UroSwords I (ΚΥΠ)
Μονοθεραπεία ή συνδυαστική φαρμακοθεραπεία;

Η μονοθεραπεία είναι επαρκής

Χαράλαμπος Κ. Μαμουλάκης

Λέκτορας Ουρολογίας

Ουρολογική Κλινική

Πανεπιστημιακό Γενικό Νοσοκομείο Ηρακλείου

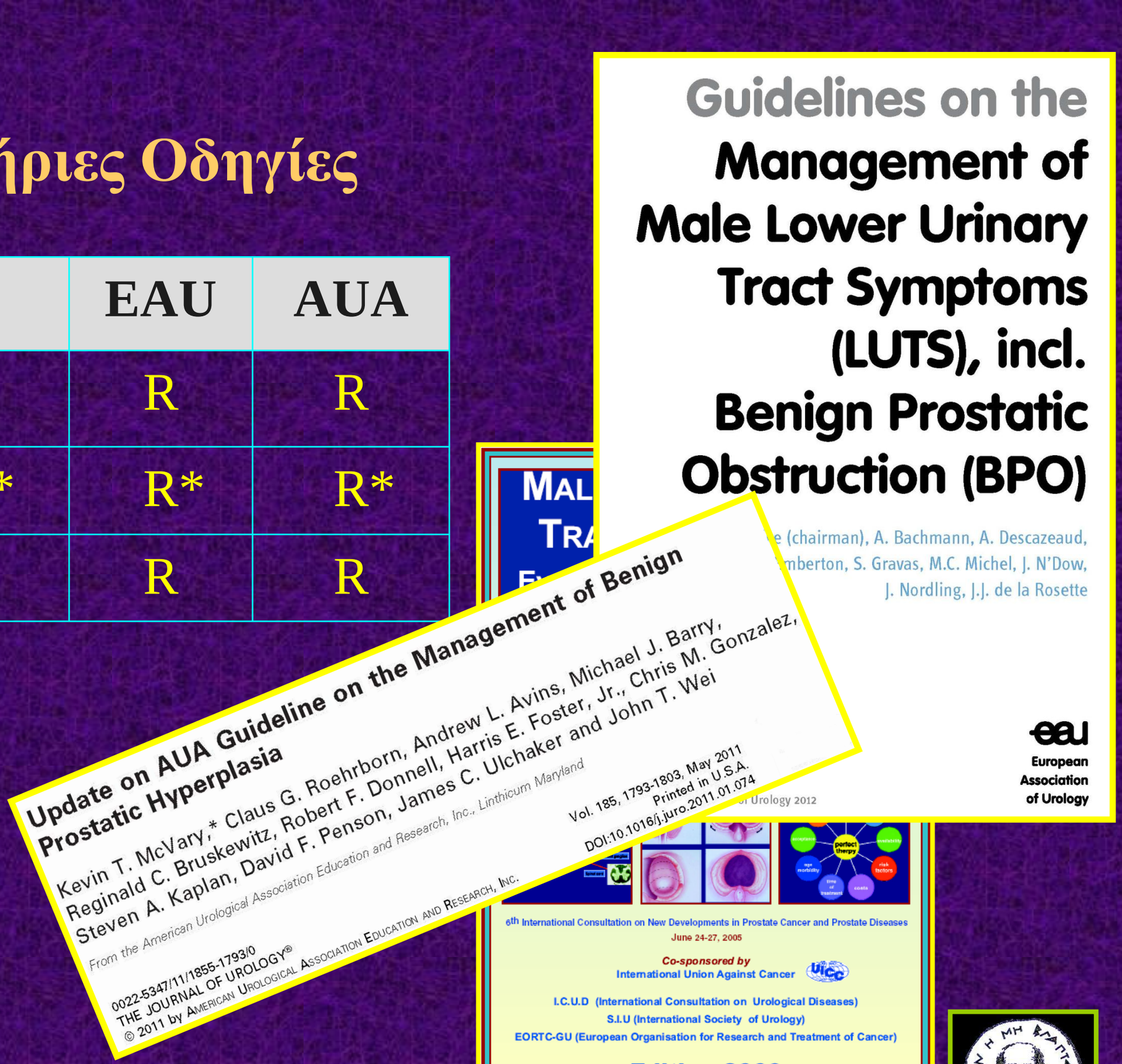
Πανεπιστήμιο Κρήτης, Τμήμα Ιατρικής

Κατευθυντήριες Οδηγίες

Medication	IC	EAU	AUA
α-blockers	R	R	R
5ARIs	R*	R*	R*
Combination	R	R	R

R: Recommended

***: Enlarged prostates**



Κατευθυντήριες Γραμμές

4.1.6 ***Recommendation***

	LE	GR
α_1-blockers should be offered to men with moderate-to-severe lower urinary tract symptoms	1a	A

4.2.6 ***Recommendations***

	LE	GR
5α-reductase inhibitors should be offered to men who have moderate-to-severe lower urinary tract symptoms and enlarged prostates (> 40 mL) or elevated prostate specific antigen concentrations (> 1.4 – 1.6 µg/L). 5α-reductase inhibitors can prevent disease progression with regard to acute urinary retention and need for surgery.	1b	A

4.6.1.6 Recommendations

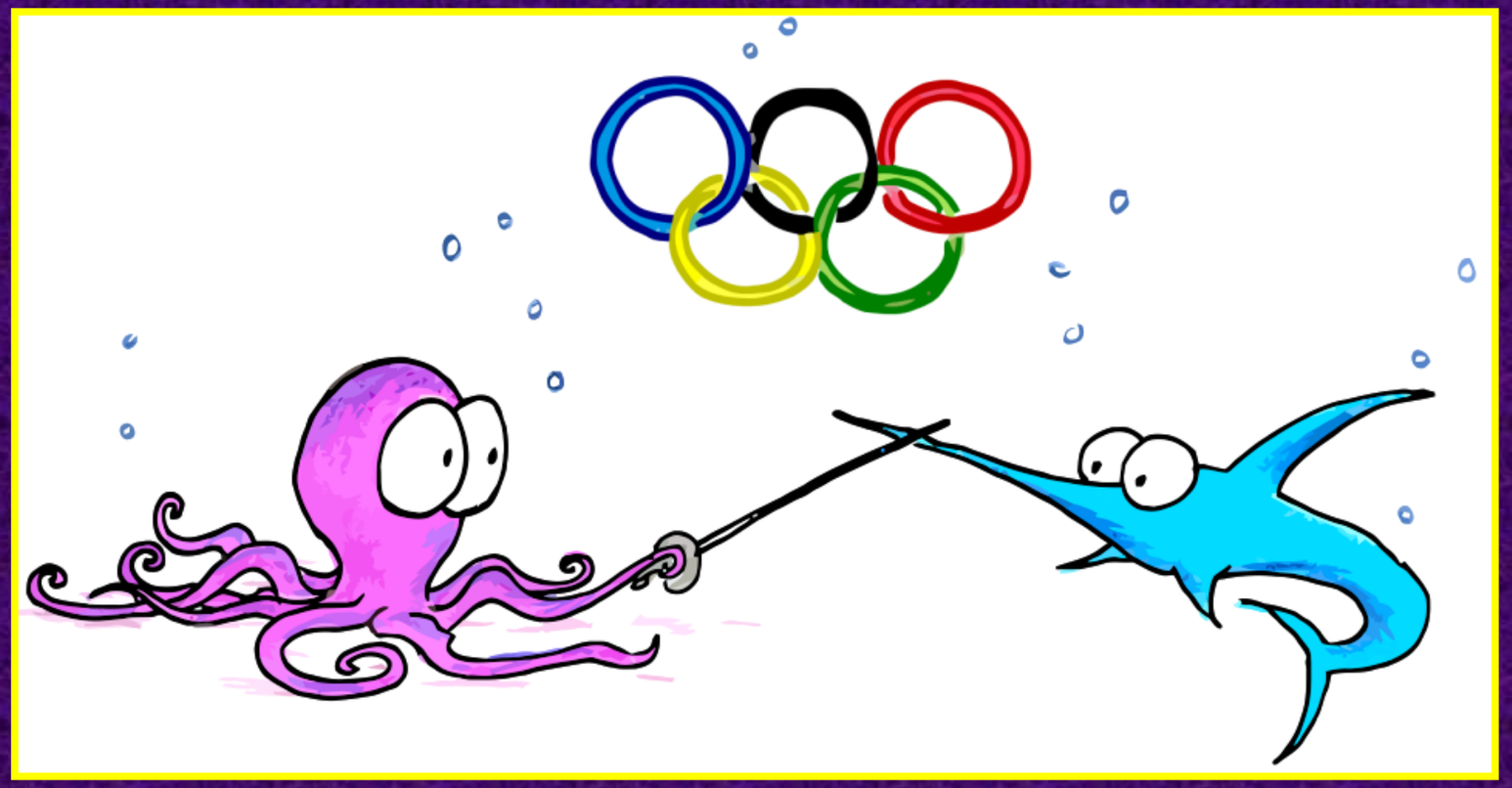
	LE	GR
Combination treatment with α_1-blocker together with 5α-reductase inhibitor should be offered to men with moderate-to-severe lower urinary tract symptoms, enlarged prostates (> 40 mL), and reduced Q_{max} (men likely to develop disease progression). Combination treatment is not recommended for short-term therapy (< 1 year).	1b	A

Guidelines on the Management of Male Lower Urinary Tract Symptoms (LUTS), incl. Benign Prostatic Obstruction (BPO)

M. Oelke (chairman), A. Bachmann, A. Descazeaud,
M. Emberton, S. Gravas, M.C. Michel, J. N'Dow,
J. Nordling, J.J. de la Rosette

European Association of Urology

ΓΥΡΟΣ 1



Αποτελεσματικότητα (IPSS – Qmax)

Table 3: Randomised, placebo-controlled trials with α_1-blockers in men with LUTS (drugs in chronological order; selection of trials)

