433 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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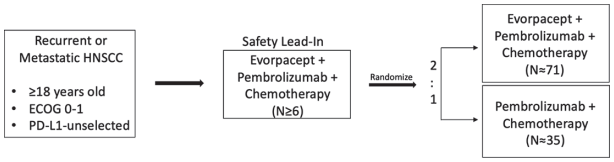
Background Anticancer immunity relies on the release of tumor antigens and subsequent activation of the innate and adaptive immune systems. After cytotoxic chemotherapy induces neoantigen release, myeloid checkpoint inhibitors can help potentiate innate immune cell activity including antigen presentation. CD47 is a marker of self that interacts with SIRPα on myeloid immune cells and is upregulated by tumors 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 that activates cytotoxic lymphocytes, is a standard 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, a combination of evorpacept + pembrolizumab + 5FU/platinum might have more anti-tumor activity in R/M HNSCC than current standard therapeutic approaches. This combination approach could be particularly beneficial to 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 ongoing Phase 1 ASPEN-01 study,[1] demonstrating initial clinical response and tolerability. In previously untreated, PD-L1-unselected R/M HNSCC patients treated with evorpacept + pembrolizumab + 5FU/platinum, patients experienced objective responses, including complete response. The ASPEN-04 study will assess the efficacy and safety of evorpacept in combination with pembrolizumab and chemotherapy in previously untreated patients with PD-L1-unselected R/M HNSCC.

Methods ASPEN-04 (figure 1) is an ongoing non-comparative, open-label, randomized Phase 2 global study of evorpacept + pembrolizumab + chemotherapy (5FU + either carboplatin or cisplatin) or pembrolizumab + chemotherapy in patients with PD-L1-unselected metastatic or unresectable recurrent HNSCC who have not yet been treated for their advanced disease. After an initial safety lead-in cohort, ~106 patients will be randomized to receive evorpacept + pembrolizumab + chemotherapy or pembrolizumab + chemotherapy. Minimization factors used to randomize patients include geography, PD-L1 combined positive score, and 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 primary endpoint in this Simon two-stage trial design is 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.



Abstract 433 Figure 1 ASPEN-04 Study Schema

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Trial Registration ClinicalTrials.gov identifier, NCT04675333

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

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