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VERSATILE-002: Overall Survival of HPV16-Positive Recurrent/Metastatic Head and Neck Squamous Cell Carcinoma Patients Treated with T Cell Stimulating Immunotherapy PDS0101 and Pembrolizumab

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Background

The overall incidence of HNC continues to rise, with a predicted 30% increase annually by 2030.[1] This rise is driven almost exclusively by HPV16.[2] Today an estimated 35–40% of recurrent/metastatic HNSCC are HPV16-positive.[3]

HPV-positive HNSCC shows different biological characteristics from HPV-negative disease with different responses to conventional therapies.[4]

HPV16 is the most carcinogenic type of HPV and has evolved to evade detection by the host system.[5] Whereas HPV-positive early stage HNSCC has better prognosis, there is evidence to suggest that advanced HPV16-positive HNSCC is implicated in disease progression and negative survival outcomes. In a published study of advanced HNSCC, HPV16 showed a significant negative impact on disease-free survival (P = 0.037), and OS (P = 0.010) when compared to HPV-negative OSCC. In contrast, HPV18 did not show a significant difference.[6]

There are no currently approved HPV-targeted therapies. In the first-line (1L) recurrent/metastatic (R/M) HNSCC setting, treatment with the immune checkpoint inhibitor (ICI) pembrolizumab is associated with a median overall survival (OS) of 12.3 months in subjects with CPS ≥1, 10.8 months with CPS 1–19, and 14.8 months with CPS ≥20.[7,8]

PDS0101 is being studied in combination with pembrolizumab in HPV16-positive R/M HNSCC.

Methods

VERSATILE-002 (NCT04260126) is a single-arm, Phase 2 study evaluating PDS0101 and pembrolizumab for 1L and 2L HPV16-positive R/M HNSCC. Subjects were ≥18-years-old, ECOG 0-1, and the 1L group had CPS ≥1.

Subjects received pembrolizumab 200 mg intravenously Q3W for up to 35 cycles (about 2 years) and PDS0101 1 mL subcutaneously Q3W during Cycles 1, 2, 3, 4, and 12. The primary study endpoint was confirmed best overall response (BOR) per RECIST v1.1.

Enrollment is complete. Herein we report data on overall survival (OS), safety, objective response rate (ORR), disease control rate (DCR), duration of response (DOR) and progression-free survival (PFS) in 1L R/M HNSCC subjects as of the latest data cut on April 3, 2025.

References

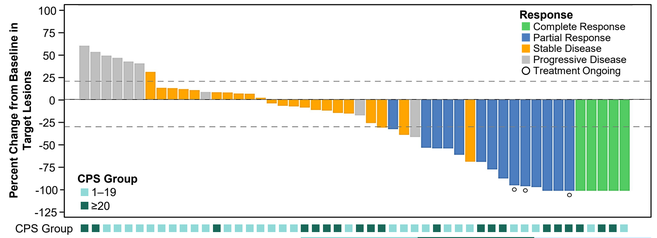
1. Gormley M et al. *British Dental Journal*. 2022; 2. Galati L et al. *Tumour Virus Research*. 2022; 3. Triangle Research Group. PDS Proprietary Market Research Report. 2024; 4. Wang HF et al. *Front Immunol*. 2019; 5. Luo X et al. *J Clin Invest*. 2020; 6. Lee LA et al. *Plos ONE*. 2012; 7. Burtness B et al. *Lancet*. 2019; 8. Burtness B et al. *J Clin Oncol*. 2022.

