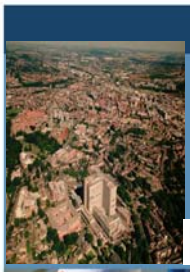
Advances in the management of BPH/LUTS



Christopher Chapple
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Sheffield Hallam University

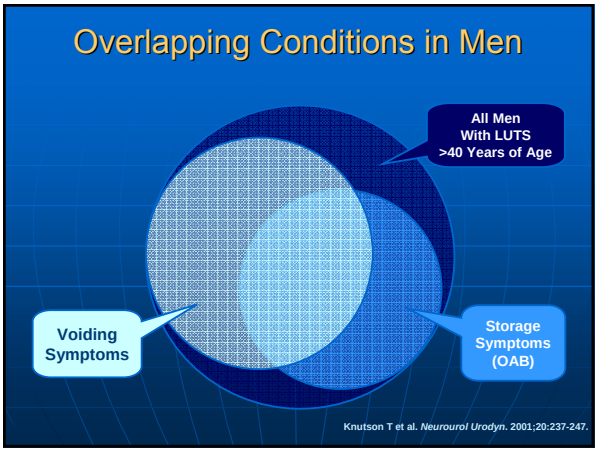
Presentation to Europa UOMO
Eau Meeting Stockholm 19th March 2009

European Association of Urology

Greetings from the Executive and Members of the European Association of Urology

Sub title (Arial Bold 24 pt Uroplus white)

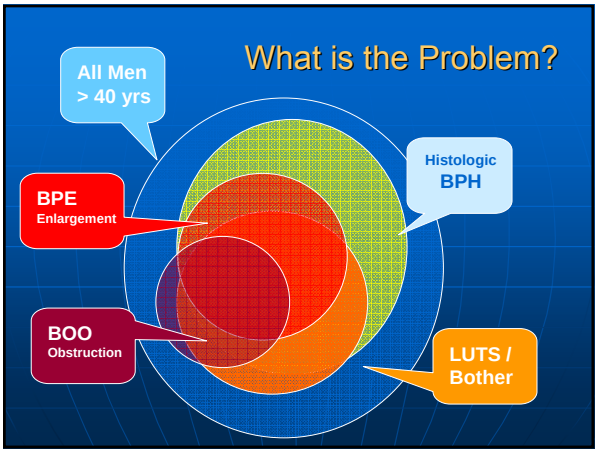
PA Abrahamsson | Chris Chapple | Walter Artibani | Manfred Wirth

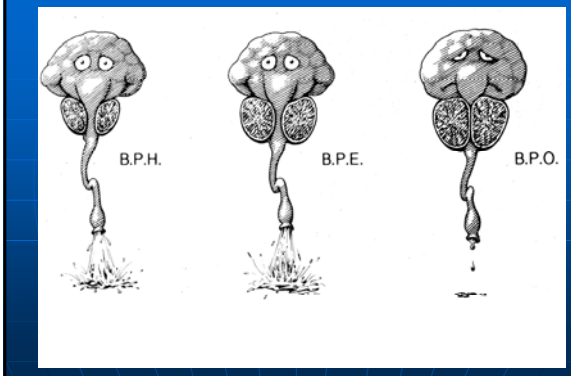


Definition of Benign Prostatic Hyperplasia

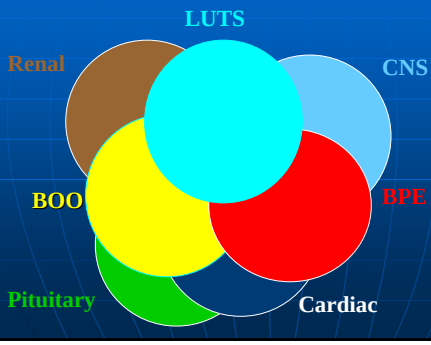
"The absence of a unifying definition, whose sensitivity and specificity can be defined has been a major problem with 'BPH'. This is a fundamental problem which still requires to be resolved…."

Barry MJ et al 1995 3rd Int Cons BPH 21-36,
Boyle P et al 2001 5th Int Cons BPH 19-68





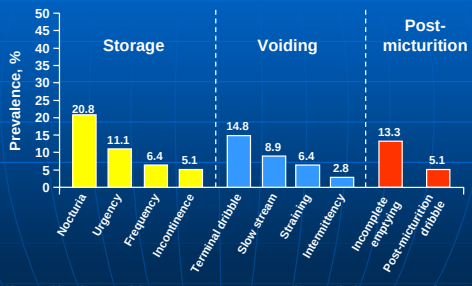
The Factors involved in LUTS



Classification of Lower Urinary Tract Symptoms (LUTS)

Storage	Voiding	Post-micturition
• Frequency • Urgency • Nocturia • Incontinence	• Slow stream • Splitting or spraying • Intermittency • Hesitancy • Straining • Terminal dribble	• Post-micturition dribble • Feeling of incomplete emptying

Prevalence of Individual LUTS in Men



Nocturia: waking to void ≥2 times per night.
Frequency: subject feels he/she urinates too often during the day.

