Abstract: 1480

Eseba-vec (HB-200) Plus Pembrolizumab as First-line Treatment of Recurrent/Metastatic HPV16-positive Head and Neck Cancer: Updated Results in PD-L1 CPS ≥20 Patients

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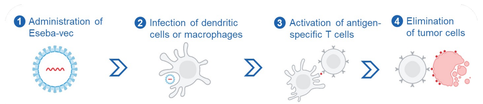
BACKGROUND

- The burden of human papillomavirus serotype 16 (HPV16+)-related head and neck squamous cell carcinoma (HNSCC) of oropharynx origin has been steadily increasing, with 20,805 new cases annually in the United States alone.[1]
- Pembrolizumab monotherapy is the preferred standard of care therapy for first-line (1L) treatment of recurrent/metastatic (R/M) HNSCC with high PD-L1 expression; however, only ~20% of patients respond to treatment with no significant differentiation by HPV status.[2]
- There are no specific treatments approved for HPV16+ cancers.
- Eseba-vec (HB-200) consists of HB-202 and HB-201 attenuated replicating arenavirus vectors delivering a non-oncogenic HPV16 E6 and E7-specific synthetic fusion protein that is recognized by antigen presenting cells (APC), resulting in enhanced and durable CD8 T-cell driven anti-tumor responses.



- We have previously reported positive clinical activity with a strong and durable HPV16-specific E7E6 CD8+ T-cell response by eseba-vec as monotherapy in the 2L+ setting and in combination with pembrolizumab as 1L treatment for patients with HPV16+ R/M HNSCC and PD-L1 CPS ≥20 in the Phase 1/2 H-200-001 study (NCT04180215).[3,4] A Phase 3 dose of eseba-vec for further clinical development has been selected.
- Here, we report updated 1L results in patients from the Phase 2 part of the H-200-001 study, including data for the selected Phase 3 dose.

STUDY DESIGN & METHODS

Main Eligibility Criteria:
- 1L recurrent or metastatic HPV16+ HNSCC
- PD-L1 CPS ≥1
- RECIST v1.1 measurable lesion
- ECOG PS 0 or 1
- No prior systemic anticancer therapy in the recurrent or metastatic setting

Eseba-vec + pembrolizumab

Treatment schedule:
- **Eseba-vec IV*:** Q3W for first 5 doses, Q6W thereafter
- **Pembrolizumab IV:** 200 mg Q3W or 400mg Q6W

→ Until unacceptable toxicity or disease progression

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

*Two eseba-vec doses explored: HB-202 1x10^7 RCV FFU and HB-201 5x10^6 RCV FFU (selected Phase 3 dose); HB-202 1x10^7 RCV FFU and HB-201 5x10^7 RCV FFU

PATIENT DISPOSITION

As of September 30, 2024, 66 participants were treated with eseba-vec + pembrolizumab (55/66 treated at the selected Phase 3 dose and 11/66 at a higher dose of eseba-vec). 30/66 (45.5%) participants remain on treatment, 15/66 (22.7%) are in long-term follow-up, and 21/66 (31.8%) discontinued the study.

66 participants treated

36 (54.5%) participants discontinued treatment
- Progressive disease (24, 66.7%)
- AEs leading to discontinuation or death (5, 13.9%)
- Clinical or pathological progression (3, 8.3%)
- Withdrew consent (2, 5.6%)
- Initiation of new anti-cancer treatment (1, 2.8%)
- Lost to follow-up (1, 2.8%)

30 (45.5%) participants still on treatment

21 (58.3%) participants discontinued study
- Death (13, 61.9%)
- Consent withdrawal (4, 19.0%)
- Lost to follow-up (3, 14.3%)
- Other (1, 4.8%)

15 (41.7%) participants in long-term follow-up

BASELINE CHARACTERISTICS

- The majority of participants had metastatic disease (~70-80%), with the oropharynx as the primary cancer site (>90%). ~45% had a smoking history. 34/66 (51.5%) had a tumor with PD-L1 CPS ≥20.
- Baseline characteristics are similar across subpopulations by PD-L1 CPS status.

