Treatment shrinks bladder cancer tumors in patients that can't tolerate chemotherapy

October 11 2016

A treatment harnesses the immune system to shrink tumors in bladder cancer patients that cannot take the most effective chemotherapy.

These are the findings of a clinical trial led by researchers at NYU Langone Medical Center and its Perlmutter Cancer Center and just presented at the ESMO 2016 Congress, the annual meeting of the European Society for Medical Oncology.

The new study found that injections of the experimental agent pembrolizumab shrank tumors by at least one third in 24 percent of patients. Of those, six percent saw their tumor lesions disappear.

All patients in the study were unable to take the current standard of care, cisplatin, which is a chemotherapy that prevents tumor cells from repairing damage to their DNA. Used widely since the 1970s, cisplatin extends survival to slightly more than a year, but nearly half of bladder cancer patients, most of them elderly and ill, cannot take it because of its toxic effects on nerves and kidneys.

"While six percent may seem like a smaller number in terms of complete responses, these patients, unable to use cisplatin, currently have no approved first-line treatment option and typically die within ten months," says lead study investigator and medical oncologist Arjun Balar, MD. "These findings offer hope to individuals with advanced disease."

About 76,000 Americans will be diagnosed with bladder cancer in 2016,

with men three times more likely than women to develop the disease.

"The need for new treatments here could not be more urgent," says Balar, an assistant professor and director of the Genitourinary Medical Oncology Program at Perlmutter.

Easier on Patients

While 67 percent of patients in the study experienced side effects linked to pembrolizumab treatment, most were tolerable, including fatigue (14 percent) as the most common along with itchy skin and diarrhea. Five percent of patients in the study stopped therapy because of side effect severity.

When compared to chemotherapy, the side effect profile with pembrolizumab was "far less severe", Balar says. In addition, 83 percent of those treated in the current trial had a response that lasted for at least six months, while responses to most chemotherapies are temporary, he says.

Part of a new class of drugs known as checkpoint inhibitors, pembrolizumab has been approved since 2014 for the treatment of head and neck squamous cell carcinoma, melanoma, and non-small cell lung cancer. The current clinical trial, called KEYNOTE-052 (ClinicalTrials.gov, NCT02335424), was designed to enroll approximately 350 patients at 50 research centers in the United States and Europe, with the results from the first 100 patients included in the current, interim analysis.

The study results revolve around the immune system, which is designed to attack foreign organisms like bacteria, while leaving the body's healthy cells alone. To spare normal cells from immune attack, the system uses "checkpoints"- sensors on immune cells that turn them off

when they receive the right signal. The body recognizes tumors as abnormal, but cancer cells hijack checkpoints to turn off immune responses.

Among the most important checkpoints is a protein called programmed death receptor 1 (PD1), which is shut down by pembrolizumab to make tumors "visible" again to the immune system.

Past studies have found that levels of PD1, as well as of its signaling partners (e.g. PD ligand 1 or PDL1), vary dramatically across patients with bladder cancer. This has frustrated efforts to arrive at a consensus threshold for when doctors should recommend that a given patient receive pembrolizumab.

To get at this question, the study authors analyzed responses to pembrolizumab in two patient groups: one with PDL1 expressed in at least 1 percent of their immune and cancer cells, and a second with PDL1 in at least 10 percent of their cells. Researchers found that 13.3 percent of patients with PDL1 levels in at least ten percent of their immune and cancer cells saw their tumors disappear compared to 6.3 percent in the group with 1 percent PDL1 expression and 6 percent in the entire patient population. The separation in results may point to the 10 percent cut-point as a good biomarker to select patients most likely to respond, Balar says, "even though PD-L1 expression is only part of the story."

Provided by New York University School of Medicine