# Traitement de l'HBP, les nouveautés en 2008

- Syndrome Métabolique
- Toxine Botulique A
- Inhibiteurs de la Phosphodiesterase
- TRT Combinés
- Radiofréquences

# Syndrome métabolique chez l'homme : définition de l'IDF (International Diabetes Federation)

Obésité central : Tour de taille > 102 cm

Plus l'un des 4 éléments suivants :

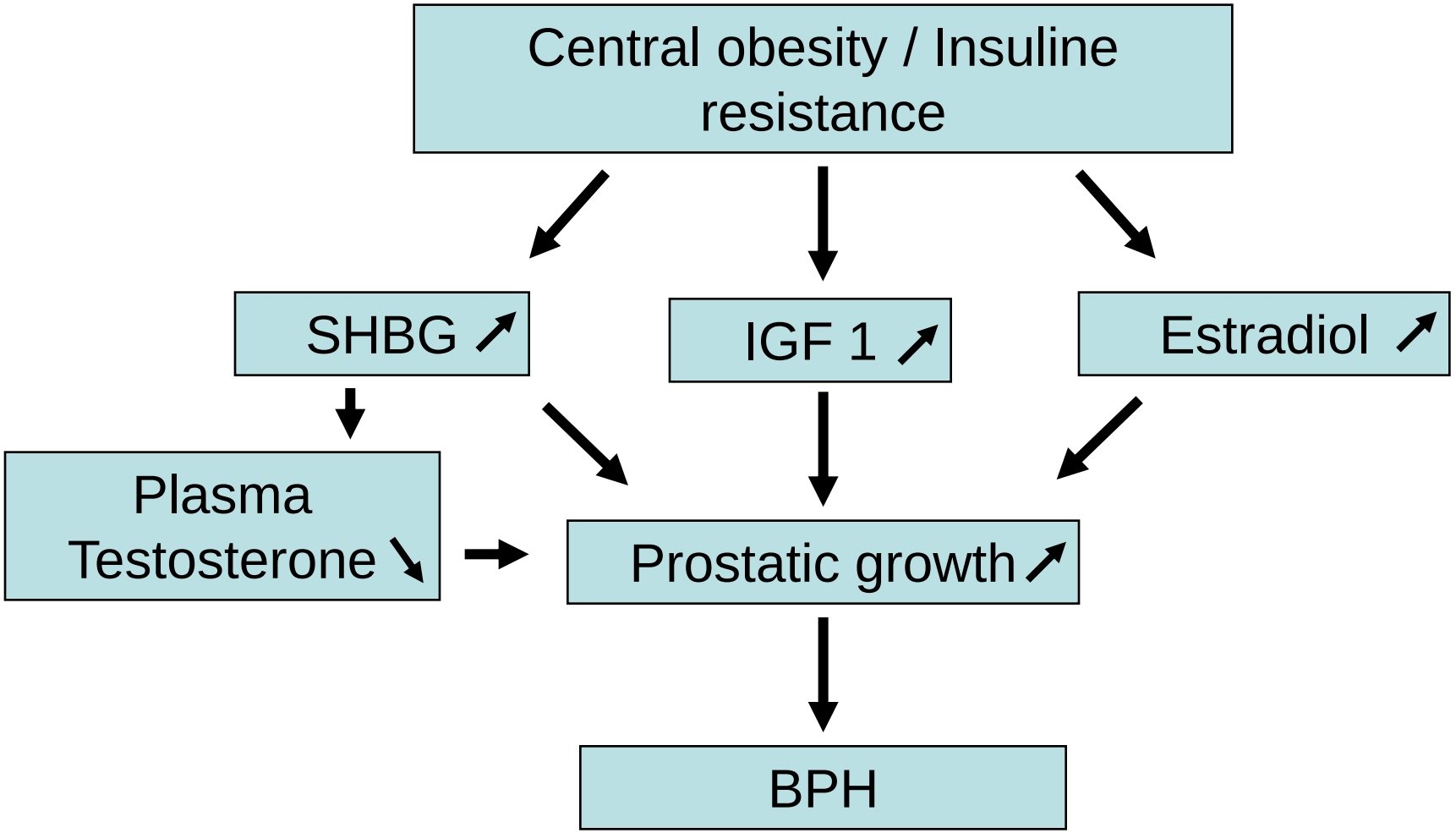
✓PA > 130 mmHg systolique, ou ≥ 85 mmHg diastolique, ou TRT en cours d'un HTA déjà diagnostiquée

✓Hyperglycémie provoquée ≥ 5.6 mmol/L ou diabète déjà diagnostiqué

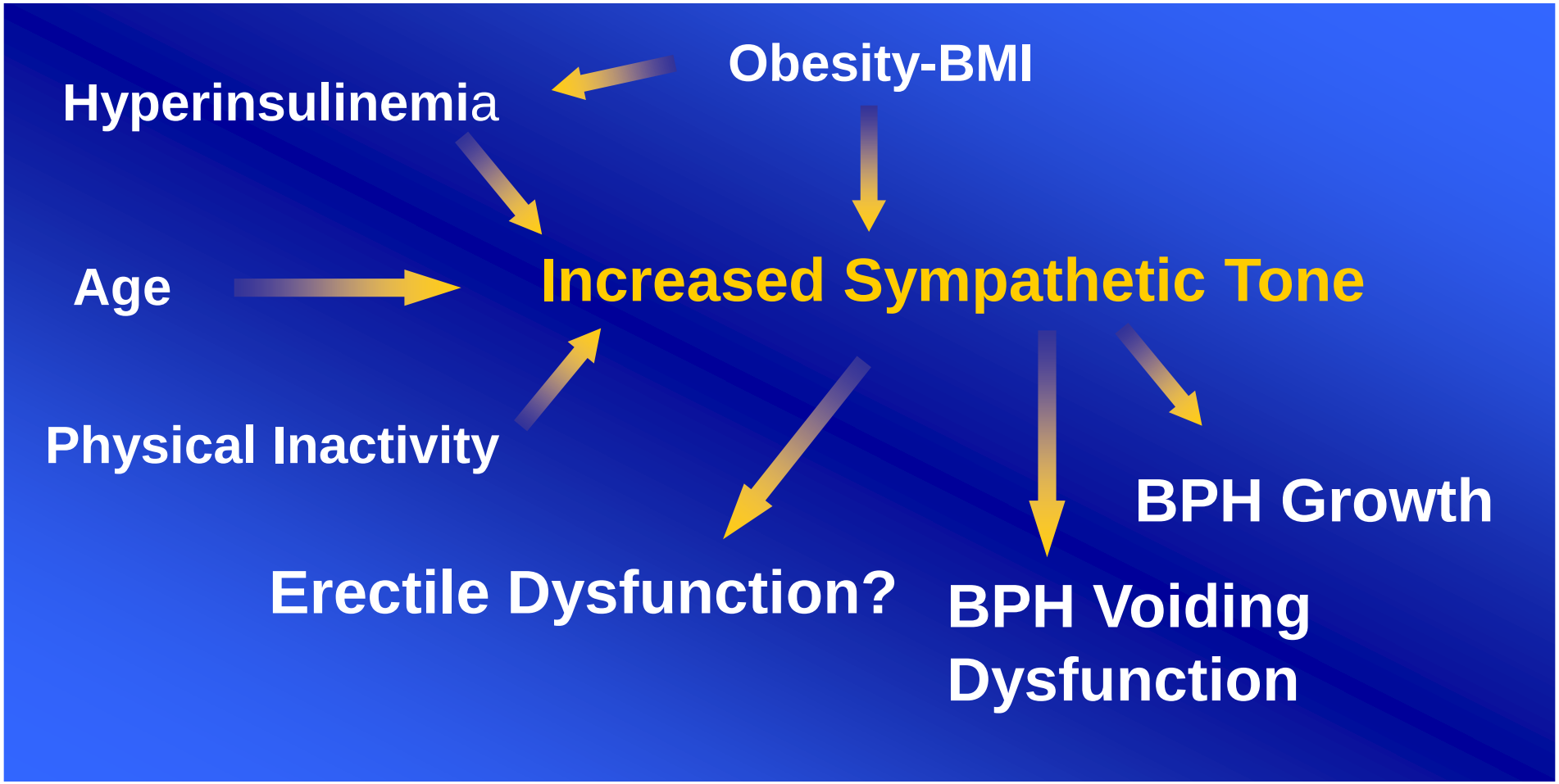
✓Triglycerides ≥ 1.7 mmol/L ou traitement en cours

