NOVARTIS

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 cMET inhibitor INC280 in adult patients with EGFR wild-type (wt), advanced non-small cell lung cancer (NSCLC)

Clinical Trial Phase

Phase 2

Phase of Drug Development

Phase II

Study Start/End Dates

Study Start Date: June 2015 (Actual)
Primary Completion Date: February 2022 (Anticipated)
Study Completion Date: March 2023 (Anticipated)

Reason for Termination (If applicable)

Not applicable

Study Design/Methodology

This is a prospectively designed, multicenter, open-label, Phase II study to evaluate the efficacy and safety of single-agent capmatinib in subjects with Epidermal Growth Factor Receptor (EGFR) wt (for exon 19 deletions and exon 21 L858R substitution mutations), Anaplastic lymphoma kinase (ALK)-negative rearrangement, advanced/metastatic (stage IIIB or IV) NSCLC harboring mesenchymal epithelial transition (MET) mutation (*MET*ex14, detected by RT-PCR) and/or amplifications (detected by fluorescence in situ hybridization (FISH)).

Patients were enrolled in 9 separate cohorts depending on their MET status and prior lines of therapy (reference the tables below). METex14 mutation and/or MET amplification status (by GCN) was determined by central laboratory. Enrollment in METex14 cohorts was irrespective of concurrent MET amplification, whereas no concurrent METex14 mutation was permitted in MET-amplified cohorts. Patients in all groups received oral capmatinib 400 mg twice daily. A treatment cycle was defined as 21 days.

Centers

155 centers in 25 countries: Norway(1), Spain(11), Lebanon(3), Netherlands(4), Austria(1), United States(33), Russia(4), Singapore(2), France(11), Korea, Republic of(5), Japan(11), Israel(4), Germany(16), Italy(18), Argentina(4), Belgium(1), Canada(2), Turkey(2), Switzerland(1), United Kingdom(4), Taiwan(5), Brazil(5), Sweden(2), Mexico(2), Poland(3)

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, by cohort.

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

Other secondary objectives were:

- To evaluate ORR and DOR by investigator assessment, by cohort
- To evaluate time to response (TTR), disease control rate (DCR) and progression-free survival (PFS) by investigator and by BIRC assessment, by cohort
- To evaluate overall survival (OS), by cohort

- 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 proportion 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 provided by cohort.

Secondary endpoint analyses were performed based on the FAS, unless otherwise specified. No adjustments for multiple testing were made. Duration of response (DOR) was described in tabular and graphical format using Kaplan-Meier (KM) methodology.

Efficacy analyses were performed for each group separately. Efficacy analyses for Cohort 1a, Cohort 5a, Cohort 6 and Cohort 7 were not available at the time of data cut-off (15-Apr-2019) and will be conducted when the protocol criteria for the primary analysis are met. At the time of the data cutoff, enrollment in Cohort 7 had not yet started.

Study Population: Key Inclusion/Exclusion Criteria

Inclusion Criteria:
- Stage IIIB or IV NSCLC (any histology) at the time of study entry
- Histologically or cytologically confirmed diagnosis of NSCLC that is:
a. EGFR wt as per patient standard of care by a validated test
b. AND ALK-negative rearrangement as part of the patient standard of care by a validated test
c. AND (by central assessment) either:
• Cohort 1: Pre-treated patients with cMET GCN ≥ 6, including:
  -Sub-cohort 1a: Patients with cMET GCN of ≥10, or
  -Sub-cohort 1b: Patients with cMET GCN of ≥ 6 and < 10, or

• Cohort 2: Pre-treated patients with cMET GCN ≥4 and < 6, or
• Cohort 3: Pre-treated patients with cMET GCN < 4, or
• Cohort 4: Pre-treated patients with cMET mutations regardless of cMET GCN, or
• Cohort 5: Treatment-naïve patients with cMET dysregulation, including:
-Sub-cohort 5a: Patients with cMET GCN of ≥10, or
-Sub-cohort 5b: Patients with cMET mutations regardless of cMET GCN, or
• Cohort 6: Pre-treated patients with either cMET GCN ≥ 10 without cMET mutations or cMET mutations regardless of cMET GCN, or
• Cohort 7: Treatment-naïve patients with cMET mutations regardless of cMET GCN
- To be eligible for Cohorts 1-4, patients must have failed one or two prior lines of systemic therapy for advanced/metastatic disease
- To be eligible for Cohort 6, patients must have failed one prior line of systemic therapy for advanced/metastatic disease
- To be eligible for Cohort 5 and Cohort 7, patients must not have received any systemic therapy for advanced/metastatic disease
- At least one measurable lesion as defined by RECIST 1.1
- Patients must have recovered from all toxicities related to prior anticancer therapies to grade ≤ 1 (CTCAE v 4.03). Patients with any grade of alopecia are allowed to enter the study.
- Patients must have adequate organ function
- ECOG performance status (PS) of 0 or 1
Details and other protocol-defined inclusion criteria may apply

Exclusion Criteria:
- Prior treatment with crizotinib, or any other cMET or HGF inhibitor
- Patients with characterized EGFR mutations that predict sensitivity to EGFR therapy, including, but not limited to exon 19 deletions and exon 21 mutations
- Patients with characterized ALK-positive rearrangement
- Clinically significant, uncontrolled heart diseases.
- Patients receiving treatment with medications that cannot be discontinued at least 1 week prior to first INC280 treatment and for the duration of the study:
• Strong inducers of CYP3A4
- Impairment of GI function or GI disease that may significantly alter the absorption of INC280
- Patients receiving treatment with any enzyme-inducing anticonvulsant
- Applicable to Cohorts 1-4 and Cohort 6 only: Previous anti-cancer and investigational agents within 4 weeks or ≤ 5 x half-life of the agent (whichever is longer) before first dose
- Pregnant or nursing women
- Women of child-bearing potential, unless they are using highly effective methods of contraception
- Sexually active males unless they use a condom during intercourse
- Presence or history of interstitial lung disease or interstitial pneumonitis, including clinically significant radiation pneumonitis

