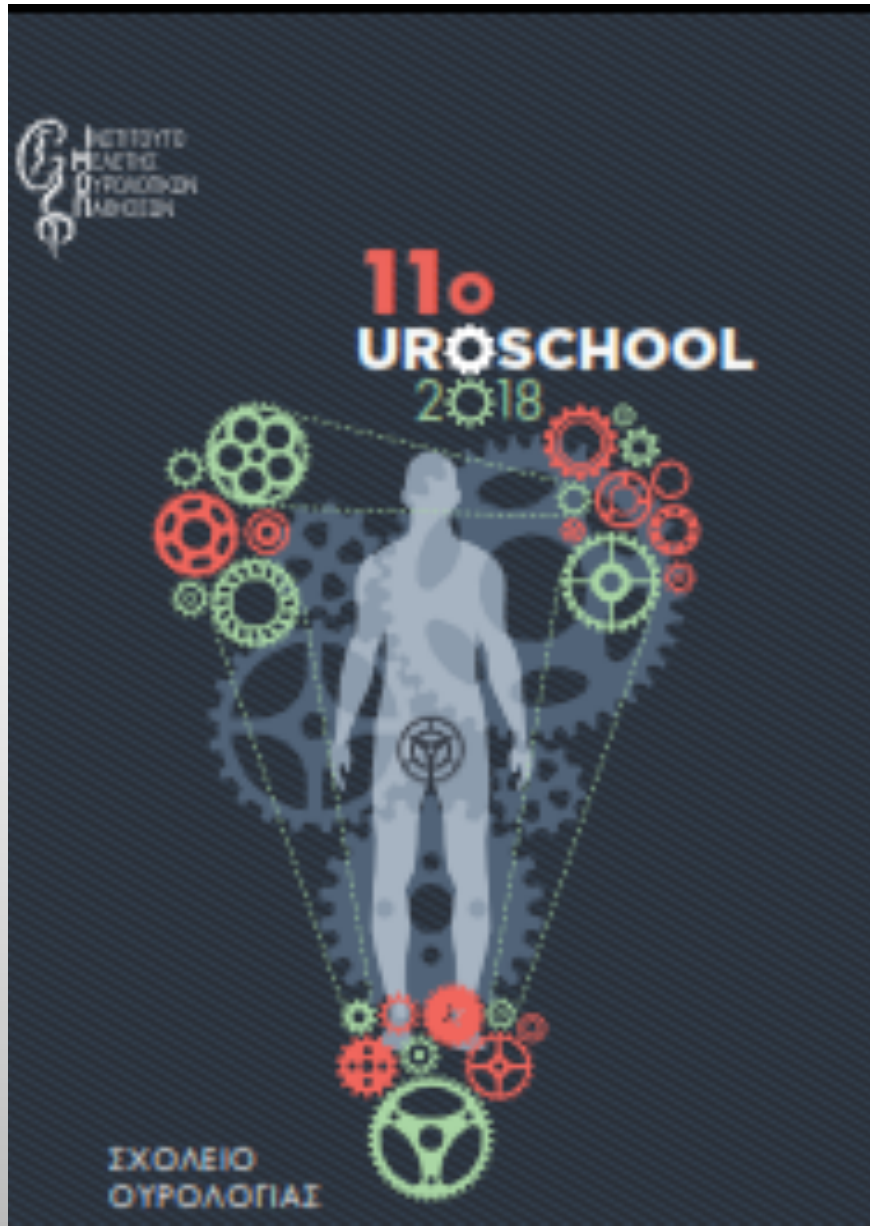
Urogold III: Οι σημαντικότερες δημοσιεύσεις της χρονιάς (Προστάτης- όρχεις)

Μουρμούρης Παναγιώτης MD, MSc, PhD, FEBU

Πανεπιστημιακός Υπότροφος ΕΚΠΑ

Β Ουρολογική Κλινική Σισμανόγλειο ΓΝΑ



- Καμία σύγκρουση συμφερόντων

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Review – Prostate Cancer

Impact of Metabolic Diseases, Drugs, and Dietary Factors on Prostate Cancer Risk, Recurrence, and Survival: A Systematic Review by the European Association of Urology Section of Oncological Urology

Riccardo Campi[a,*], Sabine D. Brookman-May[b], Jose Daniel Subiela Henríquez[c], Bülent Akdoğan[d], Maurizio Brausi[e], Tobias Klatte[f], Johan F. Langenhuijsen[g]

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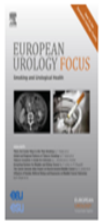


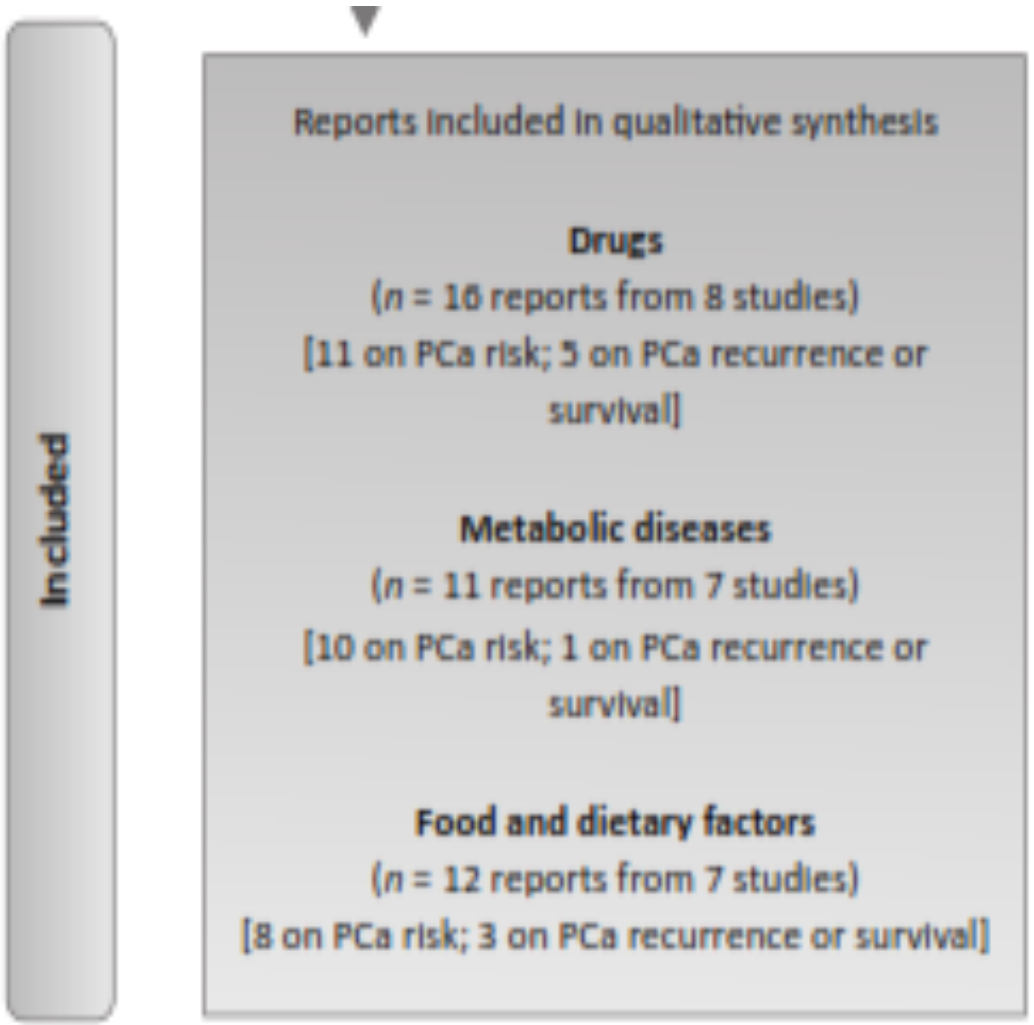
Review – Prostate Cancer

Latest Evidence on the Impact of Smoking, Sports, and Sexual Activity as Modifiable Lifestyle Risk Factors for Prostate Cancer Incidence, Recurrence, and Progression: A Systematic Review of the Literature by the European Association of Urology Section of Oncological Urology (ESOU)

Sabine D. Brookman-May[a,*], Riccardo Campi[b], Jose D.S. Henríquez[c], Tobias Klatte[d], Johan F. Langenhuijsen[e], Maurizio Brausi[f], Estefania Linares-Espinós[g], Alessandro Volpe[h], Martin Marszalek[i], Bulent Akdogan[j], Christina Roll[k], Christian G. Stief[a], Oscar Rodriguez-Faba[c,l], Andrea Minervini[b,l]

Υπάρχουν παράγοντες που επηρεάζουν την εμφάνιση και την φυσική πορεία της νόσου;

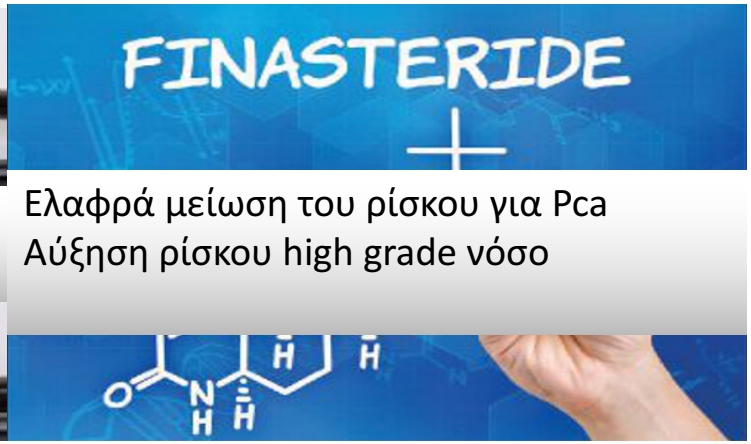
- 2003-2017
- Πληθυσμός ανδρών >18 ετών που έχουν κάνει τουλάχιστον μια εξέταση PSA
  - Χωρίς ιστορικό Pca (risk analysis)
  - Με ιστορικό Pca (recurrence/survival analysis)
- RCT ή προοπτική μελέτη με χρόνο παρακολούθησης >10 χρόνια (5 για την υποτροπή)
- Περιέχουσες στατιστική ανάλυση για ηλικία, οικογενειακό ιστορικό, PSA, στάδιο Pca, αρχική θεραπεία