Irwin DE et al. Abstract presented at EAU 2006. EPIC Study

eau
European Association of Urology

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Review – Neuro-urology – Voiding Dysfunction

A Shifted Paradigm for the Further Understanding, Evaluation, and Treatment of Lower Urinary Tract Symptoms in Men: Focus on the Bladder

Christopher R. Chapple*, Claus G. Roehrborn

Article info

Abstract

Evaluation of Symptoms

- OAB
  - No. micturition episodes/24 h
  - No. urge incontinence episodes
  - Nocturnal voids
  - Effect on urgency
- LUTS in men
  - IPSS
  - Flow rate
  - Postvoid residual (PVR)

Currently Available Treatment Guidelines for Men With LUTS

- American Urological Association (AUA)
  - Guidelines for BPH/LUTS
    http://www.auanet.org/guidelines/bph.cfm
- European Association of Urology (EAU)
  - Guidelines for BPH
    http://www.uroweb.nl/files/uploaded_files/guidelines/11%20BPH.pdf
  - Guidelines for incontinence
    http://www.uroweb.nl/files/uploaded_files/guidelines/18%20Urinary%20Incontinence.pdf
- International Consultation on New Developments in Prostate Cancer and Prostate Diseases (ICUD)
  - Evaluation of LUTS in older men

Although several treatment guidelines are available, they share relatively similar characteristics.

Diagnostic Tests

Basic Evaluation

Recommended Tests

1. History
2. Assessment of Symptoms and Bother
3. Physical Digital Rectal Examination
4. Urinalysis
5. Serum Prostate-Specific Antigen (PSA)
6. Frequency – Volume Chart (Voiding Diary)

Specialized Evaluation

Recommended Tests

1. Detailed Quantification of Symptoms by Standardized Questionnaires, moved to specialist.
2. Flow Rate Recording
3. Residual Urine
4. Pressure Flow Studies (PFS)

Optional Testing

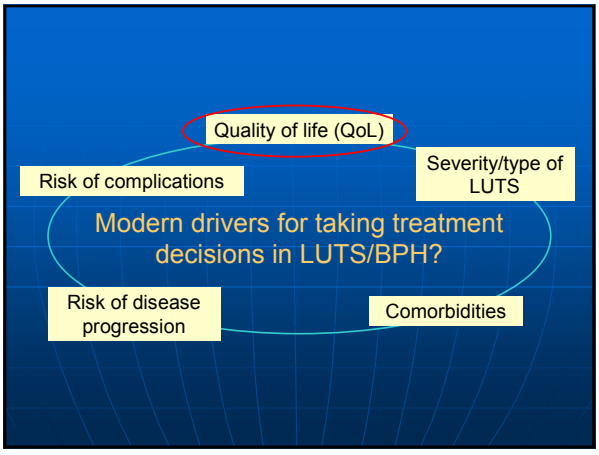
1. Imaging of the Prostate by Transabdominal or Transrectal Ultrasound (TRUS)
2. Imaging of the Upper Urinary Tract by Ultrasonography or Intravenous Uro-graphy (IVU)
3. Endoscopy of the Lower Urinary Tract

Summary

- Storage symptoms of OAB frequently occur in men with LUTS secondary to BPH and may be linked with concomitant DO
- These storage symptoms (OAB) are often the most bothersome to patients
- Multiple pathophysiological mechanisms exist that might explain the development of OAB in pts with BOO, with increased emphasis on afferent pathways

Recommendation Chapple et al 2006

- Lower urinary tract symptoms relating to voiding (LUTS) are not disease specific and hence diagnostic of BPH or BOO.
- Appropriate assessment of the symptomatic patient relies upon comprehensive evaluation.
- A major problem in the contemporaneous literature is the absence of an adequate internationally accepted and applied definition for 'BPH'
- When evaluating therapy we need to:-
  - Identify and standardise robust outcome measures pertinent to the condition - LUTS, OAB, BOO….
  - With reference to what is most bothersome to patients



PHARMACOTHERAPY FOR THE PROSTATE

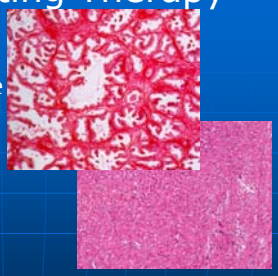
HORMONAL THERAPY
5 α reductase inhibitors

ALPHA ADRENERGIC BLOCKADE
α1, 2 antagonists
selective α1 antagonists
$\alpha 1_A$ antagonists

PHYTOTHERAPY
Various plant extracts

SYNTHETIC POLYENES

Targeting Therapy



Ratio of smooth muscle to glandular tissue increases in BPH
25% versus 40%
Nevertheless
it is an adenomatous hyperplasia

- There is insufficient evidence in the literature to recommend how to target therapy based on the morphology of the prostate
- The committee recommend this as an important area for future research

Level 2 Grade D

PHARMACOTHERAPY FOR THE PROSTATE

- **Natural history of BPH**
- **Placebo effect**
- **Precise Mechanisms / Sites of action of agents remain poorly established**

Natural History

- 16% of those with BPH have no change in symptoms
- 38% were better
- Retention is uncommon
- with a follow up ranging 2.6 - 5 years

Isaacs 1990

BPH MEDICAL MANAGEMENT

- Placebo is effective !
  - 303 patients, 25/12 FU
- FR +1.0ml/s, SS -2.3 pts
  - not age dependent
  - correlation with severity of SS & FR and prostate <40gm
- Adverse events
  - 80.2 % adverse events, urogenital 35.6%, impotence 6.3%, 13.2 % discontinued with adverse events

Nickel 1998

Recommendation

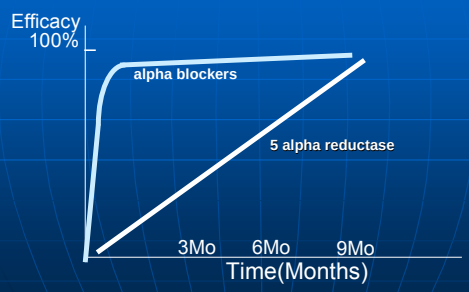
There is a lack of :-

- Data on the long-term safety and efficacy of therapy, patient compliance and therefore willingness to continue with therapy is important.
- Long-term data from real life practice
- Information on cost effectiveness and cost benefit.