Other protocol-defined exclusion criteria may apply

Participant Flow Table

Overall Study

	Cohort 1a: cMET GCN ≥ 10	Cohort 1b: cMET GCN ≥ 6 and < 10	Cohort 2: cMET GCN ≥ 4 and < 6	Cohort 3: cMET GCN < 4	Cohort 4: cMET mutations	Cohort 5a: Treatment-naïve with cMET GCN of ≥10	Cohort 5b: Treatment-naïve regardless of cMET GCN	Cohort 6: cMET dysregulation - second line	Cohort 7: cMET mutations treatment-naïve	Total
Arm/Group Description	Pre-treated patients with cMET GCN ≥ 10 treated with INC280 at 400mg BID as second or third line	Pre-treated patients with cMET GCN ≥ 6 and < 10 treated with INC280 at 400mg BID as second or third line	Pre-treated patients with cMET GCN ≥ 4 and < 6 treated with INC280 at 400 mg BID as second or third line	Pre-treated patients with cMET GCN < 4 treated with INC280 at 400mg BID as second or third line	Pre-treated patients with cMET mutations regardless of cMET GCN treated with INC280 at 400mg BID as second or third line	Treatment-naïve patients with cMET GCN of ≥10 treated with INC280 at 400mg BID	Treatment-naïve patients with cMET mutations regardless of cMET GCN treated with INC280 at 400mg BID	Pre-treated patients with either cMET GCN ≥ 10 without cMET mutations or cMET mutations regardless of cMET GCN treated with INC280 at 400 mg BID as second line	Treatment-naïve patients with cMET mutations regardless of cMET GCN treated with INC280 at 400mg BID	
Started	69	42	54	30	69	15	28	27	0	334
Completed	5	2	1	0	8	2	9	21	0	48
Not Completed	64	40	53	30	61	13	19	6	0	286
Adverse Event	11	4	8	5	14	3	6	1	0	52
Death	0	0	1	1	0	0	0	0	0	2
Physician Decision	4	4	5	1	5	0	2	1	0	22
Progressive disease	44	31	37	21	38	10	11	4	0	196

Protocol deviation	0	0	1	0	0	0	0	0	0	1
Subject/Guardian decision	5	1	1	2	4	0	0	0	0	13

Completed= Treatment ongoing at the time of the data cutoff, 15-Apr-2019

Baseline Characteristics

	Cohort 1a: cMET GCN ≥ 10	Cohort 1b: cMET GCN ≥ 6 and < 10	Cohort 2: cMET GCN ≥ 4 and < 6	Cohort 3: cMET GCN < 4	Cohort 4: cMET mutations	Cohort 5a: Treatment-naïve with cMET GCN of ≥10	Cohort 5b: Treatment-naïve regardless of cMET GCN	Cohort 6: cMET dysregulation - second line	Cohort 7: cMET mutations treatment-naïve	Total
Arm/Group Description	Pre-treated patients with cMET GCN ≥ 10 treated with INC280 at 400mg BID as second or third line	Pre-treated patients with cMET GCN ≥ 6 and < 10 treated with INC280 at 400mg BID as second or third line	Pre-treated patients with cMET GCN ≥ 4 and < 6 treated with INC280 at 400 mg BID as second or third line	Pre-treated patients with cMET GCN < 4 treated with INC280 at 400mg BID as second or third line	Pre-treated patients with cMET mutations regardless of cMET GCN treated with INC280 at 400mg BID as second or third line	Treatment-naïve patients with cMET GCN of ≥10 treated with INC280 at 400mg BID	Treatment-naïve patients with cMET mutations regardless of cMET GCN treated with INC280 at 400mg BID	Pre-treated patients with either cMET GCN ≥ 10 without cMET mutations or cMET mutations regardless of cMET GCN treated with INC280 at 400 mg BID as second line	Treatment-naïve patients with cMET mutations regardless of cMET GCN treated with INC280 at 400mg BID	
Number of Participants [units: participants]	69	42	54	30	69	15	28	27	0	334
Age Continuous (units: Years) Mean ± Standard Deviation										

	60.9±9.56	59.5±9.11	61.7±10.00	61.7±9.23	71.0±8.32	68.1±10.45	72.4±7.02	67.8±7.46		64.9±10.12
Sex: Female, Male (units: Participants) Count of Participants (Not Applicable)										
Female	15	21	15	11	40	4	18	13	0	137
Male	54	21	39	19	29	11	10	14	0	197
Race/Ethnicity, Customized (units: Participants) Count of Participants (Not Applicable)										
Asian	17	4	14	11	19	6	4	6	0	81
Black	1	0	0	0	0	0	0	1	0	2
Caucasian	51	38	40	19	49	9	24	18	0	248
Native American	0	0	0	0	1	0	0	1	0	2
Unknown	0	0	0	0	0	0	0	1	0	1

Summary of Efficacy

Primary Outcome Result(s)

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

(Time Frame: At least 18 weeks. Interim results presented with data cut-off date: 15-Apr-2019)

	Cohort 1b: cMET GCN ≥ 6 and < 10	Cohort 2: cMET GCN ≥ 4 and < 6	Cohort 3: cMET GCN < 4	Cohort 4: cMET mutations	Cohort 5b: Treatment-naïve regardless of cMET GCN
Arm/Group Description	Pre-treated patients with cMET GCN ≥ 6 and < 10 treated with INC280 at 400mg BID as second or third line	Pre-treated patients with cMET GCN ≥ 4 and < 6 treated with INC280 at 400 mg BID as second or third line	Pre-treated patients with cMET GCN < 4 treated with INC280 at 400mg BID as second or third line	Pre-treated patients with cMET mutations regardless of cMET GCN treated with INC280 at 400mg BID as second or third line	Treatment-naïve patients with cMET mutations regardless of cMET GCN treated with INC280 at 400mg BID
Number of Participants Analyzed [units: participants]	42	54	30	69	28
Overall Response Rate (ORR) by Blinded Independent Review Committee (BIRC) assessment (units: Percentage of Participants) Number (95% Confidence Interval)					
	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)	67.9 (47.6 to 84.1)

Secondary Outcome Result(s)

Duration of Response (DOR) by BIRC assessment

(Time Frame: At least 18 weeks. Interim results presented with data cut-off date: 15-Apr-2019. The DOR by BIRC assessment from a later data cut-off date (28-Oct-2019) for Cohorts 4 and 5b is presented in the approved prescribing information of capmatinib)

	Cohort 1b: cMET GCN ≥ 6 and < 10	Cohort 2: cMET GCN ≥ 4 and < 6	Cohort 3: cMET GCN < 4	Cohort 4: cMET mutations	Cohort 5b: Treatment-naïve regardless of cMET GCN
Arm/Group Description	Pre-treated patients with cMET GCN ≥ 6 and < 10 treated with INC280 at 400mg BID as second or third line	Pre-treated patients with cMET GCN ≥ 4 and < 6 treated with INC280 at 400 mg BID as second or third line	Pre-treated patients with cMET GCN < 4 treated with INC280 at 400mg BID as second or third line	Pre-treated patients with cMET mutations regardless of cMET GCN treated with INC280 at 400mg BID as second or third line	Treatment-naïve patients with cMET mutations regardless of cMET GCN treated with INC280 at 400mg BID
Number of Participants Analyzed [units: participants]	5	5	2	28	19
Duration of Response (DOR) by BIRC assessment (units: Months) Median (95% Confidence Interval)					
	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)	11.14 (5.55 to NA)[2]

[1] NA= The value was not estimable due to insufficient number of participants with events in Cohort 2 to enable estimation of the upper limit of the confidence interval.
[2] NA= The value was not estimable due to insufficient number of participants with events in Cohort 5b to enable estimation of the upper limit of the confidence interval.

