



To Print: Click your browser's PRINT button.

NOTE: To view the article with Web enhancements, go to:
<http://www.medscape.com/viewarticle/588906>

This activity is developed and funded by Medscape.



New Guidelines Recommend 5-Alpha Reductase Inhibitors for Preventing Prostate Cancer **CME**

News Author: Roxanne Nelson

CME Author: Charles Vega, MD, FAAFP

Complete author [affiliations and disclosures](#), and other [CME information](#), are available at the end of this activity.

Release Date: March 2, 2009; Valid for credit through March 2, 2010

Credits Available

Physicians - maximum of 0.25 *AMA PRA Category 1 Credit(s)TM* for physicians;

Family Physicians - up to 0.25 AAFP Prescribed credit(s) for physicians

All other healthcare professionals completing continuing education credit for this activity will be issued a certificate of participation. Physicians should only claim credit commensurate with the extent of their participation in the activity.

To participate in this internet activity: (1) review the target audience, learning objectives, and author disclosures; (2) study the education content; (3) take the post-test and/or complete the evaluation; (4) view/print certificate [View details](#).

Learning Objectives

Upon completion of this activity, participants will be able to:

1. Identify the effect of finasteride on the risks for prostate cancer and adverse events in a previous large trial.
2. Specify current recommendations regarding the use of 5-alpha reductase inhibitors to prevent prostate cancer.

Authors and Disclosures

Roxanne Nelson

Disclosure: Roxanne Nelson has disclosed no relevant financial information.

Charles Vega, MD, FAAFP

Disclosure: Charles Vega, MD, FAAFP, has disclosed an advisor/consultant relationship to Novartis, Inc.

Brande Nicole Martin

Disclosure: Brande Nicole Martin has disclosed no relevant financial information.

March 2, 2009 — A new joint guideline produced by the American Society of Clinical Oncology (ASCO) and the American Urological Association (AUA) has recommended chemoprevention for prostate cancer in healthy men.

Specifically, it recommends that asymptomatic men with a prostate-specific antigen (PSA) of 3.0 ng/mL or lower and who receive regular

screening consider using a 5-alpha reductase inhibitor (5-ARI), such as finasteride or dutasteride, to help prevent prostate cancer.

According to the new guideline, published online February 24 in the *Journal of Clinical Oncology* and scheduled to appear in the April issue of *The Journal of Urology*, men in this category might benefit from a discussion with their physicians about the benefits and risks of 5-ARIs for the prevention of prostate cancer.

In addition, patients currently using these agents to treat benign conditions, such as lower urinary tract symptoms, should discuss continuing this treatment to reduce their likelihood of developing cancer.

Chemoprevention a Reality

"The goal of developing a chemopreventive agent that can reduce the risk of prostate cancer has been achieved, and that is a major achievement in and of itself," said Barnett S. Kramer, MD, MPH, associate director for disease prevention at the National Institutes of Health, in Bethesda, Maryland, and cochair of the guideline panel. "However, very few prevention messages can be adequately delivered as a sound bite, and that is certainly the case here. Therefore, the principal focus of the panel was on shared decision making — that is, to let men who are considering chemoprevention for prostate cancer know what the known benefits are, and what the known harms and the remaining uncertainties are."

The ASCO/AUA recommendations resulted from a systematic review of the literature, and 15 randomized controlled trials met the inclusion criteria. "That body of evidence provided proof that 5-alpha reductase inhibitors will decrease the risk of prostate cancer, at least in men who are being regularly screened," said Dr. Kramer during a press briefing. "That is important to point out because all of the trials conducted to date were in men who were being regularly screened for prostate cancer."

"It has been well established that the screening process itself increases the risk of being diagnosed with prostate cancer by about 2-fold," he added.

The Prostate Cancer Prevention Trial (PCPT) is the largest and only completed randomized trial that was prospectively designed to show a reduction in period prevalence of prostate cancer in generally healthy men, and provided the bulk of the evidence for the guideline. Over half (57%) of all study subjects participated in the PCPT, and the PCPT was the only trial to report subgroup results by race/ethnicity, age, and family history of prostate cancer.

