ABSTRACT

Background and Objective: Recent clinical trials indicate that combining an alpha blocker for rapid symptom improvement and a 5-alpha reductase inhibitor (5-ARI) to reduce the risk of clinical progression of benign prostatic hyperplasia (BPH) may be an optimal approach to management; however, few studies have evaluated the effect of combination therapy on clinical progression in a real-world setting. The purpose of our study was to assess the clinical and economic impact of early versus delayed 5-ARI therapy in patients treated with an alpha blocker for BPH.

Materials and Methods: A retrospective database analysis included men 50 years of age and older who were treated for BPH between 2003 and 2007. Clinical outcomes were evaluated for patients using 5-ARIs early (within 30 days of starting an alpha blocker) compared with those using delayed 5-ARI therapy (between 30 and 180 days after starting an alpha blocker). We assessed the likelihood of clinical progression (defined as the occurrence of acute urinary retention or prostate surgery) for each group over a one-year period following the start of alpha-blocker therapy.

Data Source: The MarketScan Database, which was used to identify patients, contains medical and pharmacy claims data obtained directly from Medicare and commercial health plans and employers, representing 18 to 20 million lives annually.

Results: Of 8,617 men included in the analysis, 64.5% began 5-ARI therapy within 30 days of alpha-blocker therapy (the early cohort). These patients were less likely than those receiving delayed 5-ARI treatment to have clinical progression (12.8% vs. 17.4% respectively; P < 0.0001), acute urinary retention (10.2% vs. 13.8%, P < 0.0001), and prostate surgery (5% vs. 7%, P = 0.0002). The early group also incurred lower BPH-related medical costs ($572 vs. $730, P < 0.0001). Even though BPH-related pharmacy costs were significantly higher ($1,137 vs. $1,263, P = 0.0313), their total BPH-related costs were lower ($1,834 vs. $1,867, P = 0.0068).

Conclusion: These results suggest that early 5-ARI therapy for men with symptomatic BPH who receive an alpha blocker may significantly reduce the risk of clinical progression (i.e., acute urinary retention or prostate surgery) over the next 12 months as well as lower BPH-related medical costs and BPH-related total costs.

INTRODUCTION

Benign prostatic hyperplasia (BPH), or enlarged prostate, affects more than 50% of men 50 years of age and older and nearly 90% of men by age 80.1 The prevalence of BPH is expected to grow as the population of men 65 years of age and older increases from 17 million (in 2010) to almost 30 million (by the year 2030).2 In 2000, approximately 4.5 million visits made to physician offices resulted in a primary diagnosis of BPH, and almost 8 million physician visits resulted in a primary or secondary diagnosis of BPH.3 An enlarged prostate places a significant burden on employees and their employers because of direct medical costs (i.e., cost of treatment) and lost work time.4 Direct and indirect costs to the private sector related to BPH are estimated at $3.9 billion.4 However, few data are available regarding differences in costs associated with various therapies for BPH.

Current treatment options for BPH include watchful waiting, pharmacological therapy, minimally invasive procedures, and prostate surgery.3 In most cases, first-line therapy consists of pharmacological treatment with alpha blockers or 5-alpha reductase inhibitors (5-ARIs). Alpha blockers treat symptoms of BPH by relaxing the smooth muscle tissue in the prostate and neck of the bladder, allowing urine to flow more freely. Through their mechanism of action, these drugs achieve relatively rapid improvement of lower urinary tract symptoms (i.e., in less than one week) but have no effect on prostate growth.6

By contrast, 5-ARIs inhibit the production of dihydrotestosterone (DHT), the primary cause of prostate growth, and therefore reduce prostate size.7,8 Thus, 5-ARIs directly affect the progression of prostatic disease and its clinical sequelae (acute urinary retention and prostate-related surgery). However, the typical four- to six-month delay from the start of 5-ARI therapy to substantial prostate shrinkage causes a similar delay in relieving lower urinary tract symptoms.7,8

Disclosure: Funding for the research and preparation of this article was provided by GlaxoSmithKline, which approved the study design and manuscript. At the time of the analysis, Susan Hogue was a full-time employee of GlaxoSmithKline. Eric J. Kruep, Michael T. Eaddy, and Monica D. Chandra are employees of Xcenda, a consultant to GlaxoSmithKline.
Early Versus Delayed Therapy in Benign Prostatic Hyperplasia

Given the need for simultaneous improvement of symptoms and disease progression, there is a trend toward using combination therapy or sequential treatment with alpha blockers and 5-ARIs. Combination therapy takes advantage of the rapid symptom improvement achieved by the alpha blockers along with the disease-modifying potential offered by the 5-ARIs.

