Cost-effectiveness of Chemoprevention With Dutasteride Based on Results From the REDUCE Clinical Trial

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ABSTRACT

OBJECTIVE: The Reduction by Dutasteride of Prostate Cancer Events (REDUCE) clinical trial examined whether a dual 5-alpha reductase inhibitor (5ARI), dutasteride, reduced the rate of prostate cancer (PCa) detection on biopsy. We examined the cost-effectiveness of using dutasteride compared with usual care in preventing PCa in men at increased risk as seen in REDUCE.

METHODS: We developed a Markov model to compare the costs and outcomes of chemoprevention with dutasteride 0.5 mg/day with usual care. Subjects were men aged 50 to 75 with serum prostate-specific antigen (PSA) of 2.5 to 10 ng/mL (aged < 60 years) or 3.0 to 10 ng/mL (aged ≥ 60 years), and with single negative prostate biopsy in previous 6 months. The model simulated the REDUCE cohort of men annually through different health states (e.g., healthy male, PCa, benign prostatic hyperplasia [BPH], PCa recurrence) over a 10-year time horizon. Risk of PCa for patients receiving usual care and dutasteride was obtained from REDUCE where dutasteride showed a reduced risk of 23% and no significant increase in high-grade tumors. Additional benefits in terms of reduction in number of acute urinary retention (AUR) events and BPH-related surgeries were considered. Impact of adverse events (e.g., incontinence, erectile dysfunction, ejaculatory dysfunction) was considered. Costs and utilities were obtained from the published literature.

RESULTS: Dutasteride patients experienced fewer PCas (335 vs. 412 per 1,000 patients) and increased costs ($17,270 vs. $13,845) compared with usual care patients. Although life-years were not significantly impacted, dutasteride patients incurred an increase in quality-adjusted life-years (QALYs) of 0.15. Chemoprevention with dutasteride was found to be cost-effective, with an incremental cost per QALY of $22,460. Results were robust to changes in parameters.

CONCLUSIONS: Despite increased costs that occur due to taking a drug for prevention, the use of dutasteride 0.5 mg/day is cost-effective in men at increased risk for PCa. Use of dutasteride for PCa prevention in the appropriate population has the potential to reduce the cost associated with the treatment of PCa and prevent reductions in quality of life associated with PCa treatment.

BACKGROUND

- PCa is the most common form of solid tumor cancer and the second leading cause of death in men in the United States (US).[1]
- A 5ARI preventative treatment may have substantial clinical and economic impacts for men.[2-4]
- Recent results of the REDUCE clinical trial showed that men at increased risk for PCa treated with dutasteride as a chemoprevention agent compared with usual care had a significantly reduced risk of PCa over a 4-year period.[5]
- Because chemoprevention with dutasteride must be given prior to the diagnosis of PCa and potentially for a long period of time, decision makers may have concern about the benefit in terms of value for money. Thus, understanding the cost-effectiveness of the potential use of dutasteride to reduce the risk of PCa will be valuable for decision makers.

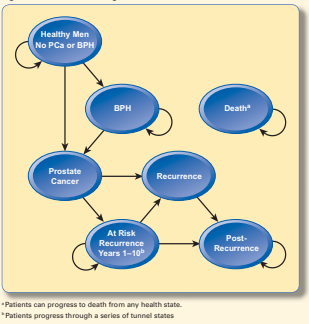
OBJECTIVE

- Using the constructs of previously published models, a decision-analytic model was created to examine the cost-effectiveness of using dutasteride compared with usual care in preventing PCa in men at increased risk as seen in the REDUCE clinical trial.[6]

METHODS

- Patient population (clinical trial population):
  - Men aged 50 to 75 years
  - Serum PSA of 2.5 to 10 ng/mL for men aged < 60
  - Serum PSA of 3.0 to 10 ng/mL for men aged ≥ 60
  - Single negative prostate biopsy (6–12 cores) in previous 6 months
- Chemoprevention with dutasteride 0.5 mg per day was compared with usual care/no preventative.
- A Markov model framework (Figure 1) simulates a cohort of patients annually through health states such as healthy male, PCa (low grade and high grade), BPH, and death over a 10-year time horizon.
- The model is based on the perspective of a US third-party payer.