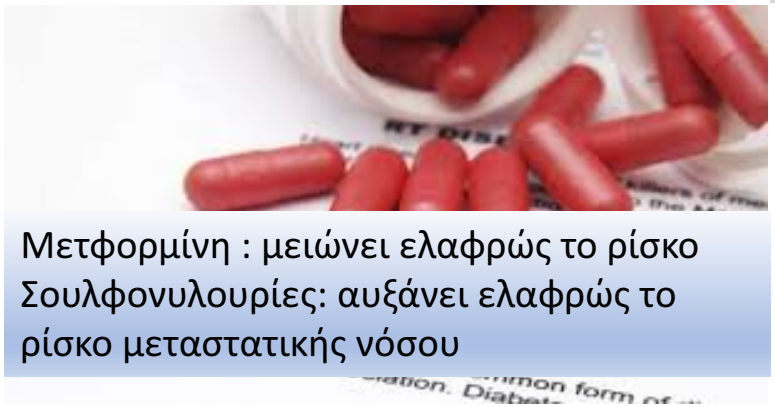
Topic (outcome)	Summary of findings
Antidiabetic drugs(PCa risk)	1. Use of metformin may be associated with a modest decreased risk of PCa, particularly of localized disease and in men with a long history of diabetes. Yet, it is difficult to disentangle the specific effect of antidiabetic drugs from that of underlying diabetes; moreover, there is a risk of detection bias. 2. Use of sulfonylureas might be associated with an increased risk of metastatic PCa. 3. There is no evidence of an effect of insulin (and other antidiabetic drugs) use on PCa risk.
Statins (PCa death)	Postdiagnostic statin use may be associated with a reduced risk of PCa death in selected patient populations, such as patients with low-medium risk PCa, those treated with ADT, and those not using antihypertensive drugs.
Aspirin and NSAIDs (PCa risk)	1. Despite findings of included studies not always being consistent and information on dose and duration being elusive, there is no evidence of an effect of regular aspirin use for the risk of advanced (high stage and/or N+ M+ disease) PCa, while regular aspirin use may be associated with a slightly decreased risk of overall PCa, especially among older men (>65 yr). 2. There was no evidence of an effect of nonaspirin NSAIDs (and in particular ibuprofen and acetaminophen) on PCa risk.
5-alpha reductase inhibitors (PCa death)	1. Despite a reduction in the overall PCa risk and a potential increased risk of high-grade disease, there was no evidence of an effect of both pre- and postdiagnostic 5-ARI use on PCa death.

Obesity (PCa risk, recurrence, or survival)	1. Interpretation of available evidence on the role of obesity for PCa risk is challenging due to highly variable definitions of exposure and outcomes, length of follow-up, and lack of data on drug doses in most studies. Moreover, detection bias due to potential PSA hemodilution among obese men cannot be ruled out entirely. 2. BMI at age 20–21 might be associated with a modest decreased risk of overall and (potentially) more advanced PCa, even if this association appeared attenuated when considering childhood body shape. 3. BMI at middle age might be associated with a modest decreased risk of overall PCa. 4. There is no evidence of an effect of both WC and WHR on PCa risk after adjustment on BMI. 5. Long-term (but not short-term) weight gain might be associated with an increased risk of lethal PCa in selected patient populations (ie, never smokers, and overweight or obese men at age 21). 6. There was no evidence of an effect of BMI on either biochemical recurrence or lethal PCa. 7. Evidence was judged too heterogeneous to evaluate the impact of BMI on grade-specific PCa.
Diabetes mellitus (PCa risk)	1. Evidence on the role of diabetes mellitus for PCa risk in populations exposed to PSA testing is not definitive. 2. The potential inverse association reported between diagnosis of diabetes mellitus and PCa among PSA-screened population seems to be restricted to total and (possibly) low-grade/localized disease. 3. The extent to which BMI, surveillance bias, and detection bias may significantly modify these associations remains undetermined.
Food and dietary factors (PCa risk)	1. Evidence on potential associations between meat consumption, and risk of overall and stage-specific PCa is conflicting. 2. Intake of specific fatty acids (ie, EPA, DHA, EPA + DHA) may be associated with a reduced risk of total PCa, while intake of other fatty acids (ALA from nonanimal sources), saturated fats, isoflavones, and high doses of calcium may be associated with an increased risk of advanced PCa. However, evidence is not conclusive. 3. There was no evidence of an effect of fruit, vegetable, and fish intake on PCa risk.

Μειώνουν την πιθανότητα θανάτου σε επιλεγμένους ασθενείς (ADT!!)



Ελαφρά μείωση του ρίσκου για Pca
Αύξηση ρίσκου high grade νόσο



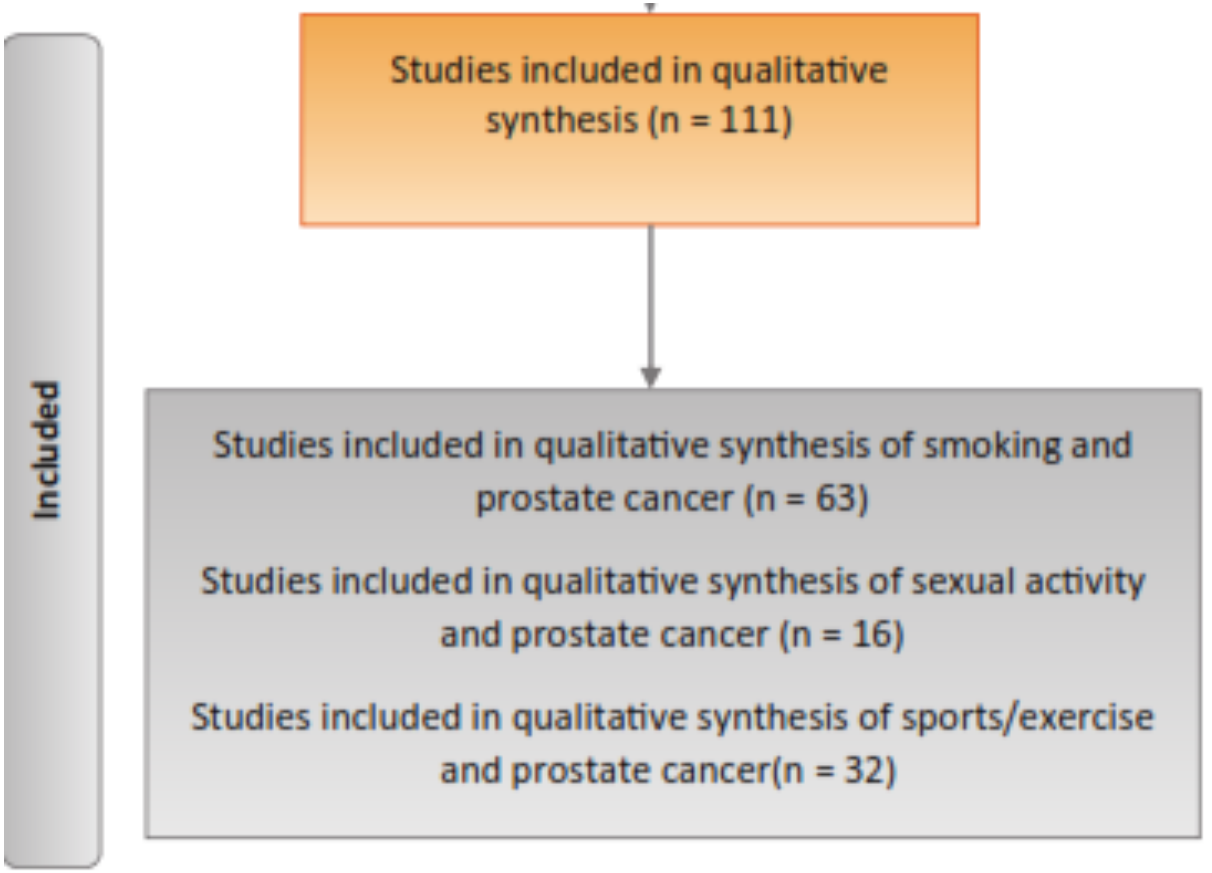
Μετφορμίνη : μειώνει ελαφρώς το ρίσκο
Σουλφονυλουρίες: αυξάνει ελαφρώς το ρίσκο μεταστατικής νόσου

Ελαφρώς μειωμένο ρίσκο

Το BMI σε ηλικίες 20-50 φαίνεται να μειώνει το ρίσκο

Τα δεδομένα δεν μας επιτρέπουν να εξάγουμε ασφαλή συμπεράσματα

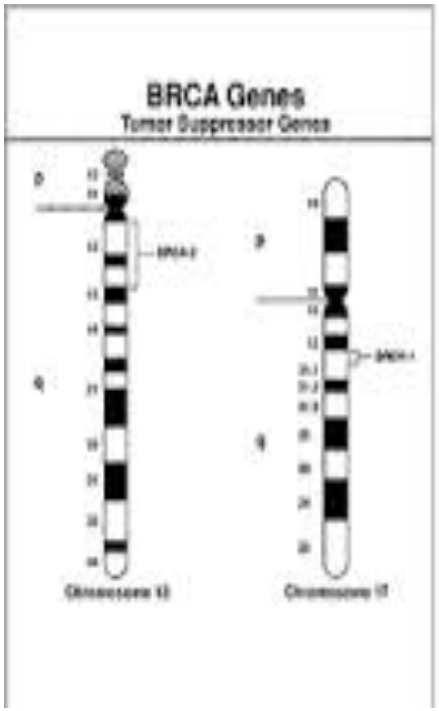
Σχεδιασμός μελέτης



Association of smoking with prostate cancer risk, tumor progression, treatment outcome, and cancer-related mortality	• There is conflicting evidence about the association of smoking with overall prostate cancer incidence. While several cohort studies have indicated reduced risks for prostate cancer diagnosis in smokers, most case-control studies show an increased risk. Potential confounders including lead-time bias due to different time points of diagnosis and different screening patterns need to be considered. • Available evidence indicates an increased risk of more advanced tumor stages and more aggressive baseline disease characteristics in smokers and former smokers. • Current epidemiological evidence suggests a robust and dose-response association between smoking and cancer-related death, which is observed in current and former smokers. Residual confounding cannot be excluded completely, but the association seems not to be related to publication bias. • There is reliable evidence that smoking is associated with adverse pathological features and a higher risk of BCR in patients undergoing RP or EBRT, which is maintained for 10 yr after smoking cessation. • Smoking status and anamnesis should be considered an important and modifiable risk factor in prostate cancer patients, and accordant advice to quit smoking should be given to patients to improve their individual prognosis. Furthermore, increased competing mortality in smokers should be considered.

