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Clinical Trial Results Website

Sponsor
Novartis Pharmaceuticals

Generic Drug Name
Capmatinib

Trial Indication(s)
Non-small cell lung cancer (NSCLC)

Protocol Number
CINC280A2201

Protocol Title
A phase II, multicenter study of oral MET inhibitor INC280 in adult patients with EGFR wild-type (wt), advanced non-small cell lung cancer (NSCLC) (Geometry mono-1)

Clinical Trial Phase
Phase 2

Phase of Drug Development
Phase IV

Study Start/End Dates
Study Start Date: June 11, 2015 (Actual)
Primary Completion Date: April 12, 2023 (Actual)
Study Completion Date: May 16, 2023 (Actual)

Reason for Termination (If applicable)

Not applicable

Study Design/Methodology

This was a Phase II, multicenter, open-label study that aimed to evaluate the efficacy and safety of capmatinib as a single-agent treatment for subjects with advanced/metastatic (stage IIIB or IV) non-small cell lung cancer (NSCLC) who had wild-type epidermal growth factor receptor (EGFR wt) (for exon 19 deletions and exon 21 L858R substitution mutations), anaplastic lymphoma kinase (ALK)-negative rearrangement, and mesenchymal epithelial transition (MET) mutations leading to exon 14 deletion (referred to as MET mutation hereafter) and/or MET amplification.

Patients were enrolled in different cohorts based on their MET status (amplification and/or mutation) and prior treatment status: Cohort 1a, Cohort 1b, Cohort 2, Cohort 3, Cohort 4, Cohort 5a, Cohort 5b, Cohort 6, and Cohort 7. MET mutation (by RT-PCR) and/or MET amplification status by gene copy number (GCN, by FISH) was determined by central laboratory.

Patients in Cohorts 1, 2, 3, and 4 had previously failed 1 or 2 prior lines of systemic therapy, while patients enrolled in Cohorts 5 and 7 were treatment-naïve for advanced disease/metastatic disease. Patients enrolled in Cohort 6 had failed 1 prior line of systemic therapy for advanced/ metastatic disease.

Patients with MET mutation were enrolled in Cohort 4 (pre-treated), Cohort 5b (treatment naïve) or Cohort 7 (treatment naïve expansion cohort of Cohort 5b), irrespective of their MET GCN. The enrollment in expansion Cohort 7 started after the completion of enrollment in Cohort 5b.

Patients without MET mutation, were enrolled in Cohorts 1a, 1b, 2, 3 (pre-treated) or 5a (treatment naïve), based on their MET GCN. Patients enrolled in Cohort 6 (expansion cohort of Cohort 1a and Cohort 4) had either MET GCN ≥10 without MET mutation (Cohort 6.1) or MET mutation, irrespective to their MET GCN (Cohort 6.2). The enrollment in Cohort 6 started upon enrollment completion of the respective Cohort 1a or Cohort 4.

Cohort	MET amplification (GCN)	MET-mutation status
Prior treatment status: pretreated (2nd/3rd line)		
Cohort 1a	≥ 10	Negative
Cohort 1b	≥ 6 and < 10	Negative
Cohort 2	≥ 4 and < 6	Negative
Cohort 3	< 4	Negative
Cohort 4	Any GCN	Positive
Prior treatment status: pretreated (2nd line)		
Cohort 6.1 (Cohort 1a expansion)	≥ 10	Negative
Cohort 6.2 (Cohort 4 expansion)	Any GCN	Positive
Prior treatment status: treatment-naive (1st line)		
Cohort 5a	≥ 10	Negative
Cohort 5b	Any GCN	Positive
Cohort 7 (Cohort 5b expansion)	Any GCN	Positive

All participants in the study received oral capmatinib 400 mg twice daily. A treatment cycle was defined as 21 days. Treatment with capmatinib continued until patient experienced any of the following: disease progression according to RECIST 1.1 as determined by investigator and confirmed by Blinded Independent Review Committee (BIRC), unacceptable toxicity that precluded further treatment, treatment discontinuation at the discretion of the Investigator or patient, lost to follow-up, or death. Treatment with capmatinib was allowed beyond RECIST 1.1-defined disease progression (as determined by investigator and confirmed by BIRC) if, in the judgment of the investigator, there was evidence of clinical benefit and the patient wished to continue on the study treatment.

All patients continued to have safety evaluations for 30 days after the last dose of study treatment.

Patients who discontinued treatment with capmatinib for any reason other than disease progression, as determined by the investigator and confirmed by BIRC, death, withdrawal of consent for further assessments, or being lost to follow-up, continued to have tumor assessments (post-treatment efficacy follow-up) until disease progression confirmed by BIRC, death, withdrawal of consent for further assessments, or lost to follow-up.

All patients who discontinued treatment with capmatinib were followed for survival (post-treatment survival follow-up) until death, loss to follow-up, withdrawal of consent to survival follow-up, or the end of the study.

Centers

95 centers in 20 countries: Norway(1), Spain(7), Lebanon(1), Netherlands(4), Austria(1), Russia(3), Singapore(2), France(10), Korea, Republic of(3), Japan(10), Israel(2), Germany(14), Italy(13), United States(13), Argentina(3), Belgium(1), Taiwan(3), United Kingdom(2), Sweden(1), Mexico(1)

Objectives

The primary objective of the study was to evaluate the antitumor activity of capmatinib, as measured by overall response rate (ORR) by Blinded Independent Review Committee (BIRC) assessment.

Key secondary objective was to evaluate duration of response (DOR) as assessed by BIRC.

Other secondary objectives were:

- To evaluate ORR and DOR by investigator assessment
- To evaluate time to response (TTR), disease control rate (DCR) and progression-free survival (PFS) by investigator and by BIRC assessment
- To evaluate overall survival (OS)
- To evaluate capmatinib safety profile as monotherapy in NSCLC subjects with advanced/metastatic disease
- To characterize the pharmacokinetics of capmatinib and metabolite CMN288.

Test Product (s), Dose(s), and Mode(s) of Administration

Capmatinib was administered orally, at a dose of 400 mg on a continuous twice daily dosing schedule.

Statistical Methods

The primary variable used to evaluate the antitumor activity of capmatinib was ORR, defined as the percentage of subjects with a confirmed best overall response (BOR) of complete response (CR) or partial response (PR), as assessed per RECIST 1.1 by BIRC. The primary analysis was performed on the Full Analysis Set (FAS). The primary efficacy endpoint ORR and the exact 95% confidence interval (CI) were assessed.

All secondary endpoint analyses were performed based on the FAS, unless otherwise specified. No adjustments for multiple testing were made.

Among subjects with a confirmed response (CR or PR), DOR was defined as the time from first documented response (CR or PR) to the date of first documented progressive disease or death due to any cause. If a subject did not have an event, DOR was censored at the date of last adequate tumor assessment. DOR was estimated using Kaplan-Meier (KM) methodology.

The distribution of other endpoints such as TTR, OS, PFS were also estimated using KM methodology and medians along with, 95% CIs provided.

Safety analyses were performed based on the Safety Set. Toxicity was assessed according to the National Cancer Institute Common Terminology Criteria for Adverse Events (NCI-CTCAE) version 4.03. All AEs were coded using Medical Dictionary of Regulatory Activities (MedDRA), Version 26.0, to ensure consistency.

Study Population: Key Inclusion/Exclusion Criteria

Key Inclusion Criteria:
- Subjects with Stage IIIB or IV NSCLC (any histology) at the time of study entry
- Subjects with histologically or cytologically confirmed diagnosis of NSCLC that is:
a. EGFR wt status (for exon 19 deletions and exon 21 L858R substitution mutations)
b. and ALK rearrangement-negative
c. and MET-mutation and/or amplification status (as defined in the protocol).
- For Cohorts 1a, 1b, 2, 3, 4 subjects must have failed one or two prior lines of systemic therapy for advanced disease (stage IIIB or IV NSCLC). For Cohort 6, subjects must have failed one prior line of systemic therapy for advanced disease (stage IIIB or IV NSCLC).
- For Cohorts 5a, 5b, and 7, subjects must not have received any systemic therapy for advanced disease (stage IIIB or IV NSCLC).
- Subjects with at least one measurable lesion as defined by RECIST 1.1. A previously irradiated site lesion may only be counted as a target lesion if there was clear sign of progression since the irradiation.
- Subjects who recovered from all toxicities related to prior anticancer therapies to grade ≤ 1 (Common Terminology Criteria for Adverse Events [CTCAE] v 4.03). Subjects with any grade of alopecia were allowed to enter the study.
- Subjects with adequate organ function
- Eastern Cooperative Oncology Group (ECOG) performance status (PS) of 0 or 1

Key Exclusion Criteria:
- Prior treatment with crizotinib, or any other MET or HGF inhibitor
- Characterized EGFR mutations that predict sensitivity to EGFR therapy, including, but not limited to exon 19 deletions and exon 21 mutations.
- Characterized ALK-positive rearrangement.

- Symptomatic central nervous system (CNS) metastases who are neurologically unstable or have required increasing doses of steroids within the 2 weeks prior to study entry to manage CNS symptoms.
- Clinically significant, uncontrolled heart diseases
- Thoracic radiotherapy to lung fields ≤ 4 weeks prior to starting capmatinib or subjects who had not recovered from radiotherapy-related toxicities. For all other anatomic sites (including radiotherapy to thoracic vertebrae and ribs), radiotherapy ≤ 2 weeks prior to starting capmatinib or subjects who had not recovered from radiotherapy-related toxicities.
Palliative radiotherapy for bone lesions ≤ 2 weeks prior to starting capmatinib was allowed.
- Receiving treatment with strong inducers of CYP3A4 and/or any enzyme-inducing anticonvulsant and could not be discontinued ≥ 1 week prior to the start of treatment with capmatinib and for the duration of the study.
- Receiving treatment with unstable or increasing doses of corticosteroids.
- Impairment of gastrointestinal (GI) function or GI disease that may significantly alter the absorption of capmatinib.
- Applicable to Cohorts 1-4 and Cohort 6 only: previous anticancer and investigational agents within 4 weeks or ≤ 5 × half-life of the agent (whichever was longer) before first dose of- capmatinib. If previous treatment was a monoclonal antibody, then the treatment must have been discontinued ≥ 4 weeks before first dose of capmatinib. If previous treatment was an oral targeted agent, then the treatment must have been discontinued ≥ 5 × half-life of the agent before the first dose of capmatinib.
- Pregnant or nursing (lactating) women.
- Women of child-bearing potential, unless they are using highly effective methods of contraception during dosing and for 7 days after stopping treatment
- Sexually active males unless they used a condom during intercourse while taking drug and for 7 days after stopping treatment and should not father a child in this period.
- Presence or history of interstitial lung disease or interstitial pneumonitis, including clinically significant radiation pneumonitis (i.e., affecting activities of daily living or requiring therapeutic intervention).

Participant Flow Table

Treatment period

	Cohort 1a: Pre-treated patients with MET GCN ≥ 10 (2/3L)	Cohort 1b:Pre-treated patients with MET GCN ≥ 6 and < 10 (2/3L)	Cohort 2: Pre-treated patients with MET GCN ≥ 4 and < 6 (2/3L)	Cohort 3: Pre-treated patients with MET GCN < 4 (2/3L)	Cohort 4: Pre-treated patients with MET mutation regardless of MET GCN (2/3L)	Cohort 5a: Treatment-naïve patients with MET GCN ≥10 (1L)	Cohort 5b: Treatment-naïve patients with MET mutation regardless of MET GCN (1L)	Cohort 6.1 (expansion of Cohort 1a): Pre-treated patients MET GCN ≥ 10 without MET mutation (2L)	Cohort 6.2 (expansion of Cohort 4): Pre-treated patients with MET mutation (2L)	Cohort 7 (expansion of Cohort 5b): Treatment-naïve with MET mutation regardless	Total

Arm/Group Description	Pre-treated patients with MET GCN ≥ 10 treated with INC280 at 400mg BID as second or third line (2/3L)	Pre-treated patients with MET GCN ≥ 6 and < 10 treated with INC280 at 400 mg BID as second or third line (2/3L)	Pre-treated patients with MET GCN ≥ 4 and < 6 treated with INC280 at 400mg BID as second or third line (2/3L)	Pre-treated patients with MET GCN < 4 treated with INC280 at 400mg BID as second or third line (2/3L)	Pre-treated patients with MET mutation regardless of MET GCN treated with INC280 at 400mg BID as second or third line (2/3L)	Treatment-naïve patients with MET GCN ≥10 treated with INC280 at 400mg BID as first-line (1L)	Treatment-naïve patients with MET mutation regardless of MET GCN treated with INC280 at 400mg BID as first line (1L)	Pre-treated patients with MET GCN ≥ 10 without MET mutation treated with INC280 at 400 mg BID as second line (2L) (expansion cohort of Cohort 1a)	Pre-treated patients with MET mutation regardless of MET GCN treated with INC280 at 400 mg BID as second line (2L)(expansion of Cohort 4)	Treatment-naïve patients with MET mutation regardless of MET GCN treated with INC280 at 400mg BID as first line (1L) (expansion cohort of Cohort 5b)	
Started	69	42	54	30	69	15	28	3	31	32	373
Completed	0	0	0	0	0	0	0	0	0	0	0
Not Completed	69	42	54	30	69	15	28	3	31	32	373
Adverse Event	11	6	8	5	14	3	6	1	6	8	68
Death	0	0	1	1	0	0	0	0	0	1	3
Physician Decision	5	4	6	1	4	0	2	0	1	4	27
Progressive disease	48	31	37	21	43	12	16	2	20	14	244
Protocol deviation	0	0	1	0	0	0	0	0	0	0	1
Subject/Guardian decision	5	1	1	2	5	0	2	0	1	1	18
Study terminated (as per protocol) by Sponsor	0	0	0	0	3	0	2	0	3	4	12

Post-treatment efficacy follow-up

	Cohort 1a: Pre-treated patients with MET	Cohort 1b:Pre-treated patients	Cohort 2: Pre-treated patients with MET	Cohort 3: Pre-treated patients with MET	Cohort 4: Pre-treated patients with MET	Cohort 5a: Treatment-naïve patients with	Cohort 5b: Treatment-naïve patients with	Cohort 6.1 (expansion of Cohort 1a): Pre-	Cohort 6.2 (expansion of Cohort 4): Pre-treated	Cohort 7 (expansion of Cohort 5b):	Total

	GCN ≥ 10 (2/3L)	with MET GCN ≥ 6 and < 10 (2/3L)	GCN ≥ 4 and < 6 (2/3L)	GCN < 4 (2/3L)	mutation regardless of MET GCN (2/3L)	MET GCN ≥10 (1L)	MET mutation regardless of MET GCN (1L)	treated patients MET GCN ≥ 10 without MET mutation (2L)	patients with MET mutation (2L)	Treatment-naïve with MET mutation regardless of MET GCN (1L)	
Arm/Group Description	Pre-treated patients with MET GCN ≥ 10 treated with INC280 at 400mg BID as second or third line (2/3L)	Pre-treated patients with MET GCN ≥ 6 and < 10 treated with INC280 at 400 mg BID as second or third line (2/3L)	Pre-treated patients with MET GCN ≥ 4 and < 6 treated with INC280 at 400mg BID as second or third line (2/3L)	Pre-treated patients with MET GCN < 4 treated with INC280 at 400mg BID as second or third line (2/3L)	Pre-treated patients with MET mutation regardless of MET GCN treated with INC280 at 400mg BID as second or third line (2/3L)	Treatment-naïve patients with MET GCN ≥10 treated with INC280 at 400mg BID as first-line (1L)	Treatment-naïve patients with MET mutation regardless of MET GCN treated with INC280 at 400mg BID as first line (1L)	Pre-treated patients with MET GCN ≥ 10 without MET mutation treated with INC280 at 400 mg BID as second line (2L) (expansion cohort of Cohort 1a)	Pre-treated patients with MET mutation regardless of MET GCN treated with INC280 at 400 mg BID as second line (2L)(expansion of Cohort 4)	Treatment-naïve patients with MET mutation regardless of MET GCN treated with INC280 at 400mg BID as first line (1L) (expansion cohort of Cohort 5b)	
Started	16	11	16	8	23	5	6	1	3	8	97
Completed	0	0	0	0	0	0	0	0	0	0	0
Not Completed	16	11	16	8	23	5	6	1	3	8	97
Adverse Event	1	0	0	0	2	0	0	0	0	0	3
Death	0	1	0	0	1	0	0	0	0	1	3
Lost to Follow-up	1	0	0	0	0	0	0	0	0	0	1
Physician Decision	4	2	4	2	4	0	1	0	0	1	18
Progressive disease	6	5	9	5	15	4	5	1	3	3	56
Study terminated by sponsor	0	1	0	0	0	0	0	0	0	1	2
Subject/guardian decision	4	2	3	1	1	1	0	0	0	2	14

Baseline Characteristics

	Cohort 1a: Pre-treated patients with MET GCN ≥ 10 (2/3L)	Cohort 1b:Pre-treated patients with MET GCN ≥ 6 and < 10 (2/3L)	Cohort 2: Pre-treated patients with MET GCN ≥ 4 and < 6 (2/3L)	Cohort 3: Pre-treated patients with MET GCN < 4 (2/3L)	Cohort 4: Pre-treated patients with MET mutation regardless of MET GCN (2/3L)	Cohort 5a: Treatment-naïve patients with MET GCN ≥10 (1L)	Cohort 5b: Treatment-naïve patients with MET mutation regardless of MET GCN (1L)	Cohort 6.1 (expansion of Cohort 1a): Pre-treated patients MET GCN ≥ 10 without MET mutation (2L)	Cohort 6.2 (expansion of Cohort 4): Pre-treated patients with MET mutation (2L)	Cohort 7 (expansion of Cohort 5b): Treatment-naïve with MET mutation regardless of MET GCN (1L)	Total
Arm/Group Description	Pre-treated patients with MET GCN ≥ 10 treated with INC280 at 400mg BID as second or third line (2/3L)	Pre-treated patients with MET GCN ≥ 6 and < 10 treated with INC280 at 400 mg BID as second or third line (2/3L)	Pre-treated patients with MET GCN ≥ 4 and < 6 treated with INC280 at 400mg BID as second or third line (2/3L)	Pre-treated patients with MET GCN < 4 treated with INC280 at 400mg BID as second or third line (2/3L)	Pre-treated patients with MET mutation regardless of MET GCN treated with INC280 at 400mg BID as second or third line (2/3L)	Treatment-naïve patients with MET GCN ≥10 treated with INC280 at 400mg BID as first-line (1L)	Treatment-naïve patients with MET mutation regardless of MET GCN treated with INC280 at 400mg BID as first line (1L)	Pre-treated patients with MET GCN ≥ 10 without MET mutation treated with INC280 at 400 mg BID as second line (2L) (expansion cohort of Cohort 1a)	Pre-treated patients with MET mutation regardless of MET GCN treated with INC280 at 400 mg BID as second line (2L)(expansion of Cohort 4)	Treatment-naïve patients with MET mutation regardless of MET GCN treated with INC280 at 400mg BID as first line (1L) (expansion cohort of Cohort 5b)	
Number of Participants [units: participants]	69	42	54	30	69	15	28	3	31	32	373
Baseline Analysis Population Description											
Age Continuous (units: Years) Analysis Population Type: Participants Mean ± Standard Deviation											
	60.9±9.56	59.5±9.11	61.7±10.00	61.7±9.23	71.0±8.32	68.2±10.36	72.4±7.02	60.7±10.69	69.0±6.29	73.3±8.35	65.7±10.18
Sex: Female, Male (units: Participants) Analysis Population Type: Participants Count of Participants (Not Applicable)											

