First prostate cancer therapy to target genes delays cancer progression

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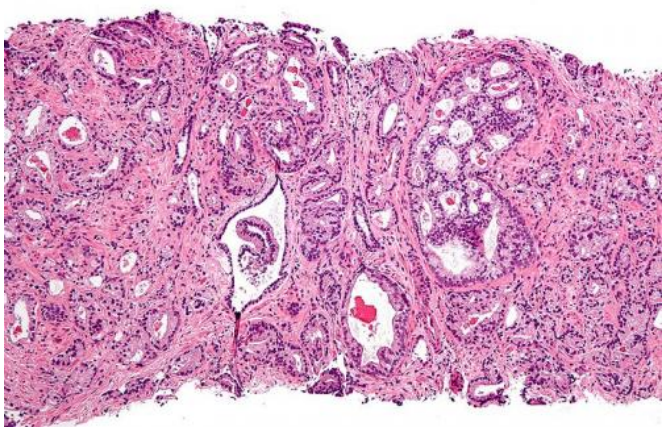

Micrograph showing prostatic acinar adenocarcinoma (the most common form of prostate cancer) Credit: Wikipedia

For the first time, prostate cancer has been treated based on the genetic makeup of the cancer, resulting in delayed disease progression, delayed time to pain progression, and potentially extending lives in patients with advanced, metastatic prostate cancer, reports a large, international phase 3 trial. One of the principal investigators is from Northwestern Medicine.

The PROfound trial treated men with metastatic prostate cancer that has progressed after several types of prior therapies, including hormone therapy .

This marks a significant advance for prostate cancer treatment, which has lagged behind other common cancers with regard to precision therapy, now the standard of care in breast, ovarian and lung cancers.

"Treatments for metastatic, hormone-resistant prostate cancer have continued to use 'one-size-fits-all' approaches, overlooking the genetic make-up of the tumor," said Northwestern principal co-investigator Dr. Maha Hussain.

"Our results show the potential of a genetically targeted treatment for patients with advanced disease," Hussain said. "I am confident we are now entering a new era of personalized care and precision medicine for metastatic prostate cancer."

Hussain is a professor of medicine at Northwestern University Feinberg School of Medicine and deputy director of the Robert H. Lurie Comprehensive Cancer Center of Northwestern University. She also is a Northwestern Medicine medical oncologist.

The results will be presented Sept. 30 during the Presidential Symposium at the 2019 European Society of Medical Oncology in Barcelona.

In 2019, there are an estimated 174,650 new cases of prostate cancer in the U.S., and 31,620 deaths from the disease, according to the National Cancer Institute. In 2016, there were an estimated 3,100,000 men living with prostate cancer in the U.S.

The trial preselected patients who have genetic alterations in the genes that enable cells to repair themselves from damage. Those most commonly known are the BRACA 1, BRACA 2 and ATM genes, but there are several others. Patients were randomly assigned to receive olaparib, which has been used in other cancers (ovarian, breast and pancreatic) with similar alterations—or standard hormone therapy with either abiraterone and prednisone or enzalutamide.

Olaparib blocks PARP, which is a protein that helps damaged cells repair themselves. Some cancer cells rely on PARP to keep their DNA healthy. When PARP is stopped from repairing DNA damage, the cancer cells die.

"We want to prevent those renegade cancer cells from repairing themselves," Hussain said.

There were two cohorts of patients based on the type of genetic alteration.

mage that must be repaired in order for the cancer cells to keep growing.

Patients in cohort A (with alterations in BRACA 1, BRACA 2 or ATM) who took olaparib had a significant extension of time before the disease grew and spread. The average time before the disease progressed was more than double: 7.4 months for the olaparib-treated patients compared to 3.6 months for the group of patients who were treated with standard hormone therapy of abiraterone and prednisone or enzalutamide.

At six months following treatment in this same cohort, about 60% of the men receiving olaparib showed no disease progression compared to 23% in the control groups. After 12 months, about three times as many men on olaparib remained progression free (28% compared to 9% in the control groups). The control groups received standard hormone treatments used for prostate cancer. As soon as men in the control groups showed disease progression, they were given olaparib.

The benefit was across the board, irrespective of the patient's cancer location, prior treatment, where the cancer had spread (bone, liver or lymph nodes), the patient's PSA (prostate-specific antigen) or age.

When prostate cancer spreads to the bone, it can cause significant pain. When patients received the drug, they had a longer time before pain occurred or progressed, Hussain said.

Scientists are still following patients who will ultimately die from their cancer, but the drug appears to prolong survival. The percentage of patients alive at six, 12 and 18 months is higher with the drug. One-year survival was 73% for the drug versus 56.94% for the control group; at 18 months, survival was 56.3 % for the drug versus 42.13% for the control group.

Trends were similar in cohort B, which was composed of a different group of genetic alternations, but were not as powerful as cohort A.

Provided by Northwestern University