Re: Quality of Life in Advanced Prostate Cancer: Results of a Randomized Therapeutic Trial

I read with interest the article by Moinpour et al. (1). I was surprised by the selection of only five primary outcome measures. Three of these measures focus on known side effects of flutamide. Given that quality of life was measured for only the first 6 months of this study, one would expect worse quality-of-life outcomes among patients taking flutamide, even when side effects occur among a relatively small group of patients (7% versus 4%).

We recently published a cross-sectional study concerning health-related quality of life among patients with metastatic prostate cancer (2). We found that men who received flutamide and were in remission had a quality of life that was similar to an equivalent norm for men in the general population of the United States. When we measured all eight domains of the SF 36 questionnaire, we noted that men who received flutamide had slightly lower scores in physical functioning, role physical, and role emotional, but had slightly higher scores in body pain, vitality, and mental health. When viewed from this perspective, quality-of-life outcomes appear to be comparable between those patients taking flutamide and those who do not. Absent any significant risks associated with flutamide, the decision to use flutamide revolves around an individual patient’s assessment of the potential for reversible side effects versus the potential for extending the time to disease progression.

Peter C. Albertsen

References


Response

Dr. Albertsen voiced concern about our selection of five primary end points for the Southwest Oncology Group (SWOG)-coordinated INT-0105 quality-of-life (QOL) study, noting that three of the five end points addressed known treatment-related side effects. We selected five end points and adjusted the significance levels accordingly to control for type I error. There was no adjustment for multiple testing in Dr. Albertsen’s QOL results (discussed below). Two of our outcomes addressed emotional and physical functioning, good surrogates for overall QOL. Our strongest outcome measure, emotional functioning, was not a known side effect of flutamide.

At first glance, data from the article by Albertsen et al. (1) cited by Dr. Albertsen appear to contradict emotional functioning findings reported in the INT-0105 randomized trial of orchietomy plus placebo versus orchietomy plus flutamide for patients with stage D2 prostate cancer. However, there are a number of important differences between the two studies that make the comparisons extremely difficult, if not meaningless. First, our study was a trial with 737 patients randomized to two different treatments: surgical castration versus surgical castration plus an antiandrogen. Albertsen’s study was not a randomized trial and did not include a comparison arm with a castration-only group. All patients received total androgen blockade with medical castration (using a leutinizing hormone-releasing hormone agonist) plus flutamide.

Forty-seven percent of the patients in Albertsen’s study were classified as “in remission” (hormone-resistant disease); these patients were required to have had 1 month or more of combination therapy. Consistent increases in prostate-specific antigen (PSA) values of 4 ng/mL or more was one of the criteria for disease progression. The SWOG QOL study had no patients with hormone-insensitive disease and did not include PSA levels as a criterion for progression. The second group of patients in Albertsen’s study was classified as “in remission” (stable disease), with 3 months or more of combination therapy; these patients had PSA values of less than 4 ng/mL. Therefore, it is difficult to compare QOL outcomes for the patients in Albertsen’s study to those in the INT-0105 patient sample. It is possible that both of the patient groups studied by Albertsen et al. represent better clinical status than the INT-0105 group.

Finally, Albertsen’s comments suggest that patients in his study were assessed considerably beyond the primary treatment phase, but the authors did not report average duration of total androgen blockade therapy for the two patient groups. This is important because we did not see statistically significant differences (with a stringent significance level of 0.003, adjusted for multiple comparisons) until months 3 and 6 after patients were randomly assigned to treatment. In the SWOG trial, both treatment arms demonstrated improvement in the Mental Health Index scores (the same measure used in Albertsen’s study) over the 6-month period, but patients treated with orchietomy alone showed significantly more improvement.

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Notes

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