A Clinical Trial Combining a Tumor Targeting Immunocytokine (PDS01ADC) and Enzalutamide without Testosterone Lowering Therapy in Biochemically Recurrent Prostate Cancer

Renee N. Donahue[1], Yo-Ting Tsai[1], Fatima Karzai[2], Lisa Cordes[2], Kathy-Lee Wisdom[2], Amy Hankin[2], Nikki Williams[2], William D. Figg[2], Jeff Schlom[1], James L. Gulley[1], Ravi A. Madan[2]

[1]Center for Immuno-oncology, Center for Cancer Research, National Cancer Institute, [2]Genitourinary Malignancies Branch, Center for Cancer Research, National Cancer Institute.

Background: Enzalutamide is an androgen receptor pathway inhibitor (ARPI). As monotherapy, enzalutamide delayed metastasis in biochemically recurrent prostate cancer (BCR), leading to recent regulatory approval in BCR. PDS01ADC is a tumor-targeting IL-12 immunocytokine with the potential to minimize immune suppression in the tumor microenvironment and to activate CD8+T-cells and Natural Killer (NK) cells (Minnar, Frontiers Oncol, 2024). NK cells have been associated with metastasis-free survival in prostate cancer (Zhao, JNCI, 2019) but NK cells are rarely the focus of immunotherapy regimens.

Methods: Enzalutamide has previously been evaluated immunologically in BCR. BCR patients were treated with enzalutamide for 84 days and peripheral blood mononuclear cells (PBMCs) were evaluated (Madan JITC, 2020). PDS01ADC was evaluated in a phase 1 study (including prostate cancer) and PBMCs were also assessed. Patients were evaluated clinically with serial prostate specific antigen (PSA) values in both studies.

Results: Enzalutamide given for BCR for 84 days controlled PSA for a median of 308 days (range:168-1330). PBMC assessment demonstrated no significant changes in T-cells, there were increases in total NK cells, including NK cells with maturity/activation markers. In a separate study, 9 patients with prostate cancer treated with PDS01ADC, 5/8 (62.5%) evaluable patients had PSA declines (8-42%). Treatment with PDS01ADC in these prostate cancer patients was associated with increases in NK cell populations, but not other immune cells consistently.

Conclusion: Both enzalutamide and PDS01ADC have been shown to increase NK cells in prostate cancer patients and increased NK cells have been associated with better clinical outcomes in prostate cancer. Clinical trial #NCT06096870 is currently evaluating enzalutamide with/without PDS01ADC at the National Cancer Institute (Bethesda, MD, USA). The key endpoints in the trial include PSA responses, changes in PSMA PET imaging and changes in NK cells. This is the first BCR trial to evaluate an ARPI with an immunocytokine.

Conflicts of Interest: none

Funding: NCI Intramural Program and via CRADAs with Astellas and PDS Biotech