

Advanced bladder cancers respond to immunotherapy regardless of gene mutation status

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UNC Lineberger's William Kim, MD, and colleagues report their research demonstrated that patients with advanced bladder cancers whose tumors have a mutated FGFR3 gene respond to immunotherapy in a manner that is similar to patients without that mutation. This discovery runs counter to previous research that suggested FGFR3-mutated bladder cancers should not be treated with immunotherapy. Credit: UNC Lineberger Comprehensive Cancer Center

A new study has demonstrated that patients with advanced bladder cancers whose tumors have a mutated FGFR3 gene respond to immunotherapy treatment in a manner that is similar to patients without that mutation, a discovery that runs counter to previous assumptions. This research, led by scientists at the University of North Carolina Lineberger Comprehensive Cancer Center, has important implications for patients who have not been offered immunotherapy because of their genetic profiles.

The findings are published in the *British Journal of Cancer*.

The National Cancer Institute estimates that 83,730 people in the United States will be diagnosed with bladder cancer in 2021, and the disease will cause 17,200 deaths. While the cancer is treatable when diagnosed early, the five-year survival rate is approximately 6 percent in advanced cases where the cancer has spread to other parts of the body. Within that low survival group of patients, about 15 percent of their tumors have [mutations](#) in the FGFR3 gene, making the gene overactive and contributing to high mortality for the disease.

"Despite prior work suggesting that FGFR3-mutated bladder cancers should not be treated with [immunotherapy](#), our study demonstrates the opposite, so we believe that immunotherapy should be offered without hesitation," said UNC Lineberger's William Y. Kim, MD, Rush S. Dickson Distinguished Professor of Medicine and professor of Genetics and the paper's corresponding author.

There have been several recent significant treatment advances for bladder cancer. In 2019, the FDA approved a drug, erdafitinib (Balversa), that targets FGFR3 and prolongs survival. Additionally, immune checkpoint blockade drugs, commonly known as immunotherapies, have recently been approved for advanced bladder cancer. Prior to this decade, treatment was primarily limited to systemic, platinum-based chemotherapy.

"Clinical trials have shown that bladder cancers with FGFR3 mutations have fewer immune cells, primarily T cells, than cancers without the mutation. Because tumors with low levels of [immune cells](#) tend to respond poorly to immune checkpoint blockades, it has been hypothesized that those patients would have low response rates to

immunotherapy," said UNC Lineberger's Tracy Rose, MD, MPH, assistant professor at the UNC School of Medicine and the paper's co-first author.

To test the hypothesis, UNC Lineberger researchers designed a study to compare tumor tissue samples and [clinical trials](#) data from 17 patients with FGFR3-mutated [bladder cancer](#) to 86 patients whose tumors did not have the mutation. The investigators found that patients with FGFR3 mutations responded to immunotherapy equally as well as those without the mutations. At a [cellular level](#), they also found equivalent diversities of T cell receptors and a similar balance of immune suppression and immune activation signals in tumors with and without FGFR3 mutations. This equivalency, or balance, indicates a similar chance of benefiting from immunotherapy.

"The standard of care for advanced [bladder cancer](#) is getting pretty complicated, but having more options is a good thing," Kim said. "Today, most patients will get chemotherapy and then, if needed, FGFR3-altered tumors can be treated with either erdafitinib or immunotherapy."

The researchers hope to establish a clinical trial to test whether patients with FGFR3 alterations benefit more from erdafitinib or immunotherapy.

"Our study does not rule out the possibility that erdafitinib will synergize with immunotherapy," said William Weir, co-first author and an MD-Ph.D. student at UNC-Chapel Hill. "If anything, the fact that FGFR3-altered patients benefit from immunotherapy argues that this may be a reasonable approach."

More information: Tracy L. Rose et al, Fibroblast growth factor receptor 3 alterations and response to immune checkpoint inhibition in metastatic urothelial cancer: a real world experience, *British Journal of Cancer* (2021). [DOI: 10.1038/s41416-021-01488-6](#)

Provided by UNC Lineberger Comprehensive Cancer Center

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