Abstracts

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

REFERENCES

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.

http://dx.doi.org/10.1136/jitc-2021-SITC2021.420