- The interpretation of data derived from studies is not standardized:-
  - With reference the criteria defining baseline values
  - Relating to the change from baseline values that occurs during the placebo run in phase prior to starting active therapy
  - In interpreting data:-
    - it is important to consider the size of the 'treatment effect' and relate this to its clinical importance and relevance.
    - remember that there is a high placebo response in BPH/LUTS.
    - untreated BPH does not necessarily progress

Level 1 Grade A

Pharmacotherapy
onset of action



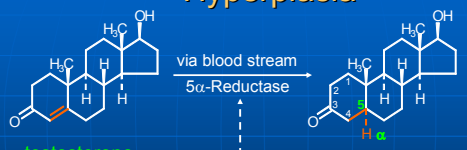
5a-Reductase Inhibitors

Two agents

- Safe and well tolerated

Level 1 Grade A

Hormonal approaches to the Treatment of Benign Prostatic Hyperplasia



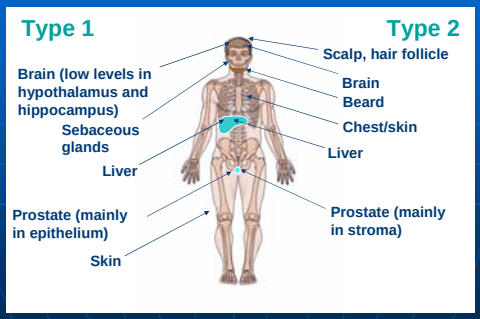
testosterone

finasteride/ dutasteride

5α-dihydrotestosterone DHT

transcription of growth factors

Type 1 and type 2 isoenzyme distribution



Enlarged Prostate International Comparator Study (EPICS):
12 months double blind
direkt comparison of dutasteride vs. finasteride

parameter	dut.(n 813)	fin.(817)
Prost. vol.	- 26.3	- 26.7
Symptoms	- 5.8	- 5.5
Qmax	2.0	1.7
Erectile dysfunction	8 %	9 %
Decreased libido	5 %	6 %

data published at www.gsk.com

Recommendations

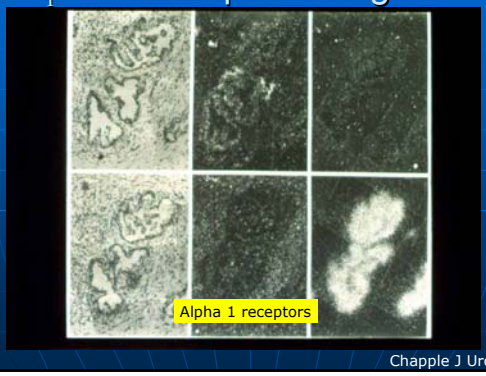
- Randomised, placebo-controlled trials have demonstrated the benefit of 5α-Reductase Inhibitors over placebo in men with clinically enlarged prostates above 30- 40cc secondary to BPH. (Level 1 Grade A)
- Randomised, placebo-controlled trials have demonstrated the benefit of 5α-Reductase Inhibitors over placebo in men. (Level 1 Grade B)
- Placebo controlled data for finasteride out to over 5 years and for dutasteride out to 2 years have confirmed the durability of the treatment response. (Level 1 Grade A)
- The efficacy and tolerability of both finasteride and dutasteride is identical. (Level 1 Grade B)
- The magnitude of benefit is greater than placebo but consistently smaller than seen with α_1-Adrenocepor Antagonists. (Level 1 Grade A)

Other Hormonal approaches to the Treatment of Benign Prostatic Hyperplasia

- **Recommendation:** Surgical castration may be effective for the treatment of BPH, but the invasiveness and risk of the procedure preclude its use.
- **Recommendation:** GnRH therapy has shown benefit in the treatment of BPH. However, cost, sexual dysfunction, decreased bone density and hot flushes preclude the use of these drugs in routine cases.
- **Recommendation:** Progestational agents have evidence of efficacy for the treatment of BPH. However, undesirable androgen withdrawal side effects (e.g. impotence, decrease of bone density) limit the widespread use of progestational agents
- **Recommendation:** Data strongly suggest that the side-effects of current androgen receptor antagonists (gynaecomastia, hepatotoxicity, diarrhoea) outweigh any potential benefit in the treatment of BPH.
- **Recommendation:** Randomised clinical trials with aromatase inhibitors have failed to show benefit. Therefore, aromatase inhibitor therapy is currently not a recommended treatment option.

