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**Sponsor**

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**Generic Drug Name**

Capmatinib

**Trial Indication(s)**

MET dependent advanced solid tumors

**Protocol Number**

CINC280X2102

**Protocol Title**

A Phase I open-label dose escalation study with expansion to assess the safety and tolerability of INC280 in subjects with c-MET dependent advanced solid tumors

**Clinical Trial Phase**

Phase I

**Phase of Drug Development**

Phase II

**Study Start/End Dates**

29-Feb-2012 (first subject first visit), 22-Oct-2014 (Primary Completion Date), 04-Jul-2017 (last subject last visit)

**Reason for Termination (If applicable)**

Not applicable.

**Study Design/Methodology**

This was a Phase I open label, multi center, non randomized dose escalation study with an expansion phase. Subjects enrolled were refractory to currently available therapies or had malignancies for which no effective treatment was available. Only subjects with advanced solid tumors with MET pathway dysregulation determined from archival or fresh tumor tissue were enrolled (either by local or Novartis designated central lab).

The maximum tolerated dose (MTD)/recommended Phase 2 dose (RP2D) of capmatinib was to be determined during the dose escalation phase, followed by an original expansion phase of approximately 30 to 90 subjects to further explore safety and preliminary efficacy of daily administration of capmatinib in selected tumor types harboring MET dysregulation as described above (1) hepatocellular carcinoma (HCC) (2) gastric cancer (3) non-small cell lung cancer (NSCLC) (4) other solid tumors (papillary renal cell carcinoma [pRCC], glioblastoma [GBM] and others).

Another expansion phase of approximately 20 subjects was added to further assess the antitumor activity of capmatinib in the pre treated NSCLC EGFRwt subjects with MET dysregulation defined as IHC3+ by Novartis designated central lab. Subjects received treatment in 28 day cycles as long as there was no evidence of disease progression or excessive toxicity. Subjects were continually reassessed for evidence of acute and cumulative toxicity.

Dose escalation: In the dose escalation phase, separate cohorts of subjects were to receive increasing doses of capmatinib until the MTD/RP2D was determined. A two parameter Bayesian logistic regression model (BLRM) employing the escalation with overdose control (EWOC) principle was used during the escalation phase for dose level selection and for determination of the MTD/RP2D.

Expansion groups (all): In the original expansion groups, approximately 30 to 90 subjects were to be enrolled and treated at the MTD/RP2D of capmatinib as determined during the escalation phase. Of the planned enrollment, a maximum of 15 subjects could have pRCC, GBM, or other advanced solid tumors with MET pathway dysregulation. Three additional groups could have enrolled 10 subjects each with MET dysregulated tumors: gastric cancer, HCC, or NSCLC. An additional 15 subjects could be enrolled to each of these three groups, for a maximum of 25 subjects per group, if additional safety or efficacy data were desired. The decision to expand one or more of these three groups was to be made no later than 16 weeks after the last subject of the group started treatment with capmatinib. This decision was made by the Novartis Clinical Trial team in consultation with Investigators after

reviewing all safety and efficacy data from the first 10 subjects available at the time. In these original expansion groups of HCC, gastric cancer, NSCLC, and other solid tumors (pRCC, GBM, and others), MET status as per eligibility criterion was determined either by local or Novartis designated central lab.

In the NSCLC EGFRwt MET IHC 3+ expansion group, approximately 20 subjects were to be enrolled and treated at the RP2D of capmatinib. To confirm study eligibility, subjects in this NSCLC EGFRwt expansion group were molecularly pre-screened for MET overexpression defined as IHC3+ at a Novartis designated central laboratory.

**Centers**

Australia (1), Canada (1), France (2), Germany (5), Hong Kong (2), Israel (3), Italy (4), Netherlands (3), Norway (1), Singapore (1), South Korea (4), Spain (1), Taiwan (2), United States (3).

**Objectives:**

**Objectives for dose escalation and original expansion groups**

Primary objective

Primary Objective: to determine the MTD/highest studied dose determined to be safe, the safety and tolerability of capmatinib as a single agent when administered orally to adult patients with MET dependent advanced solid malignancies.

Key secondary objective

To explore the antitumor activity of capmatinib in patients with MET dependent advanced solid malignancies.

Secondary objective(s)

To characterize the safety and tolerability of capmatinib.

To assess the MET inhibition and antitumor effect of capmatinib by paired pre-treatment and post-treatment tumor biopsies.

To evaluate the PK of capmatinib.

**Objectives for expansion group of NSCLC subjects EGFRwt with high MET expression in dose expansion**

Key secondary objective

To assess the antitumor activity of capmatinib as a single agent when administered orally to adult subjects with tumors characterized by genetic abnormalities in MET at MTD/ RP2D by CT/MRI.

Secondary objective(s)

To characterize the safety and tolerability of capmatinib.

To assess the anti-tumor activity of capmatinib.

To evaluate the PK of capmatinib.

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

Capmatinib was the investigational drug and is referred to as the “study drug”. Capmatinib was supplied to the Investigators as hard gelatin capsules at two dosage strengths of 10 mg and 50 mg, and as film coated tablets at dosage strengths of 50 mg, 100 mg, and 200 mg. All test materials were supplied by Novartis Drug Supply Management (DSM).

All subjects were treated with capmatinib administered orally, beginning on Cycle 1 Day 1. Each cycle had 28 days. Subjects could be discontinued from treatment earlier due to disease progression, unacceptable toxicity, the discretion of the Investigator or subject, death or if subject was lost to follow-up.

## Statistical Methods

All statistical analysis were performed by Novartis personnel.
Data were summarized using descriptive statistics (continuous data) and/or contingency tables (categorical data) for demographic and baseline characteristics, efficacy measurements, safety measurements, and all relevant PK and PD measurements.
The final analysis of study data was based on all subject data of the escalation and expansion phases when all subjects discontinued the study.

For the analysis, subjects treated at the RP2D for capmatinib during the escalation phase were pooled with those receiving the same dosing regimen and same disease during the expansion phase.
Additionally, data of the subjects with NSCLC in the original expansion group and the EGFRwt NSCLC subjects with high MET expression enrolled after protocol Amendment 6 were summarized separately.
Analyses for study treatment exposure, compliance and safety were separated for the different formulations (capsule and tablet).

**Study Population: Key Inclusion/Exclusion Criteria**

**Key inclusion criteria**

**Dose escalation and original expansion groups**

**Molecular pre-screening inclusion criteria**

- Evidence of dysregulation of the MET pathway was required to begin screening activities. This was to be demonstrated by either locally available data or through the submission of archival or newly obtained tumor samples to a central laboratory for molecular analysis.

**Other inclusion criteria**

- Subject age ≥ 18 years
- Subjects with advanced solid tumors that were refractory to currently available therapies or for which no effective treatment was available and had confirmed MET dysregulation.
- Subject had discontinued any previous anticancer and investigational therapy for at least 28 days before study treatment administration (6 weeks for GBM subjects that received nitrosoureas), and recovered fully from the adverse effects of such treatment before beginning study treatment.
- Subject had an Eastern Cooperative Oncology Group (ECOG) performance status ≤ 2.

**Additional inclusion criteria for subjects with EGFRwt NSCLC with high MET expression**:

- Availability of documentation of EGFRwt NSCLC.
- Tumors had MET positivity as defined by MET IHC intensity score +3 in ≥ 50% of tumor cells performed through a Novartis designated central laboratory.

- Subjects had not received more than three prior lines of antineoplastic therapy for NSCLC. Subjects with more than three prior lines of antineoplastic therapy were enrolled after discussion with Novartis if the Investigator considered a clinical benefit for the subject.
- Subjects had presence of at least one measurable lesion as determined by modified RECIST version 1.1

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## Participant Flow Table

### Subject disposition by cohort in dose escalation (Full analysis set)

| | Capmatinib dose bid | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | 100mg capsule | 200mg capsule | 250 mg capsule | 350 mg capsule | 450 mg capsule | 600 mg capsule | 400 mg tablets | All dose escalation subjects |
| | N=4 | N=5 | N=4 | N=3 | N=9 | N=8 | N=5 | N=38 |
| | n (%) | n (%) | n (%) | n (%) | n (%) | n (%) | n (%) | n (%) |
| **Subjects treated** | | | | | | | | |
| Treatment discontinued | 4 (100) | 5 (100) | 4 (100) | 3 (100) | 9 (100) | 8 (100) | 5 (100) | 38 (100) |
| **Primary reason for end of treatment** | | | | | | | | |
| Adverse event(s) | 0 | 0 | 0 | 0 | 1 (11.1) | 0 | 0 | 1 (2.6) |
| Disease progression | 4 (100) | 5 (100) | 4 (100) | 3 (100) | 8 (88.9) | 8 (100) | 5 (100) | 37 (97.4) |

Study evaluation completion corresponds to the evaluation performed 30-day following treatment discontinuation.

### Subject disposition by cohort in expansion groups (Full analysis set)

| | Gastric cancer | HCC | NSCLC* | pRCC + GBM + Others | All expansion subjects |
|---|---|---|---|---|---|
| | N=9 | N=11 | N=55 | N=18 | N=93 |
| | n (%) | n (%) | n (%) | n (%) | n (%) |
| **Subjects treated** | | | | | |
| Treatment discontinued | 9 (100) | 11 (100) | 55 (100) | 18 (100) | 93 (100) |
| **Primary reason for end of treatment** | | | | | |

| | Gastric cancer | HCC | NSCLC* | pRCC + GBM + Others | All expansion subjects |
|---|---|---|---|---|---|
| | N=9 | N=11 | N=55 | N=18 | N=93 |
| | n (%) | n (%) | n (%) | n (%) | n (%) |
| Adverse event(s) | 1 (11.1) | 2 (18.2) | 11 (20.0) | 3 (16.7) | 17 (18.3) |
| Subject withdrew consent | 2 (22.2) | 0 | 4 (7.3) | 0 | 6 (6.5) |
| Lost to follow-up | 0 | 0 | 1 (1.8) | 0 | 1 (1.1) |
| Administrative reasons | 0 | 0 | 1 (1.8) | 0 | 1 (1.1) |
| Death | 0 | 0 | 0 | 0 | 0 |
| Disease progression | 6 (66.7) | 8 (72.7) | 38 (69.1) | 15 (83.3) | 67 (72.0) |
| Protocol deviation | 0 | 1 (9.1) | 0 | 0 | 1 (1.1) |

*NSCLC group includes both original NSCLC group and subjects with EGFRwt NSCLC with high MET expression.
Study evaluation completion corresponds to the evaluation performed 30-day following treatment discontinuation.
All expansion subjects received 600 mg bid capmatinib capsule. Seven subjects treated with capmatinib in capsule formulation in the original expansion group switched to tablet formulation once it became available.

## Baseline Characteristics

### Demographics summary by cohort group in dose escalation (Full analysis set)

| | Capmatinib dose bid | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | 100 mg capsule | 200 mg capsule | 250 mg capsule | 350 mg capsule | 450 mg capsule | 600 mg capsule | 400 mg tablet | All dose escalation subjects |
| | N=4 | N=5 | N=4 | N=3 | N=9 | N=8 | N=5 | N=38 |
| **Age (Years, at screening)** | | | | | | | | |

| | Capmatinib dose bid | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | 100 mg capsule | 200 mg capsule | 250 mg capsule | 350 mg capsule | 450 mg capsule | 600 mg capsule | 400 mg tablet | All dose escalation subjects |
| | N=4 | N=5 | N=4 | N=3 | N=9 | N=8 | N=5 | N=38 |
| n | 4 | 5 | 4 | 3 | 9 | 8 | 5 | 38 |
| Mean | 57.5 | 54.0 | 62.3 | 50.0 | 52.0 | 54.1 | 54.4 | 54.5 |
| SD | 7.85 | 13.04 | 7.93 | 14.73 | 9.57 | 11.46 | 9.48 | 10.26 |
| Median | 57.5 | 48.0 | 64.0 | 58.0 | 53.0 | 57.5 | 56.0 | 56.0 |
| Minimum | 48.0 | 42.0 | 52.0 | 33.0 | 29.0 | 32.0 | 41.0 | 29.0 |
| Maximum | 67.0 | 74.0 | 69.0 | 59.0 | 64.0 | 66.0 | 67.0 | 74.0 |
| **Age category (Years, at screening) – n (%)** | | | | | | | | |
| <65 | 3 (75.0) | 4 (80.0) | 2 (50.0) | 3 (100) | 9 (100) | 7 (87.5) | 4 (80.0) | 32 (84.2) |
| ≥ 65 | 1 (25.0) | 1 (20.0) | 2 (50.0) | 0 | 0 | 1 (12.5) | 1 (20.0) | 6 (15.8) |
| **Sex -n (%)** | | | | | | | | |
| Female | 0 | 2 (40.0) | 1 (25.0) | 0 | 4 (44.4) | 0 | 4 (80.0) | 11 (28.9) |
| Male | 4 (100) | 3 (60.0) | 3 (75.0) | 3 (100) | 5 (55.6) | 8 (100) | 1 (20.0) | 27 (71.1) |
| **Predominant Race - n (%)** | | | | | | | | |
| Caucasian | 0 | 0 | 0 | 0 | 3 (33.3) | 0 | 3 (60.0) | 6 (15.8) |
| Asian | 4 (100) | 5 (100) | 4 (100) | 3 (100) | 5 (55.6) | 8 (100) | 2 (40.0) | 31 (81.6) |
| Other | 0 | 0 | 0 | 0 | 1 (11.1) | 0 | 0 | 1 (2.6) |
| **Ethnicity - n (%)** | | | | | | | | |
| Hispanic/Latino | 0 | 0 | 0 | 0 | 1 (11.1) | 0 | 0 | 1 (2.6) |
| Chinese | 1 (25.0) | 3 (60.0) | 1 (25.0) | 2 (66.7) | 3 (33.3) | 7 (87.5) | 2 (40.0) | 19 (50.0) |
| Indian (Indian subcontinent) | 0 | 0 | 0 | 0 | 0 | 1 (12.5) | 0 | 1 (2.6) |
| Japanese | 0 | 0 | 0 | 0 | 1 (11.1) | 0 | 0 | 1 (2.6) |
| Other | 3 (75.0) | 2 (40.0) | 3 (75.0) | 1 (33.3) | 4 (44.4) | 0 | 3 (60.0) | 16 (42.1) |

| | Capmatinib dose bid | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | 100 mg capsule | 200 mg capsule | 250 mg capsule | 350 mg capsule | 450 mg capsule | 600 mg capsule | 400 mg tablet | All dose escalation subjects |
| | N=4 | N=5 | N=4 | N=3 | N=9 | N=8 | N=5 | N=38 |
| **ECOG performance status* - n (%)** | | | | | | | | |
| 0 | 4 (100) | 3 (60.0) | 3 (75.0) | 1 (33.3) | 4 (44.4) | 5 (62.5) | 1 (20.0) | 21 (55.3) |
| 1 | 0 | 2 (40.0) | 1 (25.0) | 2 (66.7) | 4 (44.4) | 3 (37.5) | 4 (80.0) | 16 (42.1) |
| 2 | 0 | 0 | 0 | 0 | 1 (11.1) | 0 | 0 | 1 (2.6) |

*0 - Fully active, able to carry on all pre-disease performance without restriction; 1 - Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, e.g., light house work, Office work; 2 - Ambulatory and capable of all selfcare but unable to carry out any work activities. Up and about more than 50% of waking hours; 3 - Capable of only limited selfcare, confined to bed or chair more than 50% of waking hours; 4 –Completely disabled. Cannot carry on any selfcare. Totally confined to bed to chair, 5 – Dead

## Demographics summary by cohort group in expansion groups (Full analysis set)

| | Gastric cancer | HCC | NSCLC | pRCC + GBM + Others | All expansion subjects |
|---|---|---|---|---|---|
| | N=9 | N=11 | N=55 | N=18 | N=93 |
| **Age (Years, at screening)** | | | | | |
| n | 9 | 11 | 55 | 18 | 93 |
| Mean | 55.7 | 57.7 | 60.6 | 55.3 | 58.8 |
| SD | 4.09 | 9.54 | 11.33 | 12.41 | 10.98 |
| Median | 55.0 | 54.0 | 60.0 | 57.0 | 58.0 |
| Minimum | 51.0 | 44.0 | 29.0 | 28.0 | 28.0 |

| | Gastric cancer | HCC | NSCLC | pRCC + GBM + Others | All expansion subjects |
|---|---|---|---|---|---|
| | N=9 | N=11 | N=55 | N=18 | N=93 |
| Maximum | 63.0 | 76.0 | 84.0 | 72.0 | 84.0 |
| **Age category (Years, at screening) -n (%)** | | | | | |
| <65 | 9 (100) | 8 (72.7) | 35 (63.6) | 13 (72.2) | 65 (69.9) |
| ≥ 65 | 0 | 3 (27.3) | 20 (36.4) | 5 (27.8) | 28 (30.1) |
| **Sex -n (%)** | | | | | |
| Female | 2 (22.2) | 2 (18.2) | 22 (40.0) | 3 (16.7) | 29 (31.2) |
| Male | 7 (77.8) | 9 (81.8) | 33 (60.0) | 15 (83.3) | 64 (68.8) |
| **Predominant Race - n (%)** | | | | | |
| Caucasian | 9 (100) | 6 (54.5) | 40 (72.7) | 13 (72.2) | 68 (73.1) |
| Black | 0 | 1 (9.1) | 0 | 1 (5.6) | 2 (2.2) |
| Asian | 0 | 4 (36.4) | 15 (27.3) | 4 (22.2) | 23 (24.7) |
| **Ethnicity - n (%)** | | | | | |
| Hispanic/Latino | 0 | 1 (9.1) | 0 | 0 | 1 (1.1) |
| Chinese | 0 | 2 (18.2) | 3 (5.5) | 3 (16.7) | 8 (8.6) |
| Other | 9 (100) | 8 (72.7) | 52 (94.5) | 15 (83.3) | 84 (90.3) |
| **ECOG performance status* - n (%)** | | | | | |
| 0 | 3 (33.3) | 7 (63.6) | 19 (34.5) | 10 (55.6) | 39 (41.9) |
| 1 | 6 (66.7) | 4 (36.4) | 34 (61.8) | 6 (33.3) | 50 (53.8) |
| 2 | 0 | 0 | 2 (3.6) | 1 (5.6) | 3 (3.2) |
| Missing | 0 | 0 | 0 | 1 (5.6) | 1 (1.1) |

*0 - Fully active, able to carry on all pre-disease performance without restriction; 1 - Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, e.g., light house work, Office work; 2 - Ambulatory and capable of all selfcare but unable to carry out any work activities. Up and about more Than 50% of waking hours; 3 - Capable of only limited selfcare, confined to bed or chair more than 50% of waking hours; 4 – Completely disabled. Cannot carry on any selfcare. Totally confined to bed or chair; 5 – Dead

## Summary of Efficacy

## Primary Outcome Result(s)

**Dose limiting toxicities occurring during the first cycle by preferred term and cohort group in dose escalation (Dose determining set)**

| | Capmatinib dose bid | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | 100 mg capsule | 200 mg capsule | 250 mg capsule | 350 mg capsule | 450 mg capsule | 600 mg capsule | 400 mg tablet | All dose escalation subjects |
| | N=3 | N=4 | N=4 | N=3 | N=6 | N=7 | N=3 | N=30 |
| **Preferred term** | n (%) | n (%) | n (%) | n (%) | n (%) | n (%) | n (%) | n (%) |
| **Total** | 0 | 1 (25.0) | 1 (25.0) | 0 | 1 (16.7) | 0 | 0 | 3 (10.0) |
| Blood Bilirubin increased | 0 | 0 | 1 (25.0) | 0 | 0 | 0 | 0 | 1 (3.3) |
| Fatigue | 0 | 1 (25.0) | 0 | 0 | 1 (16.7) | 0 | 0 | 2 (6.7) |

Preferred terms are sorted by frequency of "All subject" Column.
A subject with multiple occurrences of DLTs under one treatment is counted only once in the AE category for that treatment.