Results

Demographic/Baseline Characteristic	Efficacy Population (N=53)
Age, Median (Min, Max)	64.0 (46, 83)
Sex, n (%)	
Male	49 (92.5)
Female	4 (7.5)
Race, n (%)	
Asian	1 (1.9)
Black or African American	1 (1.9)
White	50 (94.3)
Other	1 (1.9)
ECOG, n (%)	
0	30 (56.6)
1	23 (43.4)
CPS, n (%)	
1–19	32 (60.4)
≥20	21 (39.6)
Prior Therapy*, n (%)	
No Prior Therapy	10 (18.9)
Chemotherapy Only	3 (5.7)
Chemotherapy + Radiation Therapy	40 (75.5)

* Prior therapy at initial diagnosis of HNSCC

Waterfall Plot of Best Overall Change from Baseline in Target Lesions



	CPS 1–19 (N=32)	CPS ≥20 (N=21)	CPS ≥1 (N=53)
ORR, n (%)	9 (28.1%)	10 (47.6%)	19 (35.8%)
DCR, n (%)	24 (75.0%)	17 (81.0%)	41 (77.4%)

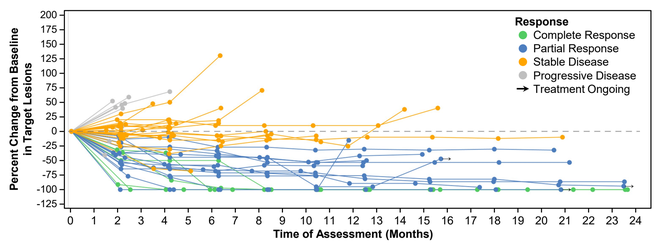
Response categories are based on confirmed Best Overall Response (BOR) by Investigator assessment per RECIST v1.1 using a minimum duration of 42 days for SD confirmation. ORR is defined as the percentage of subjects with confirmed BOR of CR or PR. DCR is defined as the percentage of subjects with confirmed BOR of CR, PR, or SD. Three subjects were still being treated at the time of the data cut. Three subjects were non-evaluable and are not included in the graph; two subjects died and one experienced disease progression before receiving an evaluable imaging scan. Eleven subjects (21%) had deep tumor responses of 90–100%.

PDS0101 or Pembrolizumab Treatment-Related Adverse Events (TRAE) (≥5%)

Preferred Term	Safety Population (N=62)
Any PDS0101 or Pembrolizumab TRAE, n (%)	55 (88.7)
Grade 1	27 (43.5)
Grade 2	17 (27.4)
Grade 3	10 (16.1)
Grade 4	1 (1.6)
Grade 5	0
Any Injection Site Reaction	46 (74.2)
Non-Injection Site TRAEs ≥ 5%, n (%)	
Fatigue	24 (38.7)
Headache	12 (19.4)
Pruritus	9 (14.5)
Diarrhea	8 (12.9)
Rash	6 (9.7)
Pain	5 (8.1)
Alanine aminotransferase increased	5 (8.1)
Arthralgia	5 (8.1)
Aspartate aminotransferase increased	4 (6.5)
Cough	4 (6.5)
Malaise	4 (6.5)
Rash maculopapular	4 (6.5)

Grade 3 Combination TRAEs were: Fatigue (2), Colitis (2), Rash, Diarrhea, Alanine aminotransferase increased, Blood alkaline phosphatase increased, Lymphocyte count decreased, Autoimmune colitis, Headache, Pancreatitis, Acute kidney injury, Hyponatremia, Hyperglycemia. Encephalitis, Abdominal pain, Hepatitis.
Grade 4 Combination TRAE: encephalitis (case recorded approximately one year after last PDS0101 dose).

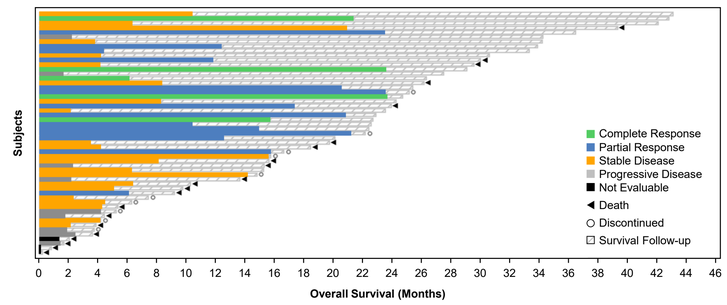
Spider Plot of Percent Change from Baseline in Target Lesions



	CPS 1–19 (N=32)	CPS ≥20 (N=21)	CPS ≥1 (N=53)
Median DOR, months (95% CI)	21.8 (4.2, NE)	NE (5.6, NE)	21.8 (11.5, NE)