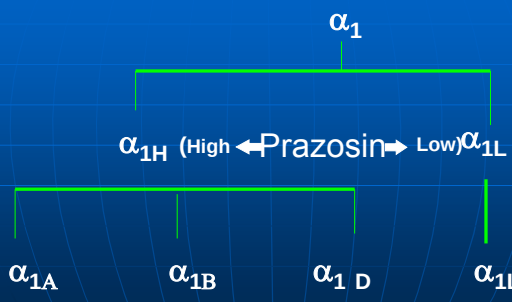
Level 2 Grade B

α_1-Adrenoceptor Antagonists

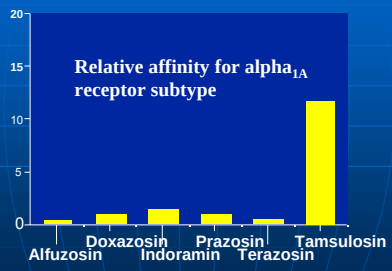


Chapple J Urol 1989

Alpha$_1$-Adrenoceptor subtypes



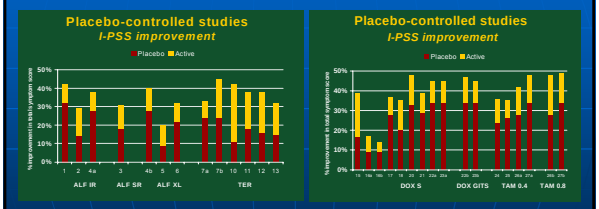
Alpha Adrenoceptor Antagonist Selectivity



adrenoreceptor antagonist ?

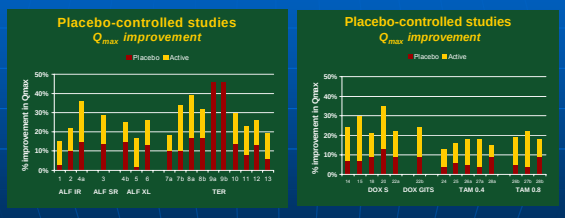
- Pharmacological 'uroselectivity?
- Prostate 'uroselectivity' ?
- Clinical 'uroselectivity'

α_1-Adrenoceptor Antagonist Treatment Outcome: IPSS



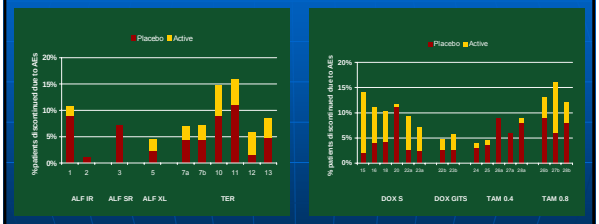
Djavan et al. Eur Urol 1999;36:1-13

α_1-Adrenoceptor Antagonist Treatment Outcome: Qmax



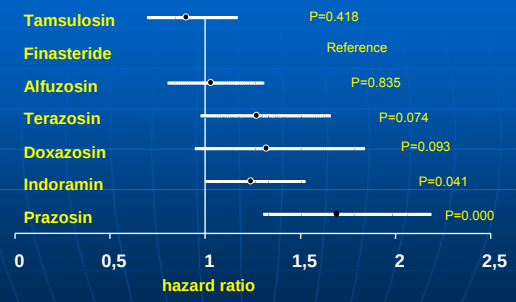
Djavan et al. Eur Urol 1999;36:1-13

α_1-Adrenoceptor Antagonist Treatment: drop outs due to side effects



Djavan et al. Eur Urol 1999;36:1-13

TRIUMPH
Switch to other therapy from *GPRD*



Logie JW, et al. Eur Urol 2001;39(Suppl 3):42-7

Recommendations

- **The efficacy of α_1 -Adrenoceptor Antagonists on symptoms has been demonstrated in placebo controlled studies out to 5 years.**
  (Level 1 Grade B)
- **The benefit of α_1-Adrenoceptor Antagonists is not related to prostate size.**
  (Level 1 Grade A)
- **The efficacy of all α_1-Adrenoceptor Antagonists is similar.** **(Level 1 Grade A)**
- **The tolerability of alfuzosin and tamsulosin is similar and better than the other agents.**
  (Level 1 Grade A)
- **Randomised, placebo-controlled trials have demonstrated the benefit of α_1-Adrenoceptor Antagonists over placebo and finasteride in men with LUTS.**
  (Level 1 Grade A)

Phytotherapy

- **A number of compounds which have been postulated to have various mechanisms of action.**
- **The nature of the 'active' chemicals and their precise mechanisms of action remain obscure.**
- **There are very few blinded controlled studies in the literature.**

PLANT DERIVED THERAPIES

- Bark of PYGEUM AFRICANUM
- POLLEN EXTRACT
- Leaves of TREMBLING POPLAR
- Roots of HYPOXIS HOOPERI
- Seeds of CUCURBITA PEPO
- Fruits of SERENOA REPENS
- Roots of ECHINACEA PURPURA …

