

## FEATURE ARTICLE

# Ketoconazole as a Secondary Hormonal Intervention in Advanced Prostate Cancer

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Prostate cancer is the most common nonskin cancer in American men, and androgen-deprivation therapy is the cornerstone of treatment for advanced prostate cancer. Unfortunately, the median duration of response to initial androgen deprivation is limited to 18–24 months. After failing primary therapy, many individuals respond to multiple secondary hormonal interventions, such as ketoconazole. A potent adrenolytic agent, ketoconazole is associated with potential hepatotoxicity, adrenal insufficiency, and drug and food interactions. Nurses can greatly impact the course of treatment for patients by being aware of the rationale for the use of secondary hormones, ketoconazole as a hormonal intervention, potential drug interactions, side effects, and management of toxicities.

**P**rostate cancer is the most common male malignancy, excluding skin cancer, among American men and is the second-leading cause of cancer-related death in males. The projected incidence for 2006 is 234,460 new cases, and the projected number of deaths is 27,350 (American Cancer Society, 2006). Prostate cancer ranks third in cancer incidence worldwide and sixth in cancer mortality among men (Parkin, Bray, Ferlay, & Pisani, 2002). However, considerable variability regarding incidence and mortality exists worldwide, with incidence rates as low as 1.08 per 100,000 in China and 5.5 per 100,000 in Japan to as high as 17.9 per 100,000 in the United States (Jemal, Thomas, Murray, & Thun, 2002), where prostate-specific antigen (PSA) screening is used widely. Prostate cancer commonly is viewed as a disease that affects older men; in fact, age 72 is the median at diagnosis (National Cancer Institute, 2005). The disease occurs more frequently in those with a family history as well as in African American men.

Microscopic foci of cancer are evident in most men with increasing age; however, only a small proportion of the slow-growing tumors progress to invasive prostate cancer, and an even smaller number result in premature death (Boyle, Severi, & Giles, 2003). For patients who develop metastases, the disease is incurable by any therapeutic modality currently available (Laufer & Eisenberger, 2002). The outcome for those patients is bleak because the disease becomes progressive and, for some, eventually fatal (Laufer & Eisenberger). The mainstay for advanced disease has been androgen-deprivation therapy since the 1940s, when Huggins and Hodges (1941) observed that surgical orchiectomy or the administration of estrogen could reduce tumor size, decrease acid phosphatase, and palliate symptoms of disease. Despite response rates to initial androgen-deprivation therapy of 80%–90%, nearly all men experience progression after an average of 18–24 months;

### At a Glance

- ◆ New therapies beyond hormones are needed to improve outcomes for patients with progressive prostate cancer; however, some patients with castrate levels of testosterone do respond to multiple, successive hormonal manipulations.
- ◆ Whether to try additional hormonal manipulations or proceed immediately to cytotoxic therapy depends on functional status, comorbidities, disease extent, and symptoms.
- ◆ Ketoconazole, an adrenolytic agent used as a hormonal therapy for prostate cancer treatment, can be administered safely and effectively. Close monitoring of drug administration, drug interaction, and toxicity assessment by nurses can greatly impact the overall effectiveness of this regimen while minimizing toxicity.

therefore, at that point, second-line hormone therapy should be considered (Dawson, 2002).

The aim of this article is to describe the role of secondary hormones, specifically ketoconazole, in the treatment of advanced

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