Female	15	21	15	11	40	4	18	1	16	23	164
Male	54	21	39	19	29	11	10	2	15	9	209
Race/Ethnicity, Customized (units: Participants) Analysis Population Type: Participants Count of Participants (Not Applicable)											
Asian	17	4	14	11	19	6	4	1	5	3	84
Black	1	0	0	0	0	0	0	0	1	1	3
Caucasian	51	38	40	19	49	9	24	1	24	26	281
Native American	0	0	0	0	1	0	0	0	1	0	2
Unknown	0	0	0	0	0	0	0	1	0	0	1
Other	0	0	0	0	0	0	0	0	0	2	2

Primary Outcome Result(s)

Overall Response Rate (ORR) by Blinded Independent Review Committee (BIRC) assessment

Description	Percentage of participants with a best overall response defined as confirmed complete response (CR) or partial response (PR) by BIRC assessment per RECIST 1.1. CR: Disappearance of all non-nodal target and non-target lesions. In addition, any pathological lymph nodes assigned as target and non-target lesions must have a reduction in short axis to < 10 mm PR: At least a 30% decrease in the sum of diameter of all target lesions, taking as reference the baseline sum of diameters.
Time Frame	Up to approximately 5 years
Analysis Population Description	Full Analysis Set (FAS)-including all subjects who received at least one dose of capmatinib

	Cohort 1a: Pre-treated patients with MET	Cohort 1b: Pre-treated patients with MET	Cohort 2: Pre-treated patients with MET	Cohort 3: Pre-treated patients with MET	Cohort 4: Pre-treated patients with MET	Cohort 5a: Treatment-naïve patients	Cohort 5b: Treatment-naïve patients	Cohort 6.1 (expansion of Cohort 1a): Pre-	Cohort 6.2 (expansion of Cohort 4): Pre-treated	Cohort 7 (expansion of Cohort 5b):	Cohort 4 + Cohort 6.2: All pre-treated	Cohort 5b + Cohort 7: All treatment-

	GCN ≥ 10 (2/3L)	GCN ≥ 6 and < 10 (2/3L)	GCN ≥ 4 and < 6 (2/3L)	GCN < 4 (2/3L)	mutation regardless of MET GCN (2/3L)	with MET GCN ≥10 (1L)	with MET mutation regardless of MET GCN (1L)	treated patients MET GCN ≥ 10 without MET mutation (2L)	patients with MET mutation (2L)	Treatment-naïve with MET mutation regardless of MET GCN (1L)	patients with MET mutation regardless of MET GCN (2/3L)	naive with MET mutation regardless of MET GCN (1L)
Arm/Group Description	Pre-treated patients with MET GCN ≥ 10 treated with INC280 at 400mg BID as second or third line (2/3L)	Pre-treated patients with MET GCN ≥ 6 and < 10 treated with INC280 at 400 mg BID as second or third line (2/3L)	Pre-treated patients with MET GCN ≥ 4 and < 6 treated with INC280 at 400mg BID as second or third line (2/3L)	Pre-treated patients with MET GCN < 4 treated with INC280 at 400mg BID as second or third line (2/3L)	Pre-treated patients with MET mutation regardless of MET GCN treated with INC280 at 400mg BID as second or third line (2/3L)	Treatment-naïve patients with MET GCN ≥10 treated with INC280 at 400mg BID as first-line (1L)	Treatment-naïve patients with MET mutation regardless of MET GCN treated with INC280 at 400mg BID as first line (1L)	Pre-treated patients with MET GCN ≥ 10 without MET mutation treated with INC280 at 400 mg BID as second line (2L) (expansion cohort of Cohort 1a)	Pre-treated patients with MET mutation regardless of MET GCN treated with INC280 at 400 mg BID as second line (2L)(expansion of Cohort 4)	Treatment-naïve patients with MET mutation regardless of MET GCN treated with INC280 at 400mg BID as first line (1L) (expansion cohort of Cohort 5b)	All pre-treated patients with MET mutation regardless of MET GCN treated with INC280 at 400mg BID as second or third line (2/3L). (Participants from Cohort 4 and Cohort 6.2)	All treatment naive patients with MET mutation regardless of MET GCN treated with INC280 at 400 mg BID as first line (1L) (Participants from Cohort 5b and Cohort 7)
Number of Participants Analyzed [units: participants]	69	42	54	30	69	15	28	3	31	32	100	60
Overall Response Rate (ORR) by Blinded Independent Review Committee (BIRC) assessment (units: Percentage of Participants)	**Number (95% Confidence Interval)**	**Number (95% Confidence Interval)**	**Number (95% Confidence Interval)**	**Number (95% Confidence Interval)**	**Number (95% Confidence Interval)**	**Number (95% Confidence Interval)**	**Number (95% Confidence Interval)**	**Number (95% Confidence Interval)**	**Number (95% Confidence Interval)**	**Number (95% Confidence Interval)**	**Number (95% Confidence Interval)**	**Number (95% Confidence Interval)**
	29.0 (18.7 to 41.2)	11.9 (4.0 to 25.6)	9.3 (3.1 to 20.3)	6.7 (0.8 to 22.1)	40.6 (28.9 to 53.1)	40.0 (16.3 to 67.7)	67.9 (47.6 to 84.1)	0.0 (0.0 to 70.8)	51.6 (33.1 to 69.8)	68.8 (50.0 to 83.9)	44.0 (34.1 to 54.3)	68.3 (55.0 to 79.7)

Secondary Outcome Result(s)

Duration of Response (DOR) by BIRC assessment

Description	Time from the date of the first documented CR or PR by BIRC per RECIST 1.1 to the first documented progression or date of death due to any cause for patients with confirmed PR or CR. The Kaplan-Meier method was used to estimate DOR, and the median DOR, along with 95% confidence intervals was reported. If a subject did not have an event, DOR was censored at the date of last adequate tumor assessment. CR: Disappearance of all non-nodal target and non-target lesions. In addition, any pathological lymph nodes assigned as target and non-target lesions must have a reduction in short axis to < 10 mm. PR: At least a 30% decrease in the sum of diameter of all target lesions, taking as reference the baseline sum of diameters.
Time Frame	Up to approximately 5 years
Analysis Population Description	Participants with confirmed CR or PR by BIRC in FAS

	Cohort 1a: Pre-treated patients with MET GCN ≥ 10 (2/3L)	Cohort 1b: Pre-treated patients with MET GCN ≥ 6 and < 10 (2/3L)	Cohort 2: Pre-treated patients with MET GCN ≥ 4 and < 6 (2/3L)	Cohort 3: Pre-treated patients with MET GCN < 4 (2/3L)	Cohort 4: Pre-treated patients with MET mutation regardless of MET GCN (2/3L)	Cohort 5a: Treatment-naïve patients with MET GCN ≥10 (1L)	Cohort 5b: Treatment-naïve patients with MET mutation regardless of MET GCN (1L)	Cohort 6.1 (expansion of Cohort 1a): Pre-treated patients MET GCN ≥ 10 without MET mutation (2L)	Cohort 6.2 (expansion of Cohort 4): Pre-treated patients with MET mutation (2L)	Cohort 7 (expansion of Cohort 5b): Treatment-naïve with MET mutation regardless of MET GCN (1L)	Cohort 4 + Cohort 6.2: All pre-treated patients with MET mutation regardless of MET GCN (2/3L)	Cohort 5b + Cohort 7: All treatment-naive with MET mutation regardless of MET GCN (1L)
Arm/Group Description	Pre-treated patients with MET GCN ≥ 10 treated with INC280 at 400mg BID as second	Pre-treated patients with MET GCN ≥ 6 and < 10 treated with INC280 at 400 mg BID as second	Pre-treated patients with MET GCN ≥ 4 and < 6 treated with INC280 at 400mg BID as second	Pre-treated patients with MET GCN < 4 treated with INC280 at 400mg BID as second	Pre-treated patients with MET mutation regardless of MET GCN treated with INC280 at 400mg BID	Treatment-naïve patients with MET GCN ≥10 treated with INC280 at 400mg BID	Treatment-naïve patients with MET mutation regardless of MET GCN treated with INC280 at	Pre-treated patients with MET GCN ≥ 10 without MET mutation treated with INC280 at 400 mg BID	Pre-treated patients with MET mutation regardless of MET GCN treated with INC280 at 400 mg BID as second line	Treatment-naïve patients with MET mutation regardless of MET GCN treated with INC280 at	All pre-treated patients with MET mutation regardless of MET GCN treated with INC280 at	All treatment naive patients with MET mutation regardless of MET GCN treated with

	or third line (2/3L)	or third line (2/3L)	or third line (2/3L)	or third line (2/3L)	as second or third line (2/3L)	as first-line (1L)	400mg BID as first line (1L)	as second line (2L) (expansion cohort of Cohort 1a)	(2L)(expansion of Cohort 4)	400mg BID as first line (1L) (expansion cohort of Cohort 5b)	400mg BID as second or third line (2/3L). (Participants from Cohort 4 and Cohort 6.2)	INC280 at 400 mg BID as first line (1L) (Participants from Cohort 5b and Cohort 7)
Number of Participants Analyzed [units: participants]	20	5	5	2	28	6	19	0	16	22	44	41
Duration of Response (DOR) by BIRC assessment (units: Months)	**Median (95% Confidence Interval)**	**Median (95% Confidence Interval)**	**Median (95% Confidence Interval)**	**Median (95% Confidence Interval)**	**Median (95% Confidence Interval)**	**Median (95% Confidence Interval)**	**Median (95% Confidence Interval)**	**Median (95% Confidence Interval)**	**Median (95% Confidence Interval)**	**Median (95% Confidence Interval)**	**Median (95% Confidence Interval)**	**Median (95% Confidence Interval)**
	8.31 (4.17 to 15.44)	24.94 (2.69 to 24.94)	9.66 (4.17 to NA)[1]	4.19 (4.17 to 4.21)	9.72 (5.55 to 12.98)	7.54 (2.56 to 14.26)	12.58 (5.55 to 38.67)		9.05 (4.17 to 27.60)	16.59 (8.34 to NA)[1]	9.72 (5.62 to 12.98)	16.59 (8.41 to 22.11)

[1] NA: not estimable due to the insufficient number of participants with events

ORR by investigator assessment

Description	Percentage of patients with a best overall response defined as confirmed CR or PR per RECIST 1.1 by investigator assessment. CR: Disappearance of all non-nodal target and non-target lesions. In addition, any pathological lymph nodes assigned as target and non-target lesions must have a reduction in short axis to < 10 mm. PR: At least a 30% decrease in the sum of diameter of all target lesions, taking as reference the baseline sum of diameters.
Time Frame	Up to approximately 5 years
Analysis Population Description	FAS, including all subjects who received at least one dose of capmatinib.

	Cohort 1a: Pre-treated patients	**Cohort 1b: Pre-treated patients**	**Cohort 2: Pre-treated patients**	**Cohort 3: Pre-treated patients**	**Cohort 4: Pre-treated patients**	**Cohort 5a: Treatment-naïve**	**Cohort 5b: Treatment-naïve**	**Cohort 6.1 (expansion of Cohort**	**Cohort 6.2 (expansion of Cohort 4):**	**Cohort 7 (expansion of Cohort**	**Cohort 4 + Cohort 6.2: All pre-**	**Cohort 5b + Cohort 7: All**

	with MET GCN ≥ 10 (2/3L)	with MET GCN ≥ 6 and < 10 (2/3L)	with MET GCN ≥ 4 and < 6 (2/3L)	with MET GCN < 4 (2/3L)	with MET mutation regardless of MET GCN (2/3L)	patients with MET GCN ≥10 (1L)	patients with MET mutation regardless of MET GCN (1L)	1a): Pre-treated patients MET GCN ≥ 10 without MET mutation (2L)	Pre-treated patients with MET mutation (2L)	5b): Treatment-naïve with MET mutation regardless of MET GCN (1L)	treated patients with MET mutation regardless of MET GCN (2/3L)	treatment-naive with MET mutation regardless of MET GCN (1L)
Arm/Group Description	Pre-treated patients with MET GCN ≥ 10 treated with INC280 at 400mg BID as second or third line (2/3L)	Pre-treated patients with MET GCN ≥ 6 and < 10 treated with INC280 at 400 mg BID as second or third line (2/3L)	Pre-treated patients with MET GCN ≥ 4 and < 6 treated with INC280 at 400mg BID as second or third line (2/3L)	Pre-treated patients with MET GCN < 4 treated with INC280 at 400mg BID as second or third line (2/3L)	Pre-treated patients with MET mutation regardless of MET GCN treated with INC280 at 400mg BID as second or third line (2/3L)	Treatment-naïve patients with MET GCN ≥10 treated with INC280 at 400mg BID as first-line (1L)	Treatment-naïve patients with MET mutation regardless of MET GCN treated with INC280 at 400mg BID as first line (1L)	Pre-treated patients with MET GCN ≥ 10 without MET mutation treated with INC280 at 400 mg BID as second line (2L) (expansion cohort of Cohort 1a)	Pre-treated patients with MET mutation regardless of MET GCN treated with INC280 at 400 mg BID as second line (2L)(expansion of Cohort 4)	Treatment-naïve patients with MET mutation regardless of MET GCN treated with INC280 at 400mg BID as first line (1L) (expansion cohort of Cohort 5b)	All pre-treated patients with MET mutation regardless of MET GCN treated with INC280 at 400mg BID as second or third line (2/3L). (Participants from Cohort 4 and Cohort 6.2)	All treatment naive patients with MET mutation regardless of MET GCN treated with INC280 at 400 mg BID as first line (1L) (Participants from Cohort 5b and Cohort 7)
Number of Participants Analyzed [units: participants]	69	42	54	30	69	15	28	3	31	32	100	60
ORR by investigator assessment (units: Percentage of participants)	**Number (95% Confidence Interval)**	**Number (95% Confidence Interval)**	**Number (95% Confidence Interval)**	**Number (95% Confidence Interval)**	**Number (95% Confidence Interval)**	**Number (95% Confidence Interval)**	**Number (95% Confidence Interval)**	**Number (95% Confidence Interval)**	**Number (95% Confidence Interval)**	**Number (95% Confidence Interval)**	**Number (95% Confidence Interval)**	**Number (95% Confidence Interval)**
	27.5 (17.5 to 39.6)	7.1 (1.5 to 19.5)	9.3 (3.1 to 20.3)	3.3 (0.1 to 17.2)	43.5 (31.6 to 56.0)	40.0 (16.3 to 67.7)	60.7 (40.6 to 78.5)	0.0 (0.0 to 70.8)	45.2 (27.3 to 64.0)	56.3 (37.7 to 73.6)	44.0 (34.1 to 54.3)	58.3 (44.9 to 70.9)

Duration of Response (DOR) by investigator assessment

Description	Time from the date of the first documented CR or PR per RECIST 1.1 by investigator assessment to the first documented progression or death due to any cause for patients with confirmed PR or CR. The Kaplan-Meier method was used to estimate DOR, and the median DOR, along with 95% confidence intervals was reported. If a subject did not have an event, DOR was censored at the date of last adequate tumor assessment. CR: Disappearance of all non-nodal target and non-target lesions. In addition, any pathological lymph nodes assigned as target and non-target lesions must have a reduction in short axis to < 10 mm. PR: At least a 30% decrease in the sum of diameter of all target lesions, taking as reference the baseline sum of diameters.
Time Frame	Up to approximately 5 years
Analysis Population Description	Participants with confirmed CR or PR by investigator assessment in FAS.

