



BPH progression:
The disease continuum & evidence –
based learnings

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Introduction

- LUTS/BPH is an prevalent condition in ageing men
- Not a life-threatening → many patients even some physicians ignore the significance of this condition
- But, substantial number of men have a progressive disease

BPH progression

- Deterioration of symptoms and HRQoL
- Decreased Qmax
- Increased prostate size
- Unfavorable outcomes
 - AUR
 - BPH-related surgery

How can we know the fact?

- Longitudinal community-based studies
 - Olmsted county study
- Placebo arms of controlled studies
 - (limitation due to selection criteria)
 - MTOPS study
 - ALTESS study



Olmsted County study

Olmsted County study

- Study subjects
 - Male residents of Olmsted County 40-79 years old on Jan 1, 1990
 - A 16% stratified random sample
 - Screen for prostatectomy, CaP, other medical conditions interfering with voiding function(=3,658 men potentially eligible)
 - 2,115 men(55%) completed study protocol
 - Followed for 12 years

Olmsted County study

TABLE 1 Changes in IPSS, peak flow rate, prostate size and cumulative incidence of serious outcomes in the Olmsted County study

Variable	Age, years				
	Overall	40-49	50-59	60-69	≥70
Number of patients	2115	839	587	434	252
IPSS [1]					
Baseline IPSS	0.18 (1.22)	0.05 (1.06)	0.18 (1.19)	0.44 (1.35)	0.14 (1.43)
Mean (SD) change/year			0.18 (1.19)	0.44 (1.35)	0.14 (1.43)
Peak flow rate [4]					
Peak flow rate	-2.1	-1.1	-2.7	-2.3	-6.2
Median change/year, %	-2.1	-1.1	-2.7	-2.3	-6.2
Prostate volume [6]					
Median growth per year, %	1.9	1.9	1.9	1.8	1.6
Prostate volume (mL)	1.9	1.9	1.9	1.8	1.6
Cumulative incidence of surgical procedures over 6 years [8], n (%)					
TURP	45 (2.1)	1 (0.1)	5 (0.9)	21 (4.8)	18 (7.1)
MIST	19 (0.9)	0	6 (1.0)	7 (1.6)	6 (2.4)
Total	64 (3.0)	1 (0.1)	11 (1.9)	28 (6.5)	24 (9.5)

MIST, minimally invasive surgical therapies.

Evidences-OCS

- A slow but measurable progression in urinary symptom severity among community dwelling men for 42months f-u (*Jacobsen et al, 1996 J Urol*)
- During the 8,344 person-years f-u, 57 men had a first episode of **AUR (6.8/1,000 person-yrs)**
(*Jacobsen et al, 1997 J Urol*)
- During 10,000 person-years f-u, 167 men were **treated (16.0/1,000 person-yrs)**
(*Jacobsen et al, 1999 J Urol*)

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- Prostate volume appears to increase steadily at about **1.6% per year** in randomly selected community men (*Rhodes et al, 1999 J Urol*)
 - Median Qmax slope was **-2.1%** per year. Qmax declined more rapidly with ↓ baseline rate, ↑ baseline age, prostate volume, symptom severity (*Roberts et al, 2000 J Urol*)

