Background Pembrolizumab alone and in combination with platinum-based chemotherapy have become standard first-line treatment options for recurrent/metastatic head and neck squamous cell carcinoma (R/M HNSCC), and there is a growing unmet need for safe and efficacious treatment options for R/M HNSCC that has progressed on or after platinum-based chemotherapy and immunotherapy. Data from Study 111/KEYNOTE-146 showed promising antitumor activity and acceptable safety for the PD-1 inhibitor pembrolizumab given in combination with the multitarget kinase inhibitor lenvatinib in patients with metastatic HNSCC.1 LEAP-009 (NCT04428151), a global, randomized, open-label, phase 2 trial, will assess the efficacy and safety of pembrolizumab in combination with lenvatinib versus SOC chemotherapy, as well as the efficacy and safety of lenvatinib monotherapy, in patients with R/M HNSCC that has progressed after platinum-based chemotherapy and a PD-(L)1 inhibitor.

Methods Eligible patients are adults with histologically confirmed, locally incurable R/M HNSCC of the oral cavity, oropharynx, hypopharynx, or larynx, disease progression at any time during or after platinum-containing chemotherapy (with or without cetuximab), disease progression within 12 weeks from the last dose of treatment with ≥2 doses of a PD-(L)1 inhibitor, measurable disease based on RECIST v1.1 as confirmed by BICR, ECOG performance status of 0 or 1, and no major blood vessel invasion/infiltration. Patients will be randomized 3:3:2 to pembrolizumab (200 mg IV Q3W for up to 35 cycles) plus lenvatinib (20 mg orally once daily), investigator’s choice of SOC chemotherapy (docetaxel, paclitaxel, cetuximab, or cetaperitabine), or lenvatinib monotherapy (24 mg orally once daily). Randomization will be stratified by PD-L1 tumor proportion score (<50% versus ≥50%) and ECOG performance status (0 versus 1). Treatment will continue until centrally verified disease progression, unacceptable toxicity, or decision to withdraw. Patients in the chemotherapy and lenvatinib monotherapy arms may be eligible to receive pembrolizumab plus lenvatinib upon disease progression. The primary endpoint is ORR according to modified RECIST v1.1 as assessed by BICR. Secondary endpoints include PFS, OS, DOR, and safety. Interim futility analysis will be conducted for the lenvatinib monotherapy arm. Tumor imaging by CT or MRI will be performed 6 weeks after randomization, every 6 weeks through year 1, and every 9 weeks thereafter. Safety will be monitored throughout the study and for 30 days after treatment end (90 days for serious AEs if no new antitumor treatment is initiated, and at any time if the AE is considered treatment-related). Recruitment is ongoing; Planned enrollment is ~400 patients.

Results N/A

Conclusions N/A

Trial Registration ClinicalTrials. gov Identifier, NCT04428151

Ethics Approval The study and protocol were approved by the Institutional Review Board or ethics committee at each site.

Consent All patients provided written informed consent to participate in the clinical trial.

REFERENCE

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352 UPDATED CLINICAL DATA FROM THE SQUAMOUS CELL CARCINOMA OF THE HEAD AND NECK (SCCHN) EXPANSION COHORT OF AN ONGOING PH1/1B STUDY OF EGANALISIB (FORMERLY IPI-549) IN COMBINATION WITH NIVOLUMAB

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Background Eganalisib is a first-in-class, oral, selective PI3K-g inhibitor. Preclinically, eganalisib reprograms macrophages/myeloid derived suppressor cells (MDSCs) from an immune-suppressive to an immune-activating phenotype and enhances efficacy of checkpoint inhibitors. Efficacy of eganalisib + nivolumab in patients with SCCHN resistant to immediate prior anti-PD-(L)1 therapy is presented.