

Celebrex-Lipitor combo may halt prostate cancer

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Researchers at Rutgers' Ernest Mario School of Pharmacy have shown that administering a combination of the widely used drugs Celebrex (celecoxib, a nonsteroidal anti-inflammatory drug) and Lipitor (atorvastatin, a cholesterol lowering drug) stops the transition of early prostate cancer to its more aggressive and potentially fatal stage.

Prostate cancer is the second leading cause of cancer death in men in the United States, with more than a quarter-million new cases appearing each year, according to the American Cancer Society. The findings are being presented by Rutgers Professor Xi Zheng at the annual meeting of the American Association for Cancer Research in San Diego, April 14th.

In the early stage of the disease, when it is typically diagnosed, prostate cancer cells depend on androgen hormones, such as testosterone, to grow. Treatment at this stage involves either decreasing the production of the hormone or blocking its actions on the cancer cells.

“Anti-androgen therapy slows the prostate cancer but eventually the cancer becomes androgen-independent, the therapy becomes ineffective and the cancer cells become more aggressive,” said Xi Zheng, assistant research professor at Rutgers, The State University of New Jersey, who conducted the study.

“Treatments available for the later stage cancers are not very good,” said Allan Conney, director of Rutgers' Susan Lehman Cullman Laboratory for Cancer Research, another researcher on the project. “Oncologists

employ classical chemotherapy drugs which are very toxic and don't work all that well."

Zheng and Conney's research objective was to find a way to indefinitely delay the transition to androgen-independence, prolonging the time during which the cancer would be responsive to effective, low-toxicity, anti-hormone therapy.

Zheng explained that their experiments were first conducted on cell cultures in the laboratory, where the researchers tested the effects of the drugs on the growth of prostate cancer cells from four different cell lines. They then moved on to test the drugs on specially bred mice in which prostate cancer tumors were introduced under the skin. Celebrex alone, Lipitor alone, and the two in combination were tested at the lab bench and on the mice.

"A combination of low doses of Lipitor and Celebrex had a more potent inhibiting effect on the formation of later stage tumors than a higher dose of either agent alone," Zheng reported. "The results from our study indicate that a combination of Lipitor and Celebrex may be an effective strategy for the prevention of prostate cancer progression from the first to the second stage."

Zheng also noted that the team is exploring the underlying molecular mechanisms to understand how Lipitor and Celebrex work on prostate cancer, perhaps identifying an important signaling pathway for tumor cell growth that the drugs inhibit.

Conney pointed out that previous experiments reported in the Sept. 15, 2007, issue of *Clinical Cancer Research* had demonstrated that the Lipitor-Celebrex combination also inhibited the growth of prostate cancer cells in the later androgen-independent stage.

“So if you can affect the early stage and prevent it from becoming the more severe form, that’s a good thing. If you can also inhibit the growth of the more severe form, that’s also a good thing,” Conney said.

Human clinical trials are being planned at the Robert Wood Johnson Medical School of the University of Medicine and Dentistry of New Jersey in New Brunswick.

“If the clinical trials go well, we could have something available in five years, but it would be nice to speed that up,” Conney said. “If the trials show that the drug therapy does a good job of preventing the cancer from advancing, we won’t need to worry about how to handle the more aggressive later stage cancer.

“This is something we hope is going to save lives,” he added.

Source: Rutgers University

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