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Polyfunctional HPV16-Specific T cell responses in subjects receiving PDS0101 and pembrolizumab combination treatment for recurrent/metastatic HPV16-positive head and neck squamous cell carcinoma (HNSCC)

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Background

- Generation of multifunctional, anti-tumor T cell responses and immune memory are critical for effective long-term control of tumor growth and clinical outcomes.
- Previously reported data suggests PDS0101 generates clinically active immune responses[1,2], and the combination of PDS0101 with other treatments has shown promising disease control by shrinking tumors, delaying disease progression and prolonging survival[3-5].
- The investigational T cell activating HPV16-targeted immunotherapy PDS0101 is being studied in combination with pembrolizumab (NCT04260126) in patients with HPV16-positive head and neck cancer.
- Biomarkers of response are undetermined.

Methods

- The ProteomeX IsoCode® Single-Cell Secretome adaptive immune proteomic assay was utilized to assess the functional state of tumor-specific CD4 and CD8 T cells.
- Cryopreserved PBMCs were thawed and rested overnight in the presence of IL-2, with magnetic bead column enrichment and surface staining for CD8/CD4 subsets following *in vitro* stimulation for 16 hours with an overlapping HPV16 E6/E7 peptide pool.
- Single-cell production of 32 immune analytes was measured and polyfunctionality was assessed at 3 timepoints: pre-treatment, and 12 and 36 weeks following 4 and 5 cycles of combination therapy, respectively.

Study Treatment Schedule

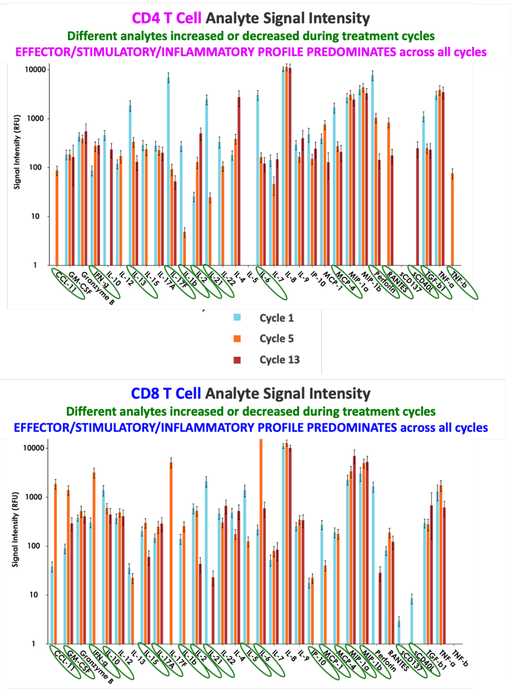
- PDS0101 1mL subcutaneous every 3 weeks
- Pembrolizumab 200mg intravenous every 3 weeks
- PDS0101 + pembrolizumab combination treatment Cycles 1-4 and Cycle 12
- **X** Immune monitoring assessments

Ethics Approval

The study protocol and all amendments were approved by the appropriate ethics committee at each institution. All subjects provided written informed consent prior to enrollment.

Results

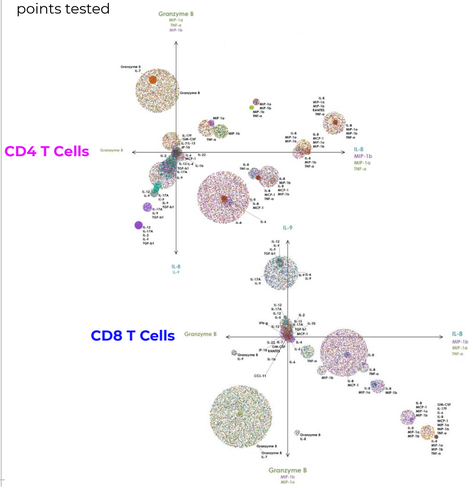
Figure 1: Analyte Signal Intensity: All Subjects at Cycles 1, 5, 13



Cohort Demographics N=18	
Median Age, (range)	63 (46-83)
Sex	
Female	1 (6%)
Male	17 (94%)
HPV16-positive	18 (100%)
PD-L1 CPS [PD-L1 IHC 22C3 pharmDx, Agilent]	
1-19*	8 (44%)
≥20	10 (56%)
*includes 1 ICI refractory subject with CPS <1	
Confirmed BOR	
OR (CR+PR)	6 (33%)
SD	10 (56%)
PD	2 (11%)
PD Occurred	
Yes	10 (56%)
No	8 (44%)
Time to PD	
≤ 183 days	10 (56%)
> 184 days	8 (44%)
Alive at Data Cut-Off	
Yes	16 (89%)
No	2 (11%)
Subjects with Specimens at:	
Cycles 1 and 5	10 (56%)
Cycles 1, 5 and 13	8 (44%)

