Dutasteride Slows Early Prostate Ca Progression

REDEEM study included men with low-risk, early-stage disease followed with active surveillance.

BY PATRICE WENDLING

FROM THE GENITOURINARY CANCERS SYMPOSIUM

Dutasteride slowed the time to prostate cancer progression in men with low-risk, early-stage disease who were followed with active surveillance in the phase III REDEEM study.

Of the 302 patients who were randomized, 38% of men given dutasteride (Avodart) 0.5 mg daily and 49% of those given placebo experienced some progression of their cancer.

This resulted in a relative risk reduction of 38.9% in the dutasteride group, lead author Dr. Neil Fleshner said during a press briefing that was held in advance of the Genitourinary Cancers Symposium.

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DR. FLESHNER

The aggregate primary end point of the Reduction With Dutasteride of Clinical Progression Events in Expectant Management (REDEEM) study was time to either therapeutic or pathological progression. Therapeutic progression was defined as prostatectomy, radiation, or hormonal therapy. Pathological progression was defined as at least four positive biopsy cores, at least 50% of any one core positive, or a Gleason pattern of 4 or more.

At final biopsy, 36% of 140 men receiving dutasteride had no cancer vs. 23% of 136 men on placebo ($P = .024$). "This is a statistically, and I think, clinically significant improvement," said Dr. Fleshner, head of urology at University Health Network in Toronto.

There was no evidence of increased Gleason score progression in patients given dutasteride in the three-year trial, he said. At final biopsy, 12% of men given dutasteride and 14% of those given placebo had a Gleason score of 7, and 2% of men in both groups had a Gleason score of 8.

This is noteworthy as an increase in high-grade prostate cancers was observed in men treated with dutasteride compared with those on placebo in the Reduction by Dutasteride of Prostate Cancer Events (REDUCE) trial.

Avodart's maker, GlaxoSmithKline, filed for a chemoprevention indication for dutasteride in the United States and Europe based mainly on the results of REDUCE, a 4-year study of 8,231 men aged 50-75 years considered at an increased risk of prostate cancer because of an elevated PSA (2.5-10 ng/mL) and one negative biopsy.

The company has since announced receiving a Complete Response Letter from the Food and Drug Administration, which signals that the indication has not been approved.

Dutasteride and finasteride, another 5-alpha reductase inhibitor, were shot down as prostate chemoprevention agents in December 2010 by the FDA's Oncologic Drugs Advisory Committee on the basis that the risk-benefit profile for either drug is not favorable when it is used to reduce the risk of prostate cancer.

The current results will not resurrect GSK's attempt to gain a chemoprevention indication for dutasteride. "They are not going to apply for it," Dr. Fleshner told reporters at the meeting.

"This was not a registration trial, and the time required to reassemble and complete another one will not fit in with their patent expiration. So, I don't think we will see a formal indication for surveillance," he said.

A separate cost-utility analysis published in February showed that dutas-

VITALS

Major Finding: Taking dutasteride 0.5 mg daily reduced relative risk of prostate cancer progression by 38.9% vs. placebo.

Data Source: Phase III REDEEM trial in 302 men with low-risk, early stage prostate cancer followed with active surveillance.

Disclosures: GlaxoSmithKline sponsored the study. The investigators disclosed relationships with GSK, including consultant/advisory roles, employment/stock ownership, and research support and honoraria. Dr. Vogelzang disclosed financial relationships with multiple pharmaceutical companies.

teride at a cost of $626 per year, down from the current $1,400, was unlikely to be cost effective for chemoprevention use in men at elevated risk for prostate cancer (Cancer Prev. Res. 2011;4:277-83).

The moderator of the press briefing, Dr. Nicholas Vogelzang of Las Vegas, who is with US Oncology, said that the paper is important because of the increased anxiety experienced by the growing number of men under watchful waiting.

"With this drug, dutasteride, the PSA [prostate-specific antigen] drops by about 50%; it makes the gland smaller, so they have [fewer] urinary symptoms," he said.

"Now we have learned that this seems to reduce the amount of cancer in the gland, and we are now able to offer the patients who wish to have watchful waiting an active treatment option. I think it's an important step forward," Dr. Vogelzang noted.

Dutasteride was approved for benign prostatic hypertrophy in men with an enlarged prostate in 2001. Currently, no drug is approved for prevention of prostate cancer.

At baseline, men in the REDEEM study were aged 48-82 years, they had a PSA level of less than 11 ng/mL, a Gleason score of 6 or less, and clinical stage T1c-T2a disease.

The data were formally presented at the symposium, which is sponsored by the American Society for Clinical Oncology, the American Society for Radiation Oncology and the Society of Urologic Oncology. ■