420 PROSTVAC IN COMBINATION WITH NIVOLUMAB ENHANCED IMMUNE CELL INFILTRATION IN PROSTATE CANCER

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Background Prostate cancer (PC) is the most common non-cutaneous diagnosed cancer among men in USA.[1] Although clinical outcomes are favorable for patients with localized disease, 20–30% of patients will develop metastatic prostate cancer (mPC) and have poor prognosis. Immunotherapy, as a single agent, provides benefit to a small subset of PC patients, which is thought to be partially due to its known cold tumor immune microenvironment (TIME). Combination studies are needed to enhance benefit.[2] Prostvac is a therapeutic cancer vaccine engineered to activate an immune response against prostate-specific Antigen (PSA).[3] Prostvac alone could induce systemic immune response by increasing immune-cell infiltrates in and around the tumor.[4] In this study, we are exploring the effect of Prostvac in combination with nivolumab in TIME in prostate cancer.

Methods We treated locally advanced prostate cancer patients (n=6) undergoing radical prostatectomy (RP) with neoadjuvant Prostvac in combination with nivolumab, an immune checkpoint PD-1 inhibitor. Dynamic changes in TIME before and after treatment were studied using multiplex immunofluorescence (Opal Method). Formalin fixed paraffin-embedded sections from matched pre-treated prostate biopsies and post-treated RP samples were stained with a validated T cell panel (DAPI, CD4, CD8, FOXP3, Ki67, Pan CK and PD-L1). To analyze the data, TIME was segmented into 3 compartments: intratumoral, invasive margin and benign.

Results Combination immunotherapy significantly increased CD4+ T cell density in the invasive margin (mean 211.5 cells/mm2 vs 592.2 cells/mm2, $p<0.05$), with similar trend in the intratumoral and the benign compartments. CD8+ T cell density increased after treatment in the invasive margin (mean 47.25 cells/mm2 vs 157cells/mm2) and the benign compartment. 5/6 and 4/6 patients showed more than 2-fold increase of CD4 and CD8 T cells in the TIME, respectively, in at least one of the three compartments. Increased proliferative indices in CD4+ and CD8+ T cells were also seen after treatment. Tregs were present in low frequencies in TIME (maximum of 12 cells/mm2) with no significant changes. Moreover, a significant drop in tumor cell Ki67 after treatment (mean 252.8 cells/mm2 vs 100.5 cells/332, $p<0.05$) suggests that the combination may control tumor growth.

Conclusions The combination of Neoadjuvant Prostvac and nivolumab was associated with increased immune cell infiltration in a cohort of early prostate cancer patients. A broader examination of the TIME and the role immune cells undertake to control tumor growth is on-going.

Trial Registration NCT02933255

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Ethics Approval This study was performed in compliance with ethical standard and was approved by the NIH IRB, 17C-0007. All patients participating in this study gave an informed consent before taking part.

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