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Docetaxel in Hormone-Refractory Metastatic Prostate Cancer

A Viewpoint by William K. Oh

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Chemotherapy for hormone-refractory prostate cancer was thought to have no established role as recently as a decade ago. The approval of mitoxantrone chemotherapy by the US FDA in the 1990s did little to change this prevailing attitude among oncologists, given its modest efficacy, even as a palliative therapy for patients with symptomatic bone metastases. It was not until 2004, when docetaxel was approved for the treatment of hormone-refractory prostate cancer, that chemotherapy was widely accepted as having a benefit in this patient population.

This benefit was clearly demonstrated in two large randomised trials described in the accompanying Drug Profile: TAX 327 and Southwest Oncology Group (SWOG) 9916. Both studies demonstrated a remarkably similar survival benefit of approximately 2–3 months. Though survival differences were modest, the trials also demonstrated that docetaxel-treated patients had superior progression-free survival, palliative benefit and response to therapy as measured by the decline in prostate-specific antigen (PSA) levels. As a result, the US FDA approved docetaxel given every 3 weeks in combination with prednisone as a new standard of care for treatment of metastatic hormone-refractory prostate cancer.

Questions arose immediately from these trials, however. For instance, estramustine was used in SWOG 9916 in combination with docetaxel, but this arm appeared excessively toxic compared to a similar arm in TAX 327 using prednisone instead. While such comparisons are not usually valid, many clinicians and the US FDA have chosen to leave this drug out of the combination for initial treatment in combination with docetaxel. In addition, because of reduced myelosuppression, weekly administration of docetaxel was popular among oncologists for use in older men who may have had prior pelvic radiotherapy. In TAX 327, this arm was not superior to the control arm (mitoxantrone) and, therefore, this is not considered a first-line alternative. That said, it could still be considered an option for patients for whom myelosuppression is considered a significant risk.

New randomised trials are evaluating docetaxel-based combinations with new drugs (e.g. imatinib, high-dose calcitriol, atrasentan, bevacizumab), as well as the earlier use of docetaxel chemotherapy in high-risk patients with localised disease prior to, or after, local treatments such as radical prostatectomy or radiotherapy, and in those with rising PSA levels. ▲