FPN: 921P

HB-200 ARENAVIRUS-BASED IMMUNOTHERAPY PLUS PEMBROLIZUMAB AS A FIRST-LINE TREATMENT IN PATIENTS WITH RECURRENT/METASTATIC HPV16-POSITIVE HEAD AND NECK CANCER

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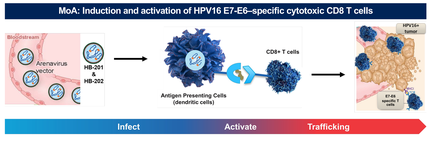
BACKGROUND

- Treatment options are limited for patients with recurrent/metastatic HPV16+ head and neck squamous cell carcinoma (HNSCC).
  - In the first-line setting, the PD-1 inhibitor pembrolizumab has been established as an appropriate treatment for tumors with a PD-L1 CPS ≥1.[1]
  - No HPV-specific treatment options are approved.
- HB-200 consists of an alternating sequence of two replicating attenuated arenavirus vectors derived from Pichinde virus (HB-202) and LCMV (HB-201) expressing the same non-oncogenic HPV16 E7-E6 fusion protein to induce E6- and E7-specific CD8+ T cell responses.[2]



- 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 recurrent/metastatic HPV16+ HNSCC.[3]
- Combination of HB-201 and an anti-PD-1 mAb resulted in superior antitumor efficacy in murine models of HPV16+ cancer.[4]

STUDY DESIGN & METHODS

Main Eligibility

- Recurrent or metastatic HPV16+ HNSCC
- RECIST v1.1 measurable lesion
- ECOG PS 0 or 1
- No prior systemic anticancer therapy in recurrent or metastatic setting
- Eligible per local regulations and guidelines (eg, package insert, SmPC) to receive pembrolizumab, including indicated PD-L1 CPS

Design: single-arm Phase 2 cohort

1L HNSCC HPV16+ PD-L1 CPS≥1 → HB-200 IV + pembrolizumab IV →

Endpoints

- Primary: ORR by RECIST v1.1 per investigator assessment
- Secondary: OS; PFS, DCR, and DOR per RECIST v1.1 / iRECIST
- Exploratory: T cell response, pharmacodynamic biomarkers

HB-200 (alternating IV administration of HB-202 first followed by HB-201) Q3W for first 5 doses followed by Q6W. Pembrolizumab administered Q3W or Q6W.

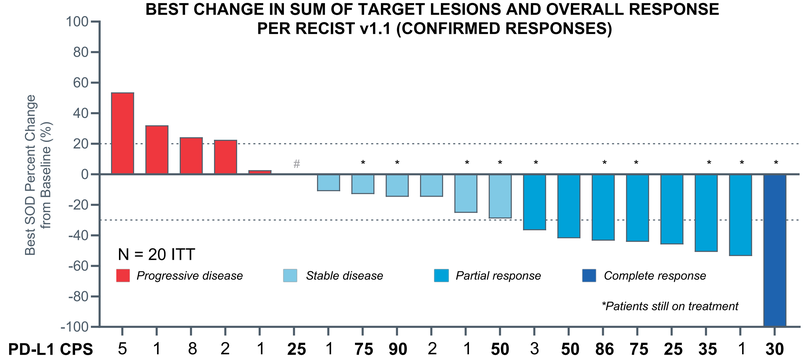
PATIENT POPULATION

Here we report the first 20 participants treated with HB-200 and pembrolizumab in the first-line setting. As of August 07, 2023, 10 (50%) participants are on treatment. Reasons for discontinuing treatment include progressive disease (8, 80%), adverse event (1, 10%), and death due to COVID-related illness (1, 10%). Of the discontinued patients, 7 (70%) are in long-term follow-up.

Baseline Characteristics	
Participants with HPV16+ HNSCC, N	20
Oropharynx primary site, n (%)	19 (95)
Hypopharynx primary site, n (%)	1 (5)
Age, years, median (range)	66 (50-76)
Gender, male, n (%)	19 (95)
Race, white, n (%)	17 (85)
Smoking history, n (%)	9 (45)
ECOG PS 1, n (%)	2 (10)
Metastatic, n (%)	18 (90)
Locally recurrent only, n (%)	2 (10)
PD-L1 CPS	
1-19, n (%)	10 (50)
≥20, n (%)	10 (50)
Prior radiation ± chemotherapy definitive treatment, n (%)	19 (95)
Prior radiation treatment, n (%)	19 (95)
Prior platinum use, n (%)	17 (85)
Prior CPI use, n (%)	0

