood (circulating tumor DNA).

Arm type	Experimental
Investigational medicinal product name	MGCD265
Investigational medicinal product code	
Other name	Glesatinib
Pharmaceutical forms	Capsule, soft, Tablet
Routes of administration	Oral use

Dosage and administration details:

MGCD265 was administered twice-daily in 21-day cycles. MGCD265 could be taken as one of two formulations; softgel capsules (1050 mg) and spray dried dispersion (750 mg).

Arm title	MET Gene Amplifications in ctDNA

Arm description:

MGCD265 (750 mg BID spray dried dispersion tablet or 1050 mg BID soft-gel capsule) in patients with mesenchymal-epithelial transition factor (MET) gene amplifications in the blood (circulating tumor DNA).

Arm type	Experimental
Investigational medicinal product name	MGCD265
Investigational medicinal product code	
Other name	Glesatinib
Pharmaceutical forms	Capsule, soft, Tablet
Routes of administration	Oral use

Dosage and administration details:

MGCD265 was administered twice-daily in 21-day cycles. MGCD265 could be taken as one of two formulations; softgel capsules (1050 mg) and spray dried dispersion (750 mg).

Number of subjects in period 2[1]	MET Activating Mutations in Tumor Tissue	MET Gene Amplifications in Tumor Tissue	MET Activating Mutations in ctDNA
Started	28	19	7
Completed	0	0	0
Not completed	28	19	7
Death	12	14	3
Other	1	-	-
Withdrawal by Subject	4	-	1
Study Terminated by Sponsor	11	4	2
Lost to follow-up	-	1	1

Number of subjects in period 2[1]	MET Gene Amplifications in ctDNA
Started	12
Completed	0
Not completed	12
Death	9
Other	-
Withdrawal by Subject	-
Study Terminated by Sponsor	3
Lost to follow-up	-

Notes:

[1] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.
Justification: Not all subjects entered follow-up period.

Baseline characteristics

Reporting groups	
Reporting group title	MET Activating Mutations in Tumor Tissue
Reporting group description:	
MGCD265 (750 mg twice a day (BID) spray dried dispersion tablet or 1050 mg BID soft-gel capsule) in patients with mesenchymal-epithelial transition factor (MET) activating mutations in tumor tissue.	
Reporting group title	MET Gene Amplifications in Tumor Tissue
Reporting group description:	
MGCD265 (750 mg BID spray dried dispersion tablet or 1050 mg BID soft-gel capsule) in patients with mesenchymal-epithelial transition factor (MET) gene amplifications in tumor tissue.	
Reporting group title	MET Activating Mutations in ctDNA
Reporting group description:	
MGCD265 (750 mg BID spray dried dispersion tablet or 1050 mg BID soft-gel capsule) in patients with mesenchymal-epithelial transition factor (MET) activating mutations in the blood (circulating tumor DNA).	
Reporting group title	MET Gene Amplifications in ctDNA
Reporting group description:	
MGCD265 (750 mg BID spray dried dispersion tablet or 1050 mg BID soft-gel capsule) in patients with mesenchymal-epithelial transition factor (MET) gene amplifications in the blood (circulating tumor DNA).	

Reporting group values	MET Activating Mutations in Tumor Tissue	MET Gene Amplifications in Tumor Tissue	MET Activating Mutations in ctDNA
Number of subjects	28	20	8
Age categorical			
Units: Subjects			
In utero			
Preterm newborn infants (gestational age < 37 wks)			
Newborns (0-27 days)			
Infants and toddlers (28 days-23 months)			
Children (2-11 years)			
Adolescents (12-17 years)			
Adults (18-64 years)			
From 65-84 years			
85 years and over			
Age continuous			
Units: years			
arithmetic mean	70.7	61.8	59.1
standard deviation	± 6.02	± 13.17	± 7.70
Gender categorical			
Units: Subjects			
Female	16	4	6
Male	12	16	2
Ethnicity			
Units: Subjects			
Hispanic or Latino	0	0	1
Not Hispanic or Latino	28	20	7
Race			
Units: Subjects			

Asian	4	6	2
Black or African American	2	1	0
White	21	13	6
Unknown or Not Reported	1	0	0
ECOG Performance Status			
0 - Fully active, able to carry on all pre-disease performance without restriction 1 - Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, e.g., light house work, office work 2 - Ambulatory and capable of all self care but unable to carry out any work activities. Up and about more than 50% of waking hours 3 - Capable of only limited self care, confined to bed or chair more than 50% of waking hours 4 - Completely disabled. Cannot carry on any self care. Totally confined to bed or chair 5 - Dead			
Units: Subjects			
ECOG Performance Status - 0	10	6	2
ECOG Performance Status - 1	16	12	6
ECOG Performance Status - 2	2	2	0
ECOG Performance Status - 3	0	0	0
ECOG Performance Status - 4	0	0	0
Primary Disease Histology Units: Subjects			
Adenocarcinoma	22	18	7
Squamous Cell Carcinoma	3	2	1
Large Cell Carcinoma	0	0	0
Other	3	0	0
Current Stage Units: Subjects			
Locally Advanced	1	1	0
Metastatic	27	19	8
Smoking History Units: Subjects			
Lifetime Non-Smoker	10	2	3
Current Smoker	0	4	1
Past Smoker	18	14	4
Height			
Some patients did not have their height recorded at baseline.			
Units: cm			
arithmetic mean	168.63	173.18	161.11
standard deviation	± 9.74	± 8.77	± 8.10
Body Mass Index			
BMI unable to be calculated in patients with no height recorded at baseline.			
Units: Kg/m^2			
arithmetic mean	25.16	24.92	22.24
standard deviation	± 4.58	± 4.46	± 2.34
Weight Units: Kg			
arithmetic mean	70.85	75.33	60.97
standard deviation	± 17.64	± 17.77	± 8.68

Reporting group values	MET Gene	Total	

	Amplifications in ctDNA		
Number of subjects	12	68	
Age categorical Units: Subjects			
In utero		0	
Preterm newborn infants (gestational age < 37 wks)		0	
Newborns (0-27 days)		0	
Infants and toddlers (28 days-23 months)		0	
Children (2-11 years)		0	
Adolescents (12-17 years)		0	
Adults (18-64 years)		0	
From 65-84 years		0	
85 years and over		0	
Age continuous Units: years			
arithmetic mean	64.8		
standard deviation	± 11.09	-	
Gender categorical Units: Subjects			
Female	6	32	
Male	6	36	
Ethnicity Units: Subjects			
Hispanic or Latino	0	1	
Not Hispanic or Latino	12	67	
Race Units: Subjects			
Asian	2	14	
Black or African American	0	3	
White	10	50	
Unknown or Not Reported	0	1	
ECOG Performance Status			
0 - Fully active, able to carry on all pre-disease performance without restriction 1 - Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, e.g., light house work, office work 2 - Ambulatory and capable of all self care but unable to carry out any work activities. Up and about more than 50% of waking hours 3 - Capable of only limited self care, confined to bed or chair more than 50% of waking hours 4 - Completely disabled. Cannot carry on any self care. Totally confined to bed or chair 5 - Dead			
Units: Subjects			
ECOG Performance Status - 0	2	20	
ECOG Performance Status - 1	6	40	
ECOG Performance Status - 2	4	8	
ECOG Performance Status - 3	0	0	
ECOG Performance Status - 4	0	0	
Primary Disease Histology Units: Subjects			

Adenocarcinoma	6	53	
Squamous Cell Carcinoma	2	8	
Large Cell Carcinoma	2	2	
Other	2	5	
Current Stage Units: Subjects			
Locally Advanced	1	3	
Metastatic	11	65	
Smoking History Units: Subjects			
Lifetime Non-Smoker	2	17	
Current Smoker	3	8	
Past Smoker	7	43	
Height			
Some patients did not have their height recorded at baseline.			
Units: cm			
arithmetic mean	167.70		
standard deviation	± 8.98	-	
Body Mass Index			
BMI unable to be calculated in patients with no height recorded at baseline.			
Units: Kg/m^2			
arithmetic mean	21.80		
standard deviation	± 4.18	-	
Weight Units: Kg			
arithmetic mean	61.58		
standard deviation	± 13.56	-	

