Abstracts

BASECAMP-1: LEVERAGING HLA LOSS OF HETEROYOSOGY IN SOLID TUMORS BY NGS TO IDENTIFY PATIENTS WITH RELAPSED SOLID TUMORS FOR FUTURE CEA AND MSLN LOGIC-GATED TMOD™ CAR T-CELL THERAPY


Background Solid tumors comprise >90% of cancers. Non-small cell lung cancer (NSCLC), metastatic colorectal cancer (CRC), and pancreatic cancer are the leading causes of cancer-related mortality (5-year overall survival: 26%, 15%, and 11%, respectively).

Chimeric antigen receptor (CAR) T-cell therapy has demonstrated clinical efficacy in hematologic malignancies.1 However, translating engineered T-cell therapies to solid tumors has proven to be challenging due to a lack of tumor-specific targets that can discriminate cancer cells from normal cells. Previous studies using carcinoembryonic antigen (CEA) T-cell receptors and mesothelin (MSLN) CARs resulted in dose-limiting on-target, off-tumor toxicities.2,3

To create a therapeutic safety window, Tmod CAR T-cell therapy utilizes dual-signaling receptors to create a robust logic gate capable of killing tumor cells, while leaving healthy cells intact.4

The 2 receptors in Tmod CAR T-cell therapy comprise an activator that recognizes an antigen on the surface of tumor cells that may also be present on normal cells, such as CEA and MSLN, and a blocker that recognizes a second surface antigen from an allele lost only in tumor cells (figure 1).1,9,10

Human leukocyte antigen (HLA) loss of heterozygosity (LOH) offers a definitive tumor versus normal discriminator (HLA) loss of heterozygosity (LOH) in solid tumors by next-generation sequencing (NGS) to identify patients with relapsed solid tumor for future logic-gated Tmod CAR T-cell therapy. Poster presented at: ASCO Annual Meeting; June 3-7, 2022; Chicago, IL. Abstract #TPS2676.


Hecht JR, Kopetz S, Patel SP, et al. Next generation sequencing (NGS) to identify relapsed gastrointestinal (GI) solid tumor patients with human leukocyte antigen (HLA) loss of heterozygosity (LOH) for future logic-gated CAR T therapy to reduce on target off tumor toxicity. J Clin Oncol. 2022;40(suppl):190-190.

Ethics Approval The study was approved by site IRBs

Abstract 639 Figure 1

Abstract 639 Figure 2


REFERENCES

Abstract 639 Figure 1

Abstract 639 Figure 2