EFFICACY

BEST CHANGE IN SUM OF TARGET LESIONS AND OVERALL RESPONSE PER RECIST v1.1 (CONFIRMED RESPONSES)

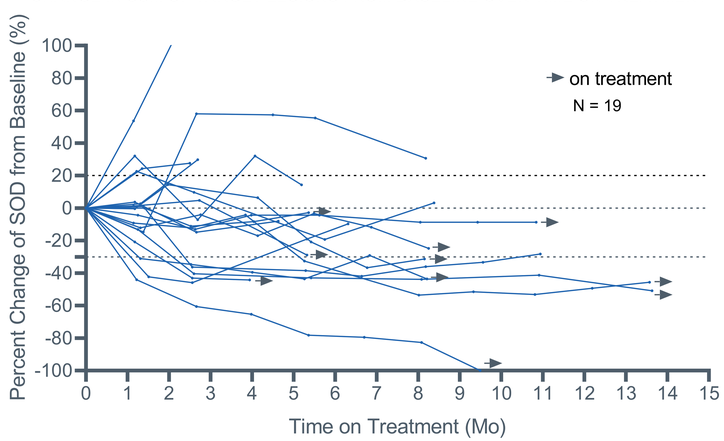


1 study participant discontinued prior to tumor scans due to COVID-related death.

Population	Confirmed Responses (RECIST v1.1)	ORR	DCR	% Participants with Target Lesion Decrease
ITT (N = 20)	8	40%	70%	70%
Evaluable* (n = 19)	8	42%	74%	74%

*Evaluable population for response consists of participants within the first 20 ITT population with ≥1 tumor scan post-treatment.

CHANGE IN SUM OF TARGET LESIONS FROM BASELINE OVER TIME ON TREATMENT

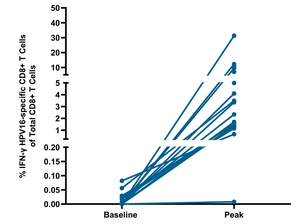


Spider plot includes participants with ≥1 tumor scan after study treatment (N = 19 evaluable). From the ITT population, 1 patient is not included (discontinued prior to tumor scans due to COVID-related death). In the ITT population, median follow-up time was 8.31 months. Median PFS and median OS data are maturing.

BIOMARKERS

CIRCULATING HPV16-SPECIFIC CD8+ T CELL RESPONSES

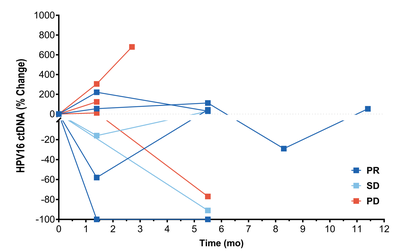
- In 94% (16/17 participants), treatment with HB-200 and pembrolizumab increased the circulating HPV16-specific T cells to >1% of PBMCs



Line graphs represent E6-E7–specific CD8+ T cells at baseline and peak response (median 3.36%, range 0.08%-31.34%). PBMC samples from 17/20 patients were available for T cell response assessment. Frozen PBMCs were stimulated for 6 hr with overlapping HPV16 E6-E7 peptides, and HPV16 E6-E7–specific T cells were measured by intracellular staining followed by flow cytometry to quantitate antigen-specific T cell functionality.

HPV16 ctDNA and RESPONSE

- Participants with partial response and stable disease showed a trend toward decreased HPV16 tumor DNA



Circulating tumor HPV16 DNA in patients treated with HB-200 + pembrolizumab was measured with NavDx® to monitor treatment response. Plasma samples available from 10 patients at baseline and on treatment were examined for HPV ctDNA.

SAFETY

SAFETY SUMMARY

All Participants (N = 20)	Treatment-Related AEs, n (%)	Treatment-Emergent AEs, n (%)
Any event	19 (95)	20 (100)
Grade ≥3	4 (20)	8 (40)
Serious	2 (10)	5 (25)
Leading to discontinuation	1 (5)*	2 (10)
Deaths	0	1 (5)

*1 study participant discontinued for a treatment-related SAE of grade 3 CPI pneumonitis, which resolved to grade 2. Treatment-emergent AEs consist of any AE occurring after the first dose and within 30 days of the last dose, regardless of attribution of relatedness to study treatment.

