**head and neck cancer**

**3160**

**RANDOMIZED PHASE II STUDY OF MEHD7945A (MEHD) VS CETUXIMAB (CET) IN >= 2ND-LINE RECURRENT/METASTATIC SQUAMOUS CELL CARCINOMA OF THE HEAD & NECK (RMSCCHN) PROGRESSIVE ON/AFTER PLATINUM-BASED CHEMOTHERAPY (PTCT)**

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**Aim:** MEHD, a novel dual-action humanized IgG1 antibody that blocks ligand binding to EGFR and HER3, inhibits signaling from all ligand-dependent HER dimers, and can elicit antibody dependent cell mediated cytotoxicity. MEHD is active in multiple tumor models, including models resistant to anti-EGFR or anti-HER3. Preclinical and early clinical data suggest that high expression of neuregulin 1 (NRG1) in tumors may enhance sensitivity to MEHD.

**Methods:** This multicenter, open-label, randomized phase II study evaluated efficacy in RMSCCHN patients (pts) progressive on/after PtCT, and in those whose tumors express high NRG1. Primary endpoint = PFS (RECIST v1.1), secondary endpoints = ORR, DOR, OS and safety (CTCAE v4.0). Pts received MEHD (1100 mg IV, q2w) or Cet (400 mg/m² load, 250 mg/m² IV, q1w) until progression or intolerable toxicity. Upon central confirmation of progression on Cet, pts could cross over to MEHD. Mandatory tumor samples are assayed for biomarkers related to mechanism of action and SCCHN, including NRG1 expression and HPV status by qRT-PCR.

**Results:** 121 pts were randomized (59 MEHD, 62 Cet; median age 62 y, ECOG 0-2). As of 28Mar14, 8 pts remain active. Efficacy results are shown (Table) with no difference between treatment arms. Grade $\geq 3$ adverse events (AE) that were more frequent with MEHD (61%) compared to Cet (51%) included infections (22.0 vs 11.5%) and GI disorders (13.6 vs 6.6%) contributing to higher rates of SAEs (40.7 vs 29.5%); metabolic disorders were less with MEHD (10.2 vs 14.8%). Any grade skin toxicity was lower with MEHD (45.8 vs 59.7%).

**Table:**

<table>
<thead>
<tr>
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<th>MEHD (n = 59)</th>
<th>Cet (n = 62)</th>
<th>HR (90% CI)</th>
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<tbody>
<tr>
<td>Pts with PFS event</td>
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<tr>
<td>Median PFS, mo</td>
<td>4.1 (2.8–4.7)</td>
<td>4.0 (3.0–5.0)</td>
<td>1.15 (0.83–1.59)</td>
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<tr>
<td>Pts with OS event</td>
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<tr>
<td>Median OS, mo</td>
<td>7.2 (4.3–9.4)</td>
<td>8.5 (6.4–10.5)</td>
<td>1.18 (0.80–1.73)</td>
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</table>

**Conclusions:** MEHD did not improve outcomes of pts with RMSCCHN compared to Cet. Crossover and biomarker analyses (ongoing) will be presented.

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