Abstract 6540: Regression of metastatic cancer and abscopal effects following *in situ* vaccination by cryosurgical tumor cell lysis and intratumoral immunotherapy: A case series

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Abstract

Purpose: To evaluate the efficacy and safety of a novel *in situ* cancer vaccination method for the treatment of aggressive solid tumors, with an initial focus on metastatic prostate cancer (PCa).

Procedure: 27 consecutive patients with metastatic cancers (21 with PCa and 6 with other cancers), were treated by *in situ* cryosurgical lysis of tumor tissue followed by injection of ipilimumab, pembrolizumab or nivolumab, and sargramostim directly into the zone of lysis. This was followed by 30 daily s.c. injections of sargramostim. Patients received 1 to 3 cycles of the above therapy at intervals of ≥ 1 month. Responses to therapy were assessed by RECIST v.1.1 and for patients with PCa, serum PSA levels. This IRB-approved study, Shulman IRB Protocol #00027107, is a retrospective analysis (with prospective follow-up) of the practice of medicine of two physicians. All patients signed informed consent.

Results: 21 patients with progressive metastatic PCa and 6 with other metastatic cancers (2 bladder, 1 pancreatic, 1 colon, 1 melanoma, and 1 unknown) were treated. RECIST responses for 2 patients (both with PCa) could not be evaluated due to a lack of follow-up imaging. Among the remaining 25 patients, CRs were seen in 9 (36%) patients and a PR in 1 (4%), for an ORR of 40%. SD was seen in 8 (32%) patients, and progression was seen in 7 (28%).

Among the 19 evaluable PCa patients, there were 9 (47%) CRs and no PRs, for an ORR of 47%. 5 (26%) patients showed SD, and 5 (26%) progressed. 13/21 (62%) of patients had post-therapy PSA reductions of >50%.

12 PCa patients were ADT-naïve (11 evaluable by RECIST) and there were 9 with mCRPC (8 evaluable by RECIST), and positive responses were seen in both groups, with ORRs of 55% and 38%, respectively, and PSA reductions of > 50% in 75% and 44% of patients, respectively.

These antitumor responses have been durable in many patients, with CRs to date ranging from 1 to over 4.5 years post-treatment. Encouragingly, this durability of response was observed both in ADT-naïve patients and in those with mCRPC.

Therapy was well tolerated, with AEs in 19/27 (70%) of patients. 24 grade 1-2 AEs were seen in 19 (70%) patients, and 8 grade 3-4 AEs were seen in 5 (19%) patients. Notably, AEs included liver enzyme elevations, hyperthyroidism and hypothyroidism, all of which are associated with autoimmune responses to immunotherapy. One death that was possibly treatment-related, 4 disease-related deaths, and 2 unrelated deaths occurred.

Conclusions: This report describes a novel therapeutic modality utilizing local cryosurgical tumor cell lysis and intratumorally-delivered immunotherapy to treat metastatic prostate cancer and other aggressive solid tumor cancers. Its combination of striking efficacy and good tolerability supports additional formal clinical studies.

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