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HB-200 arenavirus-based immunotherapy plus pembrolizumab as first-line treatment of patients with recurrent/metastatic HPV16-positive head and neck cancer: updated results

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Unmet medical need in HPV16+ head and neck squamous cell carcinoma

- HPV infection has been linked to the increasing incidence of HNSCC in the US1
 - 70% of OPC cases are related to HPV infection, with the most prominent subtype, HPV16, causing ~90% of OPC cases2
- Pembrolizumab created a paradigm shift in the management of metastatic/recurrent HNSCC, but improvements are needed
 - Only about 19% of patients with PD-L1 CPS ≥ 1 treated with pembrolizumab monotherapy have an objective response, with approximately 23% ORR and ~8% CR rate in the PD-L1 CPS ≥ 20 sub-population and ~15% ORR and ~3% CR rate in the PD-L1 CPS 1-19 sub-population3, 4
 - In the PD-L1 CPS ≥ 20 sub-population receiving pembrolizumab monotherapy, mPFS and mOS were 3.4 mo and 14.9 mo, respectively, and 12 month OS rate was ~56%3, 4
 - Pembrolizumab + chemotherapy and Cetuximab improves response rates, with increased toxicity and shorter duration of response5, 6
- HPV-positive disease is mediated via distinct biological drivers compared to HPV-negative HNSCC7
- Opportunity to improve existing therapy in HNSCC by developing immunotherapeutic approach tailored to HPV biology

CPS, combined positive score; CR, complete response; HNSCC, head and neck squamous cell carcinoma; HPV, human papillomavirus; HPV16, human papillomavirus 16; mo, month; mPFS, median progression free survival; mOS, median overall survival; OPC, oropharynx cancer.

1. Tota J, et al. *J Clin Oncol*. 2019;37:1538. 2. Chaturvedi A, et al. *J Clin Oncol*. 2011;29:4294. 3. Harrington et al. *J Clin Oncol*. 2023;41(4):790-802. 4. Burtness B, et al. *J Clin Oncol* 2022;40:2321-2332; 5. Burtness B, et al. *Lancet*. 2019;394:1915. 6. Sacco AG, et al. *Lancet Oncol* 2021; 22: 883–92; 7. Powell SF, et al. *Cancers (Basel)*. 2021;13(20):5206.

HB-200 Therapy: Activating HPV16+ Specific T Cell Response

- 1 Modification of arenavirus with target antigen

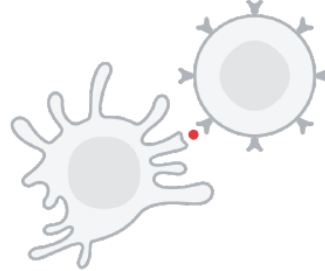


Administration of HB-200

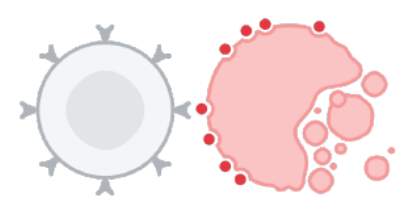
- 2 Infection of dendritic cells or macrophages



- 3 Activation of antigen-specific T cells



- 4 Elimination of tumor cells



HB-200 is an alternating treatment of replicating arenavirus vectors expressing a non-oncogenic HPV16 E7-E6 fusion protein¹

As a monotherapy, HB-200 robustly induced antigen-specific circulating T cells in patients with HPV16+ cancers, with tumor shrinkage observed^{2,3}

HPV16, human papillomavirus 16.

