594 SQZ-PBMC-HPV-101: INCREASED OVERALL SURVIVAL IN A SUBSET OF PATIENTS WITH RECURRENT, LOCALLY ADVANCED, OR METASTATIC HPV16^{+} TUMORS TREATED WITH CELL-BASED VACCINE, SQZ-PBMC-HPV

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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. Cell Squeeze® technology delivers target antigens 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. SQZ-PBMC-HPV is an autologous PBMC cell vaccine targeting HPV16 viral oncoprotein E6 and E7 using the Cell Squeeze platform.

Methods SQZ-PBMC-HPV-101 (NCT04084951) includes HLA-A*02^{+}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 with a collection-to-release time of about 1 week. SQZ-PBMC-HPV was given IV q3w without a conditioning regimen. Double antigen priming (DP) was introduced in the last 2 monotherapy cohorts. The response was assessed via RECIST 1.1. Paired biopsies were required at baseline and Day 28.

Results Twenty-two patients [head and neck (11), anal (7), and cervical (4)] were dosed in 4 monotherapy cohorts (from 0.5 to 5.0 x10e6/kg [DP]). Treatment was generally well-tolerated. There were no DLTs, Grade (G) >2 related SAEs or related G >3 AEs. Of the eighteen patients with paired biopsies, six had an increase (any increase in CD8 density compared to baseline) in CD8 density (CD8^{Inc}) in the tumor after treatment. These six patients had a median overall survival (mOS) of 607 days (95% CI [314d, 713d]), which was significantly longer than the mOS of patients with a CD8 density decrease (CD8^{Dec}) in the tumor (170 days, 95% CI [54d, 220d], p=0.008). Compared to the 12 CD8^{Dec}patients, CD8^{Inc}patients showed more favorable clinical activitywith 4 out of 6 having stable disease or better while only 2 out of 12 CD8^{Dec}patients had stable disease or better. There were no baseline patient characteristics or on treatment characteristics (e.g. dose level, number of doses received, tumor or peripheral blood biomarkers) that distinguished these groups.

Conclusions These findings suggest that a subset of patients treated with SQZ-PBMC-HPV benefit in a manner consistent with the proposed mechanism of action, namely, priming of CD8^{+} T cells. The sub-set of patients who had an increase in CD8 density within the tumor after treatment showed a 3.5-fold increase in mOS with better control of tumor growth (as measured by clinical response) compared to those without an increase.

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

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