Two trials demonstrated the clinical benefits of combination therapy—Medical Therapy of Prostate Symptoms (MTOPS) and the Combination of Avodart and Tamsulosin (COMBAT).9–11 In addition, a retrospective database analysis confirmed the clinical benefits of early versus delayed use of 5-ARI therapy with alpha-blocker therapy.12 In further support of this retrospective database analysis, our study aimed to evaluate the effects of early versus delayed initiation of 5-ARI therapy with existing alpha-blocker treatment on clinical progression, acute urinary retention, and prostate-related surgery outcomes in a different population. Our study examines the effect of early or delayed 5-ARI therapy in combination with alpha blockers on BPH-related health care costs in men with BPH over a one-year time period.

PATIENTS AND METHODS

The MarketScan Database (Thomson Reuters) was used to identify patients. This database contains medical and pharmacy claims data obtained directly from Medicare and commercial health plans and employers, representing approximately 18 to 20 million lives annually. It also profiles the health care experience of retirees with Medicare supplemental insurance paid for by employers and thus includes the Medicare-covered portion of payment, the employer-paid portion, and any patient out-of-pocket expenses.

MarketScan provides detailed cost, use, and outcomes data for health care services performed in both inpatient and outpatient settings. For most of the population, medical claims are linked to outpatient prescription drug claims and person-level enrollment data through the use of unique patient or enrollee identifiers. Beneficiaries in the MarketScan Medicare Supplemental Database have drug coverage; therefore, drug data are available.

The enrollment period spanned from July 1, 2000, to December 31, 2006. Men 50 years of age and older were eligible for inclusion if they had BPH or an enlarged prostate, according to International Classification of Disease, 9th revision, Clinical Modification (ICD-9-CM) codes 222.2 and 600.xx, respectively. Subjects also had to have used an alpha blocker and a concomitant 5-ARI within six months of starting index alpha-blocker therapy.

The index date was defined as the date of the first fill of an alpha-blocker prescription. The six-month pre-index period was used to evaluate baseline patient characteristics. Patients were required to be continuously eligible for at least six months before and 12 months after the index date.

Patients were excluded from the study:

- if they had a diagnosis of prostate cancer (ICD-9-CM codes 185, 198.82, 233.4, 236.5, 239.5, V10.46) or bladder cancer (ICD-9-CM codes 188, 198.1, 223.3, 233.7, 239.4, V10.51).
- if they had used finasteride 1-mg tablets (Proscar, Merck) to treat male-pattern baldness.
- if they had undergone prostate surgery any time before the index date and in the five months after the index date.

Patients were excluded from the outcomes analyses if they had undergone prostate surgery in the five-month period after the index date, because 5-ARIs take approximately four to six months to produce a physiological effect on this outcome.7,8 The five-month period after the index date is defined as the peri-period; the seven-month period after the peri-period is defined as the outcomes assessment period. We conducted sensitivity analyses around the time periods of the peri-period and the outcomes assessment period. The study design is depicted in Figure 1.

Patients were assigned to one of two cohorts based on timing of 5-ARI therapy in relation to index alpha-blocker therapy. The early cohort started 5-ARI therapy within 30 days of index alpha blockers, and the delayed cohort started 5-ARI therapy within 31 to 180 days of the index alpha blockers. To further assess the effect of time increment on outcomes, we assigned patients to categories based on 30-day increments (0–30 days, 31–60 days, 61–90 days, 91–120 days, 121–150 days, and 151–180 days).

Clinical outcomes of interest included clinical progression (defined by the presence of acute urinary retention or prostate surgery), acute urinary retention only, and prostate surgery only. To account for the four- to six-month delay in the effect of 5-ARIs on the prostate, we evaluated only cases of acute urinary retention and prostate surgery occurring after the five-month peri-period (during the seven-month outcomes assessment period). Associated Current Procedural Terminology (CPT) and ICD-9-CM codes for the clinical outcomes of interest are listed in Table 1.

