TPS2699 Poster Session

A phase I study of a pooled synthetic long peptide mutant KRAS vaccine in patients with pancreatic cystic neoplasms at risk for developing pancreatic cancer.

Kai-li Liang, Amanda Huff, S. Daniel Haldar, Anna Ferguson, Maureen Berg, Hao Wang, Julie Nauroth, Amy Thomas, Nancy Sun, Dan Laheru, William Burns, Richard Burkhart, Jin He, Kelly Lafaro, Laura D. Wood, Michael Goggins, Elizabeth M. Jaffee, Nilofer Saba Azad, Neeha Zaidi; Department of Oncology, Johns Hopkins Sidney Kimmel Comprehensive Cancer Center, Baltimore, MD; The University of Texas MD Anderson Cancer Center, Houston, TX; Division of Biostatistics and Bioinformatics, Department of Oncology, Johns Hopkins University School of Medicine, Baltimore, MD; Department of Surgery, Johns Hopkins University, Baltimore, MD; Department of Oncology, Sidney Kimmel Comprehensive Cancer Center, The Johns Hopkins University School of Medicine, Baltimore, MD

Background: Mutant KRAS (mKRAS) is an oncogenic driver expressed in > 90% of patients with pancreatic ductal adenocarcinoma (PDAC) and the majority of pancreatic precursors, including > 90% of intraductal papillary mucinous neoplasms (IPMNs) and pancreatic intraepithelial neoplasia (PanIN) (Kanda *et al.*, 2012). If left untreated, approximately 40-60% of high-risk IPMNs will have malignant transformation (Fonseca *et al.*, 2018). mKRAS vaccines have recently demonstrated encouraging results in generating mKRAS-specific T cell responses that correlate with clinical benefit in patients with resected PDAC. We previously reported that a mKRAS-targeted *Listeria*-based vaccine given with Treg-depleting agents results in slowing of PanIN progression to PDAC in a murine model (Keenan *et al.*, 2014). Based on these data, we have initiated a clinical trial testing this vaccine in individuals at high-risk of developing pancreatic cancer. In our first Cohort [A], we have tested this vaccine in individuals at high-risk due to a known germline mutation or familial predisposition (n = 20). Our current study [Cohort B] aims to determine the safety and immunogenicity of a pooled synthetic long peptide (SLP) mKRAS vaccine with poly-ICLC adjuvant in patients with pancreatic cystic neoplasm at risk for developing PDAC and who are scheduled to undergo surgical resection. **Methods:** This is a single-arm, open-label phase I trial evaluating mKRAS vaccine in patients with pancreatic cystic neoplasms at risk for developing PDAC and scheduled to undergo surgical resection (n = 10). The vaccine consists of SLPs corresponding to six common mKRAS mutations: G12D, G12V, G12R, G12C, G12A, G13D admixed with poly-ICLC adjuvant. A two-dose series of the mKRAS vaccine is administered at weeks 1 and 2 followed by pancreatic surgery at week 4. Peripheral blood will be collected pre-vaccination (week 1) and post-vaccination (weeks 4 and 8). Following completion of the treatment phase, patients have the option to continue annual follow-up visits until study closure. Eligible patients must have clinical, radiographic, or histologic evidence of a pancreatic cystic neoplasm with features warranting surgical resection per the discretion of the treating hepatobiliary surgeon. Co-primary endpoints include the safety profile per NCI CTCAE v5.0 and maximal percent change of mutant-KRAS-specific T cells measured by IFNg ELISPOT at weeks 4 and 8 post-vaccination compared to pre-vaccination baseline. Correlative studies of resected specimens will include characterization of the premalignant microenvironment and mKRAS-specific T cell trafficking post-vaccination. Methods of analyses include bulk RNA and T cell receptor (TCR) sequencing, spatial transcriptomics, and imaging mass cytometry. Patient accrual began in December 2024 and is currently ongoing. Clinical trial information: NCT05013216. Research Sponsor: Lustgarten Foundation for Pancreatic Cancer.