head and neck cancer

PHASE 1B STUDY OF MEHD7945A (MEHD) PLUS CISPLATIN/FLUOROURACIL (CIS/5FU) OR CARBOPLATIN/PACLITAXEL (CARBO/PAC) FOR 1ST-LINE TREATMENT OF RECURRENT/METASTATIC SQAMOUS CELL CARCINOMA OF HEAD AND NECK (RMSCCHN)

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Aim: MEHD, a novel dual-action humanized IgG1 antibody that blocks ligand binding to HER3 and EGFR, inhibits signaling from ligand-dependent HER dimers. MEHD is active in multiple tumor models, including models resistant to anti-EGFR or anti-HER3, and enhances activity of chemotherapeutic agents. Single-agent activity in Phase 1a included confirmed PR in 2 RMSCCHN patients (pts) who had high levels of the HER3 ligand NRG1.

Methods: This open-label, multicenter, Phase 1b study with a modified 3 + 3 + 3 design assesses safety, PK and preliminary anti-tumor activity (RECIST v1.1) of MEHD plus platinum-based chemotherapy in 1st-line RMSCCHN pts. MEHD 1650 mg IV every 3 wks is combined with cis 100 mg/m2 / 5FU 1000 mg/m2/d on Days 1-4 (Arm A) or carbo (AUC 6 mg/mL·min) / pac 200 mg/m2 (Arm B) on Day 1 of 21-d cycles (up to 6), followed by MEHD maintenance until disease progression / intolerable toxicity. Mandatory tumor samples are assayed by qRT-PCR for biomarkers related to mechanism of action and SCCHN.

Results: As of 28MAR14, 18 pts were treated and remain active: 6 ARM A pts have received 2-7 cycles (median 5.5) of MEHD; 13 Arm B pts have received 1-8 cycles (median 3.5). DLTs occurred in 2 pts in Arm A (1 G3 diarrhea, 1 G3 acute renal failure & G3 febrile neutropenia) and 1 pt in Arm B (G3 dehydration, anorexia). G ≥ 3 treatment-related AEs in ≥2 pts were hypokalemia (3), neutropenia (3), dehydration (3), fatigue (2), and hyponatremia (2) in Arm A and neutropenia (6), febrile neutropenia (3), and hyponatremia (2) in Arm B. Chemo dose was reduced in 9/18 pts. Preliminary MEHD PK in both arms was similar to single-agent MEHD profile. In 12 pts with on-treatment tumor assessments, best responses were 9 (75%) PR (4 confirmed) [Arm A: 4; Arm B: 5; HPV: 2 + , 5-, 2 unknown], and 3 (25%) stable disease [Arm A: 1; Arm B: 2]; after data cutoff 2 pts were reported with CR. Further biomarker data are pending.

Conclusions: MEHD plus cis/5FU or carbo/pac has been reasonably well tolerated with no new safety signals. G ≥ 3 AEs were manageable and less frequent post-Cycle 1. Both combinations had promising anti-tumor activity. Updated results will be presented.

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