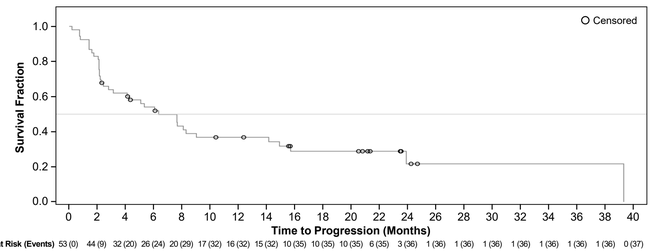
Spider plot shows the durability of the confirmed BOR by Investigator assessment per RECIST v1.1. DOR was estimated using the Kaplan-Meier method, defined as time from the first documented response (CR or PR) until disease progression or death from any cause. NE means non estimable.

Swimmer Plot of Overall Survival and Progression-Free Survival



Data reflect confirmed BOR by RECIST v1.1 by Investigator assessment for individual subjects. BOR is displayed graphically from treatment start until the last tumor assessment. Survival follow up is displayed from last tumor assessment until date of censoring or death. Subjects labeled Discontinued withdrew consent (7), were lost to follow-up (2), or discontinued due to an adverse event (1).

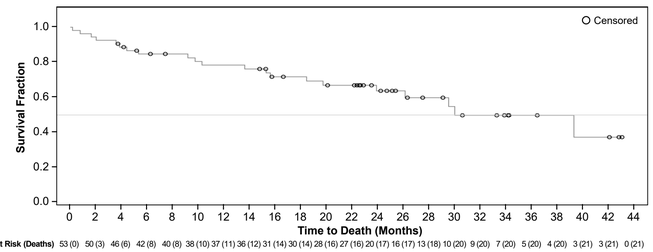
Kaplan-Meier Estimates of Progression-Free Survival



	CPS 1–19 (N=32)	CPS ≥20 (N=21)	CPS ≥1 (N=53)
Median PFS, months (95% CI)	5.1 (2.2, 8.1)	14.1 (2.1, NE)	6.3 (2.8, 14.1)

PFS was estimated based on the Kaplan-Meier method and was defined as the time from the start of study treatment until documented disease progression or death by any cause in the absence of progression. PFS was censored at the last known date of tumor assessment or Day 1 without any post-baseline tumor assessment.

Kaplan-Meier Estimates of Overall Survival



	CPS 1–19 (N=32)	CPS≥20 (N=21)	CPS≥1 (N=53)
Median OS, months (95% CI)	26.1 (15.3, NE)	39.3 (30.0, NE)	30.0 (23.9, NE)
Median Follow Up, months (Q1, Q3)	15.7 (6.8, 24.8)	24.7 (18.4, 30.5)	22.1 (9.2, 27.5)

Overall survival plotted by standard Kaplan-Meier methodology. At the time of the data cut, 22 subjects were alive and still being followed for survival, 10 subjects discontinued the study (7 withdrew consent, 2 were lost to follow up, and 1 discontinued due to an AE), and 21 subjects had died. Follow up is defined as the time from start of study treatment until death by any cause or date of censoring and includes long-term follow up period.

Conclusions

- **Enrollment in this study is complete. As of this data cut, 3 subjects remain on study treatment and 22 subjects continue to be followed for survival.**
- **PDS0101 plus pembrolizumab continues to show excellent tolerability in this 1L R/M HPV16-positive HNSCC population.**
- **Median OS of 30.0 months with lower 95% confidence interval of 23.9 months and median follow up of 22.1 months is encouraging, illustrating potential benefit of PDS0101 plus pembrolizumab to improve survival.**
- **Clinical activity remains strong with an ORR of 35.8% and DCR of 77.4%.**
- **Eleven subjects (21%) had deep tumor responses of 90–100%.**
- **A global, randomized, controlled, Phase 3 study of PDS0101 (Versamune® HPV) plus pembrolizumab vs. pembrolizumab monotherapy in patients with 1L HPV16-positive R/M HNSCC with CPS ≥1 is underway (NCT06790966).**

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Disclosures

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