ORR by investigator assessment

(Time Frame: At least 18 weeks. Interim results presented with data cut-off date: 15-Apr-2019)

	Cohort 1b: cMET GCN ≥ 6 and < 10	Cohort 2: cMET GCN ≥ 4 and < 6	Cohort 3: cMET GCN < 4	Cohort 4: cMET mutations	Cohort 5b: Treatment-naïve regardless of cMET GCN
Arm/Group Description	Pre-treated patients with cMET GCN ≥ 6 and < 10 treated with INC280 at 400mg BID as second or third line	Pre-treated patients with cMET GCN ≥ 4 and < 6 treated with INC280 at 400 mg BID as second or third line	Pre-treated patients with cMET GCN < 4 treated with INC280 at 400mg BID as second or third line	Pre-treated patients with cMET mutations regardless of cMET GCN treated with INC280 at 400mg BID as second or third line	Treatment-naïve patients with cMET mutations regardless of cMET GCN treated with INC280 at 400mg BID
Number of Participants Analyzed [units: participants]	42	54	30	69	28
ORR by investigator assessment (units: Percentage of participants) Number (95% Confidence Interval)					
	7.1 (1.5 to 19.5)	9.3 (3.1 to 20.3)	3.3 (0.1 to 17.2)	42.0 (30.2 to 54.5)	60.7 (40.6 to 78.5)

Duration of Response (DOR) by investigator assessment

(Time Frame: At least 18 weeks. Interim results presented with data cut-off date 15-Apr-2019.)

	Cohort 1b: cMET GCN ≥ 6 and < 10	Cohort 2: cMET GCN ≥ 4 and < 6	Cohort 3: cMET GCN < 4	Cohort 4: cMET mutations	Cohort 5b: Treatment-naïve regardless of cMET GCN
Arm/Group Description	Pre-treated patients with cMET GCN ≥ 6 and < 10 treated with INC280 at 400mg BID as second or third line	Pre-treated patients with cMET GCN ≥ 4 and < 6 treated with INC280 at 400 mg BID as second or third line	Pre-treated patients with cMET GCN < 4 treated with INC280 at 400mg BID as second or third line	Pre-treated patients with cMET mutations regardless of cMET GCN treated with INC280 at 400mg BID as second or third line	Treatment-naïve patients with cMET mutations regardless of cMET GCN treated with INC280 at 400mg BID
Number of Participants Analyzed [units: participants]	3	5	1	30	17
Duration of Response (DOR) by investigator assessment (units: Months) Median (95% Confidence Interval)					
	6.93 (5.75 to 8.34)	19.48 (2.83 to NA)[1]	6.93 (NA to NA)[2]	8.31 (4.34 to 12.06)	13.96 (4.27 to NA)[3]

[1] NA= The value was not estimable due to insufficient number of participants with events in Cohort 2 to enable estimation of the upper limit of the confidence interval.
[2] NA= The value was not estimable due to insufficient number of participants with events in Cohort 3 to enable estimation of the limits of the confidence interval.
[3] NA= The value was not estimable due to insufficient number of participants with events in Cohort 5b to enable estimation of the upper limit of the confidence interval.

Time to Response (TTR)

(Time Frame: at least 18 weeks)

	Cohort 1b: cMET GCN ≥ 6 and < 10	Cohort 2: cMET GCN ≥ 4 and < 6	Cohort 3: cMET GCN < 4	Cohort 4: cMET mutations	Cohort 5b: Treatment-naïve regardless of cMET GCN
Arm/Group Description	Pre-treated patients with cMET GCN ≥ 6 and < 10 treated with INC280 at 400mg BID as second or third line	Pre-treated patients with cMET GCN ≥ 4 and < 6 treated with INC280 at 400 mg BID as second or third line	Pre-treated patients with cMET GCN < 4 treated with INC280 at 400mg BID as second or third line	Pre-treated patients with cMET mutations regardless of cMET GCN treated with INC280 at 400mg BID as second or third line	Treatment-naïve patients with cMET mutations regardless of cMET GCN treated with INC280 at 400mg BID
Number of Participants Analyzed [units: participants]					
Time to Response (TTR) (units:) ()					

Disease Control Rate (DCR)

(Time Frame: at least 18 weeks)

	Cohort 1b: cMET GCN ≥ 6 and < 10	Cohort 2: cMET GCN ≥ 4 and < 6	Cohort 3: cMET GCN < 4	Cohort 4: cMET mutations	Cohort 5b: Treatment-naïve regardless of cMET GCN
Arm/Group Description	Pre-treated patients with cMET GCN ≥ 6 and < 10 treated with	Pre-treated patients with cMET GCN ≥ 4 and < 6 treated with INC280 at	Pre-treated patients with cMET GCN < 4 treated with INC280 at	Pre-treated patients with cMET mutations regardless of	Treatment-naïve patients with cMET mutations regardless of

	INC280 at 400mg BID as second or third line	400 mg BID as second or third line	400mg BID as second or third line	cMET GCN treated with INC280 at 400mg BID as second or third line	cMET GCN treated with INC280 at 400mg BID
Number of Participants Analyzed [units: participants]					
Disease Control Rate (DCR) (units:) ()					

Progression-free Survival (PFS)

(Time Frame: at least 18 weeks)

	Cohort 1b: cMET GCN ≥ 6 and < 10	**Cohort 2: cMET GCN ≥ 4 and < 6**	**Cohort 3: cMET GCN < 4**	**Cohort 4: cMET mutations**	**Cohort 5b: Treatment-naïve regardless of cMET GCN**
Arm/Group Description	Pre-treated patients with cMET GCN ≥ 6 and < 10 treated with INC280 at 400mg BID as second or third line	Pre-treated patients with cMET GCN ≥ 4 and < 6 treated with INC280 at 400 mg BID as second or third line	Pre-treated patients with cMET GCN < 4 treated with INC280 at 400mg BID as second or third line	Pre-treated patients with cMET mutations regardless of cMET GCN treated with INC280 at 400mg BID as second or third line	Treatment-naïve patients with cMET mutations regardless of cMET GCN treated with INC280 at 400mg BID

Number of Participants Analyzed [units: participants]					
Progression-free Survival (PFS) (units:) ()					

Overall Survival (OS)

(Time Frame: at least 18 weeks)

