Oral drug may improve survival in men with metastatic prostate cancer

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An investigational prostate cancer treatment slows the disease's progression and may increase survival, especially among men whose cancer has spread to the bones, according an analysis led by the Duke Cancer Institute.

The study, published on Nov. 19, 2013, in the journal *Clinical Cancer Research*, adds long-term survival and safety data for the drug tasquinimod, a new candidate for treating advanced and recurrent prostate cancer.

"While all subgroups in the clinical trial benefited from tasquinimod, those whose cancer metastasized to their bones had the greatest benefit in terms of delaying the time from the start of treatment to when the cancer progressed," said lead author Andrew J. Armstrong, M.D., ScM, associate professor of medicine at the Duke Cancer Institute. "This group of men also seemed to have a longer survival benefit when we followed them over several years."

Tasquinimod, a drug in development by Active Biotech in partnership with Ipsen, is an oral therapy that activates the body's immune system to fight cancer. Its mechanism is not fully understood, but it appears to affect the function of myeloid-derived suppressor cells, which are found in increased numbers in cancer patients. Tasquinimod is also known to block tumor blood vessel growth, a process termed angiogenesis.

New treatments approved in recent years have given physicians and patients additional options to fight prostate cancer, but the therapies typically only extend patients' lives by three to five months. New drugs that increase survival – without serious side effects – are still needed.

In this phase II clinical trial, funded by Active Biotech, researchers studied the use of tasquinimod among men with metastatic castration-resistant prostate cancer, an advanced form of the disease that does not respond to hormonal therapy. The study enrolled 201 men who were followed for approximately three years, with 134 randomly assigned to receive tasquinimod and 67 given placebo.

The researchers measured patients' overall survival, whether their cancer progressed, and the drug's safety and tolerability. They also conducted studies of biomarkers to better understand how tasquinimod stimulates the immune system.

Armstrong and his colleagues found that men taking tasquinimod saw no cancer progression for an average of 7.6 months, compared with 3.3 months for placebo. Men whose cancer had already metastasized to their bones and took tasquinimod remained progression-free for even longer – 8.8 months, compared with 3.4 months for placebo.

"By delaying the onset of symptoms or growth of metastatic tumors, tasquinimod may allow men to put off other treatments, such as chemotherapy, and maintain a high quality of life," Armstrong said. "That's an important goal for many patients and providers."

Men taking tasquinimod survived 33.4 months on average, versus 30.4 months with placebo. However, those whose cancer had already metastasized to their bones survived an average of 34.2 months, compared with 27.1 months for placebo, a seven-month difference. This improvement in survival with tasquinimod persisted when statistical adjustments were made for other factors such as PSA level, PSA doubling time, lactate dehydrogenase (LDH) levels, and the presence of anemia, each of which were important prognostic factors.

The researchers also identified certain predictors of who would benefit most from tasquinimod, such as lower baseline PSA levels or other biomarkers.

The treatment was considered safe with low to moderate side effects, which included mild gastrointestinal issues, muscle and joint pains, and fatigue.

Based on results from the phase II clinical trial, tasquinimod is now being evaluated in an international phase III trial focusing on men whose prostate cancer has spread to their bones and become resistant to hormonal therapies.

"We still need to do more research to understand the efficacy and mechanism of action of tasquinimod, who benefits the most from it, how it fits into a treatment regimen, and how it could be used in combination with other therapies," Armstrong said. "In addition, tasquinimod is not a prostate cancer-specific drug. If the phase III trial shows that tasquinimod is effective and safe, this opens the door for evaluating the immunotherapy in other cancers."

Provided by Duke University Medical Center