	Cohort 1a: Pre-treated patients with MET GCN ≥ 10 (2/3L)	Cohort 1b: Pre-treated patients with MET GCN ≥ 6 and < 10 (2/3L)	Cohort 2: Pre-treated patients with MET GCN ≥ 4 and < 6 (2/3L)	Cohort 3: Pre-treated patients with MET GCN < 4 (2/3L)	Cohort 4: Pre-treated patients with MET mutation regardless of MET GCN (2/3L)	Cohort 5a: Treatment-naïve patients with MET GCN ≥10 (1L)	Cohort 5b: Treatment-naïve patients with MET mutation regardless of MET GCN (1L)	Cohort 6.1 (expansion of Cohort 1a): Pre-treated patients MET GCN ≥ 10 without MET mutation (2L)	Cohort 6.2 (expansion of Cohort 4): Pre-treated patients with MET mutation (2L)	Cohort 7 (expansion of Cohort 5b): Treatment-naïve with MET mutation regardless of MET GCN (1L)	Cohort 4 + Cohort 6.2: All pre-treated patients with MET mutation regardless of MET GCN (2/3L)	Cohort 5b + Cohort 7: All treatment-naive with MET mutation regardless of MET GCN (1L)
Arm/Group Description	Pre-treated patients with MET GCN ≥ 10 treated with INC280 at 400mg BID as second or third line (2/3L)	Pre-treated patients with MET GCN ≥ 6 and < 10 treated with INC280 at 400 mg BID as second or third line (2/3L)	Pre-treated patients with MET GCN ≥ 4 and < 6 treated with INC280 at 400mg BID as second or third line (2/3L)	Pre-treated patients with MET GCN < 4 treated with INC280 at 400mg BID as second or third line (2/3L)	Pre-treated patients with MET mutation regardless of MET GCN treated with INC280 at 400mg BID as second or third line (2/3L)	Treatment-naïve patients with MET GCN ≥10 treated with INC280 at 400mg BID as first-line (1L)	Treatment-naïve patients with MET mutation regardless of MET GCN treated with INC280 at 400mg BID as first line (1L)	Pre-treated patients with MET GCN ≥ 10 without MET mutation treated with INC280 at 400 mg BID as second line (2L) (expansion cohort of Cohort 1a)	Pre-treated patients with MET mutation regardless of MET GCN treated with INC280 at 400 mg BID as second line (2L)(expansion of Cohort 4)	Treatment-naïve patients with MET mutation regardless of MET GCN treated with INC280 at 400mg BID as first line (1L) (expansion cohort of Cohort 5b)	All pre-treated patients with MET mutation regardless of MET GCN treated with INC280 at 400mg BID as second or third line (2/3L). (Participants from Cohort	All treatment naive patients with MET mutation regardless of MET GCN treated with INC280 at 400 mg BID as first line (1L) (Participants from Cohort

											4 and Cohort 6.2)	5b and Cohort 7)
Number of Participants Analyzed [units: participants]	19	3	5	1	30	6	17	0	14	18	44	35
Duration of Response (DOR) by investigator assessment (units: Months)	**Median (95% Confidence Interval)**	**Median (95% Confidence Interval)**	**Median (95% Confidence Interval)**	**Median (95% Confidence Interval)**	**Median (95% Confidence Interval)**	**Median (95% Confidence Interval)**	**Median (95% Confidence Interval)**	**Median (95% Confidence Interval)**	**Median (95% Confidence Interval)**	**Median (95% Confidence Interval)**	**Median (95% Confidence Interval)**	**Median (95% Confidence Interval)**
	6.80 (4.21 to 20.73)	6.93 (5.75 to 8.34)	19.48 (2.83 to NA)[1]	6.93 (NA to NA)[1]	8.31 (4.34 to 12.06)	9.66 (4.01 to 17.08)	13.83 (4.27 to 25.33)		14.57 (4.17 to 27.60)	15.21 (6.77 to 31.77)	8.38 (5.55 to 13.80)	13.96 (9.33 to 22.18)

[1] NA: not estimable due to the insufficient number of participants with events

Time to Response (TTR) by BIRC assessment

Description	Time between date of start of treatment until first documented response (confirmed CR or PR) per RECIST 1.1 by BIRC assessment. CR: Disappearance of all non-nodal target and non-target lesions. In addition, any pathological lymph nodes assigned as target and non-target lesions must have a reduction in short axis to < 10 mm. PR: At least a 30% decrease in the sum of diameter of all target lesions, taking as reference the baseline sum of diameters.
Time Frame	Up to approximately 5 years
Analysis Population Description	Participants with confirmed CR or PR by BIRC assessment in FAS.

	Cohort 1a: Pre-treated patients with MET GCN ≥ 10 (2/3L)	**Cohort 1b: Pre-treated patients with MET GCN ≥ 6 and < 10 (2/3L)**	**Cohort 2: Pre-treated patients with MET GCN ≥ 4 and < 6 (2/3L)**	**Cohort 3: Pre-treated patients with MET GCN < 4 (2/3L)**	**Cohort 4: Pre-treated patients with MET mutation regardless of MET GCN (2/3L)**	**Cohort 5a: Treatment-naïve patients with MET GCN ≥10 (1L)**	**Cohort 5b: Treatment-naïve patients with MET mutation regardless of MET GCN (1L)**	**Cohort 6.1 (expansion of Cohort 1a): Pre-treated patients MET GCN ≥ 10 without MET**	**Cohort 6.2 (expansion of Cohort 4): Pre-treated patients with MET mutation (2L)**	**Cohort 7 (expansion of Cohort 5b): Treatment-naïve with MET mutation regardless**	**Cohort 4 + Cohort 6.2: All pre-treated patients with MET mutation regardless**	**Cohort 5b + Cohort 7: All treatment-naive with MET mutation regardless**

								mutation (2L)		**of MET GCN (1L)**	**of MET GCN (2/3L)**	**of MET GCN (1L)**
Arm/Group Description	Pre-treated patients with MET GCN ≥ 10 treated with INC280 at 400mg BID as second or third line (2/3L)	Pre-treated patients with MET GCN ≥ 6 and < 10 treated with INC280 at 400 mg BID as second or third line (2/3L)	Pre-treated patients with MET GCN ≥ 4 and < 6 treated with INC280 at 400mg BID as second or third line (2/3L)	Pre-treated patients with MET GCN < 4 treated with INC280 at 400mg BID as second or third line (2/3L)	Pre-treated patients with MET mutation regardless of MET GCN treated with INC280 at 400mg BID as second or third line (2/3L)	Treatment-naïve patients with MET GCN ≥10 treated with INC280 at 400mg BID as first-line (1L)	Treatment-naïve patients with MET mutation regardless of MET GCN treated with INC280 at 400mg BID as first line (1L)	Pre-treated patients with MET GCN ≥ 10 without MET mutation treated with INC280 at 400 mg BID as second line (2L) (expansion cohort of Cohort 1a)	Pre-treated patients with MET mutation regardless of MET GCN treated with INC280 at 400 mg BID as second line (2L)(expansion of Cohort 4)	Treatment-naïve patients with MET mutation regardless of MET GCN treated with INC280 at 400mg BID as first line (1L) (expansion cohort of Cohort 5b)	All pre-treated patients with MET mutation regardless of MET GCN treated with INC280 at 400mg BID as second or third line (2/3L). (Participants from Cohort 4 and Cohort 6.2)	All treatment naive patients with MET mutation regardless of MET GCN treated with INC280 at 400 mg BID as first line (1L) (Participants from Cohort 5b and Cohort 7)
Number of Participants Analyzed [units: participants]	20	5	5	2	28	6	19	0	16	22	44	41
Time to Response (TTR) by BIRC assessment (units: Months)	**Median (Full range)**	**Median (Full range)**	**Median (Full range)**	**Median (Full range)**	**Median (Full range)**	**Median (Full range)**	**Median (Full range)**	**Median (Full range)**	**Median (Full range)**	**Median (Full range)**	**Median (Full range)**	**Median (Full range)**
	1.4 (0.5 to 6.8)	2.8 (1.4 to 16.6)	1.4 (1.2 to 6.2)	3.4 (1.3 to 5.5)	1.4 (1.2 to 5.6)	1.4 (1.2 to 2.9)	1.4 (1.3 to 6.9)		1.4 (1.1 to 9.8)	1.4 (1.2 to 7.2)	1.4 (1.1 to 9.8)	1.4 (1.2 to 7.2)

Time to Response (TTR) by investigator assessment

Description: Time between date of start of treatment until first documented response (confirmed CR or PR) per RECIST 1.1 by investigator assessment.

CR: Disappearance of all non-nodal target and non-target lesions. In addition, any pathological lymph nodes assigned as target and non-target lesions must have a reduction in short axis to < 10 mm.

PR: At least a 30% decrease in the sum of diameter of all target lesions, taking as reference the baseline sum of diameters.

Time Frame	Up to approximately 5 years
Analysis Population Description	Participants with confirmed CR or PR by investigator assessment in FAS.

	Cohort 1a: Pre-treated patients with MET GCN ≥ 10 (2/3L)	**Cohort 1b: Pre-treated patients with MET GCN ≥ 6 and < 10 (2/3L)**	**Cohort 2: Pre-treated patients with MET GCN ≥ 4 and < 6 (2/3L)**	**Cohort 3: Pre-treated patients with MET GCN < 4 (2/3L)**	**Cohort 4: Pre-treated patients with MET mutation regardless of MET GCN (2/3L)**	**Cohort 5a: Treatment-naïve patients with MET GCN ≥10 (1L)**	**Cohort 5b: Treatment-naïve patients with MET mutation regardless of MET GCN (1L)**	**Cohort 6.1 (expansion of Cohort 1a): Pre-treated patients MET GCN ≥ 10 without MET mutation (2L)**	**Cohort 6.2 (expansion of Cohort 4): Pre-treated patients with MET mutation (2L)**	**Cohort 7 (expansion of Cohort 5b): Treatment-naïve with MET mutation regardless of MET GCN (1L)**	**Cohort 4 + Cohort 6.2: All pre-treated patients with MET mutation regardless of MET GCN (2/3L)**	**Cohort 5b + Cohort 7: All treatment-naive with MET mutation regardless of MET GCN (1L)**
Arm/Group Description	Pre-treated patients with MET GCN ≥ 10 treated with INC280 at 400mg BID as second or third line (2/3L)	Pre-treated patients with MET GCN ≥ 6 and < 10 treated with INC280 at 400 mg BID as second or third line (2/3L)	Pre-treated patients with MET GCN ≥ 4 and < 6 treated with INC280 at 400mg BID as second or third line (2/3L)	Pre-treated patients with MET GCN < 4 treated with INC280 at 400mg BID as second or third line (2/3L)	Pre-treated patients with MET mutation regardless of MET GCN treated with INC280 at 400mg BID as second or third line (2/3L)	Treatment-naïve patients with MET GCN ≥10 treated with INC280 at 400mg BID as first-line (1L)	Treatment-naïve patients with MET mutation regardless of MET GCN treated with INC280 at 400mg BID as first line (1L)	Pre-treated patients with MET GCN ≥ 10 without MET mutation treated with INC280 at 400 mg BID as second line (2L) (expansion cohort of Cohort 1a)	Pre-treated patients with MET mutation regardless of MET GCN treated with INC280 at 400 mg BID as second line (2L)(expansion of Cohort 4)	Treatment-naïve patients with MET mutation regardless of MET GCN treated with INC280 at 400mg BID as first line (1L) (expansion cohort of Cohort 5b)	All pre-treated patients with MET mutation regardless of MET GCN treated with INC280 at 400mg BID as second or third line (2/3L). (Participants from Cohort 4 and Cohort 6.2)	All treatment naive patients with MET mutation regardless of MET GCN treated with INC280 at 400 mg BID as first line (1L) (Participants from Cohort 5b and Cohort 7)
Number of Participants Analyzed [units: participants]	19	3	5	1	30	6	17	0	14	18	44	35
TTR by investigator assessment	**Median (Full range)**	**Median (Full range)**	**Median (Full range)**	**Median (Full range)**	**Median (Full range)**	**Median (Full range)**	**Median (Full range)**	**Median (Full range)**	**Median (Full range)**	**Median (Full range)**	**Median (Full range)**	**Median (Full range)**

(units: Months)												
	1.4 (1.2 to 5.4)	1.4 (1.3 to 1.4)	1.3 (1.2 to 1.7)	1.3 (1.3 to 1.3)	1.4 (1.2 to 11.1)	1.4 (1.3 to 2.5)	1.4 (1.2 to 4.0)		1.4 (1.1 to 12.3)	1.4 (1.2 to 5.6)	1.4 (1.1 to 12.3)	1.4 (1.2 to 5.6)

Disease Control Rate (DCR)

Description	Percentage of participants with a best overall response of confirmed CR, PR or stable disease (SD) per RECIST 1.1 by BIRC and investigator assessment. CR: Disappearance of all non-nodal target and non-target lesions. In addition, any pathological lymph nodes assigned as target and non-target lesions must have a reduction in short axis to < 10 mm. PR: At least a 30% decrease in the sum of diameter of all target lesions, taking as reference the baseline sum of diameters. SD: Neither sufficient shrinkage to qualify for PR or CR nor an increase in lesions which would qualify for progressive disease.
Time Frame	Up to approximately 5 years
Analysis Population Description	FAS, including all subjects who received at least one dose of capmatinib.

	Cohort 1a: Pre-treated patients with MET GCN ≥ 10 (2/3L)	**Cohort 1b: Pre-treated patients with MET GCN ≥ 6 and < 10 (2/3L)**	**Cohort 2: Pre-treated patients with MET GCN ≥ 4 and < 6 (2/3L)**	**Cohort 3: Pre-treated patients with MET GCN < 4 (2/3L)**	**Cohort 4: Pre-treated patients with MET mutation regardless of MET GCN (2/3L)**	**Cohort 5a: Treatment-naïve patients with MET GCN ≥10 (1L)**	**Cohort 5b: Treatment-naïve patients with MET mutation regardless of MET GCN (1L)**	**Cohort 6.1 (expansion of Cohort 1a): Pre-treated patients MET GCN ≥ 10 without MET mutation (2L)**	**Cohort 6.2 (expansion of Cohort 4): Pre-treated patients with MET mutation (2L)**	**Cohort 7 (expansion of Cohort 5b): Treatment-naïve with MET mutation regardless of MET GCN (1L)**	**Cohort 4 + Cohort 6.2: All pre-treated patients with MET mutation regardless of MET GCN (2/3L)**	**Cohort 5b + Cohort 7: All treatment-naive with MET mutation regardless of MET GCN (1L)**
Arm/Group Description	Pre-treated patients with MET GCN ≥ 10 treated with INC280 at 400mg BID as second or third line (2/3L)	Pre-treated patients with MET GCN ≥ 6 and < 10 treated with INC280 at 400 mg BID as second	Pre-treated patients with MET GCN ≥ 4 and < 6 treated with INC280 at 400mg BID as second	Pre-treated patients with MET GCN < 4 treated with INC280 at 400mg BID as second or third line (2/3L)	Pre-treated patients with MET mutation regardless of MET GCN treated with INC280 at 400mg BID	Treatment-naïve patients with MET GCN ≥10 treated with INC280 at 400mg BID as first-line (1L)	Treatment-naïve patients with MET mutation regardless of MET GCN treated with INC280 at	Pre-treated patients with MET GCN ≥ 10 without MET mutation treated with INC280 at 400 mg BID	Pre-treated patients with MET mutation regardless of MET GCN treated with INC280 at 400 mg BID as second line	Treatment-naïve patients with MET mutation regardless of MET GCN treated with INC280 at	All pre-treated patients with MET mutation regardless of MET GCN treated with INC280 at	All treatment naive patients with MET mutation regardless of MET GCN treated with

		or third line (2/3L)	or third line (2/3L)		as second or third line (2/3L)		400mg BID as first line (1L)	as second line (2L) (expansion cohort of Cohort 1a)	(2L)(expansion of Cohort 4)	400mg BID as first line (1L) (expansion cohort of Cohort 5b)	400mg BID as second or third line (2/3L). (Participants from Cohort 4 and Cohort 6.2)	INC280 at 400 mg BID as first line (1L) (Participants from Cohort 5b and Cohort 7)
Number of Participants Analyzed [units: participants]	69	42	54	30	69	15	28	3	31	32	100	60
Disease Control Rate (DCR) (units: Percentage of participants)	**Number (95% Confidence Interval)**	**Number (95% Confidence Interval)**	**Number (95% Confidence Interval)**	**Number (95% Confidence Interval)**	**Number (95% Confidence Interval)**	**Number (95% Confidence Interval)**	**Number (95% Confidence Interval)**	**Number (95% Confidence Interval)**	**Number (95% Confidence Interval)**	**Number (95% Confidence Interval)**	**Number (95% Confidence Interval)**	**Number (95% Confidence Interval)**
By BIRC assessment	71.0 (58.8 to 81.3)	54.8 (38.7 to 70.2)	46.3 (32.6 to 60.4)	53.3 (34.3 to 71.7)	78.3 (66.7 to 87.3)	66.7 (38.4 to 88.2)	96.4 (81.7 to 99.9)	100.0 (29.2 to 100.0)	90.3 (74.2 to 98.0)	100.0 (89.1 to 100.0)	82.0 (73.1 to 89.0)	98.3 (91.1 to 100.0)
By investigator assessment	60.9 (48.4 to 72.4)	45.2 (29.8 to 61.3)	44.4 (30.9 to 58.6)	46.7 (28.3 to 65.7)	76.8 (65.1 to 86.1)	73.3 (44.9 to 92.2)	96.4 (81.7 to 99.9)	100.0 (29.2 to 100.0)	90.3 (74.2 to 98.0)	96.9 (83.8 to 99.9)	81.0 (71.9 to 88.2)	96.7 (88.5 to 99.6)

Progression-Free Survival

Description	Time from start of treatment to the date of the first documented progression or death due to any cause per RECIST 1.1 both by BIRC and investigator assessment. Clinical deterioration was not considered as a qualifying event for progression. PFS was censored at the last adequate tumor assessment if one of the following occurred: absence of event or the event occurred after two or more missing tumor assessments. The Kaplan-Meier method was used to estimate PFS, and the median PFS, along with 95% confidence intervals, was reported. Progressive disease: For target lesions, at least a 20% increase in the sum of diameter of all measured target lesions, taking as reference the smallest sum of diameter of all target lesions recorded at or after baseline. In addition to the relative increase of 20%, the sum must also demonstrate an absolute increase of at least 5 mm^2. For non-target lesions, unequivocal progression of existing non-target lesions
Time Frame	Up to approximately 5 years
Analysis Population Description	FAS, including all subjects who received at least one dose of capmatinib.

