PROTUX Clinical trial: An open label, single institution, pilot study of rituximab neoadjuvant therapy in patients with high risk prostate cancer scheduled to undergo radical prostatectomy.

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Background: A novel, immunosuppressive B cell subpopulation which accelerated the emergence of castrate resistant prostate cancer (PCa) was discovered in mouse models and PCa patients. Ablation of B lymphocytes with anti-CD20 antibody in the mouse models delayed regrowth of PCa. Our objective was to determine whether neoadjuvant treatment of high risk PCa patients with the anti-CD20 immunotherapy, Rituximab, could reduce B cell infiltration of prostate tumors. We report B cell density in tumor and adjacent tissue for 8 patients with high risk PCa who received neoadjuvant rituximab when compared to 11 historical controls.
Methods: An open label, non-randomized, single arm clinical trial for high risk PCa prior to prostatectomy ("PROTUX" NCT01804712) was performed. Subjects were candidates for prostatectomy with curative intent. Enrolled men received one cycle of rituximab (375 mg/m<sup>2<sup> IV once weekly for 28 days), followed in 2 weeks by prostatectomy. Controls were selected from a pathologic biobank with similar patient characteristics and stained concurrently for CD20. Tumor regions were marked by a blinded pathologist and a computer algorithm quantified the immunofluorescence in tumor and adjacent tissue regions. Mean immunohistochemical (IHC) staining area of CD20+ B-cells within the tumor was compared against historical controls.
Results: Mean CD20 IHC stained area in the tumor region of the untreated and treated groups was 0.044 (95% CI 0.028 – 0.062) and 0.027 (95% CI 0.021 – 0.033) p=0.02, respectively. Mean within patient difference (CD20 IHC stained area in tumor –adjacent tissue) was compared against controls, both utilizing unequal variances <I>t</I> test. Mean within patient difference of CD20 IHC stained area was 0.009 (95% CI -0.004 – 0.023) and -0.005 (95% CI -0.028 – 0.017) (p=0.11) in the untreated and treated groups, respectively.
Conclusions: Neoadjuvant rituximab treatment significantly decreased B cell density within tumors compared to historical controls (p=0.02, relative to controls) and appeared to reduce the density of tumor-resident B cells to levels comparable to adjacent normal tissue, (p=0.11 relative to controls). These results provide evidence that rituximab can modify the immune environment of the tumor.

Conflict of Interest: None

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