## Secondary Outcome Result(s)

**Summary of best overall response by cohort group as per Investigator in dose escalation (Full analysis set)**

| | Capmatinib dose bid | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | 100 mg capsule | 200 mg capsule | 250 mg capsule | 350 mg capsule | 450 mg capsule | 600 mg capsule | 400 mg tablet | All subjects |
| | N=4 | N=5 | N=4 | N=3 | N=9 | N=8 | N=5 | N=38 |
| | n (%) | n (%) | n (%) | n (%) | n (%) | n (%) | n (%) | n (%) |

| | Capmatinib dose bid | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | 100 mg capsule N=4 n (%) | 200 mg capsule N=5 n (%) | 250 mg capsule N=4 n (%) | 350 mg capsule N=3 n (%) | 450 mg capsule N=9 n (%) | 600 mg capsule N=8 n (%) | 400 mg tablet N=5 n (%) | All subjects N=38 n (%) |
| **Best overall response** | | | | | | | | |
| Complete response (CR) | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Partial response (PR) | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Stable disease (SD) | 2 (50.0) | 1 (20.0) | 1 (25.0) | 1 (33.3) | 2 (22.2) | 1 (12.5) | 2 (40.0) | 10 (26.3) |
| Progressive disease (PD) | 2 (50.0) | 4 (80.0) | 3 (75.0) | 2 (66.7) | 6 (66.7) | 6 (75.0) | 3 (60.0) | 26 (68.4) |
| Unknown* | 0 | 0 | 0 | 0 | 1 (11.1) | 1 (12.5) | 0 | 2 (5.3) |
| **Overall response rate (ORR) (CR or PR)** | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 95% CI | (0.0-60.2) | (0.0-52.2) | (0.0-60.2) | (0.0-70.8) | (0.0-33.6) | (0.0-36.9) | (0.0-52.2) | (0.0-9.3) |
| **Disease control rate** (DCR) CR or PR or SD) | 2 (50.0) | 1 (20.0) | 1 (25.0) | 1 (33.3) | 2 (22.2) | 1 (12.5) | 2 (40.0) | 10 (26.3) |
| 95% CI | (6.8-93.2) | (0.5-71.6) | (0.6-80.6) | (0.8-90.6) | (2.8-60.0) | (0.3-52.7) | (5.3-85.3) | (13.4-43.1) |

Best overall response is based on Investigator's assessment of disease status using RECIST or MacDonald criteria (for glioblastoma).
95%CI for ORR and DCR were obtained using Clopper and Pearson's method.
*Unknown refers to 1) no valid post-baseline tumor assessments 2) all post baseline assessments had overall response UNK 3) New antineoplastic therapy started before first post-baseline assessment 4) SD too early 5) PD too late.

**Summary of best overall response by cohort group as per Investigator in expansion groups (Full analysis set)**

| | Gastric cancer | HCC | NSCLC | pRCC + GBM + Others | All expansion subjects |
|---|---|---|---|---|---|

| | N=9<br>n (%) | N=11<br>n (%) | N=55<br>n (%) | N=18<br>n (%) | N=93<br>n (%) |
|---|---|---|---|---|---|
| **Best overall response** | | | | | |
| Complete response (CR) | 0 | 0 | 1 (1.8) | 0 | 1 (1.1) |
| Partial response (PR) | 0 | 0 | 10 (18.2) | 0 | 10 (10.8) |
| Stable disease (SD) | 2 (22.2) | 5 (45.5) | 17 (30.9) | 5 (27.8) | 29 (31.2) |
| Progressive disease (PD) | 3 (33.3) | 1 (9.1) | 17 (30.9) | 9 (50.0) | 30 (32.3) |
| Unknown* | 4 (44.4) | 5 (45.5) | 10 (18.2) | 4 (22.2) | 23 (24.7) |
| **Overall response rate (ORR) (CR or PR)** | 0 | 0 | 11 (20.0) | 0 | 11 (11.8) |
| 95% CI | (0.0-33.6) | (0.0-28.5) | (10.4-33.0) | (0.0-18.5) | (6.1-20.2) |
| **Disease control rate (DCR) (CR or PR or SD)** | 2 (22.2) | 5 (45.5) | 28 (50.9) | 5 (27.8) | 40 (43.0) |
| 95% CI | (2.8-60.0) | (16.7-76.6) | (37.1-64.6) | (9.7-53.5) | (32.8-53.7) |

Best overall response is based on Investigator's assessment of disease status using RECIST or MacDonald criteria (for glioblastoma)
95%CI for ORR and DCR were obtained using Clopper and Pearson's method.
*Unknown refers to 1) no valid post-baseline tumor assessments 2) all post baseline assessments had overall response UNK 3) New antineoplastic therapy started before first post-baseline assessment 4) SD too early 5) PD too late.

**Analysis of PFS based on investigator using Kaplan-Meier method by cohort in expansion NSCLC subjects (Full analysis set)**

| | NSCLC Original expansion<br>N=26 | NSCLC EGFRwt<br>N=29 | All expansion NSCLC subjects<br>N=55 |
|---|---|---|---|
| **No. of PFS events** | 21 (80.8%) | 23 (79.3%) | 44 (80.0%) |
| **Progression** | 18 (69.2%) | 20 (69.0%) | 38 (69.1%) |
| **Death** | 3 (11.5%) | 3 (10.3%) | 6 (10.9%) |
| **No. of censored** | 5 (19.2%) | 6 (20.7%) | 11 (20.0%) |

| | NSCLC Original expansion N=26 | NSCLC EGFRwt N=29 | All expansion NSCLC subjects N=55 |
|---|---|---|---|
| **Kaplan-Meier estimates@[95% CI] at**: | | | |
| 3 months | 50.3 [29.3, 68.0] | 58.2 [37.3, 74.3] | 54.4 [39.7, 66.9] |
| 6 months | 32.6 [15.1, 51.5] | 45.7 [26.0, 63.5] | 39.4 [25.8, 52.8] |
| 9 months | 16.3 [4.4, 35.0] | 33.3 [16.1, 51.5] | 25.5 [14.0, 38.6] |
| 12 months | 16.3 [4.4, 35.0] | 9.5 [1.7, 25.8] | 12.8 [4.8, 24.6] |
| Median PFS [95% CI] | 3.1 [1.6, 7.3] | 3.8 [1.8, 9.2] | 3.7 [1.8, 7.3] |

**Descriptive summary of duration of response as per investigator by RECIST 1.1 for expansion NSCLC (Full analysis set)**

| | NSCLC Original expansion N=26 | NSCLC EGFRwt N=29 | All expansion NSCLC subjects N=55 |
|---|---|---|---|
| **No. of Responders** | 5 (19.2%) | 6 (20.7%) | 11 (20.0%) |
| **Duration of response (weeks)** | | | |
| **Median** | 60.4 | 36.5 | 40.1 |
| **Min** | 20.9 | 28.4 | 20.9 |
| **Max** | 177.2 | 96 | 177.2 |
| **≥12 weeks** | 5 (19.2%) | 6 (20.7%) | 11 (20.0%) |
| **≥24 weeks** | 3 (11.5%) | 6 (20.7%) | 9 (16.4%) |
| **≥48 weeks** | 3 (11.5%) | 2 (6.9%) | 5 (9.1%) |

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**Summary statistics for H-score for IHC PD biomarkers (p-cMET, p-ERK, p-AKT, p-S6) from tumor sample by cohort in dose escalation (Full analysis set)**

**Biomarker: pAKT (AKT), Timepoint: Screening**

Cellular compartment: Cytoplasmic

| | INC280 100mg capsule N=4 | INC280 200mg capsule N=5 | INC280 250mg capsule N=4 | INC280 350mg capsule N=3 |
|---|---|---|---|---|
| Level | | | | |
| n (%) | 0 | 2(40.0) | 0 | 0 |
| Mean | 0 | 142.50 | 0 | 0 |
| SD (CV%) | 0 | 95.459 (66.99) | 0 | 0 |
| Median | 0 | 142.50 | 0 | 0 |
| IQR | 0 | 75.00 - 210.00 | 0 | 0 |
| Min-Max | 0 | 75.00 - 210.00 | 0 | 0 |

| | INC280 450mg capsule N=9 | INC280 600mg capsule N=8 | INC280 400mg tablet N=5 | All dose escalation patients N=38 |
|---|---|---|---|---|
| Level | | | | |
| n (%) | 1(11.1) | 0 | 1(20.0) | 4(10.5) |
| Mean | 280.00 | 0 | 90.00 | 163.75 |
| SD (CV%) | 0 | 0 | 0 | 98.266 (60.01) |
| Median | 280.00 | 0 | 90.00 | 150.00 |
| IQR | 280.00 - 280.00 | 0 | 90.00 - 90.00 | 82.50 - 245.00 |
| Min-Max | 280.00 - 280.00 | 0 | 90.00 - 90.00 | 75.00 - 280.00 |

- IQR (Inter-quartile range) represents the interval between the 25th and 75th percentiles.
- Only data from tumor samples collected prior to intra-patient dose escalation are included in this table.

NOVARTIS

## Biomarker: pAKT (AKT), Timepoint: Cycle 1, Day 15

**Cellular compartment: Cytoplasmic**

| | INC280 100mg capsule N=4 | INC280 200mg capsule N=5 | INC280 250mg capsule N=4 | INC280 350mg capsule N=3 |
|---|---|---|---|---|
| Level | | | | |
| n (%) | 1(25.0) | 1(20.0) | 1(25.0) | 0 |
| Mean | 130.00 | 240.00 | 250.00 | 0 |
| SD (CV%) | 0 | 0 | 0 | 0 |
| Median | 130.00 | 240.00 | 250.00 | 0 |
| IQR | 130.00 - 130.00 | 240.00 - 240.00 | 250.00 - 250.00 | 0 |
| Min-Max | 130.00 - 130.00 | 240.00 - 240.00 | 250.00 - 250.00 | 0 |
| Percentage change from baseline | | | | |
| n (%) | 0 | 1(20.0) | 0 | 0 |
| Mean | 0 | 14.29 | 0 | 0 |
| SD (CV%) | 0 | 0 | 0 | 0 |
| Median | 0 | 14.29 | 0 | 0 |
| IQR | 0 | 14.29 - 14.29 | 0 | 0 |
| Min-Max | 0 | 14.29 - 14.29 | 0 | 0 |

| | INC280 450mg capsule N=9 | INC280 600mg capsule N=8 | INC280 400mg tablet N=5 | All dose escalation patients N=38 |
|---|---|---|---|---|
| Level | | | | |
| n (%) | 1(11.1) | 0 | 1(20.0) | 5(13.2) |
| Mean | 280.00 | 0 | 80.00 | 196.00 |
| SD (CV%) | 0 | 0 | 0 | 86.197 (43.98) |
| Median | 280.00 | 0 | 80.00 | 240.00 |
| IQR | 280.00 - 280.00 | 0 | 80.00 - 80.00 | 130.00 - 250.00 |
| Min-Max | 280.00 - 280.00 | 0 | 80.00 - 80.00 | 80.00 - 280.00 |
| Percentage change from baseline | | | | |
| n (%) | 1(11.1) | 0 | 1(20.0) | 3(7.9) |
| Mean | 0.00 | 0 | -11.11 | 1.06 |
| SD (CV%) | 0 | 0 | 0 | 12.731 (1203.12) |
| Median | 0.00 | 0 | -11.11 | 0.00 |
| IQR | 0.00 - 0.00 | 0 | -11.11 - -11.11 | -11.11 - 14.29 |
| Min-Max | 0.00 - 0.00 | 0 | -11.11 - -11.11 | -11.11 - 14.29 |

- IQR (Inter-quartile range) represents the interval between the 25th and 75th percentiles.
- Only data from tumor samples collected prior to intra-patient dose escalation are included in this table.

NOVARTIS

**Biomarker: Phospho-Met (Tyr1234/1235) (D26) XP Rabbit mAb, Cell Signaling, #3077, Timepoint: Screening**

Cellular compartment: Cytoplasmic

| | INC280 100mg capsule N=4 | INC280 200mg capsule N=5 | INC280 250mg capsule N=4 | INC280 350mg capsule N=3 |
|---|---|---|---|---|
| Level | | | | |
| n (%) | 2(50.0) | 5 (100) | 0 | 0 |
| Mean | 0.00 | 0.00 | 0 | 0 |
| SD (CV%) | 0 | 0 | 0 | 0 |
| Median | 0.00 | 0.00 | 0 | 0 |
| IQR | 0.00 - 0.00 | 0.00 - 0.00 | 0 | 0 |
| Min-Max | 0.00 - 0.00 | 0.00 - 0.00 | 0 | 0 |

| | INC280 450mg capsule N=9 | INC280 600mg capsule N=8 | INC280 400mg tablet N=5 | All dose escalation patients N=38 |
|---|---|---|---|---|
| Level | | | | |
| n (%) | 3(33.3) | 6(75.0) | 1(20.0) | 17(44.7) |
| Mean | 25.00 | 0.50 | 0.00 | 4.59 |
| SD (CV%) | 43.301 (173.21) | 0.837 (167.33) | 0 | 18.152 (395.63) |
| Median | 0.00 | 0.00 | 0.00 | 0.00 |
| IQR | 0.00 - 75.00 | 0.00 - 1.00 | 0.00 - 0.00 | 0.00 - 0.00 |
| Min-Max | 0.00 - 75.00 | 0.00 - 2.00 | 0.00 - 0.00 | 0.00 - 75.00 |

- IQR (Inter-quartile range) represents the interval between the 25th and 75th percentiles.
- Only data from tumor samples collected prior to intra-patient dose escalation are included in this table.

NOVARTIS

**Biomarker: Phospho-Met (Tyr1234/1235) (D26) XP Rabbit mAb, Cell Signaling, #3077, Timepoint: Cycle 1, Day 15**

Cellular compartment: Cytoplasmic

| | INC280 100mg capsule N=4 | INC280 200mg capsule N=5 | INC280 250mg capsule N=4 | INC280 350mg capsule N=3 |
|---|---|---|---|---|
| Level | | | | |
| n (%) | 1(25.0) | 1(20.0) | 1(25.0) | 0 |
| Mean | 15.00 | 0.00 | 0.00 | 0 |
| SD (CV%) | 0 | 0 | 0 | 0 |
| Median | 15.00 | 0.00 | 0.00 | 0 |
| IQR | 15.00 - 15.00 | 0.00 - 0.00 | 0.00 - 0.00 | 0 |
| Min-Max | 15.00 - 15.00 | 0.00 - 0.00 | 0.00 - 0.00 | 0 |
| Percentage change from baseline | | | | |
| n (%) | 0 | 0 | 0 | 0 |
| Mean | 0 | 0 | 0 | 0 |
| SD (CV%) | 0 | 0 | 0 | 0 |
| Median | 0 | 0 | 0 | 0 |
| IQR | 0 | 0 | 0 | 0 |
| Min-Max | 0 | 0 | 0 | 0 |

| | INC280 450mg capsule N=9 | INC280 600mg capsule N=8 | INC280 400mg tablet N=5 | All dose escalation patients N=38 |
|---|---|---|---|---|
| Level | | | | |
| n (%) | 1(11.1) | 0 | 1(20.0) | 5(13.2) |
| Mean | 2.00 | 0 | 0.00 | 3.40 |
| SD (CV%) | 0 | 0 | 0 | 6.542 (192.42) |
| Median | 2.00 | 0 | 0.00 | 0.00 |
| IQR | 2.00 - 2.00 | 0 | 0.00 - 0.00 | 0.00 - 2.00 |
| Min-Max | 2.00 - 2.00 | 0 | 0.00 - 0.00 | 0.00 - 15.00 |
| Percentage change from baseline | | | | |
| n (%) | 1(11.1) | 0 | 0 | 1(2.6) |
| Mean | -97.33 | 0 | 0 | -97.33 |
| SD (CV%) | 0 | 0 | 0 | 0 |
| Median | -97.33 | 0 | 0 | -97.33 |
| IQR | -97.33 - -97.33 | 0 | 0 | -97.33 - -97.33 |
| Min-Max | -97.33 - -97.33 | 0 | 0 | -97.33 - -97.33 |

- IQR (Inter-quartile range) represents the interval between the 25th and 75th percentiles.
- Only data from tumor samples collected prior to intra-patient dose escalation are included in this table.

NOVARTIS

**Biomarker: Phospho-ERK, Timepoint: Screening**

Cellular compartment: Cytoplasmic

| | INC280 100mg capsule N=4 | INC280 200mg capsule N=5 | INC280 250mg capsule N=4 | INC280 350mg capsule N=3 |
|---|---|---|---|---|
| Level | | | | |
| n (%) | 0 | 2(40.0) | 0 | 0 |
| Mean | 0 | 55.00 | 0 | 0 |
| SD (CV%) | 0 | 70.711 (128.56) | 0 | 0 |
| Median | 0 | 55.00 | 0 | 0 |
| IQR | 0 | 5.00 - 105.00 | 0 | 0 |
| Min-Max | 0 | 5.00 - 105.00 | 0 | 0 |

| | INC280 450mg capsule N=9 | INC280 600mg capsule N=8 | INC280 400mg tablet N=5 | All dose escalation patients N=38 |
|---|---|---|---|---|
| Level | | | | |
| n (%) | 1(11.1) | 0 | 1(20.0) | 4(10.5) |
| Mean | 300.00 | 0 | 100.00 | 127.50 |
| SD (CV%) | 0 | 0 | 0 | 123.861 (97.15) |
| Median | 300.00 | 0 | 100.00 | 102.50 |
| IQR | 300.00 - 300.00 | 0 | 100.00 - 100.00 | 52.50 - 202.50 |
| Min-Max | 300.00 - 300.00 | 0 | 100.00 - 100.00 | 5.00 - 300.00 |

- IQR (Inter-quartile range) represents the interval between the 25th and 75th percentiles.
- Only data from tumor samples collected prior to intra-patient dose escalation are included in this table.

NOVARTIS

**Biomarker: Phospho-ERK, Timepoint: Screening**

Cellular compartment: Nuclear

| | INC280 100mg capsule N=4 | INC280 200mg capsule N=5 | INC280 250mg capsule N=4 | INC280 350mg capsule N=3 |
|---|---|---|---|---|
| Level | | | | |
| n (%) | 0 | 2(40.0) | 0 | 0 |
| Mean | 0 | 17.50 | 0 | 0 |
| SD (CV%) | 0 | 17.678 (101.02) | 0 | 0 |
| Median | 0 | 17.50 | 0 | 0 |
| IQR | 0 | 5.00 - 30.00 | 0 | 0 |
| Min-Max | 0 | 5.00 - 30.00 | 0 | 0 |

| | INC280 450mg capsule N=9 | INC280 600mg capsule N=8 | INC280 400mg tablet N=5 | All dose escalation patients N=38 |
|---|---|---|---|---|
| Level | | | | |
| n (%) | 1(11.1) | 0 | 1(20.0) | 4(10.5) |
| Mean | 300.00 | 0 | 40.00 | 93.75 |
| SD (CV%) | 0 | 0 | 0 | 138.286 (147.50) |
| Median | 300.00 | 0 | 40.00 | 35.00 |
| IQR | 300.00 - 300.00 | 0 | 40.00 - 40.00 | 17.50 - 170.00 |
| Min-Max | 300.00 - 300.00 | 0 | 40.00 - 40.00 | 5.00 - 300.00 |

- IQR (Inter-quartile range) represents the interval between the 25th and 75th percentiles.
- Only data from tumor samples collected prior to intra-patient dose escalation are included in this table.

NOVARTIS

**Biomarker: Phospho-ERK, Timepoint: Cycle 1, Day 15**

Cellular compartment: Cytoplasmic

| | INC280 100mg capsule N=4 | INC280 200mg capsule N=5 | INC280 250mg capsule N=4 | INC280 350mg capsule N=3 |
|---|---|---|---|---|
| Level | | | | |
| n (%) | 1(25.0) | 1(20.0) | 1(25.0) | 0 |
| Mean | 185.00 | 5.00 | 200.00 | 0 |
| SD (CV%) | 0 | 0 | 0 | 0 |
| Median | 185.00 | 5.00 | 200.00 | 0 |
| IQR | 185.00 - 185.00 | 5.00 - 5.00 | 200.00 - 200.00 | 0 |
| Min-Max | 185.00 - 185.00 | 5.00 - 5.00 | 200.00 - 200.00 | 0 |
| Percentage change from baseline | | | | |
| n (%) | 0 | 1(20.0) | 0 | 0 |
| Mean | 0 | 0.00 | 0 | 0 |
| SD (CV%) | 0 | 0 | 0 | 0 |
| Median | 0 | 0.00 | 0 | 0 |
| IQR | 0 | 0.00 - 0.00 | 0 | 0 |
| Min-Max | 0 | 0.00 - 0.00 | 0 | 0 |

| | INC280 450mg capsule N=9 | INC280 600mg capsule N=8 | INC280 400mg tablet N=5 | All dose escalation patients N=38 |
|---|---|---|---|---|
| Level | | | | |
| n (%) | 1(11.1) | 0 | 1(20.0) | 5(13.2) |
| Mean | 280.00 | 0 | 20.00 | 138.00 |
| SD (CV%) | 0 | 0 | 0 | 120.239 (87.13) |
| Median | 280.00 | 0 | 20.00 | 185.00 |
| IQR | 280.00 - 280.00 | 0 | 20.00 - 20.00 | 20.00 - 200.00 |

| | | | | |
|---|---|---|---|---|
| Min-Max | 280.00 - 280.00 | 0 | 20.00 - 20.00 | 5.00 - 280.00 |
| Percentage change from baseline | | | | |
| n (%) | 1(11.1) | 0 | 1(20.0) | 3(7.9) |
| Mean | -6.67 | 0 | -80.00 | -28.89 |
| SD (CV%) | 0 | 0 | 0 | 44.389 (-153.65) |
| Median | -6.67 | 0 | -80.00 | -6.67 |
| IQR | -6.67 - -6.67 | 0 | -80.00 - -80.00 | -80.00 - 0.00 |
| Min-Max | -6.67 - -6.67 | 0 | -80.00 - -80.00 | -80.00 - 0.00 |

- IQR (Inter-quartile range) represents the interval between the 25th and 75th percentiles.
- Only data from tumor samples collected prior to intra-patient dose escalation are included in this table.

