Immune and targeted therapies with radiation therapy improves outcomes for melanoma brain metastases patients

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Brain metastases are one of the most common complications of advanced melanoma, requiring multidisciplinary management. Patients who are diagnosed with these metastases have an expected median survival of only 4 to 5 months. Moffitt Cancer Center researchers hope to improve these survival rates following a new study in Annals of Oncology that shows novel immune and targeted therapies with radiation therapy improves the outcomes of patients with melanoma brain metastases over conventional chemotherapy.

Common treatment options for patients with melanoma brain metastases are surgery, whole brain radiation therapy, and focused radiation therapy called stereotactic radiation. These treatments may also be combined with conventional chemotherapy. However, according to Kamran A. Ahmed, M.D., lead study author and resident in the Department of Radiation Oncology at Moffitt, "conventional chemotherapy has failed to improve outcomes in patients with melanoma brain metastases."

Recent advances in therapies that target specific proteins have changed the standard-of-care for melanoma patients without brain metastases, suggesting that immune and targeted therapies may also be beneficial in patients with melanoma brain metastases. This is supported by past studies from the Moffitt researchers showing the immunotherapy agent, nivolumab, which targets the protein PD-1, combined with stereotactic radiation therapy, is effective and safe in patients with melanoma brain metastases.

In their most recent *Annals of Oncology* publication, Moffitt researchers sought to determine if patients with melanoma brain metastases treated with immune and targeted therapies had improved outcomes over patients treated with conventional chemotherapy. They retrospectively analyzed data from 96 patients with melanoma brain metastases who were treated with stereotactic radiation therapy within 3 months of different targeted therapies (anti–PD-1 therapy, anti–CTLA-4 therapy, BRAF inhibitor plus a MEK inhibitor, or a BRAF inhibitor alone) or conventional chemotherapy.

The researchers found that targeted treatments were better able to control tumor growth outside the irradiated field in the brain than standard conventional chemotherapy. Patients who were treated with radiation therapy after anti–PD-1 therapy or BRAF/MEK inhibitors had the best tumor control out of all treatment groups analyzed.

Patients treated with stereotactic radiation and either anti–PD-1 therapy or BRAF/MEK inhibitors also had improved survival when compared to the survival of other treatment groups. Forty-one percent of patients treated with anti–PD-1 therapy and 39 percent of patients treated with BRAF/MEK inhibitors survived 12 months without systemic disease progression, while only 5 percent of conventional chemotherapy patients survived 12 months without systemic disease progression. Similarly, the 12-month overall survival rates were 48 percent for anti–PD-1 therapy, 65 percent for BRAF/MEK inhibitors, and 10 percent for conventional chemotherapy.

"These results reveal that in patients with melanoma brain metastases, anti–PD-1 therapy and BRAF/MEK inhibitors alongside stereotactic radiosurgery offer optimal control of disease spread in the brain," said Ahmed. "Although future randomized studies will be necessary to confirm the benefit of adding anti–PD-1 agents and BRAF/MEK inhibitors to stereotactic radiation to improve the outcomes of patients with melanoma brain

metastases, these results are encouraging."

The study results were published online on Sept. 15 in *Annals of Oncology*.

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