A REAL-WORLD INVESTIGATION OF FINASTERIDE AND THE RISK OF PROSTATE CANCER

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BACKGROUND

Finasteride is a 5α-reductase inhibitor used to treat the symptoms of benign prostatic hyperplasia (BPH). It is known to also decrease prostate specific antigen (PSA). Given this effect, finasteride has been studied since 1991 for its potential role in the development and detection of prostate cancer[1].

In 1993, the National Cancer Institute funded the Prostate Cancer Prevention Trial (PCPT) which was published in 2003 and found a decreased risk of low-grade prostate cancer with finasteride compared to placebo[2]. Concerns that finasteride may cause more high-grade cancers were alleviated by a follow-up study at 18 years[3], but by this time an FDA warning had already been mandated on the medication label. Additionally, these results were found under arguably artificial clinical trial conditions, including only patients with PSA values of ≤3 ng/mL at baseline[4].

With the publication of recent long-term follow-up to the PCPT using Medicare claims[5], real-world evidence (RWE) has gained a modicum of attention in its discussion. However, a fully RWE-driven analysis of the association between finasteride treatment and prostate cancer had yet to emerge.

RESULTS

Study Cohorts:

- Of 47 million patients in the network, 2,659 finasteride patients (F) and 11,890 tamsulosin patients (T) fulfilled study criteria (Figure 1).
- 95% of clinical facts for the finasteride cohort were between 2001 to 2018 and between 2003 to 2018 for the tamsulosin cohort.
- Cohorts differed in age at index event (T: M = 64.7 yrs., SD = 9.7; F: M = 68.0 yrs., SD = 9.7), pre-existing PSA values (T: M = 1.9 ng/mL, SD = 1.9; F: M = 2.7 ng/mL, SD = 2.6), and prevalence of some pre-existing diagnoses.

Propensity Score Model:

- 2,636 matched patients were identified in each cohort (Figure 2).
- Following matching, the standardized mean difference (SMD) comparing variables in the two cohorts was <10%.

Outcomes:

- PSA values were significantly decreased for the finasteride cohort (M = 1.9 ng/mL, SD = 2.0) as compared to the tamsulosin cohort (M = 2.8 ng/mL, SD = 2.7) (t = 11.5, p < 0.0001) (Figure 3).
- A Kaplan-Meier analysis demonstrated a significantly increased survival probability without prostate cancer diagnosis (Figure 4).
- Over the 10-year observation period, 3.9% of patients in the finasteride cohort and 7.1% patients in the tamsulosin cohort received a diagnosis of prostate cancer (RR = 0.55, RD = -3.2%, p < 0.0001, NNT = 31) (Figure 5).

(1) Gormley, G. (1991). Role of 5 alpha-reductase inhibitors in the treatment of advanced prostatic carcinoma. *The Urologic Clinics of North America,18*(1), 93-8.
(2) Thompson, I. M., Goodman, P. J., Tangen, C. M., Lucia, M. S., Miller, G. J., Ford, L. G., ... Coltman, C. A. (2003). The Influence of Finasteride on the Development of Prostate Cancer. *New England Journal of Medicine, 349*(3), 215–224. https://doi.org/10.1056/NEJMoa030660
(3) Thompson, I. M., Goodman, P. J., Tangen, C. M., Parnes, H. L., Minasian, L. M., Godley, P. A., ... Ford, L. G. (2013). Long-Term Survival of Participants in the Prostate Cancer Prevention Trial. *New England Journal of Medicine, 369*(7), 603–610. https://doi.org/10.1056/NEJMoa1215932
(4) Stapff, M. P., & Palm, S. T. (2019). More on Long-Term Effects of Finasteride on Prostate Cancer Mortality. *New England Journal of Medicine, 380*(20), e38(1). https://doi.org/10.1056/NEJMc1902700
(5) Unger, J. M., Hershman, D. L., Till, C., Tangen, C. M., Barlow, W. E., Ramsey, S. D., ... Thompson, I. M. (2018). Using Medicare Claims to Examine Long-term Prostate Cancer Risk of Finasteride in the Prostate Cancer Prevention Trial. *JNCI: Journal of the National Cancer Institute*. https://doi.org/10.1093/jnci/djy035

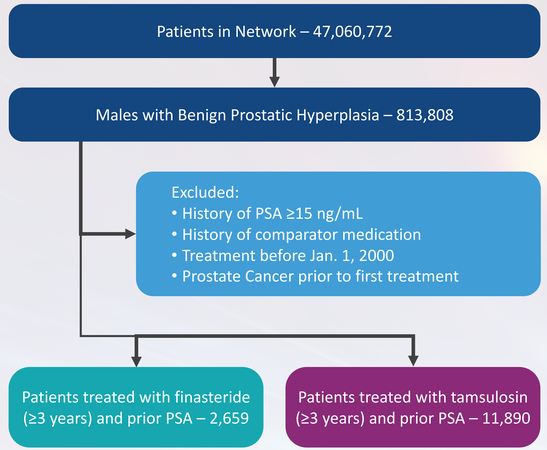


Figure 1: Study cohorts.