	Cohort 1a: Pre-treated patients with MET GCN ≥ 10 (2/3L)	Cohort 1b: Pre-treated patients with MET GCN ≥ 6 and < 10 (2/3L)	Cohort 2: Pre-treated patients with MET GCN ≥ 4 and < 6 (2/3L)	Cohort 3: Pre-treated patients with MET GCN < 4 (2/3L)	Cohort 4: Pre-treated patients with MET mutation regardless of MET GCN (2/3L)	Cohort 5a: Treatment-naïve patients with MET GCN ≥10 (1L)	Cohort 5b: Treatment-naïve patients with MET mutation regardless of MET GCN (1L)	Cohort 6.1 (expansion of Cohort 1a): Pre-treated patients MET GCN ≥ 10 without MET mutation (2L)	Cohort 6.2 (expansion of Cohort 4): Pre-treated patients with MET mutation (2L)	Cohort 7 (expansion of Cohort 5b): Treatment-naïve with MET mutation regardless of MET GCN (1L)	Cohort 4 + Cohort 6.2: All pre-treated patients with MET mutation regardless of MET GCN (2/3L)	Cohort 5b + Cohort 7: All treatment-naive with MET mutation regardless of MET GCN (1L)
Arm/Group Description	Pre-treated patients with MET GCN ≥ 10 treated with INC280 at 400mg BID as second or third line (2/3L)	Pre-treated patients with MET GCN ≥ 6 and < 10 treated with INC280 at 400 mg BID as second or third line (2/3L)	Pre-treated patients with MET GCN ≥ 4 and < 6 treated with INC280 at 400mg BID as second or third line (2/3L)	Pre-treated patients with MET GCN < 4 treated with INC280 at 400mg BID as second or third line (2/3L)	Pre-treated patients with MET mutation regardless of MET GCN treated with INC280 at 400mg BID as second or third line (2/3L)	Treatment-naïve patients with MET GCN ≥10 treated with INC280 at 400mg BID as first-line (1L)	Treatment-naïve patients with MET mutation regardless of MET GCN treated with INC280 at 400mg BID as first line (1L)	Pre-treated patients with MET GCN ≥ 10 without MET mutation treated with INC280 at 400 mg BID as second line (2L) (expansion cohort of Cohort 1a)	Pre-treated patients with MET mutation regardless of MET GCN treated with INC280 at 400 mg BID as second line (2L)(expansion of Cohort 4)	Treatment-naïve patients with MET mutation regardless of MET GCN treated with INC280 at 400mg BID as first line (1L) (expansion cohort of Cohort 5b)	All pre-treated patients with MET mutation regardless of MET GCN treated with INC280 at 400mg BID as second or third line (2/3L). (Participants from Cohort 4 and Cohort 6.2)	All treatment naive patients with MET mutation regardless of MET GCN treated with INC280 at 400 mg BID as first line (1L) (Participants from Cohort 5b and Cohort 7)
Number of Participants Analyzed [units: participants]	69	42	54	30	69	15	28	3	31	32	100	60
Progression-Free Survival (units: Months)	**Median (95% Confidence Interval)**	**Median (95% Confidence Interval)**	**Median (95% Confidence Interval)**	**Median (95% Confidence Interval)**	**Median (95% Confidence Interval)**	**Median (95% Confidence Interval)**	**Median (95% Confidence Interval)**	**Median (95% Confidence Interval)**	**Median (95% Confidence Interval)**	**Median (95% Confidence Interval)**	**Median (95% Confidence Interval)**	**Median (95% Confidence Interval)**
By BIRC assessment	4.07 (2.86 to 4.83)	2.66 (1.41 to 3.09)	2.66 (1.41 to 4.14)	3.55 (2.20 to 4.21)	5.42 (4.17 to 6.97)	4.17 (1.45 to 6.87)	12.42 (8.21 to 23.39)	2.79 (2.07 to 4.24)	6.93 (4.17 to 13.34)	12.45 (6.87 to 22.05)	5.49 (4.17 to 8.11)	12.45 (8.31 to 17.97)
By investigator assessment	4.14 (2.79 to 5.52)	2.40 (1.45 to 2.83)	2.60 (1.48 to 3.09)	2.73 (1.45 to 3.78)	4.80 (4.11 to 7.75)	2.76 (1.45 to 6.87)	11.99 (5.52 to 16.92)	2.76 (2.07 to 2.79)	6.90 (5.55 to 17.31)	9.79 (5.75 to 16.36)	6.60 (4.70 to 8.18)	11.07 (6.87 to 15.18)

Overall Survival (OS)

Description	Time from start of treatment to the date of death due to any cause. If the patient was alive at the date of the analysis cut-off or lost to follow-up, then OS was censored at the last contact date prior to data cut-off date. The Kaplan-Meier method was used to estimate OS, and the median OS, along with 95% confidence intervals, was reported.
Time Frame	Up to approximately 6 years
Analysis Population Description	FAS, including all subjects who received at least one dose of capmatinib.

	Cohort 1a: Pre-treated patients with MET GCN ≥ 10 (2/3L)	Cohort 1b:Pre-treated patients with MET GCN ≥ 6 and < 10 (2/3L)	Cohort 2: Pre-treated patients with MET GCN ≥ 4 and < 6 (2/3L)	Cohort 3: Pre-treated patients with MET GCN < 4 (2/3L)	Cohort 4: Pre-treated patients with MET mutation regardless of MET GCN (2/3L)	Cohort 5a: Treatment-naïve patients with MET GCN ≥10 (1L)	Cohort 5b: Treatment-naïve patients with MET mutation regardless of MET GCN (1L)	Cohort 6.1 (expansion of Cohort 1a): Pre-treated patients MET GCN ≥ 10 without MET mutation (2L)	Cohort 6.2 (expansion of Cohort 4): Pre-treated patients with MET mutation (2L)	Cohort 7 (expansion of Cohort 5b): Treatment-naïve with MET mutation regardless of MET GCN (1L)	Cohort 4 + Cohort 6.2: All pre-treated patients with MET mutation regardless of MET GCN (2/3L)	Cohort 5b + Cohort 7: All treatment-naive with MET mutation regardless of MET GCN (1L)
Arm/Group Description	Pre-treated patients with MET GCN ≥ 10 treated with INC280 at 400mg BID as second or third line (2/3L)	Pre-treated patients with MET GCN ≥ 6 and < 10 treated with INC280 at 400 mg BID as second or third line (2/3L)	Pre-treated patients with MET GCN ≥ 4 and < 6 treated with INC280 at 400mg BID as second or third line (2/3L)	Pre-treated patients with MET GCN < 4 treated with INC280 at 400mg BID as second or third line (2/3L)	Pre-treated patients with MET mutation regardless of MET GCN treated with INC280 at 400mg BID as second or third line (2/3L)	Treatment-naïve patients with MET GCN ≥10 treated with INC280 at 400mg BID as first-line (1L)	Treatment-naïve patients with MET mutation regardless of MET GCN treated with INC280 at 400mg BID as first line (1L)	Pre-treated patients with MET GCN ≥ 10 without MET mutation treated with INC280 at 400 mg BID as second line (2L) (expansion cohort of Cohort 1a)	Pre-treated patients with MET mutation regardless of MET GCN treated with INC280 at 400 mg BID as second line (2L)(expansion of Cohort 4)	Treatment-naïve patients with MET mutation regardless of MET GCN treated with INC280 at 400mg BID as first line (1L) (expansion cohort of Cohort 5b)	All pre-treated patients with MET mutation regardless of MET GCN treated with INC280 at 400mg BID as second or third line (2/3L). (Participants from Cohort 4 and Cohort 6.2)	All treatment naive patients with MET mutation regardless of MET GCN treated with INC280 at 400 mg BID as first line (1L) (Participants from Cohort 5b and Cohort 7)

Number of Participants Analyzed [units: participants]	69	42	54	30	69	15	28	3	31	32	100	60
Overall Survival (OS) (units: Months)	**Median (95% Confidence Interval)**	**Median (95% Confidence Interval)**	**Median (95% Confidence Interval)**	**Median (95% Confidence Interval)**	**Median (95% Confidence Interval)**	**Median (95% Confidence Interval)**	**Median (95% Confidence Interval)**	**Median (95% Confidence Interval)**	**Median (95% Confidence Interval)**	**Median (95% Confidence Interval)**	**Median (95% Confidence Interval)**	**Median (95% Confidence Interval)**
	10.61 (6.28 to 17.22)	7.46 (5.59 to 10.18)	10.15 (5.52 to 15.74)	9.46 (4.11 to 12.32)	13.57 (8.61 to 22.24)	9.56 (4.80 to NA)[1]	20.76 (12.42 to 43.93)	4.14 (2.07 to NA)[1]	25.95 (13.54 to 43.40)	21.36 (12.85 to 34.76)	16.79 (11.63 to 23.82)	21.36 (15.24 to 30.52)

[1] NA: not estimable due to the insufficient number of participants with events

Pharmacokinetic (PK) concentrations of capmatinib

Description	PK concentrations of capmatinib. Plasma concentrations of capmatinib were measured using validated liquid chromatography-tandem mass spectrometry (LCMS/MS) methods with a lower limit of quantification (LLOQ) of approximately 1.0 ng/mL. Capmatinib concentration data was summarized for Cohorts 1a, 1b, 2, 3, 4, 5a and 5b when capmatinib was administered in fasted state; and for Cohorts 6 and 7 when capmatinib was administered with or without food.
Time Frame	Cycle (C) 1 Day (D) 1 predose and 2 hours post-dose, C1D15 pre-dose and 2 hours post-dose, C3D1 pre-dose. Each Cycle is 21 days
Analysis Population Description	Participants who received at least one dose of capmatinib and provided at least one evaluable pharmacokinetic concentration for capmatinib at the specified time points. Participants who received capmatinib under the same administration conditions (fasted state or with/without food) were pooled together.

	Cohorts 1-5: Capmatinib administration in fasted state	**Cohorts 6-7: Capmatinib administration with ot without food**
Arm/Group Description	Participants from Cohorts 1a, 1b, 2, 3, 4, 5a and 5b who received capmatinib in fasted state	Participants from Cohorts 6 and 7 who received capmatinib with or without food
Number of Participants Analyzed [units: participants]	275	54
Pharmacokinetic (PK) concentrations of capmatinib (units: nanogram/mililiter (ng/ml))	**Mean ± Standard Deviation**	**Mean ± Standard Deviation**
Cycle 1 Day 1- pre-dose	0.00 ± 0.00	0.00 ± 0.00
Cycle 1 Day 1- 2 hours post-dose	3360 ± 1920	3060 ± 1780
Cycle 1 Day 15 - pre-dose	727 ± 781	663 ± 806
Cycle 1 Day 15- 2 hours post-dose	4100 ± 2100	4340 ± 2000

Cycle 3 Day 1 - pre-dose	687 ± 1000	672 ± 745

Maximum concentration (Cmax) of capmatinib

Description	Cmax of capmatinib was estimated by non-compartmental analysis. Cmax is the maximum plasma drug concentration after single dose administration. Plasma concentrations of capmatinib were measured using validated LCMS/MS methods with a LLOQ of approximately 1.0 ng/mL. Only a subset of participants from Cohorts 1a, 1b, 2, 3, 4, 5a and 5b, who had an extensive PK collection schedule, were included in this analysis
Time Frame	Cycle 1 Day 1 and Day 15 at pre-dose, 0.5, 1, 2, 4, 6 and 8 hours post-dose. Each Cycle is 21 days
Analysis Population Description	Participants from Cohorts 1a, 1b, 2, 3, 4, 5a and 5b who received at least one dose of capmatinib with extensive PK sampling collection and an evaluable PK parameter (Cmax for capmatinib) at the specified time points. Participants received capmatinib under the same administration conditions (fasted state) and were pooled together for analysis

	Cohorts 1-5: Capmatinib administration in fasted state
Arm/Group Description	Participants from Cohorts 1a, 1b, 2, 3, 4, 5a and 5b who received capmatinib in fasted state
Number of Participants Analyzed [units: participants]	55
Maximum concentration (Cmax) of capmatinib (units: ng/ml)	**Mean ± Standard Deviation**
Cycle 1 Day 1	4230 ± 2290
Cycle 1 Day 15	5450 ± 2560

Maximum concentration (Cmax) of CMN288

Description	Cmax of CMN288 (metabolite of capmatinib) was estimated by non-compartmental analysis. Cmax is the maximum plasma drug concentration after single dose administration. Plasma concentrations of metabolite CMN288 were measured using validated LCMS/MS methods with a LLOQ of approximately 1.0 ng/mL. Only a subset of participants from Cohorts 1a, 1b, 2, 3, 4, 5a and 5b, who had an extensive PK collection schedule, were included in this analysis
Time Frame	Cycle 1 Day 1 and Day 15 at pre-dose, 0.5, 1, 2, 4, 6 and 8 hours post-dose. Each Cycle is 21 days
Analysis Population Description	Participants from Cohorts 1a, 1b, 2, 3, 4, 5a and 5b who received at least one dose of capmatinib with extensive PK sampling collection and an evaluable PK parameter (Cmax for CMN288) at the specified time points. Participants received capmatinib under the same administration conditions (fasted state) and were pooled together for analysis

	Cohorts 1-5: Capmatinib administration in fasted state
Arm/Group Description	Participants from Cohorts 1a, 1b, 2, 3, 4, 5a and 5b who received capmatinib in fasted state
Number of Participants Analyzed [units: participants]	51
Maximum concentration (Cmax) of CMN288 (units: ng/ml)	**Mean ± Standard Deviation**
Cycle 1 Day 1	1910 ± 1420
Cycle 1 Day 15	1420 ± 725

Area under the plasma concentration-time curve from zero to time infinity (AUCinf) of capmatinib

Description	AUCinf of capmatinib was estimated by non-compartmental analysis. AUCinf is the area under the plasma concentration-time curve extrapolated to infinity. Plasma concentrations of capmatinib were measured using validated LCMS/MS methods with a LLOQ of approximately 1.0 ng/mL. Only a subset of participants from Cohorts 1a, 1b, 2, 3, 4, 5a and 5b, who had an extensive PK collection schedule, were included in this analysis
Time Frame	Cycle 1 Day 1 at pre-dose, 0.5, 1, 2, 4, 6 and 8 hours post-dose. Each Cycle is 21 days
Analysis Population Description	Participants from Cohorts 1a, 1b, 2, 3, 4, 5a and 5b who received at least one dose of capmatinib with extensive PK sampling collection and an evaluable PK parameter (AUCinf for capmatinib) at the specified time points. Participants received capmatinib under the same administration conditions (fasted state) and were pooled together for analysis

	Cohorts 1-5: Capmatinib administration in fasted state
Arm/Group Description	Participants from Cohorts 1a, 1b, 2, 3, 4, 5a and 5b who received capmatinib in fasted state
Number of Participants Analyzed [units: participants]	44
Area under the plasma concentration-time curve from zero to time infinity (AUCinf) of capmatinib (units: nanogram * hour / mililiter (ng*h/ml))	**Mean ± Standard Deviation**
Cycle 1 Day 1	17000 ± 7770

Area under the plasma concentration-time curve from zero to time infinity (AUCinf) of CMN288

Description	AUCinf of CMN288 (metabolite of capmatinib) was estimated by non-compartmental analysis. AUCinf is the area under the plasma concentration-time curve extrapolated to infinity. Plasma concentrations of metabolite CMN288 were measured using validated LCMS/MS methods with a LLOQ of approximately 1.0 ng/mL. Only a subset of participants from Cohorts 1a, 1b, 2, 3, 4, 5a and 5b, who had an extensive PK collection schedule, were included in this analysis

Time Frame	Cycle 1 Day 1 at pre-dose, 0.5, 1, 2, 4, 6 and 8 hours post-dose. Each Cycle is 21 days
Analysis Population Description	Participants from Cohorts 1a, 1b, 2, 3, 4, 5a and 5b who received at least one dose of capmatinib with extensive PK sampling collection and an evaluable PK parameter (AUCinf for CMN288) at the specified time points. Participants received capmatinib under the same administration conditions (fasted state) and were pooled together for analysis

	Cohorts 1-5: Capmatinib administration in fasted state
Arm/Group Description	Participants from Cohorts 1a, 1b, 2, 3, 4, 5a and 5b who received capmatinib in fasted state
Number of Participants Analyzed [units: participants]	27
Area under the plasma concentration-time curve from zero to time infinity (AUCinf) of CMN288 (units: ng*h/ml)	**Mean ± Standard Deviation**
Cycle 1 Day 1	9020 ± 5060

Time to reach maximum concentration (Tmax) of capmatinib

Description	Tmax of capmatinib was estimated by non-compartmental analysis. Tmax is the time to reach maximum plasma concentration. Actual recorded sampling times were considered for the calculations. Plasma concentrations of capmatinib were measured using validated LCMS/MS methods with a LLOQ of approximately 1.0 ng/mL. Only a subset of participants from Cohorts 1a, 1b, 2, 3, 4, 5a and 5b, who had an extensive PK collection schedule, were included in this analysis
Time Frame	Cycle 1 Day 1 and Day 15 at pre-dose, 0.5, 1, 2, 4, 6 and 8 hours post-dose. Each Cycle is 21 days
Analysis Population Description	Participants from Cohorts 1a, 1b, 2, 3, 4, 5a and 5b who received at least one dose of capmatinib with extensive PK sampling collection and an evaluable PK parameter (Tmax for capmatinib) at the specified time points. Participants received capmatinib under the same administration conditions (fasted state) and were pooled together for analysis

	Cohorts 1-5: Capmatinib administration in fasted state
Arm/Group Description	Participants from Cohorts 1a, 1b, 2, 3, 4, 5a and 5b who received capmatinib in fasted state
Number of Participants Analyzed [units: participants]	55
Time to reach maximum concentration (Tmax) of capmatinib (units: hour)	**Median (Full Range)**
Cycle 1 Day 1	1.87 (0.583 to 4.03)

Cycle 1 Day 15	1.09 (0.5 to 6.07)

Time to reach maximum concentration (Tmax) of CMN288

Description	Tmax of CMN288 (metabolite of capmatinib) was estimated by non-compartmental analysis. Tmax is the time to reach maximum plasma concentration. Actual recorded sampling times were considered for the calculations. Plasma concentrations of metabolite CMN288 were measured using validated LCMS/MS methods with a LLOQ of approximately 1.0 ng/mL. Only a subset of participants from cohorts 1-5, who had an extensive PK collection schedule, were included in this analysis
Time Frame	Cycle 1 Day 1 and Day 15 at pre-dose, 0.5, 1, 2, 4, 6 and 8 hours post-dose. Each Cycle is 21 days
Analysis Population Description	Participants from Cohorts 1a, 1b, 2, 3, 4, 5a and 5b who received at least one dose of capmatinib with extensive PK sampling collection and an evaluable PK parameter (Tmax for CMN288) at the specified time points. Participants received capmatinib under the same administration conditions (fasted state) and were pooled together for analysis

	Cohorts 1-5: Capmatinib administration in fasted state
Arm/Group Description	Participants from Cohorts 1a, 1b, 2, 3, 4, 5a and 5b who received capmatinib in fasted state
Number of Participants Analyzed [units: participants]	51
Time to reach maximum concentration (Tmax) of CMN288 (units: hour)	**Median (Full Range)**
Cycle 1 Day 1	1.93 (0.950 to 4.03)
Cycle 1 Day 15	1.91 (0.883 to 7.98)

Elimination half-life (T1/2) of capmatinib

Description	T1/2 of capmatinib was estimated by non-compartmental analysis. T1/2 is the time it takes for the concentration of capmatinib in the bloodstream to decrease by half. Plasma concentrations of capmatinib were measured using validated LCMS/MS methods with a LLOQ of approximately 1.0 ng/mL. Only a subset of participants from Cohorts 1a, 1b, 2, 3, 4, 5a and 5b, who had an extensive PK collection schedule, were included in this analysis
Time Frame	Cycle 1 Day 1 and Day 15 at pre-dose, 0.5, 1, 2, 4, 6 and 8 hours post-dose. Each Cycle is 21 days

