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ORIGINAL RESEARCH

Real-World Use of Permixon® in Benign Prostatic Hyperplasia – Determining Appropriate Monotherapy and Combination Treatment

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ABSTRACT

Introduction: Benign prostatic hyperplasia (BPH) is a major health concern for aging men. The resulting lower urinary tract symptoms may have a profound effect on a patient's quality of life and it is recognized that patient acceptability of treatment is key to decreasing the human and economic burden of the condition. Alpha-adrenergic antagonists (alpha-blockers), 5-alpha-reductase inhibitors (5-ARIs), and phytotherapy as monotherapy or in combination, form the mainstay of medical treatment.

Methods: The Adelphi Permixon Study, a cross-sectional study of representative consulting patients with BPH in two European countries, was undertaken to examine the reasons for choice of medication. Physicians completed patient record forms, and data were analyzed for clinical outcomes and their relationship with the choice of appropriate therapy.

Results: Patients receiving combination therapies for BPH are likely to be older and are more likely to be retired than those on monotherapy. Combination therapy is adopted in the real-world setting as first-line therapy on a not-infrequent basis. The analyses demonstrated an association between choice of Permixon® (Pierre Fabre Medicament, Castres, France) as appropriate monotherapy or in combination with alpha-blockers, and the following: BPH severity; treatment of general urinary symptoms, including storage and voiding symptoms; improvement of urinary flow rate; lack of a risk of sexual problems; and reduction of inflammation. Permixon combination with an alpha-blocker is associated with benefits in terms of speed of onset of action, reduction of inflammation, and a positive benefit regarding sexual problems when compared with use of alpha-blocker monotherapy.

Conclusion: In the real clinical world, Permixon is considered an appropriate treatment for BPH as both monotherapy and in combination with alpha-blockers. Prescribing Permixon

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in combination with alpha-blockers can be demonstrated to provide benefits beyond use of either therapy alone.

Keywords: Alpha-blockers; Appropriate treatment; BPH; Combination therapy; Patient acceptability; Permixon; Phytotherapy; Real-world

INTRODUCTION

Benign prostatic hyperplasia (BPH), a nonmalignant enlargement of the prostate, can lead to voiding and storage lower urinary tract symptoms (LUTS). However, not all LUTS are necessarily directly associated with BPH [1]. The true incidence of BPH is, therefore, difficult to assess, but may be up to 40% in men over 40, and 90% in those over 80 years of age [2]. BPH is a benign proliferation of the prostatic stromal and epithelial cells leading to formation of palpable nodules and enlargement of the prostate gland. This increase in size may eventually compress the urethral canal leading to physical symptoms of urinary hesitancy and frequency, dysuria, sexual dysfunction, increased risk of urinary infection, and sometimes retention. These clinical manifestations of BPH may also lead to anxiety and depression [3].

Mild LUTS may not in themselves cause sufficiently aggravating symptoms to warrant intervention and a policy of "watchful waiting" (WW) can be adopted. This will include continued patient consultation with medical assessment and monitoring, patient reassurance and education, plus advice for self-management and lifestyle changes. Progression to serious symptoms, such as retention, is infrequent [4], but deterioration from mild-to-moderate symptoms will occur within most patients over a 5-year period from diagnosis, with approximately one-third progressing to minimally invasive therapies or surgery [5–8]. The remaining two-thirds will require medication. Alpha-adrenergic antagonists (alpha-blockers), 5-alpha-reductase inhibitors (5-ARIs), and phytotherapy as monotherapy or in combination, form the foundation of medical treatment [9, 10].

The pharmacologic use of phytotherapeutic agents (plants and herbs) for the treatment of LUTS associated with BPH has been growing steadily [11–14]. Such agents are used both as monotherapy and in combination with other medications. Permixon® (Pierre Fabre Medicament, Castres, France), a lipido-sterolic extract of *Serenoa repens*, belongs to this group of compounds and has been extensively studied for the pharmacotherapeutic management of LUTS/BPH [15–18].