End points reporting groups

Reporting group title	MET Activating Mutations in Tumor Tissue
Reporting group description:	
MGCD265 (750 mg twice a day (BID) spray dried dispersion tablet or 1050 mg BID soft-gel capsule) in patients with mesenchymal-epithelial transition factor (MET) activating mutations in tumor tissue.	
Reporting group title	MET Gene Amplifications in Tumor Tissue
Reporting group description:	
MGCD265 (750 mg BID spray dried dispersion tablet or 1050 mg BID soft-gel capsule) in patients with mesenchymal-epithelial transition factor (MET) gene amplifications in tumor tissue.	
Reporting group title	MET Activating Mutations in ctDNA
Reporting group description:	
MGCD265 (750 mg BID spray dried dispersion tablet or 1050 mg BID soft-gel capsule) in patients with mesenchymal-epithelial transition factor (MET) activating mutations in the blood (circulating tumor DNA).	
Reporting group title	MET Gene Amplifications in ctDNA
Reporting group description:	
MGCD265 (750 mg BID spray dried dispersion tablet or 1050 mg BID soft-gel capsule) in patients with mesenchymal-epithelial transition factor (MET) gene amplifications in the blood (circulating tumor DNA).	
Reporting group title	MET Activating Mutations in Tumor Tissue
Reporting group description:	
MGCD265 (750 mg BID spray dried dispersion tablet or 1050 mg BID soft-gel capsule) in patients with mesenchymal-epithelial transition factor (MET) activating mutations in tumor tissue.	
Reporting group title	MET Gene Amplifications in Tumor Tissue
Reporting group description:	
MGCD265 (750 mg BID spray dried dispersion tablet or 1050 mg BID soft-gel capsule) in patients with mesenchymal-epithelial transition factor (MET) gene amplifications in tumor tissue.	
Reporting group title	MET Activating Mutations in ctDNA
Reporting group description:	
MGCD265 (750 mg BID spray dried dispersion tablet or 1050 mg BID soft-gel capsule) in patients with mesenchymal-epithelial transition factor (MET) activating mutations in the blood (circulating tumor DNA).	
Reporting group title	MET Gene Amplifications in ctDNA
Reporting group description:	
MGCD265 (750 mg BID spray dried dispersion tablet or 1050 mg BID soft-gel capsule) in patients with mesenchymal-epithelial transition factor (MET) gene amplifications in the blood (circulating tumor DNA).	
Subject analysis set title	Tablet 750 mg BID
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Tablet formulation, 750 mg, BID	
Subject analysis set title	Soft Gel 1050 mg BID
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Soft Gel formulation, 1050 mg, BID	

Primary: Objective Response Rate

End point title	Objective Response Rate
End point description:	
Objective disease response is defined as the percent of patients documented by investigator assessment to have a confirmed Complete Response (CR) or Partial Response (PR) in accordance with the Response Evaluation Criteria in Solid Tumors (RECIST 1.1) for target and non-target lesions as assessed by CT or MRI. CR is defined as complete disappearance of all target lesions with the exception of nodal disease; PR is defined as >=30% decrease under baseline of the sum of diameters of all target measurable lesions; Stable Disease (SD) is concluded when the response does not qualify for CR, PR or Progression;	

Progressive Disease (PD) is defined as a 20% increase in the sum of diameters of target measurable lesions above the smallest sum observed with a minimum absolute increase of 5 mm, or unequivocal progression of pre-existing non-target lesions.

End point type	Primary

End point timeframe:

Up to 3 months

End point values	MET Activating Mutations in Tumor Tissue	MET Gene Amplifications in Tumor Tissue	MET Activating Mutations in ctDNA	MET Gene Amplifications in ctDNA
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	28	20	8	12
Units: Percentage of patients				
number (confidence interval 95%)	10.7 (2.27 to 28.23)	15.0 (3.21 to 37.89)	25.0 (3.19 to 65.09)	0.00 (0.00 to 26.46)

Statistical analyses

Statistical analysis title	MET Activating Mutations in Tumor Tissue
Comparison groups	MET Activating Mutations in Tumor Tissue v MET Gene Amplifications in Tumor Tissue v MET Activating Mutations in ctDNA v MET Gene Amplifications in ctDNA
Number of subjects included in analysis	68
Analysis specification	Pre-specified
Analysis type	superiority[1]
P-value	= 0.94
Method	Exact test

Notes:

[1] - An exact test for single proportion (two-sided a=5%) will be performed to test H0: ORR <=20% against H1: ORR >20%.

Statistical analysis title	MET Gene Amplifications in Tumor Tissue
Comparison groups	MET Activating Mutations in Tumor Tissue v MET Gene Amplifications in Tumor Tissue v MET Activating Mutations in ctDNA v MET Gene Amplifications in ctDNA
Number of subjects included in analysis	68
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.79
Method	Exact test

Statistical analysis title	MET Activating Mutations in ctDNA
Comparison groups	MET Gene Amplifications in Tumor Tissue v MET Activating Mutations in Tumor Tissue v MET Activating Mutations in ctDNA v MET Gene Amplifications in ctDNA

Number of subjects included in analysis	68
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.47
Method	Exact test

Statistical analysis title	MET Gene Amplifications in ctDNA
Comparison groups	MET Activating Mutations in Tumor Tissue v MET Gene Amplifications in Tumor Tissue v MET Activating Mutations in ctDNA v MET Gene Amplifications in ctDNA
Number of subjects included in analysis	68
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.999
Method	Exact test

Secondary: Duration of Response

End point title	Duration of Response

End point description:

Duration of Response (DR) was defined as the time from date of the first documentation of objective tumor response (CR or PR) to the first documentation of Objective Progression of Disease (PD) or to death due to any cause in the absence of documented PD.

End point type	Secondary

End point timeframe:

From date of the first documentation of objective tumor response (CR or PR) to the first documentation of Objective Progression of Disease (PD) or to death due to any cause in the absence of documented PD, assessed up to 24 months.

End point values	MET Activating Mutations in Tumor Tissue	MET Gene Amplifications in Tumor Tissue	MET Activating Mutations in ctDNA	MET Gene Amplifications in ctDNA
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	3	2[2]	0[3]
Units: Days				
median (confidence interval 95%)	85 (82 to 132)	170 (120 to 170)	99999 (77 to 99999)	(to)

Notes:

[2] - Median DR and upper bound of 95% CI for median DR are not estimable. Median not reached.

[3] - Median DR, lower nd upper bound of 95% CI for median DR are not estimable.

Statistical analyses

No statistical analyses for this end point

Secondary: Progression Free Survival

End point title	Progression Free Survival

End point description:

Progression-free survival (PFS) was defined as the time from date of first study treatment to first PD or death due to any cause in the absence of documented PD. Per RECIST 1.1, Progressive Disease (PD) is defined as a 20% increase in the sum of diameters of target measurable lesions above the smallest sum observed (over baseline if no decrease in the sum is observed during therapy) with a minimum absolute increase of 5 mm, or unequivocal progression of pre-existing non-target lesions.

End point type	Secondary

End point timeframe:

The time from date of first study treatment to first PD or death due to any cause in the absence of documented PD, up to 24 months.

End point values	MET Activating Mutations in Tumor Tissue	MET Gene Amplifications in Tumor Tissue	MET Activating Mutations in ctDNA	MET Gene Amplifications in ctDNA
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	28	20	8[4]	12
Units: Months				
median (confidence interval 95%)	3.95 (2.11 to 4.18)	4.84 (1.35 to 5.53)	3.39 (1.28 to 99999)	2.76 (1.48 to 4.01)

Notes:

[4] - Upper bound of 95% CI for median PFS is not estimable due to small number of events.

Statistical analyses

No statistical analyses for this end point

Secondary: 1-Year Survival Rate

End point title	1-Year Survival Rate

End point description:

1-Year Survival was defined as the probability of survival at 1 year after the first dose.

End point type	Secondary

End point timeframe:

From date of first study treatment to death due to any cause, assessed up to 12 months

End point values	MET Activating Mutations in Tumor Tissue	MET Gene Amplifications in Tumor Tissue	MET Activating Mutations in ctDNA	MET Gene Amplifications in ctDNA
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	28	20	8	12
Units: Percentage				
number (confidence interval 95%)	50.47 (27.49 to 69.62)	34.92 (14.05 to 56.89)	54.69 (13.72 to 83.24)	13.89 (0.86 to 44.05)

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Survival

End point title	Overall Survival

End point description:

Overall Survival was defined as the time from date of first study treatment to death due to any cause.

