A PHASE 2 STUDY OF EVORPACEPT (ALX148) IN COMBINATION WITH PEMBROLIZUMAB AND CHEMOTHERAPY IN PATIENTS WITH ADVANCED HEAD AND NECK SQUAMOUS CELL CARCINOMA (HNSCC); ASPEN-04

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Background Anticancer immunity relies on the release of tumor antigens and subsequent activation of both the innate and adaptive immune systems. After cytotoxic chemotherapy induces neoantigen release, myeloid checkpoint inhibitors have been shown to help potentiate innate immune cell activity including antigen presentation. CD47, a marker of self, interacts with SIRPα on myeloid immune cells and can be upregulated by cancer cells to evade immune responses. Evorpacept is a high affinity CD47-blocking fusion protein with an inactive Fc region designed to safely enhance standard anticancer therapeutics. Pembrolizumab, a T cell checkpoint inhibitor, represents a standard treatment option for patients with previously untreated recurrent/metastatic (R/M) HNSCC, both as a monotherapy and in combination with 5FU + platinum. Through increased activation of the immune system, the combination of evorpacept + pembrolizumab + 5FU/platinum might have greater anti-tumor activity in R/M HNSCC than standard therapeutic approaches. This combination approach could be especially beneficial for R/M HNSCC patients with low PD-L1 expression, where anti-PD-(L)1 therapy historically has diminished efficacy. The combination of evorpacept + pembrolizumab + 5FU/platinum has undergone preliminary testing in the Phase 1 ASPEN-01 study,1 demonstrating tolerability and clinical response. In previously untreated patients with R/M HNSCC treated with evorpacept + pembrolizumab + 5FU/platinum regardless of PD-L1 expression, objective responses including complete response were demonstrated.

Methods ASPEN-04 (figure 1) is an ongoing non-comparative, open-label, randomized Phase 2 global study for patients with metastatic or unresectable recurrent HNSCC who have not yet received first-line treatment. After an initial safety lead-in cohort, ~162 patients will be randomized using a 2:1 allocation to receive evorpacept + pembrolizumab + chemotherapy (5FU + either cisplatin or carboplatin) or pembrolizumab + chemotherapy, regardless of PD-L1 expression. Minimization factors used to randomize patients include geography, PD-L1 combined positive score, and human papilloma virus (HPV) (p16) status. Patients in the evorpacept treatment arm will receive evorpacept 45 mg/kg IV Q3W. All patients will receive pembrolizumab 200 mg IV Q3W (maximum of 35 cycles) and standard administration of 5FU and platinum agents. The co-primary endpoints in this trial are 12-month overall survival rate and objective response rate using RECIST v1.1. Key secondary endpoints include duration of response, progression-free survival, overall survival, and safety. Exploratory endpoints will characterize pharmacodynamic properties.

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Trial Registration ClinicalTrials.gov identifier, NCT04675333

REFERENCE

Ethics Approval The study was approved by all participating institutions’ Ethics and/or Review Boards.

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