Chemoprevention of Prostate Cancer: An Update

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Editor's Note: This is an update of Paul Sieber's article in the first issue of the Journal that discussed the status of chemoprevention for prostate cancer.[1] Readers are referred to that article for more details about the design of the relevant studies, as well as their strengths and their shortcomings.

In 2006, the role of chemoprevention for prostate cancer was being evaluated in two clinical trials involving five alpha-reductase inhibitors that looked promising. The first trial, The Prostate Cancer Prevention Trial (PCPT), compared finasteride to a placebo and ultimately demonstrated a 25% reduction in prostate cancer. A second similar trial using dutasteride, known as Reduction by Dutasteride of Prostate Cancer Events (REDUCE), achieved similar results, with a 23% reduction in prostate cancer. Ultimately, however, the FDA did not approve the labeling of either compound as a preventive for prostate cancer.

In late 2013, long term data were published in the New England Journal of Medicine.[2] The groundbreaking PCPT trial showed that after 18 years of follow up, finasteride ultimately reduced the incidence of prostate cancer by 30%. The incidence of high-grade prostate cancer was slightly higher in the treatment group *but there was no difference in the overall survival of either group.* Unfortunately there were no data on the cancer-specific survival differences. The accompanying editorial comments on the long term results are no more clear-cut than the original data. An editorial comment from Michael LeFevre (a United States Preventive Services Task Force, USPSTF member) seems to sum it up very well: *"finasteride has no short- or long-term effect on all-cause mortality so we cannot recommend its use to prolong life. Men . . . may make a rational decision to take the drug to reduce the harm of screening. Of course, another way to reduce the harm of screening is to choose to not be screened."*[3]

It would appear that chemoprevention of prostate cancer today has been pushed aside by even tougher choices. The question facing clinicians today is whether we should even screen for prostate cancer. It is unlikely that a primary care provider will have the time to spend discussing the pros and cons of screening in addition to their already hectic schedule.

The last decade has seen a reduction in prostate cancer deaths by nearly 10,000 per year or ~30%. Few argue that screening is at least partially responsible for this reduction. Further, the long term follow-up of radical prostatectomy versus watchful waiting unequivocally shows a significant reduction in mortality, but the definitive answer required long term followup to become apparent.[4] The USPTF currently gives screening for prostate cancer a D rating! The long term effects of this policy may take a decade to emerge. This would not be surprising, considering that it took nearly 20 years of follow-up to give an unequivocal answer about radical prostatectomy. In the short term we and others have seen a significant reduction in prostate biopsies.[5] As for the long term implications, only history can tell.

It is clear today that with just a single PSA test at age 40-55 we can clearly identify whom to screen.[6] With ongoing advances in genomics and diagnostics it would appear we have a better knowledge base of whom to biopsy and whom to treat. I agree strongly with the editorial by Samir Taneja in the *Journal of Urology* that if we cannot come to a better understanding of whom we biopsy and whom we treat then maybe we should let the epidemiologists tell us how to treat our patients![7]

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