Figure 1. Markov Model Diagram



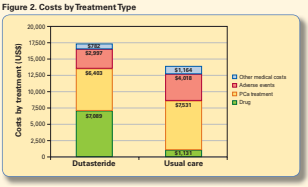
[a]Patients can progress to death from any health state.
[b]Patients progress through a series of tunnel states

- Dutasteride was shown to reduce the risk of PCa by 23% over a 4-year period.[5]
- Proportion of cancers that were high versus low grade and the probabilities of adverse events, BPH-related surgery, and AUR due to dutasteride use were obtained from the REDUCE trial.[5]
- Adverse events experienced due to PCa treatment were obtained from published clinical literature.[7-9]
- Annual cost of dutasteride was based on published wholesale acquisition costs of $981.85.[9]
- Resource use and costs for PCa workup and staging, treatment, and adverse events were taken from published literature and standard US costing sources.[10-19]
- Age-specific utilities were obtained from the published literature.[19] Utilities were adjusted for the occurrence of PCa (high versus low grade), BPH, and improvement in BPH symptoms and occurrence of adverse events due to treatment with dutasteride.[20,21]
- Mortality for PCa patients was estimated from the 1990-2004 SEER statistics.[22] Mortality for patients without PCa was obtained from US National Vital Statistics.[23]
- All costs are reported in 2009 US dollars.
- Costs and outcomes are discounted at 3% per annum.

RESULTS

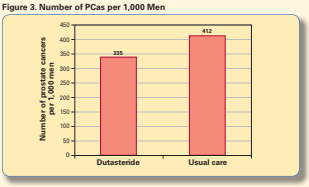
- Baseline results are presented in Figures 2 to 5.
- Patients receiving dutasteride experienced higher costs than those receiving usual care ($17,270 versus $13,845).

Figure 2. Costs by Treatment Type



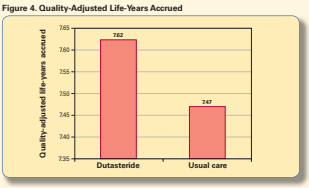
- Patients receiving dutasteride experienced fewer PCas than those receiving usual care (335 versus 412 per 1,000 men over a 10-year period).

Figure 3. Number of PCas per 1,000 Men



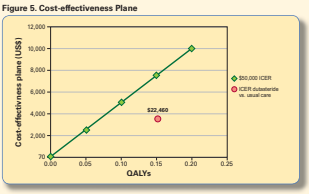
- Dutasteride patients experienced greater gains in quality-adjusted life-years than usual care patients: 7.62 versus 7.47.

Figure 4. Quality-Adjusted Life-Years Accrued



- Dutasteride is cost-effective with an incremental cost per QALY of $22,460 in patients at high risk for cancer.

Figure 5. Cost-effectiveness Plane

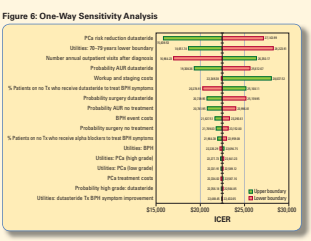


Sensitivity Analysis

One-way sensitivity analysis is presented in Figure 6.

- Results were most sensitive to changes in dutasteride's PCa risk reduction and impact on high-grade cancers.
- Additional parameters that were sensitive were PCa, BPH, and symptom improvement utilities and PCa treatment costs.
- All other parameters had very little impact on results.

Figure 6: One-Way Sensitivity Analysis



CONCLUSIONS

- Use of dutasteride increases total medical costs (due to dutasteride drug costs) while decreasing the occurrence of PCa when compared with usual care.
- QALY gains per person for men at high risk for prostate cancer seem low; however, they are similar if not greater than per person QALY gains in other disease areas.[24,25,26]
  - Pneumococcal conjugate vaccine has shown to be associated with 0.012 QALY gains.[24]
  - Influenza treatments have shown to be associated with ~0.003 QALY gains.[25,26]
- Despite increases in costs due to taking dutasteride for prevention, the use of dutasteride is cost-effective for decreasing the risk of PCa in patients at increased risk.
- Results were sensitive to changes in dutasteride's impact on the risk of PCa and high-grade tumors. However, dutasteride remained cost-effective within acceptable ranges for these values.

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