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Abstract

Safety of Stereotactic Body Radiation Therapy and Anti-PD-1 Immunotherapy in Non-Small Cell Lung Cancer Patients

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Abstract

Objectives: PD-1 inhibitors are currently being integrated into the management of patients with metastatic non-small cell lung cancer (NSCLC). Many of these patients also benefit from local therapy including integration of Stereotactic Body Radiation Therapy (SBRT). Data regarding the safety of this combination is limited. We report the toxicity of patients with metastatic NSCLC who received anti-PD-1 immunotherapy before, during, or after SBRT.

Methods: A retrospective analysis of 755 patients with NSCLC treated from 2014-2016 with SBRT to metastatic lesions and anti-PD-1 therapy was performed. We identified 45 patients treated with anti-PD-1 therapy and included 20 who received SBRT within 6 months of checkpoint inhibition. Patients with concurrent secondary malignancy were excluded. Primary outcome was toxicity, which was graded by NCI Common Terminology Criteria for Adverse Events v4.0.

Results: The median follow up was 11.2 months (range 4-23.9) and median age was 65 (range 51-83). The 20 patients included received SBRT to 58 lesions, with a median of 2 per patient (range 1-14). Thirty lesions (51.7%) were treated with SBRT within 6 months before, 25 (43.1%) concurrently with, and 3 (5.2%) within 6 months after anti-PD-1 therapy. Of 58 treated lesions, 32 (55.2%) were brain metastases, 13 (22.4%) lung, 4 spinal, 4 lymph nodes, 2 bone (not spinal), 2 liver, and 1 adrenal. The median dose to lung lesions was 54 Gy (range 40-54 in 3-5 fractions) and to brain lesions was 20 Gy (range 18-24 in 1-5 fractions). Nine grade 3-5 toxicities were experienced by 4 patients (20%) within 90 days of SBRT or anti-PD-1. Of those, 1 patient (5%) had toxicities felt to be SBRT-related. This patient had 2 acute grade 3 COPD exacerbations after receiving 54 Gy in 3 fractions to a right middle lobe lung mass (PTV 13.0cm3, lung V20 2.05%). 3 patients (15%) developed toxicities thought to be anti-PD-1 related, including grade 3 myositis, grade 3 autoimmune hepatitis, grade 5 pneumonitis, grade 3 COPD exacerbations, and grade 5 respiratory failure (in the setting of pneumonia and pleural effusion). 1 patient (5%) developed a toxicity related to both anti-PD-1 and SBRT, which was a grade 3 possible pneumonitis. The episode of grade 5 pneumonitis occurred 15 days after anti-PD-1 initiation and 5 months after SBRT. The patient received 54 Gy in 3 fractions to a left lower lobe pleural

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mass (PTV 30.8cm3, lung V20 3.75%). One patient had a possible grade 3 pneumonitis 9 days after anti-PD-1 initiation and 1.7 months after 54 Gy in 3 fractions to right upper lung (PTV 8.3cm3, lung V20 1.1%

Conclusions: In our analysis, there was one grade 5 toxicity due to pneumonitis. Combination anti-PD1 therapy and RT may be a safe combination, but prospective data is required to further understand the role and optimal combination RT and anti-PD-1 therapy in NSCLC