End point type	Secondary

End point timeframe:

From date of first study treatment to death due to any cause, assessed up to 24 months.

End point values	MET Activating Mutations in Tumor Tissue	MET Gene Amplifications in Tumor Tissue	MET Activating Mutations in ctDNA	MET Gene Amplifications in ctDNA
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	28[5]	20	8[6]	12
Units: Months				
median (confidence interval 95%)	16.32 (4.01 to 99999)	7.04 (1.84 to 14.93)	99999 (0.89 to 99999)	4.08 (1.22 to 11.05)

Notes:

[5] - Upper bound of 95% CI for median OS is not estimable due to small number of events.

[6] - Median OS and upper bound of 95% CI for median OS are not estimable. Median not reached.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Patients Experiencing Treatment-Emergent Adverse Events

End point title	Number of Patients Experiencing Treatment-Emergent Adverse Events

End point description:

End point type	Secondary

End point timeframe:

Date of first dose to 28 days after the last dose, up to an average of 5.1 months on treatment.

End point values	MET Activating Mutations in Tumor Tissue	MET Gene Amplifications in Tumor Tissue	MET Activating Mutations in ctDNA	MET Gene Amplifications in ctDNA
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	28	20	8	12
Units: Number of Patients	28	20	8	12

Statistical analyses

No statistical analyses for this end point

Secondary: Blood Plasma Concentration of MGCD265

End point title	Blood Plasma Concentration of MGCD265

End point description:

Blood samples for PK assessment were to be taken on Cycle 1, Day 1 and Day 15 at pre-dose and at 2 hours (1-3 hours) and 6 hours (4-8 hours) post-dose. On Cycle 2, samples were collected on Day 1 and Day 15 at pre-dose and at 6 hours post-dose (4-8 hours). Note: Assessment of Cmax and Tmax are limited by the sparse blood sampling schedule post dose (i.e., only 2 blood draws post-dose in Cycle 1 and only 1 sample collected post-dose in Cycle 2). The number of patients reported for each PK parameter was dependent on the actual number of blood samples collected post-dose.

End point type	Secondary

End point timeframe:

Cycle 1, Day 1 and Day 15 at pre-dose and at 2 hours (1-3 hours) and 6 hours (4-8 hours) post-dose. Cycle 2, Day 1 and Day 15 at pre-dose and at 6 hours post-dose (4-8 hours).

End point values	Tablet 750 mg BID	Soft Gel 1050 mg BID		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	46[7]	17[8]		
Units: See Parameter				
geometric mean (geometric coefficient of variation)				
AUC0-6 (h*ng/mL) C1D1	250.8 (± 98.0)	185.5 (± 98.8)		
AUC0-6 (h*ng/mL) C1D15	1565 (± 54.0)	1837 (± 51.3)		
Cmax (ng/mL) C1D1	69.77 (± 87.1)	60.49 (± 103.9)		
Cmax (ng/mL) C1D15	279.2 (± 54.6)	328.1 (± 49.8)		
Cmax (ng/mL) C2D1	214 (± 69.4)	386 (± 13.9)		
Cmax (ng/mL) C2D15	138 (± 100)	99999 (± 99999)		
Ctrough (ng/mL) C1D15	264 (± 52.5)	337 (± 59.2)		
Ctrough (ng/mL) C2D1	203 (± 80.9)	345 (± 48.5)		
Ctrough (ng/mL) C2D15	255 (± 37.5)	99999 (± 99999)		
Accumulation Ratio AUC0-6 C1D15	6.42 (± 87.2)	9.88 (± 96.4)		
Accumulation Ratio Cmax C1D15	4.07 (± 79.7)	5.35 (± 100.9)		
Peak to Trough ratio C1D15	1.09 (± 13.4)	1.08 (± 10.4)		

Notes:

[7] - PK Analysis Set consisted of all evaluabale patients who received at least one dose of study drug

[8] - PK Analysis Set consisted of all evaluabale patients who received at least one dose of study drug

Statistical analyses

No statistical analyses for this end point

Secondary: Blood Plasma Concentration of MGCD265 - Tmax

End point title	Blood Plasma Concentration of MGCD265 - Tmax

End point description:

Blood samples for PK assessment were to be taken on Cycle 1, Day 1 and Day 15 at pre-dose and at 2 hours (1-3 hours) and 6 hours (4-8 hours) post-dose. Note: Assessment of Cmax and Tmax are limited

by the sparse blood sampling schedule post dose (i.e., only 2 blood draws post-dose in Cycle 1 and only 1 sample collected post-dose in Cycle 2). The number of patients reported for each PK parameter was dependent on the actual number of blood samples collected post-dose.

End point type	Secondary

End point timeframe:

Cycle 1, Day 1 and Day 15 at pre-dose and at 2 hours (1-3 hours) and 6 hours (4-8 hours) post-dose.

End point values	Tablet 750 mg BID	Soft Gel 1050 mg BID		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	46[9]	17[10]		
Units: hours				
median (full range (min-max))				
C1D1	6 (2 to 6)	6 (6 to 6)		
C1D15	2 (2 to 6)	6 (2 to 6)		

Notes:

[9] - PK Analysis Set

[10] - PK Analysis Set

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Patients Showing a Correlation Between Selected Tumor Gene Alterations Using Different Analytical Techniques in Tumor Tissue and Circulating Tumor Deoxyribonucleic Acid (ctDNA)

End point title	Number of Patients Showing a Correlation Between Selected Tumor Gene Alterations Using Different Analytical Techniques in Tumor Tissue and Circulating Tumor Deoxyribonucleic Acid (ctDNA)

End point description:

Due to early closure of the study due to sponsor portfolio prioritization and not due to any patient safety issues, data to assess correlations between selected tumor gene alterations using different analytical techniques in tumor tissue and circulating tumor deoxyribonucleic acid (ctDNA) was not completed.

End point type	Secondary

End point timeframe:

At baseline

End point values	MET Activating Mutations in Tumor Tissue	MET Gene Amplifications in Tumor Tissue	MET Activating Mutations in ctDNA	MET Gene Amplifications in ctDNA
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0[11]	0[12]	0[13]	0[14]
Units: Patients				

Notes:

[11] - Study was early terminated so data collection to assess any correlations was not completed.

[12] - Study was early terminated so data collection to assess any correlations was not completed.

[13] - Study was early terminated so data collection to assess any correlations was not completed.

[14] - Study was early terminated so data collection to assess any correlations was not completed.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Patients Showing Change in Genetic Alteration Status in ctDNA With MGCD265 Treatment Over Time

End point title	Number of Patients Showing Change in Genetic Alteration Status in ctDNA With MGCD265 Treatment Over Time

End point description:

Due to early closure of the study due to sponsor portfolio prioritization and not due to any patient safety issues, data to assess change in genetic alteration status in ctDNA with MGCD265 treatment over time in the selected population was not completed.

End point type	Secondary

End point timeframe:

At baseline and at time of confirmation of response to treatment

End point values	MET Activating Mutations in Tumor Tissue	MET Gene Amplifications in Tumor Tissue	MET Activating Mutations in ctDNA	MET Gene Amplifications in ctDNA
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0[15]	0[16]	0[17]	0[18]
Units: Number of Patients				

Notes:

[15] - Study was early terminated so data to assess change in genetic alteration status wasn't completed.
[16] - Study was early terminated so data to assess change in genetic alteration status wasn't completed.
[17] - Study was early terminated so data to assess change in genetic alteration status wasn't completed.
[18] - Study was early terminated so data to assess change in genetic alteration status wasn't completed.