Συσχετισμός με χειρότερη πρόγνωση και πιο επιθετική συμπεριφορά
Τα παραπάνω παραμένουν για τουλάχιστον 10 χρόνια από την διακοπή
Πρέπει να συστήνεται η διακοπή

Association of sexual activity with prostate cancer risk	• Results from available studies on sexual activity and prostate cancer risk imply several limitations, and overall the current evidence cannot be considered authoritative. • Further investigations are clearly necessary to establish the role of STIs in the etiology of prostate cancer and to evaluate whether the suggested associations between prostate cancer risk and sexual behavior are real or spurious. Recent studies found either no or just a weak association between vasectomy and overall prostate cancer risk, and no significant association with high-grade, advanced-stage, or fatal prostate cancer, finally rebutting a relationship between vasectomy and prostate cancer.
Association of physical activity with prostate cancer risk, tumor progression, treatment outcome, and cancer-related mortality	• Despite a considerable volume of research addressing this topic, the value of regular physical activity on prostate cancer risk is not unequivocally established. Many investigators have drawn conflicting inferences based upon small subgroups or by reporting an impact without the accordantly needed statistical power or results. • Studies have shown significant benefits arising from regular physical activity in terms of disease progression, treatment outcome, and mortality, even though this has yet to be proved conclusively. • While the focus of this article was not occupational physical activity, aspects related to occupational activity, including exposure to chemicals, and socioeconomic and dietary differences between men with sedentary versus physical work, also need to be considered. • There remains a need for large and well-designed studies with improved and objective assessment of habitual physical activity at various ages under consideration of important covariates. • Long-term interventions testing possible risk modifications by exercise programs and further exploring possible underlying mechanisms are required to answer the question why susceptibility seems to be influenced by tumor aggressiveness and individuals' age. • The majority of data suggest a favorable impact of physical activity on several health problems; besides a potential preventive impact for cancer development might be assumed. Hence, it is certainly reasonable to advocate an active lifestyle as a potentially useful measure for prostate cancer prevention.



www.impactjournals.com/oncotarget/ Oncotarget, 2017, Vol. 8, (No. 25), pp: 40222-40232

Research Paper

BRCA2 mutations should be screened early and routinely as markers of poor prognosis: evidence from 8,988 patients with prostate cancer

Ming Cui[1], Xian-Shu Gao[1], Xiaobin Gu[1], Wei Guo[2], Xiaoying Li[1], Mingwei Ma[1], Shangbin Qin[1], Xin Qi[1], Mu Xie[1], Chuan Peng[1] and Yun Bai[1]

[1]Department of Radiation Oncology, Peking University First Hospital, Peking University, Beijing, China

[2]Graduate School of Medicine, Hebei North University, Zhangjiakou, Hebei, China

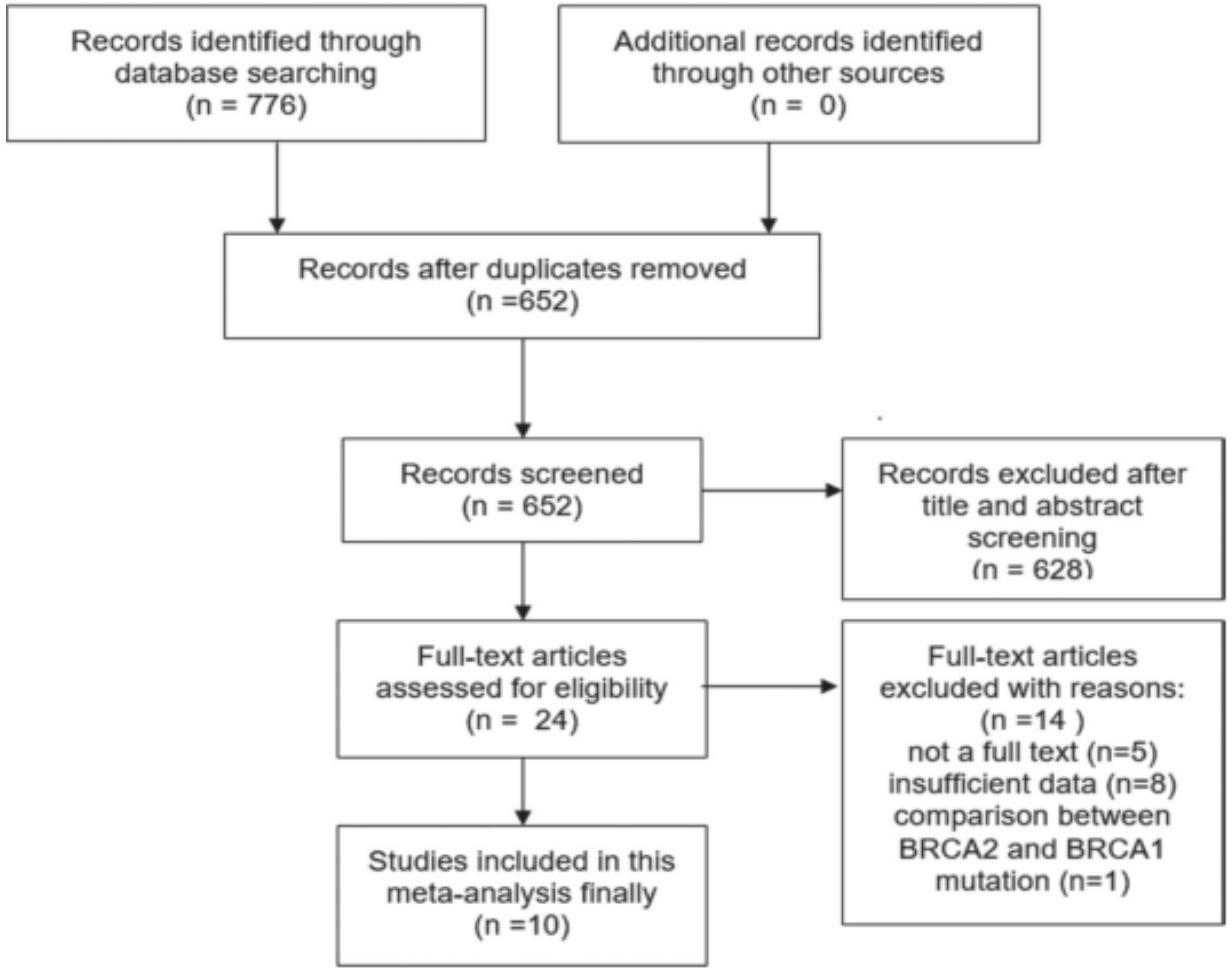
Correspondence to: Xian-Shu Gao, **email:** doctorgaoxs@126.com

Keywords: *BRCA2, mutation, prostate cancer, survival, molecular classification*

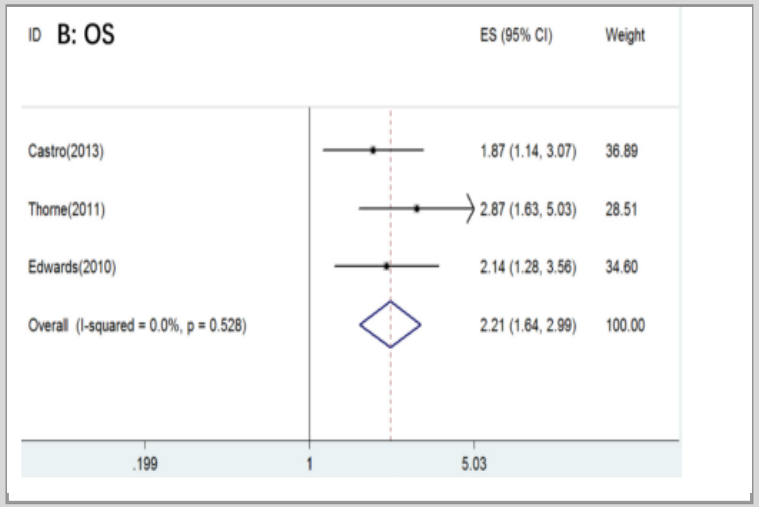
Received: *January 23, 2017* ***Accepted:*** *March 21, 2017* ***Published:*** *March 30, 2017*

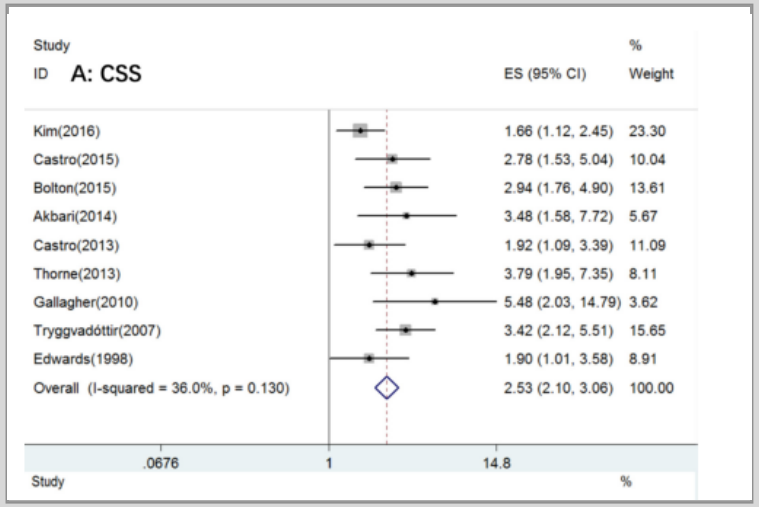
Μήπως τελικά πρέπει να ελέγχονται και οι άντρες;