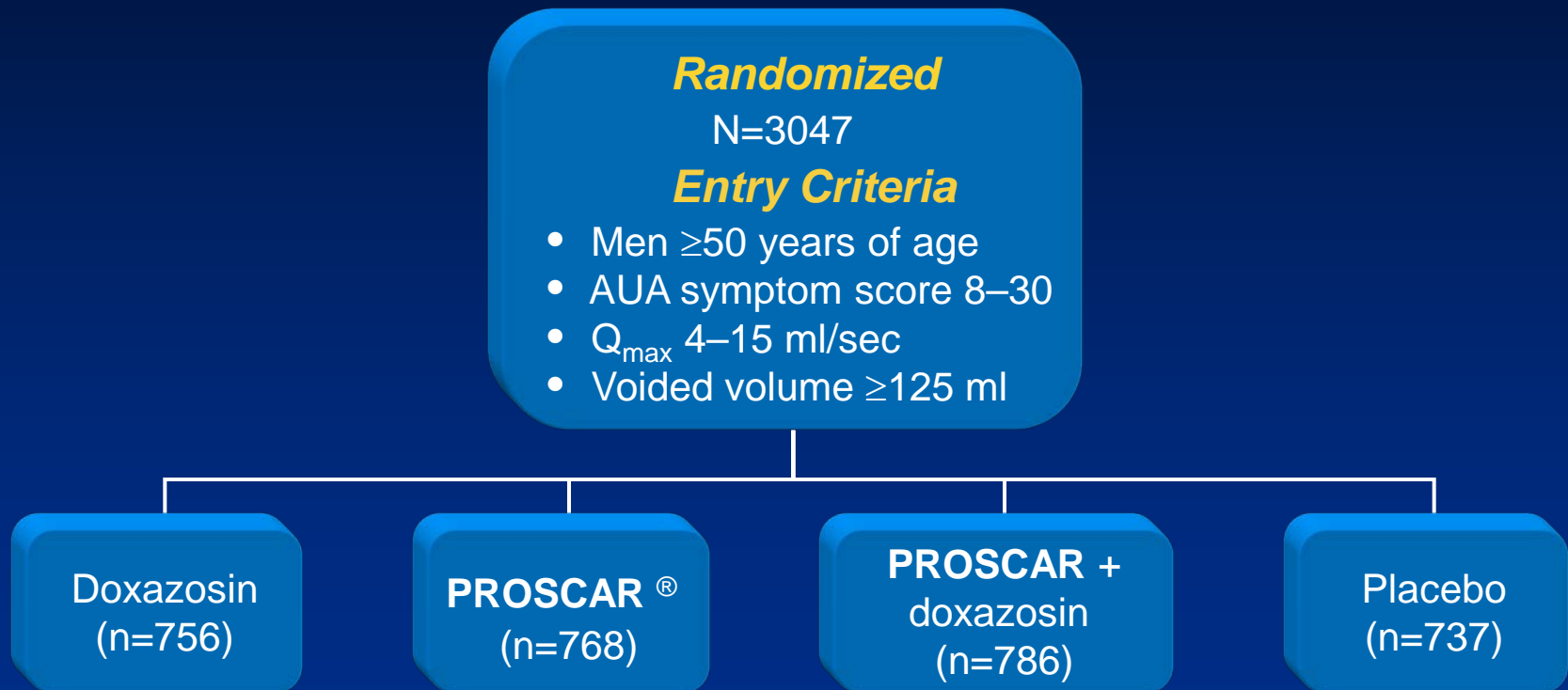
Controlled studies

- Information can be collected from placebo arms of controlled studies in men with symptomatic BPH
- Strict inclusion criteria introduce a **bias** in the analysis of outcomes
- PLESS, MTOPS, ALTESS

MTOPS study

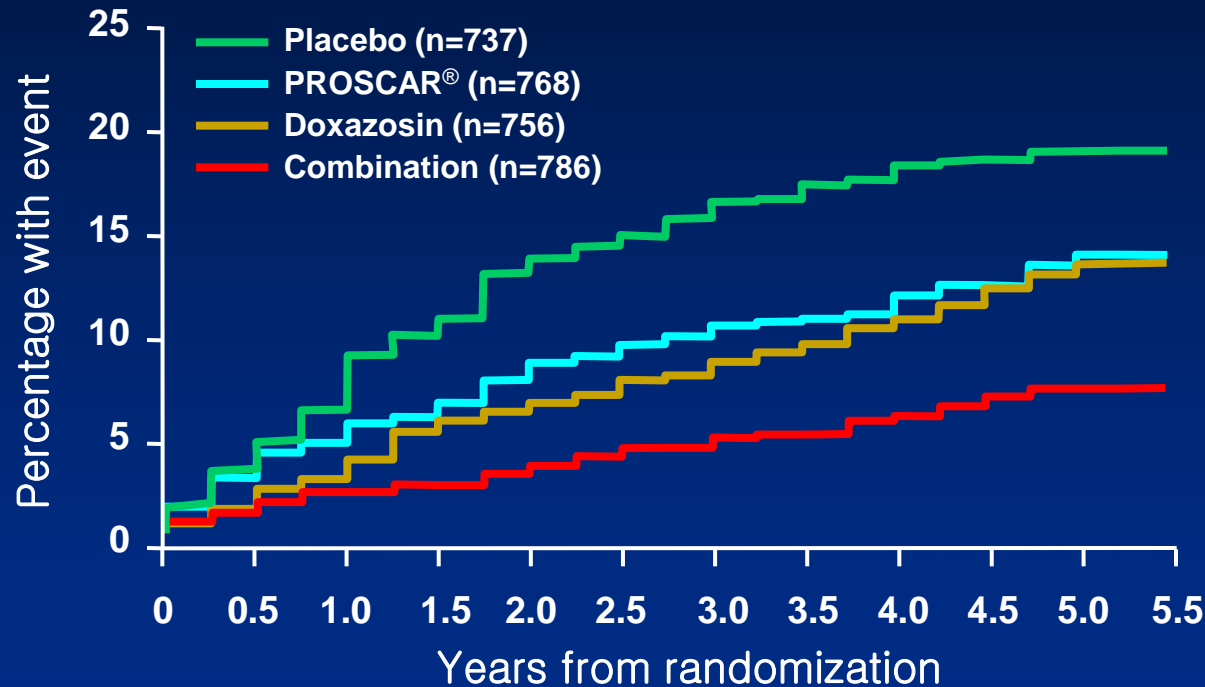
MTOPS (Medical Therapy Of Prostatic Symptoms)