Statistical analyses

No statistical analyses for this end point

Secondary: Blood Plasma Concentration of Soluble MET (sMET) Biomarker

End point title	Blood Plasma Concentration of Soluble MET (sMET) Biomarker

End point description:

MET Activating Mutations in ctDNA. Change from Baseline - Cycle 2 Day 15 - Pre-Dose Standard Deviation not evaluable.
The Pharmacodynamics Evaluable Population Population defined as all patients in the mITT population for whom PD analytical results were available.
Overall number of participants analyzed at baseline and post-baseline are different due to samples not being collected post-baseline for some patients

End point type	Secondary

End point timeframe:
Cycle 1 and Cycle 2

End point values	MET Activating Mutations in Tumor Tissue	MET Gene Amplifications in Tumor Tissue	MET Activating Mutations in ctDNA	MET Gene Amplifications in ctDNA
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	22[19]	17[20]	4[21]	9[22]
Units: pg/mL				
arithmetic mean (standard deviation)				
Baseline	443494.7 (± 228345.48)	461985.2 (± 122069.25)	450112.5 (± 80809.29)	961383.1 (± 1665608.92)
Actual - Cycle 1 Day 15 - Pre-Dose	577631.4 (± 221350.47)	568938.8 (± 129859.54)	594277.3 (± 49746.18)	775242.8 (± 679349.02)
Change from Baseline - Cycle 1 Day 15 - Pre-Dose	122074.7 (± 166978.07)	94110.4 (± 87158.09)	144164.8 (± 51740.94)	-257537.5 (± 1102955.10)
Actual - Cycle 2 Day 1 - Pre-Dose	560790.3 (± 216802.34)	582800.9 (± 140742.66)	662385.3 (± 41039.78)	742344.9 (± 620417.99)
Change from Baseline - Cycle 2 Day 15 - Pre-Dose	96641.3 (± 144021.14)	169374.6 (± 70996.25)	44093.0 (± 99999)	184161.0 (± 161224.04)

Notes:

[19] - Pharmacodynamics Evaluable Population

[20] - Pharmacodynamics Evaluable Population

[21] - Pharmacodynamics Evaluable Population

[22] - Pharmacodynamics Evaluable Population

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: Up to 12 months	
Assessment type	Non-systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	21.0

Reporting groups	
Reporting group title	MET Activating Mutations in Tumor Tissue
Reporting group description: MGCD265 (750 mg BID spray dried dispersion tablet or 1050 mg BID soft-gel capsule) in patients with mesenchymal-epithelial transition factor (MET) activating mutations in tumor tissue.	
Reporting group title	MET Gene Amplifications in Tumor Tissue
Reporting group description: MGCD265 (750 mg BID spray dried dispersion tablet or 1050 mg BID soft-gel capsule) in patients with mesenchymal-epithelial transition factor (MET) gene amplifications in tumor tissue.	
Reporting group title	MET Activating Mutations in ctDNA
Reporting group description: MGCD265 (750 mg BID spray dried dispersion tablet or 1050 mg BID soft-gel capsule) in patients with mesenchymal-epithelial transition factor (MET) activating mutations in the blood (circulating tumor DNA).	
Reporting group title	MET Gene Amplifications in ctDNA
Reporting group description: MGCD265 (750 mg BID spray dried dispersion tablet or 1050 mg BID soft-gel capsule) in patients with mesenchymal-epithelial transition factor (MET) gene amplifications in the blood (circulating tumor DNA).	

Serious adverse events	MET Activating Mutations in Tumor Tissue	MET Gene Amplifications in Tumor Tissue	MET Activating Mutations in ctDNA
Total subjects affected by serious adverse events			
subjects affected / exposed	12 / 28 (42.86%)	10 / 20 (50.00%)	4 / 8 (50.00%)
number of deaths (all causes)	12	14	3
number of deaths resulting from adverse events	9	6	1
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Malignant neoplasm progression			
subjects affected / exposed	5 / 28 (17.86%)	5 / 20 (25.00%)	1 / 8 (12.50%)
occurrences causally related to treatment / all	0 / 5	0 / 5	0 / 1
deaths causally related to treatment / all	0 / 5	0 / 5	0 / 1
Vascular disorders			
Hypotension			

subjects affected / exposed	0 / 28 (0.00%)	0 / 20 (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
Thrombosis			
subjects affected / exposed	0 / 28 (0.00%)	0 / 20 (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
Cardiac disorders			
Myocardial infarction			
subjects affected / exposed	2 / 28 (7.14%)	0 / 20 (0.00%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	0 / 4	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 2	0 / 0	0 / 0
Nervous system disorders			
Cerebrovascular accident			
subjects affected / exposed	1 / 28 (3.57%)	0 / 20 (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
Haemorrhage intracranial			
subjects affected / exposed	1 / 28 (3.57%)	0 / 20 (0.00%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Seizure			
subjects affected / exposed	1 / 28 (3.57%)	1 / 20 (5.00%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Syncope			
subjects affected / exposed	0 / 28 (0.00%)	0 / 20 (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
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	1 / 28 (3.57%)	0 / 20 (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

Multiple organ dysfunction syndrome			
subjects affected / exposed	1 / 28 (3.57%)	0 / 20 (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
Gastrointestinal disorders			
Colitis			
subjects affected / exposed	1 / 28 (3.57%)	0 / 20 (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
Enterocolitis			
subjects affected / exposed	0 / 28 (0.00%)	0 / 20 (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
Nausea			
subjects affected / exposed	0 / 28 (0.00%)	1 / 20 (5.00%)	1 / 8 (12.50%)
occurrences causally related to treatment / all	0 / 0	1 / 1	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			
subjects affected / exposed	0 / 28 (0.00%)	1 / 20 (5.00%)	1 / 8 (12.50%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Hepatic haemorrhage			
subjects affected / exposed	1 / 28 (3.57%)	0 / 20 (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 / 1	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Acute respiratory failure			
subjects affected / exposed	0 / 28 (0.00%)	1 / 20 (5.00%)	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
Bronchial fistula			

subjects affected / exposed	1 / 28 (3.57%)	0 / 20 (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
Chronic obstructive pulmonary disease			
subjects affected / exposed	1 / 28 (3.57%)	0 / 20 (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
Epistaxis			
subjects affected / exposed	0 / 28 (0.00%)	1 / 20 (5.00%)	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
Hypoxia			
subjects affected / exposed	1 / 28 (3.57%)	1 / 20 (5.00%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oesophagobronchial fistula			
subjects affected / exposed	0 / 28 (0.00%)	0 / 20 (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 / 28 (0.00%)	0 / 20 (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
Pneumothorax spontaneous			
subjects affected / exposed	0 / 28 (0.00%)	1 / 20 (5.00%)	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
Pulmonary embolism			
subjects affected / exposed	1 / 28 (3.57%)	1 / 20 (5.00%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Acute kidney injury			

subjects affected / exposed	1 / 28 (3.57%)	0 / 20 (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
Infections and infestations			
Bronchopulmonary aspergillosis			
subjects affected / exposed	0 / 28 (0.00%)	0 / 20 (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
Herpes zoster			
subjects affected / exposed	1 / 28 (3.57%)	0 / 20 (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
Lower respiratory tract infection			
subjects affected / exposed	0 / 28 (0.00%)	0 / 20 (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	1 / 28 (3.57%)	3 / 20 (15.00%)	1 / 8 (12.50%)
occurrences causally related to treatment / all	0 / 1	0 / 4	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 28 (0.00%)	3 / 20 (15.00%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	0 / 0	2 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	MET Gene Amplifications in ctDNA		
Total subjects affected by serious adverse events			
subjects affected / exposed	7 / 12 (58.33%)		
number of deaths (all causes)	9		
number of deaths resulting from adverse events	5		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Malignant neoplasm progression			

subjects affected / exposed	4 / 12 (33.33%)		
occurrences causally related to treatment / all	0 / 5		
deaths causally related to treatment / all	0 / 4		
Vascular disorders			
Hypotension			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Thrombosis			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Myocardial infarction			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Cerebrovascular accident			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Haemorrhage intracranial			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Seizure			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Syncope			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Multiple organ dysfunction syndrome			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Colitis			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Enterocolitis			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Nausea			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Vomiting			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			
Hepatic haemorrhage			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Acute respiratory failure			

subjects affected / exposed	0 / 12 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Bronchial fistula				
subjects affected / exposed	0 / 12 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Chronic obstructive pulmonary disease				
subjects affected / exposed	0 / 12 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Epistaxis				
subjects affected / exposed	0 / 12 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hypoxia				
subjects affected / exposed	0 / 12 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Oesophagobronchial fistula				
subjects affected / exposed	1 / 12 (8.33%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 1			
Pleural effusion				
subjects affected / exposed	1 / 12 (8.33%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pneumothorax spontaneous				
subjects affected / exposed	0 / 12 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pulmonary embolism				