	Cohort 1b: cMET GCN ≥ 6 and < 10	Cohort 2: cMET GCN ≥ 4 and < 6	Cohort 3: cMET GCN < 4	Cohort 4: cMET mutations	Cohort 5b: Treatment-naïve regardless of cMET GCN
Arm/Group Description	Pre-treated patients with cMET GCN ≥ 6 and < 10 treated with INC280 at 400mg BID as second or third line	Pre-treated patients with cMET GCN ≥ 4 and < 6 treated with INC280 at 400 mg BID as second or third line	Pre-treated patients with cMET GCN < 4 treated with INC280 at 400mg BID as second or third line	Pre-treated patients with cMET mutations regardless of cMET GCN treated with INC280 at 400mg BID as second or third line	Treatment-naïve patients with cMET mutations regardless of cMET GCN treated with INC280 at 400mg BID
Number of Participants Analyzed [units: participants]					
Overall Survival (OS) (units:) ()					

Number of patients with incidence of adverse events and serious adverse events, change in vital signs, laboratory results (hematology, blood chemistry, and urinalysis) and ECG.
(Time Frame: at least 18 weeks)

	Cohort 1b: cMET GCN ≥ 6 and < 10	Cohort 2: cMET GCN ≥ 4 and < 6	Cohort 3: cMET GCN < 4	Cohort 4: cMET mutations	Cohort 5b: Treatment-naïve regardless of cMET GCN
Arm/Group Description	Pre-treated patients with cMET GCN ≥ 6 and < 10 treated with INC280 at 400mg BID as second or third line	Pre-treated patients with cMET GCN ≥ 4 and < 6 treated with INC280 at 400 mg BID as second or third line	Pre-treated patients with cMET GCN < 4 treated with INC280 at 400mg BID as second or third line	Pre-treated patients with cMET mutations regardless of cMET GCN treated with INC280 at 400mg BID as second or third line	Treatment-naïve patients with cMET mutations regardless of cMET GCN treated with INC280 at 400mg BID
Number of Participants Analyzed [units: participants]					
Number of patients with incidence of adverse events and serious adverse events, change in vital signs, laboratory results (hematology, blood chemistry, and urinalysis) and ECG. (units:) ()					

Cmax, Cmin and plasma concentration-time profiles of INC280

(Time Frame: 6 weeks)

	Cohort 1b: cMET GCN ≥ 6 and < 10	Cohort 2: cMET GCN ≥ 4 and < 6	Cohort 3: cMET GCN < 4	Cohort 4: cMET mutations	Cohort 5b: Treatment-naïve regardless of cMET GCN
Arm/Group Description	Pre-treated patients with cMET GCN ≥ 6 and < 10 treated with INC280 at 400mg BID as second or third line	Pre-treated patients with cMET GCN ≥ 4 and < 6 treated with INC280 at 400 mg BID as second or third line	Pre-treated patients with cMET GCN < 4 treated with INC280 at 400mg BID as second or third line	Pre-treated patients with cMET mutations regardless of cMET GCN treated with INC280 at 400mg BID as second or third line	Treatment-naïve patients with cMET mutations regardless of cMET GCN treated with INC280 at 400mg BID
Number of Participants Analyzed [units: participants]					
Cmax, Cmin and plasma concentration-time profiles of INC280 (units:) ()					

Summary of Safety

Safety Results

All-Cause Mortality

	Cohort 1a: cMET GCN ≥ 10 N = 69	Cohort 1b: cMET GCN ≥ 6 and < 10 N = 42	Cohort 2: cMET GCN ≥ 4 and < 6 N = 54	Cohort 3: cMET GCN < 4 N = 30	Cohort 4: cMET mutations N = 69	Cohort 5a: Treatment-naïve with cMET GCN of ≥10 N = 15	Cohort 5b: Treatment-naïve regardless of cMET GCN N = 28	Cohort 6: cMET dysregulation - second line N = 27	All patients N = 334
Arm/Group Description	Pre-treated patients with cMET GCN ≥ 10 treated with INC280 at 400mg BID as second or third line	Pre-treated patients with cMET GCN ≥ 6 and < 10 treated with INC280 at 400mg BID as second or third line	Pre-treated patients with cMET GCN ≥ 4 and < 6 treated with INC280 at 400 mg BID as second or third line	Pre-treated patients with cMET GCN < 4 treated with INC280 at 400mg BID as second or third line	Pre-treated patients with cMET mutations regardless of cMET GCN treated with INC280 at 400mg BID as second or third line	Treatment-naïve patients with cMET GCN of ≥10 treated with INC280 at 400mg BID	Treatment-naïve patients with cMET mutations regardless of cMET GCN treated with INC280 at 400mg BID	Pre-treated patients with either cMET GCN ≥ 10 without cMET mutations or cMET mutations regardless of cMET GCN treated with INC280 at 400 mg BID as second line	All patients
Total participants affected	10 (14.49%)	7 (16.67%)	12 (22.22%)	4 (13.33%)	13 (18.84%)	0 (0.00%)	5 (17.86%)	2 (7.41%)	53 (15.87%)

Serious Adverse Events by System Organ Class

Time Frame	Adverse Events are collected from First Patient First Visit (FPFV) until Last Patient Last Visit (LPLV). All Adverse Events reported in this record are from first dose of study treatment until data cutoff for interim analysis (15-Apr-2019).
Additional Description	Any sign or symptom that occurs during the study treatment until data cutoff for interim analysis (15-Apr-2019)

Source Vocabulary for Table Default	MedDRA (22.0)
Assessment Type for Table Default	Systematic Assessment

