FDA Panel: Prostate Ca Therapy Trials Needed

BY JESSICA BYLANDER

GAITHERSBURG, MD. — Developers of targeted prostate cancer treatments should include randomized clinical trials with "watchful waiting" as a control, according to the Food and Drug Administration's Gastroenterology and Urology Devices Panel.

Active surveillance may be an appropriate control for studies of whole-gland therapies that treat or remove the entire prostate, as well as for studies of targeted therapies in which only the known cancerous regions are treated (focal treatments); however, the panel reached consensus only on the focal-treatment study controls.

The primary end point for active surveillance studies would measure the impact of therapy on disease progression. Because prostate cancer progresses so slowly, survival rates are not a feasible end point, the panel said.

"A win in the active surveillance arm is not needing treatment, and a win in the treatment arm is [cancer] not recurring after treatment," said panel member Dr. Peter Scardino of Memorial Sloan-Kettering Cancer Center in New York.

There is a growing interest in developing new, minimally invasive device therapies, as current treatments may pose risks that are disproportionate to the risk of the disease itself, according to the FDA. New treatment methods include high-intensity focused ultrasound, radiofrequency ablation, lasers, microwave devices, and photodynamic therapy.

Current prostate cancer treatments rely on the radical, whole-gland approach in which the entire prostate is removed or irradiated, and they are associated with significant morbidity, the FDA noted. It asked the panel whether nonrandomized study designs for new prostate cancer treatments could be considered, and to identify appropriate control groups, patient selection criteria, and effectiveness end points.

The panel agreed that randomized trials were necessary, despite the many challenges of conducting them, and that

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outcomes from focal treatments, at least, should be compared with outcomes from a watchful-waiting (or active surveillance) approach.

Few randomized studies comparing different prostate cancer treatment modalities have been completed, the FDA noted. The Southwest Oncology Group study of prostatectomy vs. external-beam radiation treatment, for example, was terminated after enrolling only 6 of 1,000 planned subjects.

According to Dr. Scardino, it would be easier to enroll patients in a trial with an active surveillance control. He pointed to non-U.S. randomized studies that were successfully completed by using an active surveillance control.

Quality of life measurements and complication rates are also important, panel members said, but they disagreed on which data elements to collect and whether quality of life should be a primary or secondary end point. Nor did the panel reach consensus on the length of follow-up for randomized studies.

Janine Morris, acting director of the Division of Reproductive, Abdominal, and Radiological Devices in the FDA's Center for Devices and Radiological Health, said that although the panel was able to answer the FDA's most important questions, she was disappointed that there was not time for further discussion when it met on Dec. 11, 2009.

"We will have to address this in another format," such as another advisory panel meeting, a public workshop, or a meeting with industry stakeholders, she said in an interview. "We have unanswered questions." ■

Jessica Bylander is with "The Gray Sheet." This publication and "The Gray Sheet" are published by Elsevier.