Analysis Population Description	Participants from Cohorts 1a, 1b, 2, 3, 4, 5a and 5b who received at least one dose of capmatinib with extensive PK sampling collection and an evaluable PK parameter (T1/2 for capmatinib) at the specified time points. Participants received capmatinib under the same administration conditions (fasted state) and were pooled together for analysis

	Cohorts 1-5: Capmatinib administration in fasted state
Arm/Group Description	Participants from Cohorts 1a, 1b, 2, 3, 4, 5a and 5b who received capmatinib in fasted state
Number of Participants Analyzed [units: participants]	47
Elimination half-life (T1/2) of capmatinib (units: hour)	**Mean ± Standard Deviation**
Cycle 1 Day 1	1.87 ± 0.947
Cycle 1 Day 15	2.40 ± 0.652

Elimination half-life (T1/2) of CMN288

Description	T1/2 of CMN288 (metabolite of capmatinib) was estimated by non-compartmental analysis. T1/2 is the time it takes for the concentration of CMN288 in the bloodstream to decrease by half. Plasma concentrations of metabolite CMN288 were measured using validated LCMS/MS methods with a LLOQ of approximately 1.0 ng/mL. Only a subset of participants from Cohorts 1a, 1b, 2, 3, 4, 5a and 5b, who had an extensive PK collection schedule, were included in this analysis
Time Frame	Cycle 1 Day 1 and Day 15 at pre-dose, 0.5, 1, 2, 4, 6 and 8 hours post-dose. Each Cycle is 21 days
Analysis Population Description	Participants from Cohorts 1a, 1b, 2, 3, 4, 5a and 5b who received at least one dose of capmatinib with extensive PK sampling collection and an evaluable PK parameter (T1/2 for CMN288) at the specified time points. Participants received capmatinib under the same administration conditions (fasted state) and were pooled together for analysis

	Cohorts 1-5: Capmatinib administration in fasted state
Arm/Group Description	Participants from Cohorts 1a, 1b, 2, 3, 4, 5a and 5b who received capmatinib in fasted state
Number of Participants Analyzed [units: participants]	40
Elimination half-life (T1/2) of CMN288 (units: hour)	**Mean ± Standard Deviation**
Cycle 1 Day 1	3.14 ± 1.42

Cycle 1 Day 15	3.06 ± 0.949

Post-Hoc Outcome Result(s)

All collected deaths

Description	On-treatment deaths were collected from start of treatment to 30 days after last dose of treatment. Post-treatment efficacy/survival follow-up deaths were collected from 31 days after last dose of treatment until the end of the study. All deaths refer to the sum of on-treatment and post-treatment efficacy/survival follow-up deaths.
Time Frame	On-treatment: Up to approximately 5.5 years. Post-treatment efficacy/survival follow-up: Up to approximately 6 years
Analysis Population Description	FAS, including all subjects who received at least one dose of capmatinib

	Cohort 1a: Pre-treated patients with MET GCN ≥ 10 (2/3L)	Cohort 1b: Pre-treated patients with MET GCN ≥ 6 and < 10 (2/3L)	Cohort 2: Pre-treated patients with MET GCN ≥ 4 and < 6 (2/3L)	Cohort 3: Pre-treated patients with MET GCN < 4 (2/3L)	Cohort 4: Pre-treated patients with MET mutation regardless of MET GCN (2/3L)	Cohort 5a: Treatment-naïve patients with MET GCN ≥10 (1L)	Cohort 5b: Treatment-naïve patients with MET mutation regardless of MET GCN (1L)	Cohort 6.1 (expansion of Cohort 1a): Pre-treated patients MET GCN ≥ 10 without MET mutation (2L)	Cohort 6.2 (expansion of Cohort 4): Pre-treated patients with MET mutation (2L)	Cohort 7 (expansion of Cohort 5b): Treatment-naïve with MET mutation regardless of MET GCN (1L)	Cohort 4 + Cohort 6.2: All pre-treated patients with MET mutation regardless of MET GCN (2/3L)	Cohort 5b + Cohort 7: All treatment-naive with MET mutation regardless of MET GCN (1L)	All patients
Arm/Group Description	Pre-treated patients with MET GCN ≥ 10 treated with INC280 at 400mg BID as	Pre-treated patients with MET GCN ≥ 6 and < 10 treated with INC280 at 400 mg BID	Pre-treated patients with MET GCN ≥ 4 and < 6 treated with INC280 at 400mg	Pre-treated patients with MET GCN < 4 treated with INC280 at 400mg BID as	Pre-treated patients with MET mutation regardless of MET GCN treated with INC280 at 400mg BID as second	Treatment-naïve patients with MET GCN ≥10 treated with INC280 at 400mg BID as first-line (1L)	Treatment-naïve patients with MET mutation regardless of MET GCN treated with INC280 at 400mg BID	Pre-treated patients with MET GCN ≥ 10 without MET mutation treated with INC280 at 400 mg BID as second line (2L) (expansion	Pre-treated patients with MET mutation regardless of MET GCN treated with INC280 at 400 mg BID as second line (2L)(expansion of Cohort 4)	Treatment-naïve patients with MET mutation regardless of MET GCN treated with INC280 at 400mg BID as first line (1L)	All pre-treated patients with MET mutation regardless of MET GCN treated with INC280 at 400mg BID as second or third line	All treatment naive patients with MET mutation regardless of MET GCN treated with INC280 at 400 mg BID as first line	All patients

	second or third line (2/3L)	as second or third line (2/3L)	BID as second or third line (2/3L)	second or third line (2/3L)	or third line (2/3L)		as first line (1L)	cohort of Cohort 1a)		(expansion cohort of Cohort 5b)	(2/3L). (Participants from Cohort 4 and Cohort 6.2)	(1L) (Participants from Cohort 5b and Cohort 7)	
Number of Participants Analyzed [units: participants]	69	42	54	30	69	15	28	3	31	32	199	60	373
All collected deaths (units: Participants)													
On-treatment	10	7	12	4	14	0	5	1	5	5	19	10	63
Post-treatment efficacy/survival follow-up	44	26	34	22	44	13	13	2	17	16	61	29	231
All deaths	54	33	46	26	58	13	18	3	22	21	80	39	294

Safety Results

All-Cause Mortality

Time Frame

Deaths were collected from first dose of study treatment to 30 days after last dose of study medication (on-treatment), up to approximately 5.5 years.

Deaths were also collected in the post treatment efficacy/survival follow-up from 31 days after last dose of study medication until the end of the study, up to approximately 6 years.

Additional Description	Deaths in the post-treatment efficacy/survival follow-up are not counted as AEs. The total number at risk in the post-treatment efficacy/survival includes patients who entered the post-treatment efficacy and/or survival follow-up periods
Source Vocabulary for Table Default	MedDRA (26.0)
Collection Approach for Table Default	Systematic Assessment

On-Treatment

	Cohort 1a: On-treatment N = 69	**Cohort 1b: On-treatment N = 42**	**Cohort 2: On-treatment N = 54**	**Cohort 3: On-treatment N = 30**	**Cohort 4: On-treatment N = 69**	**Cohort 5a: On-treatment N = 15**	**Cohort 5b: On-treatment N = 28**	**Cohort 6.1: On-treatment N = 3**	**Cohort 6.2: On-treatment N = 31**	**Cohort 7: On-treatment N = 32**	**Cohort 4 + Cohort 6.2: On-treatment N = 100**	**Cohort 5b + Cohort 7: On-treatment N = 60**	**All patients: On-treatment N = 373**
Arm/Group Description	AEs collected during on-treatment period (up to 30 days post-treatment)	AEs collected during on-treatment period (up to 30 days post-treatment)	AEs collected during on-treatment period (up to 30 days post-treatment)	AEs collected during on-treatment period (up to 30 days post-treatment)	AEs collected during on-treatment period (up to 30 days post-treatment)	AEs collected during on-treatment period (up to 30 days post-treatment)	AEs collected during on-treatment period (up to 30 days post-treatment)	AEs collected during on-treatment period (up to 30 days post-treatment)	AEs collected during on-treatment period (up to 30 days post-treatment)	AEs collected during on-treatment period (up to 30 days post-treatment)	AEs collected during on-treatment period (up to 30 days post-treatment)	AEs collected during on-treatment period (up to 30 days post-treatment)	AEs collected during on-treatment period (up to 30 days post-treatment)
Total Number Affected	10	7	12	4	14	0	5	1	5	5	19	10	63
Total Number At Risk	69	42	54	30	69	15	28	3	31	32	100	60	373

Post-treatment efficacy/survival follow-up

	Cohort 1a: Post-treatment efficacy/ survival follow-up N = 60	Cohort 1b: Post-treatment efficacy/ survival follow-up N = 40	Cohort 2: Post-treatment efficacy/ survival follow-up N = 50	Cohort 3: Post-treatment efficacy/ survival follow-up N = 25	Cohort 4: Post-treatment efficacy/ survival follow-up N = 57	Cohort 5a: Post-treatment efficacy/ survival follow-up N = 15	Cohort 5b: Post-treatment efficacy/ survival follow-up N = 20	Cohort 6.1: Post-treatment efficacy/ survival follow-up N = 2	Cohort 6.2: Post-treatment efficacy/ survival follow-up N = 20	Cohort 7: Post-treatment efficacy/ survival follow-up N = 23	Cohort 4 + Cohort 6.2: Post-treatment efficacy/ survival follow-up N = 77	Cohort 5b + Cohort 7: Post-treatment efficacy/ survival follow-up N = 43	All patients: Post-treatment efficacy/ survival follow-up N = 312
Arm/ Group Description	Deaths collected in the post-treatment efficacy/ survival follow-up period (starting from day 31 post-treatment). No AEs were collected during this period	Deaths collected in the post-treatment efficacy/ survival follow-up period (starting from day 31 post-treatment). No AEs were collected during this period	Deaths collected in the post-treatment efficacy/ survival follow-up period (starting from day 31 post-treatment). No AEs were collected during this period	Deaths collected in the post-treatment efficacy/ survival follow-up period (starting from day 31 post-treatment). No AEs were collected during this period	Deaths collected in the post-treatment efficacy/ survival follow-up period (starting from day 31 post-treatment). No AEs were collected during this period	Deaths collected in the post-treatment efficacy/ survival follow-up period (starting from day 31 post-treatment). No AEs were collected during this period	Deaths collected in the post-treatment efficacy/ survival follow-up period (starting from day 31 post-treatment). No AEs were collected during this period	Deaths collected in the post-treatment efficacy/ survival follow-up period (starting from day 31 post-treatment). No AEs were collected during this period	Deaths collected in the post-treatment efficacy/ survival follow-up period (starting from day 31 post-treatment). No AEs were collected during this period	Deaths collected in the post-treatment efficacy/ survival follow-up period (starting from day 31 post-treatment). No AEs were collected during this period	Deaths collected in the post-treatment efficacy/ survival follow-up period (starting from day 31 post-treatment). No AEs were collected during this period	Deaths collected in the post-treatment efficacy/ survival follow-up period (starting from day 31 post-treatment). No AEs were collected during this period	Deaths collected in the post-treatment efficacy/ survival follow-up period (starting from day 31 post-treatment). No AEs were collected during this period
Total Number Affected	44	26	34	22	44	13	13	2	17	16	61	29	231
Total Number At Risk	59	35	42	25	55	15	20	2	20	23	75	43	296

Serious Adverse Events by System Organ Class

Time Frame	Serious adverse events (SAEs) were collected from first dose of study treatment to 30 days after last dose of study medication (on-treatment), up to approximately 5.5 years.
Source Vocabulary for Table Default	MedDRA (26.0)

Collection Approach for Table Default Systematic Assessment

On-treatment

Arm/Group Description	Cohort 1a: On-treatment N = 69	Cohort 1b: On-treatment N = 42	Cohort 2: On-treatment N = 54	Cohort 3: On-treatment N = 30	Cohort 4: On-treatment N = 69	Cohort 5a: On-treatment N = 15	Cohort 5b: On-treatment N = 28	Cohort 6.1: On-treatment N = 3	Cohort 6.2: On-treatment N = 31	Cohort 7: On-treatment N = 32	Cohort 4 + Cohort 6.2: On-treatment N = 100	Cohort 5b + Cohort 7: On-treatment N = 60	All patients: On-treatment N = 373
	AEs collected during on-treatment period (up to 30 days post-treatment)	AEs collected during on-treatment period (up to 30 days post-treatment)	AEs collected during on-treatment period (up to 30 days post-treatment)	AEs collected during on-treatment period (up to 30 days post-treatment)	AEs collected during on-treatment period (up to 30 days post-treatment)	AEs collected during on-treatment period (up to 30 days post-treatment)	AEs collected during on-treatment period (up to 30 days post-treatment)	AEs collected during on-treatment period (up to 30 days post-treatment)	AEs collected during on-treatment period (up to 30 days post-treatment)	AEs collected during on-treatment period (up to 30 days post-treatment)	AEs collected during on-treatment period (up to 30 days post-treatment)	AEs collected during on-treatment period (up to 30 days post-treatment)	AEs collected during on-treatment period (up to 30 days post-treatment)
Total # Affected by any Serious Adverse Event	42	21	30	15	38	9	14	2	14	17	52	31	202
Total # at Risk by any Serious Adverse Event	69	42	54	30	69	15	28	3	31	32	100	60	373
Blood and lymphatic system disorders													
Anaemia	1 (1.45%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.27%)
Febrile neutropenia	0 (0.00%)	0 (0.00%)	1 (1.85%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.27%)
Thrombocytopenia	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (3.23%)	1 (3.13%)	1 (1.00%)	1 (1.67%)	2 (0.54%)
Cardiac disorders													

Atrial fibrillation	0 (0.00%)	0 (0.00%)	1 (1.85%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (3.57%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.67%)	2 (0.54%)
Cardiac arrest	0 (0.00%)	0 (0.00%)	1 (1.85%)	1 (3.33%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (0.54%)
Cardiac failure	2 (2.90%)	0 (0.00%)	1 (1.85%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (3.57%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.67%)	4 (1.07%)
Cardiopulmonary failure	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (3.13%)	0 (0.00%)	1 (1.67%)	1 (0.27%)
Coronary artery disease	0 (0.00%)	0 (0.00%)	1 (1.85%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.27%)
Myocardial infarction	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (6.67%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.27%)
Pericardial effusion	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (3.23%)	0 (0.00%)	1 (1.00%)	0 (0.00%)	1 (0.27%)
Supraventricular tachycardia	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.45%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.00%)	0 (0.00%)	1 (0.27%)
Tachycardia	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.45%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.00%)	0 (0.00%)	1 (0.27%)
Congenital, familial and genetic disorders													
Spinal muscular atrophy	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (3.57%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.67%)	1 (0.27%)
Ear and labyrinth disorders													
Hypoacusis	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.45%)	0 (0.00%)	1 (3.57%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.00%)	1 (1.67%)	2 (0.54%)
Vertigo	0 (0.00%)	0 (0.00%)	1 (1.85%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.27%)
Endocrine disorders													
Inappropriate antidiuretic hormone secretion	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.45%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.00%)	0 (0.00%)	1 (0.27%)
Primary adrenal insufficiency	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (6.67%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.27%)

Gastrointestinal disorders													
Abdominal pain	1 (1.45%)	2 (4.76%)	2 (3.70%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (3.23%)	0 (0.00%)	1 (1.00%)	0 (0.00%)	6 (1.61%)
Abdominal pain upper	1 (1.45%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.27%)
Anal prolapse	0 (0.00%)	0 (0.00%)	1 (1.85%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.27%)
Ascites	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (3.13%)	0 (0.00%)	1 (1.67%)	1 (0.27%)
Constipation	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.45%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.00%)	0 (0.00%)	1 (0.27%)
Diarrhoea	1 (1.45%)	0 (0.00%)	0 (0.00%)	1 (3.33%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (3.23%)	0 (0.00%)	1 (1.00%)	0 (0.00%)	3 (0.80%)
Duodenal stenosis	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (3.33%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.27%)
Duodenitis	1 (1.45%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.27%)
Dysphagia	2 (2.90%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.45%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.00%)	0 (0.00%)	3 (0.80%)
Intestinal obstruction	1 (1.45%)	0 (0.00%)	2 (3.70%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	3 (0.80%)
Intestinal polyp	0 (0.00%)	0 (0.00%)	1 (1.85%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.27%)
Nausea	3 (4.35%)	3 (7.14%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (3.23%)	0 (0.00%)	1 (1.00%)	0 (0.00%)	7 (1.88%)
Oesophageal stenosis	1 (1.45%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.27%)
Pancreatitis acute	1 (1.45%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.27%)
Stomatitis	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (3.57%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.67%)	1 (0.27%)
Vomiting	4 (5.80%)	2 (4.76%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (6.67%)	0 (0.00%)	0 (0.00%)	1 (3.23%)	1 (3.13%)	1 (1.00%)	1 (1.67%)	9 (2.41%)
General disorders and administration site conditions													
Asthenia	3 (4.35%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	3 (0.80%)
Drug withdrawal syndrome	0 (0.00%)	0 (0.00%)	1 (1.85%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.27%)
Fatigue	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (3.13%)	0 (0.00%)	1 (1.67%)	1 (0.27%)

General physical health deterioration	3 (4.35%)	3 (7.14%)	2 (3.70%)	1 (3.33%)	1 (1.45%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (3.13%)	1 (1.00%)	1 (1.67%)	11 (2.95%)
Generalised oedema	1 (1.45%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.27%)
Malaise	0 (0.00%)	0 (0.00%)	1 (1.85%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (3.57%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.67%)	2 (0.54%)
Non-cardiac chest pain	2 (2.90%)	1 (2.38%)	0 (0.00%)	0 (0.00%)	1 (1.45%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.00%)	0 (0.00%)	4 (1.07%)
Oedema peripheral	2 (2.90%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (6.67%)	1 (3.57%)	0 (0.00%)	0 (0.00%)	2 (6.25%)	0 (0.00%)	3 (5.00%)	6 (1.61%)
Pain	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (3.33%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (3.23%)	0 (0.00%)	1 (1.00%)	0 (0.00%)	2 (0.54%)
Peripheral swelling	0 (0.00%)	0 (0.00%)	1 (1.85%)	0 (0.00%)	2 (2.90%)	1 (6.67%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (2.00%)	0 (0.00%)	4 (1.07%)
Pyrexia	2 (2.90%)	1 (2.38%)	0 (0.00%)	0 (0.00%)	1 (1.45%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (3.23%)	0 (0.00%)	2 (2.00%)	0 (0.00%)	5 (1.34%)
Stenosis	0 (0.00%)	1 (2.38%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.27%)
Vascular device occlusion	1 (1.45%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.27%)
Hepatobiliary disorders													
Drug-induced liver injury	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (3.57%)	0 (0.00%)	1 (3.23%)	0 (0.00%)	1 (1.00%)	1 (1.67%)	2 (0.54%)
Hepatic function abnormal	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.45%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.00%)	0 (0.00%)	1 (0.27%)
Hepatitis	1 (1.45%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.27%)
Hepatotoxicity	1 (1.45%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.27%)
Hyperbilirubinaemia	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (3.23%)	0 (0.00%)	1 (1.00%)	0 (0.00%)	1 (0.27%)
Infections and infestations													
Bronchitis	0 (0.00%)	0 (0.00%)	1 (1.85%)	1 (3.33%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (0.54%)
Cellulitis	1 (1.45%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	4 (5.80%)	0 (0.00%)	1 (3.57%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	4 (4.00%)	1 (1.67%)	6 (1.61%)
COVID-19	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (3.23%)	0 (0.00%)	1 (1.00%)	0 (0.00%)	1 (0.27%)