We also examined pharmacy and medical costs associated with BPH. Costs were defined as the amounts charged on the claims (for total, medical, and pharmacy). Medical costs specific for BPH were defined as those related to medical claims with a primary diagnosis of BPH and any claim with a CPT code of interest (see Table 1). Claims with a diagnosis of acute urinary retention had to be accompanied by a corresponding

Figure 1 Study design. AUR = acute urinary retention; Rx = prescription.
TABLE 1 ICD-9-CM and CPT-4 Codes for Acute Urinary Retention and Prostate-Related Surgeries

<table>
<thead>
<tr>
<th>Outcome of Interest</th>
<th>ICD-9-CM or CPT Code</th>
</tr>
</thead>
<tbody>
<tr>
<td>Transurethral electro surgical resection of the prostate</td>
<td>52601</td>
</tr>
<tr>
<td>Transurethral resection of the prostate</td>
<td>52612, 52614, 52620, 52640</td>
</tr>
<tr>
<td>Transurethral incision of the prostate</td>
<td>52450</td>
</tr>
<tr>
<td>Laser coagulation</td>
<td>52647</td>
</tr>
<tr>
<td>Laser vaporization</td>
<td>52648</td>
</tr>
<tr>
<td>Prostatectomy</td>
<td>55801, 55821, 55831</td>
</tr>
<tr>
<td>Transurethral microwave thermotherapy</td>
<td>52850</td>
</tr>
<tr>
<td>Transurethral needle ablation</td>
<td>52852</td>
</tr>
<tr>
<td>Transurethral water-induced thermotherapy</td>
<td>52853</td>
</tr>
<tr>
<td>Acute urinary retention*</td>
<td>788.2 (excluding 788.21), 599.6</td>
</tr>
</tbody>
</table>

ICD-9-CM = International Classification of Diseases, 9th Revision, Clinical Modification; CPT = Current Procedural Terminology. * ICD-9-CM codes were used to identify this outcome.

BPH-specific code (see Table 1).

We evaluated medical costs over the seven-month outcomes assessment period and examined pharmacy costs over the entire 12-month follow-up period (the five-month peri-period and the seven-month outcomes assessment period). With this method, we could use the economic analysis to evaluate the incremental change in medical costs that might be affected by 5-ARIs as well as the total costs associated with the use of 5-ARIs.

Patients may have incurred medical costs during the five-month peri-period, including BPH-related medical costs. However, because the purpose of our analysis was to assess the effect of 5-ARIs on clinical outcomes and related costs, we did not assess those costs associated with acute urinary retention and prostate surgery until these medications were expected to be clinically effective (i.e., four to six months after initiation).²⁷⁻⁸ We evaluated the differences in baseline covariates for all treatment cohorts using the t test when data were continuous in nature and using a chi-square test when data were categorical.

We assessed the likelihood of clinical progression, acute urinary retention, and prostate-related surgery using logistic regression, modeled as a function of the treatment cohorts, and the following pre-index baseline covariates: age, the presence of acute urinary retention, BPH stage, Charlson comorbidity index, number of unique diagnosis codes, number of unique medications, hematuria, bladder dysfunction, incontinence, and bladder stones.

To assess BPH stage (Table 2), we assigned each patient to one of the seven stages of disease severity using the Thomson Medstat Disease Staging system,¹³ based on the presence of ICD-9-CM codes in the six months prior to the index date. The Thomson method is a proprietary coding criterion that has been widely used to classify diagnostic categories and disease severity. The system identifies all possible diseases and specifies various severity stages of each disease based on diagnostic codes and procedures that the patient undergoes. For BPH, the codes essentially evaluate the presence of complications, such as bladder outlet obstruction, hydronephrosis, renal failure, sepsis, or shock. We used a generalized linear model (glm) with log link function with similar baseline covariates to assess differences in medical costs.

We performed all statistical analyses using SAS version 9.1.3 with an a priori significance of α = 0.05. All costs were adjusted to 2008 annual average dollars, based on the medical care component of the Consumer Price Index, and were presented as per-patient costs.

RESULTS

A total of 8,617 patients were identified from the MarketScan database—64.5% in the early-therapy cohort and 35.5% in the delayed-therapy cohort. At baseline, patients in the early cohort had more comorbidities (as indicated by Charlson comorbidity index), more severe disease (per BPH staging criteria), and more acute urinary retention compared with the delayed cohort (Table 3). The delayed-therapy patients were significantly more likely to have clinical progression (P < 0.0001), acute urinary retention (P < 0.0001), and prostate-related surgery (P = 0.0002) compared with patients initiating 5-ARI therapy early (Figure 2). The corresponding odds ratios (ORs) and 95% confidence intervals (CIs) for the main effect (starting a 5-ARI after 30 days) and background covariates are shown in Table 4.

