The Prostate Cancer Intervention Versus Observation Trial (PIVOT)

By Gerald E. Hanks, MD

As described by Wilt et al in their review, the Prostate Cancer Intervention Versus Observation Trial (PIVOT) is asking very important questions about the effect of surgical treatment vs observation, with delayed androgen deprivation available to both groups, in patients with localized prostate cancer. Clinicians who have suffered with the old Uro-Oncology Trial comparison of prostatectomy vs radiation hope that PIVOT provides answers rather than confusion.

PIVOT: The Radiation Oncologist's Friend?

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It is reassuring that PIVOT is attempting to access representative patients, although patient accrual is proceeding at a much slower rate than was anticipated. This has required a decrease in the final number of patients from 2,000 to 1,050, as well as an extension in the time for case accession from 3 to 7 years. When this 7 years is combined with the planned 8- to 15-year follow-up, it is clear that PIVOT will be a study conducted by young men.

As best I can tell, the radiation oncology community was not invited to this party because of a basic prejudice of the organizers that there is a difference in the success of treatment with prostatectomy or radiation. I guess it was too much of a stretch for the trial to have compared both successful treatments to observation. If surgery proves worse or no better than observation, however, radiation will still be left for definitive treatment!

I also suspect that the Veterans Affairs (VA) system is the only health-care segment in the United States in which 17% of eligible patients would agree to randomization to this clinical trial.

Criticisms of the Study Design

I have three criticisms of the study design:

1. Permitting patients with pretreatment prostate-specific antigen (PSA) values of 20 to 50 ng/mL to participate in the trial permits the inclusion of a group of patients with a 70% to 95% risk of nonlocalized disease that is not curable by surgery. This defeats the main purpose of the study.

2. Including patients with presurgical hormonal downstaging is a very serious error. The 3 to 6 months of androgen deprivation will delay the failure pattern by 2 to 4 years, confusing the important end point of failure and, perhaps ultimately, the cause-specific death rate.

3. Including patients who are 70 to 75 years old should again demonstrate the increase in mortality of prostatectomy in this age group, as well as the decrease in quality-of-life functions, such as a higher rate of incontinence, following prostatectomy in this age group. Neither of these observations need to be proven again.

Two Final Questions

Finally, I have two questions about the design of this study and national acceptance of the results:

1. Are there rules for stopping the trial if the morbidity of prostatectomy in the VA hospitals is excessive?

2. Will non-VA-based urologic surgeons accept a negative result from surgery in VA hospitals as representing the care that they deliver and stop performing prostatectomy, or will these surgeons dismiss the negative finding as unique to the study site, patients, and physicians?