Trials	Duration (weeks)	Treatment (daily dose)	Patients (n)	Change in symptoms (%)	Change in Q_{max} (mL/s)	PVR change (%)	LE
Jardin et al. (1991) [14]	24	Placebo Alfuzosin 3 x 2.5 mg	267 251	-32 [a] -42 [a,b]	+1.3 [a] +1.4 [a]	-9 -39 [a,b]	1b
Buzelin et al. (1997) [15]	12	Placebo Alfuzson 2 x 5 mg	196 194	-18 -31 [a,b]	+1.1 +2.4 [a,b]	0 -17 [a,b]	1b
van Kerrebroeck et al. (2000) [16]	12	Placebo Alfuzosin 3 x 2.5 mg Alfuzosin 1 x 10 mg	154 150 143	-27.7 -38.1 [a,b] -39.9 [a,b]	+1.4 +3.2 [a,b] +2.3 [a,b]	- - -	1b
MacDonald and Wilt (2005) [17]	4-26	Placebo Alfuzosin: all formulations	1039 1928	-0.9 [b] (Boyarski) [†] -1.8 [b] (IPSS) [†]	+1.2 [b]	-	1a
Kirby et al. (2001) [18]	13	Placebo Doxazosin 1 x 1-8 mg IR Doxazosin 1 x 4-8 mg GITS	155 640 651	-34 [a] -45 [a,b] -45 [a,b]	+1.1 [a] +2.6 [a,b] +2.8 [a,b]	- - -	1b
McConnell et al. (2003) [8]	234	Placebo Doxazosin 1 x 4-8 mg	737 756	-29 -39 [b]	+1.4 +2.5 [a,b]	- -	1b
Chapple et al. (1996) [19]	12	Placebo Tamsulosin MR 1 x 0.4 mg	185 364	-25.5 -35.1 [a,b]	+0.6 +1.6 [a,b]	-13.4 -22.4 [a]	1b
Lepor (1998) [20]	13	Placebo Tamsulosin MR 1 x 0.4 mg Tamsulosin MR 1 x 0.8 mg	253 254 247	-28.1 -41.9 [a,b] -48.2 [a,b]	+0.5 +1.8 [a,b] +1.8 [a,b]	- - -	1b
Chapple et al. (2005) [21]	12	Placebo Tamsulosin MR 1 x 0.4 mg Tamsulosin OCAS 1 x 0.4 mg Tamsulosin OCAS 1 x 0.8 mg	350 700 354 707	-32 -43.2 [b] -41.7 [b] -42.4 [b]	- - - -	- - - -	1b
Wilt et al. (2002) [22]	4-26	Placebo Tamsulosin 1 x 0.4-0.8 mg	4122	-12 [b] (-1.1 Boyarski [†]) -11 [b] (-2.1 IPSS [†])	+1.1 [b]	-	1a
Brawer et al. (1993) [23]	24	Placebo Terazosin 1 x 1-10 mg	72 69	-11 -42 [a,b]	+1.2 +2.6 [a,b]	- -	1b
Roehrborn et al. (1996) [24]	52	Placebo Terazosin 1 x 1-10 mg	973 976	-18.4 -37.8 [a,b]	+0.8 [a] +2.2 [a,b]	- -	1b
Wilt et al. (2000) [25]	4-52	Placebo Terazosin	5151	-37 [b] (-2.9 Boyarski [†]) -38 [b] (IPSS [†])	+1.7 [b]	-	1a

Q_{max} = maximum urinary flow rate (free uroflowmetry); PVR = post-void residual urine; a = significant compared to baseline (indexed wherever evaluated); b = significant compared to placebo; † = absolute value.

- Ταχεία έναρξη δράσης (ώρες – ημέρες, max: λίγες εβδομάδες)
- Ήπια-Μέτρια-Σοβαρά LUTS
- ↓ IPSS (35 - 40%)
- ↑ Qmax (20 - 25%)
- Δράση ≠ Vp για περίοδο ≤ 1 έτος, καλύτερα μακροχρόνια αποτελέσματα σε ασθενείς με Vp < 40 ml
- Δράση τουλάχιστον επί 4 έτη

EAU Guidelines, 2012

Table 5: Randomised trials with 5α-reductase inhibitors in men with LUTS and benign prostatic enlargement due to BPH

Trials	Duration (weeks)	Treatment (daily dose)	Patients (n)	Change in symptoms (% IPSS)	Change in Q_{max} (mL/s)	Change in prostate volume (%)	LE
Lepor et al. (1996) [4]	52	Placebo	305	-16.5 [a]	+1.4	+1.3	1b
		Finasteride 1 x 5 mg	310	-19.8 [a]	+1.6	-16.9 [b]	
Kirby et al. (2003) [5]	52	Placebo	253	-33.1	+1.4	-	1b
		Finasteride 1 x 5 mg	239	-38.6	+1.8	-	
Andersen et al. (1995) [6]	104	Placebo	346	+1.5	-0.3	+11.5 [a]	1b
		Finasteride 1 x 5 mg	348	-14.9 [a,b]	+1.5 [a,b]	-19.2 [a,b]	
Nickel et al. (1996) [7]	104	Placebo	226	-4.2	+0.3	+8.4 [a]	1b
		Finasteride 1 x 5 mg	246	-13.3 [a,b]	+1.4 [a,b]	-21	
McConnell et al. (1998) [8]	208	Placebo	1503	-8.7	+0.2	+14 [a]	1b
		Finasteride 1 x 5 mg	1513	-22 [a,b]	+1.9 [a,b]	-18 [a,b]	
Marberger et al. (1998) [9]	104	Placebo	1452	-9.8 [†]	0.8	+9	1b
		Finasteride 1 x 5 mg	1450	-21.4 [†b]	+1.4 [b]	-15 [b]	
McConnell et al. (2003) [10]	234	Placebo	737	-23.8	+1.4 [a]	+24 [a]	1b
		Finasteride 1 x 5 mg	768	-28.4 [a,b]	+2.2 [a,b]	-19 [a,b]	
Roehrborn et al. (2002) [11]	104	Placebo	2158	-13.5 [a]	+0.6	+1.5 [a]	1b
		Dutasteride 1 x 0.5 mg	2167	-26.5 [a,b]	+2.2 [a,b]	-25.7 [a,b]	
Roehrborn et al. (2008) [12]	104	Tamsulosin 1 x 0.4 mg	1611	-27.4 [a]	+0.9	0	1b
		Dutasteride 1 x 0.5 mg	1623	-30.5 [a]	+1.9	-28 [b]	
Roehrborn et al. (2010) [13]	208	Tamsulosin 1 x 0.4 mg	1611	-23.2 [a]	+0.7	+4.6	1b
		Dutasteride 1 x 0.5 mg	1623	-32.3 [a]	+2.0	-28 [b]	

Q_{max} = maximum urinary flow rate (free uroflowmetry); IPSS = International Prostate Symptom Score; † Boyarski Score; a = significant compared to baseline (indexed wherever evaluated); b = significant compared to placebo/ active control.

- Βραδεία έναρξη δράσης (6-12 μήνες)
- Στα 2-4 έτη:
- ↓ IPSS (15 - 30%)
- ↑ Qmax (1,5 – 2,0 ml/sec)
- ↓ Vp (18 - 20%)
- Δράση f (+) base Vp (PSA): φιναστερίδη > 40 ml ντουταστερίδη >30-40 ml