1. Lauterbach H, et al. Front Oncol. 2021;11:732166. 2. Fu S, et al. ASCO 2022. Abstract 2517.

3. Ho A, et al. SITC 2023. Abstract 679.

Study Design

- Single-arm Phase 2 cohort within the Phase 1/2 H-200-001 trial

Main Eligibility

- 1L Recurrent or metastatic HPV16+ HNSCC
- PD-L1 CPS \geq 1
- RECIST v1.1 measurable lesion
- ECOG PS 0 or 1
- No prior systemic anticancer therapy in recurrent or metastatic setting

**HB-200 IV
+ pembrolizumab IV**

Treatment schedule:

- **HB-200 IV:** Q3w for first 5 doses; Q6w later
- **Pembrolizumab IV:** 200 mg Q3w or 400mg Q6w

Until unacceptable toxicity
or
disease progression

Endpoints

- Primary
 - ORR* per investigator assessment
- Secondary
 - OS
 - PFS[†]
 - DCR[†]
 - DOR[†]
- Exploratory
 - T cell response
 - PD biomarkers

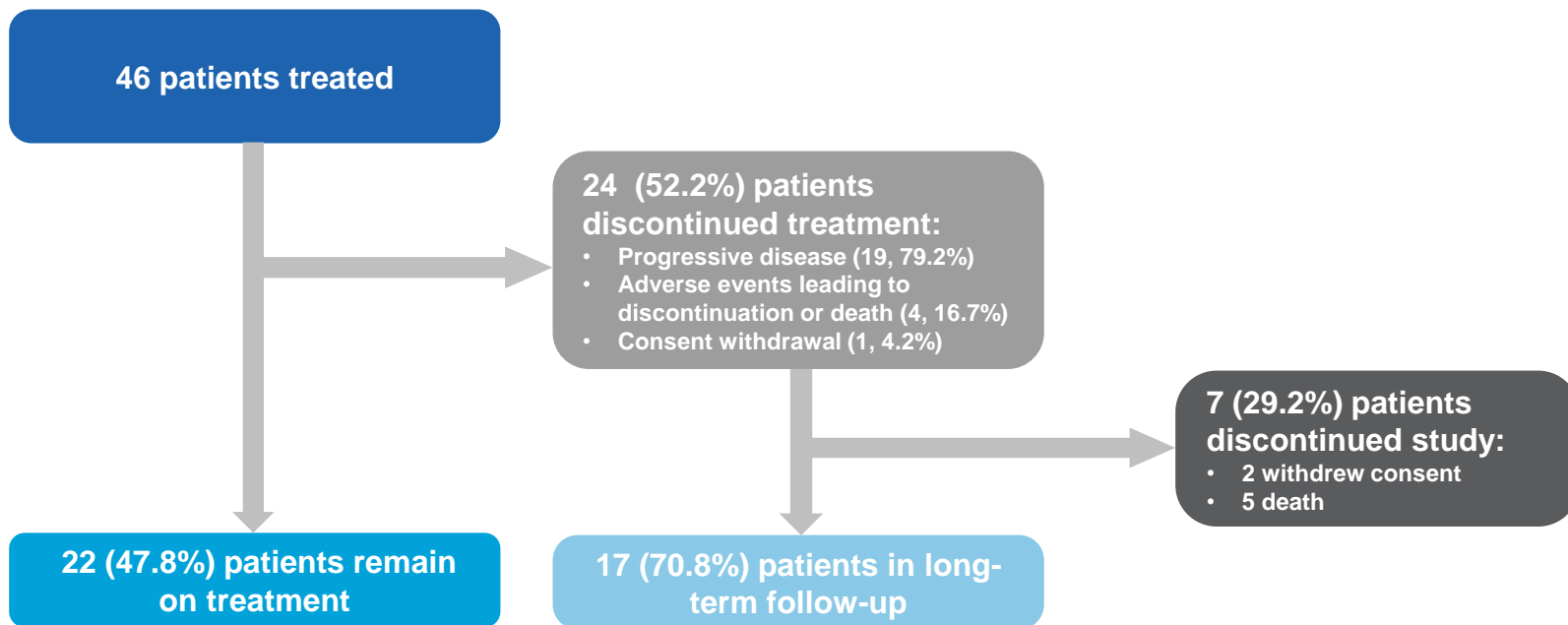
CPS, combined positive score; DCR, disease control rate; DOR, duration of response; ECOG, Eastern Cooperative Oncology Group; HNSCC, head and neck squamous cell carcinoma; HPV16, human papillomavirus 16; iRECIST, Immune Response Evaluation Criteria in Solid Tumors; IV, intravenous; ORR, objective response rate; OS, overall survival; PD, pharmacodynamic; PFS, progression-free survival; PS, performance status; Q3W, every 3 weeks; Q6W, every 6 weeks; RECIST, Response Evaluation Criteria in Solid Tumors; SmPC, summary of product characteristics.