Adelphi Real World (ARW) conducted this holistic observational study on the pharmacological treatment of BPH to understand the reasons physicians chose a particular therapy. The study, undertaken in France and Spain, was designed to describe the profile, management, and factors influencing the choice of therapy by physicians. The analyses discussed in this paper concentrate upon the use of alpha-blockers, 5-ARIs, and Permixon as monotherapy or in combination, all regarded as mainstays of therapeutic management of BPH in both France and Spain.

METHODS

Study Design

The ARW Permixon Study was conducted in January and February 2011, with urologists and primary care physicians (PCPs), and their patients recruited in France and Spain. The study method was based upon the ARW "Disease Specific Programme" approach. The full methodology for this approach, including limitations, has been outlined previously [19]. Physicians completed a patient record form (PRF) for consulting BPH

patients meeting the inclusion criteria. Included patients were not preselected and, thus, could be receiving no prescribed therapy and undergoing WW, receiving monotherapy, or combination regimens. The PRF included a list of 39 reasons for choice of therapy. The form was filled in anonymously by the physician for each patient, whether prescribed medication as monotherapy or in combination with another.

Physicians were identified by local fieldwork partners from public lists of healthcare professionals in both participating countries. Physicians were checked for their eligibility to participate in the study in terms of specialty, location (hospital or office), whether they were personally responsible for treatment decisions, and how many patients they saw in a typical week; this included total numbers and those with BPH in order to avoid recruiting physicians with an abnormally low workload. Candidate respondents who met the predefined eligibility criteria were subsequently invited to participate in the study. To avoid potential selection bias due to variable population densities in different geographical regions in a given country, an appropriately larger sample of physicians was identified in densely populated areas than in more sparsely populated areas.

All responses were anonymous to preserve doctor and patient confidentiality, and to avoid bias at the data collection and analysis phases. The study protocol followed ethical procedures, including informed consent of all patients, for anonymous and aggregated reporting of research findings based on the questionnaires employed. The analyses conducted for the purposes of this paper investigated data from the PRF records.

Statistical Analysis

By applying statistical analysis to the reasons for choice selected by physicians, it was possible to create groups ("factors") based upon associations of the 39 reasons, i.e., group together those reasons for choice that generally occur simultaneously at similar frequency in the population as a whole. Key contributing reasons for each factor were identified by large absolute values of coefficients from a factor-loading matrix. Factors were then characterized and amended to fit logically with this characterization, leaving each factor described by a mutually exclusive set of reasons for choice. Logistic regressions were then used to determine which reasons for choice are associated with given treatment group pairs.

A second statistical approach was employed in order to reduce the number of variables by focusing upon the 11 reasons for choice identified as most discriminating between therapies.

RESULTS

Holistic Overview of Demographics and Product Shares

A total of 200 physicians (120 PCPs and 80 urologists) in France and Spain provided records for 1,197 patients with BPH, in accordance with the inclusion criteria. A total of 597 patients were recruited in France and 600 patients in Spain. The mean age of the patients was 67.4 years and mean weight 78.2 kg (Table 1). The demographic data for the patients in the two countries were very similar with the only differences noted being that those in France were more likely to be described as retired (75.4% vs. 61.8% in Spain), and those in Spain were more likely to be reported to be current smokers than their counterparts in France (27.0% vs. 13.9%). The demographic data for these patients confirm that the patient sample analyzed was homogeneous, with no confounding factors, such as age and body mass index (BMI), influencing treatment decisions.

Amongst the 1,197 patients included were 1,116 (93.2%) receiving prescribed medication

Table 1 Demographic overview of population by country

Patient characteristics	France + Spain (*n* = 1,197)	France (*n* = 597)	Spain (*n* = 600)
Mean age (years)	67.4	68.0	66.9
Mean weight (kg)	78.2	78.4	77.9
Mean height (cm)	171.9	173.0	170.8
Mean BMI	26.4	26.1	26.7
Living with spouse/partner (*n*)	884	448	436
%	73.9	75.0	72.7
Retired (*n*)	821	450	371
%	68.6	75.4	61.8
Current smoker (*n*)	245	83	162
%	20.5	13.9	27.0