subjects affected / exposed	0 / 12 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Bronchopulmonary aspergillosis			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Herpes zoster			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Lower respiratory tract infection			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pneumonia			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	3 / 12 (25.00%)		
occurrences causally related to treatment / all	1 / 3		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	MET Activating Mutations in Tumor Tissue	MET Gene Amplifications in Tumor Tissue	MET Activating Mutations in ctDNA
Total subjects affected by non-serious adverse events			
subjects affected / exposed	28 / 28 (100.00%)	20 / 20 (100.00%)	7 / 8 (87.50%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Cancer pain			
subjects affected / exposed	1 / 28 (3.57%)	0 / 20 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Tumour pain			
subjects affected / exposed	0 / 28 (0.00%)	0 / 20 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	2 / 28 (7.14%)	0 / 20 (0.00%)	0 / 8 (0.00%)
occurrences (all)	2	0	0
Embolism			
subjects affected / exposed	0 / 28 (0.00%)	1 / 20 (5.00%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Haemorrhage			
subjects affected / exposed	0 / 28 (0.00%)	1 / 20 (5.00%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Hot flush			
subjects affected / exposed	0 / 28 (0.00%)	1 / 20 (5.00%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Hypertension			
subjects affected / exposed	1 / 28 (3.57%)	1 / 20 (5.00%)	0 / 8 (0.00%)
occurrences (all)	4	5	0
Hypotension			
subjects affected / exposed	3 / 28 (10.71%)	0 / 20 (0.00%)	0 / 8 (0.00%)
occurrences (all)	3	0	0
Superior vena cava syndrome			
subjects affected / exposed	0 / 28 (0.00%)	1 / 20 (5.00%)	0 / 8 (0.00%)
occurrences (all)	0	2	0
Thrombosis			
subjects affected / exposed	0 / 28 (0.00%)	0 / 20 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
General disorders and administration			

site conditions			
Asthenia			
subjects affected / exposed	2 / 28 (7.14%)	3 / 20 (15.00%)	1 / 8 (12.50%)
occurrences (all)	3	3	1
Catheter site pain			
subjects affected / exposed	0 / 28 (0.00%)	1 / 20 (5.00%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Chest discomfort			
subjects affected / exposed	0 / 28 (0.00%)	1 / 20 (5.00%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Chest pain			
subjects affected / exposed	2 / 28 (7.14%)	0 / 20 (0.00%)	0 / 8 (0.00%)
occurrences (all)	2	0	0
Face oedema			
subjects affected / exposed	1 / 28 (3.57%)	0 / 20 (0.00%)	2 / 8 (25.00%)
occurrences (all)	1	0	2
Fatigue			
subjects affected / exposed	13 / 28 (46.43%)	8 / 20 (40.00%)	5 / 8 (62.50%)
occurrences (all)	17	8	8
General physical health deterioration			
subjects affected / exposed	1 / 28 (3.57%)	1 / 20 (5.00%)	0 / 8 (0.00%)
occurrences (all)	1	1	0
Malaise			
subjects affected / exposed	2 / 28 (7.14%)	0 / 20 (0.00%)	0 / 8 (0.00%)
occurrences (all)	2	0	0
Non-cardiac chest pain			
subjects affected / exposed	0 / 28 (0.00%)	1 / 20 (5.00%)	1 / 8 (12.50%)
occurrences (all)	0	1	1
Oedema			
subjects affected / exposed	2 / 28 (7.14%)	0 / 20 (0.00%)	0 / 8 (0.00%)
occurrences (all)	3	0	0
Oedema peripheral			
subjects affected / exposed	8 / 28 (28.57%)	5 / 20 (25.00%)	3 / 8 (37.50%)
occurrences (all)	12	5	4
Pain			

subjects affected / exposed	1 / 28 (3.57%)	3 / 20 (15.00%)	0 / 8 (0.00%)
occurrences (all)	1	4	0
Peripheral swelling			
subjects affected / exposed	2 / 28 (7.14%)	1 / 20 (5.00%)	0 / 8 (0.00%)
occurrences (all)	7	1	0
Pyrexia			
subjects affected / exposed	1 / 28 (3.57%)	0 / 20 (0.00%)	1 / 8 (12.50%)
occurrences (all)	1	0	1
Reproductive system and breast disorders			
Vaginal haemorrhage			
subjects affected / exposed	0 / 28 (0.00%)	0 / 20 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	3 / 28 (10.71%)	6 / 20 (30.00%)	3 / 8 (37.50%)
occurrences (all)	7	7	5
Dysphonia			
subjects affected / exposed	1 / 28 (3.57%)	1 / 20 (5.00%)	0 / 8 (0.00%)
occurrences (all)	1	1	0
Dyspnoea			
subjects affected / exposed	6 / 28 (21.43%)	8 / 20 (40.00%)	2 / 8 (25.00%)
occurrences (all)	7	18	3
Dyspnoea exertional			
subjects affected / exposed	0 / 28 (0.00%)	0 / 20 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Haemoptysis			
subjects affected / exposed	0 / 28 (0.00%)	1 / 20 (5.00%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Hypoxia			
subjects affected / exposed	1 / 28 (3.57%)	1 / 20 (5.00%)	0 / 8 (0.00%)
occurrences (all)	2	2	0
Nasal congestion			
subjects affected / exposed	1 / 28 (3.57%)	1 / 20 (5.00%)	0 / 8 (0.00%)
occurrences (all)	1	1	0
Oropharyngeal pain			

subjects affected / exposed	1 / 28 (3.57%)	1 / 20 (5.00%)	0 / 8 (0.00%)
occurrences (all)	1	1	0
Pharyngeal erythema			
subjects affected / exposed	0 / 28 (0.00%)	1 / 20 (5.00%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Pleural effusion			
subjects affected / exposed	1 / 28 (3.57%)	2 / 20 (10.00%)	2 / 8 (25.00%)
occurrences (all)	1	3	2
Pneumonia aspiration			
subjects affected / exposed	0 / 28 (0.00%)	2 / 20 (10.00%)	0 / 8 (0.00%)
occurrences (all)	0	2	0
Pneumothorax			
subjects affected / exposed	0 / 28 (0.00%)	1 / 20 (5.00%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Productive cough			
subjects affected / exposed	2 / 28 (7.14%)	0 / 20 (0.00%)	1 / 8 (12.50%)
occurrences (all)	3	0	1
Pulmonary congestion			
subjects affected / exposed	0 / 28 (0.00%)	1 / 20 (5.00%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Pulmonary embolism			
subjects affected / exposed	1 / 28 (3.57%)	2 / 20 (10.00%)	1 / 8 (12.50%)
occurrences (all)	1	3	1
Pulmonary oedema			
subjects affected / exposed	0 / 28 (0.00%)	0 / 20 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Rales			
subjects affected / exposed	0 / 28 (0.00%)	1 / 20 (5.00%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Respiratory failure			
subjects affected / exposed	0 / 28 (0.00%)	0 / 20 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Rhinorrhoea			
subjects affected / exposed	1 / 28 (3.57%)	1 / 20 (5.00%)	0 / 8 (0.00%)
occurrences (all)	1	1	0
Sinus pain			

subjects affected / exposed	0 / 28 (0.00%)	1 / 20 (5.00%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Tachypnoea			
subjects affected / exposed	0 / 28 (0.00%)	1 / 20 (5.00%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Wheezing			
subjects affected / exposed	0 / 28 (0.00%)	1 / 20 (5.00%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Psychiatric disorders			
Agitation			
subjects affected / exposed	0 / 28 (0.00%)	1 / 20 (5.00%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Anxiety			
subjects affected / exposed	2 / 28 (7.14%)	1 / 20 (5.00%)	0 / 8 (0.00%)
occurrences (all)	2	1	0
Confusional state			
subjects affected / exposed	0 / 28 (0.00%)	1 / 20 (5.00%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Dysphemia			
subjects affected / exposed	0 / 28 (0.00%)	0 / 20 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	14 / 28 (50.00%)	8 / 20 (40.00%)	3 / 8 (37.50%)
occurrences (all)	40	20	3
Aspartate aminotransferase increased			
subjects affected / exposed	12 / 28 (42.86%)	9 / 20 (45.00%)	3 / 8 (37.50%)
occurrences (all)	40	15	3
Blood alkaline phosphatase increased			
subjects affected / exposed	3 / 28 (10.71%)	3 / 20 (15.00%)	2 / 8 (25.00%)
occurrences (all)	3	3	2
Blood alkaline phosphatase			
subjects affected / exposed	0 / 28 (0.00%)	0 / 20 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Blood lactate dehydrogenase increased			