Because it takes 5-ARIs four to six months to produce an effect on the prostate, it was assumed that the medications would not be able to prevent acute urinary retention and surgical procedures before this time period. We therefore evaluated only acute urinary retention and surgery occurring after five months of therapy (see Figure 2). During this period, the
sensitivity analysis indicated that clinical progression, acute urinary retention, and surgery findings were robust for all assessments (Table 5).

To assess the linear effect of every 30-day delay in initiating 5-ARI therapy, we used 30-day increments to classify patients based on the timing of the initiation of 5-ARI therapy. After adjusting for relevant baseline covariates, we noted that each 30-day delay in initiating 5-ARI therapy increased the risk of disease progression by 10.8% (OR, 1.108; 95% CI, 1.066, 1.152; \( P < 0.0001 \)), acute urinary retention by 12% (OR, 1.122; 95% CI, 1.075, 1.172; \( P < 0.0001 \)), and prostate-related surgery by 9% (OR, 1.094; 95% CI, 1.034, 1.158; \( P = 0.0019 \)).

After controlling for baseline covariates and pre-treatment costs of BPH, we noted that patients receiving 5-ARIs more than 30 days after initiating alpha blockers had higher BPH-related medical costs ($730 vs. $572, respectively; \( P < 0.0001 \)) in the seven-month outcomes assessment period compared with patients receiving 5-ARI therapy within 30 days (Figure 3). BPH-related pharmacy costs were significantly lower with delayed therapy ($1,263) than with early therapy ($1,137) (\( P = 0.0313 \)). Even with lower pharmacy costs, total BPH-related costs were higher in the delayed cohort ($1,867) than those in the early group ($1,834) (\( P = 0.0068 \)).

Each 30-day delay in starting 5-ARI therapy significantly increased BPH-related medical costs by 18% (\( P < 0.0001 \)) and decreased pharmacy costs by 2% (\( P = 0.001 \)). Although overall BPH-related health care costs showed an upward trend by 1% for each 30-day delay in starting 5-ARI therapy, the finding was not statistically significant (\( P = 0.0816 \)).

**Table 3  Baseline Characteristics of the Analysis Population**

<table>
<thead>
<tr>
<th>Characteristic†</th>
<th>Early-Therapy Cohort (N = 5,554)</th>
<th>Delayed-Therapy Cohort (N = 3,063)</th>
<th>( P ) Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age, years (SD)</td>
<td>68.67 (10.23)</td>
<td>67.80 (10.15)</td>
<td>0.0001</td>
</tr>
<tr>
<td>Charlson comorbidity index (SD)</td>
<td>1.03 (1.63)</td>
<td>0.86 (1.41)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Patients with previous episodes of acute urinary retention, N (%)</td>
<td>1,114 (20.06%)</td>
<td>393 (12.83%)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Mean count of unique diagnosis codes (SD)</td>
<td>7.54 (5.91)</td>
<td>6.86 (5.16)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Mean count of unique medication classes (SD)†</td>
<td>5.28 (4.09)</td>
<td>5.28 (3.96)</td>
<td>0.9494</td>
</tr>
<tr>
<td>Enlarged prostate stage (SD)</td>
<td>0.90 (1.11)</td>
<td>0.79 (0.98)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Hematuria</td>
<td>823 (14.82%)</td>
<td>297 (9.7%)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Bladder dysfunction</td>
<td>229 (4.12%)</td>
<td>121 (3.95%)</td>
<td>0.6974</td>
</tr>
<tr>
<td>Incontinence</td>
<td>127 (2.29%)</td>
<td>58 (1.89%)</td>
<td>0.2446</td>
</tr>
<tr>
<td>Bladder stones</td>
<td>292 (5.26%)</td>
<td>112 (3.66%)</td>
<td>0.0008</td>
</tr>
</tbody>
</table>

\( SD = \) standard deviation.

† All patient characteristics were calculated in the six-month pre-index period.

\( \dagger \) Includes all unique medication classes, not just those related to enlarged prostate.

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**Figure 2  Rates of clinical progression, acute urinary retention (AUR), and surgery over a period of 12 months in patients receiving alpha blockers and concurrent 5-alpha reductase inhibitors (in early-therapy versus delayed-therapy cohorts).** Clinical progression, \( P < 0.0001 \); AUR, \( P < 0.0001 \); surgery, \( P = 0.0002 \).