Είναι κακός προγνωστικός παράγοντας;



Variable	No.of studies	No.of BRCA2(+)	No.of Non-carriers	Effects model	OR (95% CI)	P
GS (> 7 vs. < = 7)	6	231	3,722	Fixed	3.24 (2.36–4.44)	< 0.001
T stage (> = T3 vs. < T3)	4	176	2,859	Fixed	1.75 (1.26–2.42)	0.001
N stage (N1 vs. N0)	3	139	2,367	Fixed	3.90 (2.17–7.03)	< 0.001
M stage (M1 vs. M0)	2	90	1,999	Fixed	2.47 (1.32–4.63)	0.005
Risk (High vs. < High)	2	101	2,510	Fixed	1.43 (0.95–2.14)	0.087

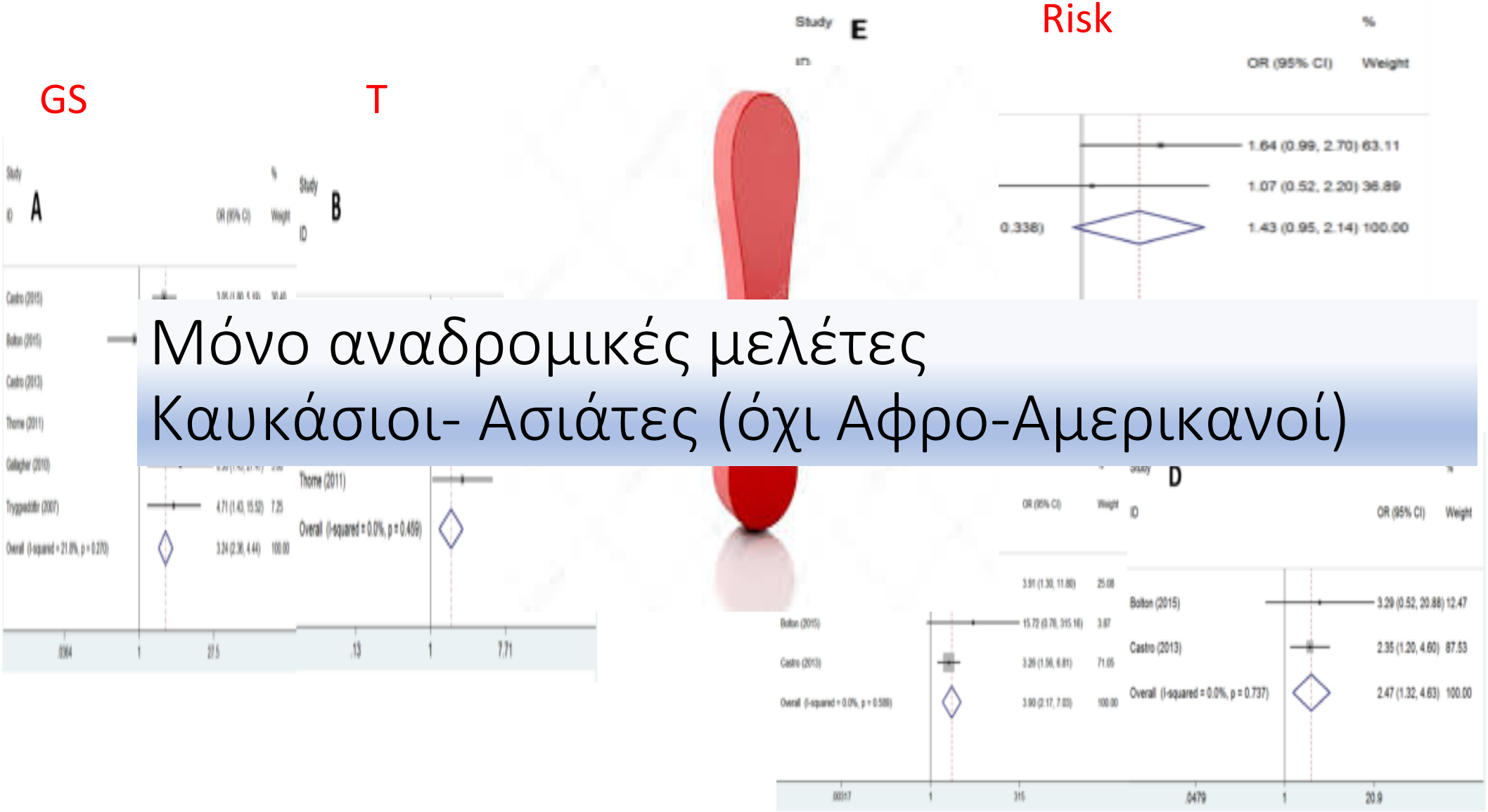




GS

T

Risk



Μόνο αναδρομικές μελέτες
Καυκάσιοι- Ασιάτες (όχι Αφρο-Αμερικανοί)

- ✓ Ασθενείς πάσχουν από καρκίνο του προστάτη και φέρουν την μετάλλαξη παρουσιάζουν μικρότερη ολική επιβίωση
- ✓ Μπορεί να θεωρηθεί κακός προγνωστικός παράγοντας
- ✓ Περαιτέρω κατηγοριοποίηση των high risk ασθενών με πιθανή τροποποίηση της θεραπείας τους
- ✓ Μοριακή ταξινόμηση των ασθενών

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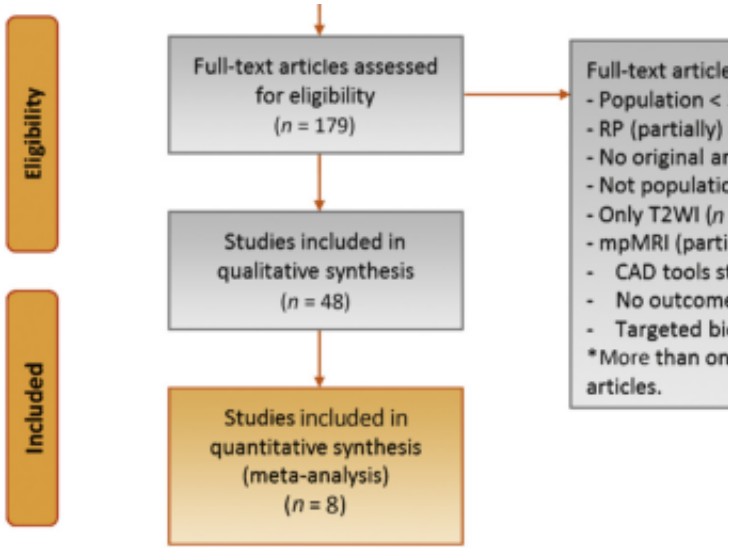
European Association of Urology

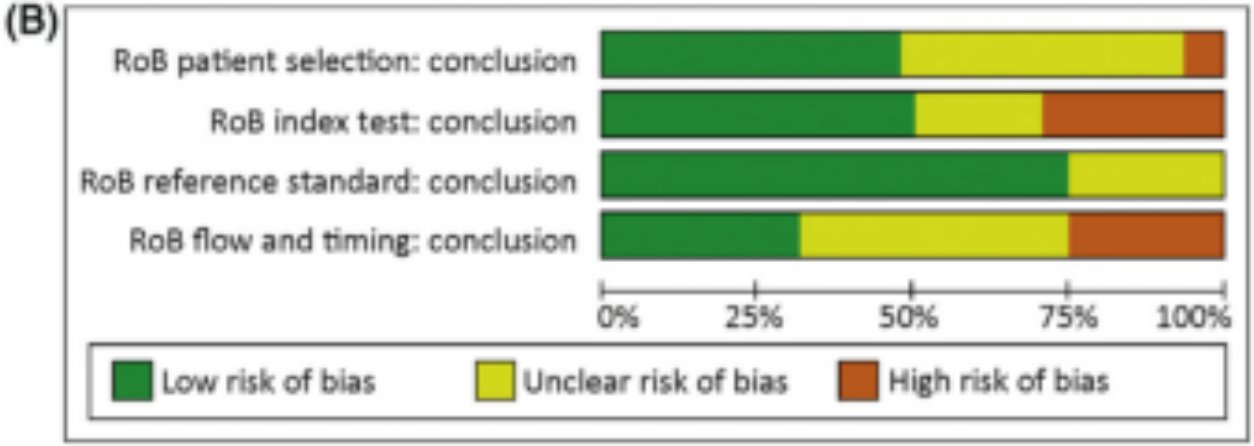
Guidelines

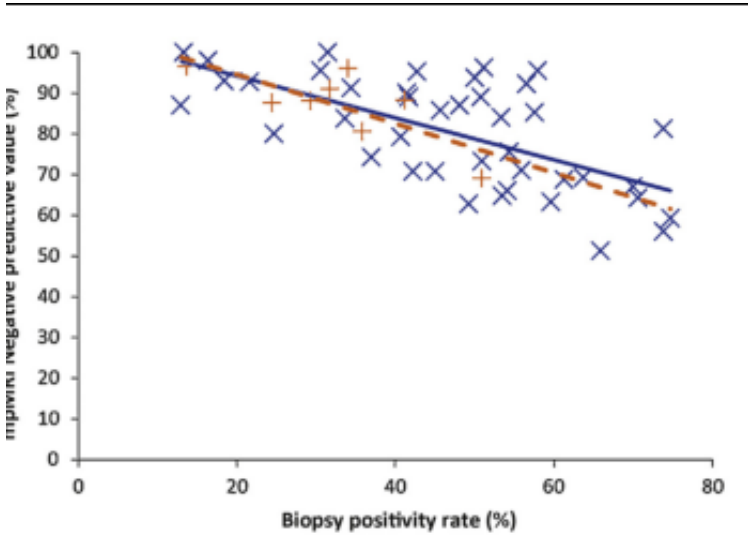
What Is the Negative Predictive Value of Multiparametric Magnetic Resonance Imaging in Excluding Prostate Cancer at Biopsy? A Systematic Review and Meta-analysis from the European Association of Urology Prostate Cancer Guidelines Panel

