Two New Clinical Trials Offer Hope for Brain Cancer Patients

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Craniopharyngiomas are a rare type of brain tumor that arise near the pituitary gland and are very difficult to treat, whether surgically or with radiation therapy, without inflicting vision loss, memory loss, or hormone disruption. Even in cases when the tumor is successfully removed, craniopharyngiomas are notorious for coming back.

But a new clinical trial led by former Damon Runyon Clinical Investigator Priscilla K. Brastianos, MD, and her colleagues at Mass General Cancer Center indicates that there may be a better way to treat these tumors—with drugs that already exist. After discovering that 95% of craniopharyngiomas carry a mutation in the BRAF gene, which controls cell growth and is commonly mutated in melanoma, Dr. Brastianos and her team tested a drug combination that has been approved for the treatment of melanoma in patients with craniopharyngiomas. The drug targets both the BRAF and MEK gene, which work closely together.

The results, published this month in the New England Journal of Medicine, were extraordinary. Fifteen of the sixteen study participants experienced a dramatic reduction (90% on average) in tumor size, a response that Dr. Brastianos called “unprecedented” in brain tumors. The team hopes their results will encourage further investment into targeted therapies for brain cancer as an alternative to high-risk surgery and radiation therapy.

Much more common than craniopharyngiomas are brain metastases, which occur when a tumor spreads from its original tissue into the brain. Incidence of brain metastasis is on the rise in the U.S., likely due to longer survival rates for patients with metastatic cancers and improved detection with MRI technology. However, patients with brain metastases continue to have poor prognoses and limited treatment options.

Fortunately, Dr. Brastianos and her colleagues offer good news on this front as well. At the 2023 ASCO Annual Meeting in June, the team presented results from a different clinical trial that tested a immunotherapy drug called pembrolizumab in patients with metastatic brain cancer. Pembrolizumab is a checkpoint inhibitor: it works by blocking a protein called PD-L1, found on the surface of some cancer cells, from binding to immune T cells and deactivating them.

The results, published in Nature Medicine, show that nearly half of the trial participants (42%) benefitted from treatment with pembrolizumab. Notably, seven patients receiving the drug survived longer than two years, compared to the estimated average of four to six months.

The next step, according to the team, is to look for other biomarkers, especially among the study's longerterm survivors, that can help predict a patient's response to the therapy. Interestingly, the seven "exceptional responders" mentioned above had different primary tumors—breast cancer, melanoma, and sarcoma—suggesting they may have had something else in common.

"Our study illustrates the promise of checkpoint inhibitors for future therapeutic strategies for brain metastases," said Dr. Brastianos. "And our work suggests that the decision to give a checkpoint inhibitor should not be based solely on the primary tumor's origin—it is likely that there are yet-to-be determined factors that may predict response. Future studies to identify these factors may help guide, inform, and personalize treatment for patients with brain metastases."

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