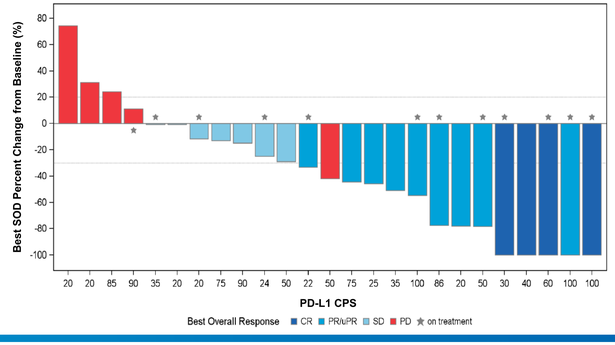
Table 1. Baseline characteristics in all treated participants

Baseline Characteristics (All Treated Participants)	PD-L1 CPS ≥1 (N = 66)	PD-L1 CPS ≥20 (N = 34)
Age, years, median (range)	64 (38–76)	68 (38–76)
Gender, male, n (%)	62 (93.9)	30 (88.2)
Race, white, n (%)	59 (89.4)	31 (91.2)
Smoking history, n (%)	30 (45.5)	15 (44.1)
ECOG PS, n (%)		
0	48 (72.7)	23 (67.6)
1	18 (27.3)	11 (32.4)
Metastatic, n (%)	51 (77.3)	24 (70.6)
Locally recurrent only, n (%)	15 (22.7)	10 (29.4)
Primary site, n (%)		
Oropharynx	64 (97.0)	32 (94.1)
Hypopharynx	1 (1.5)	1 (2.9)
Unknown	1 (1.5)	1 (2.9)
Prior definitive radiation ± chemotherapy, n (%)		
Prior radiation treatment, n (%)	62 (93.9)	31 (91.2)
Prior platinum use, n (%)	50 (75.8)	24 (70.6)
Prior CPI use, n (%)	3 (4.5)	1 (2.9)

EFFICACY

- In support of a previous report,[3] efficacy data are focused on the PD-L1 CPS ≥20 population.
- Among 55/66 participants with a minimum of 18 weeks from first dose until data cut off date, 27/55 had a PD-L1 CPS ≥20 (21/27 treated at the selected Phase 3 dose of eseba-vec).
- 25/27 participants (20/21 treated at the selected Phase 3 dose) had at least one post-baseline tumor scan (evaluable) and were assessed for best overall response per RECIST v1.1 (**Table 2** and **Figure 1**). Two participants were excluded; 1 discontinued due to COVID-19-related death and 1 withdrew consent prior to the first efficacy scan.
- ORR was 55.0% in participants treated at the selected Phase 3 dose of eseba-vec (includes confirmed and unconfirmed responses). Data are generally consistent between those receiving all dose levels and the selected Phase 3 dose (**Table 2**).
- Further deepening of responses over time seen in some participants (**Figure 2**).
- DOR is promising in the patients treated at all dose levels and at the selected Phase 3 dose with 66.7% and 60.0% of confirmed responders ongoing, respectively (**Table 2**).
- Preliminary PFS (**Figure 3**) and OS are encouraging but still maturing. The median PFS is 16.3 months (5.4 – NR). OS follow-up time is 11.1 months, with 7/27 deaths and a 12-month OS rate of 83%.

Figure 1. Best percent change in sum of target lesions from baseline and best overall response per RECIST v1.1 in evaluable participants with PD-L1 CPS ≥20 (N=25)



EFFICACY

Table 2. Best overall responses per RECIST v1.1 in the PD-L1 CPS ≥20 evaluable population

PD-L1 CPS ≥20 Evaluable	Responses (RECIST v1.1)	ORR	CR Rate	DCR (CR+PR+SD)	Ongoing Confirmed Responses
All participants (N=25)	4 CR, 8 PR, 1 uPR	52.0%	16.0%	80.0%	66.7%
Selected Phase 3 dose (N=20)	3 CR, 7 PR, 1 uPR	55.0%	15.0%	75.0%	60.0%

