Prostate cancer drug delivers benefits before chemotherapy

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This is Tomasz Beer, M.D., the lead author on the study and deputy director of the Knight Cancer Institute at Oregon Health & Science University. Credit: Oregon Health & Science University

A drug used to treat men with late-stage prostate cancer proved effective in stemming progression of the disease in research participants who had

not yet received chemotherapy and extended their survival, according to results from a multi-national Phase III clinical trial led by the Knight Cancer Institute at Oregon Health & Science University (OHSU).

A comprehensive analysis of the study's results — published in June 1 online edition of the *New England Journal of Medicine* and to be presented at the American Society of Clinical Oncology (ASCO) annual meeting in Chicago — found participants treated with enzalutamide saw an 81 percent reduction in the risk the cancer would progress and a 29 percent reduction in the risk of death. The oral medication, which is marketed under the brand name Xtandi®, also helped prevent the spread of the disease to the bones, delayed the need for chemotherapy, and reduced evidence of prostate cancer in the bloodstream.

"Based on the study results, this drug could fill an important gap in prostate cancer treatment today. The strong response to this new use of enzalutamide shows that it can provide a viable, less toxic alternative to chemotherapy in staving off the disease in men who aren't responding to standard first line hormonal treatments," said Tomasz Beer, M.D., the lead author on the study and deputy director of the Knight Cancer Institute at OHSU.

The double blind Phase III study included 1,717 research participants enrolled at 207 sites globally between September 2010 and September 2012; 872 received enzalutamide while the others received a placebo. All enrolled patients had metastatic prostate cancer that was worsening despite treatment with traditional hormone therapy. None had yet received chemotherapy.

The trial, named PREVAIL, was concluded early, after a planned interim analysis, because of overwhelming response to the treatment. At this point, 72 percent of enzalutamide patients and 63 percent of placebo patients were alive at the trial cutoff date showing a 29 percent overall

improvement in survival. Fatigue and hypertension were among the most common clinically relevant side effects.

Prostate cancer is the most common form of cancer in men and the second leading cause of cancer-related death in the US and the sixth leading cause of cancer-related death among men worldwide. Hormone therapies are used to treat prostate cancer patients whose disease either isn't responding to radiation or surgery or has already spread beyond the prostate gland. Male hormones, called androgens, cause prostate cancer cells to grow. Hormone therapies, known as androgen deprivation therapies, help arrest the disease by reducing a patient's androgen levels. Enzalutamide works differently than other hormone therapies; rather than reducing hormone levels, it blocks hormone binding to the androgen receptor – an essential step in hormone action.

"In the past few years we have vastly expanded treatment options for prostate cancer," Beer said. "We are working hard to provide answers and options for men whose disease still resists treatment. The results of this clinical trial are extremely gratifying because they represent a leap forward for those patients."

Beer's team of prostate cancer researchers at OHSU's Knight Cancer Institute have been involved in, or led, clinical trials for three of the five new treatments developed for prostate cancer in recent years.

Enzalutamide, which is taken as four pills once per day, is already approved by the Food and Drug Administration (FDA) for men whose disease has not been stopped by other treatments including, surgery, radiation, androgen deprivation therapy and chemotherapy. .

Along with Beer and the Knight Cancer Institute at OHSU, researchers who contributed to the study were from Duke University, Memorial Sloan-Kettering Cancer Center and Weill Cornell Medical College,

Institut Gustave Roussy at the University of Paris Sud, San Camillo and Forlanini Hospitals, Seattle Cancer Care Alliance, Rigshospitalet at the University of Copenhagen, Medivation Inc., Vall d'Hebron University Hospital, Medical Oncology Department, and Vall d'Hebron Institute of Oncology, Guy's Hospital, London, UK, Monash University and Eastern Health, Royal Marsden Hospital and Institute of Cancer Research, UC Davis Comprehensive Cancer Center, Princess Margaret Cancer Center, Asan Medical Center, Nippon Medical School, Icon Cancer Care, Charité-Universitätsmedizin Berlin, Astellas Pharma Global Development Inc., University of Montreal Health Center/CRCHUM, Dana-Farber Cancer Institute, Cross Cancer Institute and University of Alberta and Cliniques Universitaires Saint-Luc.

Astellas and Medivation are collaborating on a comprehensive global development program that includes studies of enzalutamide across the full spectrum of advanced prostate cancer as well as advanced breast cancer. The companies jointly commercialize XTANDI® (enzalutamide) capsules in the United States and Astellas is responsible for all global manufacturing and regulatory filings, as well as commercializing XTANDI outside the United States.

During the study, Beer had grants from Astellas Pharma Global and Medivation. Following completion of the study, Beer received consulting fees from Janssen Japan. Also following the study, he was paid by Research to Practice for participation in a Certified Nursing Educational program that was in part supported by Medivation and Astellas Pharma Global.

Provided by Oregon Health & Science University

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