BMI body mass index

Table 2 Patient demographics: monotherapy versus combination therapy

	Monotherapy (*n* = 916)	Combination therapy (*n* = 200)	Watchful waiting (*n* = 81)
France, *n* (%)	464 (50.7)	113 (56.5)	20 (24.7)
Spain, *n* (%)	452 (49.3)	87 (43.5)	61 (75.3)
Mean age (years)	67.2	69.7	65.0
Mean BMI	26.5	26.4	25.1
Home circumstances (%):			
With partner/spouse	75.7	69.5	64.2
With other family	5.6	6.5	7.4
Nursing home	1.6	3.5	1.2
Employment status (%):			
Full-time work	20.6	14.5	19.8
Retired	67.5	76.0	63.0
Current smoker (%)	21.2	15.5	24.7
Diagnosed at this visit (%)	19.4	9.0	42.0
Regimens to date			
Mean number of regimens received overall:	1.34	2.02	NA[a]
1st regimen (%)	70.7	24.0	12.3
2nd regimen (%)	17.4	50.0	2.5
Other (%)	5.6	18.5	1.2
Not stated (%)	6.3	7.5	84.0

[a] Most patients receiving watchful waiting can be assumed to have received no prior drug regimen but this is not explicitly recorded
BMI body mass index, *NA* not available

and 81 (6.8%) on a WW regimen (Table 2). Within the group of patients receiving medications, 916 (76.5% of the total population) were in receipt of monotherapy and 200 (16.7%) were receiving combinations of treatments. The use of WW was observed far more frequently in Spain, with 61 patients of the total 81 receiving WW recorded in that country. There were no major differences between the characteristics of the populations recorded in the two countries. The use of increasing numbers of medications later in the disease is demonstrated by those patients receiving combination therapies being the most elderly (mean of 69.6 years in France, 69.9 years in Spain) and the youngest receiving WW (mean of 63.8 years in France, 65.4 years in Spain). The progressive use of additional prescribed therapies is further shown in that 42.0% of WW patients were newly diagnosed, in contrast with 19.4% of those receiving monotherapy and only 9.0% of those receiving combination therapies.

In Table 2 it can be seen that the patients receiving combination therapies had the highest mean age of the three groups of patients. The employment status reflects the higher mean age, with 76.0% of patients receiving combination therapies described as retired, compared with 67.5% of monotherapy patients and 63.0% of those receiving WW.

The majority (70.7%) of the 916 patients on monotherapy were receiving their initial regimen, compared with 24.0% of the 200 patients on combination therapy. The mean number of regimens received overall was 1.40, with those on monotherapy averaging 1.34 regimens at the time of recording, compared with 2.02 for those receiving combination therapies.

Social circumstances showed little variation with treatment, although a greater proportion of those on combination therapy, seven of 200 patients (3.5%), were living in nursing homes, compared with 1.6% of those on monotherapy. Patients receiving combination therapy were less likely to be in full-time employment than other groups of patients (14.5% vs. 20.6% for those receiving monotherapy), tended to be older, and less likely to be a current smoker.

As noted earlier, the analyses concentrate upon the use of alpha-blockers, 5-ARIs, and Permixon as monotherapy or in combination. These are all mainstays of therapeutic management of BPH in France and Spain and are explored in greater detail from this point. Table 3 highlights the leading therapeutic approaches adopted in France and Spain.

Table 3 Product/regimen share

Product/regimen	France + Spain (*n* = 1,197)	France (*n* = 597)	Spain (*n* = 600)
Permixon monotherapy	161 (13.5)	108 (18.1)	53 (8.8)
Permixon + alpha-blocker	66 (5.5)	39 (6.5)	27 (4.5)
Alpha-blocker monotherapy	555 (46.4)	274 (45.9)	281 (46.8)
5-ARI monotherapy	100 (8.4)	41 (6.9)	59 (9.8)
Alpha-blocker + 5-ARI	116 (9.7)	41 (6.9)	75 (12.5)
Other drug treatments	118 (9.9)	74 (12.4)	44 (7.3)
Watchful waiting	81 (6.8)	20 (3.4)	61 (10.2)

Data are *n* (%)
5-ARI 5-alpha-reductase inhibitor

5-ARIs, as a monotherapy, were prescribed for 100 (8.4%) patients in total, 41 (6.9%) in France, and 59 (9.8%) in Spain. In combination with an alpha-blocker, the number of patients were 116 (9.7%), 41 (6.9%), and 75 (12.5%), respectively. Alpha-blockers as monotherapy were taken by 555 patients (46.4%), 274 (45.9%) in France, and 281 (46.8%) in Spain.