The vast majority of men participating in these trials were white (92%), so the results primarily apply to white males, explained Dr. Kramer. However, subgroup analyses did not reveal significant differences across any of the ethnic or racial groups.

Results of the PCPT showed a reduction in the cumulative incidence of prostate cancer, from 24.4% in the placebo group to 18.4% in the finasteride group, during the 7-year study period. The rate of prostate cancer during the 7-year period was 4.9% in the control group and 3.5% in the finasteride group, for an absolute risk reduction of 1.4%.

Increase in High-Grade Tumors?

A secondary analysis triggered concerns about harm, because finasteride was associated with an increase in higher-grade prostate cancers. Gleason scores of 7 to 10 were more common in men taking finasteride (37%, or 280 of 757 tumors) than in men taking placebo (22.2%, or 237 of 1068 tumors). This finding raised critical questions about the effect of 5-ARIs on prostate cancer morbidity and mortality, and whether the increase in high-grade prostate cancer was due to finasteride.

However, subsequent analyses of these data suggested that the finding was an artifact because finasteride decreased prostate volume and made these high-grade cancers easier to detect, as previously reported by *Medscape Oncology*.

In the guideline, the expert panel has "judged that plausible reasons could have led to a spurious increase in high-grade cancers." They note that it is unlikely for an agent to increase the incidence of high-grade tumors while simultaneously decreasing the incidence of low-grade tumors.

Although it is not definitive, the subsequent evidence suggests that the incidence of high-grade tumors is due to artifacts and not the drug, explained Dr. Kramer.

Paul F. Schellhammer, MD, past president of the AUA and cochair of the panel that developed the guideline, agrees. "It is reasonable to believe that the issue has been resolved," he told *Medscape Oncology*, "and high-grade tumors are not likely to be a concern. But it is important to tell the patient that the initial report did mention this."

Virtually all studies showed that 5-ARIs are associated with a consistently higher frequency of adverse events than placebo, although the incidence is low. A 2% to 4% increase in erectile dysfunction and gynecomastia has been reported, along with decreases in ejaculate volume and libido for men who received finasteride in clinical trials.

But overall, adverse effects are minimal, according to Dr. Schellhammer. "In 1 study, the degree of sexual dysfunction was less among men taking the drug than among the controls," he said. "The process of aging is a more important factor than the drug in that regard."

Physician-Patient Communication

Physician-patient communication is important, the guideline emphasizes, and it is essential that the available data are presented to the patient considering the use of these agents for prostate cancer prevention and that the uncertainty is highlighted.

What remains unknown is the effect of 5-ARIs on prostate-cancer-related mortality, and that can be difficult to determine. "It may take another 10 years to get an answer on that," said Dr. Schellhammer. "The length of time that 5-ARIs need to be taken is also undetermined. In the PCPT study, finasteride was used for 7 years, so that's a limitation of our data."

For men considering use of 5-ARIs for chemoprevention, physicians should explain that:

- these agents do not completely eliminate the risk for prostate cancer;
- the risk for high-grade cancer is still uncertain;
- the long-term effects of 5-ARIs on prostate cancer incidence, beyond approximately 7 years, are unknown;
- the effect on mortality is not known;
- the patient may experience potential but reversible effects on sexual dysfunction;
- there will likely be improvement in lower urinary tract symptoms.

How do physicians feel about it for their own use? Howard Sandler, MD, chair of radiation oncology at Cedars-Sinai Medical Center, in Los Angeles, California, and moderator of the press briefing, said that he would consider using finasteride as chemoprevention.

"If I was leaning toward taking [finasteride], I would try it for a month or 2 and see about side effects," he said. "If there were no significant side effects, I would continue it."

He also said that he might "sleep a little better at night," since he was reducing his risk for prostate cancer. However, when asked directly by a journalist if he was going to take it, he said, "I haven't made up my mind yet."

Coauthors Peter C. Albertsen, MD, from the University of Connecticut Health Center, in Farmington, and Paul A. Godley, MD, from the University of North Carolina at Chapel Hill, have served as consultants to GlaxoSmithKline. Janet Wittes, PhD, from Statistics Collaborative, in Washington, DC, has consulted for Merck. None of the other study authors have disclosed any relevant financial relationships.