*Per RECIST v1.1. [†]Per RECIST v1.1 / iRECIST.

Clinical trial# NCT04180215.

Patient disposition

- 46 patients treated as of March 29, 2024, with median follow-up of 7.4 months (range 0.03-23.3)



Baseline Characteristics

Baseline Characteristics	PD-L1 CPS ≥ 1 (N = 46)	PD-L1 CPS ≥ 20 (N = 23)
Age, years , median (range)	66 (50 – 76)	69 (50 – 76)
Gender, male , n (%)	44 (95.7)	21 (91.3)
Race, white , n (%)	42 (91.3)	21 (91.3)
Smoking history , n (%)	19 (41.3)	9 (39.1)
ECOG PS , n (%)		
0	38 (82.6)	18 (78.3)
1	8 (17.4)	5 (21.7)
Metastatic , n (%)	36 (78.3)	17 (73.9)
Locally recurrent only , n (%)	10 (21.7)	6 (26.1)
Primary site , n (%)		
Oropharynx	45 (97.8)	22 (95.7)
Hypopharynx	1 (2.2)	1 (4.3)
Prior definitive radiation \pm chemotherapy , n (%)		
Prior radiation treatment, n (%)	43 (93.5)	21 (91)
Prior platinum use, n (%)	34 (73.9)	16 (69.6)
Prior CPI use, n (%)	2 (4.3)	0

Safety Summary

- Manageable safety profile, in line with HB-200¹ or pembrolizumab monotherapy²
- No treatment-related AE leading to death and low rate of discontinuation
- 5 of the 7 patients with treatment-related Grade ≥3 AEs experienced transient cytopenia limited to Cycle 1

All Participants (N = 46)	Treatment-Emergent AEs, n (%)	Treatment-Related AEs, n (%)
Any event	44 (95.7)	39 (84.8)
Grade ≥3	18 (39.1)	7 (15.2)
Serious	11 (23.9)	2 (4.3)
Leading to discontinuation of HB-200	3 (6.5)	2 (4.3) ^a
Leading to discontinuation of pembrolizumab	4 (8.7)	3 (6.5) ^b
Deaths	2 (4.3)	0

a. One patient with grade 3 checkpoint inhibitor pneumonitis (noted as related to pembrolizumab), 1 patient with grade 1 cytopenia (noted as related to all treatment) along with unrelated events of grade 3 transaminitis and grade 2 abdominal pain (noted as progression related).

b. Aforementioned AEs and a grade 3 event of worsening pruritis (noted as related to pembrolizumab) leading to discontinuation of pembrolizumab but continuation of HB-200.

AEs, adverse events.

1. Fu S, et al. ASCO 2022. Abstract 2517. 2. Burtness B, et al. Lancet. 2019;394:1915-1928.

Most Common Treatment-Related Adverse Events (Incidence ≥10%)

Non-Hematologic Adverse Events

Treatment-Related AE, Preferred Term (N = 46)	All Grades, n (%)	Grade ≥3, n (%)
Fatigue	18 (39.1)	0
Nausea	16 (34.8)	0
Pyrexia	15 (32.6)	2 (4.3)
Influenza-like illness	14 (30.4)	0
Chills	13 (28.3)	0
Headache	11 (23.9)	0
Vomiting	8 (17.4)	0
Myalgia	7 (15.2)	0
Arthralgia	6 (13.0)	0
Aspartate aminotransferase increase	5 (10.9)	1 (2.2)
Lipase increased	5 (10.9)	0

