

Study provides roadmap to more personalized cancer treatment

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Researchers have found that people with advanced head and neck squamous cell carcinoma and the KRAS-variant inherited genetic mutation have significantly improved survival when given a short course of the drug cetuximab in combination with standard chemotherapy and radiation.

The study was led by UCLA Jonsson Comprehensive Cancer Center member Dr. Joanne Weidhaas in collaboration with colleagues at the NRG Oncology RTOG. They discovered that people with both head and neck squamous cell carcinoma and the KRAS-variant who were treated with standard treatment, but not with cetuximab, had a higher risk of failing treatment and developing metastatic disease, meaning the [cancer](#) spreads to distant organs and is incurable.

In 2006, researchers discovered the KRAS-variant, an inherited genetic mutation found in up to 25 percent of people with cancer. The KRAS-variant is a biomarker that disrupts a class of important regulators, called microRNAs, which were discovered in 2000. The mutation has been shown to predict response to cancer therapy for many cancers, including head and neck cancer. It was not previously understood exactly how this biomarker worked.

The current standard of care for advanced head and neck [squamous cell carcinoma](#) involves chemotherapy and radiation. However, this approach typically results in a 50 percent treatment failure. Cetuximab is a monoclonal antibody that was previously shown to be beneficial for these patients when combined with radiation and chemotherapy. Yet a randomized phase 3 trial was unable to identify those who benefited from cetuximab.

Weidhaas' team analyzed available samples from the NRG Oncology RTOG 0522 randomized phase 3 clinical trial of cetuximab in combination with chemotherapy and radiation therapy.

The researchers accessed 413 biological samples from participants in the trial. Although the sample size was not large, they found a significant benefit of cetuximab treatment for all people with the KRAS-variant. Furthermore, the team found that cetuximab may in fact be working by helping the immune system of people with the KRAS-variant better fight

their cancer.

This is the first evidence that the KRAS-variant can predict response to [radiation](#), and that individuals with the KRAS-variant may have an altered immune system. This likely explains both elevated cancer risk as well as benefit from [cetuximab](#) for these individuals. The results also indicate the KRAS-variant's potential to identify people who will respond differently to therapies that depend on the immune response. Weidhaas said that using the KRAS-variant and biomarkers like it to personalize [radiation therapy](#) as well as developing immune therapies for all cancer is very promising.

More information: Joanne B. Weidhaas et al. The-Variant and Cetuximab Response in Head and Neck Squamous Cell Cancer, *JAMA Oncology* (2016). [DOI: 10.1001/jamaoncol.2016.5478](https://doi.org/10.1001/jamaoncol.2016.5478)

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