

638

COMMANDER-001: A PHASE 1/2, FIRST-IN-HUMAN, MULTICENTER, OPEN LABEL STUDY OF SQZ-EAPC-HPV AS MONOTHERAPY AND WITH PEMBROLIZUMAB IN PATIENTS WITH HPV16+ RECURRENT, LOCALLY ADVANCED, OR METASTATIC SOLID TUMORS (TRIAL IN PROGRESS)

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Background Antigen-specific CD8+ T cells are critical for mounting a potent immune response against tumors. Creation of T cell responses requires 3 key signals from antigen presenting cells (APCs): (signal 1) the peptide-MHC complex binding to the T cell receptor, (signal 2) costimulatory molecules that bind to T cell stimulatory domains, and (signal 3) inflammatory cytokines binding to receptors on T cells. To create enhanced APCs (eAPCs) from peripheral blood mononuclear cells (PBMCs), we used the Cell Squeeze[®] technology to deliver mRNAs encoding HPV16 E6 and E7 antigens (signal 1), CD86 (signal 2), and membrane-bound IL-2 and IL-12 cytokines (signal 3). Co-localizing these signals on the eAPC surface may enable more potent T cell stimulation and limit off-target effects from systemic exposure to signal 2 and 3. SQZ-eAPC-HPV is an improved 2nd generation product, with no HLA restrictions, that builds on the clinical and manufacturing experience with the 1st generation SQZ-PBMC-HPV product. This approach may enable rapid implementation across many tumor types as it facilitates exchange of mRNA to encode for other antigens or T cell activation signals.

Methods Trial Design: COMMANDER-001 is open for enrollment to patients (pts) with HPV16 driven recurrent, locally advanced, or metastatic solid tumors and includes dose escalation for eAPC monotherapy and in combination with pembrolizumab (pembro) (Part 1), and a lead-in where eAPC is given prior to treatment with pembro (Part 2). Part 1A will assess 3 eAPC monotherapy cohorts using a Bayesian optimal interval design enrolling 3 – 12 pts per cohort. After establishing a safe and tolerable dose (RP2D), Part 1B will assess the RP2D with pembro 200mg q3 weeks (w). Part 2 will explore giving 2 doses of eAPC before the pt receives pembro. Pts will receive eAPC q3w for up to 1 year or until available eAPC is exhausted. Pembro will be given for up to 2 years. Eligible pts will undergo 1 leukapheresis. Manufacturing takes <24 hours and the vein-to-vein time for the 1st dose is expected to be ~1 week. Preconditioning is not required, and the study will be primarily conducted out-patient.

Trial Registration NCT05357898

Ethics Approval The study is registered on clinicaltrials.gov and was approved by the Ethics Board of all institutions listed as recruiting.

<http://dx.doi.org/10.1136/jitc-2022-SITC2022.0638>