J Clin Oncol. Published online February 24, 2009.

J Urol. 2009;181:1642-1657.

Learning Objectives for This Educational Activity

Upon completion of this activity, participants will be able to:

1. Identify the effect of finasteride on the risks for prostate cancer and adverse events in a previous large trial.
2. Specify current recommendations regarding the use of 5-alpha reductase inhibitors to prevent prostate cancer.

Clinical Context

5-ARIs are one of the few classes of medication that has been demonstrated to prevent the development of cancer. In a 7-year trial by Thompson and colleagues, which was published in the July 17, 2003, issue of the *New England Journal of Medicine*, finasteride reduced the risk for incident prostate cancer by 25% vs placebo. Although the rate of sexual adverse events was higher in the finasteride group, more men receiving placebo complained of urinary adverse events.

One troubling result of the Thompson study was the higher rate of prostate cancer with an elevated Gleason score in the finasteride vs placebo groups. This finding suggests potential harm and influences the larger issue of whether to use 5-ARIs to prevent prostate cancer. The current clinical practice guideline from the ASCO and AUA addresses this issue.

Study Highlights

- An expert panel reviewed randomized trials of 5-ARIs for men at least 45 years old. All included studies provided data regarding the incidence of prostate cancer, which could be reported after clinical suspicion prompted testing, or from routine screening programs as mandated by the study protocol.
- 15 clinical trials met the inclusion criteria.
- 9 trials directly measured prostate cancer incidence, and the results of these trials were generally consistent in demonstrating cancer reduction with the use of 5-ARIs.
- Only 1 of these 9 trials assessed men without lower urinary tract symptoms.
- There were limited data regarding the efficacy of 5-ARIs in reducing the risk for prostate cancer among men not receiving regular cancer screening.
- No trials were large enough to demonstrate a difference in the rates of prostate cancer-specific mortality or overall mortality in comparing 5-ARIs vs placebo.
- There were limited data regarding the effect of 5-ARIs on overall quality of life.
- The main conclusion of the expert panel is that asymptomatic men with a PSA of 3.0 ng/mL or less who receive regular screening for prostate cancer may benefit from a discussion of the benefits of chemoprevention with a 5-ARI. Men taking 5-ARIs for lower urinary

tract symptoms may benefit from the same discussion.

- Although there are plausible reasons to explain a spurious increase in the detection of high-grade prostate cancers among men receiving 5-ARIs, the current recommendations call for discussing the possibility of an increased risk for more aggressive cancers with the use of 5-ARIs.
- Finasteride has been demonstrated to lower serum PSA levels by half at 12 months. However, there is no accepted uniform scale multiplier to calculate the PSA of patients receiving 5-ARIs.
- The panel recommended that finasteride be used for at least 7 years if prescribed to prevent prostate cancer.
- Future research should compare different 5-ARIs in their ability to reduce the risk for prostate cancer; determine the best dose and duration of treatment to prevent cancer; and, importantly, investigate whether 5-ARIs select for high-grade tumors.

Pearls for Practice

- A previous study found that finasteride can reduce the overall risk for prostate cancer vs placebo, but more aggressive prostate cancer was more common in men receiving finasteride. Finasteride was also associated with a reduced rate of urinary adverse events and higher rates of sexual adverse events vs placebo.
- The current recommendations suggest that clinicians may discuss chemoprevention of prostate cancer with use of 5-ARIs in men who are regularly screened for prostate cancer.

All of the following were outcomes in comparing finasteride vs placebo in the previous study by Thompson and colleagues *except*:

- Overall reduction in the risk for prostate cancer
- Reduction in the risk for aggressive prostate cancer
- Higher rate of sexual adverse events
- Lower rate of urinary adverse events

What was the *main* recommendation from the current review of 5-ARIs by Kramer and colleagues as chemoprevention for prostate cancer?