### Biomarker: Phospho-ERK, Timepoint: Cycle 1, Day 15

Cellular compartment: Nuclear

| | INC280 100mg capsule N=4 | INC280 200mg capsule N=5 | INC280 250mg capsule N=4 | INC280 350mg capsule N=3 |
|---|---|---|---|---|
| Level | | | | |
| n (%) | 1(25.0) | 1(20.0) | 1(25.0) | 0 |
| Mean | 175.00 | 5.00 | 0.00 | 0 |
| SD (CV%) | 0 | 0 | 0 | 0 |
| Median | 175.00 | 5.00 | 0.00 | 0 |
| IQR | 175.00 - 175.00 | 5.00 - 5.00 | 0.00 - 0.00 | 0 |
| Min-Max | 175.00 - 175.00 | 5.00 - 5.00 | 0.00 - 0.00 | 0 |
| Percentage change from baseline | | | | |
| n (%) | 0 | 1(20.0) | 0 | 0 |
| Mean | 0 | 0.00 | 0 | 0 |

| | | | | |
|---|---|---|---|---|
| SD (CV%) | 0 | 0 | 0 | 0 |
| Median | 0 | 0.00 | 0 | 0 |
| IQR | 0 | 0.00 - 0.00 | 0 | 0 |
| Min-Max | 0 | 0.00 - 0.00 | 0 | 0 |

| | INC280 450mg capsule N=9 | INC280 600mg capsule N=8 | INC280 400mg tablet N=5 | All dose escalation patients N=38 |
|---|---|---|---|---|
| Level | | | | |
| n (%) | 1(11.1) | 0 | 1(20.0) | 5(13.2) |
| Mean | 300.00 | 0 | 0.00 | 96.00 |
| SD (CV%) | 0 | 0 | 0 | 136.538 (142.23) |
| Median | 300.00 | 0 | 0.00 | 5.00 |
| IQR | 300.00 - 300.00 | 0 | 0.00 - 0.00 | 0.00 - 175.00 |
| Min-Max | 300.00 - 300.00 | 0 | 0.00 - 0.00 | 0.00 - 300.00 |
| Percentage change from baseline | | | | |
| n (%) | 1(11.1) | 0 | 1(20.0) | 3(7.9) |
| Mean | 0.00 | 0 | -100.00 | -33.33 |
| SD (CV%) | 0 | 0 | 0 | 57.735 (-173.21) |
| Median | 0.00 | 0 | -100.00 | 0.00 |
| IQR | 0.00 - 0.00 | 0 | -100.00 - -100.00 | -100.00 - 0.00 |
| Min-Max | 0.00 - 0.00 | 0 | -100.00 - -100.00 | -100.00 - 0.00 |

- IQR (Inter-quartile range) represents the interval between the 25th and 75th percentiles.
- Only data from tumor samples collected prior to intra-patient dose escalation are included in this table.

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**Biomarker: Phosphoserine 240-S6 ribosomal protein, Timepoint: Screening**

Cellular compartment: Cytoplasmic

| | INC280 100mg capsule N=4 | INC280 200mg capsule N=5 | INC280 250mg capsule N=4 | INC280 350mg capsule N=3 |
|---|---|---|---|---|
| Level | | | | |
| n (%) | 0 | 2(40.0) | 0 | 0 |
| Mean | 0 | 97.50 | 0 | 0 |
| SD (CV%) | 0 | 74.246 (76.15) | 0 | 0 |
| Median | 0 | 97.50 | 0 | 0 |
| IQR | 0 | 45.00 - 150.00 | 0 | 0 |
| Min-Max | 0 | 45.00 - 150.00 | 0 | 0 |

| | INC280 450mg capsule N=9 | INC280 600mg capsule N=8 | INC280 400mg tablet N=5 | All dose escalation patients N=38 |
|---|---|---|---|---|
| Level | | | | |
| n (%) | 1(11.1) | 0 | 1(20.0) | 4(10.5) |
| Mean | 15.00 | 0 | 30.00 | 60.00 |
| SD (CV%) | 0 | 0 | 0 | 61.237 (102.06) |
| Median | 15.00 | 0 | 30.00 | 37.50 |
| IQR | 15.00 - 15.00 | 0 | 30.00 - 30.00 | 22.50 - 97.50 |
| Min-Max | 15.00 - 15.00 | 0 | 30.00 - 30.00 | 15.00 - 150.00 |

- IQR (Inter-quartile range) represents the interval between the 25th and 75th percentiles.
- Only data from tumor samples collected prior to intra-patient dose escalation are included in this table.

**Biomarker: Phosphoserine 240-S6 ribosomal protein, Timepoint: Screening**

Cellular compartment: Nuclear

| | INC280 100mg capsule N=4 | INC280 200mg capsule N=5 | INC280 250mg capsule N=4 | INC280 350mg capsule N=3 |
|---|---|---|---|---|
| Level | | | | |
| n (%) | 0 | 2(40.0) | 0 | 0 |
| Mean | 0 | 30.00 | 0 | 0 |
| SD (CV%) | 0 | 42.426 (141.42) | 0 | 0 |
| Median | 0 | 30.00 | 0 | 0 |
| IQR | 0 | 0.00 - 60.00 | 0 | 0 |
| Min-Max | 0 | 0.00 - 60.00 | 0 | 0 |

| | INC280 450mg capsule N=9 | INC280 600mg capsule N=8 | INC280 400mg tablet N=5 | All dose escalation patients N=38 |
|---|---|---|---|---|
| Level | | | | |
| n (%) | 1(11.1) | 0 | 1(20.0) | 4(10.5) |
| Mean | 0.00 | 0 | 20.00 | 20.00 |
| SD (CV%) | 0 | 0 | 0 | 28.284 (141.42) |
| Median | 0.00 | 0 | 20.00 | 10.00 |
| IQR | 0.00 - 0.00 | 0 | 20.00 - 20.00 | 0.00 - 40.00 |
| Min-Max | 0.00 - 0.00 | 0 | 20.00 - 20.00 | 0.00 - 60.00 |

- IQR (Inter-quartile range) represents the interval between the 25th and 75th percentiles.
- Only data from tumor samples collected prior to intra-patient dose escalation are included in this table.

**Biomarker: Phosphoserine 240-S6 ribosomal protein, Timepoint: Cycle 1, Day 15**

Cellular compartment: Cytoplasmic

| | INC280 100mg capsule N=4 | INC280 200mg capsule N=5 | INC280 250mg capsule N=4 | INC280 350mg capsule N=3 |
|---|---|---|---|---|
| Level | | | | |
| n (%) | 1(25.0) | 1(20.0) | 1(25.0) | 0 |
| Mean | 150.00 | 15.00 | 3.00 | 0 |
| SD (CV%) | 0 | 0 | 0 | 0 |
| Median | 150.00 | 15.00 | 3.00 | 0 |
| IQR | 150.00 - 150.00 | 15.00 - 15.00 | 3.00 - 3.00 | 0 |
| Min-Max | 150.00 - 150.00 | 15.00 - 15.00 | 3.00 - 3.00 | 0 |
| Percentage change from baseline | | | | |
| n (%) | 0 | 1(20.0) | 0 | 0 |
| Mean | 0 | -66.67 | 0 | 0 |
| SD (CV%) | 0 | 0 | 0 | 0 |
| Median | 0 | -66.67 | 0 | 0 |
| IQR | 0 | -66.67 - -66.67 | 0 | 0 |
| Min-Max | 0 | -66.67 - -66.67 | 0 | 0 |

| | INC280 450mg capsule N=9 | INC280 600mg capsule N=8 | INC280 400mg tablet N=5 | All dose escalation patients N=38 |
|---|---|---|---|---|
| Level | | | | |
| n (%) | 1(11.1) | 0 | 1(20.0) | 5(13.2) |
| Mean | 45.00 | 0 | 30.00 | 48.60 |
| SD (CV%) | 0 | 0 | 0 | 58.841 (121.07) |
| Median | 45.00 | 0 | 30.00 | 30.00 |
| IQR | 45.00 - 45.00 | 0 | 30.00 - 30.00 | 15.00 - 45.00 |
| Min-Max | 45.00 - 45.00 | 0 | 30.00 - 30.00 | 3.00 - 150.00 |
| Percentage change from baseline | | | | |
| n (%) | 1(11.1) | 0 | 1(20.0) | 3(7.9) |
| Mean | 200.00 | 0 | 0.00 | 44.44 |
| SD (CV%) | 0 | 0 | 0 | 138.778 (312.25) |
| Median | 200.00 | 0 | 0.00 | 0.00 |
| IQR | 200.00 - 200.00 | 0 | 0.00 - 0.00 | -66.67 - 200.00 |
| Min-Max | 200.00 - 200.00 | 0 | 0.00 - 0.00 | -66.67 - 200.00 |

- IQR (Inter-quartile range) represents the interval between the 25th and 75th percentiles.
- Only data from tumor samples collected prior to intra-patient dose escalation are included in this table.

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**Biomarker: Phosphoserine 240-S6 ribosomal protein, Timepoint: Cycle 1, Day 15**

Cellular compartment: Nuclear

| | INC280 100mg capsule N=4 | INC280 200mg capsule N=5 | INC280 250mg capsule N=4 | INC280 350mg capsule N=3 |
|---|---|---|---|---|
| Level | | | | |
| n (%) | 1(25.0) | 1(20.0) | 1(25.0) | 0 |
| Mean | 0.00 | 0.00 | 0.00 | 0 |
| SD (CV%) | 0 | 0 | 0 | 0 |
| Median | 0.00 | 0.00 | 0.00 | 0 |
| IQR | 0.00 - 0.00 | 0.00 - 0.00 | 0.00 - 0.00 | 0 |
| Min-Max | 0.00 - 0.00 | 0.00 - 0.00 | 0.00 - 0.00 | 0 |
| Percentage change from baseline | | | | |
| n (%) | 0 | 0 | 0 | 0 |
| Mean | 0 | 0 | 0 | 0 |
| SD (CV%) | 0 | 0 | 0 | 0 |
| Median | 0 | 0 | 0 | 0 |
| IQR | 0 | 0 | 0 | 0 |
| Min-Max | 0 | 0 | 0 | 0 |

| | INC280 450mg capsule N=9 | INC280 600mg capsule N=8 | INC280 400mg tablet N=5 | All dose escalation patients N=38 |
|---|---|---|---|---|
| Level | | | | |
| n (%) | 1(11.1) | 0 | 1(20.0) | 5(13.2) |
| Mean | 0.00 | 0 | 0.00 | 0.00 |
| SD (CV%) | 0 | 0 | 0 | 0 |
| Median | 0.00 | 0 | 0.00 | 0.00 |
| IQR | 0.00 - 0.00 | 0 | 0.00 - 0.00 | 0.00 - 0.00 |
| Min-Max | 0.00 - 0.00 | 0 | 0.00 - 0.00 | 0.00 - 0.00 |
| Percentage change from baseline | | | | |
| n (%) | 0 | 0 | 1(20.0) | 1(2.6) |
| Mean | 0 | 0 | -100.00 | -100.00 |
| SD (CV%) | 0 | 0 | 0 | 0 |
| Median | 0 | 0 | -100.00 | -100.00 |
| IQR | 0 | 0 | -100.00 - -100.00 | -100.00 - -100.00 |
| Min-Max | 0 | 0 | -100.00 - -100.00 | -100.00 - -100.00 |

- IQR (Inter-quartile range) represents the interval between the 25th and 75th percentiles.
- Only data from tumor samples collected prior to intra-patient dose escalation are included in this table.

**Summary statistics for H-score for IHC PD biomarkers (p-cMET, p-ERK, p-AKT, p-S6) from tumor sample by cohort in dose expansion (Full analysis set)**

**Biomarker: pAKT (AKT), Timepoint: Screening**

Cellular compartment: Cytoplasmic

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| | Gastric cancer N=9 n (%) | HCC N=11 n (%) | NSCLC N=55 n (%) | Other indications N=18 n (%) |
|---|---|---|---|---|
| Level | | | | |
| n (%) | 3(33.3) | 3(27.3) | 6(10.9) | 2(11.1) |
| Mean | 99.33 | 162.00 | 156.17 | 95.00 |
| SD (CV%) | 99.304 (99.97) | 119.549 (73.80) | 81.928 (52.46) | 7.071 (7.44) |
| Median | 70.00 | 96.00 | 113.50 | 95.00 |
| IQR | 18.00 - 210.00 | 90.00 - 300.00 | 100.00 - 210.00 | 90.00 - 100.00 |
| Min-Max | 18.00 - 210.00 | 90.00 - 300.00 | 100.00 - 300.00 | 90.00 - 100.00 |

| | All expansion patients N=93 n (%) |
|---|---|
| Level | |
| n (%) | 14(15.1) |
| Mean | 136.50 |
| SD (CV%) | 84.933 (62.22) |
| Median | 100.00 |
| IQR | 90.00 - 210.00 |
| Min-Max | 18.00 - 300.00 |

- IQR (Inter-quartile range) represents the interval between the 25th and 75th percentiles.
- Only data from tumor samples collected prior to intra-patient dose escalation are included in this table.

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**Biomarker: pAKT (AKT), Timepoint: Cycle 1, Day 15**

Cellular compartment: Cytoplasmic

| | Gastric cancer N=9 n (%) | HCC N=11 n (%) | NSCLC N=55 n (%) | Other indications N=18 n (%) | All expansion patients N=93 n (%) |
|---|---|---|---|---|---|
| Level | | | | | |
| n (%) | 1(11.1) | 2(18.2) | 5(9.1) | 3(16.7) | 11(11.8) |
| Mean | 125.00 | 115.00 | 120.00 | 106.33 | 115.82 |
| SD (CV%) | 0 | 21.213 (18.45) | 106.771 (88.98) | 76.814 (72.24) | 76.350 (65.92) |
| Median | 125.00 | 115.00 | 100.00 | 90.00 | 100.00 |
| IQR | 125.00 - 125.00 | 100.00 - 130.00 | 40.00 - 120.00 | 39.00 - 190.00 | 40.00 - 130.00 |
| Min-Max | 125.00 - 125.00 | 100.00 - 130.00 | 40.00 - 300.00 | 39.00 - 190.00 | |
| Percentage change from baseline | | | | | |
| n (%) | 1(11.1) | 1(9.1) | 2(3.6) | 1(5.6) | |
| Mean | -40.48 | 11.11 | -40.48 | -61.00 | |
| SD (CV%) | 0 | 0 | 57.242 (-141.42) | 0 | |
| Median | -40.48 | 11.11 | -40.48 | -61.00 | |
| IQR | -40.48 - -40.48 | 11.11 - 11.11 | -80.95 - 0.00 | -61.00 - -61.00 | |
| Min-Max | -40.48 - -40.48 | 11.11 - 11.11 | -80.95 - 0.00 | -61.00 - -61.00 | |

| | |
|---|---|
| Min-Max | 39.00 - 300.00 |
| Percentage change from baseline | |
| n (%) | 5(5.4) |
| Mean | -34.26 |
| SD (CV%) | 39.262 (-114.59) |
| Median | -40.48 |
| IQR | -61.00 - 0.00 |
| Min-Max | -80.95 - 11.11 |

- IQR (Inter-quartile range) represents the interval between the 25th and 75th percentiles.
- Only data from tumor samples collected prior to intra-patient dose escalation are included in this table.

**Biomarker: Phospho-Met (Tyr1234/1235) (D26) XP Rabbit mAb, Cell Signaling, #3077, Timepoint: Screening**

Cellular compartment: Cytoplasmic

| | Gastric cancer N=9 n (%) | HCC N=11 n (%) | NSCLC N=55 n (%) | Other indications N=18 n (%) |
|---|---|---|---|---|
| Level | | | | |
| n (%) | 3(33.3) | 3(27.3) | 6(10.9) | 2(11.1) |
| Mean | 0.00 | 93.33 | 62.17 | 0.00 |
| SD (CV%) | 0 | 161.658 (173.21) | 117.899 (189.65) | 0 |
| Median | 0.00 | 0.00 | 9.00 | 0.00 |
| IQR | 0.00 - 0.00 | 0.00 - 280.00 | 5.00 - 50.00 | 0.00 - 0.00 |
| Min-Max | 0.00 - 0.00 | 0.00 - 280.00 | 0.00 - 300.00 | 0.00 - 0.00 |

| | All expansion patients N=93 n (%) |
|---|---|
| Level | |
| n (%) | 14(15.1) |
| Mean | 46.64 |
| SD (CV%) | 104.009 (222.99) |
| Median | 0.00 |
| IQR | 0.00 - 10.00 |
| Min-Max | 0.00 - 300.00 |

- IQR (Inter-quartile range) represents the interval between the 25th and 75th percentiles.
- Only data from tumor samples collected prior to intra-patient dose escalation are included in this table.

**Biomarker: Phospho-Met (Tyr1234/1235) (D26) XP Rabbit mAb, Cell Signaling, #3077, Timepoint: Cycle 1, Day 15**

Cellular compartment: Cytoplasmic

| | Gastric cancer N=9 n (%) | HCC N=11 n (%) | NSCLC N=55 n (%) | Other indications N=18 n (%) |
|---|---|---|---|---|
| Level | | | | |
| n (%) | 1(11.1) | 2(18.2) | 6(10.9) | 3(16.7) |
| Mean | 0.00 | 2.50 | 26.00 | 5.00 |
| SD (CV%) | 0 | 3.536 (141.42) | 49.940 (192.08) | 8.660 (173.21) |
| Median | 0.00 | 2.50 | 0.50 | 0.00 |
| IQR | 0.00 - 0.00 | 0.00 - 5.00 | 0.00 - 30.00 | 0.00 - 15.00 |
| Min-Max | 0.00 - 0.00 | 0.00 - 5.00 | 0.00 - 125.00 | 0.00 - 15.00 |

| | | | | |
|---|---|---|---|---|
| Percentage change from baseline | | | | |
| n (%) | 0 | 0 | 2(3.6) | 0 |
| Mean | 0 | 0 | -95.00 | 0 |
| SD (CV%) | 0 | 0 | 7.071 (-7.44) | 0 |
| Median | 0 | 0 | -95.00 | 0 |
| IQR | 0 | 0 | -100.00 - -90.00 | 0 |
| Min-Max | 0 | 0 | -100.00 - -90.00 | 0 |

| | All expansion patients N=93 n (%) |
|---|---|
| Level | |
| n (%) | 12(12.9) |
| Mean | 14.67 |
| SD (CV%) | 35.922 (244.93) |
| Median | 0.00 |
| IQR | 0.00 - 10.00 |
| Min-Max | 0.00 - 125.00 |
| Percentage change from baseline | |
| n (%) | 2(2.2) |
| Mean | -95.00 |
| SD (CV%) | 7.071 (-7.44) |
| Median | -95.00 |
| IQR | -100.00 - -90.00 |
| Min-Max | -100.00 - -90.00 |

- IQR (Inter-quartile range) represents the interval between the 25th and 75th percentiles.
- Only data from tumor samples collected prior to intra-patient dose escalation are included in this table.

NOVARTIS

**Biomarker: Phospho-ERK, Timepoint: Screening**

Cellular compartment: Cytoplasmic

| | Gastric cancer N=9 n (%) | HCC N=11 n (%) | NSCLC N=55 n (%) | Other indications N=18 n (%) |
|---|---|---|---|---|
| Level | | | | |
| n (%) | 3(33.3) | 3(27.3) | 6(10.9) | 2(11.1) |
| Mean | 135.00 | 136.67 | 211.67 | 95.00 |
| SD (CV%) | 152.233 (112.77) | 83.865 (61.36) | 71.110 (33.60) | 63.640 (66.99) |
| Median | 105.00 | 180.00 | 230.00 | 95.00 |
| IQR | 0.00 - 300.00 | 40.00 - 190.00 | 160.00 - 250.00 | 50.00 - 140.00 |
| Min-Max | 0.00 - 300.00 | 40.00 - 190.00 | 100.00 - 300.00 | 50.00 - 140.00 |

| | All expansion patients N=93 n (%) |
|---|---|
| Level | |
| n (%) | 14(15.1) |
| Mean | 162.50 |
| SD (CV%) | 95.126 (58.54) |
| Median | 170.00 |
| IQR | 100.00 - 240.00 |
| Min-Max | 0.00 - 300.00 |

- IQR (Inter-quartile range) represents the interval between the 25th and 75th percentiles.
- Only data from tumor samples collected prior to intra-patient dose escalation are included in this table.