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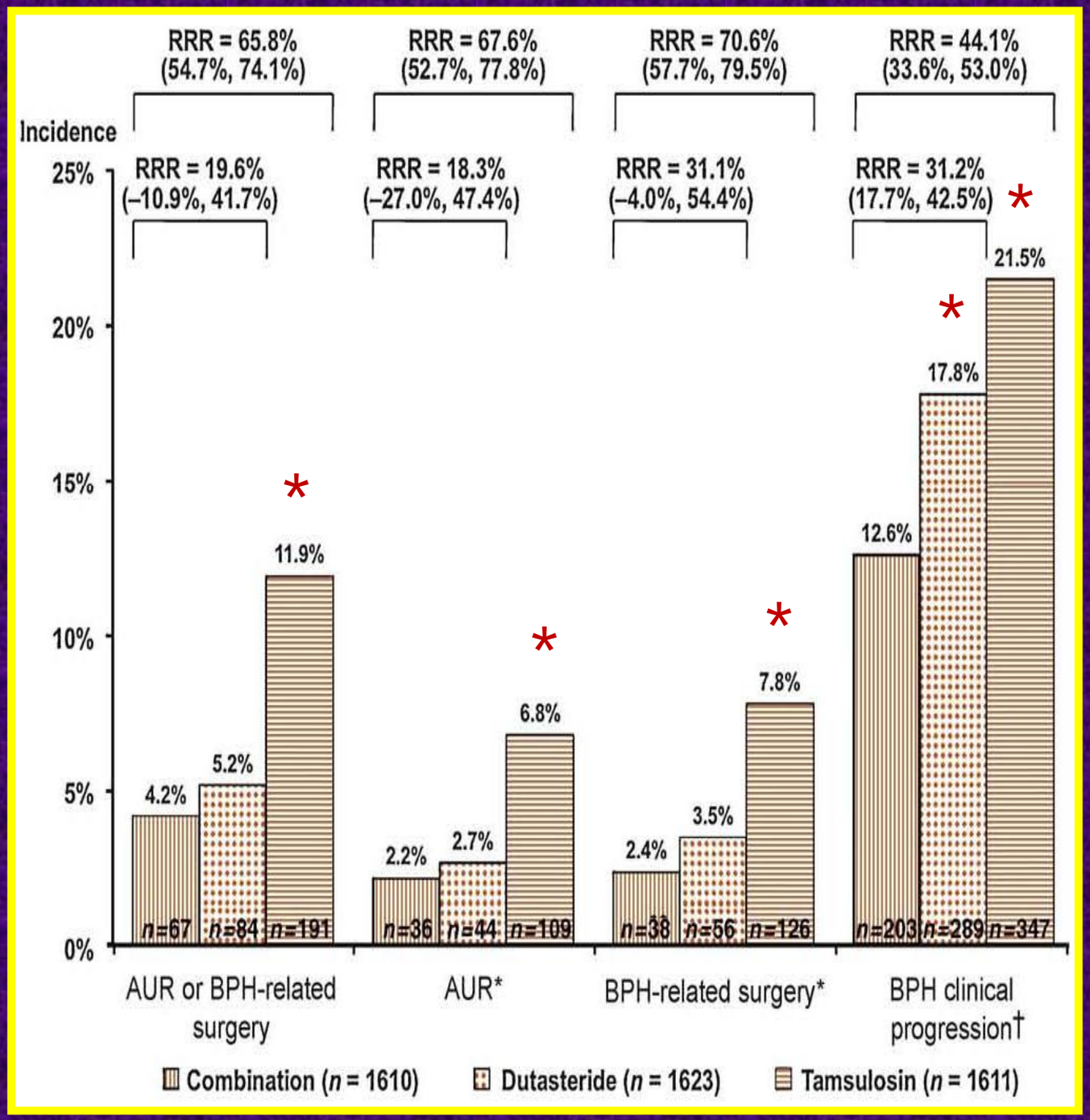
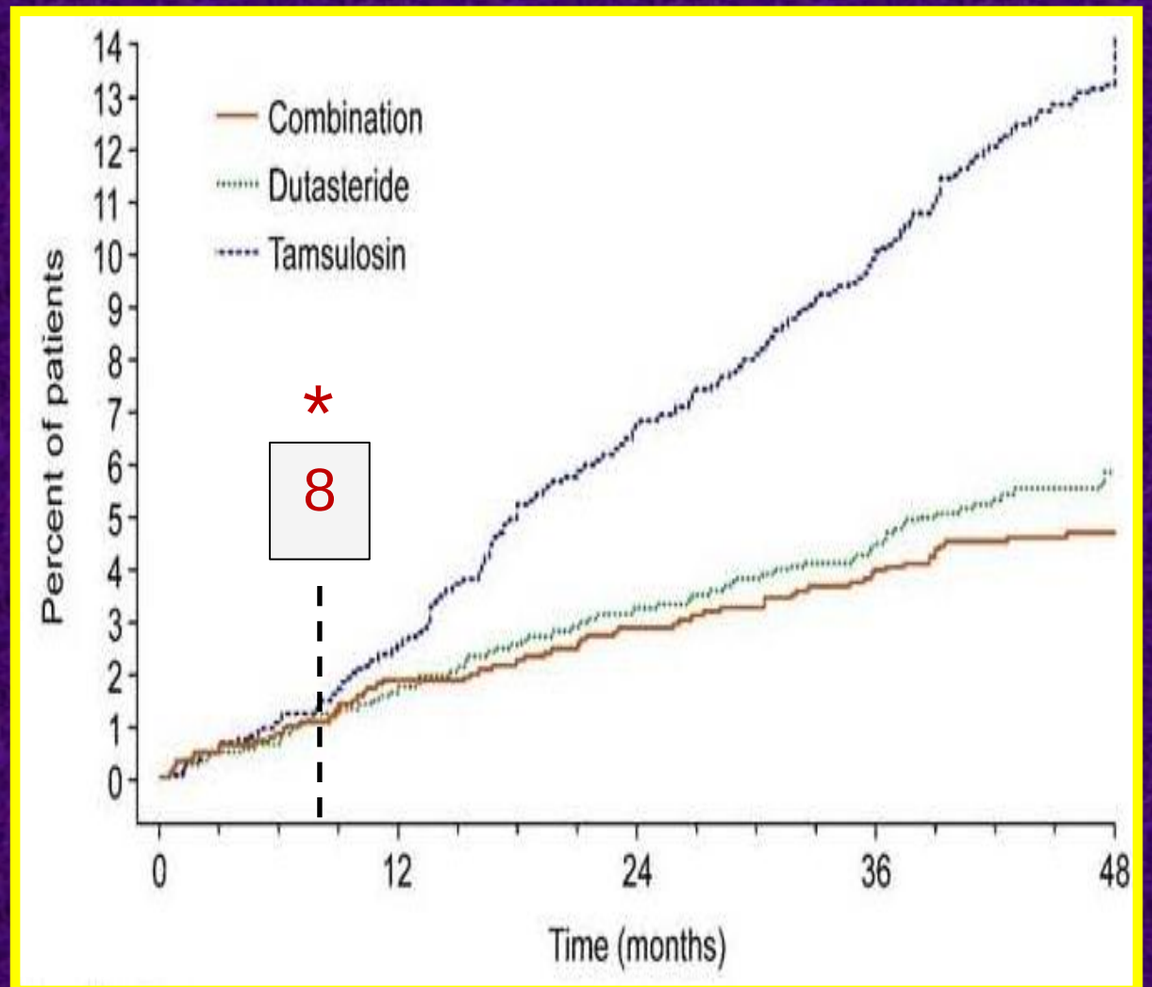
ΓΥΡΟΣ 2

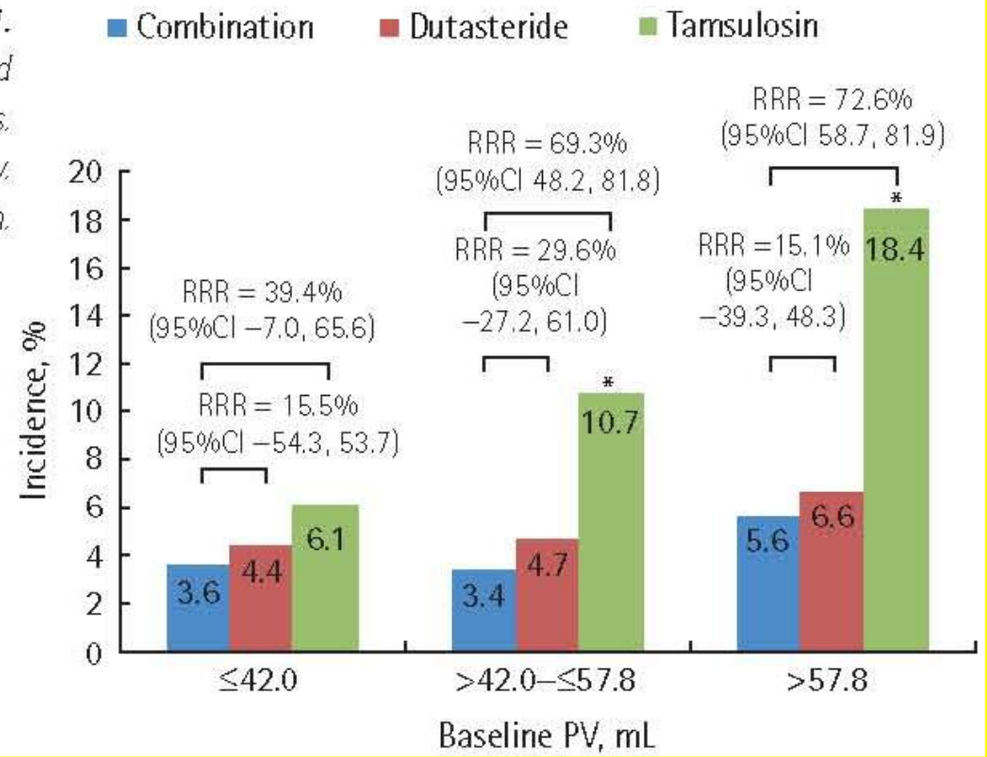
Πρόληψη προόδου





Roehrborn, et al. Eur Urol 2010; 57:123-31

FIG. 1.
*Incidence of AUR or BPH-related surgery by baseline PV tertiles. *P < 0.001 vs combined therapy. RRR, RR reduction.*



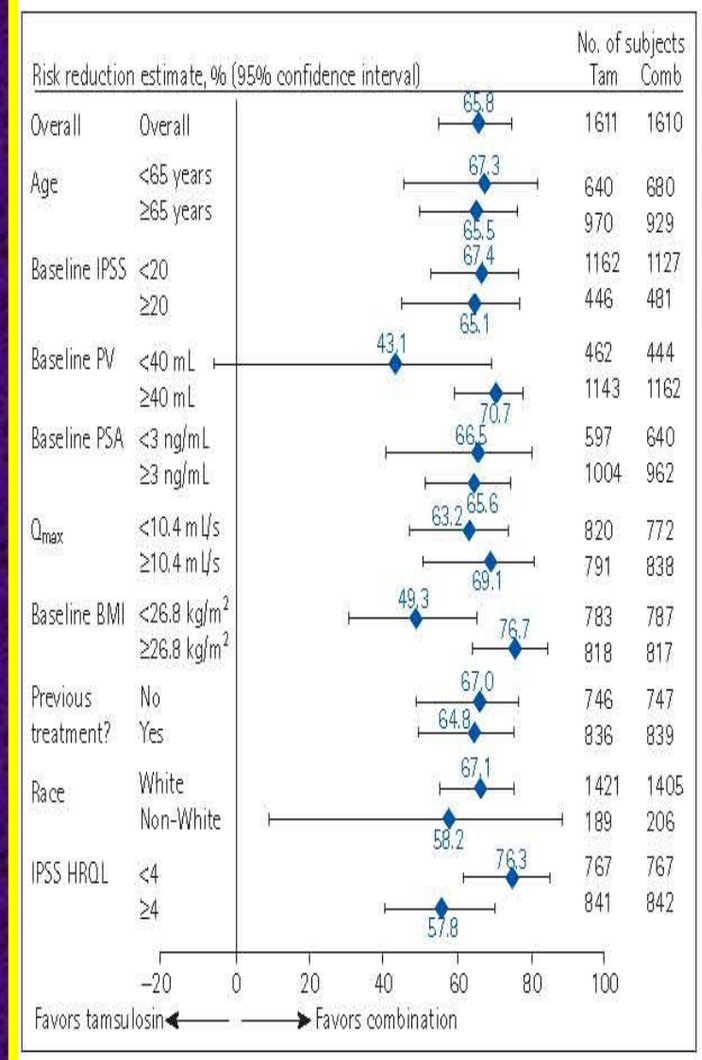


FIG. 3.
RR reduction in time to AUR or BPH-related surgery for combined therapy vs tamsulosin monotherapy by baseline subgroup.