subjects affected / exposed	0 / 28 (0.00%)	1 / 20 (5.00%)	0 / 8 (0.00%)
occurrences (all)	0	3	0
Blood magnesium decreased			
subjects affected / exposed	1 / 28 (3.57%)	0 / 20 (0.00%)	1 / 8 (12.50%)
occurrences (all)	1	0	1
Capillary nail refill test abnormal			
subjects affected / exposed	0 / 28 (0.00%)	1 / 20 (5.00%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Haemoglobin			
subjects affected / exposed	0 / 28 (0.00%)	0 / 20 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Inflammatory marker increased			
subjects affected / exposed	0 / 28 (0.00%)	1 / 20 (5.00%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
International normalised ratio increased			
subjects affected / exposed	0 / 28 (0.00%)	0 / 20 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Lymphocyte count decreased			
subjects affected / exposed	0 / 28 (0.00%)	1 / 20 (5.00%)	0 / 8 (0.00%)
occurrences (all)	0	4	0
Neutrophil count decreased			
subjects affected / exposed	3 / 28 (10.71%)	1 / 20 (5.00%)	0 / 8 (0.00%)
occurrences (all)	4	1	0
Platelet count decreased			
subjects affected / exposed	3 / 28 (10.71%)	2 / 20 (10.00%)	0 / 8 (0.00%)
occurrences (all)	3	2	0
Platelet count increased			
subjects affected / exposed	0 / 28 (0.00%)	0 / 20 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Transaminases increased			
subjects affected / exposed	0 / 28 (0.00%)	1 / 20 (5.00%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Weight decreased			
subjects affected / exposed	4 / 28 (14.29%)	1 / 20 (5.00%)	0 / 8 (0.00%)
occurrences (all)	6	1	0

Weight increased			
subjects affected / exposed	1 / 28 (3.57%)	1 / 20 (5.00%)	0 / 8 (0.00%)
occurrences (all)	1	1	0
White blood cell count decreased			
subjects affected / exposed	2 / 28 (7.14%)	0 / 20 (0.00%)	1 / 8 (12.50%)
occurrences (all)	2	0	1
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	1 / 28 (3.57%)	0 / 20 (0.00%)	1 / 8 (12.50%)
occurrences (all)	1	0	1
Fall			
subjects affected / exposed	0 / 28 (0.00%)	0 / 20 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Joint injury			
subjects affected / exposed	0 / 28 (0.00%)	0 / 20 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Laceration			
subjects affected / exposed	0 / 28 (0.00%)	1 / 20 (5.00%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Cardiac disorders			
Sinus tachycardia			
subjects affected / exposed	0 / 28 (0.00%)	0 / 20 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Tachycardia			
subjects affected / exposed	1 / 28 (3.57%)	1 / 20 (5.00%)	1 / 8 (12.50%)
occurrences (all)	1	1	1
Nervous system disorders			
Dizziness			
subjects affected / exposed	4 / 28 (14.29%)	3 / 20 (15.00%)	3 / 8 (37.50%)
occurrences (all)	10	3	3
Dysgeusia			
subjects affected / exposed	2 / 28 (7.14%)	1 / 20 (5.00%)	2 / 8 (25.00%)
occurrences (all)	2	2	4
Headache			
subjects affected / exposed	4 / 28 (14.29%)	2 / 20 (10.00%)	0 / 8 (0.00%)
occurrences (all)	4	2	0

Hemiparesis			
subjects affected / exposed	0 / 28 (0.00%)	1 / 20 (5.00%)	0 / 8 (0.00%)
occurrences (all)	0	2	0
Hypoaesthesia			
subjects affected / exposed	1 / 28 (3.57%)	1 / 20 (5.00%)	0 / 8 (0.00%)
occurrences (all)	1	1	0
Memory impairment			
subjects affected / exposed	0 / 28 (0.00%)	1 / 20 (5.00%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Neuropathy peripheral			
subjects affected / exposed	2 / 28 (7.14%)	0 / 20 (0.00%)	0 / 8 (0.00%)
occurrences (all)	2	0	0
Paraesthesia			
subjects affected / exposed	2 / 28 (7.14%)	0 / 20 (0.00%)	0 / 8 (0.00%)
occurrences (all)	2	0	0
Tremor			
subjects affected / exposed	0 / 28 (0.00%)	1 / 20 (5.00%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Insomnia			
subjects affected / exposed	2 / 28 (7.14%)	0 / 20 (0.00%)	0 / 8 (0.00%)
occurrences (all)	2	0	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	3 / 28 (10.71%)	1 / 20 (5.00%)	1 / 8 (12.50%)
occurrences (all)	10	1	1
Iron deficiency anaemia			
subjects affected / exposed	0 / 28 (0.00%)	0 / 20 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Leukocytosis			
subjects affected / exposed	1 / 28 (3.57%)	0 / 20 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Thrombocytopenia			
subjects affected / exposed	1 / 28 (3.57%)	0 / 20 (0.00%)	2 / 8 (25.00%)
occurrences (all)	1	0	2
Eye disorders			

Cataract			
subjects affected / exposed	0 / 28 (0.00%)	0 / 20 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Eye discharge			
subjects affected / exposed	0 / 28 (0.00%)	0 / 20 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Periorbital oedema			
subjects affected / exposed	0 / 28 (0.00%)	1 / 20 (5.00%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Vision blurred			
subjects affected / exposed	0 / 28 (0.00%)	0 / 20 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Visual impairment			
subjects affected / exposed	2 / 28 (7.14%)	0 / 20 (0.00%)	0 / 8 (0.00%)
occurrences (all)	2	0	0
Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	0 / 28 (0.00%)	1 / 20 (5.00%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Abdominal distension			
subjects affected / exposed	2 / 28 (7.14%)	1 / 20 (5.00%)	0 / 8 (0.00%)
occurrences (all)	2	1	0
Abdominal pain			
subjects affected / exposed	5 / 28 (17.86%)	2 / 20 (10.00%)	1 / 8 (12.50%)
occurrences (all)	6	2	2
Abdominal pain upper			
subjects affected / exposed	2 / 28 (7.14%)	1 / 20 (5.00%)	2 / 8 (25.00%)
occurrences (all)	2	1	2
Constipation			
subjects affected / exposed	4 / 28 (14.29%)	1 / 20 (5.00%)	2 / 8 (25.00%)
occurrences (all)	4	1	2
Diarrhoea			
subjects affected / exposed	22 / 28 (78.57%)	18 / 20 (90.00%)	7 / 8 (87.50%)
occurrences (all)	52	50	34
Dry mouth			

subjects affected / exposed	1 / 28 (3.57%)	0 / 20 (0.00%)	1 / 8 (12.50%)
occurrences (all)	1	0	1
Duodenal perforation			
subjects affected / exposed	0 / 28 (0.00%)	1 / 20 (5.00%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Dyspepsia			
subjects affected / exposed	1 / 28 (3.57%)	1 / 20 (5.00%)	1 / 8 (12.50%)
occurrences (all)	1	1	1
Dysphagia			
subjects affected / exposed	3 / 28 (10.71%)	1 / 20 (5.00%)	0 / 8 (0.00%)
occurrences (all)	3	1	0
Flatulence			
subjects affected / exposed	5 / 28 (17.86%)	1 / 20 (5.00%)	0 / 8 (0.00%)
occurrences (all)	6	1	0
Gastrooesophageal reflux disease			
subjects affected / exposed	3 / 28 (10.71%)	0 / 20 (0.00%)	0 / 8 (0.00%)
occurrences (all)	3	0	0
Haematochezia			
subjects affected / exposed	0 / 28 (0.00%)	0 / 20 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Nausea			
subjects affected / exposed	15 / 28 (53.57%)	9 / 20 (45.00%)	6 / 8 (75.00%)
occurrences (all)	17	12	14
Oesophagitis			
subjects affected / exposed	0 / 28 (0.00%)	0 / 20 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Rectal haemorrhage			
subjects affected / exposed	0 / 28 (0.00%)	1 / 20 (5.00%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Small intestinal obstruction			
subjects affected / exposed	0 / 28 (0.00%)	0 / 20 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Vomiting			
subjects affected / exposed	7 / 28 (25.00%)	8 / 20 (40.00%)	6 / 8 (75.00%)
occurrences (all)	11	11	17
Hepatobiliary disorders			