✓HDL Cholesterol < 1.03 mmmol/L ou traitement en cours

# Syndrome Métabolique et HBP

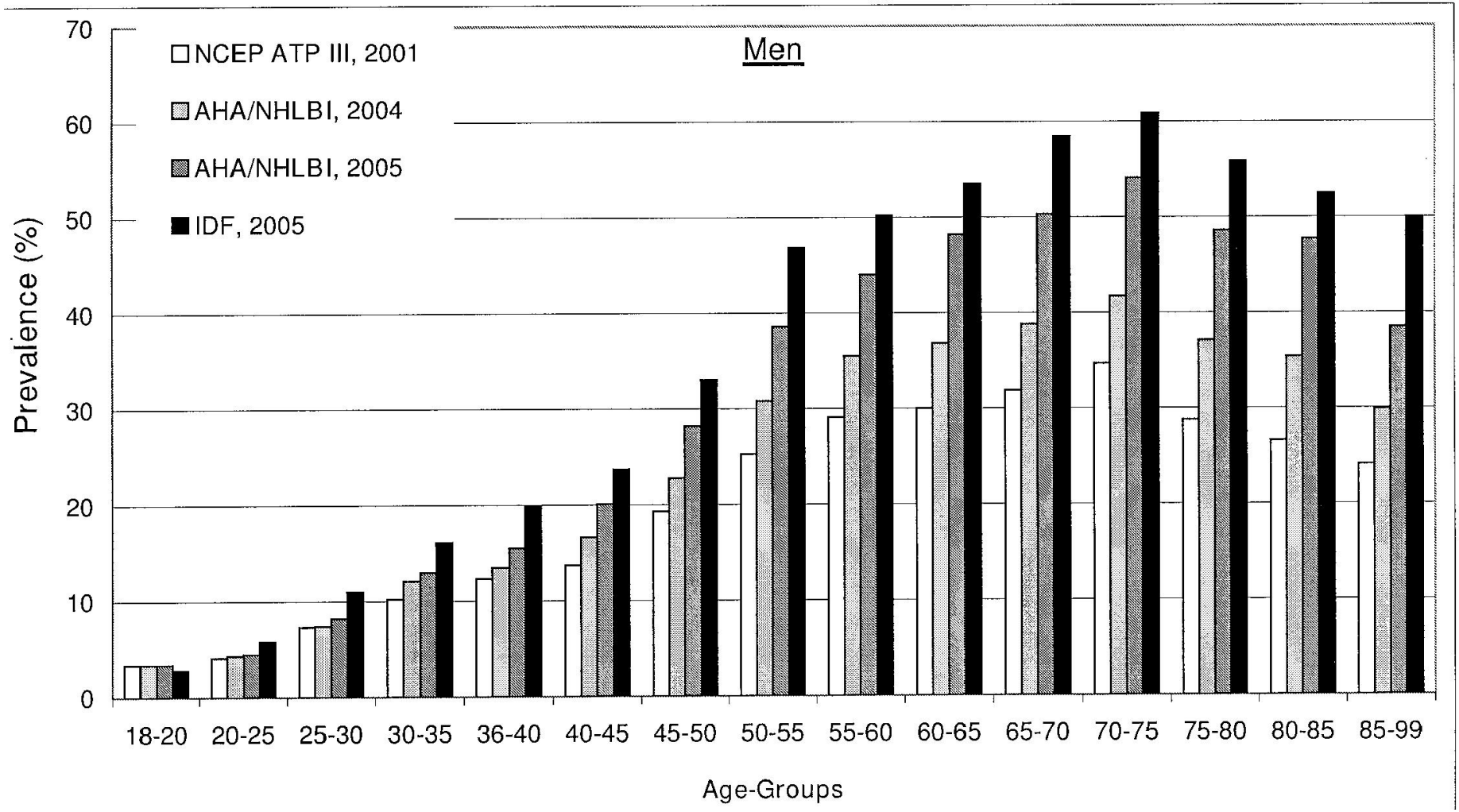


# Syndrome métabolique et hypertonie sympathique




McVary KT et al., Autonomic Nervous System Overactivity in Men with LUTS Secondary to BPH. Journal of Urology (In press) 2005

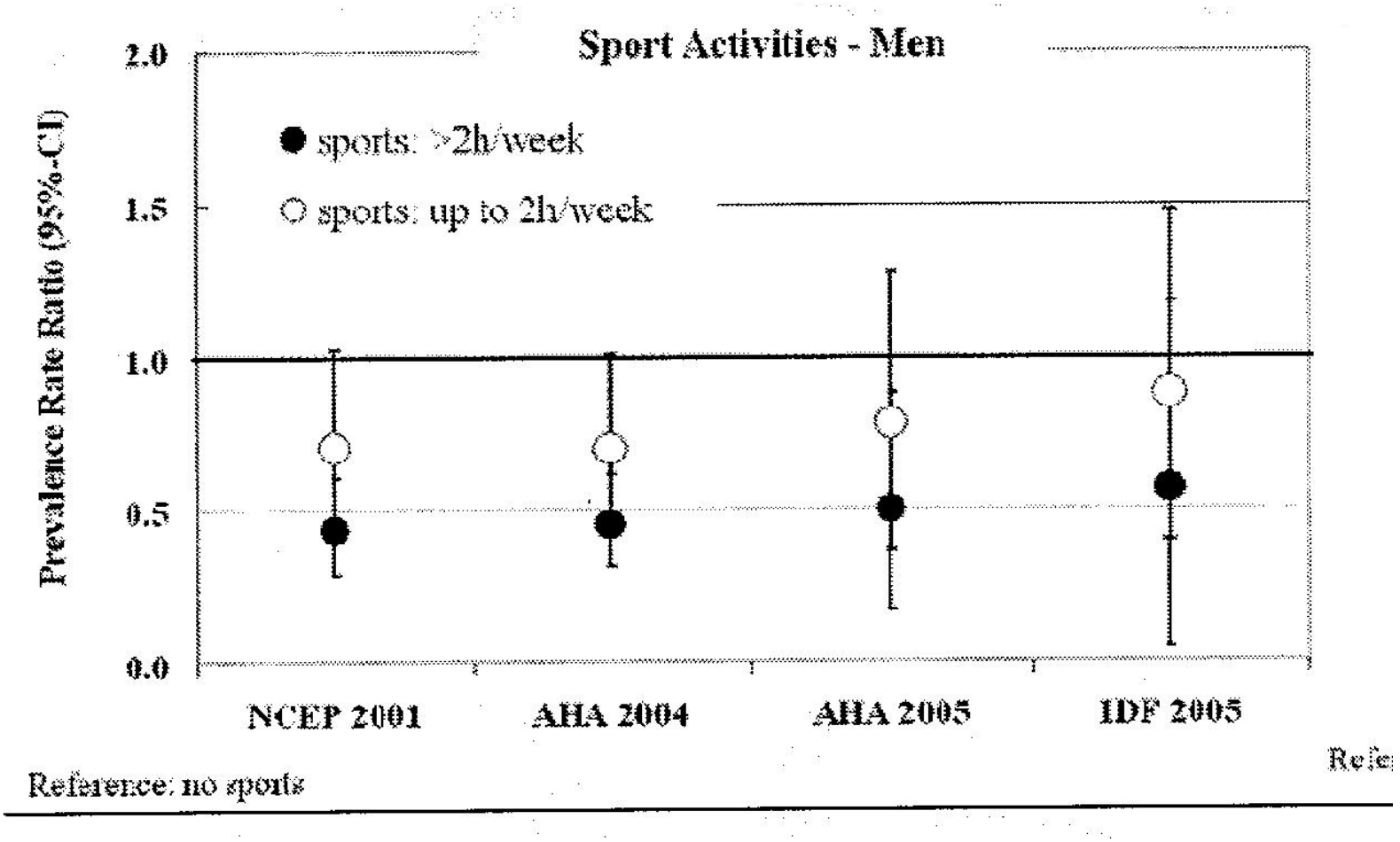
# Prévalence du syndrome métabolique Allemagne