Figure 2. Best percent change in sum of target lesions from baseline over time in evaluable participants with PD-L1 CPS ≥20 (N=25)

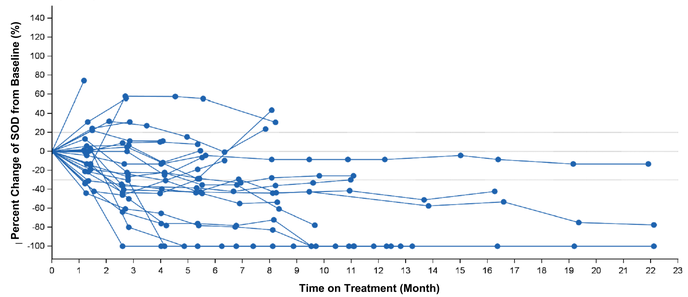
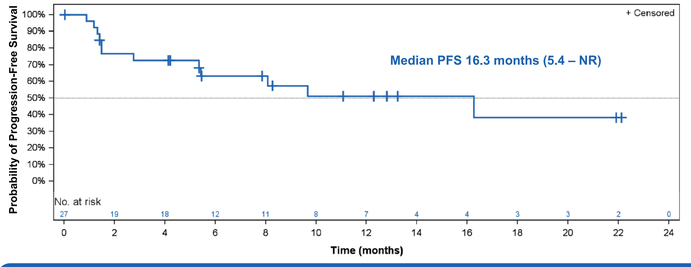
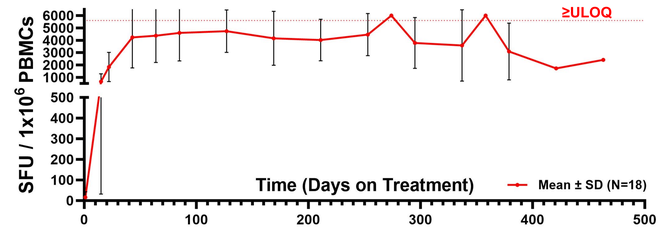


Figure 3. Progression-free survival in participants with PD-L1 CPS ≥20 (N=27)



TUMOR-SPECIFIC T-CELL RESPONSE

Figure 4. Circulating HPV16-specific CD8+ T-cell response in participants with PD-L1 CPS ≥20 (N=18)



Line graph represents the mean SFU/10^6 PBMCs of E7E6-specific T cells over time. PBMCs were stimulated for 24 hours with overlapping HPV16 E7E6 peptides and analyzed by IFN-γ ELISpot assay.

SAFETY

- Eseba-vec in combination with pembrolizumab demonstrated a favorable safety profile with manageable toxicity (**Table 4**).
- The majority of TRAEs were mild to moderate in severity, with only 7.6% serious events.
- Very few participants (4.5%) had TRAEs leading to discontinuation.
- One TRAE led to death in a participant who also received concomitant chemotherapy (carboplatin and 5-FU) in error in addition to eseba-vec and pembrolizumab (documented as critical protocol deviation).
- The most common TRAEs were grade 1-2 flu-like disease/symptoms, which were mostly short-lived, transient, and observed within a few days after the first administration (**Table 5**).

Table 4. Overall safety

All Participants (N = 66)	Treatment-Emergent AEs, n (%)	Treatment-Related AEs, n (%)
Any event	63 (95.5)	60 (90.9)
Grade ≥3	30 (45.5)	14 (21.2)
Serious	15 (22.7)	5 (7.6)
Leading to discontinuation of eseba-vec	4 (6.1)	3 (4.5)[a]
Leading to discontinuation of pembrolizumab	5 (7.6)	4 (6.1)[b]
Deaths	3 (4.5)	1 (1.5)[c]

a. One participant with grade 3 checkpoint inhibitor pneumonitis (related to pembrolizumab), one participant with grade 1 cytopenia (related to eseba-vec and pembrolizumab) along with unrelated events of grade 3 transaminitis and grade 2 abdominal pain, one participant with grade 2 pneumonitis (related to pembrolizumab).
b. Above-mentioned AEs and a grade 3 event of worsening pruritus (related to pembrolizumab) leading to discontinuation of pembrolizumab but continuation of eseba-vec.
c. Grade 5 hepatitis fulminant was reported as related to HB-202 and pembrolizumab per investigator assessment, where the participant also received chemotherapy (carboplatin and 5-FU) in error.