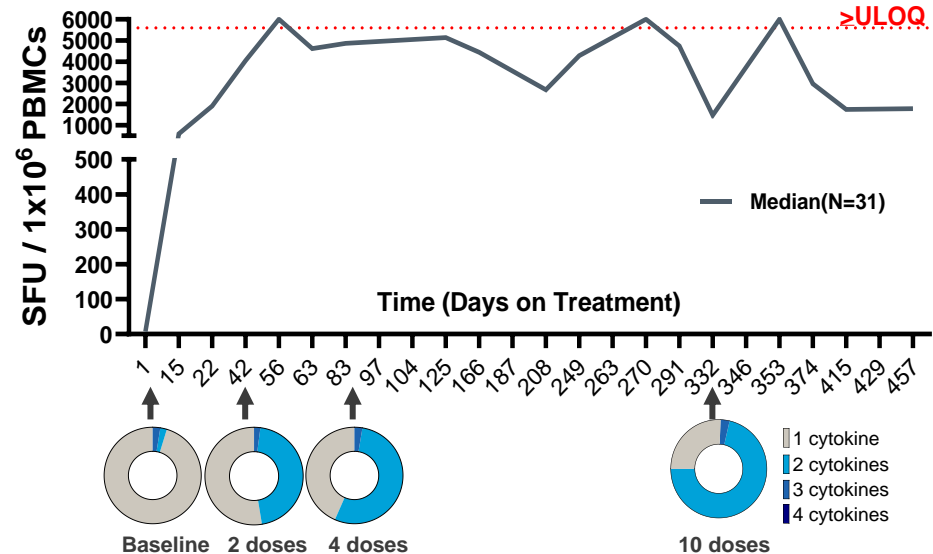
AEs, adverse event

Hematologic Adverse Events

Treatment-Related AE, Preferred Term (N = 46)	All Grades, n (%)	Grade ≥3, n (%)
White blood cell count decrease	7 (15.2)	3 (6.5)
Neutrophil count decrease	6 (13.0)	5 (10.9)
Anemia	5 (10.9)	1 (2.2)
Platelet count decreased	5 (10.9)	0

Robust & Sustained Induction of Functional HPV16+ Tumor-Specific T Cells

- In 71% (22/31 patients¹), HB-200 + pembrolizumab increased circulating HPV16-specific CD8+ T cells to >1% of all CD8+ T cells (maximum of 24% observed)
- Increasing polyfunctionality of HPV16+ tumor specific CD8+ T cells during treatment



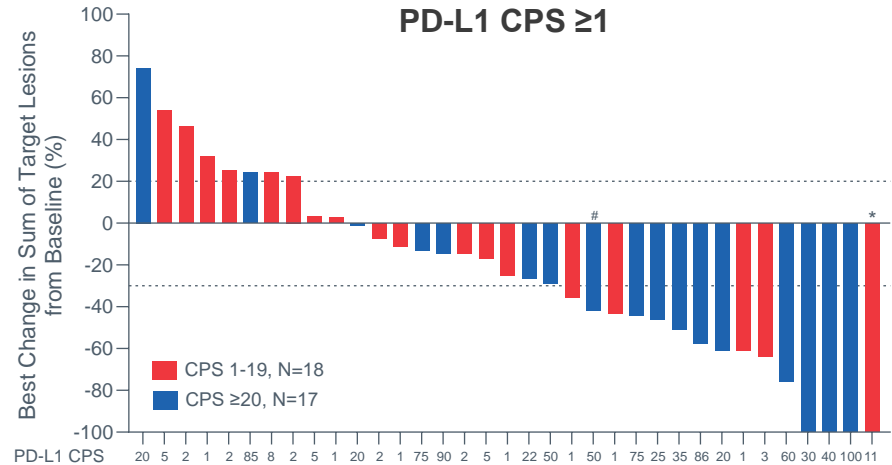
¹T cell immunogenicity data for 31 out of 38 patients available;
 Graph: Systemic T cell kinetics per HPV-16 E6/E7 specific ELISPOT (N = 31pt) and analysis of polyfunctionality of E6 / E7 specific CD8+ T cells by intracellular cytokine staining; cytokines analyzed were IFN- γ , TNF, IL-2; CD107a
 HPV16, human papillomavirus 16; PBMCs, peripheral blood mononuclear cells; SFU, spot-forming unit; ULOQ, upper limit of quantitation.