- All patients with lower urinary tract symptoms should receive 5-ARIs to prevent prostate cancer
- Clinicians may discuss chemoprevention with men undergoing regular prostate cancer screening
- Clinicians should discourage chemoprevention with 5-ARIs because of an increased risk for high-grade prostate cancer
- The adverse effects of 5-ARIs outweigh any benefit in their prevention of prostate cancer

Instructions for Participation and Credit

There are no fees for participating in or receiving credit for this online educational activity. For information on applicability and acceptance of continuing education credit for this activity, please consult your professional licensing board.

This activity is designed to be completed within the time designated on the title page; physicians should claim only those credits that reflect the time actually spent in the activity. To successfully earn credit, participants must complete the activity online during the valid credit period that is noted on the title page.

FOLLOW THESE STEPS TO EARN CME/CE CREDIT*:

1. Read the target audience, learning objectives, and author disclosures.
2. Study the educational content online or printed out.
3. Online, choose the best answer to each test question. To receive a certificate, you must receive a passing score as designated at the top of the test. Medscape encourages you to complete the Activity Evaluation to provide feedback for future programming.

You may now view or print the certificate from your CME/CE Tracker. You may print the certificate but you cannot alter it. Credits will be tallied in your CME/CE Tracker and archived for 5 years; at any point within this time period you can print out the tally as well as the certificates by accessing "Edit Your Profile" at the top of your Medscape homepage.

*The credit that you receive is based on your user profile.

Target Audience

This article is intended for primary care clinicians, urologists, oncologists, and other specialists who care for men at risk for prostate cancer.

Goal

The goal of this activity is to provide medical news to primary care clinicians and other healthcare professionals in order to enhance patient care.

Accreditation Statements

For Physicians



Medscape, LLC is accredited by the Accreditation Council for Continuing Medical Education (ACCME) to provide continuing medical education for physicians.

Medscape, LLC designates this educational activity for a maximum of 0.25 **AMA PRA Category 1 Credit(s)**[™]. Physicians should only claim credit commensurate with the extent of their participation in the activity. Medscape Medical News has been reviewed and is acceptable for up to 350 Prescribed credits by the American Academy of Family Physicians. AAFP accreditation begins 09/01/08. Term of approval is for 1 year from this date. This activity is approved for 0.25 Prescribed credits. Credit may be claimed for 1 year from the date of this activity.

Note: Total credit is subject to change based on topic selection and article length.

[AAFP Accreditation Questions](#)

For questions regarding the content of this activity, contact the accredited provider for this CME/CE activity: CME@medscape.net. For technical assistance, contact CME@webmd.net.

Authors and Disclosures

As an organization accredited by the ACCME, Medscape, LLC requires everyone who is in a position to control the content of an education activity to disclose all relevant financial relationships with any commercial interest. The ACCME defines "relevant financial relationships" as financial relationships in any amount, occurring within the past 12 months, including financial relationships of a spouse or life partner, that could create a conflict of interest.

Medscape, LLC encourages Authors to identify investigational products or off-label uses of products regulated by the US Food and Drug Administration, at first mention and where appropriate in the content.

News Author

Roxanne Nelson

is a freelance journalist for Medscape Oncology.

Disclosure: Roxanne Nelson has disclosed no relevant financial information.

CME Author

Charles P. Vega, MD, FAAFP

Associate Professor; Residency Director, Department of Family Medicine, University of California, Irvine

Disclosure: Charles Vega, MD, FAAFP, has disclosed an advisor/consultant relationship to Novartis, Inc.

Brandi Nicole Martin

is the News CME editor for Medscape Medical News.

Disclosure: Brandi Nicole Martin has disclosed no relevant financial information.

Medscape Medical News 2009. ©2009 Medscape

Legal Disclaimer

The material presented here does not necessarily reflect the views of Medscape or companies that support educational programming on www.medscape.com. These materials may discuss therapeutic products that have not been approved by the US Food and Drug Administration and off-label uses of approved products. A qualified healthcare professional should be consulted before using any therapeutic product discussed. Readers should verify all information and data before treating patients or employing any therapies described in this educational activity.

Registration for CME credit and the post test must be completed online.
To access the activity Post Test, please go to:
<http://www.medscape.com/viewarticle/588906>