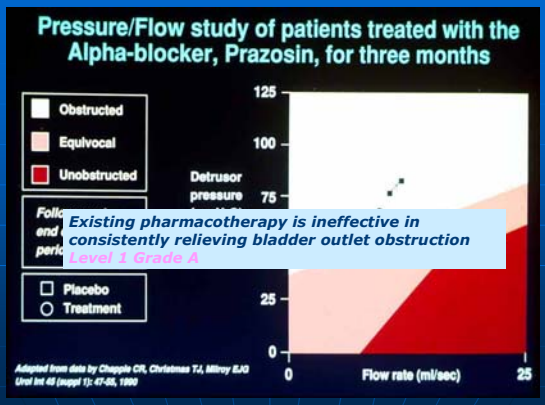
Recommendations

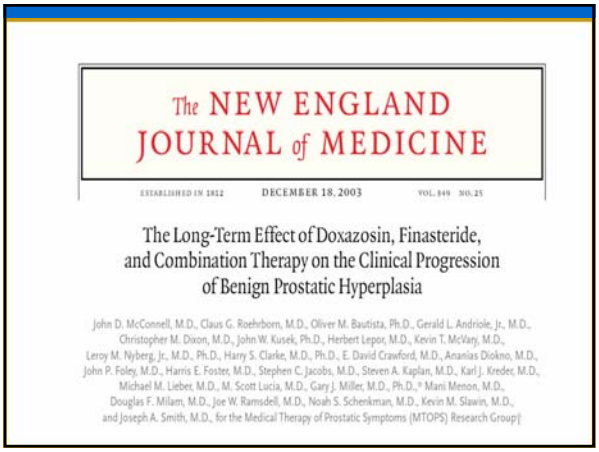
- There is a lack of adequate placebo controlled studies with phytotherapeutic agents.
- With these constraints in mind there is limited evidence to support their use as a class. **(Level 4 Grade D)**
- Permixon (serenoa repens) **(Level 2 Grade B)**
- Pygeum Africanum **(Level 3 Grade D)**
- American dwarf palm/ (fruits) **(Level 3 Grade C)**
- South African star grass (roots) (Hypoxis rooperi) **(Level 4 Grade D)**
- Pine, Spruce (Pinus, Picea) **(Level 4 Grade D)**
- Stinging nettle (roots) (Urtica dioica) **(Level 4 Grade D)**
- Rye (pollen) (Secale cereale) **(Level 4 Grade D)**
- Pumpkin (seeds) (Cucurbita pepoto) **(Level 4 Grade D)**

Head-to-head comparisons

Direct Comparative studies are strongly recommended Level 1 Grade A

Pressure/Flow study of patients treated with the Alpha-blocker, Prazosin, for three months





The NEW ENGLAND JOURNAL of MEDICINE

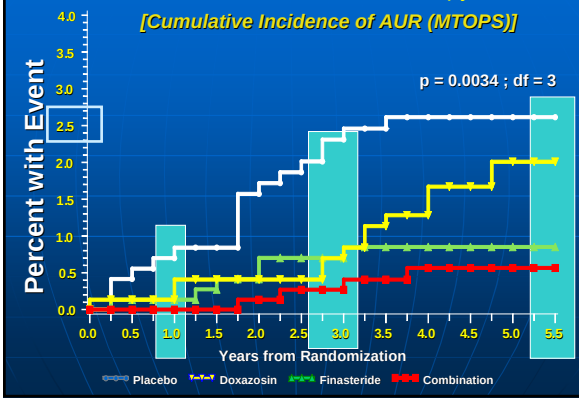
ESTABLISHED IN 1812 DECEMBER 18, 2003 VOL. 349 NO. 25

The Long-Term Effect of Doxazosin, Finasteride, and Combination Therapy on the Clinical Progression of Benign Prostatic Hyperplasia

John D. McConnell, M.D., Claus G. Roehrborn, M.D., Oliver M. Bautista, Ph.D., Gerald L. Andriole, Jr., M.D., Christopher M. Dixon, M.D., John W. Kusek, Ph.D., Herbert Lepor, M.D., Kevin T. McVary, M.D., Leroy M. Nyberg, Jr., M.D., Ph.D., Harry S. Clarke, M.D., Ph.D., E. David Crawford, M.D., Ananias Diokno, M.D., John P. Foley, M.D., Harris E. Foster, M.D., Stephen C. Jacobs, M.D., Steven A. Kaplan, M.D., Karl J. Kreder, M.D., Michael M. Lieber, M.D., M. Scott Lucia, M.D., Gary J. Miller, M.D., Ph.D.,* Mani Menon, M.D., Douglas F. Milam, M.D., Joe W. Ramsdell, M.D., Noah S. Schenkman, M.D., Kevin M. Slawin, M.D., and Joseph A. Smith, M.D., for the Medical Therapy of Prostatic Symptoms (MTOPS) Research Group†

The Value of Combination Therapy

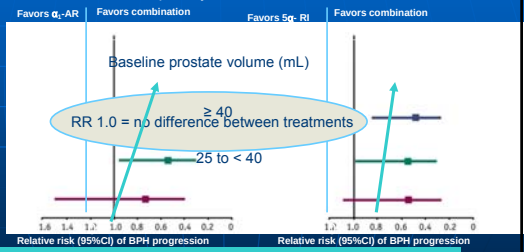
[Cumulative Incidence of AUR (MTOPS)]



α_1-AR antagonist + 5α-RI more effective in patients with enlarged prostate (1)

MTOPS trial

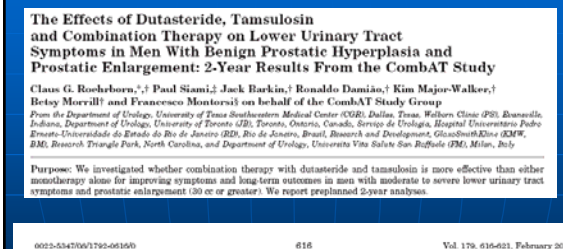
- N = 3047, mean follow-up 4.5 years



Combination therapy beneficial for patients with large prostate

Kaplan SA et al. J Urol 2006;175:217-20

CombAT



The Effects of Dutasteride, Tamsulosin and Combination Therapy on Lower Urinary Tract Symptoms in Men With Benign Prostatic Hyperplasia and Prostatic Enlargement: 2-Year Results From the CombAT Study

Claus G. Roehrborn,*,† Paul Siami,‡ Jack Barkin,† Ronaldo Damião,† Kim Major-Walker,† Betsy Morrill† and Francesco Montorsi§ on behalf of the CombAT Study Group

From the Department of Urology, University of Texas Southwestern Medical Center (CGR), Dallas, Texas, Welborn Clinic (PS), Evansville, Indiana, Department of Urology, University of Toronto (JB), Toronto, Ontario, Canada, Serviço de Urologia, Hospital Universitario Pedro Ernesto-Universidade do Estado do Rio de Janeiro (RD), Rio de Janeiro, Brazil, Research and Development, GlaxoSmithKline (KMW, BM), Research Triangle Park, North Carolina, and Department of Urology, Universita Vita Salute San Raffaele (FM), Milan, Italy

Purpose: We investigated whether combination therapy with dutasteride and tamsulosin is more effective than either monotherapy alone for improving symptoms and long-term outcomes in men with moderate to severe lower urinary tract symptoms and prostatic enlargement (30 cc or greater). We report preplanned 2-year analyses.