Permixon monotherapy was received by 161 (13.5%) of patients in total and Permixon plus an alpha-blocker combination therapy by 66 (5.5%) of patients. In France, 147 patients were recorded for these two therapy groups, of which 39 (26.5%) received Permixon with an alpha-blocker. In Spain, a lower number of patients receiving Permixon was recorded (80 in total), with 27 of these (33.8%) receiving Permixon with an alpha-blocker.

The remaining 118 (9.9%) patients receiving medication for their BPH were excluded from further detailed analysis. These include a diverse range of monotherapies and combinations. In total, 85 patients were receiving phytotherapy medication other than Permixon, with 82 of these patients prescribedpygeum africanum (a bark extract derived from *Prunusafricana,* red stinkwood), and of these the majority (54 patients) were in France.

In France, 423 patients were recorded on the three selected monotherapies (70.9%) and 80 on selected combination treatments (13.4%). There were 74 patients (12.4%) on other drug therapies and 20 (3.4%) receiving a WW regimen. In Spain, the respective proportions were 393 patients (65.5%) and 102 (17.0%) for the selected monotherapies and combinations, respectively. There were 44 (7.3%) patients on other drug treatments and 61 (10.2%) on WW.

There was little demographically to differentiate these treatment populations, though the 5-ARI monotherapy and 5-ARI plus

Table 4 Patient demographics by regimen received

	Permixon mono therapy (*n* = 161)	Permixon + alpha-blocker (*n* = 66)	Alpha-blocker mono therapy (*n* = 555)	5-ARI mono therapy (*n* = 100)	Alpha-blocker + 5-ARI (*n* = 116)	Other therapy	
						Other Rx (*n* = 118)	WW (*n* = 81)
Mean age (years)	67.0	67.9	66.8	69.6	70.8	67.3	65.0
Mean BMI	26.1	26.3	26.6	27.0	26.4	26.4	25.1
Home circumstances:							
With partner/spouse (%)	73.9	63.6	77.8	71.0	73.3	70.3	64.2
With other family (%)	6.2	3.0	4.3	9.0	8.6	7.6	7.4
Employment status:							
Retired (%)	70.8	72.7	66.7	74.0	78.5	61.9	63.0
Current smoker (%)	19.9	15.2	22.0	18.0	21.6	15.3	24.7
Mean weeks since diagnosis	175.3	143.2	164.5	132.9	123.1	194.7	208.1
Regimens nos.	1.1	1.8	1.3	1.7	2.2	1.6	0.2[a]

[a] A small number who were on WW have received a therapy in the past

5-ARI 5-alpha-reductase inhibitor, *BMI* body mass index, *Other Rx* other drug treatments, *WW* watchful waiting

alpha-blocker combination groups were slightly older (Table 4). As seen in Table 4, there appear to be no other major confounding factors.

The majority of BPH patients included in the study were retired (68.6%), with a range from 61.9% in the "other drug treatments" group to 78.5% in patients receiving a 5-ARI plus alpha-blocker combination. A significant majority of patients were living with a spouse/partner (73.9%) with a range from 63.6% (Permixon plus alpha-blocker combination) to 77.8% (alpha-blocker monotherapy). The mean time since diagnosis for all patients was 156.9 weeks (range 123.1–208.1 weeks), with the mean slightly higher in France (159.0 weeks) compared with in Spain (149.3 weeks). There was one key difference between the countries, namely that Spanish patients receiving the Permixon plus an alpha-blocker combination had received it for only 83.6 weeks (n = 27), whereas in France this population had received the combination for 184.5 weeks (n = 39). The time elapsed since diagnosis for the other patient groups showed no major difference between the two countries, with regimens, including 5-ARIs, having the shortest time interval since diagnosis.

Drivers of Choice

The current study examined the specific reasons for choice of drug(s) as recorded by physicians for each of their included patients. These reasons were answered for each individual drug prescribed and were not answered for patients receiving WW.