COVID-19 pneumonia	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (3.23%)	0 (0.00%)	1 (1.00%)	0 (0.00%)	1 (0.27%)
Device related infection	0 (0.00%)	0 (0.00%)	1 (1.85%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.27%)
Erysipelas	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (3.57%)	0 (0.00%)	0 (0.00%)	1 (3.13%)	0 (0.00%)	2 (3.33%)	2 (0.54%)
Haemophilus infection	0 (0.00%)	1 (2.38%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.27%)
Herpes zoster	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.45%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.00%)	0 (0.00%)	1 (0.27%)
Infection	0 (0.00%)	1 (2.38%)	1 (1.85%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (0.54%)
Infectious pleural effusion	0 (0.00%)	1 (2.38%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (3.23%)	0 (0.00%)	1 (1.00%)	0 (0.00%)	2 (0.54%)
Influenza	1 (1.45%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.27%)
Lung abscess	1 (1.45%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.27%)
Medical device site infection	1 (1.45%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.27%)
Pleural infection	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (6.67%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.27%)
Pneumonia	7 (10.14%)	4 (9.52%)	3 (5.56%)	1 (3.33%)	4 (5.80%)	0 (0.00%)	0 (0.00%)	1 (33.33%)	2 (6.45%)	1 (3.13%)	6 (6.00%)	1 (1.67%)	23 (6.17%)
Pneumonia aspiration	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (3.57%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.67%)	1 (0.27%)
Pneumonia bacterial	1 (1.45%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.27%)
Pneumonia influenzal	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.45%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.00%)	0 (0.00%)	1 (0.27%)
Pyelonephritis	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (2.90%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (2.00%)	0 (0.00%)	2 (0.54%)
Respiratory tract infection	1 (1.45%)	0 (0.00%)	2 (3.70%)	2 (6.67%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	5 (1.34%)
Sepsis	0 (0.00%)	1 (2.38%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.27%)
Septic shock	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.45%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.00%)	0 (0.00%)	1 (0.27%)
Urinary tract infection	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (6.67%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (0.54%)
Urosepsis	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (3.33%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.27%)

Injury, poisoning and procedural complications													
Accidental exposure to product	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.45%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.00%)	0 (0.00%)	1 (0.27%)
Femur fracture	1 (1.45%)	0 (0.00%)	1 (1.85%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (3.57%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.67%)	3 (0.80%)
Fracture displacement	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (3.23%)	0 (0.00%)	1 (1.00%)	0 (0.00%)	1 (0.27%)
Lower limb fracture	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.45%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.00%)	0 (0.00%)	1 (0.27%)
Radiation necrosis	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (6.67%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.27%)
Thoracic vertebral fracture	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (3.33%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.27%)
Toxicity to various agents	0 (0.00%)	0 (0.00%)	1 (1.85%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.27%)
Investigations													
Amylase increased	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (3.57%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.67%)	1 (0.27%)
Eastern Cooperative Oncology Group performance status worsened	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.45%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.00%)	0 (0.00%)	1 (0.27%)
General physical condition abnormal	0 (0.00%)	1 (2.38%)	1 (1.85%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (33.33%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	3 (0.80%)
Liver function test abnormal	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (3.33%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.27%)
Platelet count decreased	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (6.67%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.27%)

SARS-CoV-2 test positive	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.45%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.00%)	0 (0.00%)	1 (0.27%)
Troponin increased	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (6.67%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.27%)
Metabolism and nutrition disorders													
Decreased appetite	0 (0.00%)	1 (2.38%)	0 (0.00%)	0 (0.00%)	1 (1.45%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.00%)	0 (0.00%)	2 (0.54%)
Dehydration	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (6.45%)	1 (3.13%)	2 (2.00%)	1 (1.67%)	3 (0.80%)
Hyperkalaemia	1 (1.45%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.27%)
Hypokalaemia	0 (0.00%)	0 (0.00%)	1 (1.85%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.27%)
Hyponatraemia	2 (2.90%)	0 (0.00%)	1 (1.85%)	0 (0.00%)	0 (0.00%)	1 (6.67%)	1 (3.57%)	0 (0.00%)	0 (0.00%)	1 (3.13%)	0 (0.00%)	2 (3.33%)	6 (1.61%)
Musculoskeletal and connective tissue disorders													
Arthralgia	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (3.33%)	1 (1.45%)	1 (6.67%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (3.13%)	1 (1.00%)	1 (1.67%)	4 (1.07%)
Back pain	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (3.57%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.67%)	1 (0.27%)
Bone pain	1 (1.45%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (3.13%)	0 (0.00%)	1 (1.67%)	2 (0.54%)
Muscular weakness	1 (1.45%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.45%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (3.23%)	0 (0.00%)	2 (2.00%)	0 (0.00%)	3 (0.80%)
Musculoskeletal chest pain	0 (0.00%)	0 (0.00%)	1 (1.85%)	1 (3.33%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (0.54%)
Osteolysis	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.45%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.00%)	0 (0.00%)	1 (0.27%)
Pain in extremity	1 (1.45%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (6.67%)	1 (3.57%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.67%)	3 (0.80%)
Sacroiliitis	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (3.13%)	0 (0.00%)	1 (1.67%)	1 (0.27%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)													

Adenocarcinoma gastric	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (3.13%)	0 (0.00%)	1 (1.67%)	1 (0.27%)
Breast cancer	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (3.23%)	0 (0.00%)	1 (1.00%)	0 (0.00%)	1 (0.27%)
Cancer pain	0 (0.00%)	1 (2.38%)	0 (0.00%)	0 (0.00%)	1 (1.45%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.00%)	0 (0.00%)	2 (0.54%)
Rectal cancer	0 (0.00%)	0 (0.00%)	1 (1.85%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.27%)
Squamous cell carcinoma of skin	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (3.23%)	0 (0.00%)	1 (1.00%)	0 (0.00%)	1 (0.27%)
Tumour haemorrhage	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (3.33%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.27%)
Tumour pain	1 (1.45%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (3.13%)	0 (0.00%)	1 (1.67%)	2 (0.54%)
Nervous system disorders													
Aphasia	1 (1.45%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.27%)
Cerebral ischaemia	1 (1.45%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (6.67%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (0.54%)
Cerebral mass effect	1 (1.45%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.27%)
Cerebrovascular accident	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (3.13%)	0 (0.00%)	1 (1.67%)	1 (0.27%)
Epilepsy	1 (1.45%)	0 (0.00%)	1 (1.85%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (0.54%)
Headache	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.45%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.00%)	0 (0.00%)	1 (0.27%)
Hemiparesis	1 (1.45%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.27%)
Neurological symptom	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (6.67%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.27%)
Paraplegia	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.45%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.00%)	0 (0.00%)	1 (0.27%)
Seizure	2 (2.90%)	0 (0.00%)	1 (1.85%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	3 (0.80%)
Psychiatric disorders													
Agitation	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.45%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.00%)	0 (0.00%)	1 (0.27%)
Anxiety	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (3.13%)	0 (0.00%)	1 (1.67%)	1 (0.27%)
Confusional state	1 (1.45%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (3.13%)	0 (0.00%)	1 (1.67%)	2 (0.54%)

Disorientation	0 (0.00%)	0 (0.00%)	1 (1.85%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.27%)
Mental status changes	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (6.67%)	1 (3.57%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.67%)	2 (0.54%)
Organic brain syndrome	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (3.13%)	0 (0.00%)	1 (1.67%)	1 (0.27%)
Renal and urinary disorders													
Acute kidney injury	1 (1.45%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.27%)
Calculus urinary	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.45%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.00%)	0 (0.00%)	1 (0.27%)
Haematuria	0 (0.00%)	0 (0.00%)	1 (1.85%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.27%)
Renal failure	1 (1.45%)	1 (2.38%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (0.54%)
Renal infarct	0 (0.00%)	1 (2.38%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.27%)
Urinary retention	0 (0.00%)	0 (0.00%)	1 (1.85%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.27%)
Reproductive system and breast disorders													
Breast pain	1 (1.45%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.27%)
Genital prolapse	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.45%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.00%)	0 (0.00%)	1 (0.27%)
Pelvic pain	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (3.33%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.27%)
Scrotal oedema	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.45%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.00%)	0 (0.00%)	1 (0.27%)
Respiratory, thoracic and mediastinal disorders													
Acute respiratory failure	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.45%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.00%)	0 (0.00%)	1 (0.27%)
Aspiration	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (3.57%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.67%)	1 (0.27%)

Asthma	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.45%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.00%)	0 (0.00%)	1 (0.27%)
Chronic obstructive pulmonary disease	0 (0.00%)	0 (0.00%)	1 (1.85%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (3.57%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.67%)	2 (0.54%)
Cough	1 (1.45%)	0 (0.00%)	0 (0.00%)	1 (3.33%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (0.54%)
Dyspnoea	6 (8.70%)	4 (9.52%)	3 (5.56%)	2 (6.67%)	6 (8.70%)	1 (6.67%)	2 (7.14%)	0 (0.00%)	1 (3.23%)	1 (3.13%)	7 (7.00%)	3 (5.00%)	26 (6.97%)
Haemoptysis	1 (1.45%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (3.23%)	0 (0.00%)	1 (1.00%)	0 (0.00%)	2 (0.54%)
Interstitial lung disease	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.45%)	0 (0.00%)	1 (3.57%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.00%)	1 (1.67%)	2 (0.54%)
Organising pneumonia	0 (0.00%)	0 (0.00%)	1 (1.85%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (3.23%)	0 (0.00%)	1 (1.00%)	0 (0.00%)	2 (0.54%)
Pleural effusion	6 (8.70%)	1 (2.38%)	3 (5.56%)	0 (0.00%)	2 (2.90%)	1 (6.67%)	0 (0.00%)	0 (0.00%)	1 (3.23%)	2 (6.25%)	3 (3.00%)	2 (3.33%)	16 (4.29%)
Pleurisy	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (3.13%)	0 (0.00%)	1 (1.67%)	1 (0.27%)
Pleuritic pain	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.45%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.00%)	0 (0.00%)	1 (0.27%)
Pneumonitis	1 (1.45%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	3 (4.35%)	0 (0.00%)	1 (3.57%)	0 (0.00%)	0 (0.00%)	1 (3.13%)	3 (3.00%)	2 (3.33%)	6 (1.61%)
Pneumothorax	1 (1.45%)	1 (2.38%)	1 (1.85%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (3.23%)	0 (0.00%)	1 (1.00%)	0 (0.00%)	4 (1.07%)
Pulmonary embolism	0 (0.00%)	3 (7.14%)	1 (1.85%)	2 (6.67%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (3.13%)	0 (0.00%)	1 (1.67%)	7 (1.88%)
Pulmonary haemorrhage	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (3.23%)	0 (0.00%)	1 (1.00%)	0 (0.00%)	1 (0.27%)
Pulmonary venous thrombosis	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.45%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.00%)	0 (0.00%)	1 (0.27%)
Respiratory distress	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (3.57%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.67%)	1 (0.27%)
Respiratory failure	3 (4.35%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.45%)	0 (0.00%)	1 (3.57%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.00%)	1 (1.67%)	5 (1.34%)
Skin and subcutaneous tissue disorders													
Urticaria	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.45%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.00%)	0 (0.00%)	1 (0.27%)

Vascular disorders													
Embolism	1 (1.45%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.27%)
Hypertension	1 (1.45%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.27%)
Hypotension	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (3.13%)	0 (0.00%)	1 (1.67%)	1 (0.27%)
Jugular vein thrombosis	1 (1.45%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.27%)
Peripheral ischaemia	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (3.13%)	0 (0.00%)	1 (1.67%)	1 (0.27%)
Superior vena cava syndrome	1 (1.45%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.45%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.00%)	0 (0.00%)	2 (0.54%)
Thrombosis	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.45%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.00%)	0 (0.00%)	1 (0.27%)
Venous thrombosis	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (3.33%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.27%)

Other Adverse Events by System Organ Class

Time Frame	Non-serious adverse events (non-SAEs) were collected from first dose of study treatment to 30 days after last dose of study medication (on-treatment), up to approximately 5.5 years.
Source Vocabulary for Table Default	MedDRA (26.0)
Collection Approach for Table Default	Systematic Assessment

On-treatment

Frequent Event Reporting Threshold 5%

	Cohort 1a: On-treatment N = 69	Cohort 1b: On-treatment N = 42	Cohort 2: On-treatment N = 54	Cohort 3: On-treatment N = 30	Cohort 4: On-treatment N = 69	Cohort 5a: On-treatment N = 15	Cohort 5b: On-treatment N = 28	Cohort 6.1: On-treatment N = 3	Cohort 6.2: On-treatment N = 31	Cohort 7: On-treatment N = 32	Cohort 4 + Cohort 6.2: On-treatment N = 100	Cohort 5b + Cohort 7: On-treatment N = 60	All patients: On-treatment N = 373
Arm/Group Description	AEs collected during on-treatment period (up to 30 days post-treatment)	AEs collected during on-treatment period (up to 30 days post-treatment)	AEs collected during on-treatment period (up to 30 days post-treatment)	AEs collected during on-treatment period (up to 30 days post-treatment)	AEs collected during on-treatment period (up to 30 days post-treatment)	AEs collected during on-treatment period (up to 30 days post-treatment)	AEs collected during on-treatment period (up to 30 days post-treatment)	AEs collected during on-treatment period (up to 30 days post-treatment)	AEs collected during on-treatment period (up to 30 days post-treatment)	AEs collected during on-treatment period (up to 30 days post-treatment)	AEs collected during on-treatment period (up to 30 days post-treatment)	AEs collected during on-treatment period (up to 30 days post-treatment)	AEs collected during on-treatment period (up to 30 days post-treatment)
Total # Affected by any Other Adverse Event	66	41	53	28	66	15	28	3	29	31	95	59	360
Total # at Risk by any Other Adverse Event	69	42	54	30	69	15	28	3	31	32	100	60	373
Blood and lymphatic system disorders													
Anaemia	5 (7.25%)	2 (4.76%)	5 (9.26%)	6 (20.00%)	8 (11.59%)	1 (6.67%)	2 (7.14%)	0 (0.00%)	4 (12.90%)	2 (6.25%)	12 (12.00%)	4 (6.67%)	35 (9.38%)
Leukopenia	1 (1.45%)	0 (0.00%)	2 (3.70%)	1 (3.33%)	0 (0.00%)	1 (6.67%)	0 (0.00%)	0 (0.00%)	1 (3.23%)	0 (0.00%)	1 (1.00%)	0 (0.00%)	6 (1.61%)

Lymphopenia	0 (0.00%)	0 (0.00%)	1 (1.85%)	2 (6.67%)	1 (1.45%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (3.23%)	0 (0.00%)	2 (2.00%)	0 (0.00%)	5 (1.34%)
Neutropenia	2 (2.90%)	0 (0.00%)	1 (1.85%)	1 (3.33%)	1 (1.45%)	1 (6.67%)	2 (7.14%)	0 (0.00%)	1 (3.23%)	0 (0.00%)	2 (2.00%)	2 (3.33%)	9 (2.41%)
Thrombocytopenia	1 (1.45%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (2.90%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	3 (9.68%)	3 (9.38%)	5 (5.00%)	3 (5.00%)	9 (2.41%)
Cardiac disorders													
Atrial fibrillation	2 (2.90%)	0 (0.00%)	2 (3.70%)	0 (0.00%)	2 (2.90%)	1 (6.67%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (3.13%)	2 (2.00%)	1 (1.67%)	8 (2.14%)
Cardiac failure	0 (0.00%)	1 (2.38%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (6.25%)	0 (0.00%)	2 (3.33%)	3 (0.80%)
Palpitations	1 (1.45%)	1 (2.38%)	1 (1.85%)	0 (0.00%)	2 (2.90%)	1 (6.67%)	1 (3.57%)	0 (0.00%)	0 (0.00%)	2 (6.25%)	2 (2.00%)	3 (5.00%)	9 (2.41%)
Sinus bradycardia	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	4 (5.80%)	0 (0.00%)	1 (3.57%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	4 (4.00%)	1 (1.67%)	5 (1.34%)
Tachycardia	0 (0.00%)	3 (7.14%)	0 (0.00%)	0 (0.00%)	2 (2.90%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (2.00%)	0 (0.00%)	5 (1.34%)
Ear and labyrinth disorders													
Hypoacusis	2 (2.90%)	1 (2.38%)	1 (1.85%)	0 (0.00%)	3 (4.35%)	0 (0.00%)	2 (7.14%)	0 (0.00%)	0 (0.00%)	5 (15.63%)	3 (3.00%)	7 (11.67%)	14 (3.75%)
Tinnitus	1 (1.45%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	3 (10.71%)	0 (0.00%)	3 (9.68%)	1 (3.13%)	3 (3.00%)	4 (6.67%)	8 (2.14%)
Vertigo	2 (2.90%)	2 (4.76%)	2 (3.70%)	2 (6.67%)	5 (7.25%)	0 (0.00%)	1 (3.57%)	0 (0.00%)	1 (3.23%)	0 (0.00%)	6 (6.00%)	1 (1.67%)	15 (4.02%)
Endocrine disorders													
Hyperthyroidism	1 (1.45%)	3 (7.14%)	0 (0.00%)	0 (0.00%)	1 (1.45%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (6.25%)	1 (1.00%)	2 (3.33%)	7 (1.88%)
Gastrointestinal disorders													
Abdominal discomfort	1 (1.45%)	1 (2.38%)	0 (0.00%)	0 (0.00%)	2 (2.90%)	0 (0.00%)	0 (0.00%)	1 (33.33%)	0 (0.00%)	0 (0.00%)	2 (2.00%)	0 (0.00%)	5 (1.34%)

