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Clinical Outcomes of Patients with Melanoma Brain Metastases Receiving Stereotactic Radiosurgery and Concurrent Ipilimumab or Pembrolizumab

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Abstract

Objectives: Patients with brain metastases from melanoma historically have a very poor prognosis. Systemic therapy for metastatic melanoma now increasingly utilizes immunotherapy (IT) agents including anti-CTLA4 agents such as ipilimumab and anti-PD1 agents such as pembrolizumab. While a synergistic effect between RT and IT has been hypothesized, published data on clinical outcomes remains limited. This study sought to evaluate clinical outcomes for melanoma patients treated with SRS and concurrent IT.

Methods: We retrospectively reviewed a single institution's experience of consecutive melanoma patients undergoing intracranial RT and receiving concurrent ipilimumab or pembrolizumab between 2010-2015. Concurrent therapy was defined as receiving SRS within 30 days of IT administration. Patients were required to have measurable disease, pre-treatment MRI, and early (<100 days after RT) post-treatment MRI. Patient, treatment and imaging data were reviewed. CNS progression was defined as new enhancing lesion or >20% increase in sum of one-dimensional measurements of intracranial lesions. Intracranial progression-free survival (PFS) and overall survival (OS) were measured from time of intracranial RT, and data was analyzed using Cox proportional hazards modeling and Kaplan-Meier survival analysis.

Results: We identified 32 melanoma patients with 69 brain metastases who received intracranial RT and concurrent ipilimumab (n=24) or pembrolizumab (n=8). Among 24 patients receiving concurrent RT and ipilimumab, median age was 66.5 years old (range 49-87), and 22 (91.7%) had ECOG performance status 0-1; 22 (91.7%) had extracranial disease, and median 1 lesion treated (range 1-7, total 53). Among 8 patients receiving concurrent RT and pembrolizumab, median age was 74.5 years old (range 50-80), and 6 (75%) had ECOG performance status 0-1; 8 (100%) had extracranial disease, and median 1.5 lesions treated (range 1-4, total 16). In univariate analysis, ECOG performance status 0-1 (HR 0.145, p=0.003) was associated with improved OS. For patients receiving concurrent ipilimumab, crude median intracranial PFS was 49 days with 5 (20.8%) patients with intracranial PFS > 1 year. For patients receiving concurrent pembrolizumab, crude median intracranial PFS was 134 days with 3 (37.5%) patients with intracranial PFS > 1 year. Crude median OS was 439 days for patients receiving concurrent ipilimumab with 12 (50%) patients surviving > 1 year. Crude median OS

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was 594 days for patients receiving concurrent pembrolizumab with 5 (62.5%) patients surviving > 1 year. There was no differences by log-rank testing (p>0.05) with respect to PFS or OS for patients receiving concurrent ipilimumab vs. pembrolizumab.

Conclusions: Although the sample size is small, intracranial PFS and OS for melanoma patients with brain metastases using concurrent SRS and ipilimumab or pembrolizumab are superior compared to published historical data, including a significant proportion of patients who have intracranial disease control over one year. Prospective trials are necessary to identify optimal timing of RT and IT, optimal IT agent(s), and other factors to improve intracranial disease control and overall survival.