	Cohort 1a: cMET GCN ≥ 10 N = 69	**Cohort 1b: cMET GCN ≥ 6 and < 10 N = 42**	**Cohort 2: cMET GCN ≥ 4 and < 6 N = 54**	**Cohort 3: cMET GCN < 4 N = 30**	**Cohort 4: cMET mutations N = 69**	**Cohort 5a: Treatment-naïve with cMET GCN of ≥10 N = 15**	**Cohort 5b: Treatment-naïve regardless of cMET GCN N = 28**	**Cohort 6: cMET dysregulation - second line N = 27**	**All patients N = 334**
Arm/Group Description	Pre-treated patients with cMET GCN ≥ 10 treated with INC280 at 400mg BID as second or third line	Pre-treated patients with cMET GCN ≥ 6 and < 10 treated with INC280 at 400mg BID as second or third line	Pre-treated patients with cMET GCN ≥ 4 and < 6 treated with INC280 at 400 mg BID as second or third line	Pre-treated patients with cMET GCN < 4 treated with INC280 at 400mg BID as second or third line	Pre-treated patients with cMET mutations regardless of cMET GCN treated with INC280 at 400mg BID as second or third line	Treatment-naïve patients with cMET GCN of ≥10 treated with INC280 at 400mg BID	Treatment-naïve patients with cMET mutations regardless of cMET GCN treated with INC280 at 400mg BID	Pre-treated patients with either cMET GCN ≥ 10 without cMET mutations or cMET mutations regardless of cMET GCN treated with INC280 at 400 mg BID as second line	All patients
Total participants affected	41 (59.42%)	21 (50.00%)	30 (55.56%)	15 (50.00%)	35 (50.72%)	8 (53.33%)	13 (46.43%)	6 (22.22%)	169 (50.60%)
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%)	1 (0.30%)
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%)	1 (0.30%)
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%)	2 (0.60%)
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%)	2 (0.60%)
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%)	4 (1.20%)
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%)	1 (0.30%)
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%)	1 (0.30%)
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%)	1 (0.30%)
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%)	1 (0.30%)
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%)	2 (0.60%)
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%)	1 (0.30%)
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%)	1 (0.30%)
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%)	1 (0.30%)
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%)	1 (3.70%)	6 (1.80%)
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%)	1 (0.30%)
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%)	1 (0.30%)
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%)	1 (0.30%)
Diarrhoea	1 (1.45%)	0 (0.00%)	0 (0.00%)	1 (3.33%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (3.70%)	3 (0.90%)

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%)	1 (0.30%)
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%)	1 (0.30%)
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%)	3 (0.90%)
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%)	3 (0.90%)
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%)	1 (0.30%)
Nausea	3 (4.35%)	3 (7.14%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (3.70%)	7 (2.10%)
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%)	1 (0.30%)
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%)	1 (0.30%)
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%)	1 (0.30%)
Vomiting	4 (5.80%)	2 (4.76%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (6.67%)	0 (0.00%)	1 (3.70%)	8 (2.40%)
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%)	3 (0.90%)
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%)	1 (0.30%)
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%)	10 (2.99%)
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%)	1 (0.30%)
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%)	2 (0.60%)
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%)	4 (1.20%)
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%)	4 (1.20%)

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 (0.30%)
Peripheral swelling	0 (0.00%)	0 (0.00%)	1 (1.85%)	0 (0.00%)	1 (1.45%)	1 (6.67%)	0 (0.00%)	0 (0.00%)	3 (0.90%)
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%)	4 (1.20%)
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%)	1 (0.30%)
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 (0.30%)
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%)	1 (0.30%)
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%)	1 (0.30%)
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%)	1 (0.30%)
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%)	2 (0.60%)
Cellulitis	1 (1.45%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	4 (5.80%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	5 (1.50%)
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%)	1 (0.30%)
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%)	1 (0.30%)
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%)	1 (0.30%)
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%)	1 (0.30%)
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%)	2 (0.60%)
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 (0.30%)
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%)	1 (0.30%)
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%)	1 (0.30%)
Lung infection	1 (1.45%)	0 (0.00%)	1 (1.85%)	1 (3.33%)	1 (1.45%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	4 (1.20%)

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%)	1 (0.30%)
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%)	1 (0.30%)
Pneumonia	5 (7.25%)	4 (9.52%)	2 (3.70%)	0 (0.00%)	3 (4.35%)	0 (0.00%)	0 (0.00%)	2 (7.41%)	16 (4.79%)
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%)	1 (0.30%)
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%)	1 (0.30%)
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%)	2 (0.60%)
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%)	5 (1.50%)
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%)	1 (0.30%)
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%)	1 (0.30%)
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%)	2 (0.60%)
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%)	1 (0.30%)
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%)	1 (0.30%)
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%)	3 (0.90%)
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%)	1 (0.30%)
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%)	1 (0.30%)
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%)	1 (0.30%)
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%)	1 (0.30%)

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%)	1 (0.30%)
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%)	1 (0.30%)
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 (3.70%)	3 (0.90%)
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%)	1 (0.30%)
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%)	1 (0.30%)
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%)	1 (0.30%)
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%)	2 (0.60%)
Dehydration	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (3.70%)	1 (0.30%)
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%)	1 (0.30%)
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%)	1 (0.30%)
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%)	5 (1.50%)
Musculoskeletal and connective tissue disorders									
Arthralgia	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.45%)	1 (6.67%)	0 (0.00%)	0 (0.00%)	2 (0.60%)
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%)	1 (0.30%)

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%)	1 (0.30%)
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%)	2 (0.60%)
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%)	2 (0.60%)
Musculoskeletal pain	1 (1.45%)	0 (0.00%)	0 (0.00%)	1 (3.33%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (0.60%)
Neuropathic 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%)	1 (0.30%)
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%)	1 (0.30%)
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%)	3 (0.90%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)									
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%)	2 (0.60%)
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%)	1 (0.30%)
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%)	1 (0.30%)
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%)	1 (0.30%)
Brain midline shift	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 (0.30%)
Cerebral ischaemia	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 (0.30%)
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%)	2 (0.60%)
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%)	1 (0.30%)
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%)	1 (0.30%)

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%)	1 (0.30%)
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%)	1 (0.30%)
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%)	3 (0.90%)
Product issues									
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%)	1 (0.30%)
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%)	1 (0.30%)
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%)	1 (0.30%)
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%)	1 (0.30%)
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%)	2 (0.60%)
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%)	1 (0.30%)
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%)	1 (0.30%)
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%)	2 (0.60%)
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%)	1 (0.30%)
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%)	1 (0.30%)
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%)	1 (0.30%)
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%)	1 (0.30%)
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%)	1 (0.30%)
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%)	1 (0.30%)

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%)	1 (0.30%)
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%)	1 (0.30%)
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%)	1 (0.30%)
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%)	2 (0.60%)
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%)	2 (0.60%)
Dyspnoea	6 (8.70%)	4 (9.52%)	3 (5.56%)	2 (6.67%)	5 (7.25%)	1 (6.67%)	2 (7.14%)	0 (0.00%)	23 (6.89%)
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 (0.30%)
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%)	2 (0.60%)
Organising pneumonia	0 (0.00%)	0 (0.00%)	1 (1.85%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (3.70%)	2 (0.60%)
Pleural effusion	6 (8.70%)	1 (2.38%)	3 (5.56%)	0 (0.00%)	2 (2.90%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	12 (3.59%)
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%)	1 (0.30%)
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%)	1 (0.30%)
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%)	5 (1.50%)
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%)	3 (0.90%)
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%)	6 (1.80%)
Pulmonary haemorrhage	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (3.70%)	1 (0.30%)

