679 CHARACTERIZATION OF TUMOR SPECIFIC CD8+ T CELL RESPONSES IN PATIENTS WITH RECURRENT/METASTATIC HPV16-POSITIVE HEAD AND NECK CANCER RECEIVING HB-200 MONOTHERAPY AS SECOND OR LATER LINE TREATMENT IN A PHASE 1 STUDY

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Background Prognosis is poor for patients with recurrent/metastatic (R/M) human papillomavirus (HPV) 16+ head and neck squamous cell carcinoma (HNSCC) after first-line standard of care therapy. HB-200 is comprised of an alternating sequence of two replicating attenuated arenavirus vectors derived from LCMV (HB-201) and Pichinde virus (HB-202), respectively, expressing the same non-oncogenic HPV16 E7E6 fusion protein.[1] In a Phase 1 study, HB-200 monotherapy induced strong and long-lasting HPV16 E6 and E7-specific CD8+ T cell responses and demonstrated a favorable safety profile and antitumor activity in previously treated patients with HPV16+ R/M HNSCC.[2] Here, we report long-term circulating tumor specific immune responses and clinical benefit in these patients.

Methods Patients with HPV16+ HNSCC post at least 1 prior systemic R/M anti-cancer therapy were treated with HB-200 monotherapy (alternating intravenous administration of HB-202 and HB-201 every 3 weeks [Q3W] then Q6W) until disease progression or unacceptable toxicity. Four dose levels of HB-200 were explored. HPV16 specific T cell responses were evaluated in peripheral blood mononuclear cells (PBMCs) by both direct IFN-γ ELISpot and intracellular cytokine staining (ICS) performed without prior *in vitro* expansion. Tumor analyses including sequencing were performed for patients with available baseline and on-treatment biopsies. Antitumor activity was measured by RECIST v1.1 per investigator assessment.

Results As of March 31, 2023, 41 patients with HPV16+ R/M HNSCC (37 oropharynx, 1 larynx, 2 nasopharynx, 1 unknown primary) were treated with HB-200 monotherapy. HB-200 rapidly induced HPV16+ tumor-specific CD8+ T cells in more than 90% of patients analyzed. The E6/E7 T cell responses were maintained for more than 8 months and on-going as of data cut-off. Circulating tumor-specific T cells responses increased up to 1250-fold (median 174, range 93–1250) from baseline, with more than 57% of patients exhibiting ≥1% (maximum 48%) tumor specific CD8+ T cells out of total CD8+ T cells. Furthermore, tumor-specific CD8+ T cells increased in poly-functionality during treatment. Characterization of paired tumor biopsies revealed that HB-200 induced increased CD8+ T cell infiltration in tumors. Across all HB-200 doses, disease control rate was 48.5% in 33 heavily pre-treated patients with imaging evaluation (1 partial response, 15 stable disease), and overall survival is being assessed.

Conclusions HB-200 monotherapy induces promising HPV16+ tumor-specific T cell responses and tumor infiltration in heavily pre-treated patients. This immune response coupled with clinical benefit in monotherapy suggests that HB-200 may enhance and strengthen current immunotherapy approaches by targeting specific tumor antigens.

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