NOVARTIS

**Biomarker: Phospho-ERK, Timepoint: Screening**

Cellular compartment: Nuclear

| | Gastric cancer N=9 n (%) | HCC N=11 n (%) | NSCLC N=55 n (%) | Other indications N=18 n (%) |
|---|---|---|---|---|
| Level | | | | |
| n (%) | 3(33.3) | 3(27.3) | 6(10.9) | 2(11.1) |
| Mean | 105.00 | 109.00 | 154.17 | 52.50 |
| SD (CV%) | 169.041 (160.99) | 94.620 (86.81) | 87.431 (56.71) | 74.246 (141.42) |
| Median | 15.00 | 132.00 | 170.00 | 52.50 |
| IQR | 0.00 - 300.00 | 5.00 - 190.00 | 125.00 - 210.00 | 0.00 - 105.00 |
| Min-Max | 0.00 - 300.00 | 5.00 - 190.00 | 0.00 - 250.00 | 0.00 - 105.00 |

| | All expansion patients N=93 n (%) |
|---|---|
| Level | |
| n (%) | 14(15.1) |
| Mean | 119.43 |
| SD (CV%) | 102.259 (85.62) |
| Median | 128.50 |
| IQR | 5.00 - 190.00 |
| Min-Max | 0.00 - 300.00 |

- IQR (Inter-quartile range) represents the interval between the 25th and 75th percentiles.
- Only data from tumor samples collected prior to intra-patient dose escalation are included in this table.

NOVARTIS

**Biomarker: Phospho-ERK, Timepoint: Cycle 1, Day 15**

Cellular compartment: Cytoplasmic

| | Gastric cancer N=9 n (%) | HCC N=11 n (%) | NSCLC N=55 n (%) | Other indications N=18 n (%) | All expansion patients N=93 n (%) |
|---|---|---|---|---|---|
| Level | | | | | |
| n (%) | 1(11.1) | 2(18.2) | 5(9.1) | 3(16.7) | 11(11.8) |
| Mean | 300.00 | 57.50 | 211.00 | 86.67 | 157.27 |
| SD (CV%) | 0 | 67.175 (116.83) | 86.631 (41.06) | 55.076 (63.55) | 105.009 (66.77) |
| Median | 300.00 | 57.50 | 240.00 | 60.00 | |
| IQR | 300.00 - 300.00 | 10.00 - 105.00 | 155.00 - 270.00 | 50.00 - 150.00 | |
| Min-Max | 300.00 - 300.00 | 10.00 - 105.00 | 90.00 - 300.00 | 50.00 - 150.00 | |
| Percentage change from baseline | | | | | |
| n (%) | 1(11.1) | 1(9.1) | 2(3.6) | 1(5.6) | |
| Mean | 0.00 | -41.67 | 5.63 | -64.29 | |
| SD (CV%) | 0 | 0 | 69.827 (1241.37) | 0 | |
| Median | 0.00 | -41.67 | 5.63 | -64.29 | |
| IQR | 0.00 - 0.00 | -41.67 - -41.67 | -43.75 - 55.00 | -64.29 - -64.29 | |
| Min-Max | 0.00 - 0.00 | -41.67 - -41.67 | -43.75 - 55.00 | -64.29 - -64.29 | |

| | |
|---|---|
| Median | 150.00 |
| IQR | 60.00 - 270.00 |
| Min-Max | 10.00 - 300.00 |
| Percentage change from baseline | |
| n (%) | 5(5.4) |
| Mean | -18.94 |
| SD (CV%) | 47.471 (-250.63) |
| Median | -41.67 |
| IQR | -43.75 - 0.00 |
| Min-Max | -64.29 - 55.00 |

- IQR (Inter-quartile range) represents the interval between the 25th and 75th percentiles.
- Only data from tumor samples collected prior to intra-patient dose escalation are included in this table.

**Biomarker: Phospho-ERK, Timepoint: Cycle 1, Day 15**

Cellular compartment: Nuclear

| | Gastric cancer N=9 n (%) | HCC N=11 n (%) | NSCLC N=55 n (%) | Other indications N=18 n (%) |
|---|---|---|---|---|
| Level | | | | |
| n (%) | 1(11.1) | 2(18.2) | 5(9.1) | 3(16.7) |
| Mean | 300.00 | 17.50 | 238.00 | 50.33 |
| SD (CV%) | 0 | 24.749 (141.42) | 54.498 (22.90) | 8.386 (16.66) |
| Median | 300.00 | 17.50 | 250.00 | 46.00 |
| IQR | 300.00 - 300.00 | 0.00 - 35.00 | 240.00 - 250.00 | 45.00 - 60.00 |
| Min-Max | 300.00 - 300.00 | 0.00 - 35.00 | 150.00 - 300.00 | 45.00 - 60.00 |
| Percentage change from | | | | |

| | | | | |
|---|---|---|---|---|
| baseline | | | | |
| n (%) | 1(11.1) | 1(9.1) | 1(1.8) | 1(5.6) |
| Mean | 0.00 | -73.48 | 20.00 | -57.14 |
| SD (CV%) | 0 | 0 | 0 | 0 |
| Median | 0.00 | -73.48 | 20.00 | -57.14 |
| IQR | 0.00 - 0.00 | -73.48 - -73.48 | 20.00 - 20.00 | -57.14 - -57.14 |
| Min-Max | 0.00 - 0.00 | -73.48 - -73.48 | 20.00 - 20.00 | -57.14 - -57.14 |

| | All expansion patients N=93 n (%) |
|---|---|
| Level | |
| n (%) | 11(11.8) |
| Mean | 152.36 |
| SD (CV%) | 117.773 (77.30) |
| Median | 150.00 |
| IQR | 45.00 - 250.00 |
| Min-Max | 0.00 - 300.00 |
| Percentage change from baseline | |
| n (%) | 4(4.3) |
| Mean | -27.66 |
| SD (CV%) | 44.743 (-161.78) |
| Median | -28.57 |
| IQR | -65.31 - 10.00 |
| Min-Max | -73.48 - 20.00 |

- IQR (Inter-quartile range) represents the interval between the 25th and 75th percentiles.
- Only data from tumor samples collected prior to intra-patient dose escalation are included in this table.

NOVARTIS

**Biomarker: Phosphoserine 240-S6 ribosomal protein, Timepoint: Screening**

Cellular compartment: Cytoplasmic

| | Gastric cancer N=9 n (%) | HCC N=11 n (%) | NSCLC N=55 n (%) | Other indications N=18 n (%) |
|---|---|---|---|---|
| Level | | | | |
| n (%) | 3(33.3) | 3(27.3) | 5(9.1) | 2(11.1) |
| Mean | 108.33 | 130.00 | 138.00 | 42.50 |
| SD (CV%) | 105.159 (97.07) | 60.828 (46.79) | 74.632 (54.08) | 24.749 (58.23) |
| Median | 115.00 | 100.00 | 130.00 | 42.50 |
| IQR | 0.00 - 210.00 | 90.00 - 200.00 | 90.00 - 180.00 | 25.00 - 60.00 |
| Min-Max | 0.00 - 210.00 | 90.00 - 200.00 | 50.00 - 240.00 | 25.00 - 60.00 |

| | All expansion patients N=93 n (%) |
|---|---|
| Level | |
| n (%) | 13(14.0) |
| Mean | 114.62 |
| SD (CV%) | 74.371 (64.89) |
| Median | 100.00 |
| IQR | 60.00 - 180.00 |
| Min-Max | 0.00 - 240.00 |

- IQR (Inter-quartile range) represents the interval between the 25th and 75th percentiles.
- Only data from tumor samples collected prior to intra-patient dose escalation are included in this table.

NOVARTIS

**Biomarker: Phosphoserine 240-S6 ribosomal protein, Timepoint: Screening**

Cellular compartment: Nuclear

| | Gastric cancer N=9 n (%) | HCC N=11 n (%) | NSCLC N=55 n (%) | Other indications N=18 n (%) | All expansion patients N=93 n (%) |
|---|---|---|---|---|---|
| Level | | | | | |
| n (%) | 3(33.3) | 3(27.3) | 5(9.1) | 2(11.1) | 13(14.0) |
| Mean | 38.33 | 8.33 | 12.00 | 7.50 | 16.54 |
| SD (CV%) | 66.395 (173.21) | 7.638 (91.65) | 13.435 (111.96) | 10.607 (141.42) | 31.173 (188.49) |
| Median | 0.00 | 10.00 | 9.00 | 7.50 | 9.00 |
| IQR | 0.00 - 115.00 | 0.00 - 15.00 | 0.00 - 20.00 | 0.00 - 15.00 | 0.00 - 15.00 |
| Min-Max | 0.00 - 115.00 | 0.00 - 15.00 | 0.00 - 31.00 | 0.00 - 15.00 | 0.00 - 115.00 |

- IQR (Inter-quartile range) represents the interval between the 25th and 75th percentiles.
- Only data from tumor samples collected prior to intra-patient dose escalation are included in this table.

NOVARTIS

**Biomarker: Phosphoserine 240-S6 ribosomal protein, Timepoint: Cycle 1, Day 15**

Cellular compartment: Cytoplasmic

| | Gastric cancer N=9 n (%) | HCC N=11 n (%) | NSCLC N=55 n (%) | Other indications N=18 n (%) | All expansion patients N=93 n (%) |
|---|---|---|---|---|---|
| Level | | | | | |
| n (%) | 1(11.1) | 2(18.2) | 6(10.9) | 3(16.7) | 12(12.9) |
| Mean | 180.00 | 35.00 | 82.50 | 83.33 | 82.92 |
| SD (CV%) | 0 | 35.355 (101.02) | 58.030 (70.34) | 18.930 (22.72) | 54.625 (65.88) |
| Median | 180.00 | 35.00 | 80.00 | 75.00 | 72.50 |
| IQR | 180.00 - 180.00 | 10.00 - 60.00 | 25.00 - 135.00 | 70.00 - 105.00 | 42.50 - 120.00 |
| Min-Max | 180.00 - 180.00 | 10.00 - 60.00 | 15.00 - 160.00 | 70.00 - 105.00 | |
| Percentage change from baseline | | | | | |
| n (%) | 1(11.1) | 1(9.1) | 1(1.8) | 1(5.6) | |
| Mean | -14.29 | -33.33 | -72.22 | 200.00 | |
| SD (CV%) | 0 | 0 | 0 | 0 | |
| Median | -14.29 | -33.33 | -72.22 | 200.00 | |
| IQR | -14.29 - -14.29 | -33.33 - -33.33 | -72.22 - -72.22 | 200.00 - 200.00 | |
| Min-Max | -14.29 - -14.29 | -33.33 - -33.33 | -72.22 - -72.22 | 200.00 - 200.00 | |

| | |
|---|---|
| Min-Max | 10.00 - 180.00 |
| Percentage change from baseline | |
| n (%) | 4(4.3) |
| Mean | 20.04 |
| SD (CV%) | 122.372 (610.65) |
| Median | -23.81 |
| IQR | -52.78 - 92.86 |
| Min-Max | -72.22 - 200.00 |

- IQR (Inter-quartile range) represents the interval between the 25th and 75th percentiles.
- Only data from tumor samples collected prior to intra-patient dose escalation are included in this table.

**Biomarker: Phosphoserine 240-S6 ribosomal protein, Timepoint: Cycle 1, Day 15**

Cellular compartment: Nuclear

| | Gastric cancer N=9 n (%) | HCC N=11 n (%) | NSCLC N=55 n (%) | Other indications N=18 n (%) |
|---|---|---|---|---|
| Level | | | | |
| n (%) | 1(11.1) | 2(18.2) | 6(10.9) | 3(16.7) |
| Mean | 0.00 | 0.00 | 1.67 | 10.67 |
| SD (CV%) | 0 | 0 | 4.082 (244.95) | 10.066 (94.37) |
| Median | 0.00 | 0.00 | 0.00 | 12.00 |
| IQR | 0.00 - 0.00 | 0.00 - 0.00 | 0.00 - 0.00 | 0.00 - 20.00 |
| Min-Max | 0.00 - 0.00 | 0.00 - 0.00 | 0.00 - 10.00 | 0.00 - 20.00 |
| Percentage change from baseline | | | | |
| n (%) | 0 | 1(9.1) | 1(1.8) | 1(5.6) |
| Mean | 0 | -100.00 | 11.11 | -20.00 |

| | | | | |
|---|---|---|---|---|
| SD (CV%) | 0 | 0 | 0 | 0 |
| Median | 0 | -100.00 | 11.11 | -20.00 |
| IQR | 0 | -100.00 - -100.00 | 11.11 - 11.11 | -20.00 - -20.00 |
| Min-Max | 0 | -100.00 - -100.00 | 11.11 - 11.11 | -20.00 - -20.00 |

| | All expansion patients N=93 n (%) |
|---|---|
| Level | |
| n (%) | 12(12.9) |
| Mean | 3.50 |
| SD (CV%) | 6.722 (192.05) |
| Median | 0.00 |
| IQR | 0.00 - 5.00 |
| Min-Max | 0.00 - 20.00 |
| Percentage change from baseline | |
| n (%) | 3(3.2) |
| Mean | -36.30 |
| SD (CV%) | 57.320 (-157.92) |
| Median | -20.00 |
| IQR | -100.00 - 11.11 |
| Min-Max | -100.00 - 11.11 |

**Summary of primary PK parameters for plasma capmatinib capsule (Cycle 1 Day 1) by cohort group (Pharmacokinetic analysis set)**

| Treatment (bid) | Statistics | AUClast (hr*ng/mL) | AUC0-8h (hr*ng/mL) | AUC0-12h (hr*ng/mL) | Cmax (ng/mL) | Tmax (hr) |
|---|---|---|---|---|---|---|
| **Capmatinib 100mg capsule (N=4)** | n | 4 | 3 | 2 | 4 | 4 |

| Treatment (bid) | Statistics | AUClast (hr*ng/mL) | AUC0-8h (hr*ng/mL) | AUC0-12h (hr*ng/mL) | Cmax (ng/mL) | Tmax (hr) |
|---|---|---|---|---|---|---|
| | Mean (SD) | 1950 (1190) | 2080 (1430) | 3120 (862) | 474 (309) | N/A |
| | CV% mean | 61.0 | 68.9 | 27.7 | 65.2 | N/A |
| | Geo-mean | 1610 | 1620 | 3060 | 375 | N/A |
| | CV% geo-mean | 92.3 | 124.0 | 28.6 | 107.8 | N/A |
| | Median | 1940 | 2320 | 3120 | 478 | 3.02 |
| | [Min; Max] | [544; 3370] | [544; 3380] | [2510; 3730] | [112; 827] | [1.92; 4.33] |
| **Capmatinib 200mg capsule (N=5)** | n | 5 | 5 | 4 | 5 | 5 |
| | Mean (SD) | 9460 (5560) | 9680 (5540) | 8320 (3690) | 2470 (955) | N/A |
| | CV% mean | 58.7 | 57.3 | 44.4 | 38.6 | N/A |
| | Geo-mean | 8290 | 8500 | 7670 | 2320 | N/A |
| | CV% geo-mean | 62.4 | 62.9 | 50.4 | 41.7 | N/A |
| | Median | 9340 | 9810 | 8240 | 2460 | 2.10 |
| | [Min; Max] | [4030; 18500] | [4030; 18500] | [4380; 12400] | [1330; 3870] | [0.500; 4.00] |
| **Capmatinib 250mg capsule (N=4)** | n | 4 | 3 | 2 | 4 | 4 |
| | Mean (SD) | 4560 (2350) | 4270 (2840) | 5980 (2990) | 1140 (838) | N/A |
| | CV% mean | 51.5 | 66.5 | 49.9 | 73.7 | N/A |
| | Geo-mean | 4040 | 3650 | 5600 | 902 | N/A |
| | CV% geo-mean | 65.5 | 78.4 | 55.9 | 99.0 | N/A |
| | Median | 4580 | 3550 | 5980 | 974 | 3.19 |
| | [Min; Max] | [1850; 7230] | [1850; 7390] | [3870; 8100] | [312; 2290] | [1.00; 5.88] |
| **Capmatinib 350mg capsule (N=3)** | n | 3 | 2 | 2 | 3 | 3 |

| Treatment (bid) | Statistics | AUClast (hr*ng/mL) | AUC0-8h (hr*ng/mL) | AUC0-12h (hr*ng/mL) | Cmax (ng/mL) | Tmax (hr) |
|---|---|---|---|---|---|---|
| | Mean (SD) | 12000 (11300) | 15900 (12900) | 17800 (12800) | 3700 (4350) | N/A |
| | CV% mean | 93.9 | 80.9 | 72.1 | 117.7 | N/A |
| | Geo-mean | 9070 | 13100 | 15300 | 2280 | N/A |
| | CV% geo-mean | 110.6 | 115.3 | 93.9 | 172.7 | N/A |
| | Median | 6400 | 15900 | 17800 | 1410 | 2.05 |
| | [Min; Max] | [4650; 25000] | [6820; 25000] | [8750; 26900] | [968; 8720] | [0.833; 3.97] |
| **Capmatinib 450mg capsule (N=8)** | n | 8 | 5 | 4 | 8 | 8 |
| | Mean (SD) | 7840 (2810) | 8710 (3440) | 9240 (4330) | 2280 (985) | N/A |
| | CV% mean | 35.8 | 39.4 | 46.9 | 43.3 | N/A |
| | Geo-mean | 7300 | 7920 | 8150 | 2100 | N/A |
| | CV% geo-mean | 45.3 | 58.9 | 71.6 | 45.4 | N/A |
| | Median | 8080 | 9970 | 10700 | 2070 | 2.25 |
| | [Min; Max] | [3090; 11500] | [3090; 11500] | [3190; 12500] | [1050; 3910] | [1.13; 7.17] |
| **Capmatinib 600mg capsule (N=8)** | n | 8 | 5 | 4 | 8 | 8 |
| | Mean (SD) | 18800 (12200) | 24200 (12000) | 23600 (13300) | 4680 (3080) | N/A |
| | CV% mean | 65.2 | 49.8 | 56.5 | 65.7 | N/A |
| | Geo-mean | 12900 | 19100 | 18100 | 3260 | N/A |
| | CV% geo-mean | 153.4 | 122.8 | 135.1 | 145.2 | N/A |
| | Median | 25400 | 27600 | 28500 | 6130 | 2.04 |
| | [Min; Max] | [2020; 30900] | [3470; 34300] | [3940; 33500] | [605; 7860] | [1.00; 7.17] |

| Treatment (bid) | Statistics | AUClast (hr*ng/mL) | AUC0-8h (hr*ng/mL) | AUC0-12h (hr*ng/mL) | Cmax (ng/mL) | Tmax (hr) |
|---|---|---|---|---|---|---|
| n: number of subjects with non-missing values.<br>CV% = coefficient of variation (%) = sd/mean*100<br>CV% geo-mean = sqrt (exp (variance for log transformed data)-1)*100. | | | | | | |