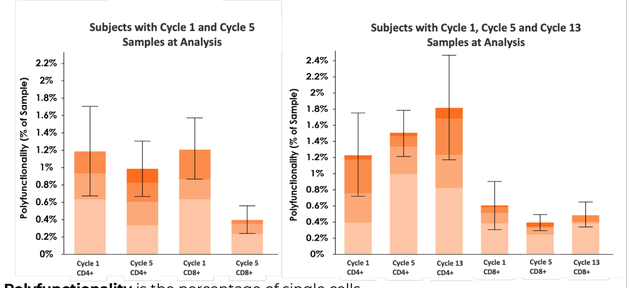
Figure 2: PAT PCA All Subjects

- The polyfunctional subsets of CD4 and CD8 T cells from subjects are visualized by single-cell **polyfunctional activation topology (PAT)- principal component analysis (PCA) plots**.
- Data shown reflects cells from all patients at all sample time points tested



- Each dot represents a *single cell* that is functionally clustered in a broader circle based on the cytokine secretion combination.
- The color-coded dots within each circle represent the frequency of single cells that secreted this group of cytokines in each sample.
- **The analytes most strongly present** (and their affiliated cytokines) **in each component are listed at the ends of the axes.**
- **For CD4 T cells these are Granzyme B** (MIP-1a, TNF-a, MIP-1b), **IL-8** (MIP-1b, MIP-1a, TNF-a) and **IL-8** (IL-9)
- **For CD8 T cells these are Granzyme B** (MIP-1a, MIP-1b), **IL-8** (MIP-1b, MIP-1a, TNF-a) and **IL-9**

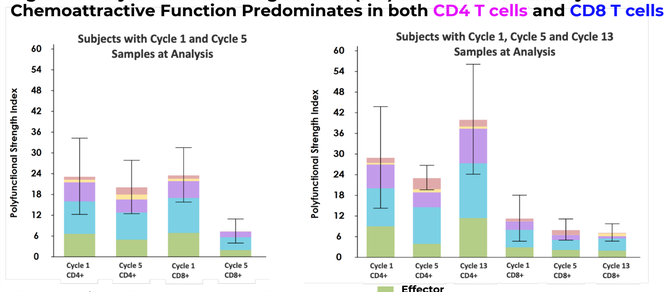
Figure 3: Both CD4 T cells and CD8 T cells demonstrate polyfunctionality



Polyfunctionality is the percentage of single cells secreting two or more cytokines in the peripheral blood (excludes T cells that may have tracked to the tumor)

- Increases in T cells with higher levels of cytokine expression are seen and vary according to cycle
- Decreases in CD8 T cells at Cycles 5 and 13 suggest possible trafficking to the tumor microenvironment
- All specimens were collected pre-treatment on Cycles 1 (baseline), 5 and 13

Figure 4: Polyfunctional Strength Index (PSI) Effector – Stimulatory – Chemoattractive Function Predominates in both CD4 T cells and CD8 T cells



Polyfunctional Strength Index (PSI) is an index combining the polyfunctionality of the sample and the average signal intensity of the analytes secreted by the polyfunctional single cells. The bars are broken down by the PSI of each cytokine group e.g., Effector, Stimulatory, Regulatory, Inflammatory, Chemoattractive.

Conclusions

- **In the current analysis, the PDS0101 + pembrolizumab combination results in significant CD4 and CD8 HPV16 tumor-specific polyfunctional T cell responses.**
- **Alterations in specific analyte profiles (increases or decreases) were observed across treatment cycles.**
- **Increases in T cells with higher levels of cytokine expression are seen and vary according to treatment cycle and T cell subpopulation.**
- **An effector / stimulatory / chemoattractive functional T cell profile predominates across all timepoints up to 13 cycles of combination treatment.**
- **Polyfunctional responses align with preclinical data[6].**
- **Decreases in polyfunctional CD8 T cells in peripheral blood at Cycles 5 and 13 may be due to T cell trafficking to and infiltration of the tumor microenvironment[6].**
- **Other potential biomarkers of anti-tumor activity and clinical outcomes are being explored.**

Acknowledgements

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Disclosure Statement

- Study sponsored by PDS Biotechnology Corporation
- Presenting Author contact: Kevin.Harrington@icr.ac.uk
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- Declaration of Interest KH: Independent Site Principal Investigator, PDS-sponsored VERSATILE-002 study (NCT04260126)
- Declaration of Interest LVW: Employee of PDS Biotechnology

Limitations

This analysis presents data from a snapshot of an ongoing Phase 2 trial, VERSATILE-002 (NCT04260126). It includes an initial subset of 18 subjects out of a total cohort of 55 immune checkpoint inhibitor (ICI) naïve subjects to be studied. Identical assessments are also planned for a cohort of 21 ICI refractory subjects.

References

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