587 NIVOLUMAB INCREASED VACCINE INDUCED T-CELL INFILTRATION IN PROSTATE CANCER

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Background Prostate cancer is the most diagnosed cancer in men worldwide, making up 21% of all cancer cases.[1] Although this disease is slow growing, 370,000 men die from prostate cancer every year. Prostate cancer is mostly a cold tumor, lacking infiltrating immune cells.[2] To switch the tumor immune microenvironment phenotype from cold to inflamed we used Prostvac, a therapeutic cancer vaccine that targets prostate-specific antigen (PSA) in monotherapy and in combination with Nivolumab, a PD1 inhibitor.

Methods Patients with localized prostate cancer were enrolled in 2 distinct clinical trials. In the 1st trial, patients received subcutaneously neoadjuvant Prostvac vaccine alone for 4 doses (NCT02153918). In the 2nd trial, patients received Prostvac and Nivolumab (NCT 02933255).

We studied the T cells infiltration in matched paired samples from pre-treatment biopsies and post-treatment Radical prostatectomy from patients enrolled in these trials (26 patients had monotherapy and 12 patients had combination therapy). Using multiplex immunofluorescence technique and opals, we immune-stained formalin fixed paraffin-embedded sections with a validated lymphocyte panel of markers that included DAPI, CD4, CD8, FOXP3, Ki67, Pan CK and PD-L1. We analyzed the data by measuring the cell densities in Invasive margin, center of the tumor and normal regions.

Results In both trials and using Prostvac alone or in combination with Nivolumab, CD4 and CD8 T cells increased in the overall prostate tumor tissues, the invasive margins and the center of the tumors. These increases are more predominant and frequent in patients who received Prostvac and Nivolumab. CD4 and CD8 densities increased by at least 2-fold in 91% and 83%, respectively and in patients who received the combination therapy, whereas this increase was found in 71% and 58% in patients who received only the vaccine. Ki67 was found higher in CD8 T-cells (Mean from 2.9 cells/mm^2 to 4.16 cells/mm^2, p=0.09) and significantly higher in CD4 T-cells in the overall tissues (Mean from 7.63 cells/mm^2 to 15.68 cells/mm^2, p=0.0019) only after the combination treatment, suggesting a role of blocking PD1 in activating these lymphocytes. T-regulatory T cells were found low in all samples (average of 10 cells/mm^2).

Conclusions Immunotherapy is standard therapy for many tumors, however PD-1 inhibitors as single agents have no clinical role in prostate cancer outside MSI high cancer. Combination immunotherapies could change the tumor immune-microenvironment landscape and enhance immune response by increasing T-cells activation and infiltration and therefore overcoming tumor immune evasion.

Trial Registration NCT: 02153918 and NCT: 02933255

REFERENCES

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Ethics Approval The study obtained ethics approval by NIH IRB. All participants gave informed consent before taking part in these trials.

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