**Summary of primary PK parameters for plasma capmatinib capsule (Cycle 1 Day 15) by cohort group (Pharmacokinetic analysis set)**

| Treatment (bid) | Statistics | AUClast (hr*ng/mL) | AUC0-8h (hr*ng/mL) | AUC0-12h (hr*ng/mL) | Cmax (ng/mL) | Tmax (hr) |
|---|---|---|---|---|---|---|
| **Capmatinib 100mg capsule (N=4)** | n | 4 | 4 | 4 | 4 | 4 |
| | Mean (SD) | 3820 (2420) | 2960 (2120) | 3820 (2420) | 660 (550) | N/A |
| | CV% mean | 63.5 | 71.4 | 63.5 | 83.3 | N/A |
| | Geo-mean | 3280 | 2450 | 3280 | 503 | N/A |
| | CV% geo-mean | 70.3 | 81.5 | 70.3 | 105.4 | N/A |
| | Median | 3220 | 2400 | 3220 | 510 | 2.86 |
| | [Min; Max] | [1770; 7070] | [1210; 5860] | [1770; 7070] | [190; 1430] | [1.88; 4.00] |
| **Capmatinib 200mg capsule (N=5)** | n | 5 | 5 | 5 | 5 | 5 |
| | Mean (SD) | 13300 (6800) | 10600 (3630) | 13500 (6530) | 2500 (856) | N/A |
| | CV% mean | 51.3 | 34.3 | 48.5 | 34.2 | N/A |
| | Geo-mean | 11900 | 10000 | 12200 | 2370 | N/A |
| | CV% geo-mean | 58.1 | 38.2 | 52.4 | 39.2 | N/A |
| | Median | 13900 | 11400 | 13900 | 2260 | 1.92 |
| | [Min; Max] | [6120; 23200] | [6500; 14400] | [7200; 23200] | [1340; 3450] | [1.85; 8.00] |
| **Capmatinib 250mg capsule (N=3)** | n | 3 | 3 | 3 | 3 | 3 |

| Treatment (bid) | Statistics | AUClast (hr*ng/mL) | AUC0-8h (hr*ng/mL) | AUC0-12h (hr*ng/mL) | Cmax (ng/mL) | Tmax (hr) |
|---|---|---|---|---|---|---|
| | Mean (SD) | 7070 (3990) | 6010 (3580) | 7070 (3990) | 1580 (1010) | N/A |
| | CV% mean | 56.4 | 59.7 | 56.4 | 63.8 | N/A |
| | Geo-mean | 6250 | 5240 | 6250 | 1270 | N/A |
| | CV% geo-mean | 70.0 | 74.8 | 70.0 | 113.5 | N/A |
| | Median | 6860 | 5700 | 6860 | 1920 | 1.00 |
| | [Min; Max] | [3190; 11200] | [2590; 9730] | [3190; 11200] | [447; 2380] | [0.450; 2.02] |
| **Capmatinib 350mg capsule (N=3)** | n | 3 | 3 | 3 | 3 | 3 |
| | Mean (SD) | 19400 (5360) | 16200 (6470) | 19400 (5360) | 4410 (3800) | N/A |
| | CV% mean | 27.7 | 39.9 | 27.7 | 86.3 | N/A |
| | Geo-mean | 18900 | 15400 | 18900 | 3500 | N/A |
| | CV% geo-mean | 26.5 | 38.3 | 26.5 | 94.4 | N/A |
| | Median | 16400 | 12500 | 16400 | 2240 | 3.93 |
| | [Min; Max] | [16200; 25600] | [12400; 23700] | [16200; 25600] | [2180; 8800] | [1.00; 4.02] |
| **Capmatinib 450mg capsule (N=7)** | n | 7 | 7 | 7 | 7 | 7 |
| | Mean (SD) | 18800 (6870) | 14600 (4550) | 18800 (6870) | 3200 (1280) | N/A |
| | CV% mean | 36.6 | 31.1 | 36.6 | 39.8 | N/A |
| | Geo-mean | 17900 | 14000 | 17900 | 2970 | N/A |
| | CV% geo-mean | 32.6 | 32.5 | 32.6 | 46.3 | N/A |
| | Median | 17100 | 14500 | 17100 | 3120 | 2.00 |
| | [Min; Max] | [12400; 33100] | [8310; 22400] | [12400; 33100] | [1400; 4840] | [1.83; 7.87] |

| Treatment (bid) | Statistics | AUClast (hr*ng/mL) | AUC0-8h (hr*ng/mL) | AUC0-12h (hr*ng/mL) | Cmax (ng/mL) | Tmax (hr) |
|---|---|---|---|---|---|---|
| **Capmatinib 600mg capsule (N=45)** | n | 45 | 44 | 43 | 45 | 45 |
| | Mean (SD) | 24700 (15200) | 20800 (13000) | 25600 (14900) | 4890 (3580) | N/A |
| | CV% mean | 61.4 | 62.5 | 58.3 | 73.2 | N/A |
| | Geo-mean | 19800 | 16900 | 21200 | 3630 | N/A |
| | CV% geo-mean | 84.9 | 79.8 | 74.4 | 103.4 | N/A |
| | Median | 21400 | 17500 | 21800 | 4180 | 2.00 |
| | [Min; Max] | [2340; 64000] | [2250; 54100] | [3370; 64000] | [407; 15300] | [0.517; 8.42] |

n: number of subjects with non-missing values.
CV% = coefficient of variation (%) = sd/mean*100
CV% geo-mean = sqrt (exp (variance for log transformed data)-1)*100.

**Summary of primary PK parameters for plasma capmatinib tablet (Cycle 1 Day 1) by cohort group (Pharmacokinetic analysis set)**

| Treatment (bid) | Statistics | AUClast (hr*ng/mL) | AUC0-8h (hr*ng/mL) | AUC0-12h (hr*ng/mL) | Cmax (ng/mL) | Tmax (hr) |
|---|---|---|---|---|---|---|
| **Capmatinib 400mg tablet (N=4)** | n | 4 | 4 | 4 | 4 | 4 |
| | Mean (SD) | 17700 (5170) | 18200 (5110) | 19600 (5480) | 5390 (2380) | N/A |
| | CV% mean | 29.3 | 28.0 | 27.9 | 44.2 | N/A |
| | Geo-mean | 17000 | 17600 | 19000 | 4970 | N/A |
| | CV% geo-mean | 34.2 | 33.2 | 33.3 | 50.0 | N/A |
| | Median | 18700 | 19600 | 21300 | 5190 | 1.88 |
| | [Min; Max] | [10600; 22700] | [11000; 22700] | [11800; 24200] | [2690; 8470] | [0.500; 2.17] |

| Treatment (bid) | Statistics | AUClast (hr*ng/mL) | AUC0-8h (hr*ng/mL) | AUC0-12h (hr*ng/mL) | Cmax (ng/mL) | Tmax (hr) |
|---|---|---|---|---|---|---|
| n: number of subjects with non-missing values.<br>CV% = coefficient of variation (%) = sd/mean*100<br>CV% geo-mean = sqrt (exp (variance for log transformed data)-1)*100. | | | | | | |

**Summary of primary PK parameters for plasma capmatinib tablet (Cycle 1 Day 15) by cohort group (Pharmacokinetic analysis set)**

| Treatment (bid) | Statistics | AUClast (hr*ng/mL) | AUC0-8h (hr*ng/mL) | AUC0-12h (hr*ng/mL) | Cmax (ng/mL) | Tmax (hr) |
|---|---|---|---|---|---|---|
| **Capmatinib 400mg tablet (N=8)** | n | 8 | 8 | 8 | 8 | 8 |
| | Mean (SD) | 22000 (7790) | 18200 (6860) | 22000 (7790) | 4910 (2510) | N/A |
| | CV% mean | 35.5 | 37.6 | 35.5 | 51.0 | N/A |
| | Geo-mean | 20600 | 17000 | 20600 | 4350 | N/A |
| | CV% geo-mean | 41.9 | 43.4 | 41.9 | 57.9 | N/A |
| | Median | 21000 | 18800 | 21000 | 4850 | 2.02 |
| | [Min; Max] | [9560; 31700] | [8610; 27400] | [9560; 31700] | [2250; 8810] | [0.500; 4.33] |
| n: number of subjects with non-missing values.<br>CV% = coefficient of variation (%) = sd/mean*100<br>CV% geo-mean = sqrt (exp (variance for log transformed data)-1)*100. | | | | | | |

## Summary of Safety

## Safety Results

**Adverse events, regardless of study drug relationship, by primary system organ class, preferred term and cohort in dose escalation**
**(Safety set)**

| Primary system organ class<br>Preferred term | INC280 100mg capsule N=4<br>n (%) | INC280 200mg capsule N=5<br>n (%) | INC280 250mg capsule N=4<br>n (%) | INC280 350mg capsule N=3<br>n (%) | INC280 450mg capsule N=9<br>n (%) | INC280 600mg capsule N=8<br>n (%) | INC280 400mg tablet N=5<br>n (%) | All dose escalation patients N=38<br>n (%) |
|---|---|---|---|---|---|---|---|---|
| -Any primary system organ class | | | | | | | | |
| -Total | 4 (100) | 5 (100) | 4 (100) | 3 (100) | 9 (100) | 8 (100) | 5 (100) | 38 (100) |
| Blood And Lymphatic System Disorders | | | | | | | | |
| -Total | 2 (50.0) | 3 (60.0) | 2 (50.0) | 2 (66.7) | 1 (11.1) | 2 (25.0) | 0 | 12 (31.6) |
| Anaemia | 1 (25.0) | 2 (40.0) | 1 (25.0) | 1 (33.3) | 0 | 2 (25.0) | 0 | 7 (18.4) |
| Disseminated Intravascular Coagulation | 1 (25.0) | 0 | 0 | 0 | 0 | 0 | 0 | 1 (2.6) |
| Lymphopenia | 0 | 1 (20.0) | 0 | 0 | 0 | 0 | 0 | 1 (2.6) |
| Neutropenia | 0 | 0 | 1 (25.0) | 0 | 1 (11.1) | 0 | 0 | 2 (5.3) |
| Thrombocytopenia | 0 | 0 | 0 | 1 (33.3) | 0 | 0 | 0 | 1 (2.6) |
| Cardiac Disorders | | | | | | | | |
| -Total | 0 | 0 | 0 | 0 | 1 (11.1) | 0 | 1 (20.0) | 2 (5.3) |
| Pericardial Effusion | 0 | 0 | 0 | 0 | 0 | 0 | 1 (20.0) | 1 (2.6) |
| Tachycardia | 0 | 0 | 0 | 0 | 1 (11.1) | 0 | 0 | 1 (2.6) |
| Ear And Labyrinth Disorders | | | | | | | | |
| -Total | 1 (25.0) | 0 | 0 | 0 | 1 (11.1) | 1 (12.5) | 1 (20.0) | 4 (10.5) |

NOVARTIS

| Primary system organ class<br>Preferred term | INC280 100mg capsule N=4<br>n (%) | INC280 200mg capsule N=5<br>n (%) | INC280 250mg capsule N=4<br>n (%) | INC280 350mg capsule N=3<br>n (%) | INC280 450mg capsule N=9<br>n (%) | INC280 600mg capsule N=8<br>n (%) | INC280 400mg tablet N=5<br>n (%) | All dose escalation patients N=38<br>n (%) |
|---|---|---|---|---|---|---|---|---|
| Ear And Labyrinth Disorders | | | | | | | | |
| Deafness | 0 | 0 | 0 | 0 | 0 | 1 (12.5) | 0 | 1 (2.6) |
| Deafness Unilateral | 0 | 0 | 0 | 0 | 1 (11.1) | 0 | 0 | 1 (2.6) |
| Eustachian Tube Patulous | 1 (25.0) | 0 | 0 | 0 | 0 | 0 | 0 | 1 (2.6) |
| Hypoacusis | 0 | 0 | 0 | 0 | 0 | 0 | 1 (20.0) | 1 (2.6) |
| Endocrine Disorders | | | | | | | | |
| -Total | 0 | 0 | 0 | 0 | 0 | 0 | 1 (20.0) | 1 (2.6) |
| Hypothyroidism | 0 | 0 | 0 | 0 | 0 | 0 | 1 (20.0) | 1 (2.6) |
| Eye Disorders | | | | | | | | |
| -Total | 0 | 0 | 0 | 0 | 0 | 1 (12.5) | 0 | 1 (2.6) |
| Vitreous Floaters | 0 | 0 | 0 | 0 | 0 | 1 (12.5) | 0 | 1 (2.6) |
| Gastrointestinal Disorders | | | | | | | | |
| -Total | 4 (100) | 5 (100) | 3 (75.0) | 1 (33.3) | 9 (100) | 8 (100) | 4 (80.0) | 34 (89.5) |
| Abdominal Discomfort | 0 | 0 | 1 (25.0) | 0 | 0 | 0 | 0 | 1 (2.6) |
| Abdominal Distension | 1 (25.0) | 1 (20.0) | 1 (25.0) | 0 | 2 (22.2) | 0 | 0 | 5 (13.2) |
| Abdominal Pain | 3 (75.0) | 0 | 0 | 0 | 3 (33.3) | 0 | 1 (20.0) | 7 (18.4) |
| Abdominal Pain Upper | 1 (25.0) | 0 | 1 (25.0) | 1 (33.3) | 0 | 1 (12.5) | 1 (20.0) | 5 (13.2) |

NOVARTIS

| Primary system organ class<br>Preferred term | INC280 100mg capsule N=4 n (%) | INC280 200mg capsule N=5 n (%) | INC280 250mg capsule N=4 n (%) | INC280 350mg capsule N=3 n (%) | INC280 450mg capsule N=9 n (%) | INC280 600mg capsule N=8 n (%) | INC280 400mg tablet N=5 n (%) | All dose escalation patients N=38 n (%) |
|---|---|---|---|---|---|---|---|---|
| Gastrointestinal Disorders | | | | | | | | |
| Abdominal Tenderness | 0 | 0 | 0 | 0 | 1 (11.1) | 0 | 0 | 1 (2.6) |
| Ascites | 1 (25.0) | 2 (40.0) | 1 (25.0) | 0 | 2 (22.2) | 1 (12.5) | 0 | 7 (18.4) |
| Constipation | 1 (25.0) | 0 | 2 (50.0) | 0 | 1 (11.1) | 1 (12.5) | 2 (40.0) | 7 (18.4) |
| Diarrhoea | 2 (50.0) | 2 (40.0) | 0 | 1 (33.3) | 1 (11.1) | 2 (25.0) | 1 (20.0) | 9 (23.7) |
| Dyspepsia | 1 (25.0) | 0 | 0 | 0 | 1 (11.1) | 1 (12.5) | 0 | 3 (7.9) |
| Epigastric Discomfort | 0 | 1 (20.0) | 0 | 0 | 0 | 0 | 0 | 1 (2.6) |
| Gastritis | 0 | 1 (20.0) | 0 | 0 | 0 | 0 | 0 | 1 (2.6) |
| Gastrooesophageal Reflux Disease | 2 (50.0) | 0 | 0 | 0 | 0 | 0 | 1 (20.0) | 3 (7.9) |
| Haemorrhoids | 0 | 0 | 0 | 0 | 0 | 1 (12.5) | 0 | 1 (2.6) |
| Impaired Gastric Emptying | 0 | 0 | 0 | 0 | 1 (11.1) | 0 | 0 | 1 (2.6) |
| Intestinal Obstruction | 0 | 0 | 0 | 0 | 2 (22.2) | 0 | 0 | 2 (5.3) |
| Nausea | 1 (25.0) | 2 (40.0) | 0 | 0 | 5 (55.6) | 3 (37.5) | 3 (60.0) | 14 (36.8) |
| Odynophagia | 1 (25.0) | 0 | 0 | 0 | 0 | 0 | 1 (20.0) | 2 (5.3) |
| Oesophageal Varices Haemorrhage | 0 | 1 (20.0) | 0 | 0 | 0 | 0 | 0 | 1 (2.6) |
| Rectal Haemorrhage | 0 | 0 | 0 | 0 | 0 | 1 (12.5) | 0 | 1 (2.6) |
| Stomatitis | 0 | 0 | 0 | 0 | 0 | 2 (25.0) | 1 (20.0) | 3 (7.9) |
| Varices Oesophageal | 0 | 0 | 0 | 0 | 0 | 1 (12.5) | 0 | 1 (2.6) |
| Vomiting | 2 (50.0) | 2 (40.0) | 2 (50.0) | 0 | 3 (33.3) | 4 (50.0) | 2 (40.0) | 15 (39.5) |

| Primary system organ class<br>Preferred term | INC280 100mg capsule N=4 n (%) | INC280 200mg capsule N=5 n (%) | INC280 250mg capsule N=4 n (%) | INC280 350mg capsule N=3 n (%) | INC280 450mg capsule N=9 n (%) | INC280 600mg capsule N=8 n (%) | INC280 400mg tablet N=5 n (%) | All dose escalation patients N=38 n (%) |
|---|---|---|---|---|---|---|---|---|
| General Disorders And Administration Site Conditions | | | | | | | | |
| -Total | 3 (75.0) | 4 (80.0) | 2 (50.0) | 2 (66.7) | 6 (66.7) | 6 (75.0) | 4 (80.0) | 27 (71.1) |
| Asthenia | 3 (75.0) | 1 (20.0) | 0 | 1 (33.3) | 1 (11.1) | 0 | 1 (20.0) | 7 (18.4) |
| Catheter Site Pain | 1 (25.0) | 0 | 0 | 0 | 0 | 0 | 0 | 1 (2.6) |
| Chills | 0 | 0 | 0 | 0 | 1 (11.1) | 0 | 0 | 1 (2.6) |
| Early Satiety | 0 | 0 | 0 | 0 | 1 (11.1) | 0 | 0 | 1 (2.6) |
| Fatigue | 0 | 2 (40.0) | 1 (25.0) | 0 | 3 (33.3) | 3 (37.5) | 1 (20.0) | 10 (26.3) |
| Non-Cardiac Chest Pain | 0 | 1 (20.0) | 0 | 0 | 1 (11.1) | 1 (12.5) | 1 (20.0) | 4 (10.5) |
| Oedema | 1 (25.0) | 0 | 0 | 0 | 0 | 0 | 0 | 1 (2.6) |
| Oedema Peripheral | 2 (50.0) | 1 (20.0) | 2 (50.0) | 2 (66.7) | 3 (33.3) | 3 (37.5) | 2 (40.0) | 15 (39.5) |
| Pain | 0 | 0 | 0 | 0 | 1 (11.1) | 0 | 1 (20.0) | 2 (5.3) |
| Pyrexia | 0 | 2 (40.0) | 0 | 0 | 2 (22.2) | 2 (25.0) | 0 | 6 (15.8) |
| Hepatobiliary Disorders | | | | | | | | |
| -Total | 1 (25.0) | 1 (20.0) | 0 | 0 | 0 | 2 (25.0) | 1 (20.0) | 5 (13.2) |
| Cholestasis | 0 | 0 | 0 | 0 | 0 | 0 | 1 (20.0) | 1 (2.6) |
| Hepatic Haematoma | 1 (25.0) | 0 | 0 | 0 | 0 | 0 | 0 | 1 (2.6) |
| Hepatitis | 0 | 0 | 0 | 0 | 0 | 1 (12.5) | 0 | 1 (2.6) |
| Hepatorenal Syndrome | 0 | 0 | 0 | 0 | 0 | 1 (12.5) | 0 | 1 (2.6) |

| Primary system organ class<br>Preferred term | INC280 100mg capsule N=4 n (%) | INC280 200mg capsule N=5 n (%) | INC280 250mg capsule N=4 n (%) | INC280 350mg capsule N=3 n (%) | INC280 450mg capsule N=9 n (%) | INC280 600mg capsule N=8 n (%) | INC280 400mg tablet N=5 n (%) | All dose escalation patients N=38 n (%) |
|---|---|---|---|---|---|---|---|---|
| Hepatobiliary Disorders | | | | | | | | |
| Hyperbilirubinaemia | 1 (25.0) | 0 | 0 | 0 | 0 | 0 | 0 | 1 (2.6) |
| Jaundice | 1 (25.0) | 1 (20.0) | 0 | 0 | 0 | 0 | 0 | 2 (5.3) |
| Immune System Disorders | | | | | | | | |
| -Total | 0 | 0 | 0 | 0 | 1 (11.1) | 0 | 0 | 1 (2.6) |
| Seasonal Allergy | 0 | 0 | 0 | 0 | 1 (11.1) | 0 | 0 | 1 (2.6) |
| Infections And Infestations | | | | | | | | |
| -Total | 1 (25.0) | 3 (60.0) | 1 (25.0) | 1 (33.3) | 3 (33.3) | 1 (12.5) | 0 | 10 (26.3) |
| Biliary Tract Infection | 0 | 1 (20.0) | 0 | 0 | 0 | 0 | 0 | 1 (2.6) |
| Catheter Site Infection | 0 | 1 (20.0) | 0 | 0 | 0 | 0 | 0 | 1 (2.6) |
| Cellulitis | 0 | 0 | 0 | 1 (33.3) | 0 | 0 | 0 | 1 (2.6) |
| Infection | 0 | 1 (20.0) | 0 | 0 | 0 | 0 | 0 | 1 (2.6) |
| Kidney Infection | 1 (25.0) | 0 | 0 | 0 | 0 | 0 | 0 | 1 (2.6) |
| Lung Infection | 0 | 0 | 0 | 0 | 0 | 1 (12.5) | 0 | 1 (2.6) |
| Pneumonia | 0 | 0 | 1 (25.0) | 0 | 1 (11.1) | 0 | 0 | 2 (5.3) |
| Septic Shock | 0 | 0 | 0 | 0 | 0 | 1 (12.5) | 0 | 1 (2.6) |
| Upper Respiratory Tract Infection | 0 | 1 (20.0) | 1 (25.0) | 0 | 1 (11.1) | 0 | 0 | 3 (7.9) |