Moebus S Cardiovasc Diab 2007

# Facteur de risque du syndrome metabolique

Sédentarité




Moebus S Cardiovasc Diab 2007

# Syndrome Metabolique et HBP

**Association Between Waist Circumference and Parameters Associated with Voiding and Sexual Health**

| Waist Circumference (inches) | 30 - 36 (n = 27) | 36 - 40 (n = 36) | > 40 (n = 25) | P value |
|---|---|---|---|---|
| Age, years | 61.39 | 62.36 | 63.89 | < 0.08 |
| PV, cc | 28.53 | 31.67 | 36.78 | < 0.001 |
| PSA, ng/mL | 2.32 | 2.92 | 3.54 | < 0.003 |
| IPSS at Screening | 11.57 | 13.67 | 15.78 | < 0.001 |
| Diabetic, % | 11.2 | 22.3 | 34.5 | 0.001 |
| Hypertension, % | 12.6 | 24.7 | 37.8 | 0.001 |
| Qmax, mL/sec | 10.6 | 9.45 | 8.65 | 0.03 |
| ED, % | 34.6 | 49.5 | 78.6 | 0.002 |
| EjD, % | 27.8 | 47.2 | 74.5 | 0.002 |

Kaplan, J Urol 2007, AUA #1508

# Syndrome Metabolique et HBP

**Association between PV and metabolic syndrome parameters**

| | Prostate volume | | | p value |
|---|---|---|---|---|
| | 5-<30 cc (n=1479) | 30-50 cc (n=3630) | >50-80 cc (n=2781) | |
| **Age, years** | 61.39 | 62.36 | 63.89 | <0.0001 |
| **PV, cc** | 23.59 | 39.80 | 61.84 | - |
| **PSA, ng/mL** | 5.48 | 5.79 | 6.25 | <0.0001 |
| **IPSS at screening** | 8.21 | 9.05 | 10.26 | <0.0001 |
| **BMI, kg/m$^2$** | 26.75 | 27.21 | 27.82 | <0.0001 |
| **Obese, %** | 15.98 | 19.07 | 24.09 | <0.0001 |
| **Diagnosed BPH, %** | 54.67 | 64.26 | 73.87 | <0.0001 |
| **Diabetic, %** | 7.78 | 8.22 | 9.22 | 0.2031 |
| **Hypertension, %** | 35.37 | 36.72 | 41.12 | 0.0001 |
| **Triglycerides, mmol/L** | 1.69 | 1.68 | 1.69 | 0.9057 |
| **Cholesterol, mmol/L** | 5.55 | 5.48 | 5.43 | 0.0055 |
| **Insulin, pmol/L** | 78.71 | 80.17 | 88.33 | 0.0004 |
| **HDL, mmol/L** | 1.32 | 1.31 | 1.27 | <0.0001 |
| **LDL, mmol/L** | 3.48 | 3.42 | 3.41 | 0.0990 |
| **Glucose, mmol/L** | 5.84 | 5.88 | 6.00 | <0.0001 |

**Data are presented as mean values unless stated otherwise**
**P values correspond to the differences among the three PV categories**

Kaplan , J Urol 2007, AUA #1548

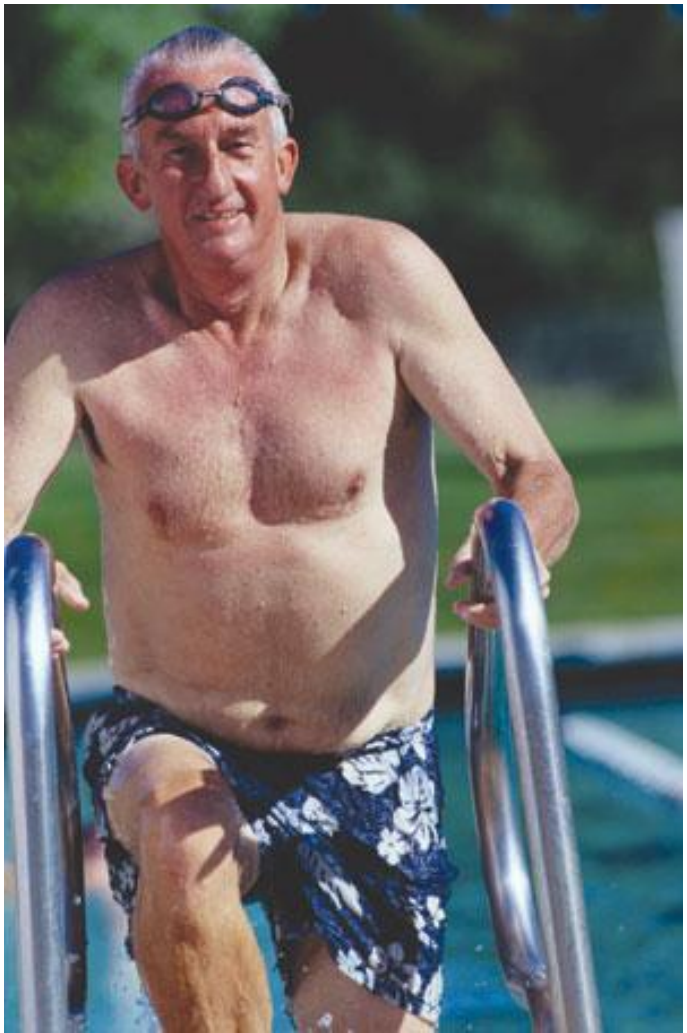
# Prevention et traitement du syndrome métabolique

**Perte de poids (7%) et activité physique régulière (120 min /semaine) …**

Meigs JB. Am J Manag Care 2002

Age: 72, IPSS: 15, Prostate: 55g, PSA: 3.5 ng/ml,
Résidu post-mictionnel: 70 ml

**TOUR DE TAILLE = 107 cm**



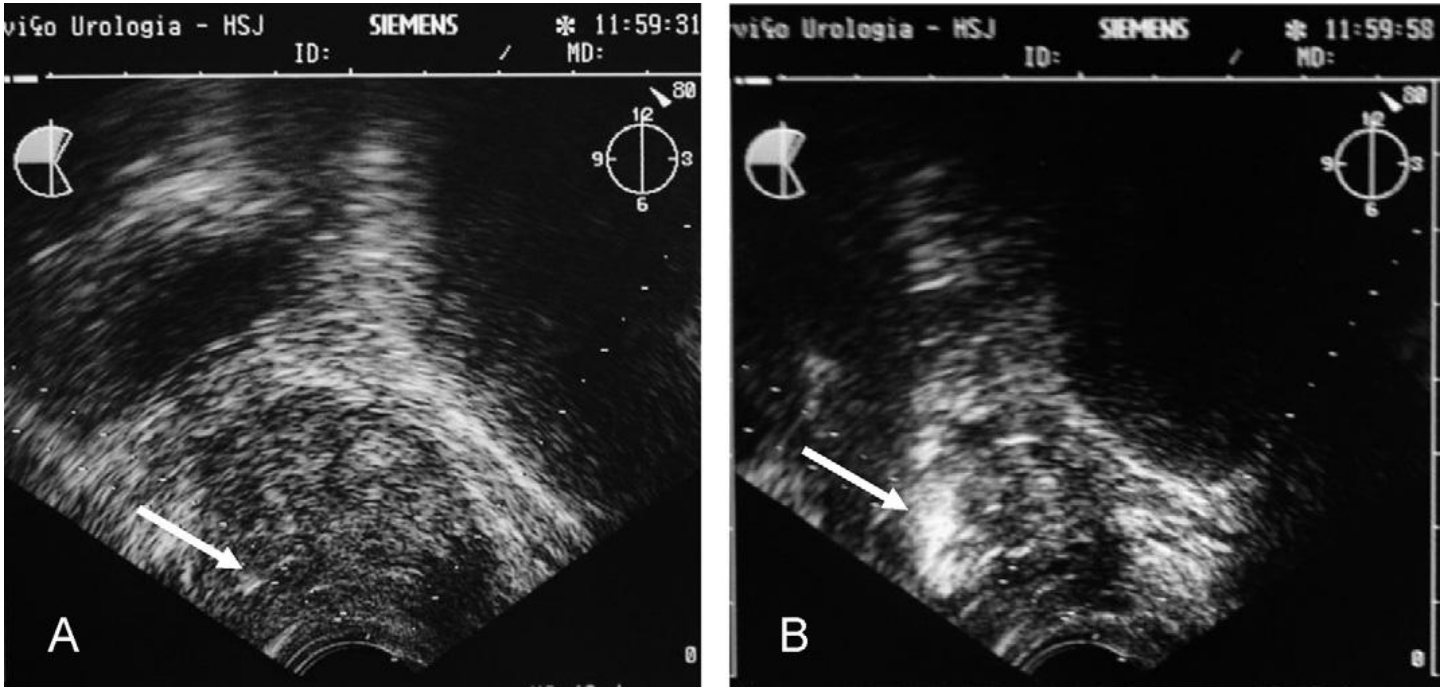
**Traitement de première intention ?**

**Durée de traitement ?**

# Toxine Botulique A

- Bloque le neurotransmission au niveau synaptique
- Son injection dans la prostate provoque une apoptose et une réduction du volume prostatique (rat) (Doggweiler R 1998)

