557P A phase I study of rebastinib and carboplatin in patients with metastatic solid tumours


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Background: Rebastinib is a switch control inhibitor of TIE2 kinase. TIE2 is expressed in endothelial cells and in a subset of macrophages with pro-angiogenic, pro-metastatic and immunosuppressive properties associated with chemotherapy resistance. This study aims to investigate the safety and preliminary efficacy of rebastinib and carboplatin in pts with solid tumors.

Methods: This is an open-label, phase Ib/II, study in which rebastinib 50 and 100 mg BID was evaluated with carboplatin AUC5/6 Q3W using 3 + 3 dose escalation rules to determine the RP2D. Dose escalation included pts with metastatic solid tumors for combination rebastinib and carboplatin at tolerable dose level.

Results: As of March 27, 2020, 22 pts were enrolled in 3 dose-escalating cohorts: rebastinib 50 mg BID + AUC5 (n=3), rebastinib 100 mg BID + AUC5 (n=14), and rebastinib 100 mg BID + AUC6 (n=5). The median age was 61 yrs. Most frequent diagnoses were breast cancer (n=5); neuroendocrine carcinoma (n=3); pancreatic cancer (n=3); NSCLC, ovarian and cholangiocarcinoma (n=2 each). The median number of prior anti-cancer therapies was 4 (1, 12). Median duration of treatment was 8.4 weeks (0.9, 22.6). Treatment-emergent adverse events >10% were Mostly Grade 1 or 2: thrombocytopenia (36%); constipation (32%); fatigue and nausea (27%)

558P Binimetinib, pemetrexed (Pem) and cisplatin (Cis), followed by maintenance of Binimetinib and Pem in patients with advanced non-squamous NSCLC and KRAS mutations: The phase Ib SAKK 19/16 trial


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Background: KRAS mutations are found in 20-25% of non-squamous NSCLC and effective therapies targeting the RAS/MEK/ERK pathway are needed. Binimetinib an oral selective MEK Inhibitor plus platinum-based chemotherapy is promising. We design a multicenter open-label phase IB trial to define the recommended phase II dose and early efficacy of Binimetinib in combination with Pem and Cis.

Methods: Eligible patients (pts) had stage III-IV NSCLC unsuitable for curative therapy due to performance status (PS) 0-1, KRAS mutation not codon 12, 13 or 61 mutations, no prior systemic therapy. Pts were enrolled into part 1: 3 + 3 design with dose escalation in 2 dose levels (DL) of Binimetinib and part 2: expansion cohort at the maximum tolerated DL. Treatment consisted of 4 cycles of Cis 75 mg/m², Pem 500 mg/m², and Binimetinib 45 mg (DL1) or 60 mg (DL2) BID d1-14 (d3-14 in cycle 1) q3w followed by Pem and Binimetinib until progressive disease (PD) or unacceptable toxicity.

Results: From May 2017 to Dec 2019, 18 pts (13 in part 1, 5 in part 2) were enrolled. Median age was 56 years (48–73); 56% were male, 65% had PS 1. KRAS mutations were 83% at codon 12, 6% at codon 13 and 6% at codon 61. In part 1, 9 pts (3 in DL1, 6 in DL2) were evaluable for DL1 and no DL occurred. Median number of cycles was 2 (1-17, range). All pts are off treatment mainly due to PD (30%) or pts/physicians decision (30%). Together with part 1, 20 pts received 45 mg Binimetinib, one of which was excluded from efficacy due to eligibility violation. Overall response rate was 33% (7 – 70% 95% CI). Median progression-free survival and overall survival were 5.7 months (1.1 - 14.0, 95% CI) and 6.5 months (1.8 – NR, 95% CI), respectively. No grade 4/5 adverse events (AEs) were observed. Most common treatment-related grade 3 AEs were fatigue (30%), nausea, anemia, hypertension and lung infection (20%). One patient experienced a grade 3 thrombocytopenic event. No grade 3 orular or cardiac AE occurred.

Conclusions: The combination of Cis, Pem and Binimetinib at 45mg BID was safe. No early signal of increased efficacy of the addition of Binimetinib to chemotherapy was observed in KRAS-mutant NSCLC.