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Vol. 179, 616-621, February 2008 Printed in U.S.A. DOI:10.1016/j.juro.2007.09.084

CombAT and MTOPS: Design

	CombAT[1]	MTOPS[2]
Treatment groups	Dutasteride monotherapy Tamsulosin monotherapy Dutasteride and tamsulosin combination NA	Finasteride monotherapy Doxazosin monotherapy Finasteride and doxazosin combination Placebo
Sponsorship	GSK	independent
n	4844	3047
Location	International	US only
Entry criteria		
Age	≥50	≥50
PV (cc)	≥30	NA
PSA (ng/mL)	≥1.5 and ≤10	≤10
Symptom index	≥12 (IPSS)	8–30 (AUA-SI)
Primary endpoints		
2-year	Improvement in IPSS	NA
4-year	Reduction in risk of AUR/surgery	Composite endpoint of BPH clinical progression
Other differences	Patients with clinical progression may continue study but not switch treatment	Patients who reached endpoint were censored but could continue on alternative medication

1. Siami *et al.* Contemp Clin Trials 2007; 28: 770–9; 2. Bautista *et al.* Control Clin Trials 2003; 24: 224–43

CombAT and MTOPS: Baseline characteristics

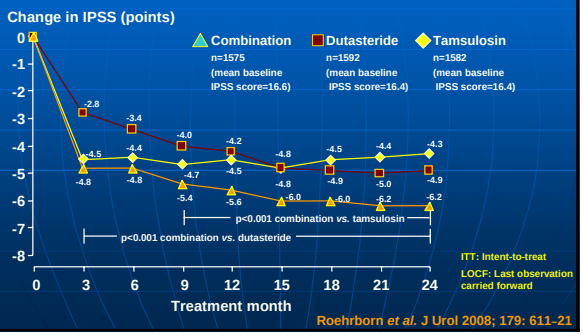
Baseline value	CombAT[1] (n=4844)	MTOPS[2] (n=3047)
Age (years)	66.1 ± 7.01	62.6 ± 7.3
Caucasian ethnicity, n (%)	4259 (88)	2509 (82)
IPSS/AUA-SI	16.4 ± 6.16	16.9 ± 5.9
PV (cc)		
Total	55.0 ± 23.58	36.3 ± 20.1
TZV	29.5 ± 21.97*	–
PSA (ng/mL)	4.0 ± 2.08	2.4 ± 2.1
Q_{max} (mL/s)	10.7 ± 3.62	10.5 ± 2.6
Post-void volume (mL)	67.7 ± 64.87	68.1 ± 82.9

Data presented are means (±SD), unless otherwise stated
*Assessed in a subset of 656 patients

[1]Roehrborn *et al.* J Urol 2008; 179: 611–21
[2]McConnell *et al.* New Engl J Med 2003; 349: 2387–98

Greater improvements in IPSS with combination *vs.* each monotherapy

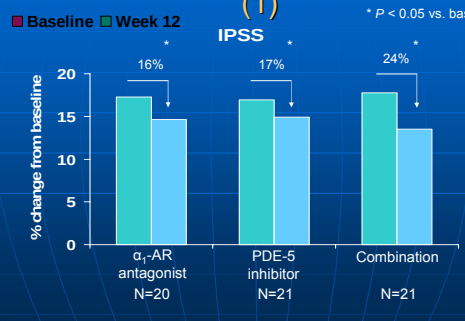
Adjusted mean change from baseline (ITT, LOCF)



ITT: Intent-to-treat
LOCF: Last observation carried forward

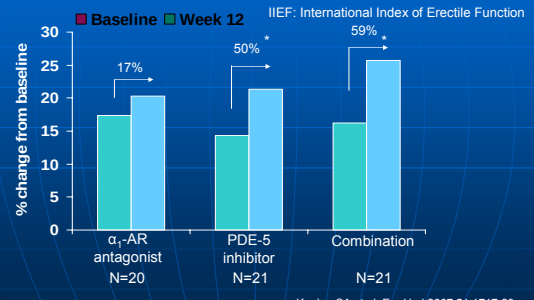
Roehrborn *et al.* J Urol 2008; 179: 611–21

α_1-AR antagonist + PDE-5 inhibitor beneficial in patients with LUTS + ED (1)



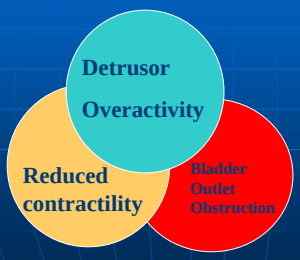
Kaplan SA et al. Eur Urol 2007;51:1717-23

α_1-AR antagonist + PDE-5 inhibitor beneficial in patients with LUTS + ED (2)