**Figure 3  Average medical costs per patient with prostate enlargement.**

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continues on page 505
DISCUSSION

Our findings indicated significant clinical and economic benefits for starting 5-ARIs on top of existing alpha-blocker therapy earlier rather than delaying the initiation of 5-ARI treatment. Specifically, men who began taking the combination early (within 30 days of initial alpha-blocker therapy), compared with men who delayed starting combination therapy (from 31 to 180 days after starting alpha blockers), had lower rates as follows:

- clinical progression: 12.8% vs. 17.4%, respectively ($P < 0.001$)
- acute urinary retention: 10.2% vs. 13.8%, respectively ($P < 0.001$)
- prostate-related surgery: 5% vs. 7%, respectively ($P < 0.001$)

Patients receiving 5-ARIs early also incurred lower BPH-related medical costs than the delayed group ($572 vs. 730$, respectively; $P < 0.0001$). In addition, the early group’s BPH-related pharmacy costs were significantly higher ($1,137 vs. 1,263$, respectively; $P = 0.0313$), but their total BPH-related costs were lower ($1,834 vs. 1,867$, respectively; $P = 0.0068$). Even though the differences were statistically significant, we recognize that the total cost differences are essentially cost-neutral.

Our study confirmed the clinical results of analyses by Naslund et al.: delaying the start of 5-ARI therapy in men with BPH was associated with higher rates of clinical progression, acute urinary retention, and prostate-related surgery. Also, each 30-day delay in initiating 5-ARI therapy resulted in an increased likelihood of these outcomes.

Examining two different databases, Naslund et al. found similar trends in early versus late cohorts as follows:

- clinical progression: Integrated Health Care Information Services (IHCIS) database: 11.2% vs. 19%, respectively ($P < 0.0001$); PharMetrics database: 10.2% vs. 14% ($P = 0.0002$)
- acute urinary retention: IHCIS database: 8.1% vs. 13.2%,

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### Table 4 Logistic Regression Comparing Early and Delayed Initiation of 5-Alpha Reductase Inhibitors (5-ARIs) In Clinical Progression, Acute Urinary Retention, and Prostate Surgery

<table>
<thead>
<tr>
<th>Variable</th>
<th>Clinical Progression ($N = 1,244$)</th>
<th>AUR ($N = 990$)</th>
<th>Surgery ($N = 492$)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Delayed</td>
<td>OR 1.454 ($1.281, 1.650$)</td>
<td>OR 1.434 ($1.245, 1.650$)</td>
<td>OR 1.428 ($1.185, 1.720$)</td>
</tr>
<tr>
<td>Age</td>
<td>OR 1.010 ($1.004, 1.016$)</td>
<td>OR 1.015 ($1.008, 1.022$)</td>
<td>OR 0.998 ($0.989, 1.007$)</td>
</tr>
<tr>
<td>Charlson comorbidity index</td>
<td>OR 1.022 ($0.975, 1.071$)</td>
<td>OR 1.041 ($0.990, 1.096$)</td>
<td>OR 0.962 ($0.891, 1.038$)</td>
</tr>
<tr>
<td>Pre-AUR</td>
<td>OR 2.346 ($2.026, 2.716$)</td>
<td>OR 2.953 ($2.527, 3.451$)</td>
<td>OR 1.259 ($0.991, 1.600$)</td>
</tr>
<tr>
<td>No. of unique diagnostic codes</td>
<td>OR 1.006 ($0.991, 1.021$)</td>
<td>OR 1.008 ($0.992, 1.025$)</td>
<td>OR 1.004 ($0.980, 1.027$)</td>
</tr>
<tr>
<td>No. of unique prescribed medication classes</td>
<td>OR 0.996 ($0.979, 1.013$)</td>
<td>OR 0.987 ($0.968, 1.006$)</td>
<td>OR 1.004 ($0.978, 1.030$)</td>
</tr>
<tr>
<td>BPH stage</td>
<td>OR 1.115 ($0.975, 1.275$)</td>
<td>OR 1.043 ($0.901, 1.208$)</td>
<td>OR 1.251 ($1.024, 1.529$)</td>
</tr>
<tr>
<td>Hematuria</td>
<td>OR 1.018 ($0.847, 1.222$)</td>
<td>OR 1.001 ($0.818, 1.225$)</td>
<td>OR 0.866 ($0.648, 1.156$)</td>
</tr>
<tr>
<td>Bladder dysfunction</td>
<td>OR 1.234 ($0.929, 1.639$)</td>
<td>OR 1.236 ($0.906, 1.687$)</td>
<td>OR 1.288 ($0.853, 1.946$)</td>
</tr>
<tr>
<td>Incontinence</td>
<td>OR 1.185 ($0.807, 1.741$)</td>
<td>OR 1.176 ($0.774, 1.785$)</td>
<td>OR 1.012 ($0.543, 1.885$)</td>
</tr>
<tr>
<td>Bladder stones</td>
<td>OR 0.836 ($0.616, 1.135$)</td>
<td>OR 0.813 ($0.557, 1.146$)</td>
<td>OR 1.259 ($0.991, 1.600$)</td>
</tr>
</tbody>
</table>