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%)	1 (0.30%)
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%)	1 (0.30%)
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%)	5 (1.50%)
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%)	1 (0.30%)
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%)	1 (0.30%)
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%)	1 (0.30%)
Ischaemia	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 (0.30%)
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%)	1 (0.30%)
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%)	2 (0.60%)
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%)	1 (0.30%)

Other Adverse Events by System Organ Class

Time Frame	Adverse Events are collected from First Patient First Visit (FPFV) until Last Patient Last Visit (LPLV). All Adverse Events reported in this record are from first dose of study treatment until data cutoff for interim analysis (15-Apr-2019).
Additional Description	Any sign or symptom that occurs during the study treatment until data cutoff for interim analysis (15-Apr-2019)
Source Vocabulary for Table Default	MedDRA (22.0)

Assessment Type for Table Default	Systematic Assessment
Frequent Event Reporting Threshold	5%

	Cohort 1a: cMET GCN ≥ 10 N = 69	**Cohort 1b: cMET GCN ≥ 6 and < 10 N = 42**	**Cohort 2: cMET GCN ≥ 4 and < 6 N = 54**	**Cohort 3: cMET GCN < 4 N = 30**	**Cohort 4: cMET mutations N = 69**	**Cohort 5a: Treatment-naïve with cMET GCN of ≥10 N = 15**	**Cohort 5b: Treatment-naïve regardless of cMET GCN N = 28**	**Cohort 6: cMET dysregulation - second line N = 27**	**All patients N = 334**
Arm/Group Description	Pre-treated patients with cMET GCN ≥ 10 treated with INC280 at 400mg BID as second or third line	Pre-treated patients with cMET GCN ≥ 6 and < 10 treated with INC280 at 400mg BID as second or third line	Pre-treated patients with cMET GCN ≥ 4 and < 6 treated with INC280 at 400 mg BID as second or third line	Pre-treated patients with cMET GCN < 4 treated with INC280 at 400mg BID as second or third line	Pre-treated patients with cMET mutations regardless of cMET GCN treated with INC280 at 400mg BID as second or third line	Treatment-naïve patients with cMET GCN of ≥10 treated with INC280 at 400mg BID	Treatment-naïve patients with cMET mutations regardless of cMET GCN treated with INC280 at 400mg BID	Pre-treated patients with either cMET GCN ≥ 10 without cMET mutations or cMET mutations regardless of cMET GCN treated with INC280 at 400 mg BID as second line	All patients
Total participants affected	65 (94.20%)	41 (97.62%)	53 (98.15%)	28 (93.33%)	66 (95.65%)	15 (100.00%)	28 (100.00%)	23 (85.19%)	319 (95.51%)
Blood and lymphatic system disorders									
Anaemia	5 (7.25%)	2 (4.76%)	5 (9.26%)	6 (20.00%)	7 (10.14%)	1 (6.67%)	2 (7.14%)	1 (3.70%)	29 (8.68%)
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%)	4 (1.20%)
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%)	7 (2.10%)
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%)	7 (2.10%)

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%)	5 (1.50%)
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%)	5 (1.50%)
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%)	9 (2.69%)
Tinnitus	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	3 (10.71%)	0 (0.00%)	3 (0.90%)
Vertigo	2 (2.90%)	2 (4.76%)	2 (3.70%)	2 (6.67%)	5 (7.25%)	0 (0.00%)	1 (3.57%)	1 (3.70%)	15 (4.49%)
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%)	5 (1.50%)
Gastrointestinal disorders									
Abdominal pain	2 (2.90%)	3 (7.14%)	7 (12.96%)	1 (3.33%)	3 (4.35%)	0 (0.00%)	3 (10.71%)	1 (3.70%)	20 (5.99%)
Abdominal pain upper	4 (5.80%)	4 (9.52%)	2 (3.70%)	2 (6.67%)	4 (5.80%)	0 (0.00%)	2 (7.14%)	1 (3.70%)	19 (5.69%)
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%)	1 (0.30%)
Constipation	16 (23.19%)	9 (21.43%)	10 (18.52%)	7 (23.33%)	9 (13.04%)	4 (26.67%)	3 (10.71%)	1 (3.70%)	59 (17.66%)
Diarrhoea	18 (26.09%)	6 (14.29%)	7 (12.96%)	8 (26.67%)	12 (17.39%)	3 (20.00%)	5 (17.86%)	1 (3.70%)	60 (17.96%)
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%)	4 (1.20%)
Dyspepsia	4 (5.80%)	3 (7.14%)	4 (7.41%)	3 (10.00%)	6 (8.70%)	0 (0.00%)	2 (7.14%)	1 (3.70%)	23 (6.89%)
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%)	16 (4.79%)
Gastrooesophageal reflux disease	3 (4.35%)	1 (2.38%)	3 (5.56%)	0 (0.00%)	1 (1.45%)	0 (0.00%)	0 (0.00%)	1 (3.70%)	9 (2.69%)
Nausea	31 (44.93%)	16 (38.10%)	24 (44.44%)	15 (50.00%)	31 (44.93%)	9 (60.00%)	12 (42.86%)	8 (29.63%)	146 (43.71%)
Stomatitis	0 (0.00%)	0 (0.00%)	3 (5.56%)	0 (0.00%)	1 (1.45%)	0 (0.00%)	0 (0.00%)	1 (3.70%)	5 (1.50%)
Vomiting	21 (30.43%)	14 (33.33%)	12 (22.22%)	9 (30.00%)	17 (24.64%)	4 (26.67%)	7 (25.00%)	6 (22.22%)	90 (26.95%)
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%)	1 (3.70%)	41 (12.28%)
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%)	6 (1.80%)
Face oedema	1 (1.45%)	0 (0.00%)	1 (1.85%)	0 (0.00%)	4 (5.80%)	0 (0.00%)	1 (3.57%)	1 (3.70%)	8 (2.40%)
Fatigue	11 (15.94%)	10 (23.81%)	16 (29.63%)	6 (20.00%)	18 (26.09%)	2 (13.33%)	4 (14.29%)	5 (18.52%)	72 (21.56%)
Malaise	1 (1.45%)	0 (0.00%)	1 (1.85%)	0 (0.00%)	3 (4.35%)	0 (0.00%)	2 (7.14%)	1 (3.70%)	8 (2.40%)
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%)	2 (7.41%)	31 (9.28%)
Oedema	1 (1.45%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	3 (10.71%)	0 (0.00%)	4 (1.20%)
Oedema peripheral	34 (49.28%)	18 (42.86%)	24 (44.44%)	11 (36.67%)	36 (52.17%)	8 (53.33%)	21 (75.00%)	13 (48.15%)	165 (49.40%)
Pain	5 (7.25%)	0 (0.00%)	1 (1.85%)	1 (3.33%)	2 (2.90%)	1 (6.67%)	0 (0.00%)	0 (0.00%)	10 (2.99%)
Performance status 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%)	1 (0.30%)
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%)	7 (2.10%)
Pyrexia	8 (11.59%)	7 (16.67%)	8 (14.81%)	5 (16.67%)	9 (13.04%)	3 (20.00%)	2 (7.14%)	2 (7.41%)	44 (13.17%)
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 (0.30%)
Infections and infestations									
Bronchitis	1 (1.45%)	1 (2.38%)	3 (5.56%)	0 (0.00%)	2 (2.90%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	7 (2.10%)
Cellulitis	2 (2.90%)	0 (0.00%)	1 (1.85%)	0 (0.00%)	4 (5.80%)	0 (0.00%)	1 (3.57%)	0 (0.00%)	8 (2.40%)
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%)	2 (0.60%)
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%)	4 (1.20%)
Lung infection	2 (2.90%)	1 (2.38%)	0 (0.00%)	2 (6.67%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	5 (1.50%)
Nasopharyngitis	7 (10.14%)	4 (9.52%)	1 (1.85%)	1 (3.33%)	2 (2.90%)	1 (6.67%)	2 (7.14%)	2 (7.41%)	20 (5.99%)
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%)	4 (1.20%)
Pneumonia	5 (7.25%)	4 (9.52%)	1 (1.85%)	1 (3.33%)	3 (4.35%)	1 (6.67%)	1 (3.57%)	1 (3.70%)	17 (5.09%)
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%)	1 (0.30%)

