Background Human Papillomavirus (HPV) cancers are uniquely antigenic with a ubiquitous and essential expression of the viral proteins E6 and E7. Radiation therapy is essential in treating locally advanced HPV-associated cancers, including cervical cancers. Radiation therapy (RT) may synergize with immunotherapy to stimulate T-cell mediated anti-tumor affects by increasing T-cell flux in tumors and promoting pathways that result in increased antigen presentation. To evaluate this, we are conducting a single-arm phase II trial combining PDS0101, an E6/7 HPV16 T-cell activating immunotherapy delivered subcutaneously, combined with the standard of care chemoradiation for patients with locally advanced squamous cell cervical cancer with either lymph node metastasis or tumors of >5 cm.

Methods 17 patients of a planned 35 have enrolled in the study. Patients receive 5 doses of PDS0101 starting 10 days before RT, then on Days 7, 28, and 49 (± 5 days) during the 7-week course of treatment and again after chemoradiation is complete at Day 170 (± 14 days). To date, eight patients have completed treatment and were evaluated with a post-treatment Positron Emission Tomography (PET) scan to assess the response. Tumor specimens were collected at baseline and end of treatment and were evaluated for changes in T-cell activation.

Results Seven of 8 patients (87.5%) enrolled on IMMUNOCERV demonstrated a complete response (CR) on PET at 3 months. For comparison, 40 of 54 (74.1%) patients treated on a prospective tissue collection protocol with standard of care chemoradiation had a CR on PET after 3 months. The observed 1-year disease-free survival rate for IMMUNOCERV patients is 85.7%, and the 1-year overall survival is 100%. The percentage of polyfunctional CD8+ T-cells expressing granzyme B and Ki67 increased from baseline to end of treatment (38.5% vs. 65.4%, p = 0.0253). There were also enhanced signals in the single function CD8+ T-cells (granzyme B, Ki67, and CD69). However, there were no significant changes in these markers for patients treated with a prospective tissue collection protocol. Toxicity attributable to PDS0101 included self-limited Grade 1 and 2 local injection site reactions in 7 patients (3 Grade 1 and 4 Grade 2).

Conclusions In an ongoing trial, PDS0101 HPV-specific immunotherapy is safe and well tolerated in combination with chemoradiation. The combination treatment appears to result in an expansion of intratumoral activated T-cells expressing granzyme B. Further analysis will determine if the combination results in sufficiently high disease-free survival rates in patients with locally advanced cervical cancer.

Acknowledgements We thank PDS biotechnology (Dr. F. Bedu-Addo, Dr. L. Wood) for providing PDS0101.

Trial Registration NCT04580771

Ethics Approval All patients were enrolled under a protocol approved by the UT M.D. Anderson Cancer Center Institutional Review Board (MDACC 2019–1260) and written informed consent were obtained from all patients.