AUR = acute urinary retention; BPH = benign prostatic hyperplasia; CI = confidence interval; OR = odds ratio.
respectively ($P < 0.0001$); PharMetrics database: 7% vs. 10% ($P = 0.0006$)

• prostate-related surgery: IHCIS database: 4.8% vs. 9.5%, respectively ($P < 0.0001$); PharMetrics database: 5% vs. 6.3% ($P = 0.0699$)

Our results validated those of Naslund et al. in a third database, adding to the growing body of literature supporting the benefits of 5-ARI/alpha-blocker combination therapy for improving lower urinary tract symptoms while addressing disease progression. The clinical burden of BPH often includes lower urinary tract symptoms, acute urinary retention, and the need for prostate surgery. The clinical advantages of combining the two classes for the treatment of BPH come from the strengths and limitations of each class for treating the constellation of clinical features of the disease.

First, alpha blockers alleviate lower urinary tract symptoms rapidly, but they have little effect on disease progression (acute urinary retention, surgery), because they do not have a physiological effect on prostate size. Second, 5-ARIs have proved their ability to reduce rates of acute urinary retention and prostate surgery in clinical trials as confirmed with real-world retrospective database analyses. However, it takes approximately five months for 5-ARIs to reduce prostate size and thus to alleviate lower urinary tract symptoms. As a result, patients may benefit by combining alpha blockers with 5-ARIs to achieve rapid symptom improvement as well as control of disease progression of BPH.

The clinical benefits of combination therapy have been investigated in key clinical trials. The MTOPS study demonstrated even greater symptom improvement with combination alpha blockers plus 5-ARIs as well as reductions in acute urinary retention and surgery that were similar to the 5-ARI monotherapy. In CombAT, combination therapy was significantly superior to monotherapy with tamsulosin (Flomax, Boehringer Ingelheim)—but not dutasteride monotherapy.
Early Versus Delayed Therapy in Benign Prostatic Hyperplasia

(Avodart, GlaxoSmithKline)—in reducing the relative risk of acute urinary retention or BPH-related surgery. The combination was also significantly superior to each monotherapy in reducing the relative risk of BPH clinical progression and provided significantly greater symptom improvement than either monotherapy at four years. The benefits of combination therapy were also confirmed in a real-world retrospective database analysis.

Specifically, early initiation of 5-ARI therapy with existing alpha-blocker therapy, compared with the late addition of 5-ARI to existing alpha-blocker therapy, was significantly associated with lower rates of clinical progression, acute urinary retention, and surgery. Furthermore, every 30-day delay in adding 5-ARI therapy to existing alpha-blocker therapy resulted in an increased risk of disease progression, acute urinary retention, and surgery.

LIMITATIONS OF THE STUDY

Although these results provide additional evidence for early concomitant use of alpha blockers and 5-ARIs for the treatment of BPH, some limitations should be highlighted. The retrospective design of this analysis did not allow for treatment randomization; consequently, the results might have been influenced by confounding factors such as symptom severity and prostate volume, variables that are not available in the MarketScan database. This claims database is based on a large convenience sample.

Because the sample was not random, it might have contained biases or failed to generalize well to other populations. Most of the data were obtained from large employers; medium and small employers were not represented.

Typical limitations associated with retrospective database research, such as coding errors and misclassification, should also be noted. Potential confounding by indication has been addressed by excluding patients who are receiving low-dose finasteride and only including uroselective alpha blockers in the analysis.

Finally, we drew our conclusions on the basis of the class-effect level; we did not assess the effect of unique pairings of specific 5-ARIs and alpha blockers.

CONCLUSION

These study results add to a growing body of literature that supports the use of combination alpha blockers plus 5-ARIs for rapid symptom improvement of an enlarged prostate along with control of disease progression. Results suggest that early initiation of 5-ARI therapy in men with BPH who are taking alpha blockers versus delaying add-on therapy is associated with a lower risk of clinical progression, acute urinary retention, and prostate-related surgery, as well as a corresponding decrease in BPH-related medical costs and total BPH-related costs.

REFERENCES