# Botox dans la rétention urinaire

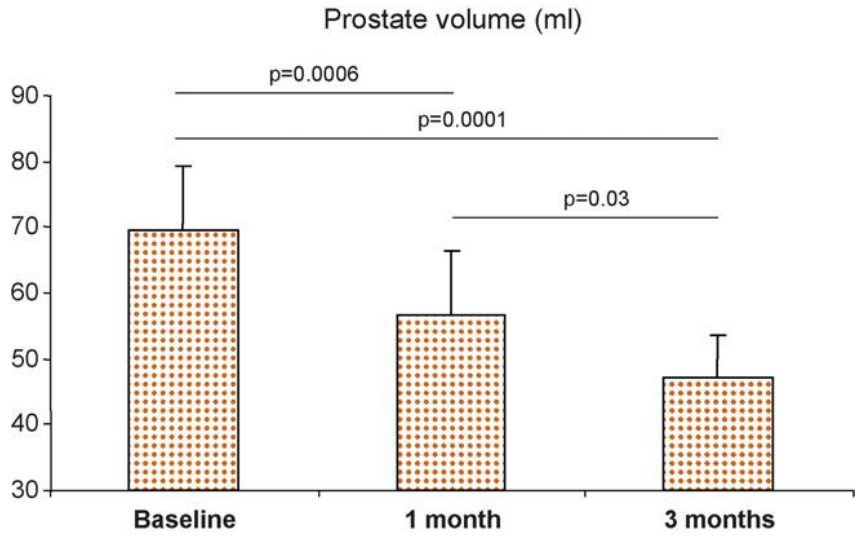


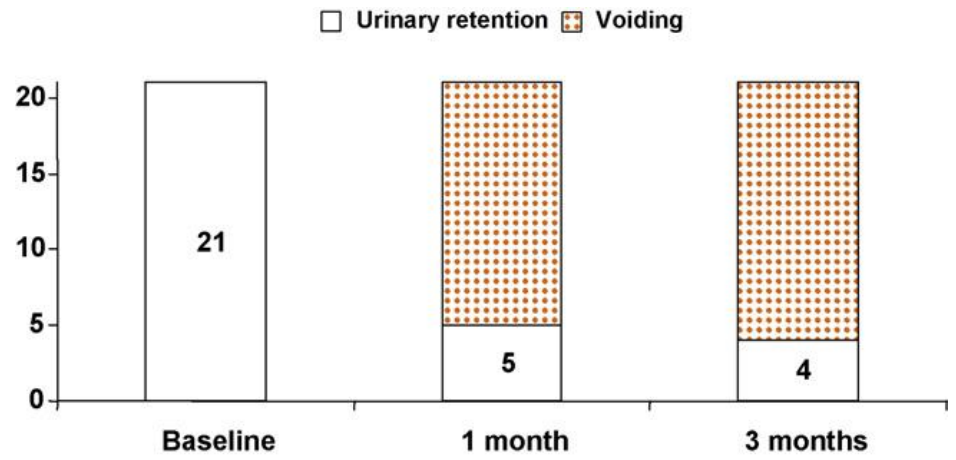

Two vials of Botox1,each one containing 100 U of neurotoxin (Allergan, Irvine, CA, USA) were diluted in 8 ml of saline. Transperineally injected in the TZ under local anesthesia.

22 patients on chronic indwelling catheter for at least 3 months

Silva J Eur Urol 2007

# Botox dans la rétention urinaire




Silva J Eur Urol 2007

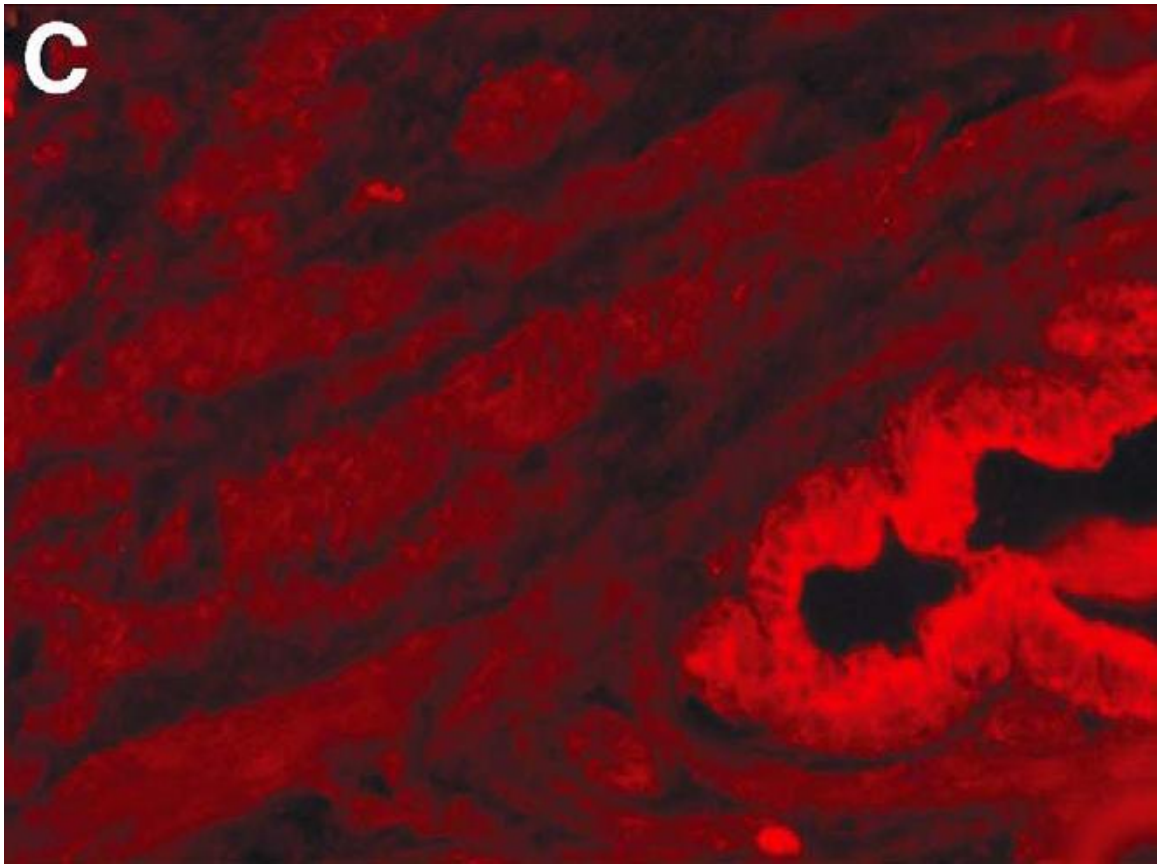
# Inhibitors Phosphodiesterase type 5

- le NO (Nitric oxide) est responsable de la relaxation musculaire dans les corps caverneux, la vessie et la prostate.
- Les inhibiteurs sildenafil, tadalafil, vardenafil augmentent la concentration du NO dans les muscles lisses, facilitant l'érection et la relaxation du col vésical et de la prostate.

