423 A PHASE 2 STUDY OF IBRUTINIB AS NEOADJUVANT THERAPY IN PATIENTS WITH LOCALIZED PROSTATE CANCER

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Background Treatment of localized prostate cancer with surgery or radiotherapy remains suboptimal with failure rates of 35–40%.[1] Neoadjuvant androgen deprivation therapy improved pathologic outcomes, but did not significantly impact progression-free or overall survival.[2] Prostate cancer with higher density of B cells correlates with higher stage disease and higher risk of recurrence or progression.[3] Elevated levels of BTK (Bruton's tyrosine kinase) – an enzyme known to have critical roles in B cell function - have also been noted in prostate cancer compared to normal prostate tissue, correlate with cancer grade, and may play a role in prostate tumorigenesis. Preclinical modeling shows pharmacologic suppression of BTK inhibits growth of prostate cancer.[4] Ibrutinib, a potent BTK inhibitor, can target B-cell signaling pathways and has an established safety profile. Ibrutinib may act to reduce immunosuppression by intratumoral B cells, which can secrete anti-inflammatory IL-10 and inhibit Th1 and cytotoxic CD8 T cell activity.[5] Therefore, we hypothesized that ibrutinib will augment anti-tumor immune responses in localized prostate cancer.

Methods Accrual began in July 2016 for this ongoing trial (NCT02643667). 23 of 24 planned patients have been enrolled to date. Eligible patients have received no prior treatment for their histologically confirmed prostatic adenocarcinoma and have no evidence of metastatic disease. Patients must have decided upon surgery and been deemed suitable candidates to undergo a radical prostatectomy. Following completion of an initial three patient safety cohort of 840 mg, qd ibrutinib dosing for 14 days, all remaining patients receive treatment with 840 mg/day oral ibrutinib for 28 days. Radical prostatectomy will occur 7–12 days after the last dose of ibrutinib. Patients are assessed 4 weeks after surgery. The primary objectives are to assess safety of ibrutinib and characterize B and T cell infiltration within prostate tissue in the ibrutinib treated patients compared to a reference population. Correlative tissue samples will be obtained to characterize the B and T cell infiltration within prostate tissue treated with ibrutinib compared to an untreated reference population. Correlative blood samples will be used to investigate circulating B and T cells induced by ibrutinib. BTK and PD-L1 expression in tumor and immune-infiltrating immune cells will also be examined. This is the first clinical trial of ibrutinib in prostate cancer, lays the foundation for larger future studies.

Trial Registration NCT02643667

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Ethics Approval This study obtained ethics approval from the Washington University School of Medicine IRB (#201808057), and participating individuals gave informed consent before taking part.

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