ASCO: Calcitriol Fails in ASCENT-2 Prostate CA Trial

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CHICAGO -- Treatment with high-dose calcitriol (DN-101) plus docetaxel resulted in more deaths compared with controls in patients with castration-resistant prostate cancer, researchers reported here.

Action Points

- The drug used in this study is not available due to its failure in clinical trials.
- Note that this study was published as an abstract and presented at a conference. These data and conclusions should be considered preliminary until published in a peer-reviewed journal.

In the open-label safety and efficacy trial, ASCENT-2 (Androgen-independent prostate cancer Study of Calcitriol ENhancing Taxotere), 477 men were randomized to weekly treatment with docetaxel plus the experimental high-dose calcitriol, and 476 men were assigned to treatment with docetaxel (Taxotere) every three weeks.

The final analysis, completed six months after the trial was halted in November 2007, showed that 174 men in the calcitriol arm died (36.5% of patients) compared with 138 of the docetaxel patients (29%), researchers reported at the 2010 annual meeting of the American Society of Clinical Oncology here.

In an oral presentation, Howard I. Scher, MD, chief of the genitourinary service at Memorial Sloan-Kettering, reviewed the history of studies of calcitriol leading up to the failed trial.

In ASCENT-1, researchers reported that the study failed to achieve their primary endpoint of an improvement in the prostate specific antigen (PSA) response rate in that phase II trial. However, Scher said the investigators were intrigued that there appeared to be a median survival benefit with the combination therapy -- about eight months longer median survival.

The combination treatment also appeared to have a better safety profile. The hazard ratio for survival was 0.67 (P=0.035) in the adjusted calculations.

In ASCENT-2, patients received prednisone 5 mg orally twice a day with docetaxel on day one and day 22 of a 24-day cycle, while the second group of patients was given calcitriol on days one, seven, and 14; docetaxel on days two, eight, and 15 of a 28-day cycle; and dexamethasone orally at 12, three, and one hour prior to docetaxel administration. The planned treatment period was 30 weeks.

Enrollment was begun in February 2006. The trial was stopped by the Data Safety and Monitoring Board on Nov. 2, 2007, when it appeared that deaths were excessive in the treatment arm compared with the control arm. Patients on high-dose calcitriol were then switched to the control regimen.

When the trial was halted, researchers reported 81 deaths among those on high-dose calcitriol plus docetaxel (17%) compared with 48 deaths among the patients on docetaxel (10.2%), Scher said.

"What we can learn from ASCENT-2 is that even large randomized phase II trials may be poor predictors of results in phase III," commented Ian Tannock, MD, PhD, senior scientist at the Ontario Cancer Institute, Princess Margaret Hospital, Toronto, who discussed the trial at the oral session.

"We also have found that docetaxel is a difficult partner -- as yet, no drug has augmented its benefit for men with castration-resistant prostate cancer," he added.

Scher and colleagues reported a financial relationship with Novacea, the company that sponsored the study.

Tannock disclosed financial relationships with sanofi-aventis and Novacea.

Primary source: Journal of Clinical Oncology
Source reference: Scher H, et al "Docetaxel (D) plus high-dose calcitriol versus D plus prednisone (P) for patients (Pts) with progressive castration-resistant prostate cancer (CRPC): Results from the phase III ASCENT2 trial" *J Clin Oncol* 2010; 28: Abstract 4509.

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