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%)	2 (0.60%)
Sepsis	0 (0.00%)	1 (2.38%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (6.67%)	0 (0.00%)	1 (3.70%)	3 (0.90%)
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%)	1 (0.30%)
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%)	9 (2.69%)
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%)	1 (0.30%)
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%)	1 (0.30%)
Fall	1 (1.45%)	0 (0.00%)	1 (1.85%)	0 (0.00%)	1 (1.45%)	1 (6.67%)	1 (3.57%)	0 (0.00%)	5 (1.50%)
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%)	1 (0.30%)
Pubis fracture	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 (0.30%)
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%)	3 (0.90%)
Investigations									
Alanine aminotransferase increased	11 (15.94%)	4 (9.52%)	5 (9.26%)	3 (10.00%)	8 (11.59%)	3 (20.00%)	4 (14.29%)	4 (14.81%)	42 (12.57%)
Amylase increased	8 (11.59%)	3 (7.14%)	2 (3.70%)	1 (3.33%)	7 (10.14%)	3 (20.00%)	2 (7.14%)	3 (11.11%)	29 (8.68%)
Aspartate aminotransferase increased	9 (13.04%)	2 (4.76%)	4 (7.41%)	3 (10.00%)	5 (7.25%)	3 (20.00%)	2 (7.14%)	1 (3.70%)	29 (8.68%)
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%)	11 (3.29%)
Blood alkaline phosphatase increased	8 (11.59%)	1 (2.38%)	3 (5.56%)	0 (0.00%)	4 (5.80%)	1 (6.67%)	1 (3.57%)	1 (3.70%)	19 (5.69%)
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%)	10 (2.99%)

Blood creatinine increased	16 (23.19%)	8 (19.05%)	14 (25.93%)	5 (16.67%)	23 (33.33%)	3 (20.00%)	10 (35.71%)	6 (22.22%)	85 (25.45%)
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%)	1 (0.30%)
Gamma-glutamyltransferase increased	9 (13.04%)	2 (4.76%)	5 (9.26%)	0 (0.00%)	3 (4.35%)	0 (0.00%)	2 (7.14%)	3 (11.11%)	24 (7.19%)
Lipase increased	4 (5.80%)	4 (9.52%)	1 (1.85%)	4 (13.33%)	7 (10.14%)	1 (6.67%)	4 (14.29%)	1 (3.70%)	26 (7.78%)
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%)	2 (0.60%)
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%)	3 (0.90%)
Platelet count decreased	2 (2.90%)	0 (0.00%)	3 (5.56%)	1 (3.33%)	4 (5.80%)	0 (0.00%)	1 (3.57%)	2 (7.41%)	13 (3.89%)
Weight decreased	7 (10.14%)	4 (9.52%)	2 (3.70%)	4 (13.33%)	9 (13.04%)	3 (20.00%)	3 (10.71%)	2 (7.41%)	34 (10.18%)
Weight increased	6 (8.70%)	0 (0.00%)	2 (3.70%)	0 (0.00%)	4 (5.80%)	1 (6.67%)	3 (10.71%)	0 (0.00%)	16 (4.79%)
Metabolism and nutrition disorders									
Decreased appetite	14 (20.29%)	6 (14.29%)	12 (22.22%)	8 (26.67%)	15 (21.74%)	3 (20.00%)	8 (28.57%)	2 (7.41%)	68 (20.36%)
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%)	6 (1.80%)
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%)	8 (2.40%)
Hypoalbuminaemia	8 (11.59%)	4 (9.52%)	5 (9.26%)	0 (0.00%)	5 (7.25%)	1 (6.67%)	3 (10.71%)	3 (11.11%)	29 (8.68%)
Hypocalcaemia	1 (1.45%)	1 (2.38%)	0 (0.00%)	0 (0.00%)	5 (7.25%)	1 (6.67%)	3 (10.71%)	1 (3.70%)	12 (3.59%)
Hypokalaemia	5 (7.25%)	1 (2.38%)	2 (3.70%)	3 (10.00%)	3 (4.35%)	1 (6.67%)	1 (3.57%)	2 (7.41%)	18 (5.39%)
Hyponatraemia	1 (1.45%)	2 (4.76%)	3 (5.56%)	0 (0.00%)	2 (2.90%)	1 (6.67%)	0 (0.00%)	1 (3.70%)	10 (2.99%)
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%)	2 (0.60%)
Hypophosphataemia	9 (13.04%)	0 (0.00%)	1 (1.85%)	0 (0.00%)	4 (5.80%)	0 (0.00%)	3 (10.71%)	1 (3.70%)	18 (5.39%)
Musculoskeletal and connective tissue disorders									
Arthralgia	3 (4.35%)	2 (4.76%)	5 (9.26%)	0 (0.00%)	4 (5.80%)	2 (13.33%)	4 (14.29%)	1 (3.70%)	21 (6.29%)

