Abstract: 6012

Safety and Efficacy of Immune Checkpoint Inhibitor (ICI) Naïve Cohort from Study of PDS0101 and Pembrolizumab in HPV16-positive Head and Neck Squamous Cell Carcinoma (HNSCC)

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Background

Up to 70% of oropharyngeal cancers in the US are HPV-mediated with most caused by HPV16 infection.[1, 2] PDS0101 is a novel, investigational, T cell activating, HPV16-targeted immunotherapy that stimulates a targeted T cell response against HPV16-positive cancers.

Methods

VERSATILE-002 (NCT04260126) is a Phase 2, open-label, non-randomized, adaptive design study evaluating the combination of PDS0101 and pembrolizumab in subjects with HPV16-positive recurrent and/or metastatic (R/M) HNSCC in 2 cohorts: ICI-naïve and ICI-refractory. All ICI naïve subjects must be ≥18 years of age and have a combined positive score (CPS) ≥1.

All subjects receive pembrolizumab 200mg IV Q3W with PDS0101 administered SC in two 0.5 mL injections during Cycles 1, 2, 3, 4, and 12 (max 5 doses).

This study is in collaboration with Merck Sharp & Dohme LLC, a subsidiary of Merck & Co., Inc., Rahway, NJ, USA.

Results

Forty-eight subjects who received at least one cycle of combination therapy made up the intent to treat (ITT) population. They had a median age of 62.5 (range 45–83), were 93.8% male, 93.8% White, 62.5% ECOG 0, and 41.7% CPS ≥20.

In the ITT population, the median overall treatment duration was 3.5 months (range 0.0–19.5). The median number of PDS0101 doses was 4 (range 1–5); 56.3% received 4 doses and 22.9% received 5 doses. The median number of pembrolizumab doses was 5 (range 1–29); 27.1% received ≥10 doses.

Efficacy was evaluated in the modified ITT (mITT) population (n=34) which consisted of all ITT subjects who had imaging assessment following treatment. They had a median age of 63.5 (range 46–83), were 94.1% male, 97.1% White, 58.8% ECOG 0, and 50.0% CPS ≥20.

Only 4 subjects had Grade 3 TRAEs: fatigue, injection site reaction, blood alkaline phosphatase increased, hyperglycemia, colitis, and rash. No subject came off study due to toxicity.

Conclusions

- **PDS0101 with pembrolizumab is well tolerated in this ICI-naïve R/M HPV16-positive HNSCC population**
- **Median PFS was 10.4 months which compares favorably to published median PFS of 2–3 months for approved ICIs when used as monotherapy in patients with similar PD-L1 levels[3, 4]**
- **The estimated 12-month OS rate of 87.1% is promising compared to published results of 36–50%[3, 4]**
- **These results justify a confirmatory randomized, controlled study**

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Limitations

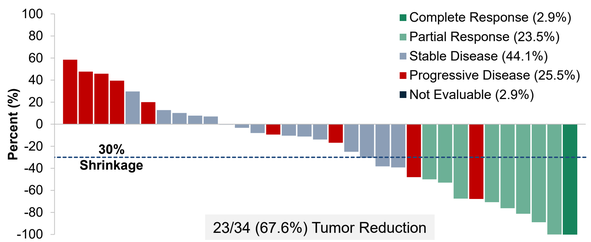
This study presents data from a snapshot of an ongoing Phase 2 study. Fourteen subjects were enrolled but had not yet received their first imaging assessment. Final results may differ for reasons including: outcomes from additional subjects enrolled in the study, new outcomes from existing subjects, delays in data entry at the research site, ongoing monitoring and clarification of data queries.

References

1. https://www.cdc.gov/cancer/hpv/basic_info/hpv_oropharyngeal.htm. Published October 3, 2022.
2. Cochicho D, et al. *Virol J*. 2021;18(217).
3. Burtness B, et al. *Lancet*. 2019;394:1915–1928.
4. Ferris RJ, et al. *Oral Oncol*. 2018;81:45–51.