Anti-Tumor Activity in Patients Treated With 1L HB-200 + Pembrolizumab

38 patients in efficacy population with minimum follow-up of 4.5 months or discontinued early during this period

PD-L1 CPS ≥ 1 Evaluable Population	Confirmed Responses (RECIST v1.1)	ORR	CR Rate	DCR (CR+PR+SD)
N = 35	13	37.1%	11.4%	68.6%

Excludes 3 patient who did not have a post-baseline tumor evaluation on trial. One patient had a sudden death on Study Day 2; 1 patient had a grade 5 COVID pneumonia event on Study Day 27; 1 patient withdrew consent prior to the first scan.

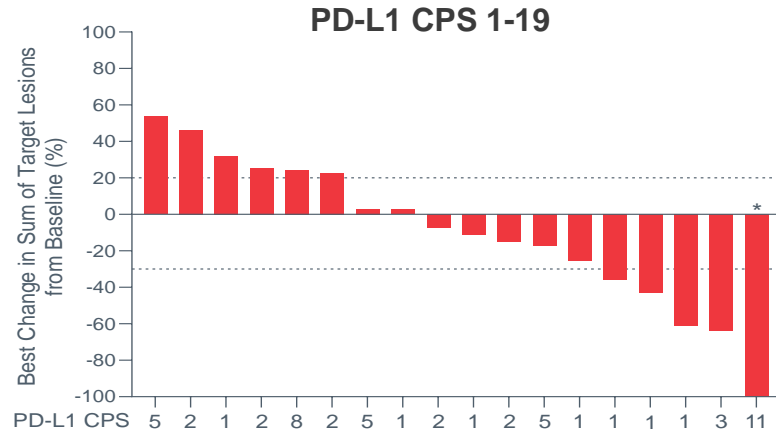


* Confirmed PR at data cutoff, confirmed CR after data cutoff date
PD per RECIST v1.1, iPR per iRECIST

Data as of 29-Mar-2024. Efficacy dataset includes 38 patients with minimum 4.5 months of follow-up time after first dose as of data cutoff or discontinued early during this period.

1L, first-line; CPS, combined positive score; CR, complete response; DCR, disease control rate; iPR, immune partial response; iRECIST, immune Response Evaluation Criteria in Solid Tumors; ORR, objective response rate; PD, progressive disease; PR, partial response; RECIST, Response Evaluation Criteria in Solid Tumors; SD, stable disease.

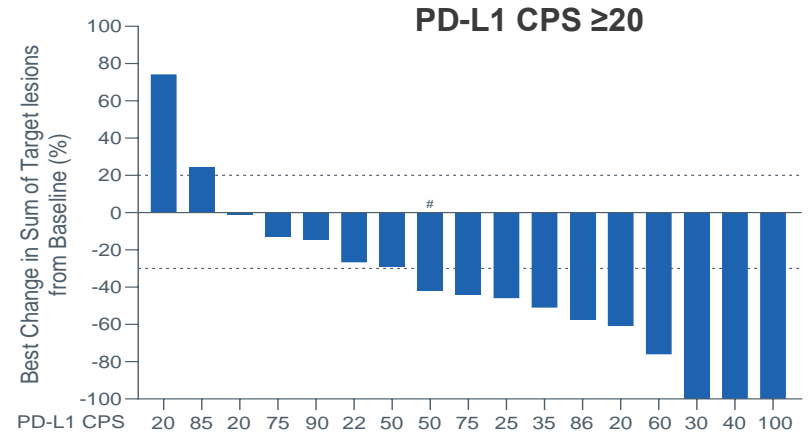
Anti-Tumor Activity in Patients Treated With 1L HB-200 + Pembrolizumab