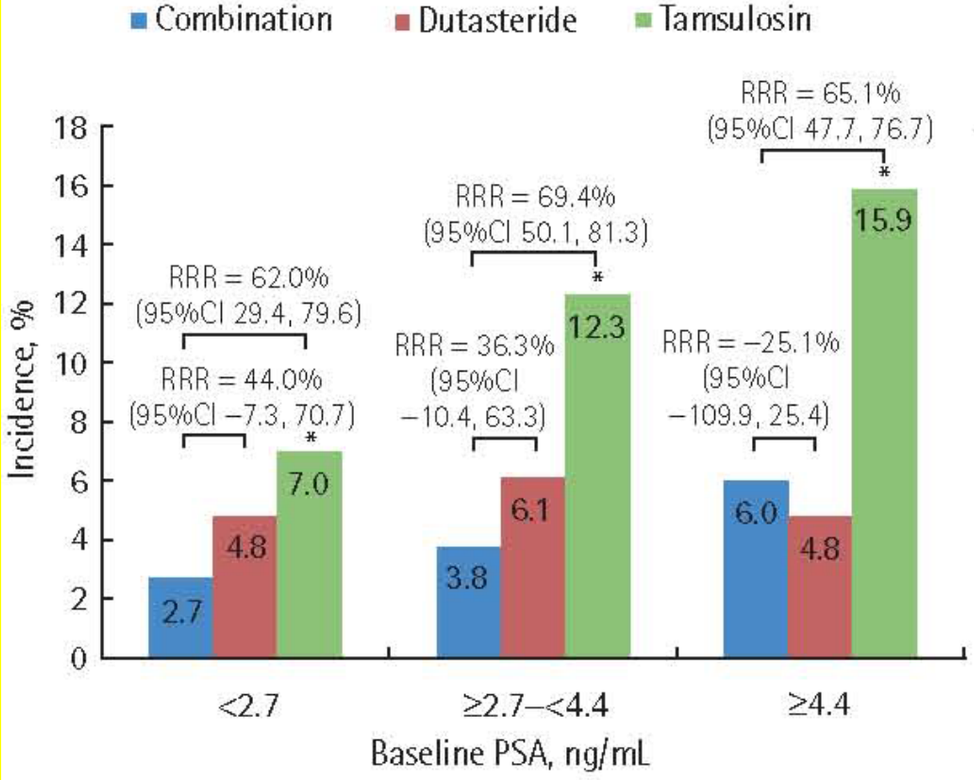


FIG. 2.
*Incidence of AUR or BPH-related surgery by baseline PSA level tertiles.*P ≤ 0.001 vs combined therapy. RRR, RR reduction.*

Roehrborn, et al. BJU Int 2011; 107:946-54

TABLE 3 RR reduction of time to BPH clinical progression after 4 years of treatment for combined therapy vs dutasteride and combined therapy vs tamsulosin, by baseline characteristic

	Incidence at 4 years, % (95% CI)			RR reduction, % (95% CI)	
Baseline variable	Combined therapy (dutasteride/tamsulosin)	Dutasteride	Tamsulosin	Combined therapy vs dutasteride	Combined therapy vs tamsulosin
Age,years					
<65	11.2 (8.8, 13.5)	16.3 (13.6, 19.1)	21.7 (18.5, 24.9)	32.0 (9.0, 49.1)	50.6 (34.7, 62.7)
≥65	13.7 (11.5, 15.9)	18.9 (16.4, 21.4)	21.4 (18.9, 24.0)	31.0 (13.3, 45.1)	38.9 (23.8, 51.0)
IPSS					
<20	15.0 (12.9, 17.1)	21.2 (18.8, 23.5)	23.2 (20.8, 25.7)	32.2 (17.6, 44.3)	38.4 (25.3, 49.2)
≥20	7.1 (4.8, 9.4)	9.5 (6.8, 12.1)	17.3 (13.8, 20.8)	25.2 (–17.0, 52.2)	60.6 (41.0, 73.7)
PV, mL					
<40	11.5 (8.5, 14.5)	18.3 (14.8, 21.7)	16.7 (13.3, 20.1)	39.3 (14.2, 57.0)	31.3 (2.2, 51.8)
≥40	13.1 (11.1, 15.0)	17.6 (15.4, 19.8)	23.6 (21.2, 26.1)	27.8 (10.8, 41.5)	47.8 (36.3, 57.2)
PSA level, ng/mL					
<3	11.1 (8.7, 13.5)	19.1 (16.1, 22.1)	19.6 (16.4, 22.8)	44.7 (26.0, 58.6)	43.8 (24.5, 58.1)
≥3	13.7 (11.5, 15.9)	17.0 (14.6, 19.4)	22.9 (20.3, 25.5)	20.8 (0.3, 37.0)	43.8 (30.3, 54.6)
Q_{max}, mL/s					
<10.4	13.2 (10.8, 15.6)	17.7 (15.1, 20.3)	21.5 (18.7, 24.3)	28.7 (8.2, 44.7)	39.7 (23.1, 52.8)
≥10.4	12.1 (9.8, 14.3)	18.0 (15.3, 20.6)	21.6 (18.7, 24.5)	33.4 (14.1, 48.4)	47.6 (32.9, 59.0)
BMI, kg/m^2					
<26.8	13.3 (11.0, 15.7)	16.1 (13.6, 18.6)	20.7 (17.9, 23.5)	18.6 (–5.2, 36.9)	36.9 (19.3, 50.6)
≥26.8	12.0 (9.8, 14.2)	19.6 (16.8, 22.3)	22.2 (19.4, 25.1)	40.9 (23.9, 54.1)	49.1 (35.0, 60.2)
Previous treatment?					
No	11.9 (9.6, 14.3)	16.9 (14.2, 19.6)	19.9 (17.1, 22.8)	30.3 (8.6, 46.8)	40.8 (23.1, 54.5)
Yes	13.0 (10.8, 15.3)	18.5 (15.9, 21.2)	23.1 (20.3, 26.0)	32.7 (14.0, 47.3)	47.2 (33.2, 58.2)
Race					
White	12.1 (10.4, 13.8)	17.7 (15.7, 19.7)	20.4 (18.3, 22.5)	33.1 (18.8, 44.9)	42.6 (30.7, 52.5)
Non-White	16.4 (11.1, 21.7)	18.4 (12.9, 23.9)	29.6 (23.4, 35.8)	19.4 (–30.8, 50.3)	49.3 (21.9, 67.1)
IPSS HRQL					
<4	15.3 (12.7, 17.8)	21.7 (18.8, 24.6)	22.9 (20.0, 25.9)	32.2 (14.0, 46.5)	35.1 (18.0, 48.7)
≥4	10.2 (8.2, 12.3)	14.4 (12.0, 16.7)	20.3 (17.6, 23.0)	30.7 (8.7, 47.3)	52.6 (38.5, 63.4)

TABLE 4 RR reduction of time to symptom deterioration after 4 years of treatment for combined therapy vs dutasteride and combined therapy vs tamsulosin, by baseline characteristic

	Incidence at 4 years, % (95% CI)			RR reduction, % (95% CI)	
Baseline variable	Combined therapy (dutasteride/tamsulosin)	Dutasteride	Tamsulosin	Combined therapy vs dutasteride	Combined therapy vs tamsulosin
Age, years					
<65	7.9 (5.9, 10.0)	12.0 (9.6, 14.4)	14.7 (11.9, 17.4)	34.0 (7.0, 53.2)	47.4 (26.5, 62.4)
≥65	9.1 (7.3, 11.0)	13.9 (11.6, 16.1)	13.9 (11.7, 16.1)	36.2 (16.2, 51.5)	36.3 (16.4, 51.4)
IPSS					
<20	11.3 (9.4, 13.1)	16.9 (14.8, 19.1)	17.6 (15.4, 19.7)	36.2 (20.2, 48.9)	38.5 (23.2, 50.7)
≥20	2.5 (1.1, 3.9)	3.4 (1.8, 5.1)	5.6 (3.5, 7.7)	25.5 (–57.5, 64.8)	55.6 (11.6, 77.7)
PV, mL					
<40	9.0 (6.3, 11.7)	14.7 (11.5, 17.9)	11.5 (8.6, 14.4)	40.0 (11.5, 59.3)	20.3 (–20.2, 47.1)
≥40	8.5 (6.9, 10.1)	12.4 (10.5, 14.3)	15.4 (13.3, 17.5)	32.5 (12.7, 47.8)	47.3 (32.5, 58.8)
PSA level, ng/mL					
<3	8.8 (6.6, 10.9)	15.2 (12.4, 17.9)	13.1 (10.4, 15.8)	44.2 (22.7, 59.8)	32.1 (4.3, 51.8)
≥3	8.6 (6.9, 10.4)	11.8 (9.7, 13.8)	15.0 (12.8, 17.3)	27.6 (3.9, 45.5)	45.8 (29.1, 58.5)
Q_{max}, mL/s					
<10.4	9.3 (7.3, 11.4)	12.9 (10.7, 15.2)	13.5 (11.2, 15.9)	30.6 (6.4, 48.5)	31.9 (8.4, 49.4)
≥10.4	8.0 (6.2, 9.8)	13.2 (10.8, 15.5)	14.9 (12.4, 17.4)	39.6 (17.9, 55.5)	48.8 (30.9, 62.1)
BMI, kg/m^2					
<26.8	8.8 (6.8, 10.7)	11.6 (9.4, 13.8)	14.3 (11.9, 16.8)	25.3 (–1.7, 45.2)	39.8 (18.8, 55.4)
≥26.8	8.6 (6.6, 10.5)	14.5 (12.1, 17.0)	14.3 (11.9, 16.7)	42.5 (22.7, 57.3)	42.4 (22.5, 57.1)
Previous treatment?					
No	8.6 (6.6, 10.6)	12.4 (10.1, 14.8)	12.6 (10.2, 15.0)	31.6 (6.0, 50.2)	32.0 (6.5, 50.5)
Yes	8.6 (6.7, 10.5)	13.5 (11.2, 15.8)	16.0 (13.5, 18.5)	38.2 (17.0, 54.0)	48.8 (31.8, 61.6)
Race					
White	8.5 (7.1, 10.0)	12.9 (11.2, 14.6)	13.1 (11.3, 14.9)	34.9 (18.2, 48.2)	36.5 (20.2, 49.6)
Non-White	9.5 (5.3, 13.7)	14.2 (9.2, 19.2)	21.8 (16.2, 27.5)	37.5 (–13.4, 65.6)	59.4 (29.8, 76.5)
IPSS HRQL					
<4	12.1 (9.8, 14.4)	16.7 (14.1, 19.4)	16.2 (13.6, 18.8)	29.3 (7.6, 45.9)	26.0 (3.2, 43.5)
≥4	5.5 (3.9, 7.0)	9.9 (7.9, 11.9)	12.5 (10.2, 14.7)	45.4 (21.9, 61.9)	58.1 (40.7, 70.4)

Roehrborn, et al. BJU Int 2011; 107:946-54

ΓΥΡΟΣ 3

Ασφάλεια - ανεπιθύμητες ενέργειες - παρακολούθηση PSA

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 I
Leroy M
John P.
D
and

Table 4. The Ten Most Frequent Adverse Events Reported among the Groups.*

Variable	Placebo	Doxazosin	Finasteride	Combination Therapy
Total no. of person-yr	3489	3652	3600	3832
	rate/100 person-yr of follow-up			
Adverse event				
Erectile dysfunction	3.32	3.56	4.53†	5.11†
Dizziness	2.29	4.41†	2.33	5.35†
Postural hypotension	2.29	4.03†	2.56	4.33†
Asthenia	2.06	4.08†	1.56	4.20†
Decreased libido	1.40	1.56	2.36†	2.51†
Abnormal ejaculation	0.83	1.10	1.78†	3.05†
Peripheral edema	0.66	0.88	0.72	1.25†
Dyspnea	0.57	0.93	0.56	1.20†
Allergic reaction	0.46	0.85†	0.58	0.73
Somnolence	0.37	0.82†	0.39	0.78†

* The numbers shown are the rates per 100 person-years of follow-up (incidence density) as of September 30, 2002.
† P<0.05 for the comparison with the placebo group.