| Primary system organ class<br>Preferred term | INC280 100mg capsule N=4 n (%) | INC280 200mg capsule N=5 n (%) | INC280 250mg capsule N=4 n (%) | INC280 350mg capsule N=3 n (%) | INC280 450mg capsule N=9 n (%) | INC280 600mg capsule N=8 n (%) | INC280 400mg tablet N=5 n (%) | All dose escalation patients N=38 n (%) |
|---|---|---|---|---|---|---|---|---|
| Infections And Infestations | | | | | | | | |
| Urinary Tract Infection | 0 | 0 | 0 | 0 | 1 (11.1) | 0 | 0 | 1 (2.6) |
| Injury, Poisoning And Procedural Complications | | | | | | | | |
| -Total | 0 | 1 (20.0) | 0 | 0 | 1 (11.1) | 1 (12.5) | 0 | 3 (7.9) |
| Anastomotic Ulcer | 0 | 0 | 0 | 0 | 0 | 1 (12.5) | 0 | 1 (2.6) |
| Fall | 0 | 0 | 0 | 0 | 1 (11.1) | 0 | 0 | 1 (2.6) |
| Post Procedural Inflammation | 0 | 1 (20.0) | 0 | 0 | 0 | 0 | 0 | 1 (2.6) |
| Investigations | | | | | | | | |
| -Total | 2 (50.0) | 4 (80.0) | 4 (100) | 2 (66.7) | 5 (55.6) | 5 (62.5) | 3 (60.0) | 25 (65.8) |
| Alanine Aminotransferase Increased | 0 | 1 (20.0) | 0 | 0 | 2 (22.2) | 1 (12.5) | 1 (20.0) | 5 (13.2) |
| Amylase Increased | 0 | 0 | 2 (50.0) | 1 (33.3) | 0 | 0 | 0 | 3 (7.9) |
| Aspartate Aminotransferase Increased | 0 | 1 (20.0) | 1 (25.0) | 0 | 3 (33.3) | 3 (37.5) | 1 (20.0) | 9 (23.7) |
| Blood Albumin Decreased | 0 | 0 | 0 | 0 | 0 | 2 (25.0) | 0 | 2 (5.3) |
| Blood Alkaline Phosphatase Increased | 1 (25.0) | 2 (40.0) | 2 (50.0) | 0 | 0 | 0 | 0 | 5 (13.2) |

| Primary system organ class<br>Preferred term | INC280 100mg capsule N=4 n (%) | INC280 200mg capsule N=5 n (%) | INC280 250mg capsule N=4 n (%) | INC280 350mg capsule N=3 n (%) | INC280 450mg capsule N=9 n (%) | INC280 600mg capsule N=8 n (%) | INC280 400mg tablet N=5 n (%) | All dose escalation patients N=38 n (%) |
|---|---|---|---|---|---|---|---|---|
| Investigations | | | | | | | | |
| Blood Bilirubin Increased | 1 (25.0) | 1 (20.0) | 2 (50.0) | 0 | 0 | 3 (37.5) | 0 | 7 (18.4) |
| Blood Creatine Phosphokinase Increased | 0 | 0 | 1 (25.0) | 0 | 0 | 0 | 0 | 1 (2.6) |
| Blood Creatinine Increased | 0 | 2 (40.0) | 0 | 1 (33.3) | 1 (11.1) | 2 (25.0) | 2 (40.0) | 8 (21.1) |
| Blood Iron Decreased | 0 | 0 | 0 | 0 | 0 | 1 (12.5) | 0 | 1 (2.6) |
| Blood Lactate Dehydrogenase Increased | 0 | 0 | 0 | 0 | 0 | 1 (12.5) | 0 | 1 (2.6) |
| Electrocardiogram Qt Prolonged | 0 | 0 | 0 | 1 (33.3) | 0 | 1 (12.5) | 0 | 2 (5.3) |
| Gamma-Glutamyltransferase Increased | 0 | 0 | 2 (50.0) | 0 | 1 (11.1) | 0 | 0 | 3 (7.9) |
| International Normalised Ratio Increased | 0 | 0 | 0 | 1 (33.3) | 0 | 0 | 0 | 1 (2.6) |
| Lipase Increased | 0 | 0 | 1 (25.0) | 0 | 0 | 0 | 0 | 1 (2.6) |
| Neutrophil Count Decreased | 0 | 0 | 0 | 0 | 0 | 1 (12.5) | 0 | 1 (2.6) |
| Oxygen Saturation Decreased | 0 | 0 | 0 | 0 | 1 (11.1) | 0 | 0 | 1 (2.6) |
| Platelet Count Decreased | 0 | 0 | 0 | 0 | 1 (11.1) | 0 | 0 | 1 (2.6) |
| Protein Total Decreased | 0 | 0 | 0 | 1 (33.3) | 0 | 1 (12.5) | 0 | 2 (5.3) |
| Troponin T Increased | 0 | 1 (20.0) | 0 | 0 | 0 | 0 | 0 | 1 (2.6) |
| Weight Decreased | 2 (50.0) | 0 | 1 (25.0) | 0 | 0 | 0 | 0 | 3 (7.9) |

| Primary system organ class<br>Preferred term | INC280 100mg capsule N=4<br>n (%) | INC280 200mg capsule N=5<br>n (%) | INC280 250mg capsule N=4<br>n (%) | INC280 350mg capsule N=3<br>n (%) | INC280 450mg capsule N=9<br>n (%) | INC280 600mg capsule N=8<br>n (%) | INC280 400mg tablet N=5<br>n (%) | All dose escalation patients N=38<br>n (%) |
|---|---|---|---|---|---|---|---|---|
| Metabolism And Nutrition Disorders | | | | | | | | |
| -Total | 3 (75.0) | 4 (80.0) | 3 (75.0) | 1 (33.3) | 5 (55.6) | 5 (62.5) | 2 (40.0) | 23 (60.5) |
| Decreased Appetite | 2 (50.0) | 2 (40.0) | 3 (75.0) | 1 (33.3) | 4 (44.4) | 3 (37.5) | 1 (20.0) | 16 (42.1) |
| Hyperglycaemia | 2 (50.0) | 0 | 0 | 0 | 0 | 0 | 0 | 2 (5.3) |
| Hyperkalaemia | 1 (25.0) | 1 (20.0) | 0 | 0 | 0 | 1 (12.5) | 0 | 3 (7.9) |
| Hypoalbuminaemia | 2 (50.0) | 2 (40.0) | 1 (25.0) | 1 (33.3) | 0 | 1 (12.5) | 2 (40.0) | 9 (23.7) |
| Hypocalcaemia | 0 | 0 | 0 | 0 | 0 | 1 (12.5) | 0 | 1 (2.6) |
| Hypoglycaemia | 0 | 1 (20.0) | 0 | 0 | 0 | 0 | 0 | 1 (2.6) |
| Hypokalaemia | 0 | 0 | 0 | 0 | 0 | 1 (12.5) | 0 | 1 (2.6) |
| Hyponatraemia | 0 | 0 | 0 | 0 | 1 (11.1) | 2 (25.0) | 0 | 3 (7.9) |
| Hypophagia | 1 (25.0) | 1 (20.0) | 0 | 0 | 0 | 0 | 0 | 2 (5.3) |
| Hypouricaemia | 0 | 0 | 0 | 0 | 0 | 1 (12.5) | 0 | 1 (2.6) |
| Musculoskeletal And Connective Tissue Disorders | | | | | | | | |
| -Total | 1 (25.0) | 1 (20.0) | 1 (25.0) | 1 (33.3) | 2 (22.2) | 2 (25.0) | 2 (40.0) | 10 (26.3) |
| Arthralgia | 0 | 0 | 0 | 0 | 1 (11.1) | 0 | 1 (20.0) | 2 (5.3) |
| Back Pain | 0 | 0 | 0 | 0 | 0 | 1 (12.5) | 0 | 1 (2.6) |
| Bone Pain | 0 | 0 | 0 | 0 | 0 | 1 (12.5) | 0 | 1 (2.6) |
| Flank Pain | 1 (25.0) | 0 | 0 | 0 | 1 (11.1) | 0 | 0 | 2 (5.3) |

| Primary system organ class<br>Preferred term | INC280 100mg capsule N=4 n (%) | INC280 200mg capsule N=5 n (%) | INC280 250mg capsule N=4 n (%) | INC280 350mg capsule N=3 n (%) | INC280 450mg capsule N=9 n (%) | INC280 600mg capsule N=8 n (%) | INC280 400mg tablet N=5 n (%) | All dose escalation patients N=38 n (%) |
|---|---|---|---|---|---|---|---|---|
| Musculoskeletal And Connective Tissue Disorders | | | | | | | | |
| Joint Range Of Motion Decreased | 0 | 0 | 0 | 0 | 0 | 0 | 1 (20.0) | 1 (2.6) |
| Muscular Weakness | 0 | 0 | 0 | 0 | 0 | 1 (12.5) | 0 | 1 (2.6) |
| Myalgia | 0 | 1 (20.0) | 0 | 1 (33.3) | 0 | 0 | 0 | 2 (5.3) |
| Pain In Extremity | 0 | 0 | 1 (25.0) | 0 | 0 | 0 | 0 | 1 (2.6) |
| Neoplasms Benign, Malignant And Unspecified (Incl Cysts And Polyps) | | | | | | | | |
| -Total | 0 | 1 (20.0) | 1 (25.0) | 0 | 1 (11.1) | 0 | 0 | 3 (7.9) |
| Tumour Pain | 0 | 1 (20.0) | 1 (25.0) | 0 | 1 (11.1) | 0 | 0 | 3 (7.9) |
| Nervous System Disorders | | | | | | | | |
| -Total | 3 (75.0) | 2 (40.0) | 1 (25.0) | 2 (66.7) | 2 (22.2) | 3 (37.5) | 2 (40.0) | 15 (39.5) |
| Dizziness | 1 (25.0) | 0 | 0 | 1 (33.3) | 1 (11.1) | 1 (12.5) | 2 (40.0) | 6 (15.8) |
| Embolic Cerebral Infarction | 0 | 0 | 1 (25.0) | 0 | 0 | 0 | 0 | 1 (2.6) |
| Encephalopathy | 1 (25.0) | 1 (20.0) | 0 | 0 | 0 | 0 | 0 | 2 (5.3) |
| Headache | 1 (25.0) | 1 (20.0) | 0 | 0 | 1 (11.1) | 0 | 0 | 3 (7.9) |
| Hemiparesis | 0 | 0 | 0 | 1 (33.3) | 0 | 0 | 0 | 1 (2.6) |
| Hypoaesthesia | 0 | 0 | 0 | 0 | 0 | 2 (25.0) | 0 | 2 (5.3) |

| Primary system organ class<br>Preferred term | INC280 100mg capsule N=4 n (%) | INC280 200mg capsule N=5 n (%) | INC280 250mg capsule N=4 n (%) | INC280 350mg capsule N=3 n (%) | INC280 450mg capsule N=9 n (%) | INC280 600mg capsule N=8 n (%) | INC280 400mg tablet N=5 n (%) | All dose escalation patients N=38 n (%) |
|---|---|---|---|---|---|---|---|---|
| Psychiatric Disorders | | | | | | | | |
| -Total | 2 (50.0) | 1 (20.0) | 0 | 0 | 1 (11.1) | 2 (25.0) | 1 (20.0) | 7 (18.4) |
| Anxiety | 1 (25.0) | 0 | 0 | 0 | 1 (11.1) | 0 | 0 | 2 (5.3) |
| Depression | 0 | 0 | 0 | 0 | 0 | 0 | 1 (20.0) | 1 (2.6) |
| Insomnia | 1 (25.0) | 1 (20.0) | 0 | 0 | 0 | 2 (25.0) | 0 | 4 (10.5) |
| Renal And Urinary Disorders | | | | | | | | |
| -Total | 1 (25.0) | 1 (20.0) | 0 | 1 (33.3) | 1 (11.1) | 1 (12.5) | 0 | 5 (13.2) |
| Haematuria | 0 | 0 | 0 | 0 | 0 | 1 (12.5) | 0 | 1 (2.6) |
| Nocturia | 0 | 0 | 0 | 1 (33.3) | 0 | 0 | 0 | 1 (2.6) |
| Pollakiuria | 0 | 0 | 0 | 0 | 1 (11.1) | 0 | 0 | 1 (2.6) |
| Proteinuria | 0 | 1 (20.0) | 0 | 0 | 0 | 0 | 0 | 1 (2.6) |
| Urinary Hesitation | 1 (25.0) | 0 | 0 | 0 | 0 | 0 | 0 | 1 (2.6) |
| Reproductive System And Breast Disorders | | | | | | | | |
| -Total | 1 (25.0) | 0 | 0 | 0 | 2 (22.2) | 0 | 0 | 3 (7.9) |
| Erectile Dysfunction | 1 (25.0) | 0 | 0 | 0 | 0 | 0 | 0 | 1 (2.6) |
| Pelvic Pain | 0 | 0 | 0 | 0 | 1 (11.1) | 0 | 0 | 1 (2.6) |
| Vaginal Haemorrhage | 0 | 0 | 0 | 0 | 1 (11.1) | 0 | 0 | 1 (2.6) |

| Primary system organ class<br>Preferred term | INC280 100mg capsule N=4<br>n (%) | INC280 200mg capsule N=5<br>n (%) | INC280 250mg capsule N=4<br>n (%) | INC280 350mg capsule N=3<br>n (%) | INC280 450mg capsule N=9<br>n (%) | INC280 600mg capsule N=8<br>n (%) | INC280 400mg tablet N=5<br>n (%) | All dose escalation patients N=38<br>n (%) |
|---|---|---|---|---|---|---|---|---|
| Respiratory, Thoracic And Mediastinal Disorders | | | | | | | | |
| -Total | 2 (50.0) | 1 (20.0) | 3 (75.0) | 1 (33.3) | 3 (33.3) | 3 (37.5) | 1 (20.0) | 14 (36.8) |
| Cough | 0 | 1 (20.0) | 3 (75.0) | 1 (33.3) | 0 | 1 (12.5) | 1 (20.0) | 7 (18.4) |
| Dyspnoea | 0 | 1 (20.0) | 1 (25.0) | 1 (33.3) | 0 | 2 (25.0) | 0 | 5 (13.2) |
| Haemoptysis | 0 | 0 | 1 (25.0) | 0 | 0 | 2 (25.0) | 0 | 3 (7.9) |
| Hiccups | 1 (25.0) | 0 | 0 | 0 | 0 | 0 | 0 | 1 (2.6) |
| Oropharyngeal Pain | 0 | 0 | 0 | 0 | 1 (11.1) | 0 | 0 | 1 (2.6) |
| Pleural Effusion | 0 | 0 | 0 | 0 | 2 (22.2) | 0 | 0 | 2 (5.3) |
| Productive Cough | 1 (25.0) | 1 (20.0) | 0 | 0 | 1 (11.1) | 0 | 0 | 3 (7.9) |
| Skin And Subcutaneous Tissue Disorders | | | | | | | | |
| -Total | 1 (25.0) | 1 (20.0) | 1 (25.0) | 1 (33.3) | 4 (44.4) | 2 (25.0) | 2 (40.0) | 12 (31.6) |
| Alopecia | 0 | 0 | 0 | 0 | 0 | 0 | 1 (20.0) | 1 (2.6) |
| Dry Skin | 0 | 0 | 0 | 0 | 0 | 1 (12.5) | 0 | 1 (2.6) |
| Palmar-Plantar Erythrodysaesthesia Syndrome | 1 (25.0) | 0 | 1 (25.0) | 0 | 0 | 0 | 0 | 2 (5.3) |
| Pruritus | 0 | 1 (20.0) | 0 | 0 | 2 (22.2) | 1 (12.5) | 1 (20.0) | 5 (13.2) |
| Rash | 0 | 0 | 0 | 0 | 1 (11.1) | 0 | 1 (20.0) | 2 (5.3) |

| Primary system organ class<br>Preferred term | INC280 100mg capsule N=4 n (%) | INC280 200mg capsule N=5 n (%) | INC280 250mg capsule N=4 n (%) | INC280 350mg capsule N=3 n (%) | INC280 450mg capsule N=9 n (%) | INC280 600mg capsule N=8 n (%) | INC280 400mg tablet N=5 n (%) | All dose escalation patients N=38 n (%) |
|---|---|---|---|---|---|---|---|---|
| Skin And Subcutaneous Tissue Disorders | | | | | | | | |
| Rash Maculo-Papular | 0 | 0 | 0 | 0 | 2 (22.2) | 0 | 0 | 2 (5.3) |
| Skin Ulcer | 0 | 0 | 0 | 1 (33.3) | 0 | 0 | 0 | 1 (2.6) |
| Urticaria | 1 (25.0) | 0 | 0 | 0 | 0 | 0 | 0 | 1 (2.6) |
| Vascular Disorders | | | | | | | | |
| -Total | 0 | 1 (20.0) | 0 | 0 | 0 | 1 (12.5) | 0 | 2 (5.3) |
| Hypotension | 0 | 0 | 0 | 0 | 0 | 1 (12.5) | 0 | 1 (2.6) |
| Phlebitis | 0 | 1 (20.0) | 0 | 0 | 0 | 0 | 0 | 1 (2.6) |

- Primary system organ classes are presented alphabetically; preferred terms are sorted by frequency of “All subject” Column.
- A subject with multiple occurrences of an AE under one treatment is counted only once in the AE category for that treatment.
- A subject with multiple adverse events within a primary system organ class is counted only once in the total row.
- Only AEs occurring during treatment or within 30 days of the last study medication are reported.

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**Adverse events, regardless of study drug relationship, by primary system organ class, preferred term and cohort in dose expansion (Safety set)**

| Primary system organ class<br>Preferred term | Gastric cancer<br>N=9<br>n (%) | HCC<br>N=11<br>n (%) | NSCLC<br>N=55<br>n (%) | Other indications<br>N=18<br>n (%) | All expansion patients<br>N=93<br>n (%) |
|---|---|---|---|---|---|
| -Any primary system organ class | | | | | |
| -Total | 9 (100) | 11 (100) | 55 (100) | 17 (94.4) | 92 (98.9) |
| Blood And Lymphatic System Disorders | | | | | |
| -Total | 1 (11.1) | 4 (36.4) | 11 (20.0) | 4 (22.2) | 20 (21.5) |
| Anaemia | 0 | 1 (9.1) | 4 (7.3) | 2 (11.1) | 7 (7.5) |
| Febrile Neutropenia | 0 | 0 | 1 (1.8) | 0 | 1 (1.1) |
| Leukopenia | 0 | 1 (9.1) | 2 (3.6) | 1 (5.6) | 4 (4.3) |
| Lymphopenia | 0 | 0 | 2 (3.6) | 1 (5.6) | 3 (3.2) |
| Neutropenia | 0 | 1 (9.1) | 0 | 1 (5.6) | 2 (2.2) |
| Pancytopenia | 0 | 0 | 1 (1.8) | 1 (5.6) | 2 (2.2) |
| Thrombocytopenia | 1 (11.1) | 2 (18.2) | 4 (7.3) | 0 | 7 (7.5) |
| Cardiac Disorders | | | | | |
| -Total | 0 | 1 (9.1) | 2 (3.6) | 0 | 3 (3.2) |
| Pericardial Effusion | 0 | 0 | 2 (3.6) | 0 | 2 (2.2) |
| Tachycardia | 0 | 1 (9.1) | 0 | 0 | 1 (1.1) |
| Ear And Labyrinth Disorders | | | | | |
| -Total | 0 | 0 | 7 (12.7) | 2 (11.1) | 9 (9.7) |
| Deafness | 0 | 0 | 0 | 1 (5.6) | 1 (1.1) |

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| Primary system organ class<br>Preferred term | Gastric cancer<br>N=9<br>n (%) | HCC<br>N=11<br>n (%) | NSCLC<br>N=55<br>n (%) | Other indications<br>N=18<br>n (%) | All expansion patients<br>N=93<br>n (%) |
|---|---|---|---|---|---|
| Ear And Labyrinth Disorders | | | | | |
| Ear Pain | 0 | 0 | 1 (1.8) | 0 | 1 (1.1) |
| Hypoacusis | 0 | 0 | 3 (5.5) | 0 | 3 (3.2) |
| Motion Sickness | 0 | 0 | 0 | 1 (5.6) | 1 (1.1) |
| Tinnitus | 0 | 0 | 1 (1.8) | 0 | 1 (1.1) |
| Vertigo | 0 | 0 | 3 (5.5) | 0 | 3 (3.2) |
| Eye Disorders | | | | | |
| -Total | 0 | 1 (9.1) | 5 (9.1) | 0 | 6 (6.5) |
| Cataract | 0 | 0 | 1 (1.8) | 0 | 1 (1.1) |
| Eye Pain | 0 | 0 | 1 (1.8) | 0 | 1 (1.1) |
| Eyelid Oedema | 0 | 0 | 1 (1.8) | 0 | 1 (1.1) |
| Vision Blurred | 0 | 1 (9.1) | 1 (1.8) | 0 | 2 (2.2) |
| Visual Impairment | 0 | 0 | 1 (1.8) | 0 | 1 (1.1) |
| Gastrointestinal Disorders | | | | | |
| -Total | 7 (77.8) | 9 (81.8) | 41 (74.5) | 13 (72.2) | 70 (75.3) |
| Abdominal Discomfort | 0 | 1 (9.1) | 0 | 0 | 1 (1.1) |
| Abdominal Distension | 0 | 1 (9.1) | 5 (9.1) | 1 (5.6) | 7 (7.5) |
| Abdominal Pain | 3 (33.3) | 2 (18.2) | 7 (12.7) | 1 (5.6) | 13 (14.0) |
| Abdominal Pain Upper | 1 (11.1) | 0 | 4 (7.3) | 1 (5.6) | 6 (6.5) |

