Medical Xpress

Rush clinical trial provides new kidney cancer immunotherapy option

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Rush University Medical Center is among the first hospitals in the nation, and the only one in Illinois, to provide patients fighting advanced kidney access to a new combination immunotherapy that targets different immune system cells and processes than a widely used therapy that has been proven effective for some patients but had little effect on others.

"Ten years ago, patients with advanced kidney cancer had few options and little hope. But just in the last few years, new drug combinations have resulted in long-lasting remission for many, but more investigations need to be done to help those kidney cancer patients who have not yet benefited," said Dr. Timothy Kuzel, Rush's chief of Hematology, Oncology and Cell Therapy and the clinical trial's principal investigator. Patients over the age of 18 who have been diagnosed with renal cell carcinoma—the most common form of kidney cancer—that has metastasized, or spread, are potential candidates for this investigational therapy.

The nationwide, multisite phase two clinical trial, titled FRACTION-RCC, is designed to test whether the new immunotherapy combination (combining nnivolumab with other investigational immunotherapy agents) is more effective than the currently used drug combination (nivolumab and ipilimumab) that has become an important kidney cancer treatment in recent years. While the current immunotherapy drugs have proven to extend kidney cancer patients' survival rate and enhance quality of life for some patients, many patient have no response

at all.

The American Cancer Society estimates that 14,000 Americans died of kidney cancer in 2016, and more than 63,000 of new cases were diagnosed. Surgery has been the standard treatment for kidney cancer for decades because the disease is often resistant to both chemotherapy and radiation. And while a class of drugs known as immune modulators has been used successfully on a small percentage of kidney cancer patients since the 1990s, the approval of new drugs including nivolumab in 2015 and subsequent use of the nivolumab in combination with another drug, ipilimumab, have made treatments that use a patient's immune system potentially the most effective treatment option.

Developing 'immunotherapy cocktails,' identifying immune biomarkers

Both nivolumab and ipilimumab are monoclonal) antibodies which help the immune system's main weapon, called T cells, to detect and destroy diseased or infected cells. Nivolumab helps block the molecular signals that cancer cells send to fool the immune system into not recognizing them as a threat, while ipilimumab targets a protein cancer cells use to signal the body to produce fewer T cells.

"Nivolumab removes the brakes that cancer cells have put on the immune system, while ipilimumab steps on the gas and accelerates the production of T cells," Kuzel explains. "But we know this combination doesn't work for everyone and that there are several other potential targets that activate the immune system's tumor-fighting capabilities. Thus we're excited about the new study to learn whether a series of novel immunotherapy combinations—immunotherapy cocktails—can be integrated into kidney cancer treatments."

The new clinical trial adds to Rush's wider research efforts towards identifying immune system biomarkers that can help oncologists predict which immunotherapy is best suited for individual patients battling several types of cancer.

Blood samples of many cancer patients undergoing immunotherapy treatments at Rush are analyzed to measure immune biomarkers secreted by the tumor detected in peripheral blood mononuclear cells, a critical component of the immune system. A biomarker is a biological substance that can indicate the presence of a disease, or predict how well someone may respond to a treatment. But because of the complex interactions between the immune system and a tumor, immune-biomarkers are more difficult to identify.

"Most cancer biomarkers, such as specific genetic mutations or proteins, are binary—they are either present or not. But as we better measure and understand the intricate ways in which our immune system and cancer cells do battle, the quicker we can develop new ways for more people to activate their immune systems to win that battle." Kuzel added.

Kuzel has led the development of a series of immune-oncology therapies, authored or co-authored more than 250 journal articles, editorials and book chapters, and oversaw in 2016 the Society for Immunotherapy of Cancer's regional Immunotherapy 101 program designed to help clinical oncologists integrate immunotherapies into the clinical management for their patients. Learn more about the full range of Rush University Medical Center's cancer care and research.

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