Bile duct obstruction			
subjects affected / exposed	0 / 28 (0.00%)	1 / 20 (5.00%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Hepatic failure			
subjects affected / exposed	0 / 28 (0.00%)	0 / 20 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Perforation bile duct			
subjects affected / exposed	0 / 28 (0.00%)	1 / 20 (5.00%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	3 / 28 (10.71%)	0 / 20 (0.00%)	0 / 8 (0.00%)
occurrences (all)	3	0	0
Decubitus ulcer			
subjects affected / exposed	1 / 28 (3.57%)	0 / 20 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Dry skin			
subjects affected / exposed	0 / 28 (0.00%)	0 / 20 (0.00%)	2 / 8 (25.00%)
occurrences (all)	0	0	2
Pruritus			
subjects affected / exposed	1 / 28 (3.57%)	0 / 20 (0.00%)	1 / 8 (12.50%)
occurrences (all)	1	0	1
Pruritus generalised			
subjects affected / exposed	0 / 28 (0.00%)	0 / 20 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Rash			
subjects affected / exposed	4 / 28 (14.29%)	3 / 20 (15.00%)	0 / 8 (0.00%)
occurrences (all)	6	3	0
Rash erythematous			
subjects affected / exposed	1 / 28 (3.57%)	0 / 20 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Rash generalised			
subjects affected / exposed	0 / 28 (0.00%)	1 / 20 (5.00%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Rash maculo-papular			

subjects affected / exposed	0 / 28 (0.00%)	1 / 20 (5.00%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Renal and urinary disorders			
Dysuria			
subjects affected / exposed	1 / 28 (3.57%)	1 / 20 (5.00%)	0 / 8 (0.00%)
occurrences (all)	1	1	0
Haematuria			
subjects affected / exposed	1 / 28 (3.57%)	1 / 20 (5.00%)	0 / 8 (0.00%)
occurrences (all)	1	1	0
Oliguria			
subjects affected / exposed	0 / 28 (0.00%)	1 / 20 (5.00%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Urinary hesitation			
subjects affected / exposed	0 / 28 (0.00%)	1 / 20 (5.00%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Urinary tract disorder			
subjects affected / exposed	0 / 28 (0.00%)	1 / 20 (5.00%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 28 (3.57%)	1 / 20 (5.00%)	1 / 8 (12.50%)
occurrences (all)	1	1	1
Back pain			
subjects affected / exposed	3 / 28 (10.71%)	2 / 20 (10.00%)	2 / 8 (25.00%)
occurrences (all)	3	2	3
Bone pain			
subjects affected / exposed	0 / 28 (0.00%)	0 / 20 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Flank pain			
subjects affected / exposed	2 / 28 (7.14%)	2 / 20 (10.00%)	0 / 8 (0.00%)
occurrences (all)	2	2	0
Joint swelling			
subjects affected / exposed	2 / 28 (7.14%)	0 / 20 (0.00%)	0 / 8 (0.00%)
occurrences (all)	2	0	0
Muscle spasms			

subjects affected / exposed	4 / 28 (14.29%)	5 / 20 (25.00%)	0 / 8 (0.00%)
occurrences (all)	8	6	0
Muscular weakness			
subjects affected / exposed	0 / 28 (0.00%)	1 / 20 (5.00%)	2 / 8 (25.00%)
occurrences (all)	0	1	2
Musculoskeletal pain			
subjects affected / exposed	2 / 28 (7.14%)	0 / 20 (0.00%)	1 / 8 (12.50%)
occurrences (all)	2	0	1
Neck pain			
subjects affected / exposed	0 / 28 (0.00%)	0 / 20 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Pain in extremity			
subjects affected / exposed	1 / 28 (3.57%)	1 / 20 (5.00%)	2 / 8 (25.00%)
occurrences (all)	1	2	2
Pain in jaw			
subjects affected / exposed	1 / 28 (3.57%)	1 / 20 (5.00%)	0 / 8 (0.00%)
occurrences (all)	1	1	0
Infections and infestations			
Aspergillus infection			
subjects affected / exposed	0 / 28 (0.00%)	0 / 20 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Bronchitis			
subjects affected / exposed	0 / 28 (0.00%)	0 / 20 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Clostridium difficile infection			
subjects affected / exposed	0 / 28 (0.00%)	1 / 20 (5.00%)	0 / 8 (0.00%)
occurrences (all)	0	2	0
Conjunctivitis			
subjects affected / exposed	0 / 28 (0.00%)	0 / 20 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Diverticulitis			
subjects affected / exposed	0 / 28 (0.00%)	0 / 20 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Influenza			
subjects affected / exposed	0 / 28 (0.00%)	1 / 20 (5.00%)	0 / 8 (0.00%)
occurrences (all)	0	1	0

Lower respiratory tract infection			
subjects affected / exposed	0 / 28 (0.00%)	0 / 20 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	3
Lung infection			
subjects affected / exposed	1 / 28 (3.57%)	1 / 20 (5.00%)	0 / 8 (0.00%)
occurrences (all)	1	1	0
Mucosal infection			
subjects affected / exposed	0 / 28 (0.00%)	1 / 20 (5.00%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Oral candidiasis			
subjects affected / exposed	1 / 28 (3.57%)	1 / 20 (5.00%)	0 / 8 (0.00%)
occurrences (all)	1	1	0
Pneumonia			
subjects affected / exposed	3 / 28 (10.71%)	1 / 20 (5.00%)	0 / 8 (0.00%)
occurrences (all)	4	7	0
Respiratory tract infection			
subjects affected / exposed	0 / 28 (0.00%)	0 / 20 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Sinusitis			
subjects affected / exposed	0 / 28 (0.00%)	1 / 20 (5.00%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Urinary tract infection			
subjects affected / exposed	2 / 28 (7.14%)	0 / 20 (0.00%)	0 / 8 (0.00%)
occurrences (all)	3	0	0
Spinal column injury			
subjects affected / exposed	0 / 28 (0.00%)	0 / 20 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	12 / 28 (42.86%)	6 / 20 (30.00%)	3 / 8 (37.50%)
occurrences (all)	13	8	7
Dehydration			
subjects affected / exposed	6 / 28 (21.43%)	2 / 20 (10.00%)	0 / 8 (0.00%)
occurrences (all)	8	5	0
Hyperglycaemia			

subjects affected / exposed	0 / 28 (0.00%)	2 / 20 (10.00%)	0 / 8 (0.00%)
occurrences (all)	0	4	0
Hyperkalaemia			
subjects affected / exposed	2 / 28 (7.14%)	0 / 20 (0.00%)	0 / 8 (0.00%)
occurrences (all)	2	0	0
Hypernatraemia			
subjects affected / exposed	0 / 28 (0.00%)	1 / 20 (5.00%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Hypoalbuminaemia			
subjects affected / exposed	4 / 28 (14.29%)	2 / 20 (10.00%)	1 / 8 (12.50%)
occurrences (all)	8	4	1
Hypocalcaemia			
subjects affected / exposed	3 / 28 (10.71%)	1 / 20 (5.00%)	1 / 8 (12.50%)
occurrences (all)	3	3	1
Hypochloraemia			
subjects affected / exposed	0 / 28 (0.00%)	1 / 20 (5.00%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Hypokalaemia			
subjects affected / exposed	5 / 28 (17.86%)	5 / 20 (25.00%)	1 / 8 (12.50%)
occurrences (all)	5	7	1
Hypomagnesaemia			
subjects affected / exposed	9 / 28 (32.14%)	4 / 20 (20.00%)	2 / 8 (25.00%)
occurrences (all)	14	7	2
Hyponatraemia			
subjects affected / exposed	2 / 28 (7.14%)	0 / 20 (0.00%)	0 / 8 (0.00%)
occurrences (all)	4	0	0
Hypophosphataemia			
subjects affected / exposed	5 / 28 (17.86%)	2 / 20 (10.00%)	0 / 8 (0.00%)
occurrences (all)	8	3	0

Non-serious adverse events	MET Gene Amplifications in ctDNA		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	12 / 12 (100.00%)		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			