The Effects of Combination Therapy with Dutasteride and Tamsulosin on Clinical Outcomes in Men with Symptomatic Benign Prostatic Hyperplasia: 4-Year Results from the CombAT Study

Claus G. Roehrborn[a,], Paul Siami[b], Jack Barkin[c], Ronaldo Damião[d], Kim Major-Walker[e], Indrani Nandy[e], Betsy B. Morrill[e], R. Paul Gagnier[e], Francesco Montorsi[f]*
on behalf of the CombAT Study Group

Table 4 – Adverse events

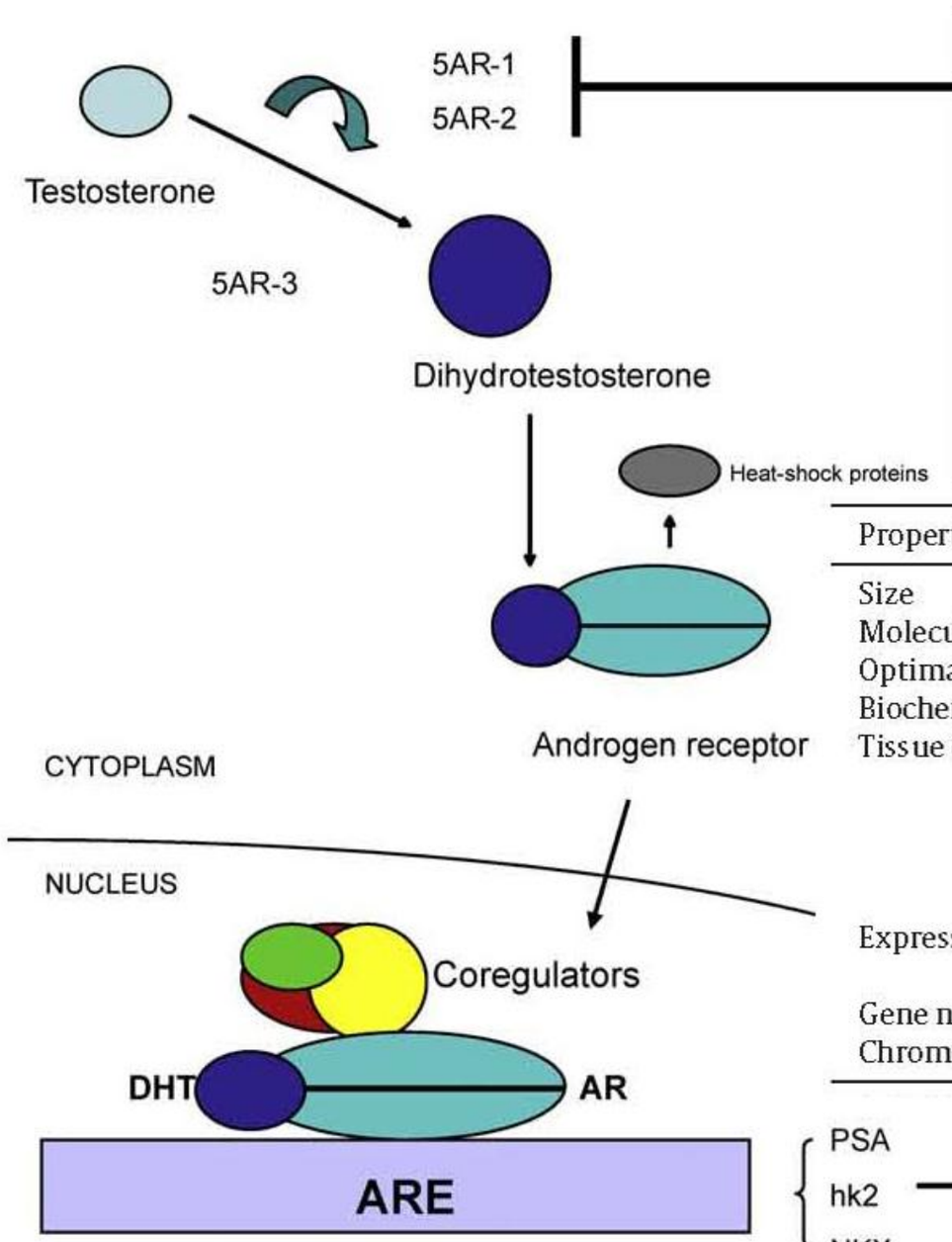
	Combination, % (*n* = 1610)	Dutasteride, % (*n* = 1623)	Tamsulosin, % (*n* = 1611)
Any adverse event	73	73	72
Any serious adverse event	19	21	22
Any drug-related adverse event	28*	21	19
Any serious drug-related adverse event	<1	<1	<1
Any adverse event leading to study withdrawal	13	12	14
Any drug-related adverse event leading to study withdrawal	6	4	4
Drug-related adverse events occurring in >1% of subjects in any treatment group			
Erectile dysfunction	9	7	5
Retrograde ejaculation	4	<1	1
Altered (decreased) libido	4	3	2
Ejaculation failure	3	<1	<1
Semen volume decreased	2	<1	<1
Loss of libido	2	1	1
Dizziness	2	<1	2
Gynaecomastia	2	2	<1
Nipple pain	1	<1	<1
Breast tenderness	1	1	<1

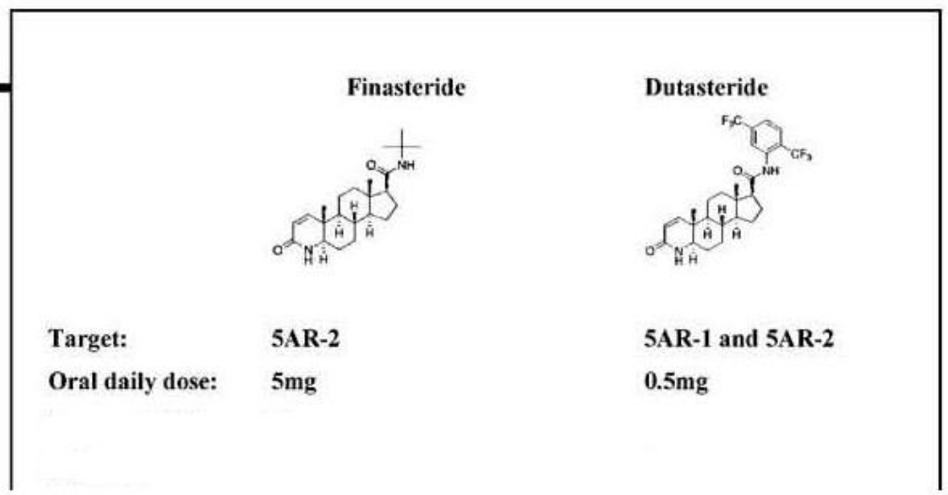
* Combination vs dutasteride and tamsulosin $p < 0.001$.

Mc Connell, et al. N Engl J Med 2003; 349:2387-2398

Roehrborn et al. Eur Urol 2010; 57:123-131

Ορμονικοί χειρισμοί (5 ARIs)



