Traditional chemotherapy superior to new alternative for oropharyngeal cancers

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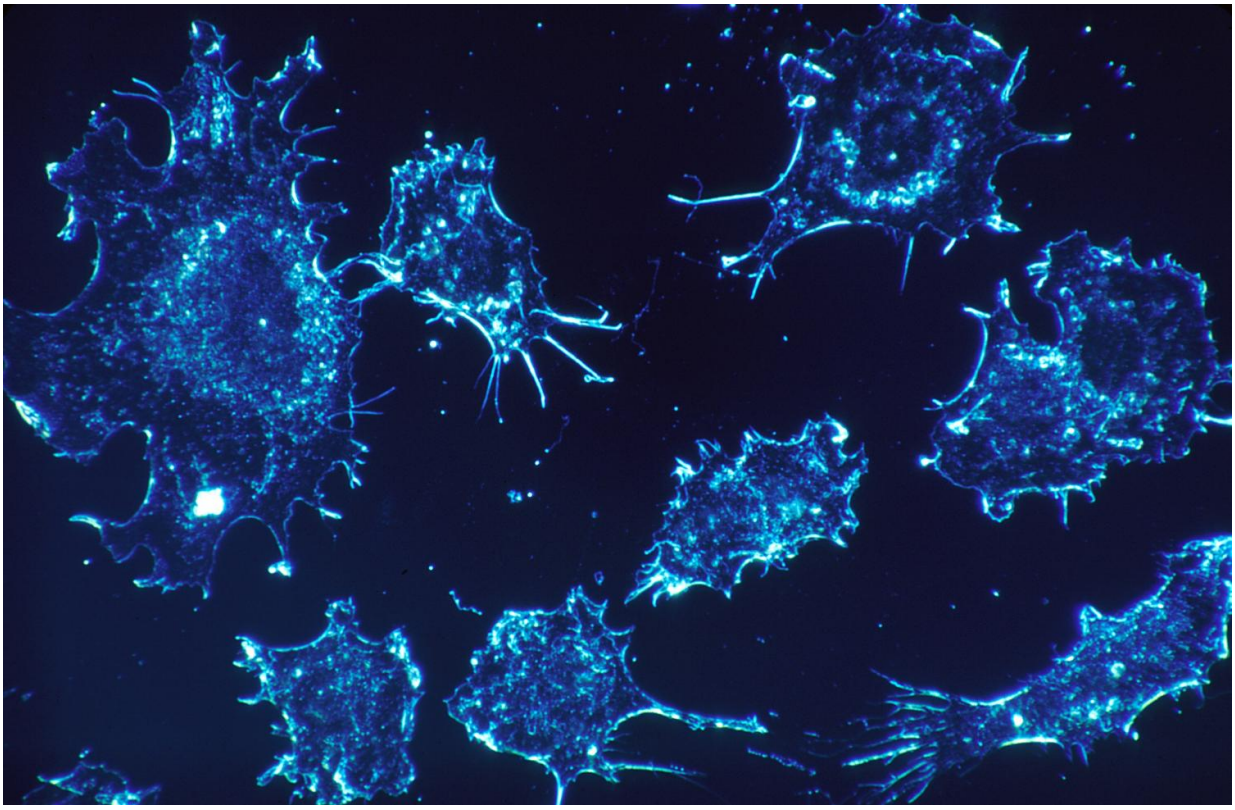

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A drug increasingly used in combination with radiotherapy to treat a type of cancer that forms in the tonsils or the base of the tongue is inferior to a previously favored option, according to a large, clinical trial led by School of Medicine researchers that tracked patient survival and disease

progression.

Patients randomized to receive the newer drug, cetuximab, had poorer outcomes than those who were randomized to receive the older drug, cisplatin, the trial found. Both drugs were administered in combination with radiotherapy.

The results of the trial, which included nearly 1,000 participants at 182 health care centers across the country, were published online Nov. 15 in *The Lancet*.

The trial was sponsored by the National Cancer Institute and conducted through NRG-Oncology, which is part of the National Clinical Trials Network. Patients from across North America were enrolled by NRG-Oncology researchers.

"Although one prior study suggested that cetuximab may provide survival benefits of similar magnitude as cisplatin when combined with radiation but with fewer long-term side effects, these two regimens have not been compared head to head in such a large study before. The result of our study showed that this is not the case," said Quynh-Thu Le, MD, professor and chair of radiation oncology. "Unfortunately, this means we are back to square one. We have to figure out a better way to reduce toxicity for these patients."

Le, who also holds the Katharine Dexter McCormick and Stanley McCormick Memorial Professorship and chairs the head and neck cancer committee of NRG-Oncology, is the senior author of the study. Maura Gillison, MD, Ph.D., professor of thoracic/head and neck medical oncology at MD Anderson Cancer Center in Houston, and Andy Trotti, MD, a professor of radiation oncology at Moffitt Cancer Center in Florida, share lead authorship.

HPV-positive cancer

The trial focused on patients with oropharyngeal cancers that are positive for the presence of human papillomavirus, or HPV. It's long been known that infection with specific subtypes of HPV confers an increased risk for cervical, anal and oropharyngeal cancers arising in the soft palate, the base of the tongue and the tonsils. The National Cancer Institute estimates that about 70 percent of oropharyngeal cancers are caused by HPV infection.

Fortunately, many of these cancers are highly treatable with radiation and chemotherapy. But because many of these patients are diagnosed at a relatively young age, it is particularly important to minimize any toxic, long-term side effects of their treatment. Although effective in promoting survival, cisplatin can cause potentially lasting adverse effects, including hearing loss and kidney damage. Physicians have increasingly been turning to cetuximab plus radiotherapy after one study suggested cetuximab conferred a survival benefit of similar magnitude as cisplatin when combined with radiation but with fewer side effects.

Le and her colleagues conducted a randomized, prospective multicenter trial to determine whether the drugs were equally effective at treating HPV-positive oropharyngeal cancer. From June 2011 to July 2014, 987 people with the disease were enrolled and randomly assigned to receive either cetuximab or cisplatin, both in combination with radiotherapy. (Some patients were subsequently deemed to be ineligible.)

The researchers found that the estimated five-year overall survival of the 399 patients assigned to receive cetuximab was 77.9 percent, compared with 84.6 percent for the 406 patients who received cisplatin.

Another measure of effectiveness is progression-free survival, or the period of time after treatment during which the cancer does not

progress. The researchers estimated that 67.3 percent of the patients in the cetuximab group would achieve five years of progression-free survival, compared with 74.8 percent of those who had received cisplatin .

In addition, the proportions of patients who suffered short-term and long-term toxicity as a result of their treatments were not significantly different between the two groups.

Assumption 'did not pan out'

"Unfortunately, our assumption that cetuximab would be less toxic but confer similar survival advantages did not pan out," Le said. "Cisplatin should still be the standard of care for most of these patients while we investigate other potentially less toxic treatments, such as immunotherapy."

More information: Maura L Gillison et al. Radiotherapy plus cetuximab or cisplatin in human papillomavirus-positive oropharyngeal cancer (NRG Oncology RTOG 1016): a randomised, multicentre, non-inferiority trial, *The Lancet* (2018). DOI: 10.1016/S0140-6736(18)32779-X

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