CABOZANTINIB PLUS ATEZOLIZUMAB IN ADVANCED HEAD AND NECK CANCER PREVIOUSLY TREATED WITH PLATINUM-CONTAINING CHEMOTHERAPY: RESULTS FROM COHORT 17 OF THE COSMIC-021 STUDY

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Background Cabozantinib, a multiple receptor tyrosine kinase inhibitor, promotes an immune-permissive environment which might enhance activity of immune checkpoint inhibitors (ICI). COSMIC-021 (NCT03170960), a multicenter phase 1b study, is evaluating cabozantinib plus atezolizumab in advanced solid tumors; here we present outcomes in patients with platinum-pretreated advanced head and neck cancer (cohort 17).

Methods Patients with head and neck squamous cell carcinoma who had progressed during or following prior platinum-containing chemotherapy for advanced or metastatic disease were enrolled. Primary tumors in the oropharynx, oral cavity, hypopharynx, or larynx were allowed (nasopharynx was excluded). Up to two prior lines of systemic therapy were allowed. Prior ICI, EGFR-targeted therapy, and radiotherapy were permitted. Patients received cabozantinib, 40 mg PO QD, plus atezolizumab, 1200 mg IV Q3W. The primary endpoint was ORR per RECIST 1.1 as assessed by the investigator. Other endpoints included safety, DOR, PFS, and OS.

Results As of May 31, 2022, 30 patients were enrolled. Baseline characteristics were, median age, 62 y (range, 44-78); male, 83%; ECOG PS 0 and 1, 33% and 67%; HPV positive, negative, and unknown, 17%, 33%, and 50%; primary tumor in oropharynx, oral cavity, hypopharynx, and larynx, 40%, 33%, 10%, and 7%; lung, lymph node, and bone metastasis, 60%, 53%, and 10%; ≥3 metastatic sites, 43%; two lines of therapy for locally advanced or metastatic disease, 40%; median (range) number of prior lines of systemic therapy, 2.5 (1-10); prior ICI, 30%; prior radiation, 97%. The median follow-up was 25.9 mo. Clinical activity was observed with cabozantinib plus atezolizumab (table 1). Most common treatment-related adverse events (TRAEs) of any grade included fatigue (30%), stomatitis (30%), hypertension (27%), hypothyroidism (23%), nausea (23%), diarrhea (20%), decreased appetite (20%), and aspartate aminotransferase increased (20%); grade 3/4 TRAEs occurred in 47%. There were no grade 5 TRAEs.

Conclusions Cabozantinib plus atezolizumab demonstrated moderate clinical activity with manageable toxicity in patients with platinum-pretreated advanced head and neck cancer.

Trial Registration This study is registered with ClinicalTrials.gov (NCT03170960).

Ethics Approval The study Protocol (online only) was reviewed and approved by the institutional review board or ethics committee at participating sites. The study was conducted in accordance with the International Conference on Harmonisation Good Clinical Practice guidelines, the principles of the Declaration of Helsinki, and any local regulations.

Consent All patients provided written informed consent.