Double-blind, placebo-controlled, multicenter, randomized
Average follow-up: 4.5 years



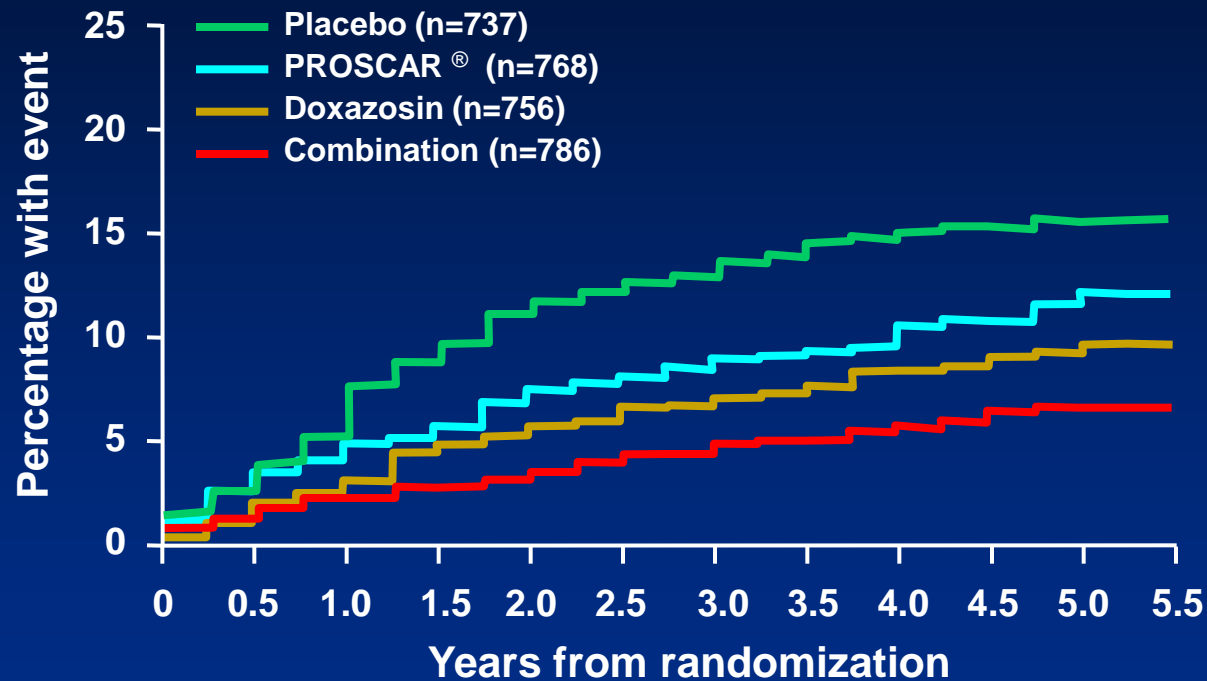
Impact on clinical progression of BPH

Cumulative incidence of BPH progression



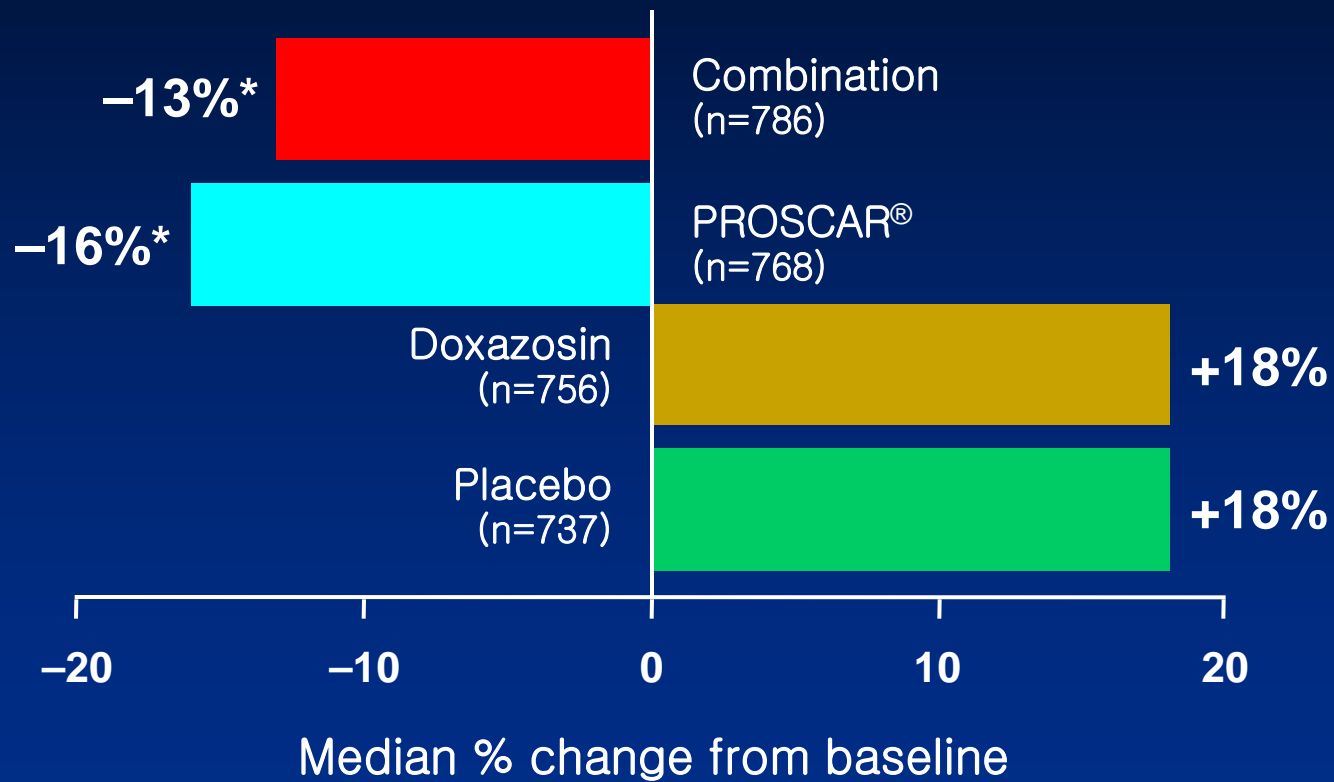
Impact on Symptom Control

Cumulative incidence of ≥ 4 -point increase in symptom score*



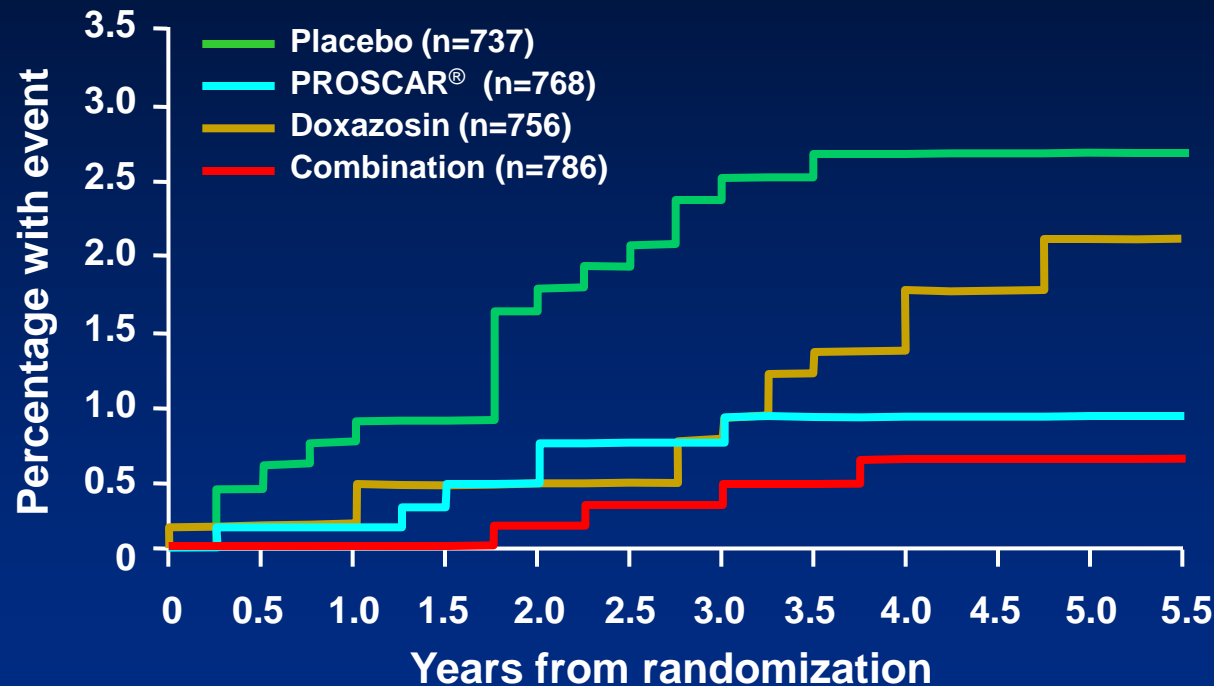
Effect on Prostate Volume

Change from baseline in prostate volume



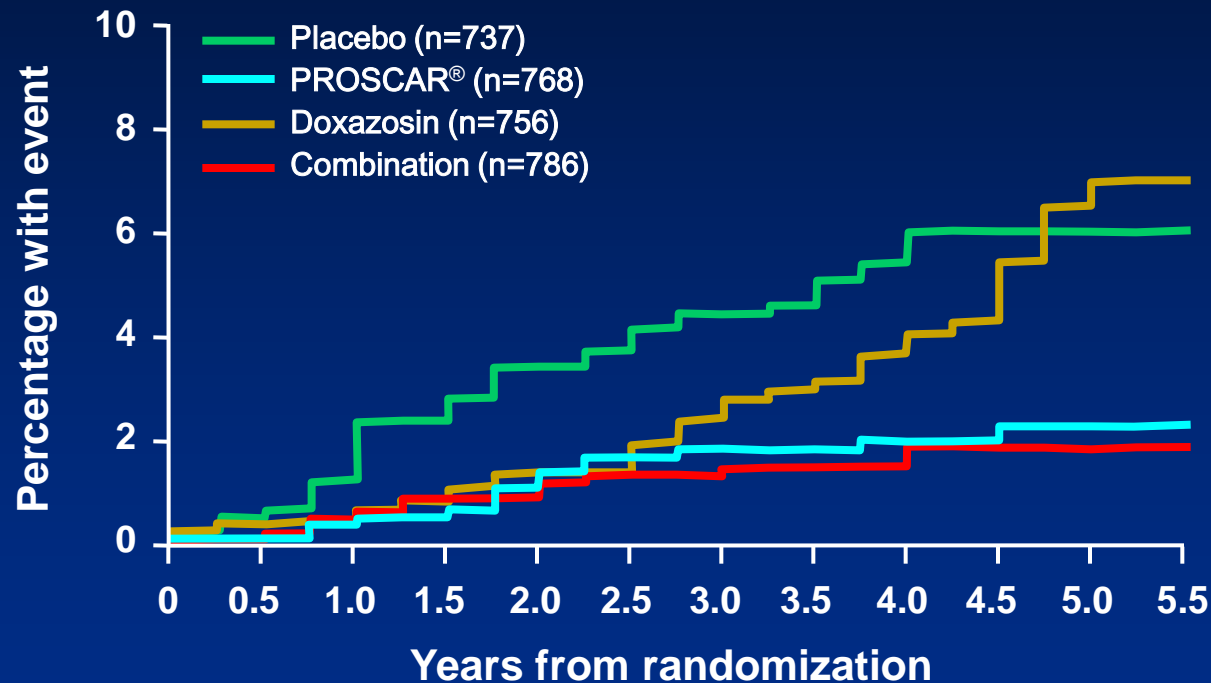
Impact on the Risk of AUR

Cumulative incidence of AUR



Impact on the Need for BPH-Related Surgery

Cumulative incidence of BPH-related surgery



In the placebo arms,

- The cumulative incidence of overall clinical progression was 16.6%((122/737)) over 5 years
- Symptom deterioration(IPSS worsening by ≥ 4 points) was the main contributor(97/122, 79.5%) with a cumulative incidence of 14% over 5 years