Kaplan SA et al. Eur Urol 2007;51:1717-23

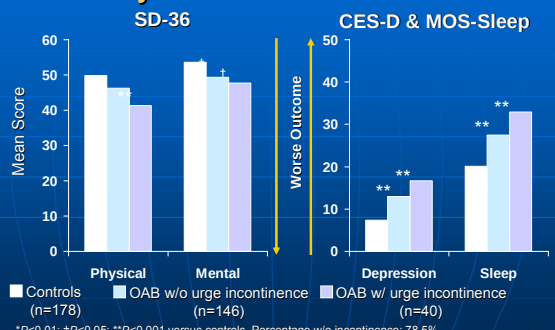
Patho-physiology of LUTS



Other important topics in LUTS

- Nocturia
- OAB

Quality of Life and OAB: Men



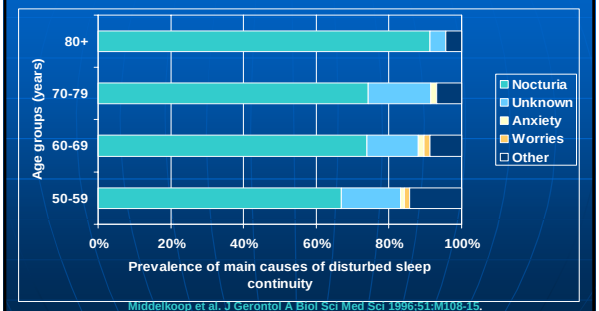
*P<0.01; †P<0.05; **P<0.001 versus controls. Percentage w/o incontinence: 78.5%.
Stewart et al. 2003 *World J Urol.* 20; 327-336.

Nocturia: a common problem in the elderly

- ICS definition of nocturia: "the complaint that the individual has to wake up at night to void; each void is preceded and followed by sleep"
- Working definition of nocturia in epidemiological surveys: "at least two nocturnal voiding episodes"
- Prevalence of nocturia (≥ 2 voids): 9%-17% in adult population
- Increasing prevalence in the higher age groups

Abrams et al. Urology 2003;61:37-49; Van Kerrebroeck et al. BJU Int 2002;90(Suppl 3):11-5; Van Dijk et al. BJU Int 2002;90:644-8; Jolleys et al. Br J Urol 1994;74:551-5; Schatzl et al. Urology 2000;56:71-5.

Nocturia as the main cause of sleep disturbance in men aged 50-93 years



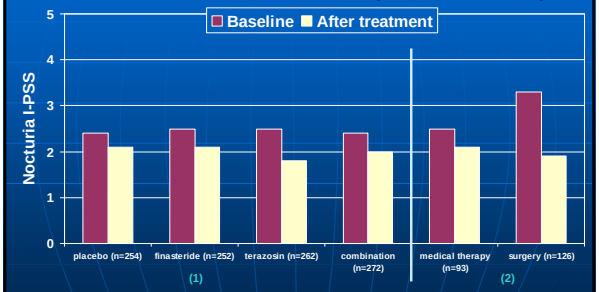
Middelkoop et al. J Gerontol A Biol Sci Med Sci 1996;51:M108-15.

Aetiology of nocturia

- **Polyuria**: overproduction of urine
- **Nocturnal polyuria**: nocturnal overproduction of urine
- **Reduced bladder capacity** due benign prostatic obstruction (with PVR)
- **Detrusor overactivity with OAB symptoms**
- **Combinations of these**

Abrams et al. Urology 2003;61:37-49; Van Kerrebroeck et al. BJU Int 2002;90(Suppl 3):11-5; Van Dijk et al. BJU Int 2002;90:644-8; Jolleys et al. Br J Urol 1994;74:551-5.

Impact of LUTS/BPO treatment on relief of nocturia (continued)



(1) Johnson et al. J Urol 2003;170:145-8; (2) Homma et al. J Urol 2002;167:172-6.

Recommendation

- OAB symptoms are more bothersome than voiding LUTS in men & may occur in the presence or absence of BOO.
- The treatment of OAB in the absence of BOO should be as suggested by the 3rd ICI
  Level 1 Grade A
- The management of OAB occurring in the presence of BOO is the subject of ongoing research
  - Antimuscarinic therapy as solo therapy can not be recommended for routine use Level 2 Grade B
  - Combination therapy of an antimuscarinic and alpha blocker may be efficacious
    Level 3 Grade C

Clinical Concerns: Antimuscarinic Therapy in Male OAB Patients

- Safety
  - Urinary retention, especially in patients with BOO
- Efficacy
  - What should be treated:
    - OAB without BOO
    - OAB with BOO
    - Combined with BPH treatments
  - How to evaluate the efficacy
    - Patient-reported treatment outcomes
    - Diary end points
      - Urgency
      - Frequency
      - Incontinence
    - IPSS
    - Quality-of-life (QOL) improvement

Well-Designed, Double-Blind, Placebo-Controlled Trials

Completed in 2006

TIMES

- **Efficacy/safety of tolterodine SR 4 mg in men with LUTS including OAB symptoms**
- **4-arm study (200 patients/arm)**
  - **Placebo**
  - **Tamsulosin**
  - **Tolterodine SR**
  - **Tolterodine SR + tamsulosin**

Completed in Sep 2007

ADAM

- **Efficacy/safety of tolterodine SR 4 mg in men *with persistent OAB symptoms on stable α-blocker therapy***
- **2-arm study (304 patients/arm)**
  - **Placebo + α-blocker (stable dose for ≥ 1 month)**
  - **Tolterodine SR + α-blocker (stable dose for ≥ 1 month)**

Studies collected OAB end points, IPSS and data on PSA, PVR and flow rate

PSA = prostate-specific antigen.

Kaplan SA et al. JAMA 2006;296:2319–2328.

