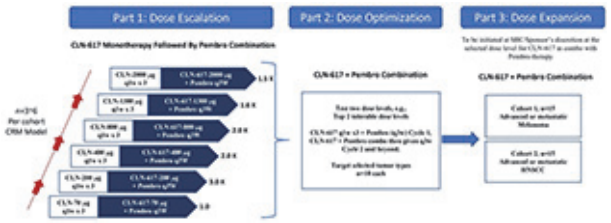
771 A PHASE 1 STUDY TO ASSESS SAFETY, EFFICACY, PHARMACOKINETICS, AND PHARMACODYNAMICS OF INTRATUMORAL CLN-617 (IL2/IL12 FUSION PROTEIN) COMBINED WITH PEMBROLIZUMAB IN PATIENTS WITH ADVANCED SOLID TUMORS

[1]Adi Diab*, [2]Anthony El-Khoueiry, [1]Reham Abdel-Wahab, [3]Sajeve Thomas, [4]Evan Hall, [5]Kaida Wu, [6]Benjamin S Maciejewski, [5]Naveen K Mehta, [5]Laura Liu, [5]Jennifer S Michaelson, [56]Jeffrey A JonesRandy Sweis. [1]*The University of Texas MD Anderson Cancer Center, Houston, TX, USA*; [2]*USC Norris Comprehensive Cancer Center, Los Angeles, CA, USA*; [3]*Orlando Health Cancer Institute, Windermere, FL, USA*; [4]*University of Washington, Seattle, WA, USA*; [5]*Cullinan Oncology, Inc., Cambridge, MA, USA*; [6]*The University of Chicago, Chicago, IL, USA*

Background The use of pro-inflammatory cytokines as systemic therapies has been explored in the oncology field due to their ability to promote the function and proliferation of immune cells. However, high toxicity and limited efficacy have been reported. CLN-617 is a single-chain fusion protein comprised of human cytokines IL2 and IL12, leukocyte-associated immunoglobulin-like receptor 2 (LAIR2), and human serum albumin (HSA), specifically engineered for intratumoral (IT) delivery and retention within the tumor microenvironment via LAIR2-mediated collagen binding. The murine surrogate to CLN-617 has preclinically demonstrated robust tumor growth inhibition in multiple checkpoint inhibitor refractory syngeneic tumor models, a memory response upon tumor rechallenge, an abscopal response when only a single tumor is injected, and synergy with systemic anti-PD1 treatment. Building upon these preclinical findings, we propose this first-in-human trial to explore the safety and efficacy of IT CLN-617 combined with intravenous (IV) pembrolizumab.

Methods This Phase-1, open-label, dose-escalation, optimization, and expansion trial will assess the safety, tolerability, and efficacy of IT CLN-617 in combination with pembrolizumab in patients with advanced/metastatic solid tumors that have accessible tumors for injection.

The trial consists of 3 parts (figure 1). In Part 1, we will conduct a dose-escalation study of weekly IT CLN-617 monotherapy for the first 21-day cycle, followed by dosing every 3 weeks thereafter in combination with IV pembrolizumab starting in cycle 2. In Part 2, CLN-617 will be administered weekly for the first 21-day cycle in combination with IV pembrolizumab every 3 weeks in cycle 1, followed by CLN-617 and pembrolizumab every 3 weeks thereafter. This part of the trial will focus on patients with specific tumor types, and two dose levels of CLN-617 will be selected to optimize a dose for the expansion part. In Part 3, we will explore an optimized dose of CLN-617 in combination with Pembrolizumab in patients with advanced melanoma and head and neck squamous cell carcinoma (HNSCC). Dose escalation will be guided following the two-parameter logistic continual reassessment model (CRM) to discover an optimized dose. The primary objectives are determining the maximum tolerated dose and the recommended phase 2 dose in Part 1 and evaluating the objective response according to immune Response Evaluation Criteria in Solid Tumors in Parts 2 and 3. Secondary endpoints involve the assessment of pharmacokinetics, pharmacodynamics, and immunogenicity across the 3 parts of the trial. Patients' enrollment is currently ongoing, and updates will be provided at the time of the presentation.



Abstract 771 Figure 1

http://dx.doi.org/10.1136/jitc-2023-SITC2023.0771