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Docetaxel in Hormone-Refractory Metastatic Prostate Cancer

A Viewpoint by William R. Berry

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With the publication of the TAX 327 and Southwest Oncology Group (SWOG) 9916 phase III trials, a survival benefit has been convincingly demonstrated for docetaxel-containing regimens versus the previous chemotherapy standard of mitoxantrone plus prednisone in hormone-refractory prostate cancer. These trials are landmark studies, as they are the first ever to show that any chemotherapy regimen can prolong survival in prostate cancer. There are several points worth further commentary.

1. The increase in median overall survival in the two trials (1.9 months [SWOG 9916] and 2.4 months [TAX 327]) might, at first glance, appear to be marginal. However, the demonstration of a survival benefit of any degree in any metastatic cancer is difficult to achieve. This feat requires large numbers of patients and a treatment with a real difference in efficacy. The hazard ratios for survival difference in the docetaxel groups of 0.76 (TAX 327) and 0.80 (SWOG 9916) are actually quite impressive, as these ratios measure the entire difference in the survival curves and not just the single point of median survival.

2. The 50% decline in prostate-specific antigen (PSA) levels remains a helpful and yet problematic measure of disease response in hormone-refractory prostate cancer. Because of the rarity of measurable disease in hormone-refractory prostate cancer, we would still have great difficulty determining the activity of any therapy without the ability to monitor changes in PSA. However, as the TAX 327 trial so accurately demonstrated, a significant difference in the rate of reduction of PSA levels does not necessarily correlate with improvement in survival. Both the once-weekly and the every 3 weeks docetaxel plus prednisone regimens showed similar reductions in PSA levels (48% and 45%) that were statistically superior to that with mitoxantrone and prednisone (32%). However, only docetaxel every 3 weeks plus prednisone showed a survival benefit versus mitoxantrone plus prednisone. Pending the discovery of better measures of response, difference in survival should remain the primary endpoint for phase III trials in hormone-refractory prostate cancer.

3. Docetaxel given every 3 weeks with daily oral prednisone is now the chemotherapy standard of care for hormone-refractory prostate cancer, and can be given with acceptable risk. Although docetaxel plus estramustine in the SWOG 9916 trial showed a survival benefit over mitoxantrone plus prednisone similar to that with docetaxel plus prednisone in the TAX 327 trial, the additional cardiovascular toxicity attributed to estramustine has led most observers to conclude that docetaxel every 3 weeks plus prednisone should be the accepted chemotherapy standard of care in hormone-refractory prostate cancer.

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