All therapy regimens indicated that three efficacy measures were always chosen as the "key drivers" irrespective of therapy selected and patient symptomatology, namely: effect on total urinary symptoms, effect on storage symptoms, and effect upon voiding symptoms.

The drivers of choice recorded for patients receiving each of the five selected treatment regimens beyond these top three efficacy measures are shown in Table 5. This table includes results for the total study population and individual results for France and Spain. For each regimen the drivers indicated are the next six most frequently recorded after the top three efficacy measures. All figures relate to the percentage of patients receiving a regimen for whom a particular driver was indicated to have been an influence upon the treating physician's therapy selection.

The main drivers for choice indicated for patients prescribed Permixon monotherapy, after the key efficacy parameters, were shown to be the avoidance of sexual dysfunction and ejaculation disorders, patient acceptability, value for money, and familiarity with the drug. Reduction of inflammation was also a leading driver for selection of Permixon. When a patient was prescribed Permixon in combination with an alpha-blocker, there was a focus upon drivers that are also noted with alpha-blocker monotherapy (fast onset of action, positive effect on the urinary flow rate, clinical symptom alleviation, and the mechanism of action) plus strong association with the lack of sexual dysfunction risk and reduction of inflammation.

When a 5-ARI was selected, the additional key drivers, beyond the major efficacy measures, include effect on urinary flow rate, single daily dose, mechanism of action, clinical evidence of prostate shrinkage, and reduced risk of urinary retention. Notable, additional key reasons that were associated with the choice of 5-ARI in combination with an alpha-blocker, compared with 5-ARI monotherapy, were clinical symptom alleviation, reduced likelihood of future surgery, and delay of surgery.

The importance of inflammation as a differential reason for selection of Permixon is shown in Table 6. Whilst a very large minority of Permixon patients was indicated to have a

Table 5 Drivers of physicians' choice of therapy (excluding relief of total, storage, and voiding symptoms)

	Permixon monotherapy			Permixon + alpha-blocker			Alpha-blocker monotherapy			5-ARI monotherapy			5-ARI + alpha-blocker		
	Total	France	Spain	Total	France	Spain	Total	France	Spain	Total	France	Spain	Total	France	Spain
	% patients			% patients			% patients			% patients			% patients		
Sexual dysfunction risk	61	58	68	68	79	52	-	-	-	-	-	-	-	-	-
Patient acceptability	53	50	58	-	-	-	-	-	-	-	-	-	-	-	-
Ejaculation-disorder risk	47	43	55	-	-	-	-	-	-	-	-	-	-	-	-
Value for money	47	43	55	-	-	-	-	-	-	-	-	-	-	-	-
Familiarity with drug	47	41	58	-	-	-	-	-	-	-	-	-	-	-	-
Reduces inflammation	38	37	40	44	44	44	-	-	-	-	-	-	-	-	-
Fast onset of action	-	-	-	68	67	70	52	52	52	-	-	-	-	-	-
Urinary flow rate	-	-	-	64	69	56	54	57	50	61	56	64	59	63	56
Clinical symptom alleviation	-	-	-	59	77	33	55	66	44	-	-	-	59	73	51
Single daily dose	-	-	-	-	-	-	62	58	66	67	66	68	61	54	65
Mechanism of action	-	-	-	59	64	52	56	53	59	67	59	73	64	73	59
Reduces future surgery risk	-	-	-	-	-	-	-	-	-	-	-	-	63	51	69
Clinical evidence of prostate shrinkage	-	-	-	-	-	-	-	-	-	48	66	36	-	-	-
Reduced risk of urinary retention	-	-	-	-	-	-	49	54	44	48	41	53	-	-	-
Nocturia	-	-	-	-	-	-	-	-	-	42	32	49	-	-	-
Delay of surgery	-	-	-	-	-	-	-	-	-	-	-	-	54	49	57

5-ARI 5-alpha-reductase inhibitor

Table 6 Inflammation reduction as physicians' driver for choice (% patients)

	France + Spain (%)	France (%)	Spain (%)
Permixon monotherapy	38	37	40
Permixon + alpha-blocker	44	44	44
Alpha-blocker monotherapy	15	13	18
5-ARI monotherapy	27	20	32
5-ARI + alpha-blocker	22	17	19

5-ARI 5-alpha-reductase inhibitor

reduction of inflammation shown as a driver of choice, this was not the case for the other selected options.

