**Abstract 678**

**A PHASE 2 STUDY OF EVORPACEPT (ALX148) IN COMBINATION WITH PEMBROLIZUMAB IN PATIENTS WITH ADVANCED HEAD AND NECK SQUAMOUS CELL CARCINOMA (HNSCC); ASPEN-03**

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**Background** Both innate and adaptive immune responses are important components of anticancer immunity. CD47 is a marker of self that interacts with SIRPa on myeloid immune cells, inhibiting their function. Evorpacept is a high affinity CD47-blocking fusion protein with an inactive Fc region designed to be safely combined with and to enhance the efficacy of standard anticancer therapeutics. Pembrolizumab inhibits PD-1/PD-L1 signaling, which is a T cell immune checkpoint, and pembrolizumab has demonstrated anti-tumor efficacy through activation of tumor-infiltrating lymphocytes. Evorpacept used in combination with pembrolizumab has the potential to augment both innate and adaptive anti-tumor immune responses. Pembrolizumab as a single agent is a standard treatment option for patients with previously untreated recurrent or metastatic (R/M) HNSCC with PD-L1-positive (combined positive score [CPS] ≥1) tumors. The combination of evorpacept + pembrolizumab has shown acceptable tolerability and preliminary efficacy in patients with advanced HNSCC in ≥2nd line in the ongoing Phase 1 ASPEN-01 study. Patients who had not received prior checkpoint inhibitor treatment and who were treated with evorpacept + pembrolizumab regardless of PD-L1 expression level (n=10) experienced a 40% objective response rate (ORR) and 22.1 months median overall survival (OS), comparing favorably with historical controls.

**Methods** ASPEN-03 (figure 1) is an ongoing non-comparative, open-label, randomized Phase 2 global study of evorpacept + pembrolizumab or pembrolizumab alone in patients with metastatic or unresectable recurrent, PD-L1-positive (CPS ≥1) HNSCC who have not yet received first-line treatment. After an initial safety lead-in cohort, ~177 patients will be randomized 2:1 to receive evorpacept + pembrolizumab or pembrolizumab alone. Minimization factors used to randomize patients include geography, CPS, and human papilloma virus (HPV) (p16) status. Patients in the evorpacept + pembrolizumab treatment arm will receive evorpacept 45 mg/kg IV Q3W and pembrolizumab 200 mg IV Q3W (maximum of 35 cycles). The co-primary endpoints in this trial are 12-month overall survival (OS) rate and ORR using RECIST v1.1. Key secondary endpoints include duration of response, progression-free survival, OS, and safety. Exploratory endpoints will characterize pharmacodynamic properties.

**Acknowledgements** We would like to thank all the participating patients, their families, and site research teams.

**Trial Registration** ClinicalTrials. gov identifier, NCT04675294

**REFERENCE**


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

![Abstract 678 Figure 1 ASPEN-03 study schema](http://dx.doi.org/10.1136/jtc-2022-SITC2022.0678)