

The Effect of Immunotherapy Treatment on Local Control for Melanoma Brain Metastases Treated with Stereotactic Radiosurgery

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Introduction

We evaluated the local control of melanoma brain metastases (MBM) following stereotactic radiosurgery (SRS) in the setting of treatment with or without sequential/concurrent immunotherapy.

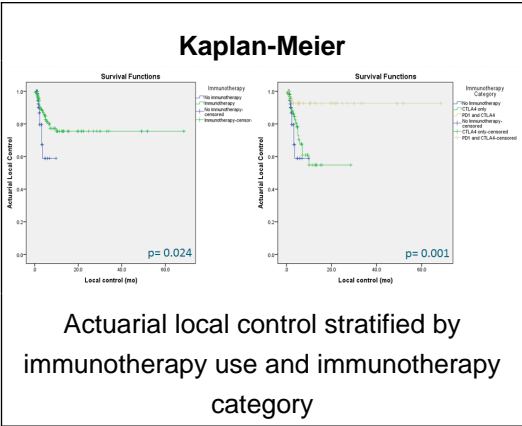
Methods

A single-institution IRB-approved retrospective review was conducted on 68 MBM patients with 228 total metastases treated with SRS between November 2008 to February 2017. We compared local control of metastases in the setting of no immunotherapy versus sequential/concurrent immunotherapy (ipilimumab) versus sequential/concurrent immunotherapy (nivolumab or pembrolizumab with ipilimumab). Local failure was defined as an increase of at least 20% in the sum of longest diameter of a metastasis and its perpendicular diameter. Statistical analysis was performed using Kaplan-Meier estimates with log-rank testing using SPSS

Summary of Characteristics	
Variable	No. (%)
Tumor Volume (cm ³)	
Median	.42
Range	.025-17.16
Dose (Gy)	
Median	22
Range	15-24
Time to local failure (mos) for metastases with local failure	
Median	2.30
Range	1.28-9.99

Results

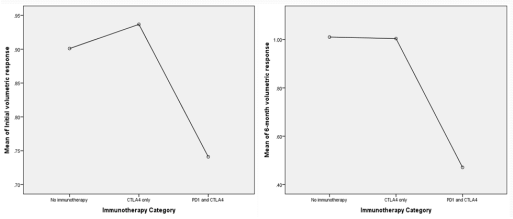
The 6-month LC rate for all lesions was 76.4%. 96 of the 228 lesions (42.1%) received ipilimumab treatments while 60 of the 228 lesions (26.3%) received nivolumab or pembrolizumab with ipilimumab. The 6-month LC rate for the metastases treated only with ipilimumab was 67.7% and the 6-month LC rate for the metastases treated with combined immunotherapy was 92.6%. In comparison, the 6-month LC rate for metastases in the cohort not treated with immunotherapy was 58.9% (p<0.0003). Patient pre-treatment characteristics including GPA score, number of brain metastases treated, and treatment volume were not significantly different between the immunotherapy and non-immunotherapy treatment groups. The mean initial (p<0.002) and 6 month (p<0.0003) volumetric response following SRS was significantly improved for patients receiving combined immunotherapy versus no immunotherapy or ipilimumab alone.



Univariate Analysis of Tumor and Treatment Parameters Versus Local Control

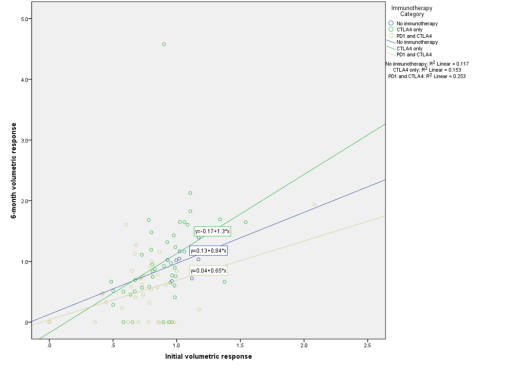
Characteristic	P-Value (log-rank)
Immunotherapy Status (Immunotherapy vs. No Immunotherapy)	0.024
Immunotherapy Category (PD1 and CTLA4 vs. CTLA4 only vs. No Immunotherapy)	0.001
BRAF Mutation Status (Positive vs. Negative)	0.050
BRAF Inhibitor Timing (0-2 months post-SRS vs. 2-6 months post-SRS)	0.688
Tumor Location (Infratentorial vs. Supratentorial)	0.124
Tumor Morphology (Cystic vs. Solid)	0.050
Tumor Volume (<1cc vs ≥1cc)	0.303
Prescription Dose (<21Gy vs ≥21Gy)	0.018
Max Dose (<26Gy vs. ≥26Gy)	0.018

Means Plots



Mean initial volumetric response and 6 month volumetric response stratified by immunotherapy category

Initial Volumetric Response Versus 6 Month Volumetric Response by Immunotherapy Category



2, 6, and 12 Month Actuarial Local Control

Treatment Category	2 Month	6 Month	12 Month
Immunotherapy Immunotherapy No Immunotherapy	95.0% 90.0%	80.1% 58.9%	75.5% 58.9%
Immunotherapy No Immunotherapy CTLA4 only PD1 and CTLA4	90.0% 93.9% 96.4%	58.9% 67.7% 92.6%	58.9% 54.8% 92.6%

Conclusions

Addition of immunotherapy in melanoma brain metastases treated with stereotactic radiosurgery may improve local intracranial tumor control. Our study suggests that local control is significantly impacted by the class of immunotherapy used. Additional studies on volumetric response and radiation necrosis rates following combined radiosurgery/immunotherapy are underway.

Learning Objectives

By the conclusion of this session, participants should be able to:

- 1) Identify an effective treatment for melanoma brain metastases.
- 2) Evaluate outcomes for melanoma brain metastases treated with stereotactic radiosurgery in the setting of sequential/concurrent immunotherapy.
- 3) Discuss, in small groups, the synergistic effect of immunotherapy and radiosurgery on local control for melanoma brain metastases.