TPS6115 **Poster Session**

FIERCE-HN: A multicenter, randomized, double-blind, placebo-controlled, phase 3 study of ficlatuzumab (HGF/cMET MAb) in combination with cetuximab in participants with recurrent or metastatic (R/M) HPV negative head and neck squamous cell carcinoma (HNSCC).

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Background: Patients with HPV-negative R/M HNSCC have a worse median overall survival (OS) than HPV-positive patients and current treatments options are limited.[1] Ficlatuzumab is a humanized IgG1 MAb that binds HGF, the ligand for the c-MET tyrosine kinase receptor. HGF/c-MET pathway dysregulation is frequently observed in HPV-negative HNSCC, and has been linked to EGFR inhibitor resistance, limiting the potential efficacy of EGFR-targeting drugs like cetuximab. In a phase 2 study, both pathways were targeted using ficlatuzumab plus cetuximab in patients with HPV-negative R/M HNSCC resistant to cetuximab, platinum, and anti-PD1 immune checkpoint inhibitors (ICI) who have a very poor historical prognosis. A PFS of 4.1 months, median OS of 7.4 months, and overall response rate (ORR) of 38% (6/16; 2 CR, 4 PR) was observed.[2] FIERCE-HN compares the efficacy/safety of ficlatuzumab+cetuximab vs placebo+cetuximab in patients with R/M HPV-negative HNSCC. **Methods:** This is an international, multicenter, randomized, double-blind, placebo-controlled phase 3 study. Major enrollment criteria include confirmed diagnosis of R/M HNSCC primary tumors of the oropharynx (p-16 negative only), oral cavity, hypopharynx, or larynx. Participants must have progressed on, or be intolerant to, previous anti-PD-1/PD-L1 ICI and platinum-based chemotherapy; have 2 or fewer prior lines of anticancer therapy; and have no prior treatment with cetuximab/alternative EGFR inhibitors in the R/M setting. Patients with feeding tubes are eligible. The primary endpoint is OS; key secondary endpoints include PFS and ORR. Other secondary endpoints are DCR, DoR, safety, PK, immunogenicity and QoL. Patients will receive cetuximab 500mg/m2 and are randomized 1:1:1 to Arm A: ficlatuzumab 10mg/kg, Arm B: ficlatuzumab 20mg/kg, or Arm C: placebo. Treatments will be on Days 1 and 15 of a 28-day cycle. This is an adaptive study with two interim analyses (IAs). IA 1 will be conducted after 70 OS events, when futility and optimal dose assessments will be performed. Participants enrolled after IA 1 will be randomized 1:1 to the optimal ficlatuzumab dose or placebo, plus cetuximab. IA 2 will be conducted after 163 OS events to assess whether an event count re-estimation is needed. The final analysis will occur after 232 (or up to 279) OS events, depending on the re-estimation outcome. The study has statistical power of 80%, assuming a true OS hazard ratio of 0.667. Between 410 to 500 patients will be enrolled. The study is ongoing and actively recruiting in North America, Europe, United Kingdom, and Asia-Pacific. Clinical trial information: NCT06064877 (collaborator Eli Lilly provided cetuximab). 1. Cohen E et al., JITC. 2019;7:184. 2. Bauman JE et al., JCO. 2023. 41:3851. Clinical trial information: NCT06064877. Research Sponsor: AVEO Oncology.