Table 5. Most common treatment-related adverse events (incidence ≥10%)

Treatment-Related AE, Preferred Term (N = 66)	All Grades, n (%)	Grade ≥3, n (%)
Fatigue	28 (42.4)	0 (0.0)
Influenza-like illness	23 (34.8)	1 (1.5)
Nausea	20 (30.3)	0 (0.0)
Pyrexia	20 (30.3)	0 (0.0)
Chills	17 (25.8)	2 (3.0)
Headache	17 (25.8)	1 (1.5)
Myalgia	11 (16.7)	0 (0.0)
Vomiting	10 (15.2)	0 (0.0)
Platelet count decreased	8 (12.1)	0 (0.0)
Arthralgia	8 (12.1)	0 (0.0)
Pruritus	7 (10.6)	1 (1.5)

MedDRA version 22.1, CTCAE 5.0

CONCLUSIONS

- Combining eseba-vec with pembrolizumab resulted in an ORR of 55%, a ~2-fold increase over historical data reported for pembrolizumab monotherapy, and suggests a meaningful improvement in participants with 1L HPV16+ PD-L1 CPS ≥20 R/M HNSCC.[3]
- Clinical activity is supported by a rapid, robust, and durable tumor antigen specific T-cell response.
- The rate, depth, and durability of responses were accompanied by encouraging preliminary PFS and OS, suggesting a meaningful contribution of eseba-vec to pembrolizumab in 1L treatment.
- The differentiated benefit observed is supported by biological plausibility: high PD-L1 expressing tumors are more permissive of infiltration by HPV-specific T-cells.[4]
- The combination showed a manageable safety profile and no significant toxicities beyond those observed with either eseba-vec or pembrolizumab alone.[5,6]
- The Phase 3 eseba-vec dose in combination with pembrolizumab has been determined.

The H-200-001 data support the confirmatory, pivotal Phase 2/3 AVALON-1 study in HPV16+ OPSCC patients with PD-L1 CPS ≥20 (NCT06513884).

AVALON-1

Acknowledgments: We thank the patients who are participating in this study, as well as their families and caregivers. Thank you to all Investigators and site personnel!

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

ABBREVIATIONS

1L, first line; 2L+, second-line and beyond; 5-FU, 5-fluorouracil; AEs, adverse events; APC, antigen-presenting cells; CD8, cluster of differentiation 8; CPI, checkpoint inhibitor; CPS, combined positive score; CR, complete response; CTCAE, Common Terminology Criteria for Adverse Events; DCR, disease control rate; DOR, duration of response; ECOG, Eastern Cooperative Oncology Group; ELISpot, enzyme-linked immunospot; HNSCC, head and neck squamous cell carcinoma; HPV16, human papillomavirus serotype 16; IFN-γ, interferon-γ; iRECIST, Immune Response Evaluation Criteria in Solid Tumors; IV, intravenous; MedDRA, Medical Dictionary for Regulatory Activities; NR, not reached; OPSCC, oropharyngeal squamous cell carcinoma; ORR, overall response rate; OS, overall survival; PBMCs, peripheral blood mononuclear cells; PD, progressive disease; PD-L1, programmed cell death-ligand 1; PFS, progression-free survival; PR, partial response; PS, performance status; Q3W, every 3 weeks; Q6W, every 6 weeks; RCV FFU, replication-competent virus focus-forming units; RECIST v1.1, Response Evaluation Criteria in Solid Tumors version 1.1; R/M, recurrent and/or metastatic; SD, stable disease; SFU, spot-forming units; SOD, sum of diameters; TRAEs, treatment-related adverse events; ULOQ, upper limit of quantification; uPR, unconfirmed partial response.

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