
Male Breast Cancer During Finasteride Therapy

Male breast cancer is an uncommon disease, with an estimated incidence of one case per 100 000 man-years (1). Conditions that result in relative estrogen excess or lack of androgen are associated with an increased risk of breast cancer in both women (2) and

men (3). An example of increased rates of male breast cancer associated with increased estrogen-to-testosterone ratios can be seen in men with Klinefelter's syndrome, who are 50 times more likely to develop breast cancer than their normal counterparts (4). This ratio may be affected by finasteride (Proscar), which has been widely marketed and used to treat benign prostate hyperplasia (BPH). Proscar shrinks androgen-dependent prostate tissue by inhibiting steroid 5 α -reductase, an enzyme that converts testosterone to dihydrotestosterone (DHT). However, inhibition of DHT production alters the estrogen-to-androgen ratio and may also increase the risk of gynecomastia and male breast cancer. Reports to the U.S. Food and Drug Administration (FDA) from June 1992 through February 1995 showed that gynecomastia had been observed in 214 men receiving Proscar therapy. Two of these men were subsequently found to have invasive ductal breast carcinoma (5). There was also a higher incidence of gynecomastia in men participating in the Prostate Cancer Prevention Trial. The rate of gynecomastia was 426 (4.5%) of 9423 subjects randomly assigned to the Proscar arm compared with 261 (2.8%) of 9457 subjects randomly assigned to the placebo arm. There was one case of breast cancer in each arm of the trial (6).

Evidence of the association of Proscar with male breast cancer comes from the Medical Therapy of Prostatic Symptoms (MTOPS) study, a National Institutes of Health (NIH)-sponsored study of about 3047 men that compared Proscar, doxazosin, and the combination for the treatment of BPH (7). Men were randomly assigned to one of four treatment arms: Proscar and doxazosin (n = 786), Proscar (n = 768), doxazosin (n = 756), and placebo (n = 737). Four cases of breast cancer were reported. According to a letter from the NIH to the MTOPS principal investigators, one man in the Proscar/doxazosin group and three in the Proscar-alone group developed male breast cancer. The rate of breast cancer in this trial for men taking Proscar either alone or with doxazosin was therefore 4 in 1554, or nearly 200 times that of the general population. One of us (S. C. Lee) was patient No. 14–214 who participated in the MTOPS trial from 1997 through 2002 and was

randomly assigned to receive 5 mg of Proscar daily. This patient was a previously healthy 69-year-old man with no family history of cancer who developed lymph node–positive estrogen and progesterone receptor–positive breast cancer (tumor–node–metastasis [TNM] staging T1cN1M0). He was subsequently treated with modified radical mastectomy with axillary lymph node dissection, chemotherapy, and tamoxifen. He was one of the four breast cancer cases mentioned in the letter from the NIH to the MTOPS.

As this patient and his physician, we strongly recommend that the FDA require that information about the possible association between male breast cancer and Proscar be clearly stated in the manufacturer's patient information leaflet for prescriptions and in its advertisements. Proscar has been well established to improve quality of life in men suffering from BPH. Patients and their physicians need to be better informed about this potential life-threatening risk. Men who take Proscar need to be aware of any changes in their breasts and report these changes immediately to their physicians.

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NOTES

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