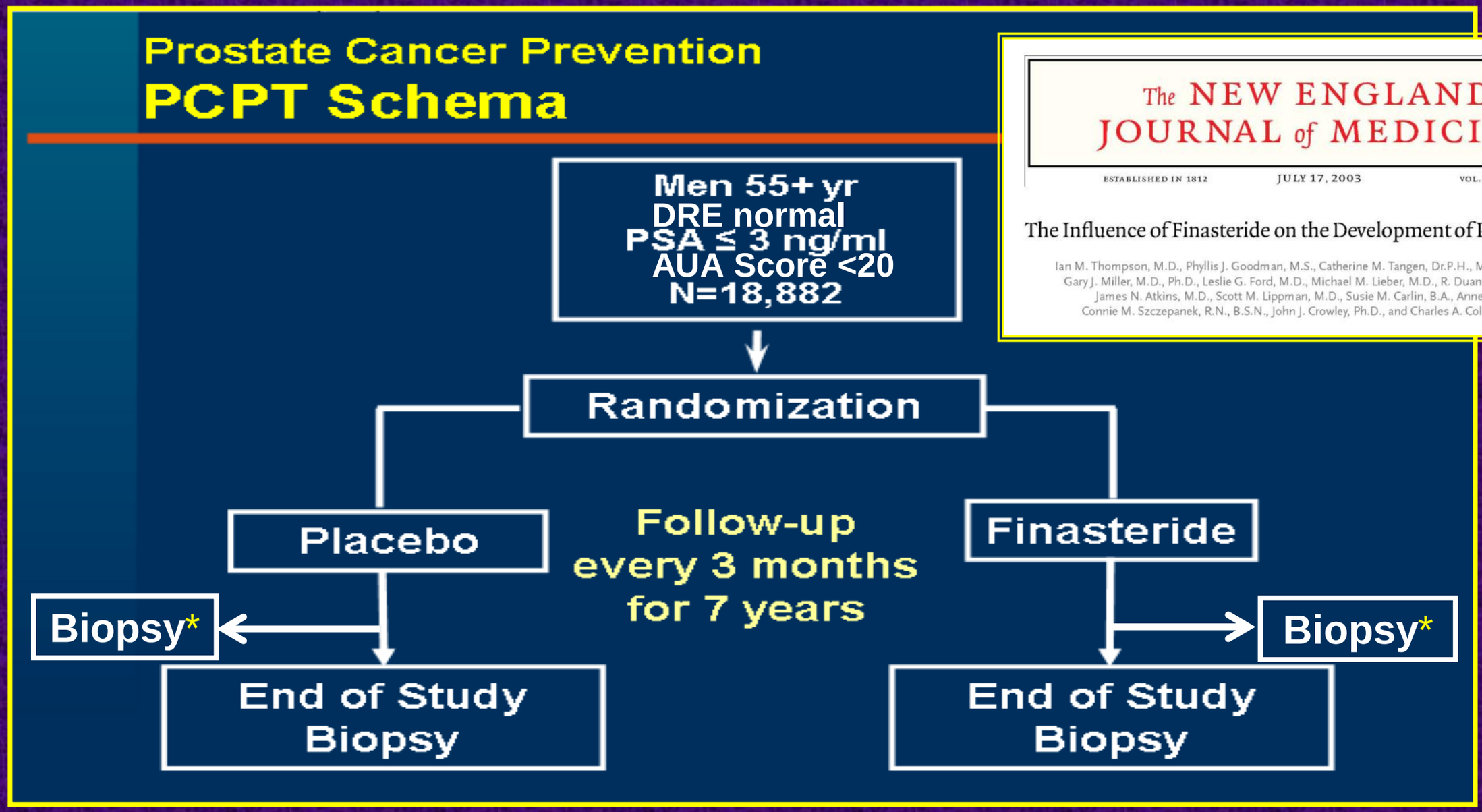


Properties	5AR-1	5AR-2
Size	259 amino acids	254 amino acids
Molecular weight	29.5 kDa	28.4 kDa
Optimal pH	6–8.5	5–5.5
Biochemical state	Hydrophobic	Hydrophobic
Tissue distribution	Liver, skin, brain, ovary, prostate, testis	Prostate, epididymis, seminal vesicle, genital skin, uterus, breast, hair follicle, placenta, testis
Expression in prostate	Normal (low), high in BPH and cancer	Normal and BPH (high) low in cancer
Gene name	SRD5A1	SRD5A2
Chromosome location	5p15	2p23

PSA
hk2
NKX

Schmidt & Tindall. J Steroid Biochem Mol Biol 2011;125:32-8

Ορμονικοί χειρισμοί: PCPT



The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 JULY 17, 2003 VOL. 349 NO. 3

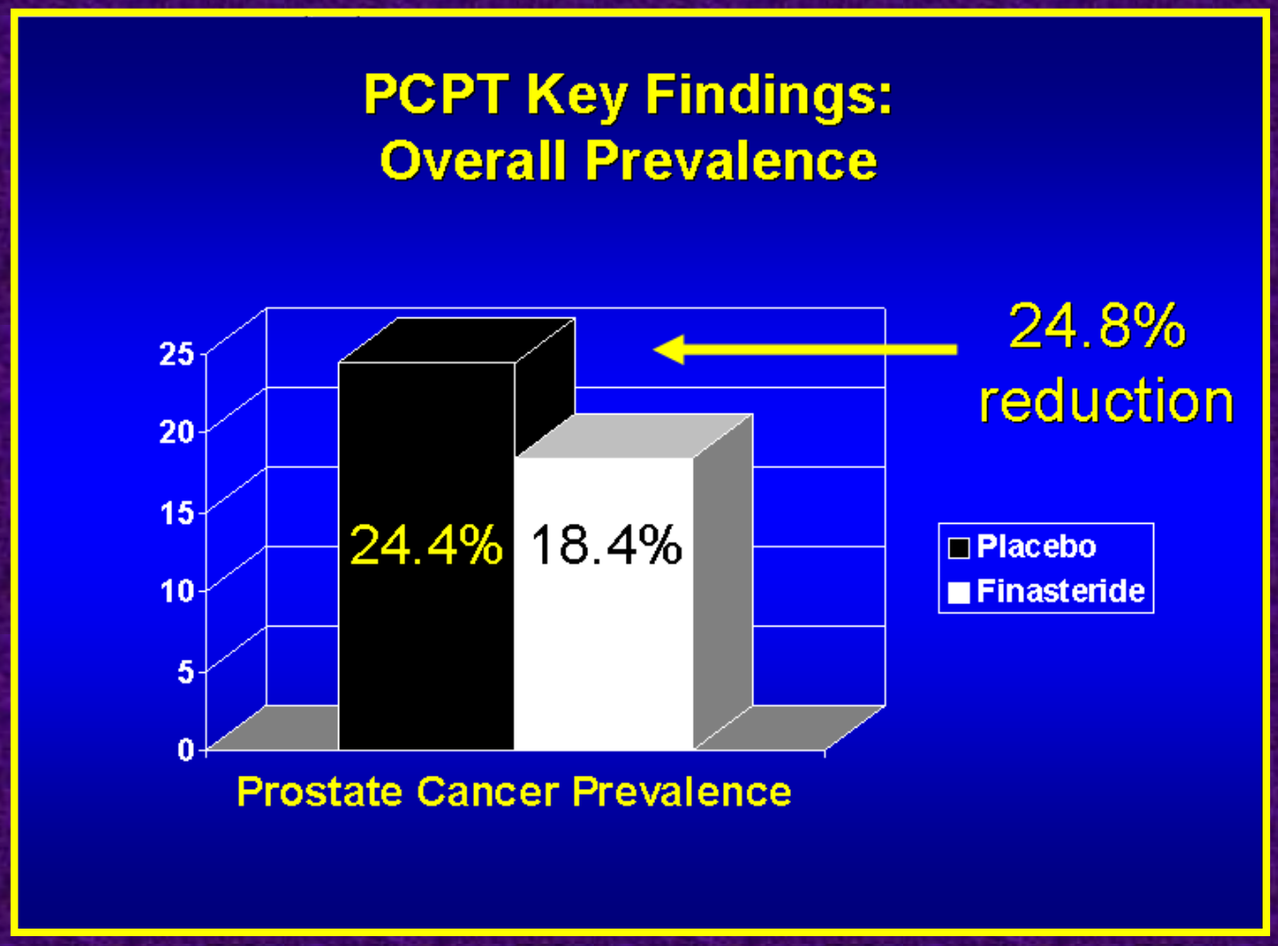
The Influence of Finasteride on the Development of Prostate Cancer

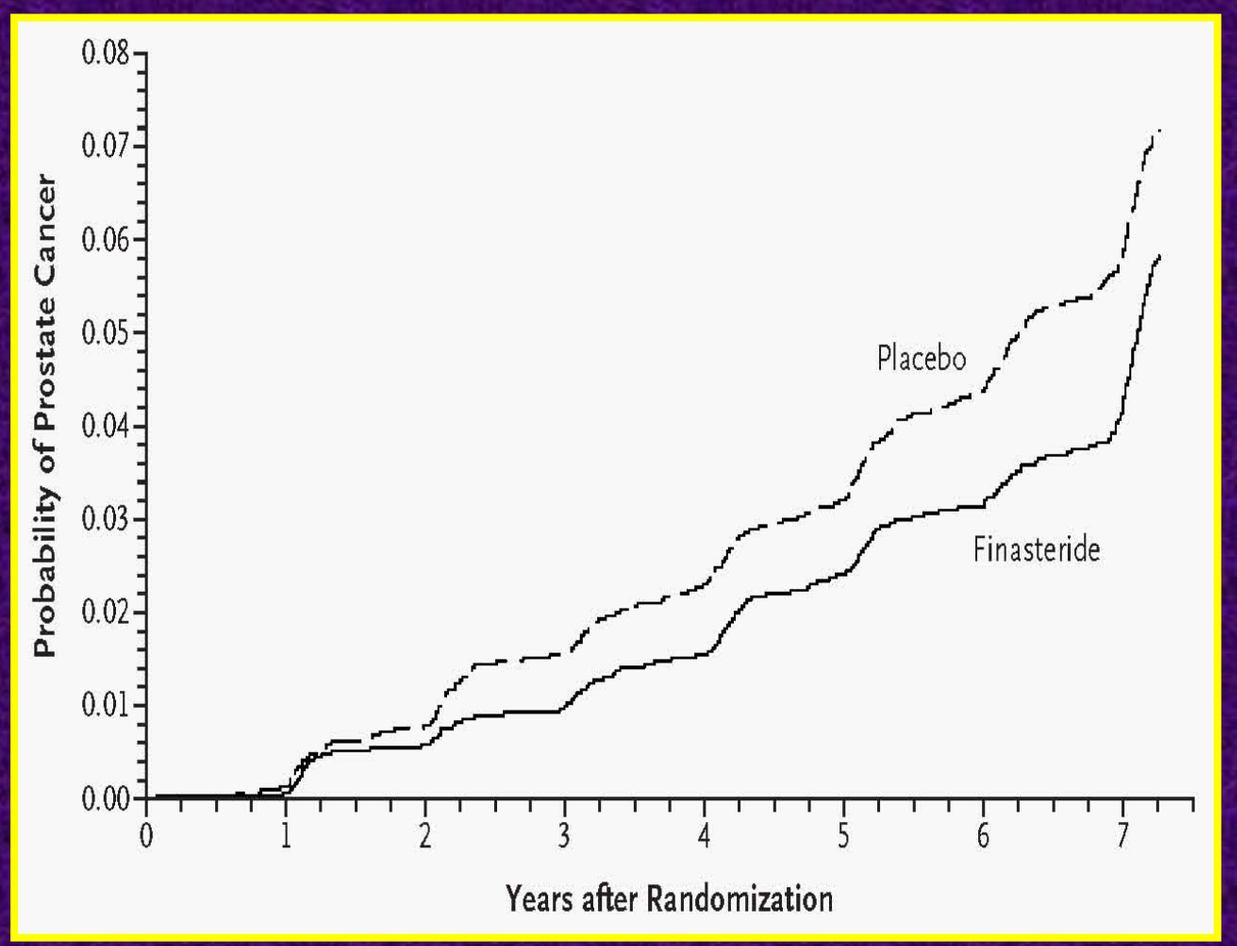
Ian M. Thompson, M.D., Phyllis J. Goodman, M.S., Catherine M. Tangen, Dr.P.H., M. Scott Lucia, M.D., Gary J. Miller, M.D., Ph.D., Leslie G. Ford, M.D., Michael M. Lieber, M.D., R. Duane Cespedes, M.D., James N. Atkins, M.D., Scott M. Lippman, M.D., Susie M. Carlin, B.A., Anne Ryan, R.N., Connie M. Szczepanek, R.N., B.S.N., John J. Crowley, Ph.D., and Charles A. Coltman, Jr., M.D.