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| Primary system organ class<br>Preferred term | Gastric cancer<br>N=9<br>n (%) | HCC<br>N=11<br>n (%) | NSCLC<br>N=55<br>n (%) | Other indications<br>N=18<br>n (%) | All expansion patients<br>N=93<br>n (%) |
|---|---|---|---|---|---|
| Gastrointestinal Disorders | | | | | |
| Aphthous Ulcer | 0 | 0 | 1 (1.8) | 0 | 1 (1.1) |
| Ascites | 1 (11.1) | 4 (36.4) | 1 (1.8) | 0 | 6 (6.5) |
| Constipation | 3 (33.3) | 2 (18.2) | 6 (10.9) | 2 (11.1) | 13 (14.0) |
| Diarrhoea | 1 (11.1) | 4 (36.4) | 11 (20.0) | 4 (22.2) | 20 (21.5) |
| Dry Mouth | 1 (11.1) | 0 | 1 (1.8) | 3 (16.7) | 5 (5.4) |
| Duodenal Ulcer | 0 | 0 | 1 (1.8) | 0 | 1 (1.1) |
| Dyspepsia | 1 (11.1) | 0 | 5 (9.1) | 3 (16.7) | 9 (9.7) |
| Dysphagia | 0 | 0 | 2 (3.6) | 1 (5.6) | 3 (3.2) |
| Eructation | 0 | 1 (9.1) | 0 | 0 | 1 (1.1) |
| Flatulence | 0 | 1 (9.1) | 1 (1.8) | 0 | 2 (2.2) |
| Gastric Ulcer | 0 | 0 | 1 (1.8) | 0 | 1 (1.1) |
| Gastritis | 0 | 0 | 1 (1.8) | 0 | 1 (1.1) |
| Gastroduodenitis | 0 | 0 | 1 (1.8) | 0 | 1 (1.1) |
| Gastrointestinal Motility Disorder | 0 | 1 (9.1) | 0 | 0 | 1 (1.1) |
| Gastrooesophageal Reflux Disease | 0 | 2 (18.2) | 1 (1.8) | 0 | 3 (3.2) |
| Gingival Swelling | 0 | 0 | 1 (1.8) | 0 | 1 (1.1) |
| Haematemesis | 0 | 1 (9.1) | 0 | 0 | 1 (1.1) |
| Hiatus Hernia | 0 | 0 | 1 (1.8) | 0 | 1 (1.1) |
| Ileus | 0 | 0 | 1 (1.8) | 0 | 1 (1.1) |
| Lip Blister | 0 | 0 | 0 | 1 (5.6) | 1 (1.1) |

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| Primary system organ class<br>Preferred term | Gastric cancer<br>N=9<br>n (%) | HCC<br>N=11<br>n (%) | NSCLC<br>N=55<br>n (%) | Other indications<br>N=18<br>n (%) | All expansion patients<br>N=93<br>n (%) |
|---|---|---|---|---|---|
| Gastrointestinal Disorders | | | | | |
| Lower Gastrointestinal Haemorrhage | 1 (11.1) | 0 | 0 | 0 | 1 (1.1) |
| Nausea | 3 (33.3) | 5 (45.5) | 28 (50.9) | 8 (44.4) | 44 (47.3) |
| Odynophagia | 0 | 0 | 1 (1.8) | 0 | 1 (1.1) |
| Oesophagitis | 0 | 0 | 1 (1.8) | 0 | 1 (1.1) |
| Oral Dysaesthesia | 0 | 0 | 1 (1.8) | 0 | 1 (1.1) |
| Pancreatitis | 0 | 0 | 1 (1.8) | 0 | 1 (1.1) |
| Peritoneal Haemorrhage | 0 | 1 (9.1) | 0 | 0 | 1 (1.1) |
| Retching | 0 | 0 | 0 | 1 (5.6) | 1 (1.1) |
| Stomatitis | 0 | 0 | 6 (10.9) | 1 (5.6) | 7 (7.5) |
| Tongue Ulceration | 0 | 0 | 1 (1.8) | 0 | 1 (1.1) |
| Tooth Loss | 0 | 0 | 1 (1.8) | 0 | 1 (1.1) |
| Toothache | 0 | 0 | 0 | 1 (5.6) | 1 (1.1) |
| Upper Gastrointestinal Haemorrhage | 0 | 0 | 1 (1.8) | 0 | 1 (1.1) |
| Vomiting | 3 (33.3) | 3 (27.3) | 22 (40.0) | 5 (27.8) | 33 (35.5) |
| General Disorders And Administration Site Conditions | | | | | |
| -Total | 6 (66.7) | 7 (63.6) | 47 (85.5) | 12 (66.7) | 72 (77.4) |
| Asthenia | 0 | 1 (9.1) | 11 (20.0) | 2 (11.1) | 14 (15.1) |
| Chest Pain | 0 | 0 | 2 (3.6) | 0 | 2 (2.2) |

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| Primary system organ class<br>Preferred term | Gastric cancer<br>N=9<br>n (%) | HCC<br>N=11<br>n (%) | NSCLC<br>N=55<br>n (%) | Other indications<br>N=18<br>n (%) | All expansion patients<br>N=93<br>n (%) |
|---|---|---|---|---|---|
| General Disorders And Administration Site Conditions | | | | | |
| Chills | 0 | 0 | 1 (1.8) | 0 | 1 (1.1) |
| Face Oedema | 0 | 0 | 2 (3.6) | 0 | 2 (2.2) |
| Fatigue | 5 (55.6) | 3 (27.3) | 15 (27.3) | 5 (27.8) | 28 (30.1) |
| General Physical Health Deterioration | 2 (22.2) | 1 (9.1) | 2 (3.6) | 0 | 5 (5.4) |
| Generalised Oedema | 0 | 0 | 3 (5.5) | 0 | 3 (3.2) |
| Localised Oedema | 0 | 0 | 0 | 2 (11.1) | 2 (2.2) |
| Malaise | 0 | 0 | 1 (1.8) | 1 (5.6) | 2 (2.2) |
| Non-Cardiac Chest Pain | 0 | 0 | 5 (9.1) | 1 (5.6) | 6 (6.5) |
| Oedema | 0 | 0 | 1 (1.8) | 1 (5.6) | 2 (2.2) |
| Oedema Peripheral | 4 (44.4) | 6 (54.5) | 26 (47.3) | 5 (27.8) | 41 (44.1) |
| Pain | 0 | 0 | 1 (1.8) | 0 | 1 (1.1) |
| Peripheral Swelling | 0 | 0 | 1 (1.8) | 0 | 1 (1.1) |
| Puncture Site Discharge | 0 | 0 | 1 (1.8) | 0 | 1 (1.1) |
| Puncture Site Haemorrhage | 0 | 0 | 1 (1.8) | 0 | 1 (1.1) |
| Pyrexia | 2 (22.2) | 0 | 8 (14.5) | 2 (11.1) | 12 (12.9) |
| Secretion Discharge | 0 | 0 | 0 | 1 (5.6) | 1 (1.1) |
| Sensation Of Foreign Body | 0 | 0 | 2 (3.6) | 0 | 2 (2.2) |

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| Primary system organ class<br>Preferred term | Gastric cancer<br>N=9<br>n (%) | HCC<br>N=11<br>n (%) | NSCLC<br>N=55<br>n (%) | Other indications<br>N=18<br>n (%) | All expansion patients<br>N=93<br>n (%) |
|---|---|---|---|---|---|
| Hepatobiliary Disorders | | | | | |
| -Total | 1 (11.1) | 2 (18.2) | 2 (3.6) | 0 | 5 (5.4) |
| Cholestasis | 1 (11.1) | 0 | 0 | 0 | 1 (1.1) |
| Hepatic Haematoma | 0 | 1 (9.1) | 0 | 0 | 1 (1.1) |
| Hyperbilirubinaemia | 0 | 1 (9.1) | 1 (1.8) | 0 | 2 (2.2) |
| Hypertransaminasaemia | 0 | 0 | 1 (1.8) | 0 | 1 (1.1) |
| Jaundice | 1 (11.1) | 0 | 0 | 0 | 1 (1.1) |
| Immune System Disorders | | | | | |
| -Total | 0 | 0 | 2 (3.6) | 0 | 2 (2.2) |
| Hypersensitivity | 0 | 0 | 2 (3.6) | 0 | 2 (2.2) |
| Infections And Infestations | | | | | |
| -Total | 2 (22.2) | 2 (18.2) | 20 (36.4) | 5 (27.8) | 29 (31.2) |
| Abdominal Infection | 1 (11.1) | 0 | 1 (1.8) | 0 | 2 (2.2) |
| Bronchitis | 0 | 0 | 1 (1.8) | 0 | 1 (1.1) |
| Candida Infection | 0 | 0 | 1 (1.8) | 0 | 1 (1.1) |
| Cellulitis | 1 (11.1) | 0 | 2 (3.6) | 1 (5.6) | 4 (4.3) |
| Conjunctivitis | 0 | 0 | 1 (1.8) | 0 | 1 (1.1) |
| Cystitis | 0 | 0 | 1 (1.8) | 0 | 1 (1.1) |
| Erysipelas | 0 | 0 | 0 | 1 (5.6) | 1 (1.1) |

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| Primary system organ class<br>Preferred term | Gastric cancer<br>N=9<br>n (%) | HCC<br>N=11<br>n (%) | NSCLC<br>N=55<br>n (%) | Other indications<br>N=18<br>n (%) | All expansion patients<br>N=93<br>n (%) |
|---|---|---|---|---|---|
| Infections And Infestations | | | | | |
| Herpes Simplex | 0 | 1 (9.1) | 0 | 0 | 1 (1.1) |
| Herpes Zoster | 0 | 0 | 1 (1.8) | 0 | 1 (1.1) |
| Influenza | 0 | 0 | 1 (1.8) | 0 | 1 (1.1) |
| Oral Candidiasis | 0 | 0 | 2 (3.6) | 0 | 2 (2.2) |
| Otitis Media Acute | 0 | 0 | 1 (1.8) | 0 | 1 (1.1) |
| Paronychia | 0 | 0 | 1 (1.8) | 0 | 1 (1.1) |
| Pneumonia | 0 | 0 | 7 (12.7) | 1 (5.6) | 8 (8.6) |
| Pyelonephritis Acute | 0 | 0 | 1 (1.8) | 0 | 1 (1.1) |
| Respiratory Tract Infection | 0 | 1 (9.1) | 0 | 0 | 1 (1.1) |
| Rhinitis | 0 | 0 | 3 (5.5) | 1 (5.6) | 4 (4.3) |
| Septic Shock | 0 | 0 | 1 (1.8) | 0 | 1 (1.1) |
| Sinusitis | 0 | 1 (9.1) | 0 | 0 | 1 (1.1) |
| Upper Respiratory Tract Infection | 0 | 0 | 3 (5.5) | 0 | 3 (3.2) |
| Urinary Tract Infection | 1 (11.1) | 0 | 2 (3.6) | 1 (5.6) | 4 (4.3) |
| Viral Upper Respiratory Tract Infection | 0 | 0 | 3 (5.5) | 0 | 3 (3.2) |
| Injury, Poisoning And Procedural Complications | | | | | |
| -Total | 0 | 0 | 8 (14.5) | 2 (11.1) | 10 (10.8) |

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| Primary system organ class<br>Preferred term | Gastric cancer<br>N=9<br>n (%) | HCC<br>N=11<br>n (%) | NSCLC<br>N=55<br>n (%) | Other indications<br>N=18<br>n (%) | All expansion patients<br>N=93<br>n (%) |
|---|---|---|---|---|---|
| Injury, Poisoning And Procedural Complications | | | | | |
| Excoriation | 0 | 0 | 0 | 1 (5.6) | 1 (1.1) |
| Femur Fracture | 0 | 0 | 1 (1.8) | 0 | 1 (1.1) |
| Head Injury | 0 | 0 | 1 (1.8) | 0 | 1 (1.1) |
| Injury | 0 | 0 | 1 (1.8) | 0 | 1 (1.1) |
| Post Procedural Swelling | 0 | 0 | 0 | 1 (5.6) | 1 (1.1) |
| Procedural Pain | 0 | 0 | 2 (3.6) | 1 (5.6) | 3 (3.2) |
| Skin Abrasion | 0 | 0 | 1 (1.8) | 0 | 1 (1.1) |
| Stoma Site Pain | 0 | 0 | 0 | 1 (5.6) | 1 (1.1) |
| Stress Fracture | 0 | 0 | 2 (3.6) | 0 | 2 (2.2) |
| Tooth Fracture | 0 | 0 | 1 (1.8) | 0 | 1 (1.1) |
| Wound | 0 | 0 | 1 (1.8) | 0 | 1 (1.1) |
| Investigations | | | | | |
| -Total | 4 (44.4) | 4 (36.4) | 30 (54.5) | 5 (27.8) | 43 (46.2) |
| Alanine Aminotransferase Increased | 1 (11.1) | 3 (27.3) | 8 (14.5) | 1 (5.6) | 13 (14.0) |
| Amylase Increased | 0 | 0 | 7 (12.7) | 0 | 7 (7.5) |
| Aspartate Aminotransferase Increased | 1 (11.1) | 3 (27.3) | 6 (10.9) | 2 (11.1) | 12 (12.9) |
| Blood Albumin Decreased | 0 | 0 | 1 (1.8) | 0 | 1 (1.1) |
| Blood Alkaline Phosphatase Increased | 0 | 0 | 2 (3.6) | 0 | 2 (2.2) |

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| Primary system organ class<br>Preferred term | Gastric cancer<br>N=9<br>n (%) | HCC<br>N=11<br>n (%) | NSCLC<br>N=55<br>n (%) | Other indications<br>N=18<br>n (%) | All expansion patients<br>N=93<br>n (%) |
|---|---|---|---|---|---|
| Investigations | | | | | |
| Blood Antidiuretic Hormone Abnormal | 0 | 0 | 1 (1.8) | 0 | 1 (1.1) |
| Blood Bilirubin Increased | 1 (11.1) | 2 (18.2) | 1 (1.8) | 1 (5.6) | 5 (5.4) |
| Blood Cholesterol Increased | 0 | 1 (9.1) | 0 | 1 (5.6) | 2 (2.2) |
| Blood Creatinine Increased | 0 | 1 (9.1) | 13 (23.6) | 2 (11.1) | 16 (17.2) |
| Blood Iron Decreased | 0 | 0 | 0 | 1 (5.6) | 1 (1.1) |
| Blood Magnesium Decreased | 0 | 0 | 1 (1.8) | 0 | 1 (1.1) |
| Blood Sodium Decreased | 0 | 0 | 1 (1.8) | 0 | 1 (1.1) |
| Blood Urea Increased | 0 | 0 | 1 (1.8) | 0 | 1 (1.1) |
| C-Reactive Protein Increased | 1 (11.1) | 0 | 1 (1.8) | 0 | 2 (2.2) |
| Gamma-Glutamyltransferase Increased | 0 | 1 (9.1) | 2 (3.6) | 0 | 3 (3.2) |
| Haemoglobin Decreased | 0 | 0 | 1 (1.8) | 0 | 1 (1.1) |
| International Normalised Ratio Increased | 0 | 0 | 1 (1.8) | 0 | 1 (1.1) |
| Lipase Increased | 0 | 2 (18.2) | 5 (9.1) | 1 (5.6) | 8 (8.6) |
| Lymphocyte Count Decreased | 0 | 0 | 1 (1.8) | 0 | 1 (1.1) |
| Neutrophil Count Decreased | 0 | 0 | 1 (1.8) | 0 | 1 (1.1) |
| Occult Blood | 1 (11.1) | 0 | 0 | 0 | 1 (1.1) |
| Oxygen Saturation Decreased | 0 | 0 | 1 (1.8) | 0 | 1 (1.1) |
| Platelet Count Decreased | 0 | 0 | 1 (1.8) | 0 | 1 (1.1) |
| Protein Total Decreased | 0 | 0 | 1 (1.8) | 0 | 1 (1.1) |

NOVARTIS

| Primary system organ class<br>Preferred term | Gastric cancer<br>N=9<br>n (%) | HCC<br>N=11<br>n (%) | NSCLC<br>N=55<br>n (%) | Other indications<br>N=18<br>n (%) | All expansion patients<br>N=93<br>n (%) |
|---|---|---|---|---|---|
| Investigations | | | | | |
| Transaminases Increased | 0 | 0 | 1 (1.8) | 0 | 1 (1.1) |
| Weight Decreased | 0 | 0 | 2 (3.6) | 0 | 2 (2.2) |
| Weight Increased | 0 | 0 | 3 (5.5) | 0 | 3 (3.2) |
| White Blood Cell Count Decreased | 0 | 0 | 1 (1.8) | 0 | 1 (1.1) |
| Metabolism And Nutrition Disorders | | | | | |
| -Total | 3 (33.3) | 6 (54.5) | 33 (60.0) | 7 (38.9) | 49 (52.7) |
| Decreased Appetite | 1 (11.1) | 2 (18.2) | 17 (30.9) | 4 (22.2) | 24 (25.8) |
| Dehydration | 1 (11.1) | 2 (18.2) | 2 (3.6) | 0 | 5 (5.4) |
| Hypercalcaemia | 0 | 0 | 1 (1.8) | 0 | 1 (1.1) |
| Hypercreatininaemia | 0 | 0 | 1 (1.8) | 0 | 1 (1.1) |
| Hyperglycaemia | 0 | 1 (9.1) | 2 (3.6) | 1 (5.6) | 4 (4.3) |
| Hyperlipasaemia | 0 | 0 | 3 (5.5) | 0 | 3 (3.2) |
| Hyperlipidaemia | 0 | 0 | 1 (1.8) | 1 (5.6) | 2 (2.2) |
| Hypertriglyceridaemia | 0 | 0 | 2 (3.6) | 0 | 2 (2.2) |
| Hypoalbuminaemia | 0 | 0 | 9 (16.4) | 1 (5.6) | 10 (10.8) |
| Hypocalcaemia | 0 | 0 | 4 (7.3) | 0 | 4 (4.3) |
| Hypoglycaemia | 0 | 0 | 1 (1.8) | 0 | 1 (1.1) |
| Hypokalaemia | 1 (11.1) | 0 | 8 (14.5) | 0 | 9 (9.7) |
| Hypomagnesaemia | 1 (11.1) | 0 | 2 (3.6) | 0 | 3 (3.2) |

NOVARTIS

| Primary system organ class<br>Preferred term | Gastric cancer<br>N=9<br>n (%) | HCC<br>N=11<br>n (%) | NSCLC<br>N=55<br>n (%) | Other indications<br>N=18<br>n (%) | All expansion patients<br>N=93<br>n (%) |
|---|---|---|---|---|---|
| Metabolism And Nutrition Disorders | | | | | |
| Hyponatraemia | 1 (11.1) | 1 (9.1) | 3 (5.5) | 1 (5.6) | 6 (6.5) |
| Hypophosphataemia | 0 | 1 (9.1) | 5 (9.1) | 0 | 6 (6.5) |
| Hypouricaemia | 0 | 0 | 0 | 1 (5.6) | 1 (1.1) |
| Musculoskeletal And Connective Tissue Disorders | | | | | |
| -Total | 2 (22.2) | 3 (27.3) | 29 (52.7) | 9 (50.0) | 43 (46.2) |
| Arthralgia | 0 | 2 (18.2) | 6 (10.9) | 1 (5.6) | 9 (9.7) |
| Back Pain | 1 (11.1) | 1 (9.1) | 10 (18.2) | 3 (16.7) | 15 (16.1) |
| Bone Pain | 0 | 0 | 4 (7.3) | 0 | 4 (4.3) |
| Flank Pain | 0 | 1 (9.1) | 3 (5.5) | 0 | 4 (4.3) |
| Groin Pain | 0 | 0 | 2 (3.6) | 0 | 2 (2.2) |
| Muscle Atrophy | 0 | 1 (9.1) | 0 | 0 | 1 (1.1) |
| Muscle Spasms | 0 | 0 | 5 (9.1) | 0 | 5 (5.4) |
| Muscle Twitching | 0 | 0 | 0 | 1 (5.6) | 1 (1.1) |
| Muscular Weakness | 1 (11.1) | 0 | 1 (1.8) | 0 | 2 (2.2) |
| Musculoskeletal Chest Pain | 0 | 0 | 0 | 1 (5.6) | 1 (1.1) |
| Musculoskeletal Discomfort | 0 | 0 | 2 (3.6) | 0 | 2 (2.2) |
| Musculoskeletal Pain | 0 | 0 | 8 (14.5) | 0 | 8 (8.6) |
| Myalgia | 0 | 0 | 1 (1.8) | 3 (16.7) | 4 (4.3) |