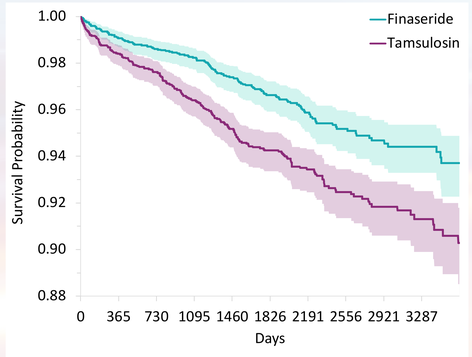


Figure 4: 10-year Kaplan-Meier survival probability, starting from index event of first recorded use of tamsulosin or finasteride, and 95% confidence interval. Patients were censored the day following the final clinical fact in their EMR record.

OBJECTIVES

Following the results of clinical trial analyses investigating the association between finasteride and prostate cancer, this research aimed to:

- Explore the risk of developing prostate cancer with finasteride treatment as compared to first-line treatment with an alpha-blocker
- Provide conclusions supported by additional forms of evidence to randomized clinical trials (RCTs) to inform the decisions of physicians
- Demonstrate the potential of using electronic medical records (EMR) to generate medical RWE as an alternative to costly and long-term RCTs

METHODS

EMR data from a research network representing 39 healthcare organizations, accessed via the TriNetX platform, were used to analyze the association between finasteride treatment and prostate cancer diagnosis. Two cohorts of patients were defined by requiring three years of treatment with finasteride or tamsulosin after January 2000, a history of BPH, and no history of treatment with the comparator medication. The first treatment with the respective medication was considered the patient's index event. Patients must also have had a PSA value recorded prior to the index event, but could not have had a diagnosis of prostate cancer during this same time. Patients with a history of a PSA value ≥15 ng/mL were not included in this study.

Cohorts were matched 1:1 on age at index event, pre-existing PSA values, and specific diagnoses in pre-determined therapeutic areas (genitourinary, metabolic, cardiovascular, neoplastic, and psychiatric) prior to the index event using a greedy nearest neighbor matching algorithm with a caliper of 0.25 times the SD.

Prostate cancer outcomes were analyzed over a 10-year observation period comparing total risk and Kaplan-Meier survival probability without prostate cancer diagnosis over that period. Additionally, the distributions of PSA values for each cohort following the index event were compared via a t-test.

CONCLUSIONS

The findings of the PCPT have not been validated under real-world conditions prior to this study. Using EMR, patients treated with finasteride were found to have significantly lower PSA values as compared to patients treated with tamsulosin. More importantly, patients treated with finasteride were found to have a significantly lower risk of being diagnosed with prostate cancer than those treated with an alpha-blocker commonly prescribed as a first-line treatment of BPH (tamsulosin). Therefore, real-world data provide robust retrospective evidence of a protective effect of finasteride against the development of prostate cancer. These results support expanded use for finasteride by physicians as a prophylactic measure against prostate cancer.

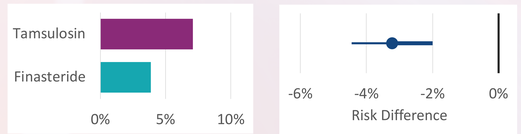
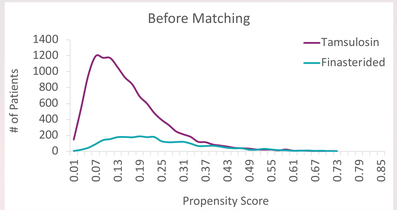


Figure 5: Total risk and risk difference (including 95% confidence intervals).



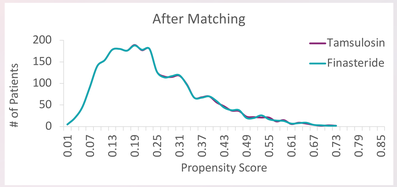


Figure 2. Propensity score matching.

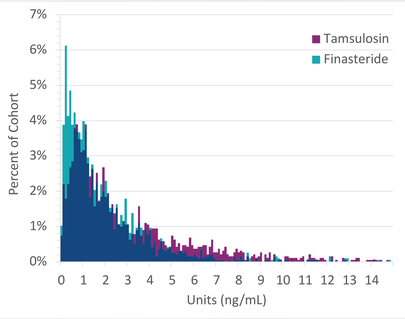


Figure 3: Distribution of PSA values measured following index event.

DISCLOSURES

Both Stephan Palm and Manfred Stapff conducted this research as employees of TriNetX, Inc.