Kaplan SA. Rev Urol 2007

# Phosphodiesterase type 5 inhibitors

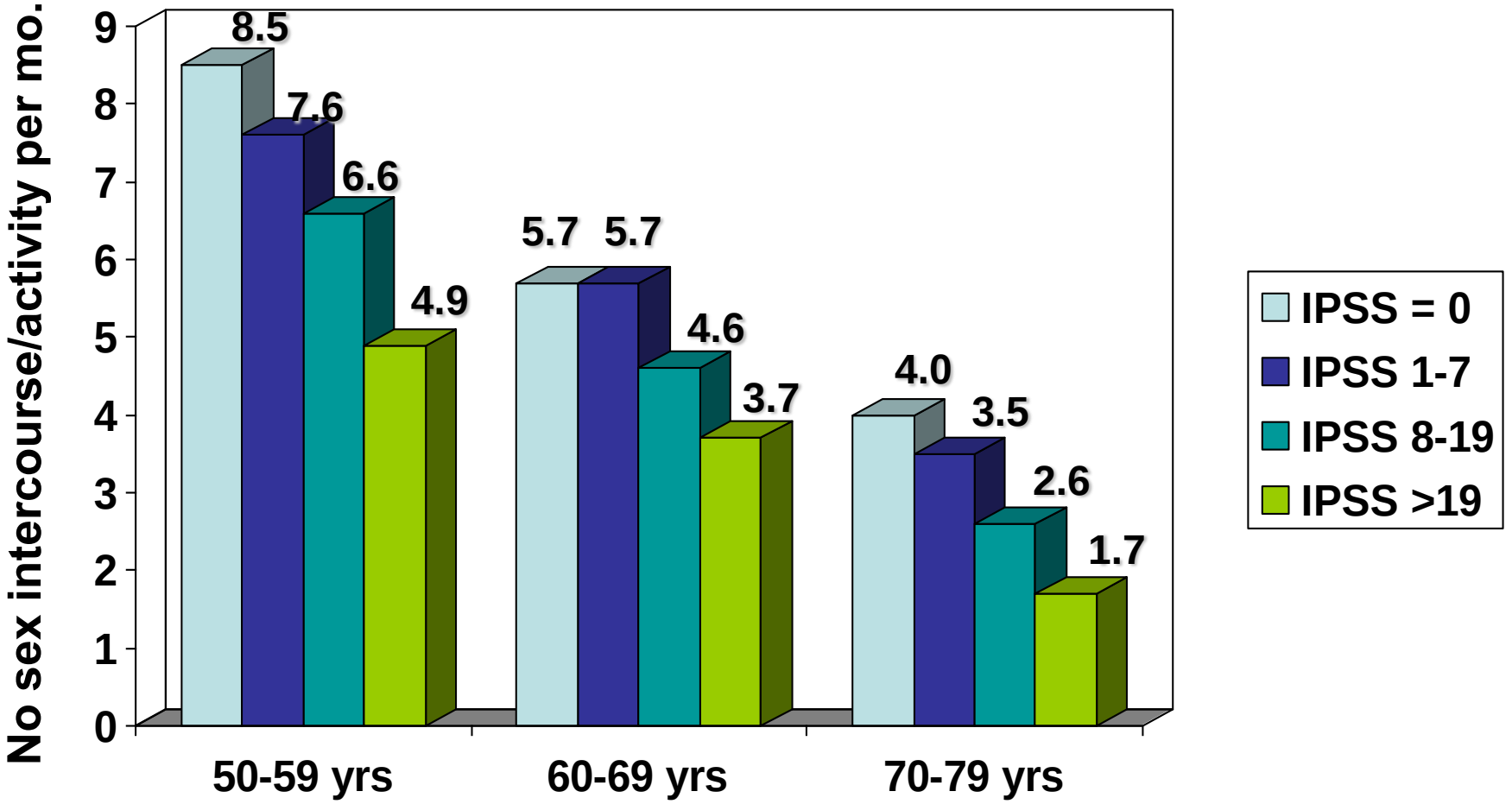
Presence of PDE isoenzymes 4, 5 and 11 in the transition zone of the human normal prostate




Dense immunofluorescence (TR) specific for PDE5 (cGMP-specific PDE) in glandular and subglandular structures of the transition zone

Uckert S Eur Urol 2007

# L’activité sexuelle décroit avec l’âge et les TUBA




MSAM-7 Multinational Survey of the Ageing Male in 7 countries

# PDE 5 : Sildenafil et HBP

**Table 1**
**Results of the Use of Alfuzosin, Sildenafil, or a Combination of Both on Lower Urinary Tract Symptoms and Erectile Dysfunction Measures**

| | Alfuzosin Baseline (n = 20) | Alfuzosin at 12 Weeks | Sildenafil Baseline (n = 21) | Sildenafil at 12 Weeks | Combination Baseline (n = 21) | Combination at 12 Weeks |
|---|---|---|---|---|---|---|
| IPSS | 17.3 | 14.6 | 17.8 | 14.9 | 17.3 | 13.5 |
| $Q_{max}$ (mL/s) | 9.4 | 10.5 | 9.7 | 10.3 | 9.5 | 11.5 |
| PVR (mL) | 54 | 31 | 46 | 34 | 53 | 32 |
| Frequency (voids/day) | 8.7 | 6.4 | 9.1 | 7.8 | 9.3 | 6.1 |
| Nocturia (voids/night) | 2.9 | 1.8 | 2.6 | 2.1 | 3.1 | 1.8 |
| IIEF | 17.4 | 20.3 | 14.3 | 21.4 | 16.2 | 25.7 |

IPSS, International Prostate Symptom Score; $Q_{max}$, peak urinary flow rate; PVR, postvoid residual urine; IIEF, International Index of Erectile Function.
Reproduced from Kaplan SA et al.[19] with permission from the American Urological Association.

Kaplan SA J Urol 2006

# PDE 5 : Tadalafil et HBP

**Table 2**
**Efficacy Results for Use of Daily-Dosed Tadalafil 5 mg, Tadalafil 5/20 mg, and Placebo at 6 and 12 Weeks**

| | Placebo 6 wk | Tadalafil 5 mg 6 wk | *P* Value | Placebo 12 wk | Tadalafil 5/20 mg 12 wk | *P* Value |
|---|---|---|---|---|---|---|
| n | 143 | 138 | | 143 | 138 | |
| IPSS* | −1.2 ± 0.47 | −2.8 ± 0.48 | .003 | −1.7 ± 0.49 | −3.8 ± 0.50 | < .001 |
| IPSS QOL* | −0.2 ± 0.11 | −0.5 ± 0.11 | .017 | −0.3 ± 0.12 | −0.7 ± 0.12 | .008 |
| BII* | −0.4 ± 0.21 | −0.7 ± 0.22 | .107 | −0.6 ± 0.23 | −1.3 ± 0.23 | .008 |
| LUTS GAQ, endpoint (% yes) | 32.6 | 55.9 | < .001 | 37.7 | 57.4 | < .001 |

*Change from baseline, least-squares mean ± standard error.
IPSS, International Prostate Symptom Score; QOL, quality of life; BII, Benign prostatic hyperplasia Impact Index; LUTS GAQ, lower urinary tract symptoms global assessment question. Reproduced from Roehrborn C et al.[20] with permission from the American Urological Association.

Roehrborn C  SA J Urol 2006

# PDE 5 : Vardenafil et HBP

Vardenafil : prospective randomised study

Vardenafil 10 mg x 2 / jour (n=108) vs  placebo (n=113)

At 8 weeks :

IPSS reduction of 5.8 vs 3.8 points (p=0.0013)

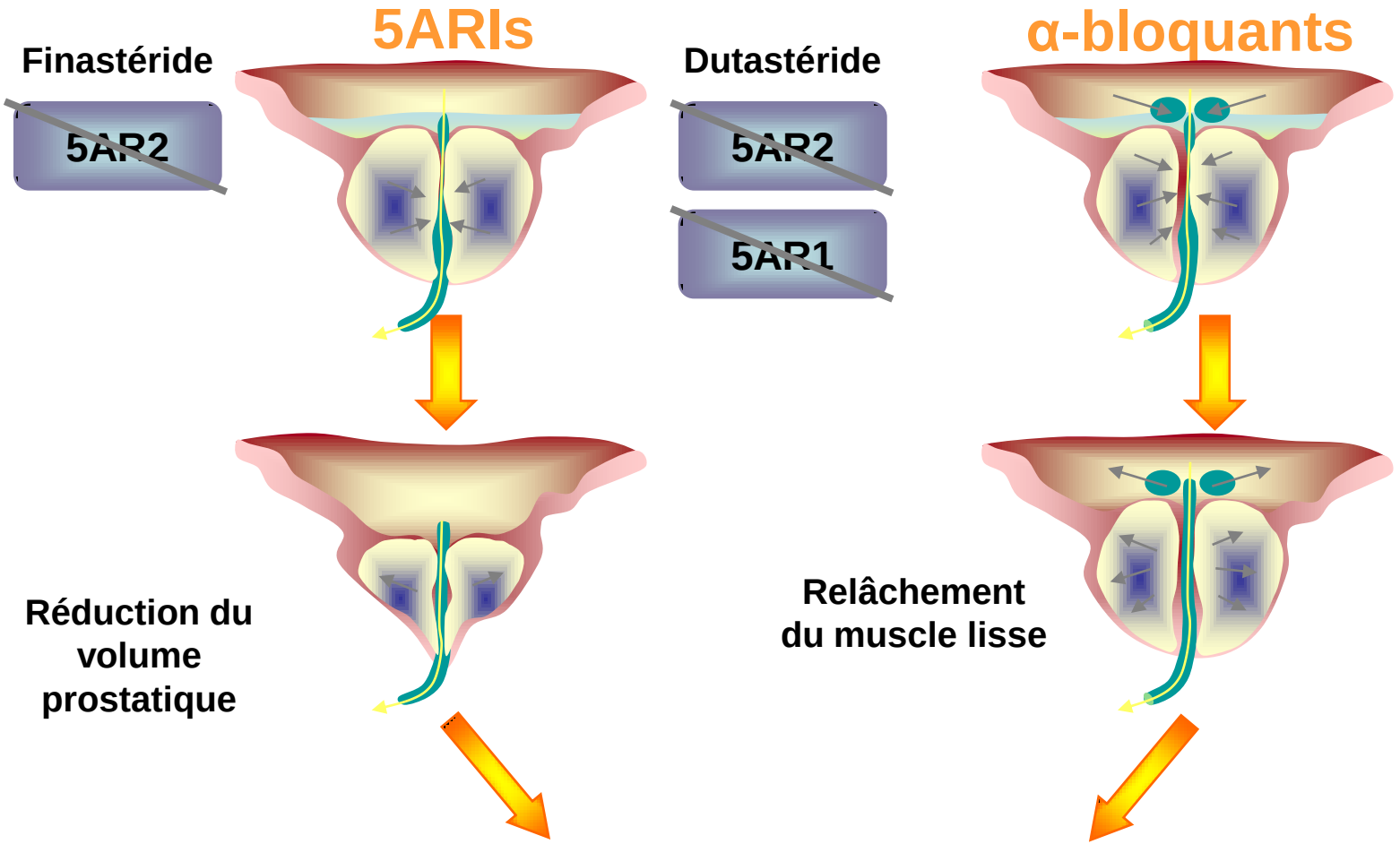
IIEF increase of 7.5 vs 1.5 points (p=0.0001)

