Phase II Trial of a Novel Immunotherapy Combination of Pembrolizumab and HER2Bi-armed Activated T Cells (BATS) in Metastatic Castrate Resistant Prostate Cancer

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Background: Metastatic castrate resistant prostate cancer (mCRPC) is a terminal condition and there remains an unmet need for more effective therapies. Immunotherapy has the potential to provide prolonged remission and is worthy of investigation. We conducted a phase 1 study with anti-CD3 x anti-Her2 bispecific antibody (HER2Bi) armed activated autologous T cells that transformed immune cells to exhibit cytotoxicity against prostate cancer. Safety was proven and preliminary efficacy was seen with decrease in PSA and relief in bone pain in three of seven patients. Bone metastasis in prostate cancer have increased PD-1 expression and over expression of CTLA-4 and rationale for synergy led to a phase II trial of combination of immune checkpoint inhibitor, pembrolizumab and BATS in mCRPC.

Patients and Methods: mCRPC patients with 0-1 performance status (PS) and normal liver, kidney and marrow function, pre or post docetaxel chemotherapy are eligible. Primary endpoint of this ongoing study is the rate of 6 month progression free survival. Patients underwent pheresis for mononuclear cell collection which was shipped to the University of Virginia for processing of cells and manufacturing. BATS infusions were given twice weekly for 4 weeks. Pembrolizumab was administered every 21 days starting 1 week prior to BATS infusion and continued for a maximum duration of 6 months. Progression was determined by clinical evaluation, monthly PSA, and radiologic assessment at 3 and 6 months and every 6 month intervals thereafter.

Results: Twelve patients have been enrolled on the study of which one withdrew consent. Median age is 69 years (Range 57 to 76 years). Five of eleven patients had prior docetaxel chemotherapy. Eight of eleven patients had bone and lymph node .metastases, one had lymph node metastases only, and two had peritoneal metastasis. Median PSA was 111ng/ml [Range 5.2 to 378 ng/ml] and 5 and 6 pts had PS of 0 and 1 respectively. The regimen was well tolerated with no unexpected toxicities. Three patients have completed study treatment and remain progression free at 6 months, one death occurred due to unrelated cause and two patients progressed at 12 weeks of therapy. Two patients are demonstrating a 88% and 36% PSA decline. Five patients are not yet evaluable.

Conclusions: The combination regimen of pembrolizumab and BATS is worthy of future exploration in this ongoing trial.

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