

Study suggests best order of treatment for brain metastases in EGFR lung cancer

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About 10 percent of lung cancers in the United States and as many as 40 percent in Asia are driven by mutations in the EGFR gene. EGFR targeted treatment advances over the previous decade now result in multiple options for controlling the disease in the body, but due to the reduced ability of many of these drugs to penetrate into the brain, treating of disease in the brain remains challenging. When brain metastases are seen at diagnosis before a patient has tried EGFR-targeted drugs, it has been an open question whether doctors should try drugs alone just in case they work in the brain or move directly to whole-brain radiotherapy or stereotactic radiosurgery (a tightly focused form of radiation) first, followed by targeted medicines. A study published in the *Journal of Clinical Oncology* looks back at 351 patients with EGFR mutant lung cancer and brain metastases treated at six institutions to offer compelling preliminary evidence as to the best sequence of these techniques: Radiation followed by targeted medicines resulted in the longest overall survival.

"This particular study illustrates a remarkable finding and raises an interesting question. First of all, these [patients](#) all had tumors that had spread to the [brain](#). Before we had these EGFR-directed medicines, their average survival would have been less than a year. But for patients treated with the newer medications, even if the cancer has spread to the brain, we are seeing survival ranging from 2-4 years on average, and that is a sign of fantastic progress for at least some [lung cancer](#) patients," says Brian Kavanagh, MD, MPH, FASTRO, professor and chair of Radiation Oncology at the University of Colorado Cancer Center, and President of

the American Society for Radiation Oncology (ASTRO).

"Because these drugs do not penetrate into the brain very well, we still have to figure out what the best thing to do for tumors that have spread to that location. Do we just use the medicines alone and watch these patients carefully and react accordingly if they have a problem in the brain, or do we take action sooner rather than later and treat the tumors in the brain before they cause a problem? Our observations suggest that the second choice may be a better one for the drugs commonly used as first line EGFR therapy to date," says D. Ross Camidge, MD, PhD, Joyce Zeff Chair in Lung Cancer Research at the CU Cancer Center and director of Thoracic Oncology at the CU School of Medicine.

Specifically, the study evaluated patients in three groups. As above, those that received [stereotactic radiosurgery](#) and then an EGFR-directed drug had a median overall survival of 46 months. Those that received whole-brain radiotherapy followed by drug survived a median 30 months. And those that received drug first, followed by either of the radiation protocols as needed, survived a median 25 months.

However, Camidge also adds, "The study wasn't randomized, though, so we can't exclude other factors that might also have influenced the results. For example, radiosurgery may be used in those with a lesser burden of brain disease, whereas whole-brain radiation may be preferred in patients with more disease shortening their survival separately from the impact of the drug or radiation technique."

The study is a collaboration between Kavanagh and Camidge at CU Cancer Center and colleagues at the Yale, Vanderbilt, Memorial Sloan Kettering, Cleveland Clinic, and UCSF Cancer Centers. While this retrospective analysis offers powerful initial evidence for the best use of these therapies, the team hopes that it will also inform a more definitive trial that could test these interventions prospectively.

"Ultimately, it is possible that there is some middle path that is best. We suspect that some patients with very tiny tumors in the brain, maybe ones that measure only 2-3 millimeters or so, can probably be safely watched closely for a while, and maybe we only need to treat them with radiosurgery when the tumors grow to a somewhat larger size," Kavanagh says. "We are currently in discussions with our colleagues at the collaborating institutions who contributed to this paper to design a study that might answer that question to everyone's satisfaction."

More information: *Journal of Clinical Oncology*, [DOI: 10.1200/JCO.2016.69.7144](https://doi.org/10.1200/JCO.2016.69.7144)

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