NOVARTIS

| Primary system organ class<br>Preferred term | Gastric cancer<br>N=9<br>n (%) | HCC<br>N=11<br>n (%) | NSCLC<br>N=55<br>n (%) | Other indications<br>N=18<br>n (%) | All expansion patients<br>N=93<br>n (%) |
|---|---|---|---|---|---|
| Musculoskeletal And Connective Tissue Disorders | | | | | |
| Neck Pain | 0 | 0 | 2 (3.6) | 0 | 2 (2.2) |
| Pain In Extremity | 0 | 1 (9.1) | 5 (9.1) | 0 | 6 (6.5) |
| Soft Tissue Disorder | 0 | 0 | 1 (1.8) | 0 | 1 (1.1) |
| Spinal Pain | 0 | 0 | 2 (3.6) | 0 | 2 (2.2) |
| Neoplasms Benign, Malignant And Unspecified (Incl Cysts And Polyps) | | | | | |
| -Total | 3 (33.3) | 0 | 7 (12.7) | 0 | 10 (10.8) |
| Cancer Pain | 2 (22.2) | 0 | 0 | 0 | 2 (2.2) |
| Malignant Pleural Effusion | 0 | 0 | 2 (3.6) | 0 | 2 (2.2) |
| Sarcoma | 0 | 0 | 1 (1.8) | 0 | 1 (1.1) |
| Tumour Pain | 2 (22.2) | 0 | 4 (7.3) | 0 | 6 (6.5) |
| Nervous System Disorders | | | | | |
| -Total | 3 (33.3) | 2 (18.2) | 19 (34.5) | 6 (33.3) | 30 (32.3) |
| Ataxia | 0 | 0 | 1 (1.8) | 0 | 1 (1.1) |
| Cerebral Ischaemia | 0 | 0 | 1 (1.8) | 0 | 1 (1.1) |
| Cerebral Venous Thrombosis | 0 | 0 | 1 (1.8) | 0 | 1 (1.1) |
| Dizziness | 0 | 1 (9.1) | 6 (10.9) | 2 (11.1) | 9 (9.7) |

NOVARTIS

| Primary system organ class<br>Preferred term | Gastric cancer<br>N=9<br>n (%) | HCC<br>N=11<br>n (%) | NSCLC<br>N=55<br>n (%) | Other indications<br>N=18<br>n (%) | All expansion patients<br>N=93<br>n (%) |
|---|---|---|---|---|---|
| Nervous System Disorders | | | | | |
| Dysaesthesia | 0 | 1 (9.1) | 1 (1.8) | 0 | 2 (2.2) |
| Dysgeusia | 0 | 0 | 2 (3.6) | 0 | 2 (2.2) |
| Headache | 1 (11.1) | 0 | 7 (12.7) | 3 (16.7) | 11 (11.8) |
| Hemiparesis | 0 | 0 | 0 | 1 (5.6) | 1 (1.1) |
| Lethargy | 1 (11.1) | 0 | 0 | 0 | 1 (1.1) |
| Memory Impairment | 0 | 0 | 1 (1.8) | 1 (5.6) | 2 (2.2) |
| Nervous System Disorder | 0 | 0 | 1 (1.8) | 0 | 1 (1.1) |
| Neuralgia | 1 (11.1) | 0 | 0 | 0 | 1 (1.1) |
| Neuropathy Peripheral | 0 | 0 | 3 (5.5) | 0 | 3 (3.2) |
| Paraesthesia | 0 | 0 | 2 (3.6) | 0 | 2 (2.2) |
| Peripheral Motor Neuropathy | 0 | 0 | 2 (3.6) | 0 | 2 (2.2) |
| Peripheral Sensory Neuropathy | 0 | 0 | 1 (1.8) | 0 | 1 (1.1) |
| Polyneuropathy | 1 (11.1) | 0 | 0 | 0 | 1 (1.1) |
| Somnolence | 0 | 0 | 0 | 2 (11.1) | 2 (2.2) |
| Spinal Cord Compression | 0 | 0 | 1 (1.8) | 0 | 1 (1.1) |
| Syncope | 0 | 1 (9.1) | 0 | 0 | 1 (1.1) |
| Product Issues | | | | | |
| -Total | 0 | 0 | 0 | 1 (5.6) | 1 (1.1) |
| Stent Malfunction | 0 | 0 | 0 | 1 (5.6) | 1 (1.1) |

NOVARTIS

| Primary system organ class<br>Preferred term | Gastric cancer<br>N=9<br>n (%) | HCC<br>N=11<br>n (%) | NSCLC<br>N=55<br>n (%) | Other indications<br>N=18<br>n (%) | All expansion patients<br>N=93<br>n (%) |
|---|---|---|---|---|---|
| Psychiatric Disorders | | | | | |
| -Total | 4 (44.4) | 0 | 11 (20.0) | 4 (22.2) | 19 (20.4) |
| Affective Disorder | 0 | 0 | 1 (1.8) | 0 | 1 (1.1) |
| Agitation | 1 (11.1) | 0 | 0 | 0 | 1 (1.1) |
| Anxiety | 0 | 0 | 1 (1.8) | 2 (11.1) | 3 (3.2) |
| Confusional State | 1 (11.1) | 0 | 1 (1.8) | 1 (5.6) | 3 (3.2) |
| Delirium | 0 | 0 | 1 (1.8) | 0 | 1 (1.1) |
| Hallucination, Auditory | 0 | 0 | 1 (1.8) | 0 | 1 (1.1) |
| Insomnia | 2 (22.2) | 0 | 3 (5.5) | 1 (5.6) | 6 (6.5) |
| Mental Status Changes | 0 | 0 | 2 (3.6) | 0 | 2 (2.2) |
| Sleep Disorder | 1 (11.1) | 0 | 1 (1.8) | 1 (5.6) | 3 (3.2) |
| Renal And Urinary Disorders | | | | | |
| -Total | 1 (11.1) | 0 | 2 (3.6) | 1 (5.6) | 4 (4.3) |
| Acute Kidney Injury | 0 | 0 | 2 (3.6) | 0 | 2 (2.2) |
| Dysuria | 1 (11.1) | 0 | 0 | 0 | 1 (1.1) |
| Haematuria | 0 | 0 | 0 | 1 (5.6) | 1 (1.1) |
| Leukocyturia | 1 (11.1) | 0 | 0 | 0 | 1 (1.1) |
| Urinary Retention | 0 | 0 | 0 | 1 (5.6) | 1 (1.1) |

NOVARTIS

| Primary system organ class<br>Preferred term | Gastric cancer<br>N=9<br>n (%) | HCC<br>N=11<br>n (%) | NSCLC<br>N=55<br>n (%) | Other indications<br>N=18<br>n (%) | All expansion patients<br>N=93<br>n (%) |
|---|---|---|---|---|---|
| Reproductive System And Breast Disorders | | | | | |
| -Total | 1 (11.1) | 0 | 3 (5.5) | 0 | 4 (4.3) |
| Benign Prostatic Hyperplasia | 1 (11.1) | 0 | 1 (1.8) | 0 | 2 (2.2) |
| Scrotal Swelling | 0 | 0 | 1 (1.8) | 0 | 1 (1.1) |
| Testicular Oedema | 0 | 0 | 1 (1.8) | 0 | 1 (1.1) |
| Respiratory, Thoracic And Mediastinal Disorders | | | | | |
| -Total | 2 (22.2) | 2 (18.2) | 28 (50.9) | 5 (27.8) | 37 (39.8) |
| Cough | 0 | 0 | 8 (14.5) | 2 (11.1) | 10 (10.8) |
| Dysphonia | 0 | 0 | 1 (1.8) | 0 | 1 (1.1) |
| Dyspnoea | 1 (11.1) | 1 (9.1) | 14 (25.5) | 2 (11.1) | 18 (19.4) |
| Dyspnoea Exertional | 0 | 1 (9.1) | 0 | 0 | 1 (1.1) |
| Haemoptysis | 0 | 0 | 1 (1.8) | 0 | 1 (1.1) |
| Hiccups | 0 | 0 | 2 (3.6) | 0 | 2 (2.2) |
| Increased Bronchial Secretion | 0 | 0 | 1 (1.8) | 0 | 1 (1.1) |
| Laryngeal Oedema | 0 | 0 | 1 (1.8) | 0 | 1 (1.1) |
| Nasal Polyps | 0 | 0 | 1 (1.8) | 0 | 1 (1.1) |
| Nasal Septum Deviation | 0 | 0 | 1 (1.8) | 0 | 1 (1.1) |
| Pleural Effusion | 0 | 0 | 2 (3.6) | 0 | 2 (2.2) |
| Pneumothorax | 1 (11.1) | 0 | 2 (3.6) | 0 | 3 (3.2) |

NOVARTIS

| Primary system organ class<br>Preferred term | Gastric cancer<br>N=9<br>n (%) | HCC<br>N=11<br>n (%) | NSCLC<br>N=55<br>n (%) | Other indications<br>N=18<br>n (%) | All expansion patients<br>N=93<br>n (%) |
|---|---|---|---|---|---|
| Respiratory, Thoracic And Mediastinal Disorders | | | | | |
| Productive Cough | 0 | 0 | 3 (5.5) | 1 (5.6) | 4 (4.3) |
| Pulmonary Embolism | 0 | 0 | 3 (5.5) | 0 | 3 (3.2) |
| Pulmonary Haemorrhage | 0 | 0 | 1 (1.8) | 0 | 1 (1.1) |
| Respiratory Failure | 0 | 0 | 1 (1.8) | 1 (5.6) | 2 (2.2) |
| Rhinorrhoea | 0 | 0 | 1 (1.8) | 1 (5.6) | 2 (2.2) |
| Skin And Subcutaneous Tissue Disorders | | | | | |
| -Total | 3 (33.3) | 1 (9.1) | 17 (30.9) | 5 (27.8) | 26 (28.0) |
| Acne | 1 (11.1) | 0 | 0 | 0 | 1 (1.1) |
| Alopecia | 0 | 0 | 1 (1.8) | 0 | 1 (1.1) |
| Decubitus Ulcer | 0 | 0 | 1 (1.8) | 0 | 1 (1.1) |
| Dermal Cyst | 0 | 0 | 1 (1.8) | 0 | 1 (1.1) |
| Dermatitis | 0 | 0 | 1 (1.8) | 0 | 1 (1.1) |
| Dermatitis Acneiform | 0 | 0 | 1 (1.8) | 0 | 1 (1.1) |
| Dry Skin | 0 | 0 | 1 (1.8) | 0 | 1 (1.1) |
| Eczema | 0 | 0 | 1 (1.8) | 0 | 1 (1.1) |
| Eczema Nummular | 0 | 0 | 1 (1.8) | 0 | 1 (1.1) |
| Erythema | 0 | 0 | 1 (1.8) | 0 | 1 (1.1) |
| Madarosis | 0 | 0 | 1 (1.8) | 0 | 1 (1.1) |

NOVARTIS

| Primary system organ class<br>Preferred term | Gastric cancer<br>N=9<br>n (%) | HCC<br>N=11<br>n (%) | NSCLC<br>N=55<br>n (%) | Other indications<br>N=18<br>n (%) | All expansion patients<br>N=93<br>n (%) |
|---|---|---|---|---|---|
| Skin And Subcutaneous Tissue Disorders | | | | | |
| Nail Discolouration | 0 | 0 | 0 | 1 (5.6) | 1 (1.1) |
| Palmar-Plantar Erythrodysaesthesia Syndrome | 0 | 0 | 0 | 1 (5.6) | 1 (1.1) |
| Pruritus | 0 | 1 (9.1) | 6 (10.9) | 1 (5.6) | 8 (8.6) |
| Pruritus Generalised | 1 (11.1) | 0 | 0 | 0 | 1 (1.1) |
| Rash | 0 | 0 | 5 (9.1) | 0 | 5 (5.4) |
| Rash Erythematous | 0 | 0 | 1 (1.8) | 0 | 1 (1.1) |
| Rash Macular | 0 | 0 | 1 (1.8) | 0 | 1 (1.1) |
| Rash Maculo-Papular | 0 | 0 | 2 (3.6) | 2 (11.1) | 4 (4.3) |
| Skin Hyperpigmentation | 1 (11.1) | 0 | 0 | 1 (5.6) | 2 (2.2) |
| Skin Lesion | 0 | 0 | 1 (1.8) | 0 | 1 (1.1) |
| Swelling Face | 0 | 0 | 1 (1.8) | 0 | 1 (1.1) |
| Vascular Disorders | | | | | |
| -Total | 1 (11.1) | 1 (9.1) | 7 (12.7) | 1 (5.6) | 10 (10.8) |
| Aortic Aneurysm | 0 | 0 | 1 (1.8) | 0 | 1 (1.1) |
| Deep Vein Thrombosis | 1 (11.1) | 0 | 1 (1.8) | 0 | 2 (2.2) |
| Hot Flush | 0 | 0 | 2 (3.6) | 0 | 2 (2.2) |
| Hypotension | 0 | 0 | 2 (3.6) | 1 (5.6) | 3 (3.2) |
| Intermittent Claudication | 0 | 0 | 1 (1.8) | 0 | 1 (1.1) |

NOVARTIS

| Primary system organ class<br>Preferred term | Gastric cancer<br>N=9<br>n (%) | HCC<br>N=11<br>n (%) | NSCLC<br>N=55<br>n (%) | Other indications<br>N=18<br>n (%) | All expansion patients<br>N=93<br>n (%) |
|---|---|---|---|---|---|
| Vascular Disorders | | | | | |
| Thrombosis | 0 | 1 (9.1) | 0 | 0 | 1 (1.1) |

- Primary system organ classes are presented alphabetically; preferred terms are sorted by frequency of “All subject” Column.
- A subject with multiple occurrences of an AE under one treatment is counted only once in the AE category for that treatment.
- A subject with multiple adverse events within a primary system organ class is counted only once in the total row.
- Only AEs occurring during treatment or within 30 days of the last study medication are reported.

## Conclusion:

**Demographic and background characteristics**:

**Dose escalation**

A total of 38 subjects were enrolled in the dose escalation phase. The median age of the subjects was 56 years (range: 29 to 74 years) and 6/38 subjects (15.8%) were ≥ 65 years of age.

**Expansion groups (all)**

Subjects with HCC, gastric cancer, NSCLC, and other solid tumors (pRCC, GBM, and others) were included in the expansion groups. Overall, 93 subjects were enrolled in the expansion groups with 55 NSCLC subjects. The median age of the subjects was 58 years (range: 28 to 84 years).

**Expansion groups of NSCLC subjects**

The median age of the subjects was 60 years (range: 29 to 84 years) and 20/55 subjects (36.4%) were ≥ 65 years of age. All 55 subjects in the expansion groups of NSCLC subjects had prior surgery. 29/55 subjects (52.7%) had prior radiotherapy and 52/55 subjects (94.5%) received prior antineoplastic medication.

**Determination of MTD/RP2D**

- The MTD/RP2D was determined in 30 subjects in the dose determining analysis set. The MTD was not reached. The RP2D was determined to be 600 mg bid in capsule formulation and 400 mg bid in tablet formulation.

**Pharmacokinetics**

- Capmatinib tablet provided higher dose normalized exposures than the capsule, as also observed in other capmatinib studies (Study CINC280X1101 and Study CINC280X2202). At RP2D, the capmatinib tablet formulation at 400 mg bid provided comparable mean AUC0-12hr,ss and slightly higher Cmax,ss (1.20-fold) compared with the capmatinib capsule at 600 mg bid.

**Safety results**: The safety results are reported for all 38 subjects in the dose escalation phase, 93 subjects in the expansion groups (including 55 NSCLC subjects in the expansion groups). The safety findings in the study were consistent with the known safety profile of capmatinib and no new or unexpected safety signals were identified. The safety results were as expected in a population of subjects with advanced solid tumors.

**Dose escalation groups**

- The median duration of exposure with capmatinib bid dosing was 8 weeks (range: 1.0 to 37.9 weeks) and median actual dose intensity was 793.8 mg/day (range: 200.0 to 1200.0 mg/day).

- Out of 30 subjects in the dose determining analysis set, 3 subjects (10%) experienced DLTs: one subject in the 200 mg bid capsule dose level and one subject in the 450 mg bid capsule dose level experienced fatigue (grade 3). One subject in the 250 mg bid capsule dose level had blood bilirubin increased (grade 3).
- All subjects had at least one AE regardless of study drug relationship of which 22 subjects (57.9%) had grade 3/4 AEs.
- Dose reductions/dose interruptions were reported in 50% of the subjects most frequently due to fatigue and increased blood bilirubin (3 subjects each, 7.9%).
- Serious adverse events were reported in 19 subjects (50%) mainly ascites, intestinal obstruction, asthenia, pneumonia, and tumor pain (2 subjects each, 5.3%).
- Four (10.5%) deaths were reported in the dose escalation phase, all due to the study indication: gastric adenocarcinoma, colon cancer, rectal adenocarcinoma (on-treatment deaths) and one subject died due to hepatocellular carcinoma 40 days after the last dose of the study medication.

**Expansion groups (all)**

- The median duration of exposure with capmatinib bid dosing was 8 weeks (range: 1.0 to 187.0 weeks) and the median actual dose intensity was 844.7 mg/day (range: 224.4 to 1200.0 mg/day).
- The majority of the subjects (92 subjects, 98.9%) had at least one AE regardless of study drug relationship in the expansion groups of which 59 subjects (63.4%) had grade 3/4 AEs.
- Dose reductions/dose interruptions were reported in 59.1% of the subjects and adverse events leading to study drug discontinuation were reported in 18.3% of subjects.
- Serious adverse events were reported in 45 subjects (48.4%) mainly abdominal pain and pneumonia (each in 5 subjects, 5.4%).
- Eighteen (19.4%) deaths were reported in the expansion groups due to NSCLC (14 subjects), gastric cancer (2 subjects), and GBM (1 subject), and 1 subject with advanced adenocarcinoma of esophagus died due to infectious pneumonia (bacterial, not study drug related). Twelve deaths reported were on-treatment.

**Expansion groups of NSCLC subjects**

- The median duration of exposure with capmatinib bid dosing was 10.4 weeks (range: 0.1 to 187.0 weeks) and the median actual dose intensity for capmatinib was 800.0 mg/day (range: 224.4 to 1200.0 mg/day).
- All subjects had at least one AE regardless of study drug relationship of which 44 subjects (74.5%) had grade 3/4 AEs.
- Serious adverse events were reported in 30 subjects (54.5%) mainly pneumonia (4 subjects, 7.3%) and pulmonary embolism (3 subjects, 5.5%).
- Dose reductions/dose interruptions were reported in 61.8% of the subjects and adverse events leading to study drug discontinuation were reported in 20% of subjects.
- Fourteen (25.5%) deaths were reported due to NSCLC. Eight deaths reported were on-treatment.

**Efficacy results**: This Phase I study was conducted in heavily pretreated subjects with advanced solid tumors with limited treatment options.

**Dose escalation**

- As per Investigator's review, out of 38 subjects, 10 subjects (26.3%) had a BOR of SD and 26 subjects (68.4%) had a BOR of PD and the DCR was 26.3% (95% CI: 13.4-43.1).

**Expansion groups (all)**

The expansion groups included subjects with gastric cancer, HCC, NSCLC and other solid tumors (including pRCC, GBM and others). As per Investigator's review,

- Out of 9 subjects with gastric cancer, 2 subjects had a BOR of SD (22.2%), 3 subjects (33.3%) had a BOR of PD. The DCR was 22.2% (95% CI: 2.8, 60.0).
- Out of 11 subjects with HCC, 5 subjects had a BOR of SD (45.5%) and 1 subject (9.1%) had a BOR of PD. The DCR was 45.5% (95% CI: 16.7, 76.6).
- Out of 18 subjects with other solid tumors (pRCC, GBM, and others), 5 subjects (27.8%) had a BOR of SD, 9 subjects (50.0%) had a BOR of PD. The DCR was 27.8% (95% CI: 9.7, 53.5).

**Expansion groups of NSCLC subjects**

- Overall, out of 55 evaluable subjects in the expansion groups of NSCLC subjects, as per Investigator's review, 1 subject (1.8%) had a BOR of CR, 10 subjects (18.2%) had PR, 17 subjects (30.9%) had a BOR of SD, and 17 subjects (30.9%) had PD. The ORR was 20.0% (95% CI: 10.4, 33.0) and DCR was 50.9% (95% CI: 37.1, 64.6). The estimated median PFS was 3.7 months (95% CI: 1.8, 7.3).

Overall, study CINC280X2102 is a well conducted Phase I study which established the RP2D for capmatinib both in capsule and tablet formulation. The study also provides preliminary evidence of the clinical activity of capmatinib for the treatment of subjects with MET dysregulated advanced solid malignancies, in particular NSCLC, highlighting the importance of an appropriate biomarker selection to identify the subjects who will benefit most from treatment with capmatinib.

## Date of Clinical Trial Report

01-Jun-2018 – Original CSR

09-Oct-2019 – Amended CSR