74 – Final Results of a Phase II Prospective Trial Evaluating the Combination of Stereotactic Body Radiotherapy (SBRT) with Concurrent Pembrolizumab in Patients with Metastatic Non-Small Cell Lung Cancer (NSCLC)

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Purpose/Objective(s): We report the final results of a phase II prospective trial designed to assess the systemic or "abscopal" response rate in patients who received SBRT after progression on anti-PD-1 immunotherapy.

Materials/Methods: Patients with metastatic NSCLC and two or more measurable lesions were eligible. Histologic analysis of biopsy samples was performed at enrollment, and the number of tumor infiltrating lymphocytes (TILs) was given a qualitative score between 0-3. If patients had progressed on prior anti-PD-1 therapy at the time of enrollment they received SBRT up front and continued on pembrolizumab. If patients were immunotherapy naïve, they were enrolled and received pembrolizumab q3 weeks until disease progression, at which point they received SBRT and continued pembrolizumab. The systemic response to radiotherapy was evaluated using RECIST v 1.1 criteria (with omission of the radiated lesion). The overall response rate after SBRT was defined as the percentage of patients achieving a complete response (CR) or partial response (PR). The disease control rate was defined as the percentage of patients achieving a CR, PR, or stable disease (SD). Adverse events were measured using the common terminology criteria for adverse events (CTCAE) v4. Mass cytometry by time-of-flight (CyTOF) was performed on the peripheral blood of a subset of patients.

Results: 56 NSCLC patients enrolled in the phase II portion of the study. 50 patients were immunotherapy naïve and began pembrolizumab on trial. Of these 50 patients, 16 experienced disease progression and were deemed suitable candidates for SBRT. 6 patients had progressed on anti-PD-1 therapy at enrollment and received SBRT up front. Of the 22 patients allocated to SBRT, 21 completed treatment. The addition of SBRT to pembrolizumab resulted in a mean of 150.67 days before further disease progression. The disease control rate was 57.14%. There were 2 patients (9.52%) who achieved a PR sustained for > 1 year. There were 10 patients (47.62%) who achieved SD after SBRT. Patients with elevated TIL scores (2-3) who achieved SD after SBRT. Patients with elevated TIL scores (2-3) showed improved progression free survival (PFS) when compared with patients that had lower TIL scores (0-1), with a mean of 215 versus 59 days respectively. Patients with an immune-related adverse event survived longer than patients with no immune-related adverse event, with a mean of 208 versus 88 days. CyTOF analysis showed patients with a systemic PR after SBRT had a population of CD8+ CD127- Ki-67+ CD45RO+ T cells that correlated with response.

Conclusion: The addition of SBRT after progression on immunotherapy resulted in increased PFS, a systemic response rate of 9.52%, and a disease control rate of 57.14%. Improved PFS correlated with an increased TIL score, the presence of an immune-related adverse event, and T cell activation status.