Paul C. Moldovan [a,†], Thomas Van den Broeck [b,c,†], Richard Sylvester [d], Lorenzo Marconi [e], Joaquim Bellmunt [f,g], Roderick C.N. van den Bergh [h], Michel Bolla [i], Erik Briers [j], Marcus G. Cumberbatch [k], Nicola Fossati [l], Tobias Gross [m], Ann M. Henry [n], Steven Joniau [b,c], Theo H. van der Kwast [o], Vsevolod B. Matveev [p], Henk G. van der Poel [h], Maria De Santis [q], Ivo G. Schoots [r,s], Thomas Wiegel [t], Cathy Yuhong Yuan [u], Philip Cornford [v], Nicolas Mottet [w], Thomas B. Lam [x,y], Olivier Rouvière [a,z,]*

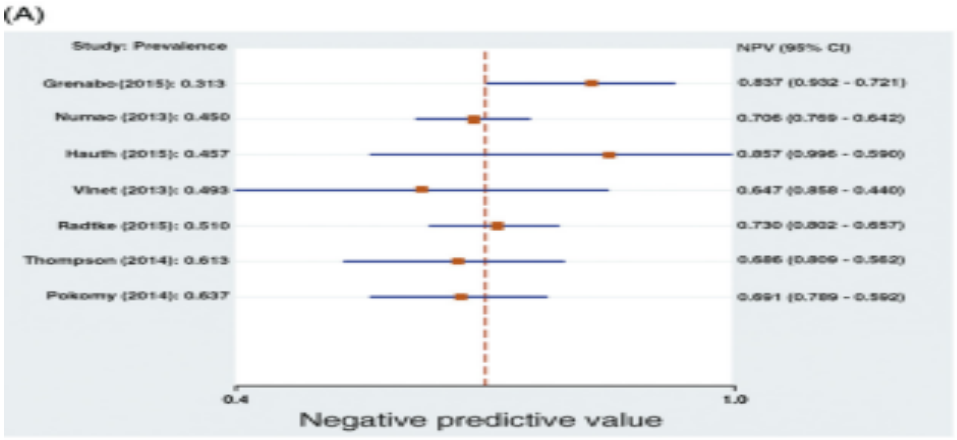
Πολυπαραμετρική MRI: Μπορεί να χρησιμοποιηθεί για να αποκλείσει την πρώτη βιοψία;







- Χωρίς προηγούμενη βιοψία ή με αρνητική βιοψία και
  1. Τουλάχιστον 10 ιστοτεμάχια
  2. T2WI και DWI
  3. PIRADS v1 (και Likert)
  4. GS >=7 (csPCa)



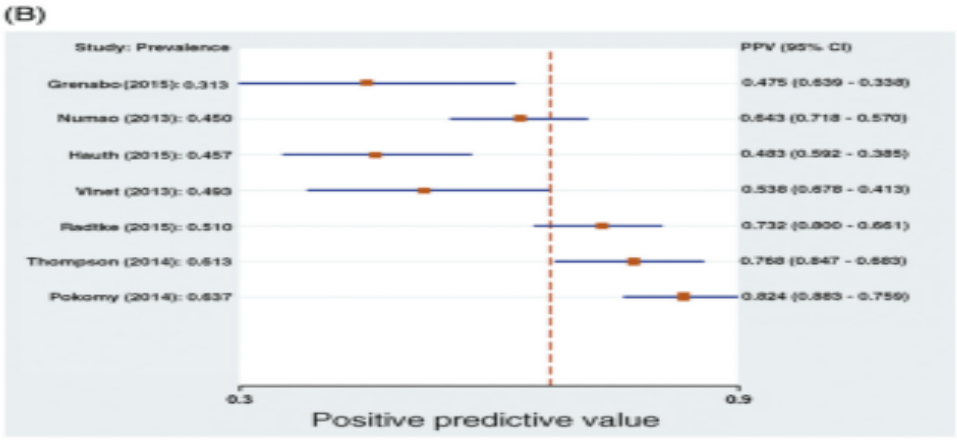


Table 3 – Reported ranges of negative predictive values for prebiopsy multiparametric MRI

	Nb of studies	Median PCa prevalence	Median mpMRI NPV	Nb of studies	Median csPCa prevalence	Median mpMRI NPV
Biopsy-naïve patients	8	51.4% (45.5–56.7)	69.9% (64.2–78)	1	35.8% (NA)	80.4% (NA)
Repeat biopsy	14	42% (35.1–52.6)	82.6% (75.5–93.1)	3	24.4% (19.1–32.8)	88.2% (87.9–92.3)
TRUS-guided biopsy	36	49.7% (34.3–57.7)	84.6% (68.6–92.8)	4	28.1% (21.7–36.5)	89.3% (82.9–92.4)
TTP biopsy	4	53.8% (47.5–57.8)	73.6% (72–78.7)	2	31.6% (30.5–32.8)	92% (89.9–94)
Biopsy with ≤16 cores	28	48.7% (39.2–54.8)	81.9% (66.8–89.3)	5	28.1% (21.8–36.5)	89.3% (82.9–92.4)
Biopsy with >16 cores	5	56.6% (51–61.3)	81.1% (73.1–92.2)	2	31.7% (30.5–32.8)	92% (89.9–93.9)
Positive DRE	1	73.9% (NA)	56% (NA)	0	–	–
Negative DRE	6	36% (34.6–46.8)	82.7% (74.2–93.1)	0	–	–
Endorectal coil	17	41.7% (30.6–55.9)	92.8% (79.3–95.4)	1	31.7% (NA)	91% (NA)
No endorectal coil	22	50.9% (41.7–56.1)	77.7% (69.5–86.6)	7	34% (26.9–46.1%)	87.9% (78.2–92.1)

PCa = prostate cancer; csPCa = clinically significant prostate cancer; NPV = negative predictive value; TRUS = transrectal ultrasound; TTP = template transperineal; DRE = digital rectal examination; PSA = prostate-specific antigen; NA = not applicable; mpMRI = multiparametric magnetic resonance imaging; MRI = magnetic resonance imaging; Nb = number.
Intervals in parenthesis are interquartile ranges.

- ✓ Η mpMRI μπορεί να ανιχνεύσει τον επιθετικό καρκίνο του προστάτη με μεγάλη ευαισθησία
- ✓ Απαιτείται να ανευρεθεί ένας κοινώς αποδεκτός τρόπος να εκτιμηθεί η πιθανότητα ύπαρξης κλινικά σημαντικού Pca πριν την βιοψία
- ✓ Μετά την βιοψία απαιτείται κοινώς αποδεκτός ορισμός του κλινικά σημαντικού Pca
- ✓ Αύξηση ειδικότητας της εξέτασης μέσω βελτίωσης της αναφοράς των αποτελεσμάτων

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European Association of Urology

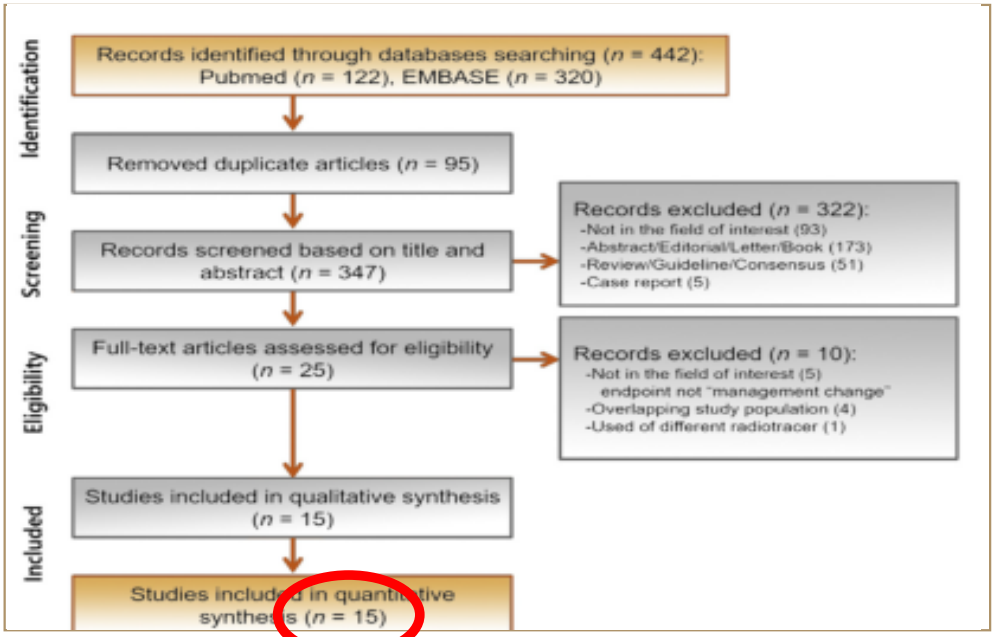
Review – Prostate Cancer

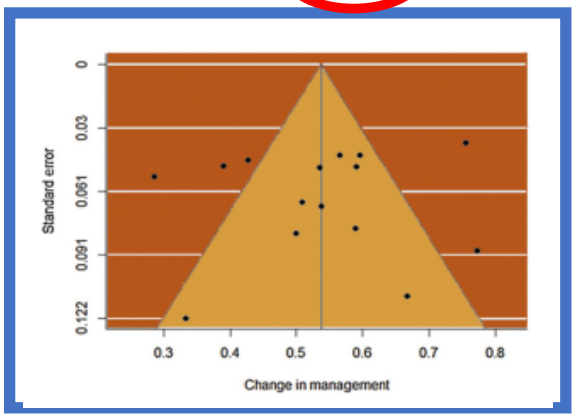
Impact of ^{68}Ga-PSMA PET on the Management of Patients with Prostate Cancer: A Systematic Review and Meta-anal