N=18
* Confirmed PR at data cutoff, confirmed CR after data cutoff

PD-L1 CPS 1-19 Evaluable Population	Confirmed Responses (RECIST v1.1)	ORR	CR Rate	DCR (CR+PR+SD)
N = 18	4	22.2%	5.6%	55.6%

Excludes 1 patient who had a sudden death on Study Day 2 and did not have a post-baseline tumor evaluation on trial.

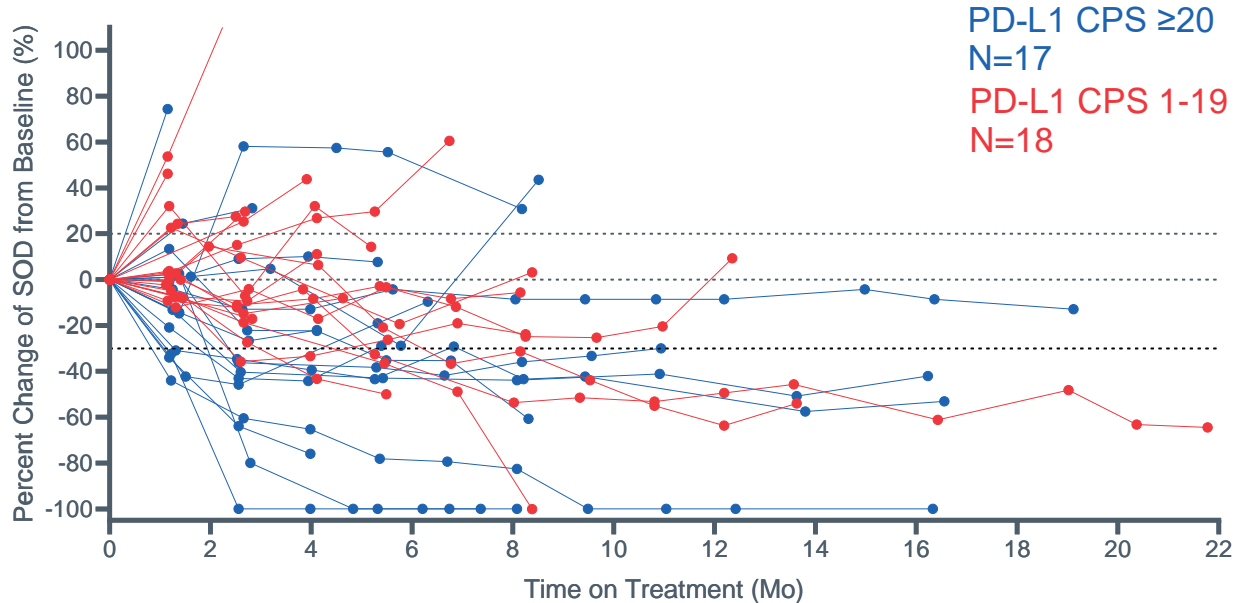


N=17
PD per RECIST v1.1, iPR per iRECIST

PD-L1 CPS ≥20 Evaluable Population	Confirmed Responses (RECIST v1.1)	ORR	CR Rate	DCR (CR+PR+SD)
N = 17	9	52.9%	17.6%	82.4%

Excludes 2 patients who did not have a post-baseline tumor evaluation on trial. One patient had a grade 5 COVID pneumonia event on Study Day 27; 1 patient withdrew consent prior to the first scan.

Anti-Tumor Activity in Patients Treated With 1L HB-200 + Pembrolizumab



- Deepening of responses observed over time
- 61.5% of responders ongoing, median DOR not yet mature
- Deeper responses observed in a subset of patients with PD-L1 CPS ≥ 20

Data as of 29-Mar-2024. Efficacy dataset includes 38 patients with minimum 4.5 months of follow-up time after first dose as of data cutoff or discontinued early during this period.