Abdominal pain	2 (2.90%)	3 (7.14%)	7 (12.96%)	1 (3.33%)	3 (4.35%)	0 (0.00%)	3 (10.71%)	0 (0.00%)	1 (3.23%)	3 (9.38%)	4 (4.00%)	6 (10.00%)	23 (6.17%)
Abdominal pain upper	4 (5.80%)	4 (9.52%)	2 (3.70%)	2 (6.67%)	5 (7.25%)	0 (0.00%)	5 (17.86%)	0 (0.00%)	2 (6.45%)	3 (9.38%)	7 (7.00%)	8 (13.33%)	27 (7.24%)
Abnormal faeces	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (6.67%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.27%)
Constipation	16 (23.19%)	9 (21.43%)	10 (18.52%)	7 (23.33%)	9 (13.04%)	6 (40.00%)	5 (17.86%)	1 (33.33%)	3 (9.68%)	3 (9.38%)	12 (12.00%)	8 (13.33%)	69 (18.50%)
Diarrhoea	18 (26.09%)	6 (14.29%)	7 (12.96%)	8 (26.67%)	13 (18.84%)	4 (26.67%)	5 (17.86%)	0 (0.00%)	5 (16.13%)	4 (12.50%)	18 (18.00%)	9 (15.00%)	70 (18.77%)
Dry mouth	0 (0.00%)	1 (2.38%)	0 (0.00%)	2 (6.67%)	0 (0.00%)	0 (0.00%)	1 (3.57%)	0 (0.00%)	1 (3.23%)	0 (0.00%)	1 (1.00%)	1 (1.67%)	5 (1.34%)
Dyspepsia	4 (5.80%)	3 (7.14%)	4 (7.41%)	3 (10.00%)	6 (8.70%)	0 (0.00%)	2 (7.14%)	1 (33.33%)	1 (3.23%)	2 (6.25%)	7 (7.00%)	4 (6.67%)	26 (6.97%)
Dysphagia	2 (2.90%)	4 (9.52%)	6 (11.11%)	1 (3.33%)	1 (1.45%)	2 (13.33%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (3.13%)	1 (1.00%)	1 (1.67%)	17 (4.56%)
Gastrooesophageal reflux disease	3 (4.35%)	1 (2.38%)	3 (5.56%)	0 (0.00%)	1 (1.45%)	0 (0.00%)	1 (3.57%)	0 (0.00%)	1 (3.23%)	2 (6.25%)	2 (2.00%)	3 (5.00%)	12 (3.22%)
Nausea	32 (46.38%)	16 (38.10%)	24 (44.44%)	15 (50.00%)	32 (46.38%)	9 (60.00%)	13 (46.43%)	2 (66.67%)	12 (38.71%)	15 (46.88%)	44 (44.00%)	28 (46.67%)	170 (45.58%)
Stomatitis	1 (1.45%)	0 (0.00%)	3 (5.56%)	0 (0.00%)	3 (4.35%)	1 (6.67%)	0 (0.00%)	0 (0.00%)	1 (3.23%)	2 (6.25%)	4 (4.00%)	2 (3.33%)	11 (2.95%)
Vomiting	22 (31.88%)	14 (33.33%)	12 (22.22%)	9 (30.00%)	19 (27.54%)	4 (26.67%)	7 (25.00%)	1 (33.33%)	8 (25.81%)	6 (18.75%)	27 (27.00%)	13 (21.67%)	102 (27.35%)
General disorders and administration site conditions													
Asthenia	6 (8.70%)	8 (19.05%)	11 (20.37%)	3 (10.00%)	6 (8.70%)	2 (13.33%)	4 (14.29%)	0 (0.00%)	3 (9.68%)	6 (18.75%)	9 (9.00%)	10 (16.67%)	49 (13.14%)
Chest discomfort	1 (1.45%)	1 (2.38%)	1 (1.85%)	0 (0.00%)	1 (1.45%)	1 (6.67%)	1 (3.57%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.00%)	1 (1.67%)	6 (1.61%)

Face oedema	1 (1.45%)	0 (0.00%)	1 (1.85%)	0 (0.00%)	4 (5.80%)	0 (0.00%)	2 (7.14%)	0 (0.00%)	1 (3.23%)	0 (0.00%)	5 (5.00%)	2 (3.33%)	9 (2.41%)
Fatigue	11 (15.94%)	10 (23.81%)	16 (29.63%)	6 (20.00%)	19 (27.54%)	2 (13.33%)	4 (14.29%)	1 (33.33%)	11 (35.48%)	6 (18.75%)	30 (30.00%)	10 (16.67%)	86 (23.06%)
Generalised oedema	0 (0.00%)	1 (2.38%)	0 (0.00%)	0 (0.00%)	1 (1.45%)	0 (0.00%)	1 (3.57%)	0 (0.00%)	1 (3.23%)	2 (6.25%)	2 (2.00%)	3 (5.00%)	6 (1.61%)
Malaise	2 (2.90%)	0 (0.00%)	1 (1.85%)	0 (0.00%)	3 (4.35%)	0 (0.00%)	2 (7.14%)	0 (0.00%)	1 (3.23%)	0 (0.00%)	4 (4.00%)	2 (3.33%)	9 (2.41%)
Non-cardiac chest pain	8 (11.59%)	5 (11.90%)	7 (12.96%)	1 (3.33%)	4 (5.80%)	3 (20.00%)	1 (3.57%)	0 (0.00%)	3 (9.68%)	0 (0.00%)	7 (7.00%)	1 (1.67%)	32 (8.58%)
Oedema	1 (1.45%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	4 (14.29%)	0 (0.00%)	0 (0.00%)	3 (9.38%)	0 (0.00%)	7 (11.67%)	8 (2.14%)
Oedema peripheral	34 (49.28%)	18 (42.86%)	24 (44.44%)	11 (36.67%)	38 (55.07%)	10 (66.67%)	21 (75.00%)	1 (33.33%)	23 (74.19%)	23 (71.88%)	61 (61.00%)	44 (73.33%)	203 (54.42%)
Pain	4 (5.80%)	0 (0.00%)	1 (1.85%)	1 (3.33%)	2 (2.90%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (3.13%)	2 (2.00%)	1 (1.67%)	9 (2.41%)
Peripheral swelling	1 (1.45%)	1 (2.38%)	1 (1.85%)	1 (3.33%)	1 (1.45%)	1 (6.67%)	1 (3.57%)	0 (0.00%)	0 (0.00%)	3 (9.38%)	1 (1.00%)	4 (6.67%)	10 (2.68%)
Pyrexia	8 (11.59%)	7 (16.67%)	8 (14.81%)	5 (16.67%)	9 (13.04%)	3 (20.00%)	2 (7.14%)	1 (33.33%)	2 (6.45%)	4 (12.50%)	11 (11.00%)	6 (10.00%)	49 (13.14%)
Hepatobiliary disorders													
Hepatic steatosis	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (6.67%)	0 (0.00%)	0 (0.00%)	1 (3.23%)	0 (0.00%)	1 (1.00%)	0 (0.00%)	2 (0.54%)
Immune system disorders													
Contrast media allergy	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (7.14%)	0 (0.00%)	0 (0.00%)	1 (3.13%)	0 (0.00%)	3 (5.00%)	3 (0.80%)
Infections and infestations													

Bronchitis	1 (1.45%)	1 (2.38%)	3 (5.56%)	0 (0.00%)	4 (5.80%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (3.23%)	0 (0.00%)	5 (5.00%)	0 (0.00%)	10 (2.68%)
Cellulitis	3 (4.35%)	0 (0.00%)	1 (1.85%)	0 (0.00%)	4 (5.80%)	0 (0.00%)	2 (7.14%)	0 (0.00%)	3 (9.68%)	0 (0.00%)	7 (7.00%)	2 (3.33%)	13 (3.49%)
COVID-19	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.45%)	0 (0.00%)	1 (3.57%)	0 (0.00%)	2 (6.45%)	3 (9.38%)	3 (3.00%)	4 (6.67%)	7 (1.88%)
Epididymitis	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (6.25%)	0 (0.00%)	2 (3.33%)	2 (0.54%)
Erysipelas	0 (0.00%)	0 (0.00%)	1 (1.85%)	0 (0.00%)	0 (0.00%)	1 (6.67%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (6.25%)	0 (0.00%)	2 (3.33%)	4 (1.07%)
Herpes zoster	1 (1.45%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (3.57%)	0 (0.00%)	2 (6.45%)	0 (0.00%)	2 (2.00%)	1 (1.67%)	4 (1.07%)
Influenza	0 (0.00%)	3 (7.14%)	1 (1.85%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (3.13%)	0 (0.00%)	1 (1.67%)	5 (1.34%)
Nasopharyngitis	7 (10.14%)	4 (9.52%)	1 (1.85%)	1 (3.33%)	3 (4.35%)	1 (6.67%)	2 (7.14%)	0 (0.00%)	3 (9.68%)	2 (6.25%)	6 (6.00%)	4 (6.67%)	24 (6.43%)
Oral candidiasis	0 (0.00%)	0 (0.00%)	3 (5.56%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (3.57%)	0 (0.00%)	0 (0.00%)	1 (3.13%)	0 (0.00%)	2 (3.33%)	5 (1.34%)
Pneumonia	6 (8.70%)	5 (11.90%)	1 (1.85%)	3 (10.00%)	5 (7.25%)	1 (6.67%)	2 (7.14%)	0 (0.00%)	2 (6.45%)	2 (6.25%)	7 (7.00%)	4 (6.67%)	27 (7.24%)
Pyuria	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (6.67%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.27%)
Rhinitis	0 (0.00%)	1 (2.38%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (6.67%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (0.54%)
Sepsis	0 (0.00%)	1 (2.38%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (6.67%)	0 (0.00%)	1 (33.33%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	3 (0.80%)
Staphylococcal infection	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (6.67%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.27%)
Upper respiratory tract infection	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (3.33%)	1 (1.45%)	0 (0.00%)	1 (3.57%)	1 (33.33%)	0 (0.00%)	1 (3.13%)	1 (1.00%)	2 (3.33%)	5 (1.34%)
Urinary tract infection	0 (0.00%)	1 (2.38%)	1 (1.85%)	0 (0.00%)	7 (10.14%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (6.45%)	2 (6.25%)	9 (9.00%)	2 (3.33%)	13 (3.49%)

Injury, poisoning and procedural complications													
Anastomotic ulcer	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (6.67%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.27%)
Face injury	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (6.67%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.27%)
Fall	1 (1.45%)	0 (0.00%)	1 (1.85%)	0 (0.00%)	2 (2.90%)	1 (6.67%)	2 (7.14%)	0 (0.00%)	2 (6.45%)	2 (6.25%)	4 (4.00%)	4 (6.67%)	11 (2.95%)
Head injury	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (6.67%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.27%)
Limb injury	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.45%)	0 (0.00%)	1 (3.57%)	0 (0.00%)	2 (6.45%)	0 (0.00%)	3 (3.00%)	1 (1.67%)	4 (1.07%)
Pelvic fracture	0 (0.00%)	0 (0.00%)	1 (1.85%)	0 (0.00%)	0 (0.00%)	1 (6.67%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (0.54%)
Spinal compression fracture	1 (1.45%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (13.33%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	3 (0.80%)
Investigations													
Alanine aminotransferase increased	13 (18.84%)	4 (9.52%)	5 (9.26%)	3 (10.00%)	9 (13.04%)	5 (33.33%)	4 (14.29%)	0 (0.00%)	7 (22.58%)	3 (9.38%)	16 (16.00%)	7 (11.67%)	53 (14.21%)
Amylase increased	9 (13.04%)	3 (7.14%)	2 (3.70%)	1 (3.33%)	7 (10.14%)	3 (20.00%)	2 (7.14%)	0 (0.00%)	4 (12.90%)	5 (15.63%)	11 (11.00%)	7 (11.67%)	36 (9.65%)
Aspartate aminotransferase increased	11 (15.94%)	2 (4.76%)	4 (7.41%)	3 (10.00%)	6 (8.70%)	5 (33.33%)	2 (7.14%)	0 (0.00%)	4 (12.90%)	2 (6.25%)	10 (10.00%)	4 (6.67%)	39 (10.46%)
Blood albumin decreased	3 (4.35%)	0 (0.00%)	1 (1.85%)	1 (3.33%)	5 (7.25%)	1 (6.67%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (6.25%)	5 (5.00%)	2 (3.33%)	13 (3.49%)
Blood alkaline	8 (11.59%)	1 (2.38%)	3 (5.56%)	0 (0.00%)	5 (7.25%)	1 (6.67%)	1 (3.57%)	0 (0.00%)	3 (9.68%)	3 (9.38%)	8 (8.00%)	4 (6.67%)	25 (6.70%)

phosphatase increased													
Blood bilirubin increased	3 (4.35%)	2 (4.76%)	1 (1.85%)	1 (3.33%)	1 (1.45%)	0 (0.00%)	2 (7.14%)	0 (0.00%)	1 (3.23%)	2 (6.25%)	2 (2.00%)	4 (6.67%)	13 (3.49%)
Blood creatinine increased	16 (23.19%)	8 (19.05%)	14 (25.93%)	5 (16.67%)	24 (34.78%)	3 (20.00%)	10 (35.71%)	1 (33.33%)	10 (32.26%)	12 (37.50%)	34 (34.00%)	22 (36.67%)	103 (27.61%)
Blood urine present	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (6.67%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.27%)
C-reactive protein increased	3 (4.35%)	2 (4.76%)	0 (0.00%)	1 (3.33%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (33.33%)	0 (0.00%)	2 (6.25%)	0 (0.00%)	2 (3.33%)	9 (2.41%)
Eastern Cooperative Oncology Group performance status worsened	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (6.67%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.27%)
Gamma-glutamyltransferase increased	9 (13.04%)	2 (4.76%)	5 (9.26%)	0 (0.00%)	3 (4.35%)	0 (0.00%)	2 (7.14%)	0 (0.00%)	3 (9.68%)	0 (0.00%)	6 (6.00%)	2 (3.33%)	24 (6.43%)
Lipase increased	5 (7.25%)	4 (9.52%)	1 (1.85%)	4 (13.33%)	7 (10.14%)	1 (6.67%)	5 (17.86%)	0 (0.00%)	3 (9.68%)	7 (21.88%)	10 (10.00%)	12 (20.00%)	37 (9.92%)
Liver function test abnormal	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (3.33%)	0 (0.00%)	1 (6.67%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (0.54%)
Liver function test increased	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.45%)	1 (6.67%)	1 (3.57%)	0 (0.00%)	0 (0.00%)	1 (3.13%)	1 (1.00%)	2 (3.33%)	4 (1.07%)
Lymphocyte count decreased	0 (0.00%)	0 (0.00%)	1 (1.85%)	0 (0.00%)	1 (1.45%)	0 (0.00%)	1 (3.57%)	0 (0.00%)	0 (0.00%)	2 (6.25%)	1 (1.00%)	3 (5.00%)	5 (1.34%)
Neutrophil count decreased	3 (4.35%)	0 (0.00%)	2 (3.70%)	1 (3.33%)	2 (2.90%)	1 (6.67%)	1 (3.57%)	0 (0.00%)	1 (3.23%)	3 (9.38%)	3 (3.00%)	4 (6.67%)	14 (3.75%)

Platelet count decreased	3 (4.35%)	0 (0.00%)	3 (5.56%)	1 (3.33%)	5 (7.25%)	1 (6.67%)	1 (3.57%)	1 (33.33%)	1 (3.23%)	1 (3.13%)	6 (6.00%)	2 (3.33%)	17 (4.56%)
Procalcitonin increased	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (33.33%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.27%)
Protein total decreased	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (6.45%)	1 (3.13%)	2 (2.00%)	1 (1.67%)	3 (0.80%)
Weight decreased	7 (10.14%)	4 (9.52%)	2 (3.70%)	4 (13.33%)	9 (13.04%)	3 (20.00%)	4 (14.29%)	1 (33.33%)	1 (3.23%)	6 (18.75%)	10 (10.00%)	10 (16.67%)	41 (10.99%)
Weight increased	7 (10.14%)	0 (0.00%)	2 (3.70%)	0 (0.00%)	4 (5.80%)	1 (6.67%)	3 (10.71%)	0 (0.00%)	2 (6.45%)	2 (6.25%)	6 (6.00%)	5 (8.33%)	21 (5.63%)
White blood cell count decreased	2 (2.90%)	0 (0.00%)	1 (1.85%)	1 (3.33%)	1 (1.45%)	1 (6.67%)	1 (3.57%)	0 (0.00%)	0 (0.00%)	1 (3.13%)	1 (1.00%)	2 (3.33%)	8 (2.14%)
Metabolism and nutrition disorders													
Decreased appetite	15 (21.74%)	6 (14.29%)	12 (22.22%)	8 (26.67%)	15 (21.74%)	4 (26.67%)	8 (28.57%)	0 (0.00%)	6 (19.35%)	6 (18.75%)	21 (21.00%)	14 (23.33%)	80 (21.45%)
Hypercalcaemia	1 (1.45%)	0 (0.00%)	3 (5.56%)	1 (3.33%)	1 (1.45%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.00%)	0 (0.00%)	6 (1.61%)
Hyperkalaemia	1 (1.45%)	1 (2.38%)	4 (7.41%)	1 (3.33%)	1 (1.45%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (3.13%)	1 (1.00%)	1 (1.67%)	9 (2.41%)
Hypoalbuminaemia	9 (13.04%)	4 (9.52%)	5 (9.26%)	0 (0.00%)	5 (7.25%)	1 (6.67%)	3 (10.71%)	0 (0.00%)	6 (19.35%)	5 (15.63%)	11 (11.00%)	8 (13.33%)	38 (10.19%)
Hypocalcaemia	1 (1.45%)	1 (2.38%)	0 (0.00%)	0 (0.00%)	5 (7.25%)	1 (6.67%)	3 (10.71%)	0 (0.00%)	4 (12.90%)	8 (25.00%)	9 (9.00%)	11 (18.33%)	23 (6.17%)
Hypokalaemia	5 (7.25%)	2 (4.76%)	2 (3.70%)	3 (10.00%)	3 (4.35%)	1 (6.67%)	1 (3.57%)	0 (0.00%)	2 (6.45%)	4 (12.50%)	5 (5.00%)	5 (8.33%)	23 (6.17%)
Hypomagnesaemia	2 (2.90%)	0 (0.00%)	1 (1.85%)	0 (0.00%)	1 (1.45%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (3.23%)	2 (6.25%)	2 (2.00%)	2 (3.33%)	7 (1.88%)
Hyponatraemia	1 (1.45%)	2 (4.76%)	3 (5.56%)	0 (0.00%)	3 (4.35%)	2 (13.33%)	1 (3.57%)	1 (33.33%)	0 (0.00%)	2 (6.25%)	3 (3.00%)	3 (5.00%)	15 (4.02%)
Hypophagia	0 (0.00%)	0 (0.00%)	1 (1.85%)	0 (0.00%)	0 (0.00%)	1 (6.67%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (0.54%)