- AUR was uncommon(18/122, 14.8%) with a cumulative incidence of 2%
- BPH-related surgery(2° endpoint) was required in 5% of men(37/737) over 5 years

Placebo effects

- Positive effect on LUTS and Qmax
 - Median improvement of 4 points and 1.4mL/s
- No effect on volume and PSA
 - Volume increased by a median of 24%
 - Serum PSA level: a 15% increase
- Placebo arms $\hat{=}$ but, \neq natural history

ALTESS

ALTESS

- Alfuzosin 10mg once daily long-term efficacy and safety study
- Study (duration: 2 years)
 - Men enrolled: at high risk of developing LUTS/BPH progression events
 - ≥ 55 years
 - moderate to severe symptoms
 - $Q_{max}=5-12\text{mL/s}$
 - $\text{Size(DRE)} \geq 30\text{g}$
 - Baseline s-PSA: $1.4-10\text{ng/mL}$

-
- 167/775(placebo arm)=**22.1%** had at least one BPH progression event
 - Main event was **symptom worsening** of ≥ 4 points(16.8%)
 - AUR=2.2%
 - BPH related surgery=6.5%(49/757)

ALTESS & MTOPS

Variable	ALTESS (2 years)	MTOPS* (4 years)
N placebo-treated patients	757	737
N (%):		
IPSS worsening of ≥ 4 points	127 (16.8)	97 (14.0)
AUR	14 (1.8)	18 (2.0)
BPH-related surgery	49 (6.5)	37 (5.0)
Incontinence	ND	6 (0.8)
UTI or urosepsis	ND	1 (0.1)

**patients having a progression event were censored in other progression-event analyses; ND, not done.*

Risk factors: BPH progression

- PSA
- Large prostate
 - Old age
 - Severe LUTS
 - Low Qmax
 - Increased PVR

Study for Asian?

Change in International Prostate Symptom Score, prostate-specific antigen and prostate volume in patients with benign prostatic hyperplasia followed longitudinally

International Journal of Urology (2007) 14, 321–324

- Retrospective cohort study
- Inclusion: 2 measurements of PV & IPSS
- Exclusion: hormone therapy, CaP, surgery
- 67 patients were eligible
- alpha blockers only? Or watchful waiting?

Prostate volume increase

PV at baseline (mL)	Number of BPH patients (<i>n</i> = 46)	Mean change in PV per year of follow-up (mL)
<20	10	5.1
20–29	16	11.9
30–39	7	3.8
≥40	13	22.0

BPH, benign prostatic hyperplasia.

- PV increased in 46(70%) men, remained the same in 10 and decreased in 11
- Rather small sized study
- The only Asian study appeared in PubMed

Summary

- There is evidence from longitudinal studies and in some extent from the placebo arms of the large controlled studies, that BPH is a progressive disease
- Symptom worsening is the most frequently occurring event
- Risk factors of BPH progression should be considered to optimize the management of individual patient
- Maybe, we need to have Asian data

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Thank you very much!