1L, first-line; CPS, combined positive score; DOR, duration of response; OS, overall survival, SOD, sum of diameters.

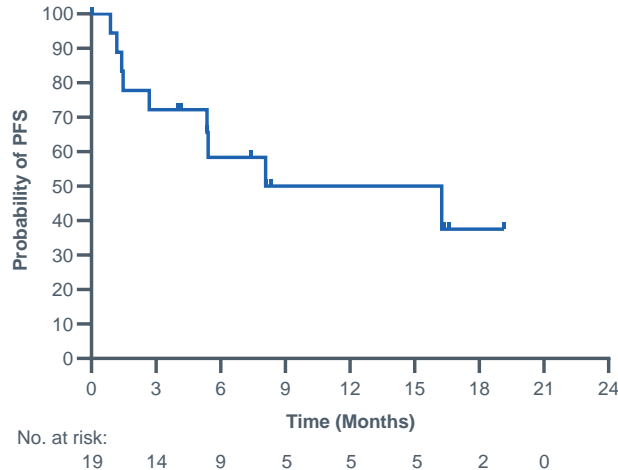
Objective Response, PFS and OS in Patients With PD-L1 CPS ≥ 20

Objective Response

ORR	52.9%
CR Rate	17.6%
DCR	82.4%

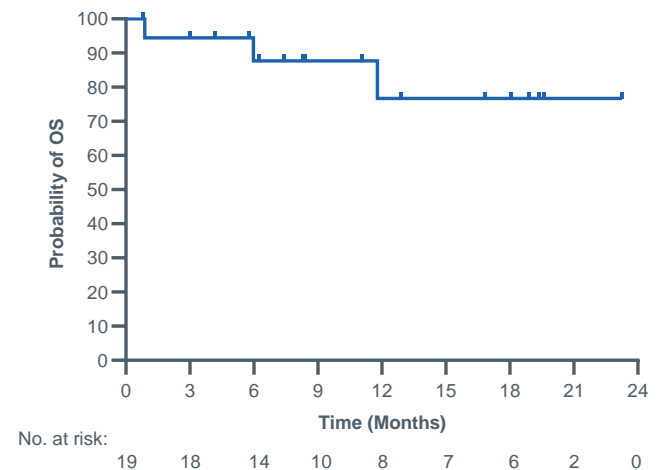
PFS

No. of events/
No. of subjects (%) mPFS
9/19 (47.4%) 16.3



OS

No. of deaths/
No. of subjects (%) mOS (Mo)
3/19 (15.8%) Unreached



- PFS and OS are promising, but not yet mature with 9 PFS events (n=19) and median follow-up of 8.4 mo (0.8-23.3), respectively
- PD-L1 CPS ≥ 20 population identified to benefit most from HB-200 + pembrolizumab combination therapy

Data as of 29-Mar-2024. Efficacy dataset includes 38 patients with minimum 4.5 months of follow-up time after first dose as of data cutoff or discontinued early during this period.

1L, first line; CI, confidence interval; CPS, combined positive score; CR, complete response; DCR, disease control rate; Mo, month; mPFS, median progression-free survival; mOS, median overall survival; n.c., not calculable; No, number; ORR, objective response rate

Conclusions

- HB-200 arenavirus-based immunotherapy in combination with pembrolizumab demonstrate:
 - Rapid and durable induction of robust tumor-specific circulating T cells consistent with previously reported data^{1,2}
 - Favorable efficacy and safety profile, compared to historical pembrolizumab monotherapy in patients with PD-L1 CPS ≥ 1 ^{3,4}
 - Compelling clinical activity in patients with PD-L1 CPS ≥ 20 in the first-line setting, with a confirmed ORR of 53% and a complete response rate of 18%
 - Majority of responses ongoing with durable tumor control
 - Promising preliminary PFS and OS data

Randomized Ph2/3 trial of HB-200 in combination with pembrolizumab in the first-line setting in patients with HPV16+ PD-L1 CPS ≥ 20 oropharynx cancer

CPS, combined positive score; HPV16, human papillomavirus 16; ORR, objective response rate.