Hypophosphataemia	9 (13.04%)	0 (0.00%)	1 (1.85%)	0 (0.00%)	3 (4.35%)	0 (0.00%)	3 (10.71%)	0 (0.00%)	4 (12.90%)	0 (0.00%)	7 (7.00%)	3 (5.00%)	20 (5.36%)
Musculoskeletal and connective tissue disorders													
Arthralgia	6 (8.70%)	3 (7.14%)	7 (12.96%)	0 (0.00%)	8 (11.59%)	3 (20.00%)	7 (25.00%)	1 (33.33%)	2 (6.45%)	2 (6.25%)	10 (10.00%)	9 (15.00%)	39 (10.46%)
Back pain	8 (11.59%)	7 (16.67%)	10 (18.52%)	2 (6.67%)	11 (15.94%)	2 (13.33%)	4 (14.29%)	1 (33.33%)	11 (35.48%)	7 (21.88%)	22 (22.00%)	11 (18.33%)	63 (16.89%)
Flank pain	0 (0.00%)	1 (2.38%)	0 (0.00%)	0 (0.00%)	1 (1.45%)	0 (0.00%)	1 (3.57%)	1 (33.33%)	1 (3.23%)	0 (0.00%)	2 (2.00%)	1 (1.67%)	5 (1.34%)
Joint swelling	0 (0.00%)	1 (2.38%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (6.67%)	2 (7.14%)	1 (33.33%)	1 (3.23%)	0 (0.00%)	1 (1.00%)	2 (3.33%)	6 (1.61%)
Muscle spasms	4 (5.80%)	6 (14.29%)	3 (5.56%)	1 (3.33%)	1 (1.45%)	3 (20.00%)	3 (10.71%)	0 (0.00%)	2 (6.45%)	3 (9.38%)	3 (3.00%)	6 (10.00%)	26 (6.97%)
Muscular weakness	1 (1.45%)	1 (2.38%)	1 (1.85%)	0 (0.00%)	1 (1.45%)	0 (0.00%)	1 (3.57%)	0 (0.00%)	3 (9.68%)	2 (6.25%)	4 (4.00%)	3 (5.00%)	10 (2.68%)
Musculoskeletal chest pain	2 (2.90%)	1 (2.38%)	3 (5.56%)	2 (6.67%)	6 (8.70%)	1 (6.67%)	1 (3.57%)	0 (0.00%)	1 (3.23%)	1 (3.13%)	7 (7.00%)	2 (3.33%)	18 (4.83%)
Musculoskeletal pain	3 (4.35%)	1 (2.38%)	1 (1.85%)	0 (0.00%)	1 (1.45%)	1 (6.67%)	2 (7.14%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.00%)	2 (3.33%)	9 (2.41%)
Myalgia	4 (5.80%)	3 (7.14%)	1 (1.85%)	1 (3.33%)	5 (7.25%)	2 (13.33%)	1 (3.57%)	0 (0.00%)	2 (6.45%)	0 (0.00%)	7 (7.00%)	1 (1.67%)	19 (5.09%)
Neck pain	0 (0.00%)	0 (0.00%)	1 (1.85%)	0 (0.00%)	4 (5.80%)	0 (0.00%)	1 (3.57%)	0 (0.00%)	1 (3.23%)	1 (3.13%)	5 (5.00%)	2 (3.33%)	8 (2.14%)
Pain in extremity	6 (8.70%)	2 (4.76%)	3 (5.56%)	1 (3.33%)	7 (10.14%)	1 (6.67%)	3 (10.71%)	0 (0.00%)	5 (16.13%)	3 (9.38%)	12 (12.00%)	6 (10.00%)	31 (8.31%)
Nervous system disorders													
Disturbance in attention	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (6.67%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.27%)

Dizziness	4 (5.80%)	5 (11.90%)	1 (1.85%)	2 (6.67%)	9 (13.04%)	2 (13.33%)	3 (10.71%)	1 (33.33%)	3 (9.68%)	4 (12.50%)	12 (12.00%)	7 (11.67%)	34 (9.12%)
Dysarthria	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (6.67%)	0 (0.00%)	0 (0.00%)	1 (3.23%)	0 (0.00%)	1 (1.00%)	0 (0.00%)	2 (0.54%)
Dysgeusia	3 (4.35%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (3.57%)	0 (0.00%)	0 (0.00%)	2 (6.25%)	0 (0.00%)	3 (5.00%)	6 (1.61%)
Headache	6 (8.70%)	4 (9.52%)	3 (5.56%)	2 (6.67%)	9 (13.04%)	1 (6.67%)	2 (7.14%)	0 (0.00%)	2 (6.45%)	1 (3.13%)	11 (11.00%)	3 (5.00%)	30 (8.04%)
Hypoaesthesia	1 (1.45%)	1 (2.38%)	0 (0.00%)	1 (3.33%)	2 (2.90%)	1 (6.67%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (2.00%)	0 (0.00%)	6 (1.61%)
Neuropathy peripheral	1 (1.45%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (2.90%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	3 (9.38%)	2 (2.00%)	3 (5.00%)	6 (1.61%)
Paraesthesia	1 (1.45%)	3 (7.14%)	2 (3.70%)	0 (0.00%)	3 (4.35%)	0 (0.00%)	1 (3.57%)	0 (0.00%)	3 (9.68%)	2 (6.25%)	6 (6.00%)	3 (5.00%)	15 (4.02%)
Somnolence	2 (2.90%)	0 (0.00%)	1 (1.85%)	0 (0.00%)	1 (1.45%)	1 (6.67%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.00%)	0 (0.00%)	5 (1.34%)
Syncope	0 (0.00%)	1 (2.38%)	1 (1.85%)	0 (0.00%)	1 (1.45%)	0 (0.00%)	2 (7.14%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.00%)	2 (3.33%)	5 (1.34%)
Taste disorder	0 (0.00%)	0 (0.00%)	1 (1.85%)	0 (0.00%)	1 (1.45%)	1 (6.67%)	0 (0.00%)	0 (0.00%)	1 (3.23%)	1 (3.13%)	2 (2.00%)	1 (1.67%)	5 (1.34%)
Tremor	0 (0.00%)	2 (4.76%)	2 (3.70%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (6.45%)	0 (0.00%)	2 (2.00%)	0 (0.00%)	6 (1.61%)
Psychiatric disorders													
Anxiety	0 (0.00%)	3 (7.14%)	4 (7.41%)	0 (0.00%)	3 (4.35%)	1 (6.67%)	2 (7.14%)	0 (0.00%)	1 (3.23%)	1 (3.13%)	4 (4.00%)	3 (5.00%)	15 (4.02%)
Confusional state	2 (2.90%)	0 (0.00%)	0 (0.00%)	1 (3.33%)	0 (0.00%)	1 (6.67%)	1 (3.57%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.67%)	5 (1.34%)
Depression	1 (1.45%)	1 (2.38%)	2 (3.70%)	0 (0.00%)	3 (4.35%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	3 (9.68%)	2 (6.25%)	6 (6.00%)	2 (3.33%)	12 (3.22%)
Dysphoria	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (6.67%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.27%)
Insomnia	7 (10.14%)	3 (7.14%)	3 (5.56%)	1 (3.33%)	6 (8.70%)	0 (0.00%)	5 (17.86%)	0 (0.00%)	3 (9.68%)	6 (18.75%)	9 (9.00%)	11 (18.33%)	34 (9.12%)

Sleep disorder	1 (1.45%)	1 (2.38%)	1 (1.85%)	0 (0.00%)	0 (0.00%)	2 (13.33%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	5 (1.34%)
Renal and urinary disorders													
Dysuria	1 (1.45%)	0 (0.00%)	1 (1.85%)	0 (0.00%)	1 (1.45%)	0 (0.00%)	0 (0.00%)	1 (33.33%)	0 (0.00%)	0 (0.00%)	1 (1.00%)	0 (0.00%)	4 (1.07%)
Renal failure	1 (1.45%)	1 (2.38%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (6.67%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	3 (0.80%)
Reproductive system and breast disorders													
Breast pain	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (7.14%)	0 (0.00%)	1 (3.23%)	0 (0.00%)	1 (1.00%)	2 (3.33%)	3 (0.80%)
Breast swelling	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (6.67%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.27%)
Oedema genital	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (7.14%)	0 (0.00%)	0 (0.00%)	1 (3.13%)	0 (0.00%)	3 (5.00%)	3 (0.80%)
Respiratory, thoracic and mediastinal disorders													
Cough	9 (13.04%)	9 (21.43%)	9 (16.67%)	4 (13.33%)	11 (15.94%)	2 (13.33%)	7 (25.00%)	0 (0.00%)	7 (22.58%)	3 (9.38%)	18 (18.00%)	10 (16.67%)	61 (16.35%)
Dysphonia	4 (5.80%)	1 (2.38%)	0 (0.00%)	1 (3.33%)	2 (2.90%)	0 (0.00%)	1 (3.57%)	0 (0.00%)	2 (6.45%)	0 (0.00%)	4 (4.00%)	1 (1.67%)	11 (2.95%)
Dyspnoea	11 (15.94%)	15 (35.71%)	11 (20.37%)	5 (16.67%)	16 (23.19%)	5 (33.33%)	6 (21.43%)	2 (66.67%)	6 (19.35%)	6 (18.75%)	22 (22.00%)	12 (20.00%)	83 (22.25%)
Dyspnoea exertional	0 (0.00%)	0 (0.00%)	1 (1.85%)	1 (3.33%)	3 (4.35%)	1 (6.67%)	1 (3.57%)	0 (0.00%)	0 (0.00%)	1 (3.13%)	3 (3.00%)	2 (3.33%)	8 (2.14%)
Emphysema	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (6.67%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.27%)
Epistaxis	0 (0.00%)	1 (2.38%)	0 (0.00%)	1 (3.33%)	3 (4.35%)	2 (13.33%)	1 (3.57%)	0 (0.00%)	0 (0.00%)	3 (9.38%)	3 (3.00%)	4 (6.67%)	11 (2.95%)

Haemoptysis	3 (4.35%)	3 (7.14%)	3 (5.56%)	0 (0.00%)	1 (1.45%)	0 (0.00%)	1 (3.57%)	1 (33.33%)	3 (9.68%)	1 (3.13%)	4 (4.00%)	2 (3.33%)	16 (4.29%)
Hypoxia	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (2.90%)	0 (0.00%)	1 (3.57%)	0 (0.00%)	2 (6.45%)	0 (0.00%)	4 (4.00%)	1 (1.67%)	5 (1.34%)
Interstitial lung disease	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.45%)	1 (6.67%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.00%)	0 (0.00%)	2 (0.54%)
Oropharyngeal pain	1 (1.45%)	1 (2.38%)	1 (1.85%)	0 (0.00%)	1 (1.45%)	0 (0.00%)	0 (0.00%)	1 (33.33%)	3 (9.68%)	0 (0.00%)	4 (4.00%)	0 (0.00%)	8 (2.14%)
Pleural effusion	3 (4.35%)	4 (9.52%)	3 (5.56%)	0 (0.00%)	3 (4.35%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (6.45%)	2 (6.25%)	5 (5.00%)	2 (3.33%)	17 (4.56%)
Pleurisy	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.45%)	0 (0.00%)	1 (3.57%)	0 (0.00%)	1 (3.23%)	2 (6.25%)	2 (2.00%)	3 (5.00%)	5 (1.34%)
Pneumonitis	3 (4.35%)	0 (0.00%)	0 (0.00%)	1 (3.33%)	4 (5.80%)	0 (0.00%)	1 (3.57%)	1 (33.33%)	0 (0.00%)	1 (3.13%)	4 (4.00%)	2 (3.33%)	11 (2.95%)
Productive cough	3 (4.35%)	0 (0.00%)	2 (3.70%)	4 (13.33%)	4 (5.80%)	0 (0.00%)	3 (10.71%)	0 (0.00%)	1 (3.23%)	2 (6.25%)	5 (5.00%)	5 (8.33%)	19 (5.09%)
Pulmonary embolism	1 (1.45%)	4 (9.52%)	2 (3.70%)	0 (0.00%)	2 (2.90%)	2 (13.33%)	2 (7.14%)	0 (0.00%)	0 (0.00%)	2 (6.25%)	2 (2.00%)	4 (6.67%)	15 (4.02%)
Rhinitis allergic	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (3.57%)	0 (0.00%)	3 (9.68%)	1 (3.13%)	3 (3.00%)	2 (3.33%)	5 (1.34%)
Rhinorrhoea	1 (1.45%)	1 (2.38%)	0 (0.00%)	1 (3.33%)	2 (2.90%)	0 (0.00%)	1 (3.57%)	0 (0.00%)	2 (6.45%)	1 (3.13%)	4 (4.00%)	2 (3.33%)	9 (2.41%)
Skin and subcutaneous tissue disorders													
Alopecia	0 (0.00%)	3 (7.14%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (6.67%)	1 (3.57%)	0 (0.00%)	2 (6.45%)	3 (9.38%)	2 (2.00%)	4 (6.67%)	10 (2.68%)
Dermatitis acneiform	1 (1.45%)	0 (0.00%)	1 (1.85%)	0 (0.00%)	2 (2.90%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (3.23%)	2 (6.25%)	3 (3.00%)	2 (3.33%)	7 (1.88%)
Dry skin	9 (13.04%)	1 (2.38%)	2 (3.70%)	1 (3.33%)	2 (2.90%)	2 (13.33%)	0 (0.00%)	0 (0.00%)	1 (3.23%)	1 (3.13%)	3 (3.00%)	1 (1.67%)	19 (5.09%)
Eczema	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.45%)	0 (0.00%)	1 (3.57%)	0 (0.00%)	2 (6.45%)	0 (0.00%)	3 (3.00%)	1 (1.67%)	4 (1.07%)
Pruritus	7 (10.14%)	6 (14.29%)	3 (5.56%)	0 (0.00%)	10 (14.49%)	2 (13.33%)	2 (7.14%)	0 (0.00%)	3 (9.68%)	2 (6.25%)	13 (13.00%)	4 (6.67%)	35 (9.38%)

Pruritus allergic	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (6.67%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.27%)
Rash	3 (4.35%)	1 (2.38%)	4 (7.41%)	1 (3.33%)	6 (8.70%)	2 (13.33%)	0 (0.00%)	0 (0.00%)	4 (12.90%)	3 (9.38%)	10 (10.00%)	3 (5.00%)	24 (6.43%)
Rash maculo-papular	2 (2.90%)	0 (0.00%)	2 (3.70%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (6.45%)	0 (0.00%)	2 (2.00%)	0 (0.00%)	6 (1.61%)
Skin induration	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (6.67%)	0 (0.00%)	0 (0.00%)	1 (3.23%)	0 (0.00%)	1 (1.00%)	0 (0.00%)	2 (0.54%)
Skin lesion	0 (0.00%)	1 (2.38%)	0 (0.00%)	0 (0.00%)	1 (1.45%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (6.25%)	1 (1.00%)	2 (3.33%)	4 (1.07%)
Stasis dermatitis	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (6.67%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.27%)
Vascular disorders													
Deep vein thrombosis	0 (0.00%)	2 (4.76%)	2 (3.70%)	0 (0.00%)	1 (1.45%)	1 (6.67%)	0 (0.00%)	0 (0.00%)	1 (3.23%)	2 (6.25%)	2 (2.00%)	2 (3.33%)	9 (2.41%)
Embolism	1 (1.45%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.45%)	1 (6.67%)	0 (0.00%)	0 (0.00%)	1 (3.23%)	1 (3.13%)	2 (2.00%)	1 (1.67%)	5 (1.34%)
Hypertension	4 (5.80%)	0 (0.00%)	1 (1.85%)	1 (3.33%)	2 (2.90%)	1 (6.67%)	1 (3.57%)	0 (0.00%)	2 (6.45%)	1 (3.13%)	4 (4.00%)	2 (3.33%)	13 (3.49%)
Hypotension	4 (5.80%)	1 (2.38%)	2 (3.70%)	1 (3.33%)	5 (7.25%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (3.23%)	5 (15.63%)	6 (6.00%)	5 (8.33%)	19 (5.09%)
Superficial vein thrombosis	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (6.25%)	0 (0.00%)	2 (3.33%)	2 (0.54%)

Other Relevant Findings

None

Conclusion

Geometry mono-1 study results demonstrated consistent rapid, robust, durable and clinically meaningful efficacy (regardless of treatment setting) and long-term survival in the challenging to treat study population with advanced NSCLC and MET exon skipping mutation.

Capmatinib also showed activity in participants with MET-amplified advanced NSCLC and GCN≥10, however the primary endpoint was not met.

Long-term exposure to capmatinib treatment showed a consistent, manageable, predictable and well-tolerated safety profile in participants with advanced MET-mutated and MET amplified NSCLC, irrespective of prior lines of treatment.

This is especially noteworthy for the NSCLC population with MET exon 14 skipping mutation (relative to populations with other molecular drivers) that is typically older, frequently presenting with comorbidities and frailties in the context of their metastatic lung cancer. This has a considerable clinical relevance, as chemotherapy-based regimens maybe less tolerable and an oral targeted therapy could offer a favorable treatment alternative with sustained quality of life.

Overall, the efficacy and safety data reported demonstrates that capmatinib is a valuable targeted treatment option for subjects with advanced NSCLC and MET exon 14 skipping mutation.

Date of Clinical Trial Report

First interim CSR (data cut-off date 15-Apr-2019): 27-Aug-2019

Supplementary CSR (data cut-off date 28-Oct-2019): 13-Dec-2019

Second interim CSR (data cut-off date 28-Oct-2019): 13-Jul-2020

Supplementary CSR (data cut-off date 18-Sep-2020): 05-Mar-2021

Third interim CSR (data cut-off date 30-Aug-2021): 19-Jan-2022

Final CSR (data cut-off date 16-May-2023): 10-Nov-2023