Patient Selection Criteria

TIMES

- Male patients with bothersome OAB symptoms & other LUTS
- Patients met symptom entry criteria for OAB and BPH trials
  - Urinary frequency ≥ 8 per 24 hr
  - Urgency ≥ 3 per 24 hr, with/without UUI
  - PPBC rated as at least moderate
  - IPSS ≥ 12; IPSS QOL item ≥ 3

ADAM

- Male patients with bothersome OAB symptoms persisting during treatment with an α-blocker
- Patients met symptom entry criteria for OAB trials
  - Urinary frequency ≥ 8 per 24 hr
  - Urgency **≥ 1 per 24 hr**, with/without UUI
  - PPBC rated as at least moderate
  - IPSS measured but not utilized for enrollment

TIMES Summary: Efficacy

Statistically Significant Differences versus Placebo

	Tolterodine SR	*Tamsulosin*	*tolterodine SR + tamsulosin*
Patient Perception of Treatment Benefit			***P* < 0.01**
Micturition frequency/24 hours			*P* < 0.01
Nighttime micturition frequency			*P* < 0.05
UUI episodes/24 hours	*P* < 0.01		*P* < 0.01
Urgency episodes/24 hours			*P* < 0.05
Sum of urgency severity			*P* < 0.01
IPSS total		*P* < 0.01	*P* < 0.01
IPSS storage			*P* < 0.01
IPSS voiding		*P* < 0.01	
IPSS QoL			*P* < 0.01
PPBC			*P* < 0.05
OAB-q/Symptom Severity score			*P* < 0.01
OAB-q/HRQL total score			*P* < 0.05

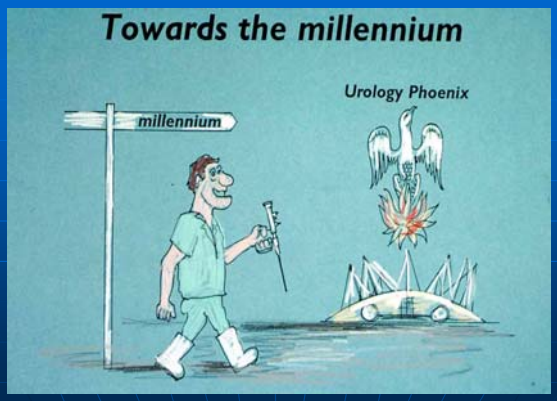
Kaplan SA. *et al. JAMA* 2006;296:2319–2328

Summary of ADAM Study

- Study did not meet the primary end point: improvement in PPBC
- Antimuscarinic significantly improved OAB symptoms/ storage LUTS, whether measured by bladder diary or by IPSS, in men with persistent OAB symptoms after previous α-blocker therapy
  - Significant improvements in micturition frequency, urgency, and severe urgency episodes, as measured by bladder diary
  - Improved IPSS storage score
  - No increase in the incidence of AUR or AEs suggestive of urinary retention compared with placebo
  - No decrease in Q_{max} versus placebo
  - Statistically significant increase in PVR (13.6 ml) was not accompanied by an increase in urinary AEs, reduction in Q_{max}, or increase in voiding subscale of IPSS

Recommendation

- OAB symptoms are more bothersome than voiding LUTS in men & may occur in the presence or absence of BOO.
- The treatment of OAB in the absence of BOO should be as suggested by the 3rd ICI
  Level 1 Grade A
- The management of OAB occurring in the presence of BOO is the subject of ongoing research
  - Antimuscarinic therapy as solo therapy can not be recommended for routine use Level 2 Grade B
  - Combination therapy of an antimuscarinic and alpha blocker may be efficacious
    Level 1 Grade B

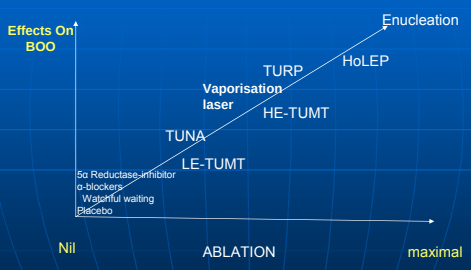


Minimally Invasive and Surgical therapies for BPH
Where is the evidence?

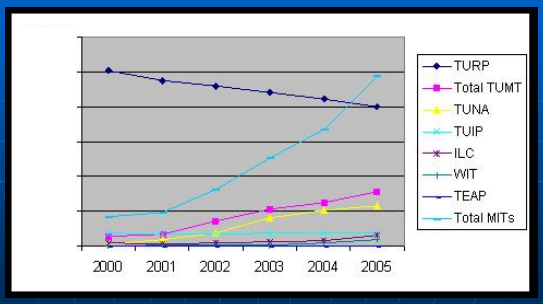
Data on efficacy and safety of the following BPH treatments were reviewed

TURP	(transurethral resection of the prostate)
TUVP	(transurethral vaporization of the prostate)
VLAP	(visual laser ablation of the prostate)
HoLEP	(holmium laser enucleation of the prostate)
HIFU	(high intensity focus ultrasonography)
TUNA	(transurethral needle ablation)
TUMT	(transurethral microwave thermotherapy)
ILCP	(interstitial laser coagulation of the prostate)

Spectrum of MIT for BPO and ablative qualities



Number of publications on minimal invasive treatments per year



In summary we can conclude that:

- The efficacy of TURP is greater than the efficacy of MIT. However: HOLEP is equal to TURP
- The morbidity of TURP is higher than the morbidity of MIT
- The durability of TURP is longer than the durability of MIT