Few Physicians Prescribe 5-Alpha Reductase Inhibitors for Prostate Cancer Prevention

A recent study has demonstrated that despite randomized clinical trials showing that 5-alpha reductase inhibitors (5-ARIs) decrease the incidence of prostate cancer by approximately 25%, most physicians are reluctant to prescribe them for the prevention of prostate cancer (Cancer Epidemiol Biomarkers Prev. 2010;19:2164-2171).

Robert Hamilton, MD, and colleagues tracked the number of new prescriptions for 5-ARIs in the Veterans Health Administration (VHA) prescription database from 2000 through 2005. Finasteride comprised most of these prescriptions, with dutasteride accounting for less than 0.05%. The authors also surveyed all VHA urologists and a random sample of VHA primary care physicians to investigate their knowledge and attitudes concerning this topic.

Analysis of VHA prescription data revealed that, although the number of new prescriptions for finasteride increased steadily throughout the study period, the publication of a randomized trial showing the utility of finasteride for the prevention of prostate cancer did not change prescribing patterns. Among physicians who responded to the survey, 64% of the 135 urologists and 80% of the 464 primary care physicians indicated that they never prescribed 5-ARIs for prostate cancer chemoprevention.

Corresponding author Linda Kinsinger, MD, MPH, chief consultant for preventive medicine at the VHA National Center for Health Promotion and Disease Prevention, says the findings validate that chemoprevention of prostate cancer with 5-ARIs has not yet been widely accepted or applied in practice. “More clinicians should be aware of the possibility of chemoprevention and it probably should be discussed with patients more often as an option to be considered,” she says.

To help put the study in context, the authors note that in 2003, the results of the Prostate Cancer Prevention Trial (PCPT) showed a 25% relative risk reduction in the incidence of prostate cancer with finasteride. The PCPT included more than 8000 men and was a randomized, placebo-controlled trial. However, 6.4% of cancers diagnosed in patients receiving finasteride were high grade (Gleason score ≥7), as opposed to 5.1% in the placebo arm, representing a 27% higher proportion of tumors. Several subsequent reports have provided contrary evidence, and the current consensus is that 5-ARIs do not significantly increase the risk of high-grade disease. However, these follow-up articles were published after the completion of the pharmacy data and survey results used in this article.

Eric Klein, MD, professor of surgery and chairman of the Glickman Urological and Kidney Institute at the Cleveland Clinic, explains that 3 observations from a subsequent analysis of the PCPT do not support concerns regarding an increased risk of high-grade prostate cancer. First, if a 5-ARI caused high-grade cancer, one would expect it to increase the risk disproportionately over placebo with longer duration of use. In the PCPT, the excess risk of men treated with finasteride was increased over one year, but the excess risk did not increase compared with placebo over time. Second, the characteristics on biopsy that are associated with aggressive behavior, including the number of positive cores, aggregate tumor length, and perineural invasion, were present in more patients receiving placebo than finasteride. Lastly, patients who were treated with finasteride did not have higher stage disease noted on radical prostatectomy specimens.
In 2010, a second randomized, placebo-controlled trial, the Reduction by Dutasteride of Prostate Cancer Events (REDUCE) trial, which included almost 7000 men, reported a 23% reduction in prostate cancer incidence after 4 years with dutasteride treatment. Although a statistically insignificant trend for higher grade disease was observed in those men treated with dutasteride, the authors of the REDUCE study believe this observation is most likely due to the drug’s effect in reducing prostate volume, which increases the likelihood that a biopsy will detect areas of high-grade cancer.

Finasteride and dutasteride are both approved for benign prostatic hyperplasia (BPH) and finasteride is also approved for male pattern baldness at a lower dose. Neither drug is currently approved by the US Food and Drug Administration for the chemoprevention of prostate cancer, although guidelines released jointly in 2009 by the American Society of Clinical Oncologists and the American Urological Association recommend that, “Asymptomatic men with a prostate-specific antigen (PSA) ≤3.0 ng/mL who are regularly screened with PSA or are anticipating undergoing annual PSA screening for early detection of prostate cancer may benefit from a discussion of both the benefits of 5-ARIs for 7 years for the prevention of prostate cancer and the potential risks (including the possibility of high-grade prostate cancer).”

Survey Results

In addition to asking whether physicians ever prescribed 5-ARIs for prostate cancer risk reduction, the survey was also designed to understand why these drugs were not prescribed more frequently. Approximately 55% of urologists were concerned over the potential to induce high-grade cancers. According to Dr. Kinsinger, although concerns over this were reasonable at the time the study was done, “subsequent evidence has been reasonably convincing to overcome this initial finding.”

Lack of awareness was the main barrier for primary care physicians: 52% were not aware that 5-ARIs could be used for prostate cancer prevention.

Less than 2% of either group of physicians stated they were influenced by the publication of the PCPT. Respondents also said that few patients inquire about using finasteride for chemoprevention: 84% of primary care physicians and 57% of urologists said that patients had never or only a few times asked about chemoprevention of prostate cancer.

Interestingly, the majority of the survey respondents said that moderate to severe BPH would be the patient characteristic most likely to make them prescribe finasteride for cancer chemoprevention. However, BPH is not a risk factor for prostate cancer, implying they are reluctant to use finasteride for chemoprevention alone and are more comfortable if a second indication is present.

The authors concluded that lack of awareness in primary care physicians, urologists’ concerns over inducing high-grade tumors, and lack of patient awareness seem to be the primary barriers to the use of 5-ARIs for chemoprevention.

A Tough Sell

Dr. Kinsinger says the use of these drugs for prostate cancer chemoprevention is low because the idea of taking a drug, with potential harms and non-negligible costs, to prevent a cancer that they will likely never get is a tough sell to patients. Regarding side effects, she says the ones related to decreased sexual function are probably the most important to patients.

“Unless someone feels particularly susceptible to getting the cancer, most people aren’t going to want to bother with chemoprevention,” she says. “For providers, it’s hard to know who is at highest risk and it is also hard to explain all the pros and cons. It is much easier to simply not bring up the subject.”

Dr. Klein agrees that many physicians do not view the risk-benefit ratio favorably. “We need to work as a field to identify the group that will benefit from 5-ARIs. Future work needs to focus on patient selection to optimize patient benefits,” he says.

Note: The name of this section has been changed from “News & Views” to “Perspectives: Research in Context.” It continues to provide the context for major developments in cancer prevention, detection, and treatment.