1. Nabell L, et al. ESMO 2023. Abstract 921P. 2. Ho A, et al. SITC 2023. Abstract 679.

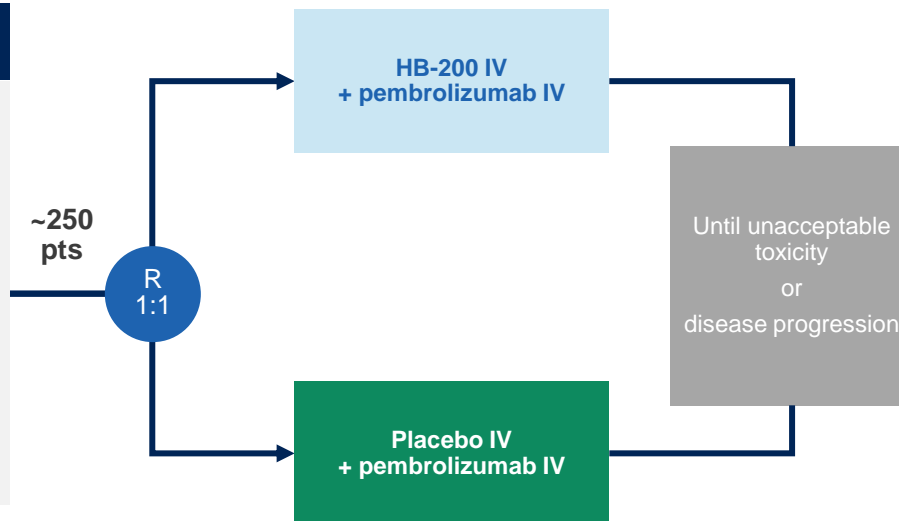
3. Harrington et al. *J Clin Oncol*. 2023;41(4):790-802. 4. Burtneß B, et al. *Lancet*. 2019;394(0212):1915-1928.

H-200-004 Study Design in HPV16+ OPSCC Patients with PD-L1 CPS ≥ 20

Randomized, blinded, placebo-controlled, adaptive Phase 2/3 study, aligned with FDA

Main Eligibility

- 1L Recurrent or metastatic HPV16+ OPSCC
- PD-L1 CPS ≥ 20
- RECIST v1.1 measurable lesion
- ECOG PS 0 or 1
- No prior systemic anticancer therapy in recurrent or metastatic setting



Treatment schedule:

- **HB-200 IV:** Q3W for first 5 doses, then Q6W **Pembrolizumab IV:** 200 mg Q3W for first 5 doses, then 400 mg Q6W
- **Duration:** up to about 20 doses

Endpoints

Primary

- ORR by BICR (Phase 2)
- OS (Phase 3)

Secondary

- PFS, DOR, DCR, PFS2 (RECIST v.1.1/iRECIST)
- Safety and tolerability (AE, SAE, ECI, irAE)
- Global QoL score

Exploratory

- Pharmacodynamic biomarkers

AE, adverse events; CPS, combined positive score; BICR, blinded independent central review; DCR, disease control rate; DOR, duration of response; ECI, events of clinical interest; ECOG, Eastern Cooperative Oncology Group; HPV16, human papillomavirus 16; irAE, immune-related adverse events; iRECIST, Immune Response Evaluation Criteria in Solid Tumors; IV, intravenous; OPSCC, oropharyngeal squamous cell carcinoma; ORR, objective response rate; OS, overall survival; PFS, progression-free survival; PFS2, time from randomization to progression on second-line therapy; PS, performance status; Q3W, every 3 weeks; Q6W, every 6 weeks; QoL, quality of life; RECIST, Response Evaluation Criteria in Solid Tumors; SAE, serious adverse events.

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