Re: Dutasteride in Localised Prostate Cancer Management: The REDEEM Randomised, Double-Blind, Placebo-Controlled Trial
Fleshner NE, Lucia MS, Egerdie B, et al.
Lancet 2012;379:1103–11

Expert’s summary:
The Reduction by Dutasteride of Clinical Progression Events in Expectant Management (REDEEM) trial assessed the efficacy of dutasteride in preventing disease progression in men with low-risk prostate cancer on active surveillance.

Investigators randomized 302 participants to receive dutasteride 0.5 mg once daily or placebo. Entry criteria included clinical stage T2a or lower, prostate-specific antigen (PSA) ≤11 ng/ml, and Gleason 6 cancer diagnosed in <4 cores of a minimum 10-core biopsy with <50% of any core positive. Follow-up continued for 3 yr, with a 12-core prostate biopsy performed at 18 and 36 mo. The final analysis included the 96% of participants who had at least one biopsy.

The primary end point was time to progression. The investigators defined progression as pathologic (four or more cores involved, ≥50% of any core, or Gleason pattern ≥4) or therapeutic (surgical or nonsurgical prostate cancer treatment).

By 3 yr, 38% and 48% of the dutasteride and control participants, respectively, had progressed by pathologic or therapeutic criteria, a risk reduction of 38% for dutasteride (p = 0.009). Adverse event rates were similar between groups.

Expert’s comments:
Effective interventions for preventing clinical progression and unnecessarily aggressive treatment in active surveillance patients are lacking. REDEEM was the first trial to test a medical therapy to reduce progression in an active surveillance population. Strengths of this study included its randomized structure, well-defined inclusion criteria, and adequate power.

A prominent design issue that tempered enthusiasm for these results was the association of a primary outcome measure, therapeutic progression, with dutasteride-induced changes in PSA. Participants were not blinded to their PSA values, and knowing them promotes anxiety and influences treatment decisions in active surveillance patients [1]. Dutasteride participants reported greater declines in prostate cancer–related anxiety compared with controls (p = 0.017), suggesting they were less inclined to pursue aggressive treatment. Analyses stratified by pathologic and therapeutic progression approached but did not attain between-group significance.

If reducing the incidence of aggressive treatment is the primary therapeutic goal in this population, there may be little clinical significance in distinguishing between biologic and therapeutic progression, particularly for a generally well-tolerated class of medications that improves PSA operating characteristics [2] and prevents the incidence of clinical benign prostatic hyperplasia [3].

Other prevention studies are currently under way for low-risk prostate cancer. The Men’s Eating and Living study [4] is a nationwide trial of 464 US men investigating the efficacy of dietary change in preventing disease progression in active surveillance patients.

Conflicts of interest: The author has nothing to disclose.

References

J. Kellogg Parsons
Division of Urologic Oncology, Moores Cancer Center, University of California, San Diego, La Jolla, CA, USA
E-mail address: k0parsons@ucsd.edu.

http://dx.doi.org/10.1016/j.eururo.2013.04.022