Cancer pain			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	2		
Tumour pain			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Embolism			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Haemorrhage			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Hot flush			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Hypertension			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Hypotension			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Superior vena cava syndrome			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Thrombosis			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Catheter site pain			

subjects affected / exposed	0 / 12 (0.00%)			
occurrences (all)	0			
Chest discomfort				
subjects affected / exposed	0 / 12 (0.00%)			
occurrences (all)	0			
Chest pain				
subjects affected / exposed	1 / 12 (8.33%)			
occurrences (all)	1			
Face oedema				
subjects affected / exposed	0 / 12 (0.00%)			
occurrences (all)	0			
Fatigue				
subjects affected / exposed	7 / 12 (58.33%)			
occurrences (all)	11			
General physical health deterioration				
subjects affected / exposed	0 / 12 (0.00%)			
occurrences (all)	0			
Malaise				
subjects affected / exposed	0 / 12 (0.00%)			
occurrences (all)	0			
Non-cardiac chest pain				
subjects affected / exposed	1 / 12 (8.33%)			
occurrences (all)	1			
Oedema				
subjects affected / exposed	0 / 12 (0.00%)			
occurrences (all)	0			
Oedema peripheral				
subjects affected / exposed	0 / 12 (0.00%)			
occurrences (all)	0			
Pain				
subjects affected / exposed	0 / 12 (0.00%)			
occurrences (all)	0			
Peripheral swelling				
subjects affected / exposed	1 / 12 (8.33%)			
occurrences (all)	1			
Pyrexia				

subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Reproductive system and breast disorders			
Vaginal haemorrhage			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Dysphonia			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Dyspnoea			
subjects affected / exposed	4 / 12 (33.33%)		
occurrences (all)	5		
Dyspnoea exertional			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	3		
Haemoptysis			
subjects affected / exposed	3 / 12 (25.00%)		
occurrences (all)	3		
Hypoxia			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Nasal congestion			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Oropharyngeal pain			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Pharyngeal erythema			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Pleural effusion			

subjects affected / exposed	2 / 12 (16.67%)			
occurrences (all)	3			
Pneumonia aspiration				
subjects affected / exposed	0 / 12 (0.00%)			
occurrences (all)	0			
Pneumothorax				
subjects affected / exposed	0 / 12 (0.00%)			
occurrences (all)	0			
Productive cough				
subjects affected / exposed	0 / 12 (0.00%)			
occurrences (all)	0			
Pulmonary congestion				
subjects affected / exposed	0 / 12 (0.00%)			
occurrences (all)	0			
Pulmonary embolism				
subjects affected / exposed	1 / 12 (8.33%)			
occurrences (all)	1			
Pulmonary oedema				
subjects affected / exposed	1 / 12 (8.33%)			
occurrences (all)	1			
Rales				
subjects affected / exposed	0 / 12 (0.00%)			
occurrences (all)	0			
Respiratory failure				
subjects affected / exposed	1 / 12 (8.33%)			
occurrences (all)	1			
Rhinorrhoea				
subjects affected / exposed	0 / 12 (0.00%)			
occurrences (all)	0			
Sinus pain				
subjects affected / exposed	0 / 12 (0.00%)			
occurrences (all)	0			
Tachypnoea				
subjects affected / exposed	0 / 12 (0.00%)			
occurrences (all)	0			
Wheezing				

subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Psychiatric disorders			
Agitation			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Anxiety			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Confusional state			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Dysphemia			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	5 / 12 (41.67%)		
occurrences (all)	5		
Aspartate aminotransferase increased			
subjects affected / exposed	4 / 12 (33.33%)		
occurrences (all)	13		
Blood alkaline phosphatase increased			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Blood alkaline phosphatase			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Blood lactate dehydrogenase increased			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Blood magnesium decreased			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Capillary nail refill test abnormal			

subjects affected / exposed	0 / 12 (0.00%)			
occurrences (all)	0			
Haemoglobin				
subjects affected / exposed	1 / 12 (8.33%)			
occurrences (all)	1			
Inflammatory marker increased				
subjects affected / exposed	0 / 12 (0.00%)			
occurrences (all)	0			
International normalised ratio increased				
subjects affected / exposed	1 / 12 (8.33%)			
occurrences (all)	1			
Lymphocyte count decreased				
subjects affected / exposed	0 / 12 (0.00%)			
occurrences (all)	0			
Neutrophil count decreased				
subjects affected / exposed	0 / 12 (0.00%)			
occurrences (all)	0			
Platelet count decreased				
subjects affected / exposed	1 / 12 (8.33%)			
occurrences (all)	2			
Platelet count increased				
subjects affected / exposed	0 / 12 (0.00%)			
occurrences (all)	0			
Transaminases increased				
subjects affected / exposed	1 / 12 (8.33%)			
occurrences (all)	1			
Weight decreased				
subjects affected / exposed	0 / 12 (0.00%)			
occurrences (all)	0			
Weight increased				
subjects affected / exposed	0 / 12 (0.00%)			
occurrences (all)	0			
White blood cell count decreased				
subjects affected / exposed	0 / 12 (0.00%)			
occurrences (all)	0			

Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Fall			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Joint injury			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Laceration			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Cardiac disorders			
Sinus tachycardia			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Tachycardia			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Nervous system disorders			
Dizziness			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Dysgeusia			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Headache			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Hemiparesis			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Hypoaesthesia			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		

Memory impairment			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Neuropathy peripheral			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Paraesthesia			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Tremor			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Insomnia			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	3		
Iron deficiency anaemia			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Leukocytosis			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Thrombocytopenia			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Eye disorders			
Cataract			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Eye discharge			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Periorbital oedema			

subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Vision blurred			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Visual impairment			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Abdominal distension			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Abdominal pain			
subjects affected / exposed	4 / 12 (33.33%)		
occurrences (all)	4		
Abdominal pain upper			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Constipation			
subjects affected / exposed	3 / 12 (25.00%)		
occurrences (all)	4		
Diarrhoea			
subjects affected / exposed	10 / 12 (83.33%)		
occurrences (all)	20		
Dry mouth			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Duodenal perforation			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Dyspepsia			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		

Dysphagia			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Flatulence			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Haematochezia			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Nausea			
subjects affected / exposed	6 / 12 (50.00%)		
occurrences (all)	12		
Oesophagitis			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Rectal haemorrhage			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Small intestinal obstruction			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Vomiting			
subjects affected / exposed	6 / 12 (50.00%)		
occurrences (all)	33		
Hepatobiliary disorders			
Bile duct obstruction			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Hepatic failure			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Perforation bile duct			

subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Decubitus ulcer			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Dry skin			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Pruritus			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Pruritus generalised			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Rash			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Rash erythematous			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Rash generalised			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Rash maculo-papular			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Renal and urinary disorders			
Dysuria			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Haematuria			

subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Oliguria			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Urinary hesitation			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Urinary tract disorder			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Back pain			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Bone pain			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Flank pain			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Joint swelling			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Muscle spasms			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Muscular weakness			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Musculoskeletal pain			

subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Neck pain			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Pain in extremity			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Pain in jaw			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Infections and infestations			
Aspergillus infection			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Bronchitis			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Clostridium difficile infection			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Conjunctivitis			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Diverticulitis			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Influenza			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Lower respiratory tract infection			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Lung infection			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		

Mucosal infection subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0		
Oral candidiasis subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0		
Pneumonia subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0		
Respiratory tract infection subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1		
Sinusitis subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0		
Urinary tract infection subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0		
Spinal column injury subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0		
Metabolism and nutrition disorders Decreased appetite subjects affected / exposed occurrences (all)	4 / 12 (33.33%) 4		
Dehydration subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 4		
Hyperglycaemia subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0		
Hyperkalaemia subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0		
Hypernatraemia			

subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Hypoalbuminaemia			
subjects affected / exposed	3 / 12 (25.00%)		
occurrences (all)	3		
Hypocalcaemia			
subjects affected / exposed	2 / 12 (16.67%)		
occurrences (all)	3		
Hypochloraemia			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Hypokalaemia			
subjects affected / exposed	2 / 12 (16.67%)		
occurrences (all)	2		
Hypomagnesaemia			
subjects affected / exposed	2 / 12 (16.67%)		
occurrences (all)	3		
Hyponatraemia			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Hypophosphataemia			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
17 May 2016	Updates made to the following sections: - Background information - Study population/patient eligibility - Study objective - Region or country specific requirements - Assessments - Study treatments - Concomitant Medications - Safety Reporting - Study Analysis
23 March 2017	Updates made to the following sections: - Study summary - Schedule of Assessments - Schedule for PK, Triplicate ECG, and PD Assessments - Introduction and Rationale - Clinical Data - Study Design - Inclusion Criteria - Study Treatment - Reporting of SAEs and AEs - References

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported