692 COMMANDER-001: SAFETY DATA FROM A PHASE I/II DOSE ESCALATION/EXPANSION STUDY OF SQZ-EAPC-HPV, A CELL-BASED MRNA THERAPEUTIC CANCER VACCINE FOR HPV16+ SOLID TUMORS

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Background Cancer vaccines aim to generate antigen-specific $CD8^+$ T cell responses. However, their efficacy has been hampered by inefficient targeting of delivered antigens to the MHC-I complex. SQZ-eAPC-HPV is an autologous, HLA agnostic, PBMC cell vaccine targeting HPV16 viral oncoproteins, E6 and E7, using the Cell Squeeze® platform. This technology simultaneously delivers 5 mRNAs encoding for full length HPV16 E6 and E7 proteins, CD86, and membrane-bound (mb) IL-2 and mbIL-12 cytokines directly into the cytosol of peripheral blood mononuclear cells (PBMC) via temporary cell membrane disruption using a microfluidic chip, which results in increased MHC-I antigen.

Methods COMMANDER-001 (NCT05357898) includes patients with advanced HPV16+ cancers progressing after standard therapy who have an ECOG of 0–1, proper organ function, and RECIST measurable lesion(s). After leukapheresis, the cell product is manufactured in <24 hours and cryopreserved with a collection-to-release time of about 1 week. SQZ-eAPC-HPV was given IV q3w for up to one year. Paired biopsies were required at baseline and Day 28.

Results Sixteen patients [head and neck (7), anal (4), cervical (4), vaginal (1)] were dosed in 3 monotherapy cohorts (from 0.5 to 5.0 $x10^6$/kg). These patients were heavily pre-treated (median prior systemic therapies = 3), the majority of whom received prior treatment with an immune checkpoint inhibitor. All patients in the safety patient population had successful SQZ-eAPC-HPV manufacture with at least 7 doses made. Cohort 3, the high dose cohort, produced a median of 10.5 doses. There were no dose limiting toxicities, adverse events of special interest, related serious adverse events or related Grade >3 adverse events reported.

Conclusions SQZ-eAPC-HPV has been well tolerated across all dose escalation cohorts. Enrollment in Cohort 3 ($5.0x10^6$/kg) is ongoing. Recommended phase 2 dose is expected to be declared in 2023. The presentation will include safety, preliminary efficacy, and pharmacokinetic/pharmacodynamic data from a cut-off proximal to presentation.

Acknowledgements We thank the patients, their families, and their caregivers for their time and their willingness to participate in this study. We also thank theinvestigators and the investigational site staff for their contributions to the study.

Ethics Approval The study was performed in accordance with ethical principles that originated in the Declaration of Helsinki consistent with the ICH/GCPand applicable regulatory requirements. The protocol was approved by IRBs/IECs at each center. Patients provided written informedconsent to participate.

http://dx.doi.org/10.1136/jitc-2023-SITC2023.0692