Stief, J Urol 2007

# Traitements combinés

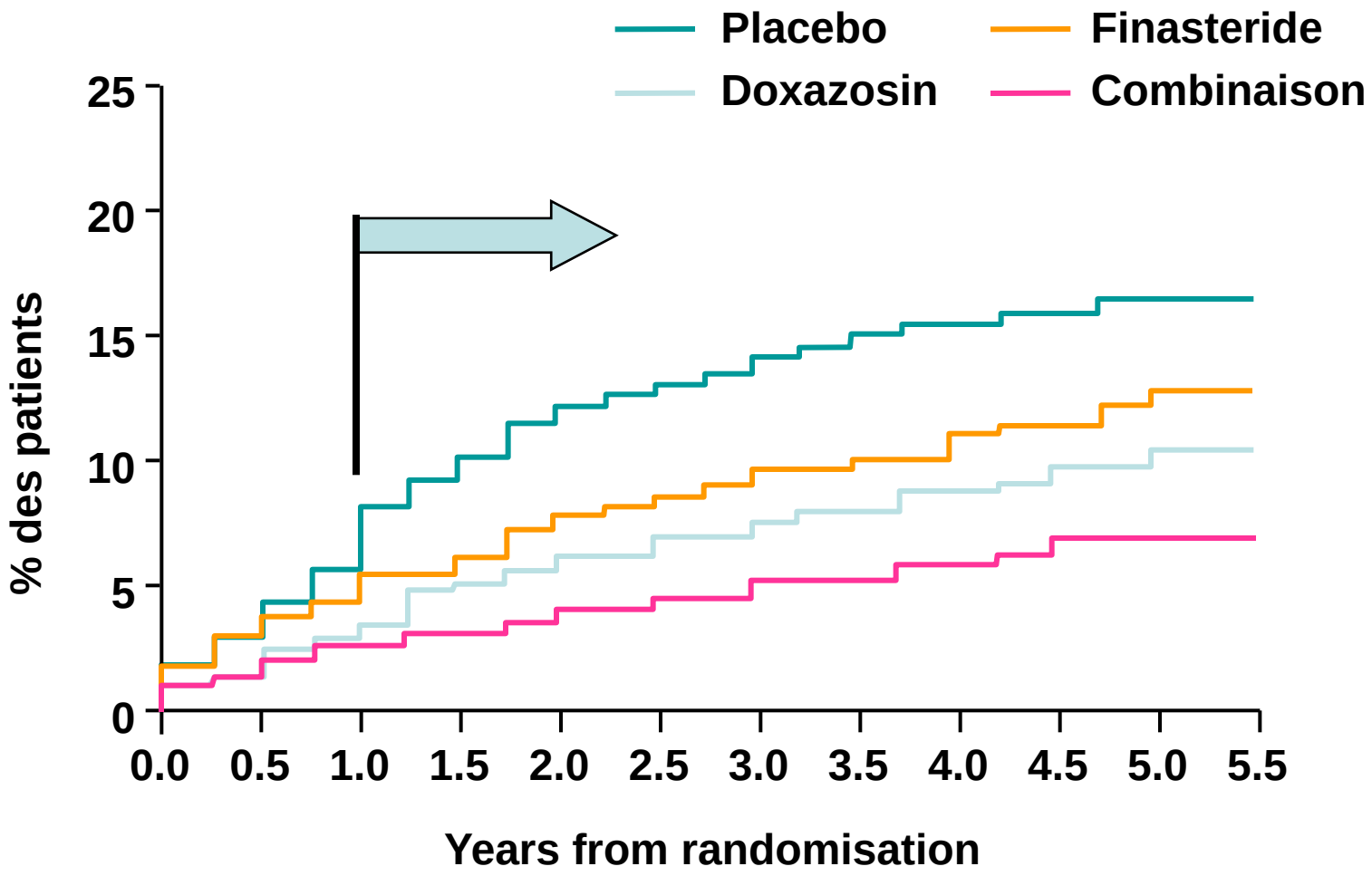
- ✓ Alpha-bloqueurs et 5 ARI

- ✓ Alpha-bloqueurs et anticholinergiques



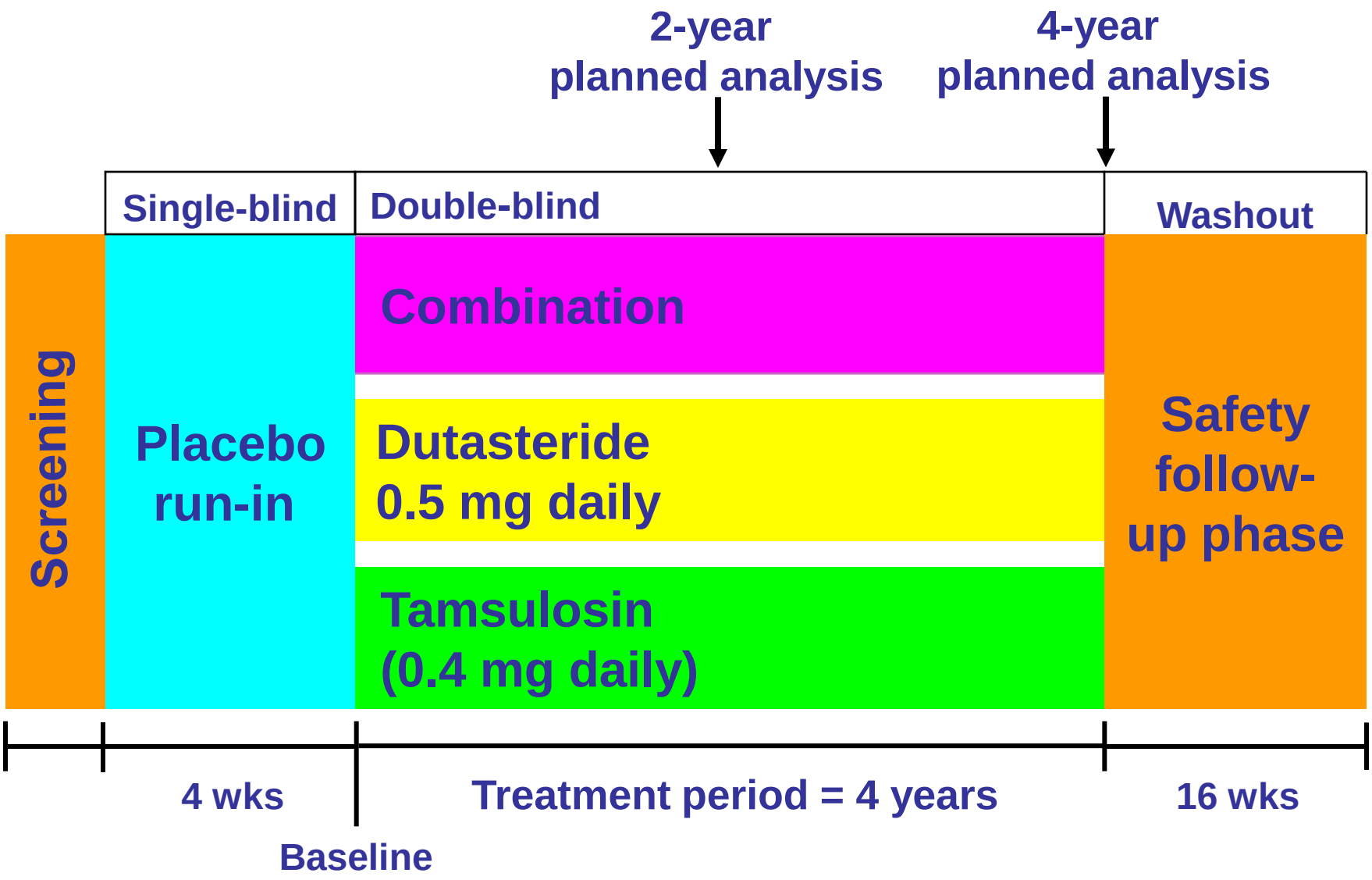

**Le traitement par association permet une diminution rapide et durable de la gêne due aux symptômes et la réduction de