Taking RTKI drugs during radiotherapy may not aid survival, worsens side effects

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Taking certain cancer-fighting drugs while undergoing radiation therapy may not increase survival for patients, but may, instead, increase side effects, according to a team of researchers. The drugs, however, may be beneficial for patients who are not undergoing radiation therapy.

In a meta-analysis of 11 different studies, the researchers said that treatments that included both radiotherapy and receptor tyrosine kinase inhibitor—or RTKI—drugs did not significantly improve survival rates of patients, but appeared to worsen negative side effects, such as fatigue, nausea and diarrhea, according to Nicholas G. Zaorsky, assistant professor of radiation oncology and public health sciences, Penn State College of Medicine.

"In the 1990s and 2000s there was a push in oncology to study these receptor tyrosine kinase inhibitor drugs, which target receptors that are either expressed on the cancer cells, or expressed on cells that surround cancer cells," said Zaorsky. "The receptors are thought to help cancer cells grow, essentially pressing the gas pedals for the cancer cells. Thus, blocking the gas pedal with RTKIs has been thought to slow down cancer cells."

Understanding how RTKI drugs, which include names like Avastin, Erbitux, Iressa and Tarceva, react with radiation therapy is important because of the radiotherapy's widespread use, he added.

"Radiation therapy is prescribed to about two-thirds of cancer patients

and a lot of these patients are also receiving receptor tyrosine kinase inhibitor (RTKI) drugs," said Zaorsky. "What hasn't been known is if these drugs added to patients receiving radiation therapy help or hurt patients."

In a meta-analysis, researchers statistically analyzed the results of 11 large clinical trials that featured both RTKI and radiation therapy. The researchers who undertook these trials, which focused on solid forms of cancer and included 5,284 patients, evaluated both survival rates and side effects. The results of the meta-analysis reveal that adding RTKI drugs to radiation therapy did not significantly improve survival, but it was associated with increased side effects for patients undergoing both treatments.

"Because it's such a broad question and because there are so many drugs available for so many different types of cancers, we decided to do a meta-analysis using all of the published data from around the world," said Zaorsky.

Because the combination of radiation therapy and RTKI drugs does not appear to improve survival, that does not mean the effectiveness of the drugs alone are in question, said Zaorsky. For many cancer patients who have not undergone simultaneous radiation therapy, these drugs have been immensely helpful, he added.

The study may help guide future clinical trials looking into RTKI and radiation therapies, as well as doctors prescribing these therapies to current cancer patients, according to the researchers, who released their findings at the 2019 American Society for Radiation Oncology annual meeting and in an issue of the *International Journal of Radiation Oncology*. For example, these results suggest that further clinical trials of radiation therapy and RKTIs may not be effective. Further, in some cases, it may be beneficial to hold RTKI drugs while the patient is

receiving radiation therapy because it could increase side effects without necessarily improving the patient's chances of survival.

More information: E. Batchelder et al. Radiotherapy and Receptor Tyrosine Kinase Inhibition for Solid Cancers: An International Meta-Analysis of 11 Studies with 5,284 Patients, *International Journal of Radiation Oncology*Biology*Physics* (2019). DOI: 10.1016/j.ijrobp.2019.06.229

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