*Ετήσια παρακολούθηση (DRE-PSA): Βιοψία: DRE + ή PSA>4 ng/ml

Thompson, et al. N Engl J Med 2003; 349:215-24

Ορμονικοί χειρισμοί: PCPT

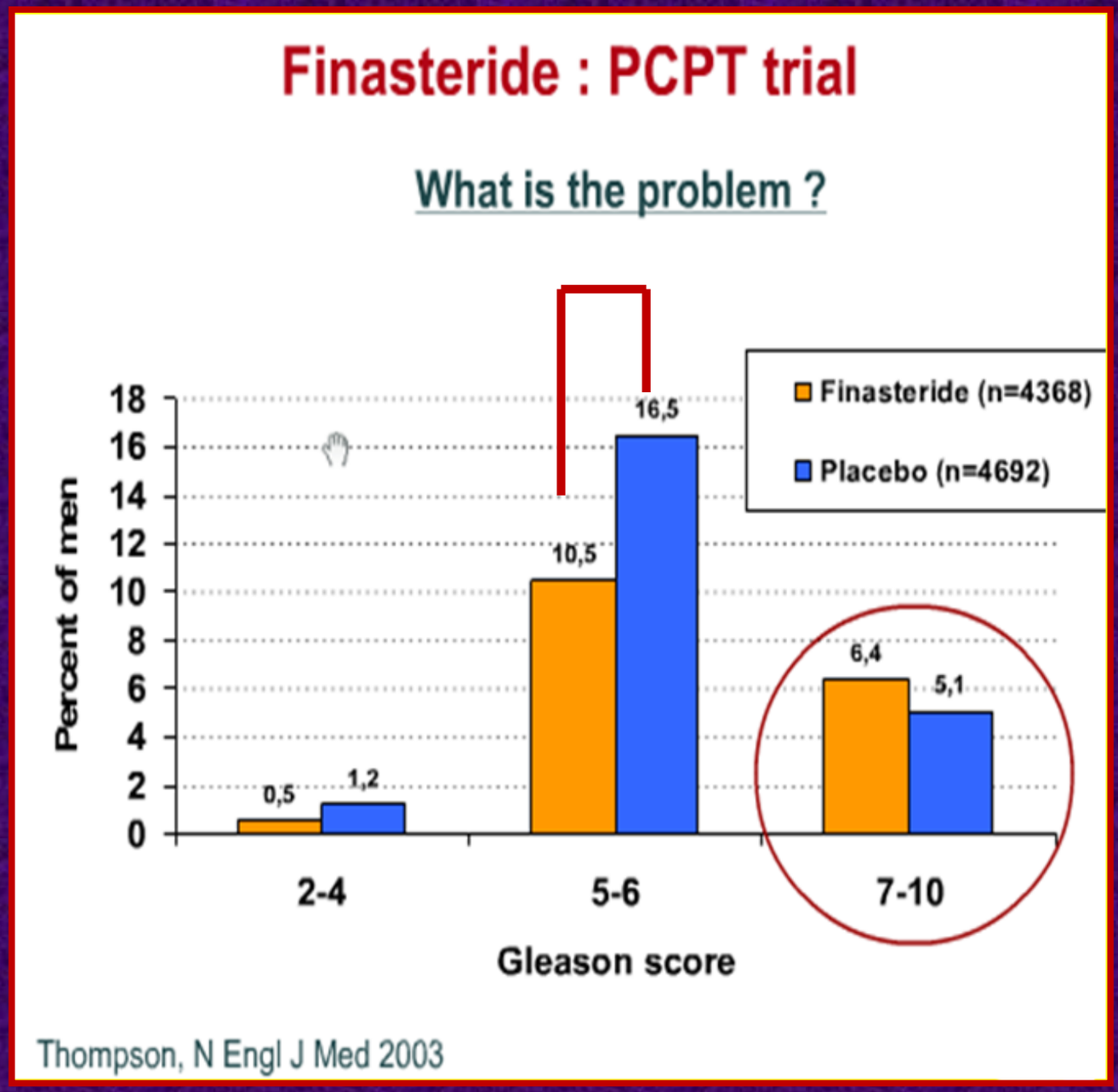




Η μελέτη τελείωσε 15 μήνες νωρίτερα λόγω σημαντικής μείωσης της επίπτωσης καρκίνου προστάτη στην ομάδα φιναστερίδης

Thompson, et al. N Engl J Med 2003; 349:215-24

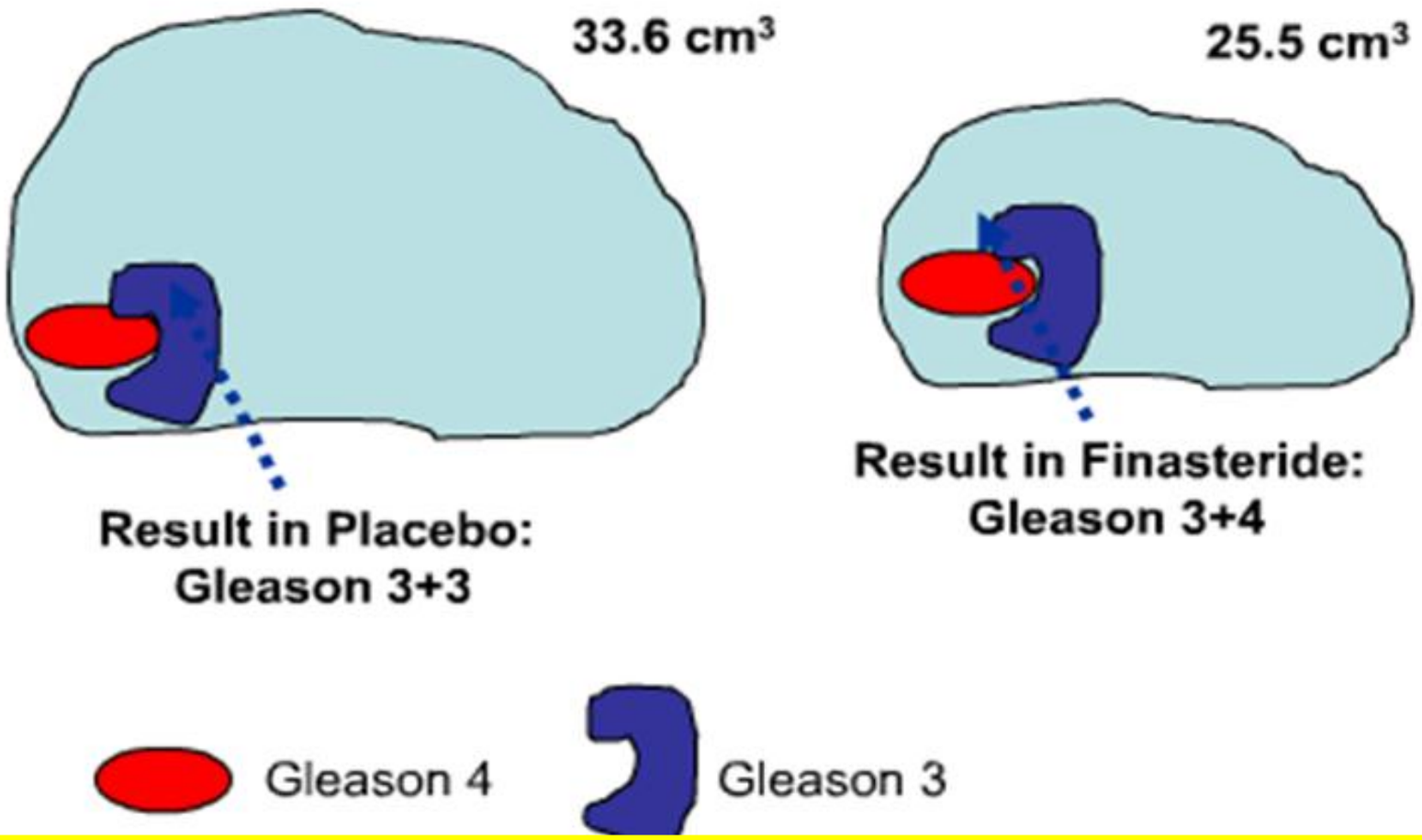
Ορμονικοί χειρισμοί: PCPT



Επιλεκτική μείωση συχνότητας των όγκων χαμηλού grade

Αύξηση ≈ 25% των όγκων GS > 6 (P = 0.005)

Finasteride induces a reduction in prostate volume that allow a better identification of high grade cancer



Η φιναστερίδη πιθανόν δεν επάγει όγκους υψηλής κακοήθειας αλλά μειώνοντας τον όγκο του προστάτη (≈ 25%) αυξάνει την πιθανότητα ανεύρεσης τους (αύξηση ευαισθησίας PSA-DRE)

Lucia, et al. Cancer Prev Res 2008; 1:167–73

Ορμονικοί χειρισμοί: Reduction by Dutasteride of PCa Events (REDUCE)