Statistical Analysis

By use of factoring in order to create groups, four reasons for choice groups emerged, and the number of reasons that had to be recorded for each factor to be said to be "positive" was also indicated. Factor 1, "Efficacy," required three from: effect on obstructive (voiding) symptoms; mechanism of action; clinical evidence of prostate shrinkage; clinical evidence of symptom alleviation; other physician recommendation; reduced risk of urinary retention; reduced likelihood of surgery; fast onset of action; and delay of surgery. Factor 2, "Sexual Problems," required two from: avoidance of sexual dysfunction risk; avoidance of ejaculatory disorder; and risk of impairing sexual drive. Factor 3, "Acceptability," required two from: value for money; patient acceptability; familiarity with drug; single daily dosage; and can be used with other BPH therapies. Factor 4, "Safety," required three from: risk of dry mouth; inhibiting detection of carcinoma; weight gain; drug interaction/sedation/dizziness; testicular pain; and risk of intraoperative floppy iris syndrome in case of cataract surgery.

These factors were used within the regressions and highlight that "safety" was not a differentiator in therapy selection to a significant extent. Permixon monotherapy was strongly associated with two factors: not being seen to cause sexual problems and acceptable to patients, whilst efficacy measures were less likely to be drivers of selection compared with the other options considered here. Alpha-blockers used as monotherapy were associated with two factors: delivering efficacy, seen to cause sexual problems, whilst adding Permixon in combination with alpha-blockers was associated with an increase in efficacy and a positive benefit regarding sexual problems.

Monotherapy with 5-ARI was positively associated with efficacy but negatively with risk of sexual problems and patient acceptability. When in combination with an alpha-blocker, efficacy was viewed as very positive and the risk of sexual problems was suggested to greatly diminish as a concern.

The second statistical approach focused upon the 11 reasons for choice identified as providing the greatest discrimination between the therapies. In this exercise, logistic regressions identified that three drivers were significantly more associated with Permixon in combination with

alpha-blockers than alpha-blocker monotherapy: greater association with fast onset of action (a synergistic benefit perceived over alpha-blocker alone); reduction in inflammation; and a negative association with delay in surgery. There was also a suggestion that the combination had a perceived advantage over alpha-blockers alone with regards to prostate shrinkage.

A further logistic regression (Table 7) identified that only one driver was very significantly more associated with Permixon in combination with alpha-blockers than 5-ARI in combination: reduction in inflammation.

Additionally, both fast onset of action and improvement of urinary flow rate were associated with the Permixon combination. The 5-ARI combination was more positively associated with: delay in surgery, reduction in likelihood of surgery, prostate shrinkage, and effect on voiding symptoms.

DISCUSSION

In the last decade, pharmacological treatment has become the primary choice for effective symptomatic relief of BPH, with phytotherapy recognized as fulfilling a role in that choice of treatments [9, 20].

The ARW Permixon Study provides an insight into real-world prescribing behavior for France and Spain. These observational data provide a number of findings that might be expected, such as WW may precede use of pharmacologic interventions (although patients will more frequently receive a prescribed therapy); patients receiving combination therapies tend to be older and more likely to be retired compared with other BPH patients; and all treatments are primarily suggested to be selected owing to their perceived efficacy. Not all findings are, perhaps, necessarily expected, such as approximately one in four (24.0%) patients

Table 7 Logistic regression: efficacy reasons for choosing permixon combination with alpha-blockers over 5-ARI combination with alpha-blockers

Odds ratio[a]	95% CI	Reason for choice
0.44	0.15–1.40	Effect on obstructive (voiding) symptoms
1.16	0.52–2.59	Mechanism of action
0.27	0.12–0.60	Clinical evidence of prostate shrinkage
1.35	0.58–3.12	Clinical evidence of symptom alleviation
0.87	0.37–2.04	Recommendation of specialist/other physician
0.77	0.35–1.67	Reduces risk of urinary retention
0.38	0.17–0.85	Reduces the likelihood of future surgery
1.58	0.71–3.54	Fast onset of action
1.63	0.75–3.52	Improvement of urinary flow rate
3.36	1.35–8.20	Reduces inflammation
0.43	0.20–0.94	Delay of surgery