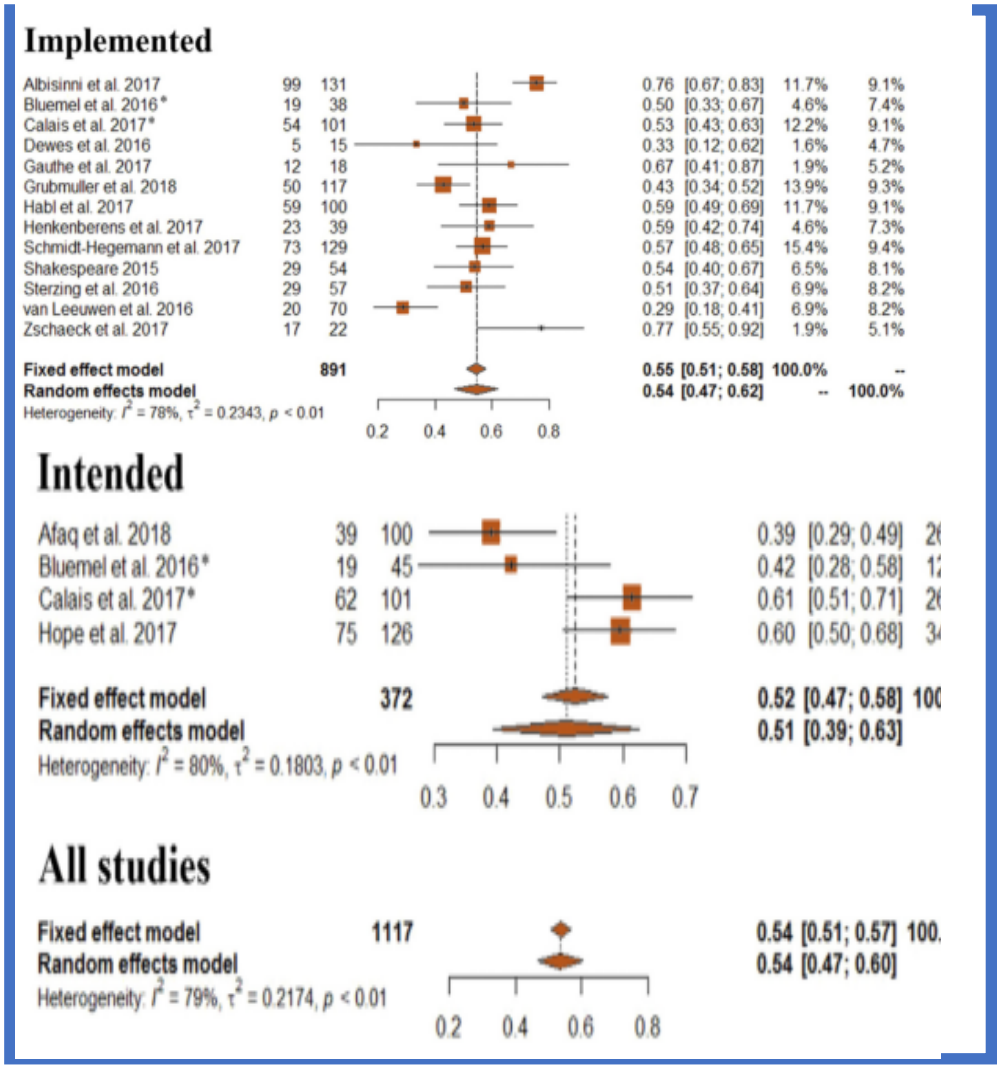
Sangwon Han [a], Sungmin Woo [b,1,*], Yeon Joo Kim [c], Chong Hyun Su

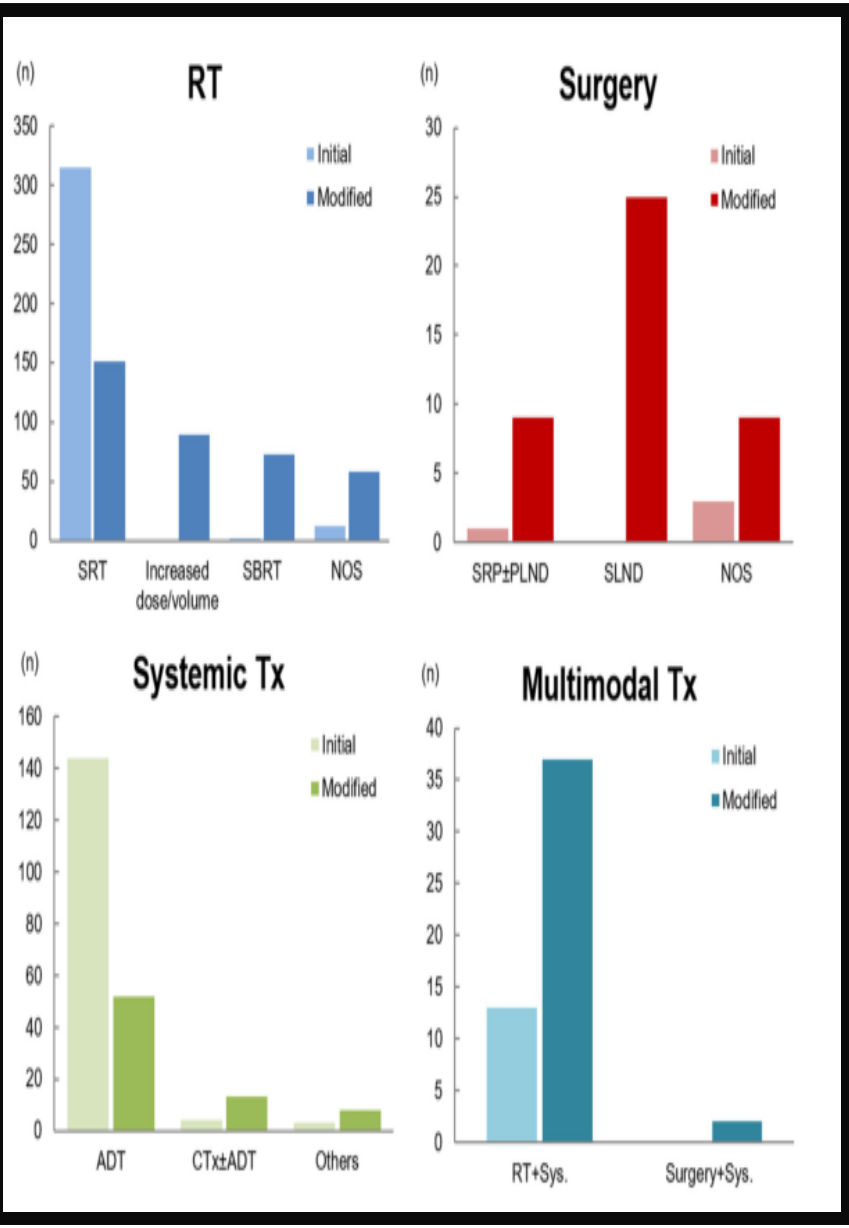
[a] Department of Nuclear Medicine, University of Ulsan College of Medicine, Asan Medical Center, 86 Asanby
Korea; [b] Department of Radiology, Seoul National University College of Medicine, 101 Daehak-ro, Jongno-g
Radiation Oncology, University of Ulsan College of Medicine, Asan Medical Center, 86 Asanbyeongwon
[d] Department of Radiology and Research Institute of Radiology, University of Ulsan College of Medicine, A
Songpa-Gu, Seoul, Republic of Korea

•Υπάρχουν νέες τεχνικές απεικόνισης που μπορούν να βοηθήσουν στην καλύτερη αντιμετώπιση του Pca;


Identification
Records identified through databases searching (n = 442): Pubmed (n = 122), EMBASE (n = 320)
Removed duplicate articles (n = 95)
Screening
Records screened based on title and abstract (n = 347)
Records excluded (n = 322):
-Not in the field of interest (93)
-Abstract/Editorial/Letter/Book (173)
-Review/Guideline/Consensus (51)
-Case report (5)
Eligibility
Full-text articles assessed for eligibility (n = 25)
Records excluded (n = 10):
-Not in the field of interest (5)
endpoint not "management change"
-Overlapping study population (4)
-Used of different radiotracer (1)
Included
Studies included in qualitative synthesis (n = 15)
Studies included in quantitative synthesis (n = 15)


Standard error
0
0.03
0.061
0.091
0.122
0.3
0.4
0.5
0.6
0.7
0.8
Change in management


Implemented
Albisinni et al. 2017 99 131 0.76 [0.67; 0.83] 11.7% 9.1%
Bluemel et al. 2016* 19 38 0.50 [0.33; 0.67] 4.6% 7.4%
Calais et al. 2017* 54 101 0.53 [0.43; 0.63] 12.2% 9.1%
Dewes et al. 2016 5 15 0.33 [0.12; 0.62] 1.6% 4.7%
Gauthe et al. 2017 12 18 0.67 [0.41; 0.87] 1.9% 5.2%
Grubmuller et al. 2018 50 117 0.43 [0.34; 0.52] 13.9% 9.3%
Habl et al. 2017 59 100 0.59 [0.49; 0.69] 11.7% 9.1%
Henkenberens et al. 2017 23 39 0.59 [0.42; 0.74] 4.6% 7.3%
Schmidt-Hegemann et al. 2017 73 129 0.57 [0.48; 0.65] 15.4% 9.4%
Shakespeare 2015 29 54 0.54 [0.40; 0.67] 6.5% 8.1%
Sterzing et al. 2016 29 57 0.51 [0.37; 0.64] 6.9% 8.2%
van Leeuwen et al. 2016 20 70 0.29 [0.18; 0.41] 6.9% 8.2%
Zschaeck et al. 2017 17 22 0.77 [0.55; 0.92] 1.9% 5.1%
Fixed effect model 891 0.55 [0.51; 0.58] 100.0% --
Random effects model 0.54 [0.47; 0.62] -- 100.0%
Heterogeneity: I^2 = 78%, τ^2 = 0.2343, p < 0.01
0.2
0.4
0.6
0.8
Intended
Afaq et al. 2018 39 100 0.39 [0.29; 0.49] 2
Bluemel et al. 2016* 19 45 0.42 [0.28; 0.58] 1
Calais et al. 2017* 62 101 0.61 [0.51; 0.71] 2
Hope et al. 2017 75 126 0.60 [0.50; 0.68] 3
Fixed effect model 372 0.52 [0.47; 0.58] 10
Random effects model 0.51 [0.39; 0.63]
Heterogeneity: I^2 = 80%, τ^2 = 0.1803, p < 0.01
0.3
0.4
0.5
0.6
0.7
All studies
Fixed effect model 1117 0.54 [0.51; 0.57] 100.
Random effects model 0.54 [0.47; 0.60]
Heterogeneity: I^2 = 79%, τ^2 = 0.2174, p < 0.01
0.2
0.4
0.6
0.8