Back pain	8 (11.59%)	7 (16.67%)	10 (18.52%)	2 (6.67%)	11 (15.94%)	2 (13.33%)	3 (10.71%)	3 (11.11%)	46 (13.77%)
Flank pain	0 (0.00%)	1 (2.38%)	0 (0.00%)	0 (0.00%)	1 (1.45%)	0 (0.00%)	1 (3.57%)	2 (7.41%)	5 (1.50%)
Joint swelling	0 (0.00%)	1 (2.38%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (6.67%)	1 (3.57%)	1 (3.70%)	4 (1.20%)
Muscle spasms	4 (5.80%)	6 (14.29%)	3 (5.56%)	1 (3.33%)	1 (1.45%)	3 (20.00%)	1 (3.57%)	1 (3.70%)	20 (5.99%)
Musculoskeletal chest pain	2 (2.90%)	1 (2.38%)	3 (5.56%)	2 (6.67%)	5 (7.25%)	1 (6.67%)	1 (3.57%)	1 (3.70%)	16 (4.79%)
Musculoskeletal pain	5 (7.25%)	2 (4.76%)	3 (5.56%)	0 (0.00%)	4 (5.80%)	0 (0.00%)	3 (10.71%)	1 (3.70%)	18 (5.39%)
Myalgia	3 (4.35%)	3 (7.14%)	0 (0.00%)	1 (3.33%)	5 (7.25%)	2 (13.33%)	1 (3.57%)	2 (7.41%)	17 (5.09%)
Pain in extremity	6 (8.70%)	2 (4.76%)	3 (5.56%)	1 (3.33%)	5 (7.25%)	1 (6.67%)	2 (7.14%)	2 (7.41%)	22 (6.59%)
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%)	1 (0.30%)
Dizziness	4 (5.80%)	5 (11.90%)	1 (1.85%)	2 (6.67%)	8 (11.59%)	2 (13.33%)	3 (10.71%)	4 (14.81%)	29 (8.68%)
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 (0.30%)
Headache	6 (8.70%)	4 (9.52%)	3 (5.56%)	2 (6.67%)	8 (11.59%)	1 (6.67%)	1 (3.57%)	1 (3.70%)	26 (7.78%)
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%)	6 (1.80%)
Paraesthesia	1 (1.45%)	3 (7.14%)	2 (3.70%)	0 (0.00%)	3 (4.35%)	0 (0.00%)	1 (3.57%)	2 (7.41%)	12 (3.59%)
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%)	5 (1.50%)
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%)	5 (1.50%)
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%)	3 (0.90%)
Psychiatric disorders									
Anxiety	0 (0.00%)	3 (7.14%)	4 (7.41%)	0 (0.00%)	3 (4.35%)	1 (6.67%)	1 (3.57%)	1 (3.70%)	13 (3.89%)
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%)	5 (1.50%)
Depression	1 (1.45%)	1 (2.38%)	2 (3.70%)	0 (0.00%)	3 (4.35%)	0 (0.00%)	0 (0.00%)	2 (7.41%)	9 (2.69%)
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%)	1 (0.30%)
Insomnia	7 (10.14%)	3 (7.14%)	3 (5.56%)	1 (3.33%)	6 (8.70%)	0 (0.00%)	5 (17.86%)	2 (7.41%)	27 (8.08%)

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%)	5 (1.50%)
Renal and urinary disorders									
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%)	3 (0.90%)
Reproductive system and breast disorders									
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%)	1 (0.30%)
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%)	2 (0.60%)
Respiratory, thoracic and mediastinal disorders									
Cough	9 (13.04%)	9 (21.43%)	9 (16.67%)	4 (13.33%)	10 (14.49%)	2 (13.33%)	6 (21.43%)	4 (14.81%)	53 (15.87%)
Dyspnoea	11 (15.94%)	15 (35.71%)	11 (20.37%)	5 (16.67%)	14 (20.29%)	5 (33.33%)	6 (21.43%)	2 (7.41%)	69 (20.66%)
Dyspnoea exertional	0 (0.00%)	0 (0.00%)	1 (1.85%)	1 (3.33%)	1 (1.45%)	1 (6.67%)	1 (3.57%)	0 (0.00%)	5 (1.50%)
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%)	1 (0.30%)
Epistaxis	0 (0.00%)	1 (2.38%)	0 (0.00%)	1 (3.33%)	2 (2.90%)	2 (13.33%)	1 (3.57%)	0 (0.00%)	7 (2.10%)
Haemoptysis	3 (4.35%)	3 (7.14%)	3 (5.56%)	0 (0.00%)	1 (1.45%)	0 (0.00%)	1 (3.57%)	1 (3.70%)	12 (3.59%)
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%)	2 (0.60%)
Pleural effusion	3 (4.35%)	4 (9.52%)	3 (5.56%)	0 (0.00%)	3 (4.35%)	0 (0.00%)	0 (0.00%)	1 (3.70%)	14 (4.19%)
Pneumonitis	3 (4.35%)	0 (0.00%)	0 (0.00%)	1 (3.33%)	4 (5.80%)	0 (0.00%)	1 (3.57%)	1 (3.70%)	10 (2.99%)
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%)	16 (4.79%)
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%)	13 (3.89%)
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%)	1 (3.70%)	6 (1.80%)
Dry skin	9 (13.04%)	1 (2.38%)	2 (3.70%)	1 (3.33%)	1 (1.45%)	1 (6.67%)	0 (0.00%)	0 (0.00%)	15 (4.49%)
Pruritus	7 (10.14%)	6 (14.29%)	2 (3.70%)	0 (0.00%)	10 (14.49%)	2 (13.33%)	2 (7.14%)	1 (3.70%)	30 (8.98%)

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%)	1 (0.30%)
Rash	3 (4.35%)	1 (2.38%)	4 (7.41%)	1 (3.33%)	6 (8.70%)	1 (6.67%)	0 (0.00%)	2 (7.41%)	18 (5.39%)
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 (0.30%)
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%)	6 (1.80%)
Embolism	1 (1.45%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.45%)	1 (6.67%)	0 (0.00%)	1 (3.70%)	4 (1.20%)
Hypertension	4 (5.80%)	0 (0.00%)	1 (1.85%)	1 (3.33%)	1 (1.45%)	1 (6.67%)	1 (3.57%)	2 (7.41%)	11 (3.29%)
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%)	13 (3.89%)

Other Relevant Findings

None

Conclusion:

Results from this study show a substantial, durable and rapid antitumor response to capmatinib in the clinically challenging population of subjects with MET-mutated advanced NSCLC, irrespective of the line of therapy (Cohort 4 and 5b). The efficacy of capmatinib is further corroborated by the secondary endpoints conducted in the study. The results of ORR based on Investigator assessment supported the primary ORR analysis based on BIRC assessment.

The safety and tolerability of capmatinib has been well characterized in the large dataset of all subjects enrolled in this study and is considered representative and acceptable for advanced METex14-mutated NSCLC patients, irrespective of prior line of treatment. The AEs are manageable with medical therapies and/or dose modifications

Date of Clinical Trial Report

21-Aug-2019