Background

Little is known of the synergy of combination intratumoral immunotherapy and ablation. We undertook a Phase 2 trial (Abscopal 5001) for patients with metastatic solid cancer (NCT04713371) to assess the safety and efficacy of cryoaablation with concurrent injections of low-dose checkpoint inhibitors and chemotherapy, referred to as Multiplex Combination Intratumoral Immunotherapy (MCII).

Methods

Twelve patients with metastatic cancer and one with sacral chordoma received at least one intratumoral treatment of MCII, preceded by 3–5 days of oral cyclophosphamide. MCII consisted of CT-guided cryoaablation followed by intratumoral injection of ipilimumab, pembrolizumab, and cyclophosphamide. GM-CSF was subcutaneously administered daily for a total of 4 weeks. Treatment was repeated every 4–6 weeks if tumor burden remained stable or reduced as noted by iRECIST criteria. Criteria were modified when follow-up biopsies revealed pathology with minimal or no cancer despite persistent mass(es) on imaging.

Results

Cancers included prostate (4 patients), sarcoma (2), and 1 each of breast, colon, bladder, uterine cervix, tongue, kidney, and sacral chordoma. Eight patients received at least 3 cycles of treatment, two received 2, and three received 1. All patients tolerated the outpatient procedure well and were discharged within 2 hours. Adverse event rate was 69%, all of which were Grade 1 or 2 except for one with delayed cryo-surgical complication. At completion of up to 3 cycles of treatment, partial response (iPR) was observed in 5 patients (38.5%) and stable disease (iSD) in 5 (38.5%), for a disease control rate (iDCR) of 77%; progression was observed in 23%. Disparity between post-treatment imaging and pathologic findings was observed in 4 patients, requiring modification of the iRECIST criteria. Best response ranged from 0–91%, with a mean for responding patients of 38%. Injection site response was observed in 9 (69%), and distal abscopal effect was seen in 4 (31%), including one sarcoma patient with complete abscopal response of lung metastases. Biopsy-confirmed resolution of liver metastases was also noted in the bladder cancer patient. Patients are being followed to determine duration of response.

Conclusions

MCII appears promising, providing 77% disease control rate with manageable, predominantly low-grade adverse events in patients with metastatic cancer. Modification of iRECIST criteria for intratumoral treatment is needed to redefine the primary treatment site response and accommodate disparities between imaging (positive) and pathologic findings (minimal or negative disease).

Trial Registration NCT04713371

Ethics Approval

Ethics approval was granted by Institutional Review Board (Advarra, Columbia, MD; Pro 00045172). The study was also cleared by the US Food and Drug Administration (IND 151900). Each patient provided written informed consent prior to participation and prior to each treatment.

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