TPS2675 Poster Session

A phase 1/2 study of KSQ-004EX: Autologous tumor infiltrating lymphocytes, engineered to inactivate genes encoding SOCS1 and Regnase-1, in patients with select advanced solid tumors.

Rodabe Navroze Amaria, Scott Kopetz, Maria Pia Morelli, George R. Blumenschein, Mehmet Altan, Khaled Sanber, Amir A. Jazaeri, Michael A. Davies, Adi Diab, Isabella Claudia Glitza, Jennifer Leigh McQuade, Alexandra Ikeguchi, Hussein A. Tawbi, Chantale Bernatchez, Marie-Andree Forget, Cara L Haymaker, Karrie Wong, Erica Tobin, Micah J. Benson, Anna Truppel-Hartmann; The University of Texas MD Anderson Cancer Center, Melanoma Medical Oncology, Houston, TX; The University of Texas MD Anderson Cancer Center, Houston, TX; Department of Thoracic Head and Neck Medical Oncology, The University of Texas MD Anderson Cancer Center, Houston, TX; Department of Melanoma Medical Oncology, The University of Texas MD Anderson Cancer Center, Houston, TX; Cell Therapy Manufacturing Center, a joint venture between MD Anderson Cancer Center and Resilience, Houston, TX; Cell Therapy Manufacturing Center, Houston, TX; KSQ Therapeutics, Cambridge, MA; KSQ Therapeutics, Lexington, MA; KSQ Therapeutics, Inc, Lexington, MA

Background: The effectiveness and durability of TIL therapy may be limited by the immunosuppressive tumor microenvironment and baseline functionality of transferred T cells. Through KSQ Therapeutics' CRISPR^2 platform, a novel method for screening optimal combinatorial targets for enhancing T cell anti-tumor efficacy in vivo, SOCS1 and Regnase-1 were identified as the most potent gene editing combination. KSQ-004EX, an engineered TIL product with CRISPR/Cas9 mediated dual-inactivation of SOCS1 and Regnase-1, is anticipated to in enhance T cell tumor infiltration, persistence, and efficacy. This first-in-human clinical study (NCT06598371) evaluates KSQ-004EX in patients with melanoma, non-small cell lung cancer (NSCLC), head and neck squamous cell carcinoma (HNSCC), colorectal carcinoma (CRC), pancreatic cancer, and cervical cancer. **Methods:** The phase 1/2, single-arm, open-label study will assess the safety, tolerability, and efficacy of KSQ-004EX in patients with select advanced solid tumors. Patients with melanoma, NSCLC, HNSCC, CRC, pancreatic, and cervical cancer who have progressed following treatment with 1 to 3 lines of prior standard therapy including standard directed therapy (as applicable), are eligible. KSQ-004EX is manufactured from the patient's tumor, which is collected through surgical resection or core needle biopsy. All patients must have at least 1 measurable lesion following resection. Patients receive lymphodepleting chemotherapy with cyclophosphamide and fludarabine prior to KSQ-004EX infusion. Patients in the initial dose escalation cohorts do not receive dosing with IL-2; IL-2 dosing may be included in subsequent cohorts. Approximately 6 patients will be enrolled in Phase 1 dose escalation, in escalating dose levels. The primary objective of Phase 1 is to evaluate the safety and tolerability of KSQ-004EX. In Phase 2, patients will be enrolled in indication-specific cohorts. The primary objective of Phase 2 is to assess the anti-tumor activity of KSQ-004EX in patients with advanced solid tumors by ORR per RECIST v1.1. This is currently a single-institution study that is actively enrolling/recruiting patients. Clinical trial information: NCT06598371. Research Sponsor: KSQ Therapeutics, Inc.