

Study reveals potential new treatment for patients with metastatic melanoma

February 26 2020

Researchers at the University of Cincinnati have uncovered a potentially more beneficial treatment regimen for patients with metastatic melanoma.

The results, published in the *International Journal of Radiation Oncology, Biology and Physics*, show that radiation before immunotherapy may prolong lives of patients with melanoma that has spread to the brain.

"Melanoma brain metastases occur in more than 50% of melanoma patients," says corresponding author Dr. Soma Sengupta, associate professor of neurology at UC, UC Health physician and co-director of the UC Gardner Neuroscience Institute's Brain Tumor Center. She is also the inaugural recipient of the Harold C. Schott Endowed Chair of Molecular Therapeutics.

"While both [radiation therapy](#) and '[immune checkpoint inhibitors](#),' a form of immunotherapy, are used alone or in combination for treatment of this cancer, the role of combination therapies and how these treatments could best be sequenced remains unclear," Sengupta adds.

Immunotherapy is a type of cancer treatment that boosts the body's natural defenses to fight cancer. It uses substances made by the body or in a laboratory to improve or restore immune system function and may work by stopping or slowing the growth of cancer cells. Immune checkpoint inhibitors work by blocking checkpoint proteins from

binding with their partner proteins. This prevents the "off" signal from being sent, allowing the T-cells to kill cancer cells.

In this study, the team conducted a retrospective analysis of patients with surgically removed melanoma brain metastases who underwent treatment with either radiation, immunotherapy or a combination of both between 2010 and 2018. Of 79 specimens, only 17 samples were eligible for this study.

"Among the latter, we specifically investigated the [gene expression](#) between patients who received radiation therapy first then immune checkpoint inhibitors in comparison to the reverse," says Daniel Pomeranz Krummel, research associate professor of neurology at UC and lead author of the paper. "We used a melanoma brain metastases animal model for validation experiments, as well."

Pomeranz Krummel says results showed that the combination of radiation therapy and immune checkpoint inhibitors correlated to better patient survival when compared to radiation therapy alone.

"Specifically, we found that radiation followed by immunotherapy was superior compared to immunotherapy followed by radiation therapy," he says, adding that his observation in patients was also observed in the melanoma animal model. "More genetic analysis of the tissue showed that [radiation](#) therapy followed by immunotherapy showed that the genes causing [cell death](#) signaling, usually fighting the cancer, were restricted and key indicators of inflammation were present."

"Our study provides initial insights into the optimal sequence of treatment following surgical removal of melanoma brain metastases," adds Sengupta, noting that this was a small sample of patients and that follow up studies are needed. "Clinical trials examining the best sequence of these treatments are necessary."

More information: Daniel A. Pomeranz Krummel et al, Impact of Sequencing Radiation Therapy and Immune Checkpoint Inhibitors in the Treatment of Melanoma Brain Metastases, *International Journal of Radiation Oncology*Biology*Physics* (2020). [DOI: 10.1016/j.ijrobp.2020.01.043](https://doi.org/10.1016/j.ijrobp.2020.01.043)

Provided by University of Cincinnati

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