Capmatinib (INC280) in METΔex14-mutated advanced non-small cell lung cancer (NSCLC): Efficacy data from the phase II GEOMETRY mono-1 study.

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Background:

Capmatinib is a highly potent and selective MET inhibitor. Previous data of GEOMETRY mono-1 study showed a clinically meaningful overall response rate (ORR) and manageable toxicity profile in patients (pts) with METΔex14-mutated NSCLC who received 1–2 prior lines of treatment (tx) (Cohort 4) and in particular a high ORR in tx-naïve pts (Cohort 5b). Here we report the results in METΔex14-mutated NSCLC for duration of response (DOR) and progression-free survival (PFS) as well as the updated results for ORR.

Methods:

GEOMETRY mono-1 is a phase 2, multi-cohort, multicenter study evaluating capmatinib in pts with METΔex14-mutated or MET-amplified advanced NSCLC across 6 cohorts. Pts (≥18 yrs) with ECOG PS 0–1, ALK and EGFR wt, and stage IIIB/IV NSCLC were eligible. Pts with METΔex14 mutation (centrally confirmed) were assigned (regardless of MET amplification status/gene copy number) to Cohorts 4 and 5b and received capmatinib tablets 400 mg BID. Primary endpoint was ORR by Blinded Independent Review Committee (BIRC) per RECIST v1.1. Key secondary endpoint was DOR by BIRC.

Results:

As of Nov 08, 2018, 97 pts with METΔex14-mutated NSCLC (Cohort 4: 69 pts; Cohort 5b: 28 pts) were evaluable for efficacy. ORR (95% CI) by BIRC was 39.1% (27.6–51.6) in Cohort 4 and 71.4% (51.3–86.8) in Cohort 5b. While still immature at the time of this analysis, data on durability are promising: median DOR (95% CI) by BIRC was 9.72 (4.27–11.14) and 8.41 (5.55–NE) mo for Cohorts 4 and 5b, respectively; median PFS (95% CI) by BIRC was 5.42 (4.17–6.97) and 9.13 (5.52–13.86) mo for Cohorts 4 and 5b, respectively. Safety profile remains favourable and unchanged. Most common AEs (≥25% all grades) across all cohorts (n = 315), were peripheral edema (49.2%), nausea (43.2%), and vomiting (28.3%); majority of the AEs were grade 1/2. Final efficacy analysis (12-mo f-u on DOR) including biomarker data will be presented during meeting.
Conclusions:

These data confirm capmatinib to be a promising new treatment option for pts with METΔex14-mutated advanced NSCLC regardless of the line of therapy with deep and durable responses and manageable toxicity profile. Clinical trial information: NCT02414139

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