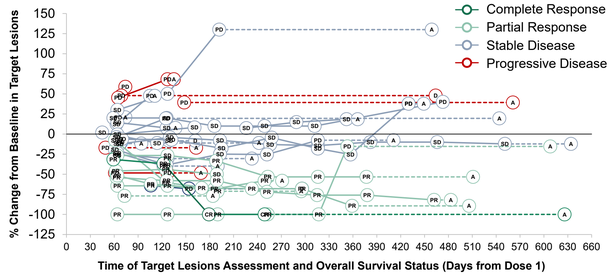
Results

Waterfall Plot of Maximum % Change from Baseline in Target Lesions*



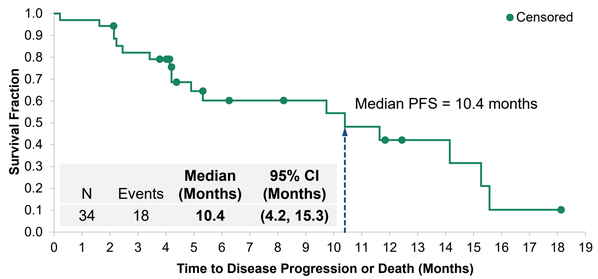
* Confirmed best overall response was determined based on confirmed CR or confirmed PR per RECIST 1.1 per investigator assessment. One subject (NE) died prior to target lesion measurement and is included in the mITT population denominator. Four subjects experienced unconfirmed tumor shrinkage and subsequently experienced progressive disease.

Spider Plot of % Change from Baseline in Target Lesions and Overall Survival Status*



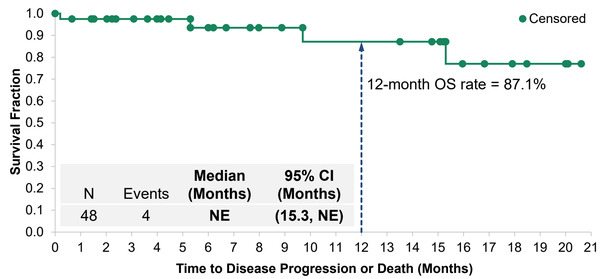
* Line color by confirmed best overall response by investigator assessment per RECIST 1.1.
Overall response: CR=Complete Response; PR=Partial Response; SD=Stable Disease; PD=Progressive Disease; NE=Not Evaluable.
Survival status: A=Alive; D=Deceased. Alive subjects were based on the last contact date.

Kaplan-Meier Estimates of PFS per Investigator Assessment (mITT Population)



N	Events	Median (Months)	95% CI (Months)
34	18	**10.4**	**(4.2, 15.3)**

Kaplan-Meier Estimates of OS (ITT Population)



N	Events	Median (Months)	95% CI (Months)
48	4	**NE**	**(15.3, NE)**

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

Preferred Term	n (%)
Any PSD0101-Pembrolizumab TRAE	**37 (77.1)**
Injection site pain	24 (50.0)
Fatigue	18 (37.5)
Injection site swelling	13 (27.1)
Injection site erythema	8 (16.7)
Headache	7 (14.6)
Injection site discoloration	7 (14.6)
Injection site warmth	7 (14.6)
Injection site inflammation	6 (12.5)
Diarrhea	5 (10.4)
Injection site pruritus	5 (10.4)
Pruritus	5 (10.4)
Dyspnea	4 (8.3)
Pain	4 (8.3)
Alanine aminotransferase increased	3 (6.3)
Arthralgia	3 (6.3)
Aspartate aminotransferase increased	3 (6.3)
Blood creatinine increased	3 (6.3)
Blood thyroid stimulating hormone increased	3 (6.3)
Cough	3 (6.3)
Hypothyroidism	3 (6.3)
Rash	3 (6.3)
Weight decreased	3 (6.3)
PSD0101-Pembrolizumab TRAE by Grade	
Grade 1	13 (27.1)
Grade 2	19 (39.6)
Grade 3	4 (8.3)
Grade 4	0
Grade 5	0

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