progression**

# MTOPS: Aggravation symptomatique



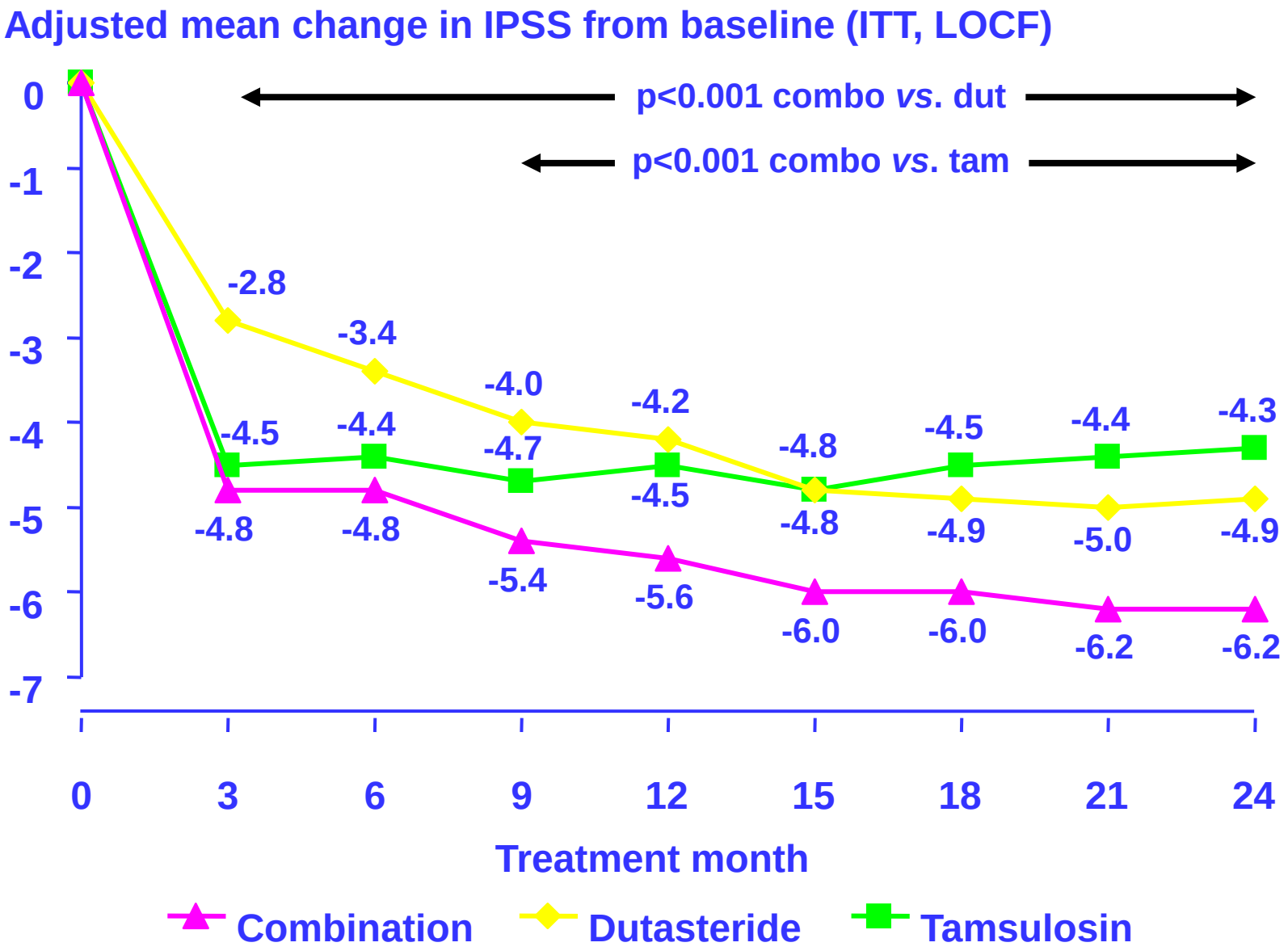

McConnell *et al*. NEJM 2003

# CombAT study design



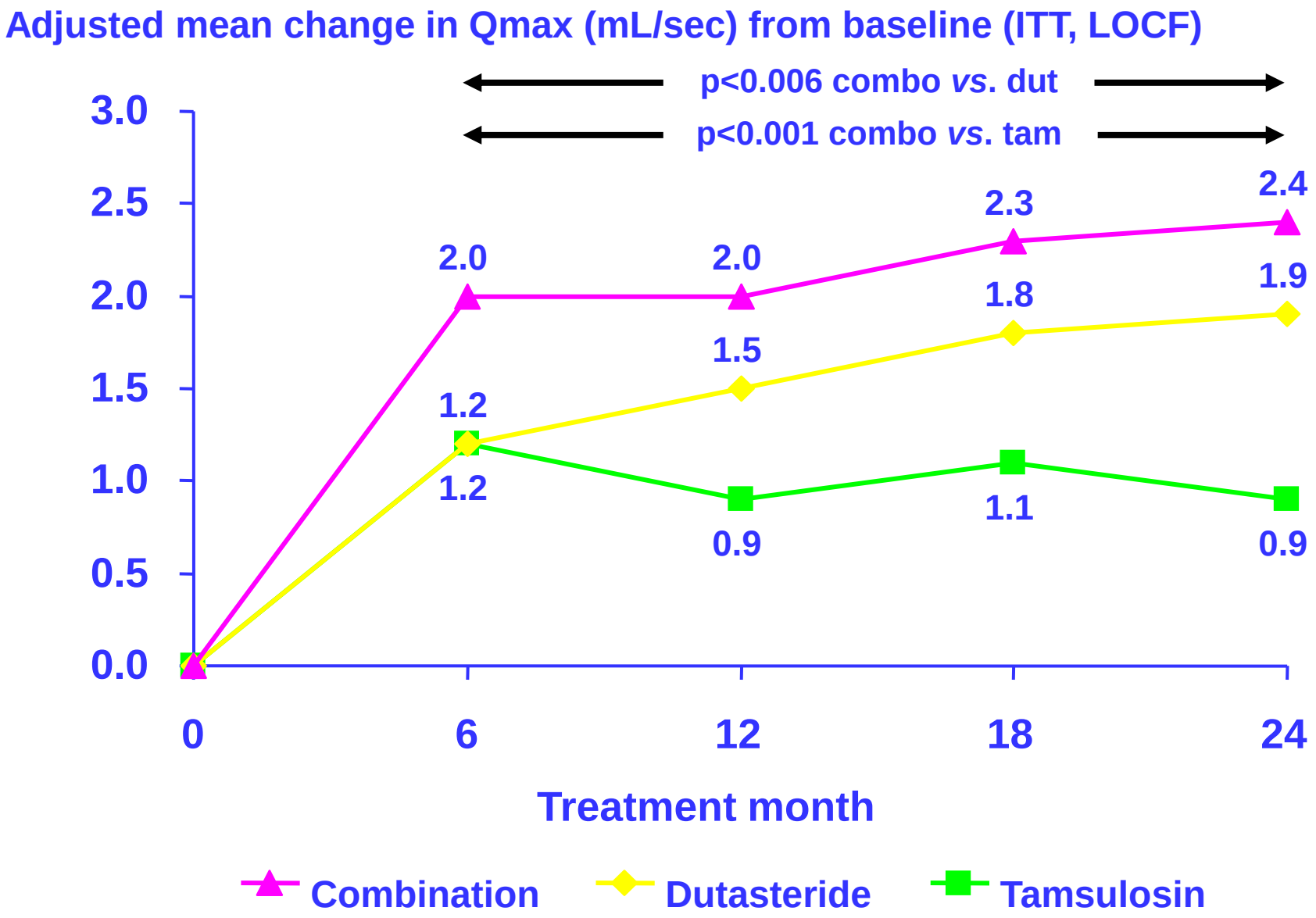

Siami *et al*. Contemp Clin Trials, August 2007 Epub

# CombAT : Evolution symptomatique




Roehrborn *et al*. J Urol (In Press)

