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

[1]Kevin Harrington*, [2]Ezra Cohen, [3]Bhumsuk Keam, [4]Jean-Pascal Machiels, [5]Sjoukje Oosting, [6]Brett Hughes, [7]Jong Chul Park, [8]Tim Welliver, [8]Christine Ju, [8]Feng Jin, [8]Alison Forgie, [8]Jaume Pons, [8]Sophia Randolph, [8]Athanasios Tsiatis. *[1]The Royal Marsden Hospital, Sutton, UK; [2]University of California San Diego, La Jolla, CA, USA; [3]Seoul National University Hospital, Seoul, Republic of Korea; [4]Cliniques Universitaires Saint-Luc, Brussels, Belgium; [5]University Medical Center Groningen, Groningen, Netherlands; [6]Royal Brisbane and Women's Hospital, Brisbane, Australia; [7]Massachusetts General Hospital Cancer Ce, Boston, MA, USA; [8]ALX Oncology Inc, South San Francisco, CA, USA*

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. CD47 is upregulated by tumors to evade immune responses and its expression is associated with poor prognosis. 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] $\geq$1) tumors. The combination of evorpacept + pembrolizumab has shown acceptable tolerability and preliminary efficacy in patients with advanced HNSCC in $\geq$2nd line in the ongoing Phase 1 ASPEN-01 study.[1]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 $\geq$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. All patients will receive 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.

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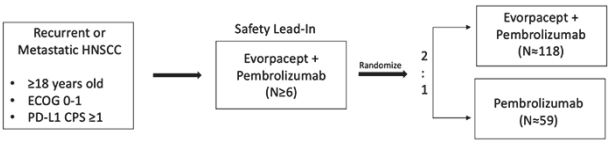
Trial Registration ClinicalTrials. gov identifier, NCT04675294

REFERENCE

1. Keun-Wook Lee, Hyun Cheol Chung, Won Seog Kim, *et al*. ALX148, a CD47 blocker, in combination with standard chemotherapy and antibody regimens in patients with gastric/gastroesophageal junction (GC) cancer and head and neck squamous cell carcinoma (HNSCC); ASPEN-01. Poster presented at: Society for Immunotherapy of Cancer Annual Meeting; November 2020.

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



Abstract 678 Figure 1 ASPEN-03 study schema

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