FIERCE-HN: A MULTICENTER, RANDOMIZED, PLACEBO-CONTROLLED, PHASE 3 STUDY OF FICLATUZUMAB + CETUXIMAB IN PTS W/RECURRENT OR METASTATIC (R/M) HPV-NEGATIVE HEAD AND NECK SQUAMOUS CELL CARCINOMA (HNSCC)

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Background For patients with R/M HNSCC, current treatments are palliative with anti-PD-1 checkpoint inhibitor +/- platinum and 5-fluorouracil chemotherapy for first-line followed by taxanes, methotrexate, and cetuximab as later-line options. The median overall survival (OS) for R/M patients is 10–13 months, and those with HPV-negative HNSCC face the worst outcomes. 1 Ficlatuzumab is a humanized IgG1 mAb against HGF, the ligand for the c-MET tyrosine kinase receptor. HGF/c-MET pathway dysregulation is frequently observed in HPV-negative HNSCC. In a phase 2 study, ficlatuzumab 20mg/kg plus cetuximab 500mg/m² every 2 weeks was assessed in R/M HNSCC patients that were anti-PD-1, cetuximab, and platinum-resistant, a pan-refractory population with a median PFS of 2 months. 2 In this study, HPV-negative patients had a progression-free survival (PFS) of 4.1 months, median OS of 7.4 months, and overall response rate (ORR) of 38% (6/16; 2 CR, 4 PR). 2 The objective of the FIERCE-HN study is to compare the efficacy/safety of ficlatuzumab +cetuximab vs placebo+cetuximab in patients with R/M HPV-negative HNSCC.

Methods FIERCE-HN is an international, multicenter, randomized, double-blind, placebo-controlled phase 3 study. Major enrollment criteria include confirmed primary diagnosis of HPV-negative R/M HNSCC; primary tumor of oropharynx, oral cavity, hypopharynx, or larynx; failed or intolerant to previous anti-PD-1/PD-L1 and platinum chemotherapy; no more than 2 prior lines of anticancer therapy; no prior treatment with cetuximab/alternative EGFR inhibitors in the R/M setting. Patients with feeding tubes are eligible. Approximately 410 patients will be randomized 1:1:1 to Arm A: ficlatuzumab 10mg/kg plus cetuximab 500mg/m², Arm B: ficlatuzumab 20mg/kg plus cetuximab 500mg/m², or Arm C: placebo plus cetuximab 500mg/m². Treatments will be on Days 1 and 15 of a 28-day cycle. An interim analysis will be done to determine optimal dose of ficlatuzumab for further study progression when 70 patients each in Arms A and B have completed their first restaging scans (the inferior ficlatuzumab arm will be discontinued; final target n of ~163 in each the optimal ficlatuzumab and control arms). The primary endpoint is OS; additional endpoints include PFS, ORR, DCR, DoR, safety, PK/PD, QoL, and antidrug antibodies. A total of 239 events are required to have 87.5% power to detect a difference assuming a true HR=0.67 in favor of the optimal ficlatuzumab+cetuximab arm after the interim analysis. Analysis will use a 1-sided log-rank test at a significance level= 0.025 and the uniformly most powerful conditionally unbiased criterion to control the Type I error.

Trial Registration NCT number TBD

REFERENCES

Ethics Approval Investigators will submit the study protocol, any protocol modifications, and the participant consent form to be utilized in this study to the appropriate IRB or EC for review and approval. This committee must operate in accordance with the US Code of Federal Regulations (CFR), Title 21 CFR Part 56 or ICH GCP or European regulations. Investigators also agree to protect the rights, safety, and welfare of the participants entering the study, including obtaining informed consent prior to performing any study-related procedures and informing each participant that the study drugs are being used for investigational purposes.

http://dx.doi.org/10.1136/jitc-2023-SITC2023.0673