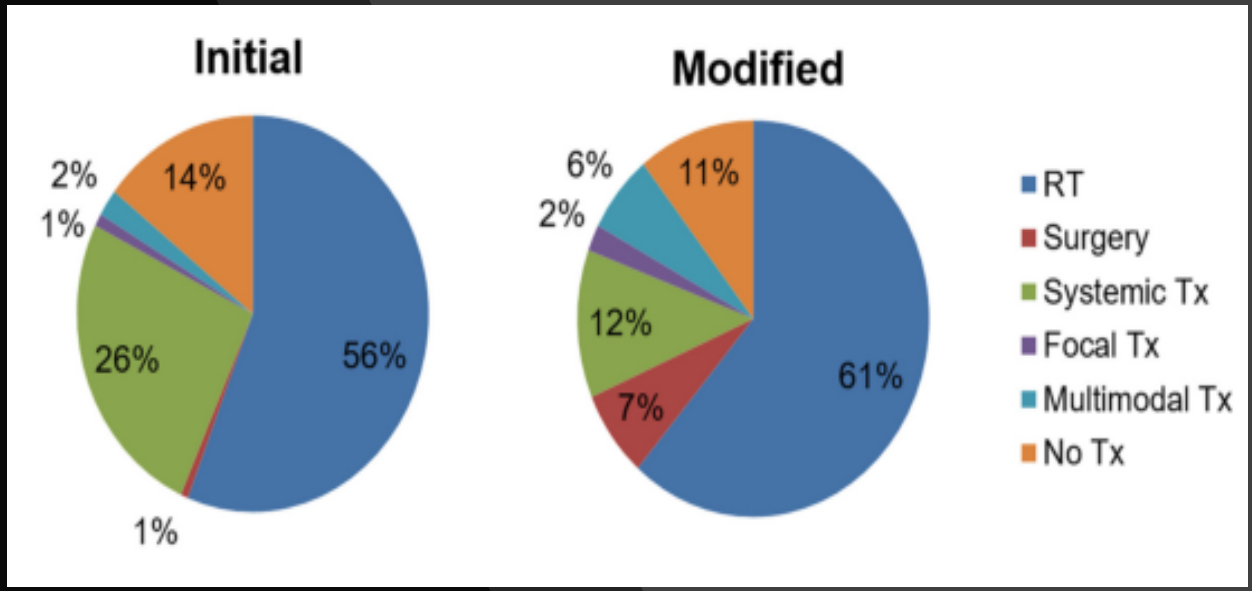


Table 4 – Results of meta-regression analyses for impact of ^{68}Ga-PSMA PET on management

Variable	Categories or cut-off	Regression coefficient	95% CI	*p* value
Study design	Prospective versus retrospective	−0.0156	−0.1744–0.1432	0.8474
Clinical setting	BCF versus primary staging + mixed population	−0.0474	−0.2210–0.1263	0.5928
Change type	Intended versus implemented	−0.0507	−0.2626–0.1612	0.6392
Responding entity	Referring physician versus multidisciplinary oncology committee	0.0176	−0.1422–0.1773	0.8294
D'Amico risk classification	High (%)	0.0013	−0.0015–0.0041	0.3529
	Intermediate + high (%)	0.0038	−0.0314–0.0389	0.8332
Gleason score	≥7 (%)	−0.0015	−0.0134–0.0105	0.8098
Patients on ADT (%)		−0.0013	−0.0061–0.0035	0.5877
PSA level at initial diagnosis (ng/ml)		0.0036	−0.0078–0.0149	0.5388
Pre-PET PSA level (ng/ml)		−0.0004	−0.0169–0.0160	0.9574
PSA doubling time (mo)		0.0303	−0.0247–0.0854	0.2802
PET positivity (%)		0.0055	0.0000–0.0110	0.0486

ADT = androgen deprivation therapy; BCF = biochemical failure; CI = confidence interval; ^{68}Ga-PSMA PET = ^{68}Gallium prostate-specific membrane antigen positron emission tomography; PET = positron emission tomography; PSA = prostate-specific antigen; PSMA = prostate-specific membrane antigen.

Στο ½ των ασθενών τροποποιήθηκε η απόφαση

>95% των ασθενών ήταν ενδιαμέσου και υψηλού ρίσκου

Οι περισσότεροι που μελετήθηκαν ήταν σε βιοχημική υποτροπή

Δεν μπορεί να γενικευτεί σε αρχική διάγνωση (υπάρχουν δεδομένα)

Δεν είναι σαφές αν η αλλαγή στην αντιμετώπιση οδήγησε σε βελτιωμένα αποτελέσματα ή πρόγνωση

JAMA | Original Investigation

Radical Prostatectomy, External Beam Radiotherapy, or External Beam Radiotherapy With Brachytherapy Boost and Disease Progression and Mortality in Patients With Gleason Score 9-10 Prostate Cancer

Amar U. Kishan, MD; Ryan R. Cook, MSPH; Jay P. Ciezki, MD; Ashley E. Ross, MD, PhD; Mark M. Pomerantz, MD; Paul L. Nguyen, MD; Talha Shaikh, MD; Phuoc T. Tran, MD, PhD; Kiri A. Sandler, MD; Richard G. Stock, MD; Gregory S. Merrick, MD; D. Jeffrey Demanes, MD; Daniel E. Spratt, MD; Eyad I. Abu-Isa, MD; Trude B. Wedde, MD; Wolfgang Lilleby, MD, PhD; Daniel J. Krauss, MD; Grace K. Shaw, BA; Ridwan Alam, MPH; Chandana A. Reddy, MS; Andrew J. Stephenson, MD; Eric A. Klein, MD; Daniel Y. Song, MD; Jeffrey J. Tosoian, MD; John V. Hegde, MD; Sun Mi Yoo, MD, MPH; Ryan Fiano, MPH; Anthony V. D'Amico, MD, PhD; Nicholas G. Nickols, MD, PhD; William J. Aronson, MD; Ahmad Sadeghi, MD; Stephen Greco, MD; Curtiland Deville, MD; Todd McNutt, PhD; Theodore L. DeWeese, MD; Robert E. Reiter, MD; Johnathan W. Said, MD; Michael L. Steinberg, MD; Eric M. Horwitz, MD; Patrick A. Kupelian, MD; Christopher R. King, MD, PhD

Ποια θεραπεία θα ωφελήσει τελικά την συγκεκριμένη κατηγορία ασθενών ;

Clinical tumor stage						
1c	327 (51.2)	212 (28.9)	148 (33.9)			
2a	138 (21.8)	137 (18.7)	63 (14.4)			
2b	72 (11.3)	111 (15.1)	88 (20.2)			
2c	20 (3.1)	52 (7.1)	44 (10.1)	<.001	<.001	<.001
3a	36 (5.6)	103 (14.0)	63 (14.4)			
3b	21 (3.3)	75 (10.2)	17 (3.9)			
4	24 (3.8)	44 (6.0)	3 (3.0)			

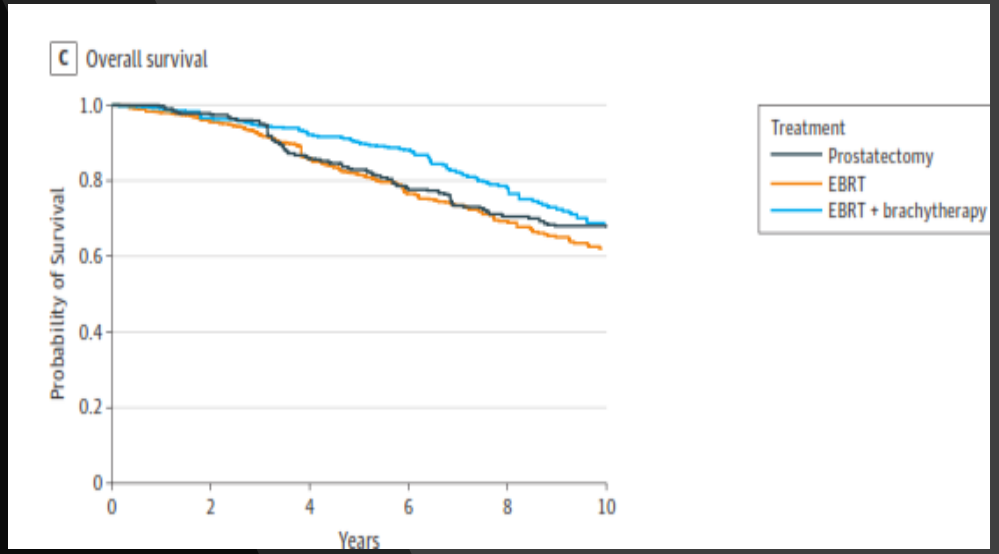
	Unadjusted, No. (%)			*P* Value[a]		
	Prostatectomy (n=639)	EBRT (n=734)	EBRT+BT (n=436)	EBRT vs Prostatectomy	EBRT+BT vs Prostatectomy	EBRT+BT vs EBRT
Clinical Characteristics						
Age, mean (median) [range], y	61.0 (61.2) [39-77.1]	67.7 (68) [39.7-98]	67.5 (68.0) [48-83]	< .001	<.001	>.52
Initial PSA level, mean (median) [range], ng/mL	11.26 (6.9) [0.4-378.6]	21.5 (9.93) [0.4-525.5]	14.8 (9.6) [0.1-273.5]	<.001	<.001	<.001
Biopsy Gleason score						
9	613 (95.9)	686 (93.5)	398 (91.3)	<.001	<.001	>.15
10	26 (4.1)	48 (6.5)	38 (8.7)			

