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Finasteride Counseling for Male Androgenetic Alopecia Should Reflect Updated Findings on Prostate Cancer Risk

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Dear Editor,

Multiple clinical trials demonstrate marked improvement in hair growth and reduced rates of hair loss following finasteride administration for which the medication gained FDA-approval for male androgenetic alopecia (AGA). While initial epidemiological data suggested that finasteride increased the risk of high-grade prostate cancer (PC), subsequent investigations revealed that a detection bias existed in which finasteride might enhance PC detection by shrinking prostate size and unmasking high-grade neoplasia. Despite these new findings, we continue to encounter patients and providers operating under viewpoints not supported by current evidence. We suggest that physician counseling for finasteride administration in the treatment of AGA should reflect updated findings on PC risk.

Finasteride is a specific type II 5- α reductase inhibitor (5-ARI) that impedes the conversion of testosterone into the more potent metabolite dihydrotestosterone responsible for AGA. As one of only two FDA-approved medications for AGA, it remains a key member of the dermatologic armamentarium in treating male pattern hair loss. The 7-year Prostate Cancer Prevention Trial (PCPT) showed an increased risk of high-grade PC in those taking oral finasteride daily, which may have limited its use for AGA by some physicians; however, more recent data reveal a reduced overall risk of PC and high-grade PC without a change in PC-related or overall mortality (Table 1).

Detection of PC, one of the most commonly diagnosed neoplasia in men, involves measuring serum prostate-specific antigen (PSA), digital rectal exam (DRE), and, if necessary, biopsy. Because the prostate is responsive to the trophic effects of androgens, 5-ARIs are used clinically for several purposes, including reducing organ size with benign prostate hypertrophy. The 2003 PCPT consisted of 18,882 men aged 55 years or older randomized to receive either oral 5 mg/day finasteride or placebo for 7 years [1]. PC was diagnosed via biopsy and subsequent histology in 24.4% of men in the placebo group compared to 18.4% in the finasteride group ($p < 0.001$) (Table 2). These results indicated a protective effect of

finasteride with a 24.8% reduction in the relative risk of developing PC [1]. Despite a lower overall incidence of PC, men in the finasteride group were more likely to have high-grade tumors (Gleason grade 7–10) compared to those in the placebo group ($p < 0.001$) (Table 2) [1].

Further investigation into the cause of this paradox revealed that the PCPT study findings of increased high-grade malignancy were influenced largely by the effect of finasteride on PC detection rather than as a causal agent. A series of publications showed that finasteride improves the sensitivity of DRE, PSA, and biopsy screening tests as well as the accuracy of grading individuals with high-grade PC (Table 2) [2–4]. Taken together, the differences in detection, rather than promotion of malignancy, could contribute to a higher prevalence of high-grade PC encountered in the finasteride group.

A 2008 epidemiological study adjusted for the DRE, PSA, and biopsy screening biases resulting from finasteride administration in the PCPT [5]. Using the same cohort of men from the original report, PC was estimated to be diagnosed in 21.1% of men in the placebo group, but only 14.7% of participants in the finasteride group – a relative risk reduction in PC of 30% in men taking finasteride ($p < 0.0001$) (Table 2). Moreover, the newfound bias-adjusted analyses demonstrated a decrease in high-grade PC risk in the finasteride group (6.0%) compared to the placebo group (8.2%). These data indicate that, in addition to lower overall risk of PC, finasteride may in fact reduce the risk of high-grade PC as well (Table 2).

In 2013, an 18-year follow-up PCPT study examined the long-term survival of patients who received finasteride against placebo in the initial 7-year trial. Contrasting the finasteride and placebo group, no significant difference existed in the overall survival following a PC diagnosis [6]. The 15-year survival rate was similar for men in the finasteride group (78.0%) and the placebo group (78.2%). In men diagnosed with PC, the adjusted hazard ratio for death in the finasteride group was no different compared to those taking placebo (Table 2) [6]. Along these lines, similar analyses showed no significant difference in PC-related mortality (Table 2) [7].

We highlight the updated findings from the PCPT epidemiological studies showing a favorable pharmacologic profile on PC risk such that more patients may benefit from its use in AGA. While the 5 mg/day oral dose used in the PCPT trials is higher than the FDA-approved dose of 1 mg/day for male AGA, either dose achieves a similar level of dihydrotestosterone inhibition [8]. Therefore, in our counseling we assume that the prostate effects are similar, although a head-to-head study would be needed to prove parity with respect to the different doses. Many patients remain concerned about the side effects of taking finasteride. Post-finasteride syndrome is a highly controversial condition consisting

Table 1. Counseling recommendations for men taking finasteride based on epidemiological data before and after 2008

Counseling parameter for taking finasteride	Old counseling (before 2008)	New counseling (after 2008)
PC risk	Lower [1]	Lower [6]
High-grade PC risk	Higher [1]	Equivalent or lower [5]
Overall survival	Unknown	Equivalent [6]
Prostate cancer-related mortality	Unknown	Equivalent [7]

Table 2. Summary of PCPT data on oral finasteride and PC risk in older men^a

Author, year [Ref. No.]	Total sample size	Results (finasteride group vs. placebo) ^b
Thompson, 2003 [1]	9,060	Overall PC: 18.4 vs. 24.4% ($p < 0.001$) High-grade PC: 37.0 vs. 22.2% ($p < 0.001$)
Thompson, 2006 [2]	9,691	Increased sensitivity of PSA for detecting PC ($p < 0.001$)
Thompson, 2007 [3]	9,691	Increased sensitivity of DRE for detecting PC ($p = 0.02$)
Lucia, 2007 [4]	526	Increased detection of high-grade PC with biopsy ($p = 0.01$)
Redman, 2008 [5]	15,990	Overall PC: RR = 0.70, 95% CI: 0.64–0.76; $p < 0.0001$ High-grade PC: RR = 0.73, 95% CI: 0.56–0.96; $p = 0.02$
Thompson, 2013 [6]	18,880	HR = 0.93, 95% CI: 0.78–1.12
Goodman, 2019 [7]	18,880	HR = 0.75, 95% CI: 0.50–1.12

PCPT, Prostate Cancer Prevention Trial; PSA, prostate-specific antigen; DRE, digital rectal exam; RR, relative risk; CI, confidence interval; HR, hazard ratio. ^a Median age of 63 years at study entry. ^b The finasteride group received 5 mg/day in the randomized controlled trial.

of reduced libido, erectile dysfunction, depression, and gynecostasia reported by men who have taken oral finasteride and discontinued it [9]. It is worth noting that a 2016 study using Medicare claims from the PCPT participants found no increase in sexual dysfunction and only a moderate increase in depression with long-term use of finasteride [10].

We proffer that when counseling patients considering finasteride for AGA, dermatologists can consider the updated epidemiology that shows that the medication at 5 mg/day (1) confers reduced lifetime PC risk, (2) might actually lower the risk for high-grade PC, and (3) does not change prognosis for overall survival nor prostate-cancer mortality. Although many of the side effects from finasteride are reversible, physicians should provide additional counseling for patients with a history of depression or sexual dysfunction. In our practice, we recommend finasteride as a relatively safe and effective treatment of AGA in men.

Disclosure Statement

C.C.A. declares no conflicts of interest. K.S. has ownership interest in Pilaris Inc.

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Author Contributions

C.C.A. and K.S. prepared the manuscript. All authors read and approved the final version.

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