# CombAT : Evolution du débit



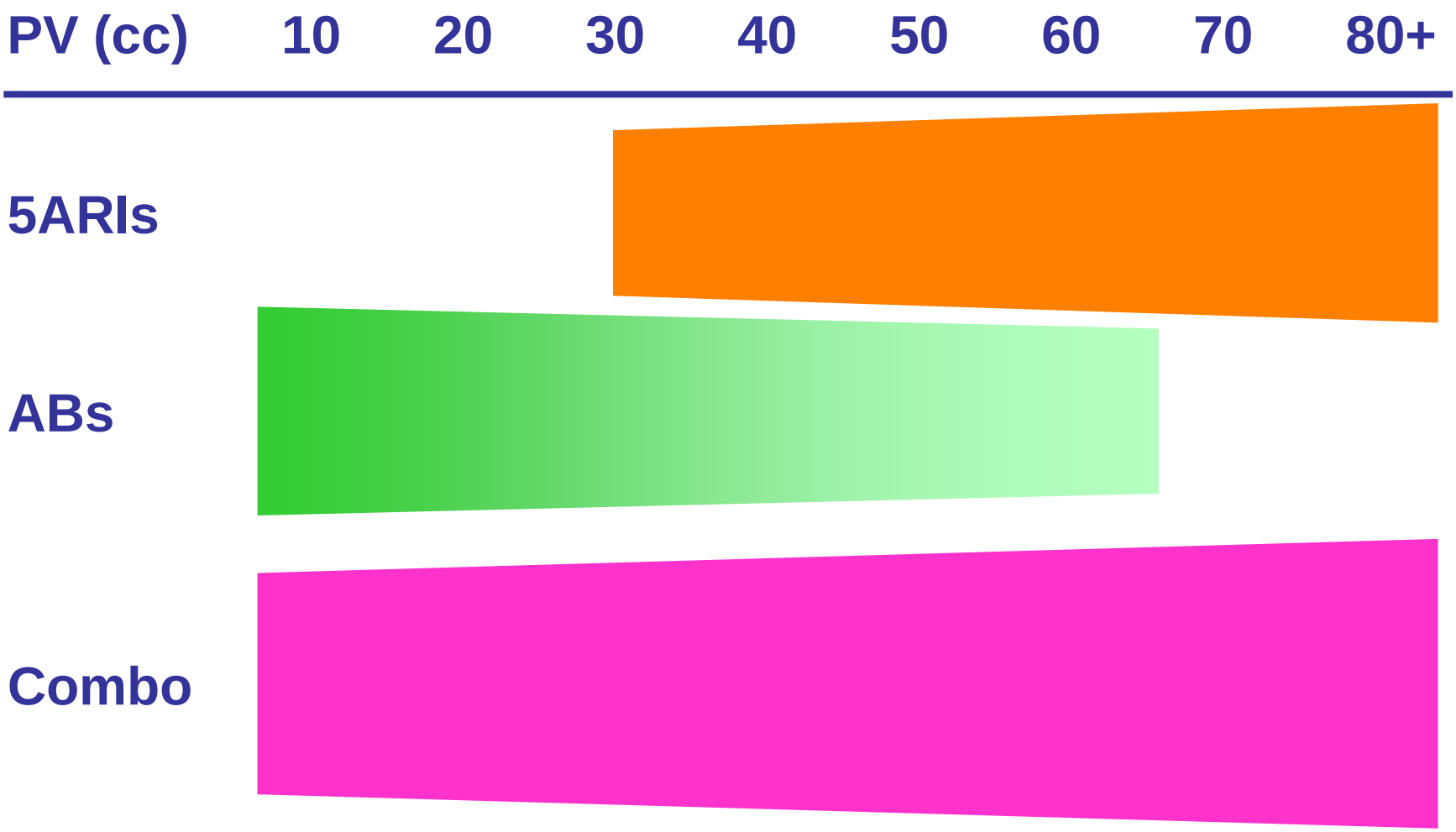

Roehrborn *et al*. J Urol (In Press)

# CombAT : Effets secondaires

| | Combination (n=1610) | Dutasteride (n=1623) | Tamsulosin (n=1611) |
|---|---|---|---|
| Erectile dysfunction | 7.4% | 6.0% | 3.8% |
| Retrograde ejaculation | 4.2% | 0.6% | 1.1% |
| Altered (decreased) libido | 3.4% | 2.8% | 1.7% |
| Ejaculation failure | 2.4% | 0.5% | 0.8% |
| Semen volume decreased | 1.8% | 0.3% | 0.8% |
| Loss of libido | 1.7% | 1.3% | 0.9% |
| Dizziness | 1.6% | 0.7% | 1.7% |
| Breast enlargement | 1.4% | 1.8% | 0.8% |
| Nipple pain | 1.2% | 0.6% | 0.3% |
| Breast tenderness | 1.0% | 1.0% | 0.3% |

Roehrborn *et al*. J Urol (In Press)

# Traitement médical de l'HBP : Conclusion ?



# Traitements combinés

- ✓ Alpha-bloqueurs et 5 ARI

- ✓ Alpha-bloqueurs et anticholinergiques

# Alpha-bloqueurs et anticholinergiques

Etude randomisée prospective
Placebo vs tolderodine vs tamsulosine
vs toldérodine + tamsulosine

879 patients with HBP and vessie hyperactive

(pollakiurie > 8/24h + urgences >3 avec ou sans incontinence, moderée à sévère (IPSS >12) )

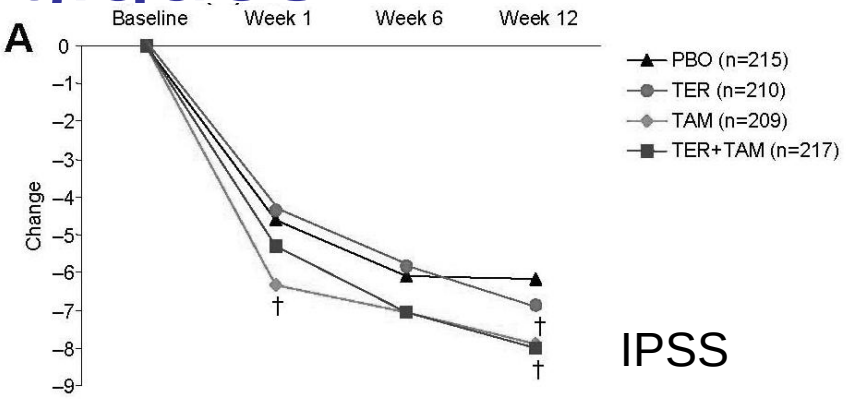
**Roehrborn C, J Urol 2007**

# Alpha-bloqueurs et anticholinergiques

TER+TAM > PBO symptômes

pas de modification Q max et PVR

AUR: 0.4% TER+TAM 0.5% TER et 0% PBO and TAM




IPSS

**Table. Changes in IPSS Item Scores***

| Item | PBO (n=215) | TER (n=210) | TAM (n=209) | TER+TAM (n=217) |
|---|---|---|---|---|
| Straining | –0.64 | –0.51 | –0.83 | –0.62 |
| Sensation of incomplete emptying | –0.94 | –1.05 | –1.21† | –1.14 |
| Frequency | –1.10 | –1.34 | –1.31 | –1.60‡ |
| Intermittency | –0.81 | –0.95 | –1.15‡ | –0.99 |
| Urgency | –1.12 | –1.27 | –1.22 | –1.56‡ |
| Weak stream | –0.81 | –0.88 | –1.25‡ | –1.00 |
| Nocturia | –0.72 | –0.85 | –0.91 | –1.09‡ |

*Values are adjusted means (ie, least squares means).
† $P \leq 0.05$ vs PBO.
‡ $P \leq 0.01$ vs PBO.