[a] The odds ratio shows the difference in odds of being in the treatment group if the reason for choice is selected. An odds ratio > 1 indicates an increase in odds (e.g., an odds ratio of 2 indicates a 100% increase in the odds of receiving Permixon combination with alpha-blockers rather than the alternative combination), whereas an odds ratio < 1 indicates a decrease in odds (e.g., an odds ratio of 0.9 indicates a 10% decrease in odds)
5-ARI 5-alpha-reductase inhibitor

receiving a combination approach received this as first-line treatment; those receiving 5-ARIs as monotherapy or in combination with an alpha-blocker have been diagnosed for the shortest time; and those receiving WW have been diagnosed the longest time.

The ARW Permixon study has shown that in real-world practice in France and Spain, Permixon is prescribed both as monotherapy, with a 13.5% share of presenting patients, and in combination with alpha-blockers (5.5% share). In the current study, 66 Permixon patients out of 227 (29.1%) received Permixon in combination with an alpha-blocker, despite the fact that this combination of medications is not currently supported by the guidelines for BPH treatment. This would appear to indicate that Permixon, as both a monotherapy and in combination with an alpha-blocker, is recognized by physicians as having a clear role as a rational treatment option for men with BPH. Association with key efficacy needs, patient acceptability, and lack of sexual problems makes Permixon particularly suitable for those who are younger, sexually active, have less severe symptoms, and are less likely to require surgery. Permixon is additionally associated with an ability to reduce inflammation associated with BPH.

Permixon, both as a monotherapy and in combination with alpha-blockers, provides physicians with a familiar option, which is likely to be well received by patients due to its perceived effectiveness and avoidance of sexual problems. Patient acceptability and the lack of sexual problems are the two key factors that appear to constitute the most significant drivers for physicians for the use of Permixon over other therapy options in the real world.

Physicians are influenced by the clinical objectives necessary for each patient and severity of symptoms is an essential mix in that choice; however, patient acceptability is receiving greater emphasis as part of clinical decision-making [21]. The variability of relationships between symptom severity and the likelihood that the symptoms will be bothersome implies that reliance on an aggregate symptom score alone will not capture the true impact of symptoms in individual men. Rather, treatment success will depend on improvements in the aspects of the disease that are of most concern to the patient. To factor patient acceptability into treatment decisions, the physician should be able to adequately inform the patient of the benefits and risks of the appropriate treatments. Selecting an inappropriate treatment, or not considering patient acceptability, may lead to a cascade of therapies, unmet expectations, discontinuance of therapy, and increase the economic and human burden of the disease [22].

A number of limitations of the methodology should be noted. Although respondent physicians were requested to collect data on a series of consecutive patients to avoid selection bias, in the absence of randomization, this was contingent upon the integrity of the participating respondent rather than formalized source verification procedures. Respondents were also required to be prescribers of combinations of therapy, although this again was not verified against prescribing records.

Although the study can be used to identify association, a further limitation is that, being cross-sectional in nature, it cannot be used to demonstrate cause and effect. BPH diagnosis in the target patient group was based primarily on the judgment and diagnostic skills of the respondent physician rather than on a formalized diagnostic checklist. Physicians also provided a subjective assessment of the severity (mild, moderate, or severe) of each patient's condition.

In conclusion, Permixon is prescribed in the clinical real world as both monotherapy and in combination with alpha-blockers.

This study shows that, when asked for the reasons that drive choice of Permixon monotherapy for individual patients, physicians are guided by the drug's effect on total urinary symptoms, including voiding and storage symptoms, plus the added advantages of its lack of sexual side effects, and acceptability to patients. When prescribed in combination with alpha-blockers, the rationale for choice is suggested to be driven by the synergy of the quick symptomatic relief provided by the alpha-blocker plus the lack of sexual problems and reduction in inflammation provided by Permixon.

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