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

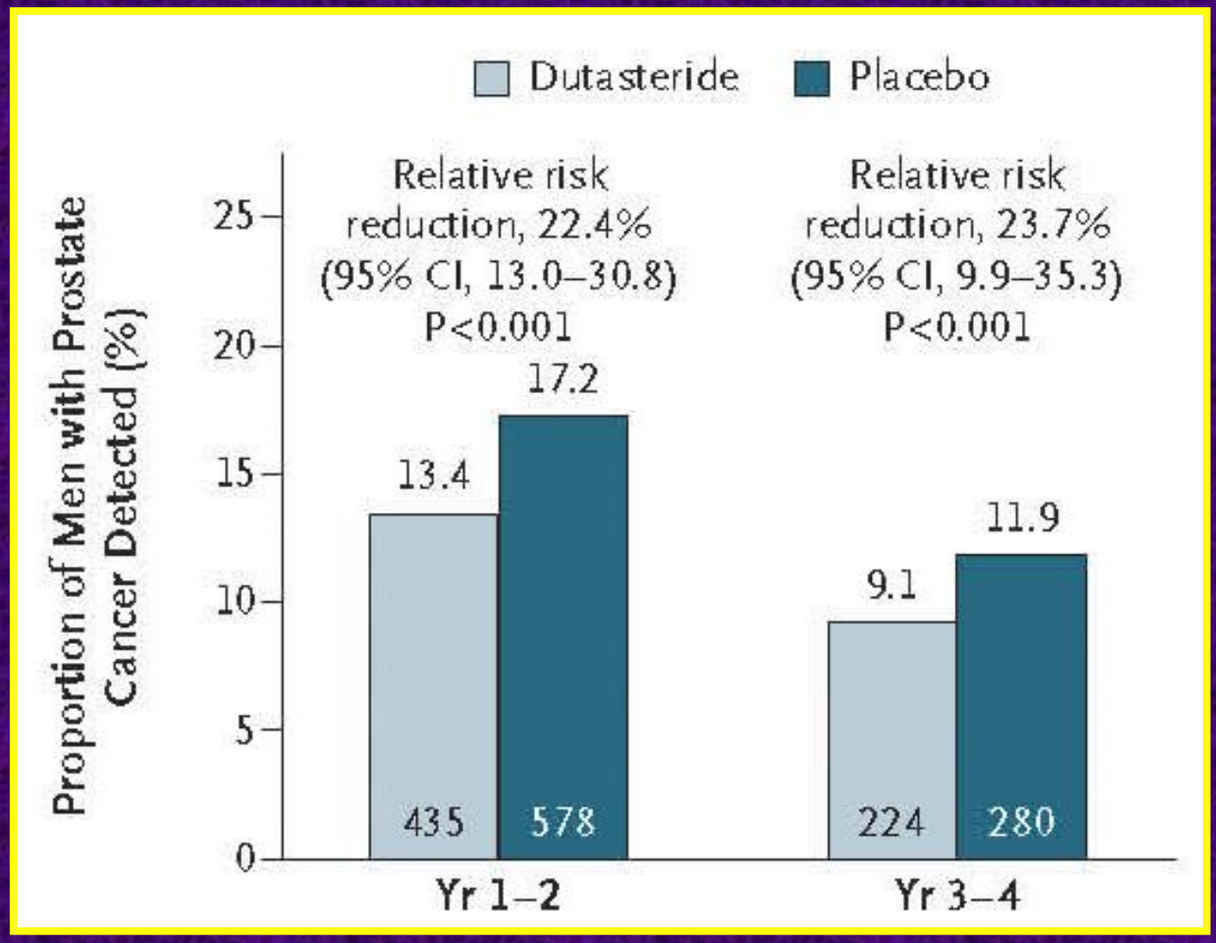
Effect of Dutasteride on the Risk of Prostate Cancer

Gerald L. Andriole, M.D., David G. Bostwick, M.D., Otis W. Brawley, M.D., Leonard G. Gomella, M.D., Michael Marberger, M.D., Francesco Montorsi, M.D., Curtis A. Pettaway, M.D., Teuvo L. Tammela, M.D., Claudio Teloken, M.D., Ph.D., Donald J. Tindall, Ph.D., Matthew C. Somerville, M.S., Timothy H. Wilson, M.S., Ivy L. Fowler, B.S.N., and Roger S. Rittmaster, M.D., for the REDUCE Study Group*

- Dutasteride vs. placebo, 4 έτη διάρκεια, πολυκεντρική RCT
- 8231 άνδρες 50-70 ετών, PSA 2,5-10ng/ml, αρνητική βιοψία 6 μήνες πριν (HGPIN, PCa), Vp<80ml, AUA SS<25
- Βιοψία προστάτου: επί κλινικής υποψίας, 2 & 4 χρόνια

Andriole, et al. N Engl J Med 2010; 362:1192-202

Ορμονικοί χειρισμοί: REDUCE



- Μείωση κινδύνου για καρκίνο κατά 23%
- Μη σημαντική αύξηση συχνότητας όγκων 7-10 GS
- Σαφής τάση αύξησης κινδύνου για εμφάνιση όγκων 8-10 GS

Andriole, et al. N Engl J Med 2010; 362:1192-202

Ορμονικοί χειρισμοί: REDUCE

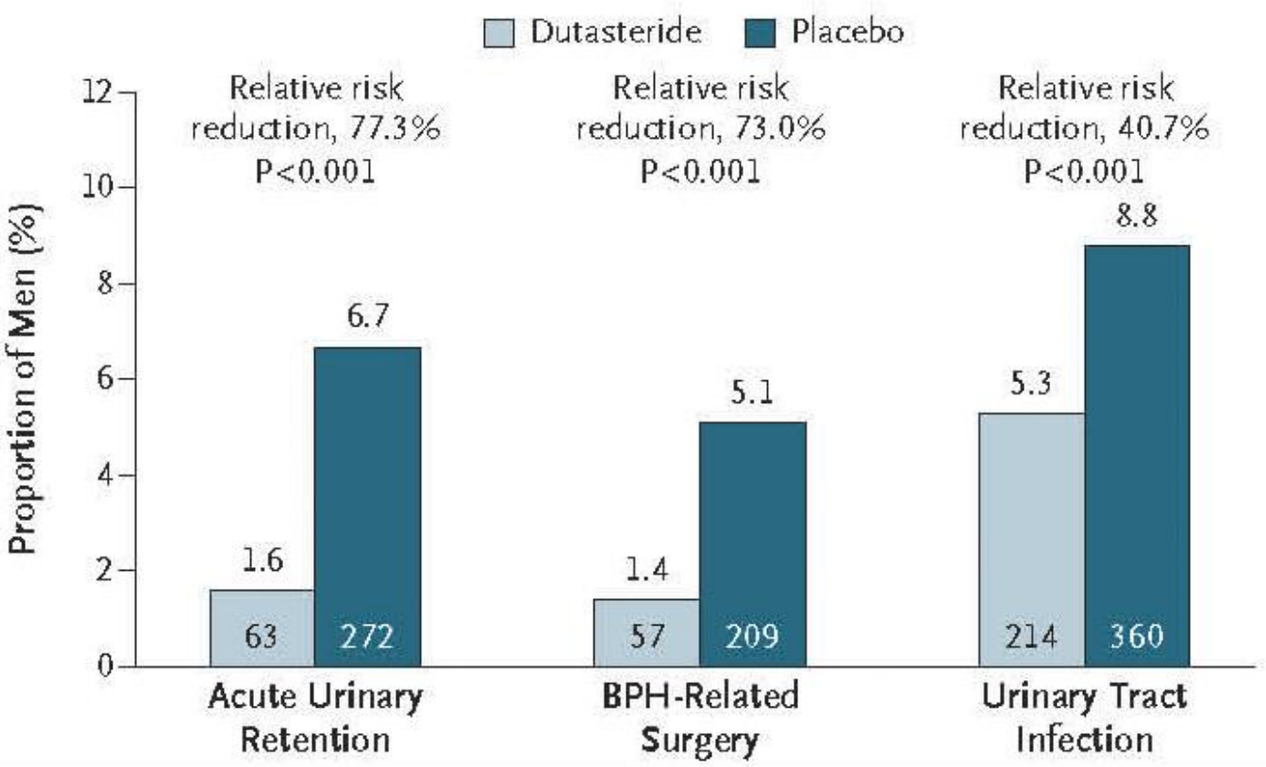


Table 4. Incidence of Adverse Events.*

Event	Dutasteride (N=4105)	Placebo (N=4126)	P Value†
	no. (%)		
Any adverse event	3017 (73.5)	2966 (71.9)	0.10
Any serious adverse event	748 (18.2)	837 (20.3)	0.02
Drug-related adverse event			
Any	904 (22.0)	604 (14.6)	<0.001
Leading to permanent discontinuation of treatment	176 (4.3)	83 (2.0)	<0.001
Occurring in ≥1% of subjects in either study group			
Decreased libido	137 (3.3)	65 (1.6)	<0.001
Loss of libido	79 (1.9)	54 (1.3)	0.03
Erectile dysfunction	369 (9.0)	237 (5.7)	<0.001
Decreased semen volume‡	56 (1.4)	9 (0.2)	<0.001
Gynecomastia	76 (1.9)	43 (1.0)	0.002
Death§	70 (1.7)	77 (1.9)	0.65

- Βελτίωση αποτελεσμάτων που σχετίζονται με BPH
- Επίπτωση παρενεργειών παρόμοια με αυτή μετά από χορήγηση για BPH (Dutasteride: 22%, Placebo: 15%)
- Συχνότερα επεισόδια καρδιακής ανεπάρκειας

Andriole, et al. N Engl J Med 2010; 362:1192-202

Ορμονικοί χειρισμοί (5ARIs): Κατευθυντήριες οδηγίες

- Ασυμπτωματικοί άνδρες με PSA ≤ 3 ng/ml που το μετρούν τακτικά ή είναι πρόθυμοι να υποβάλλονται σε ετήσιο έλεγχο, μπορεί να ωφεληθούν από τη συζήτηση για τα υπέρ της χρήσης για πρόληψη του PCa και τους δυνητικούς κινδύνους
- Το ίδιο ισχύει και για τους ασθενείς που λαμβάνουν 5ARIs για καλοήθεις καταστάσεις (BPH/LUTS)

Kramer, et al. J Urol 2009; 181:1642-57

Αλλά…

ASCO/AUA Special Announcement on FDA Decision Re:Dutasteride

Special Announcement (2/22/11):
In December, 2010, the FDA's Oncologic Drugs Advisory Committee (ODAC) voted against recommending dutasteride (Avodart, GlaxoSmithKline) for the indication to reduce prostate cancer risk because in the view of the ODAC members, the risk for more aggressive tumors outweighed the potential for chemoprevention.

ODAC recommended against prostate cancer chemoprevention labeling for the 5-alpha reductase inhibitors - dutasteride (vote 14 (no) to 2 (yes), with 2 abstentions) and finasteride (vote 17 (no) to 0 (yes), with 1abstention).

- Αμφισβητούμενη ασφάλεια:
  "Not provided compelling evidence confirming that there is not an increased risk of high-grade PCa"

- Αμφισβητούμενη αποτελεσματικότητα:
  "Cancers prevented in each trial belonged to the categories least likely to be clinically significant"

- *Τα αποτελέσματα δεν μπορούν να γενικευτούν:*
  "…end of study biopsies do not mirror clinical practice"

ΕΥΧΑΡΙΣΤΩ