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HPV16-specific CD4 and CD8 T-cell activation and functionality in patients receiving combination PDS0101 immunotherapy

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Background

- The novel HPV-targeted immunotherapy PDS0101 is being studied in combination with pembrolizumab in a Phase 2 clinical trial (VERSATILE-002, NCT04260126) in patients with HPV16-positive head and neck cancer.
- In this pilot study, we sought to establish optimal stimulation conditions for *in vitro* activation with selected HPV16 peptide pools that would enable downstream single cell analysis of functional cytokine profiles of HPV-specific CD4 and CD8 T cell subpopulations.

Ethics Approval

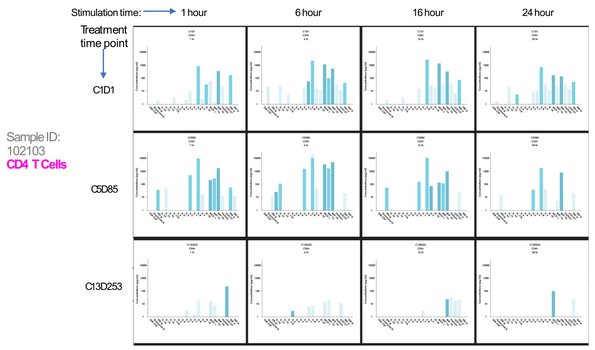
The study protocol and all amendments were approved by the appropriate ethics committee at each institution. All subjects provided written informed consent prior to enrollment.

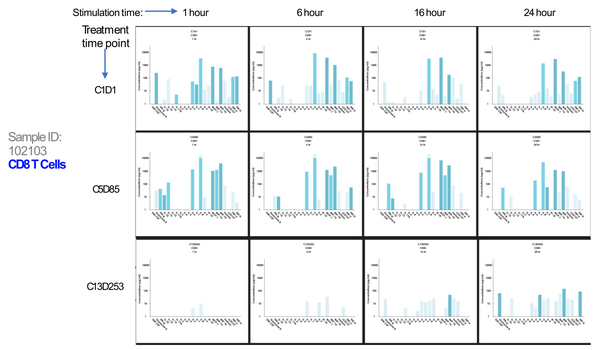
Methods

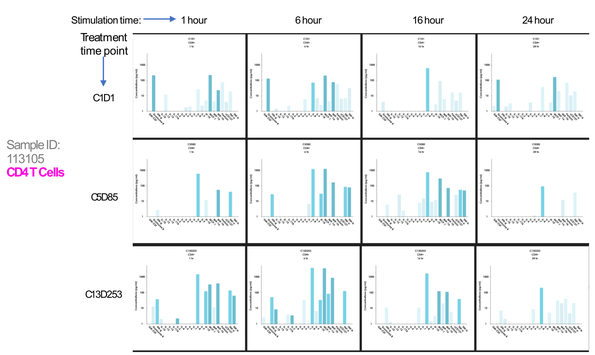
- The Isoplexis CodePlex platform was used to track cytokine profiles generated over time by peptide-activated CD4 and CD8 T-cells.
- Cryopreserved PBMCs from 2 study subjects collected at 3 timepoints (pre-treatment [C1D1], 12 weeks following 4 cycles [C5D85] and 36 weeks following 5 cycles [C13D253] of combination therapy) and were thawed and recovered overnight in the presence of IL-2, before stimulation with overlapping HPV16 E6 and E7 peptide pools (40mcg/mL) for 1hr, 6hr, 16hrs or 24hrs.
- Recovered stimulated cells were enriched for CD4 and CD8 populations using magnetic bead separation and the cells plated overnight.
- The supernatants from each of these populations were recovered and frozen at -80ºC until all supernatants were available for analysis.
- Supernatants were loaded on to CodePlex chips and analyzed using the IsoLight instrument.

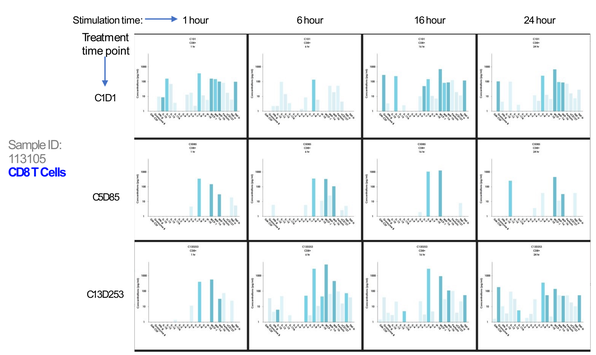
Results

Strong HPV-specific CD4 and CD8 T-cell responses were documented after only 1hr of peptide stimulation and at all time course timepoints. Detection of multiple cytokines (background subtracted) was captured by concentration (pg/mL) and demonstrated post-treatment increases in granzyme B, IFN-g, TNF-a/b, MCP-1, MIP-1a/1b and perforin reflecting development of HPV-specific CD8 and CD4 T cell reactivity and immune memory. **Stimulation between 6-16hrs provided the most multiparametric and robust cytokine signals.**









Key: CodePlex supernatant analysis on the IsoLight instrument allows for analyte detection by signal intensity (expressed as RFU) or concentration (expressed in pg/mL). Samples below the limit of detection (LOD) (faint blue bars) or above the upper limit of quantitation (ULOQ) (faint blue bar top only) are outside the individual analyte's assay limits, but still provide visual results.

Conclusion

- PDS0101 is an HPV-targeted immunotherapy that stimulates a potent targeted T cell attack against HPV-associated cancers.
- Interim data suggests PDS0101 generates clinically effective immune responses[1,2], and the combination of PDS0101 with other treatments demonstrates significant disease control by shrinking tumors, delaying disease progression and/or prolonging survival[3,4].
- Polyfunctional T cells (co-secretion of 2+ cytokines per single cell) are an important functional attribute of a quality human T cell immune response to antigen.
- PDS0101 treatment, when co-administered with pembrolizumab, induces polyfunctional, HPV-specific CD4 and CD8 T cell responses across multiple timepoints. The optimal stimulation conditions for *in vitro* activation is 6-16 hours.
- Additional studies of cell-specific functional profiles in larger numbers of subjects and correlation with clinical outcomes are planned.

Acknowledgements

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Disclosure Statement

- Presenting author Lauren V Wood, MD is an employee of PDS Biotechnology.
- Study sponsored by PDS Biotechnology
- Author contact: lwood@pdsbiotech.com

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