- Manageable and acceptable toxicity profile, in line with HB-200 monotherapy[3]
- No treatment-related AE leading to death and minimal discontinuations
- Incidence of grade ≥3 treatment-related AEs comparable to pembrolizumab monotherapy in the first-line setting (17% across 300 participants)[5]

SAFETY (Continued)

MOST COMMON TREATMENT-RELATED AEs (≥2 TREATED PARTICIPANTS)

Treatment-Related AE, Preferred Term	All Grades n (%)	Grade ≥3 n (%)
Chills	9 (45)	0
Fatigue	8 (40)	0
Pyrexia	7 (35)	0
Nausea	7 (35)	0
Influenza-like illness	6 (30)	0
Platelet count decrease	5 (25)	0
Headache	5 (25)	0
Neutrophil count decrease	4 (20)	2 (10)
Arthralgia	4 (20)	0
Vomiting	4 (20)	0
White blood cell count decrease	3 (15)	2 (10)
Myalgia	3 (15)	0
Dizziness	3 (15)	0
Pruritis	2 (10)	1 (5)
Stomatitis	2 (10)	0
Peripheral sensory neuropathy	2 (10)	0
Rash maculopapular	2 (10)	0
Anemia	2 (10)	0

CONCLUSIONS

Preliminary data with HB-200 arenavirus-based immunotherapy in combination with pembrolizumab demonstrate:

- Favorable safety profile, consistent with HB-200 or pembrolizumab monotherapy
- Promising clinical activity in the first-line setting with a confirmed ORR of 40% in the ITT population, doubling the historical data observed with pembrolizumab monotherapy (19%)[6]
- Robust induction of antigen-specific circulating T cells, as demonstrated previously for HB-200 monotherapy[3]
- Potential utility of ctDNA in follow-up of patients in the metastatic setting based on preliminary data

Results warrant further evaluation of HB-200 in combination with pembrolizumab in patients with HPV16+ HNSCC.

ACKNOWLEDGEMENTS

We thank the patients who are participating in this study, as well as their caregivers, the trial investigators, and site personnel.

Poster produced with support from Catalyst medical writer and graphic designer.

ABBREVIATIONS

1L = first line; AEs = adverse events; CPI = checkpoint inhibitor; CPS = combined positive score; DCR = disease control rate; DOR = duration of response; ECOG = Eastern Cooperative Oncology Group; HNSCC = head and neck squamous cell carcinoma; HPV16+ = human papillomavirus 16–positive; iRECIST = modified RECIST 1.1 for immune-based therapeutics; ITT = intent-to-treat; IV = intravenous; LCMV = lymphocytic choriomeningitis virus; mAb = monoclonal antibody; ORR = overall response rate; OS = overall survival; PBMCs = peripheral blood mononuclear cells; PD = progressive disease; PFS = progression-free survival; PR = partial response; PS = performance status; Q3W = every 3 weeks; Q6W = every 6 weeks; RECIST = Response Evaluation Criteria in Solid Tumors; SAE = serious adverse event; SD = stable disease; SmPC = summary of product characteristics; SOD = sum of diameters.

Preliminary data (baseline, efficacy, safety) from 07Aug2023; data subject to change. Circulating T cell data analyzed 29Jul2023. ctDNA data analyzed 08Jun2023.

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DECLARATIONS OF INTEREST

Dr. Ho: Affyimmune, Ayala, Coherus, Eisai, Exelixis, Kura Oncology, Merck, Prelude Therapeutics, Remix Therapeutics, Rgenta (advisory board); ASTRO, Chinese American Hematologist and Oncologist Network, Clinical Endocrinology Update (Endocrinology Society), Lurie Cancer Center (Northwestern), MGH, New York University, Physician Education Resource, Rasopathy Conference, Shanghai Jia Tong University School of Medicine, University of Pittsburgh Medical Center, Winship (Emory) (speaker); ExpertConnect, McKinney Global Advisors (consulting); Astellas, AstraZeneca, Ayala, Bayer, Bioatla, BMS, Celldex, Eisai, Elevar Therapeutics, Genentech Roche, Hookipa, Kura Oncology, Lilly, Merck, Novartis, OncoC4, Poseida Therapeutics, TILT Biotherapeutics, Pfizer, Verastem (principal investigator); Rgenta (briefly held options, but donated proceeds to charity); Klus Pharma (advisory board—food); pending patent with MSK; National Cancer Institute (head/neck steering committee);
Dr. Nabell: NCCN Executive Committee.

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