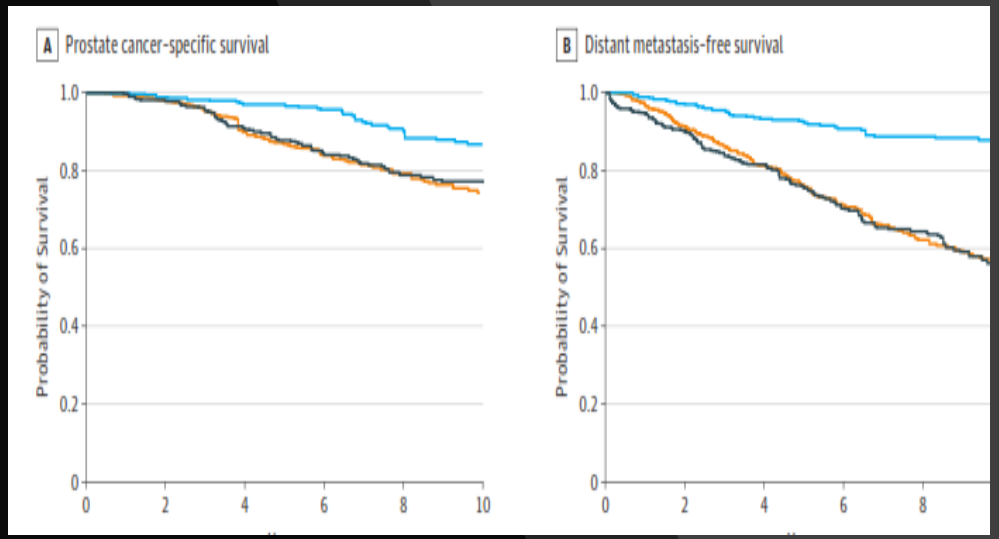
Χαμηλότερο PSA, λιγότεροι ασθενείς με GS 10 και χαμηλότερο T για την ομάδα της RP

- EBRT+BT δείχνει καλύτερα αποτελέσματα σε
  - Prostate Cancer Survival
  - Distant Metastasis free survival
- Αλλά όχι όσο αν αφορά την Συνολική Επιβίωση
- Δεν αποδεικνύεται υπεροχή της RP έναντι της EBRT ακόμα και σε εντοπισμένη νόσο
- Μικρότερα ποσοστά salvage θεραπείας στην EBRT και EBRT+BT (η ADT δεν επέδρασε στα τελικά αποτελέσματα)

Table 5. Competing Risks Regression Model of Prostate Cancer-Specific Mortality, Treating Other-Cause Mortality as a Competing Risk

Model and Parameter	Subdistribution Hazard Ratio (95% CI)	*P* Value
Unadjusted		
EBRT vs radical prostatectomy	1.13 (0.98-1.30)	.10
EBRT+BT vs radical prostatectomy	0.39 (0.20-0.76)	.005
EBRT+BT vs EBRT	0.34 (0.18-0.67)	.002
Propensity score adjusted[a]		
EBRT vs radical prostatectomy	1.05 (0.88-1.24)	.61
EBRT+BT vs radical prostatectomy	0.38 (0.19-0.73)	.004
EBRT+BT vs EBRT	0.36 (0.18-0.70)	.003





- Αναδρομική μελέτη
  - Πιθανό bias όσο αν αφορά την συνοσηρότητα (αντοχή στις επιθετικές θεραπείες)
  - Μη γνωστά στοιχεία για την τοξικότητα των θεραπειών
  - Χαμηλό follow up (μόλις 4 χρόνια για την ριζική 6 για την EBRT)
  - Δυσκολία στην συλλογή δεδομένων λόγω των λίγων κέντρων που προσφέρουν BT

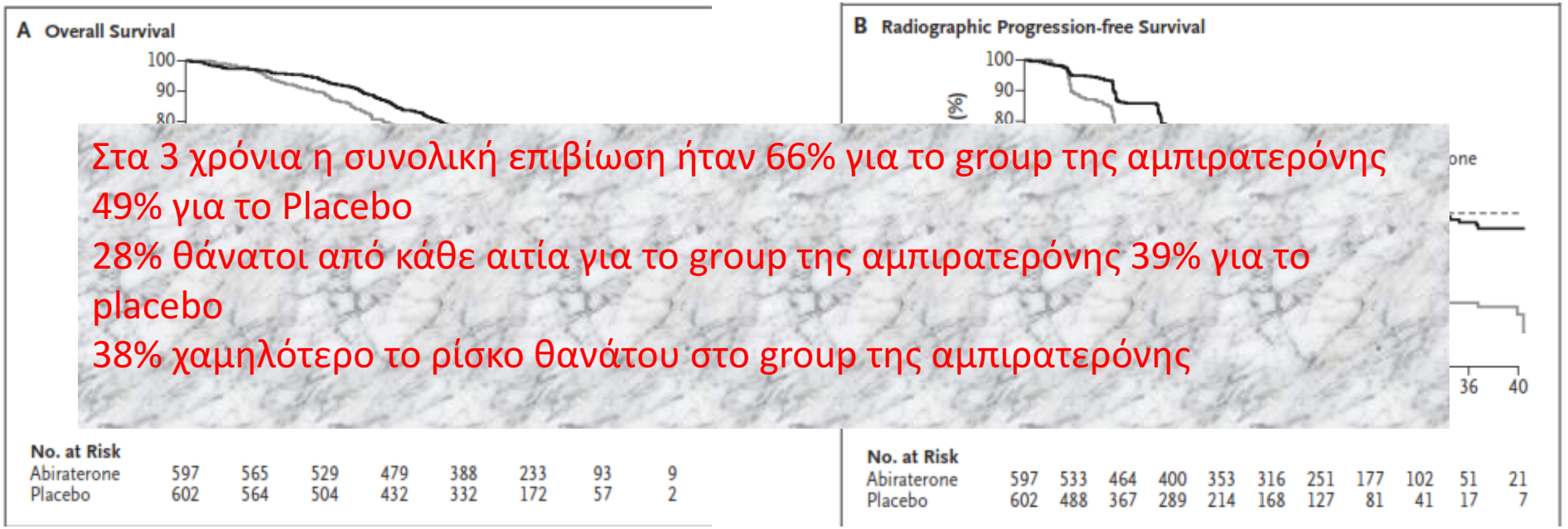
- Οι ασθενείς με Gleason Score 9-10 φαίνεται να ευνοούνται περισσότεροο από τον συνδυασμό ΑΚΘ-βραχυθεραπείας
- Καμιά όμως διαφορά όσο αν αφορά την ολική επιβίωση
- Δεν φαίνεται η ριζική προστατεκτομή να υπερέχει τις ΑΚΘ ακόμα και σε εντοπισμένη νόσο
- Προσοχή όμως στις επιπλοκές και στους σημαντικούς περιορισμούς

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

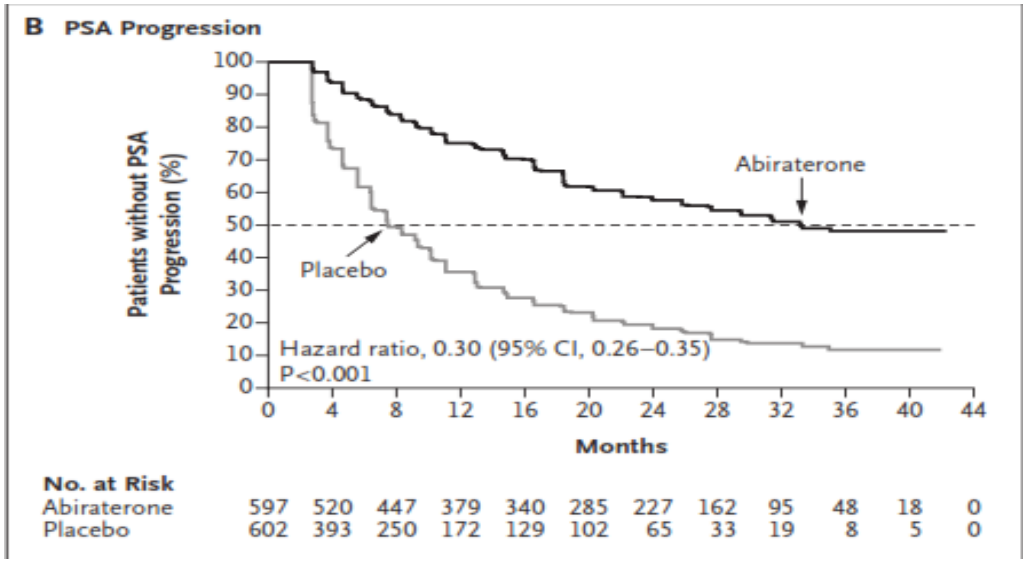
Abiraterone plus Prednisone in Metastatic, Castration-Sensitive Prostate Cancer

Karim Fizazi, M.D., Ph.D., NamPhuong Tran, M.D., Luis Fein, M.D., Nobuaki Matsubara, M.D., Alfredo Rodriguez-Antolin, M.D., Ph.D., Boris Y. Alekseev, M.D., Mustafa Özgüroğlu, M.D., Dingwei Ye, M.D., Susan Feyerabend, M.D., Andrew Protheroe, M.D., Ph.D., Peter De Porre, M.D., Thian Kheoh, Ph.D., Youn C. Park, Ph.D., Mary B. Todd, D.O., and Kim N. Chi, M.D., for the LATITUDE Investigators*



Στα 3 χρόνια η συνολική επιβίωση ήταν 66% για το group της αμπιρατερόνης
49% για το Placebo
28% θάνατοι από κάθε αιτία για το group της αμπιρατερόνης 39% για το placebo
38% χαμηλότερο το ρίσκο θανάτου στο group της αμπιρατερόνης

Προσοχή στο median



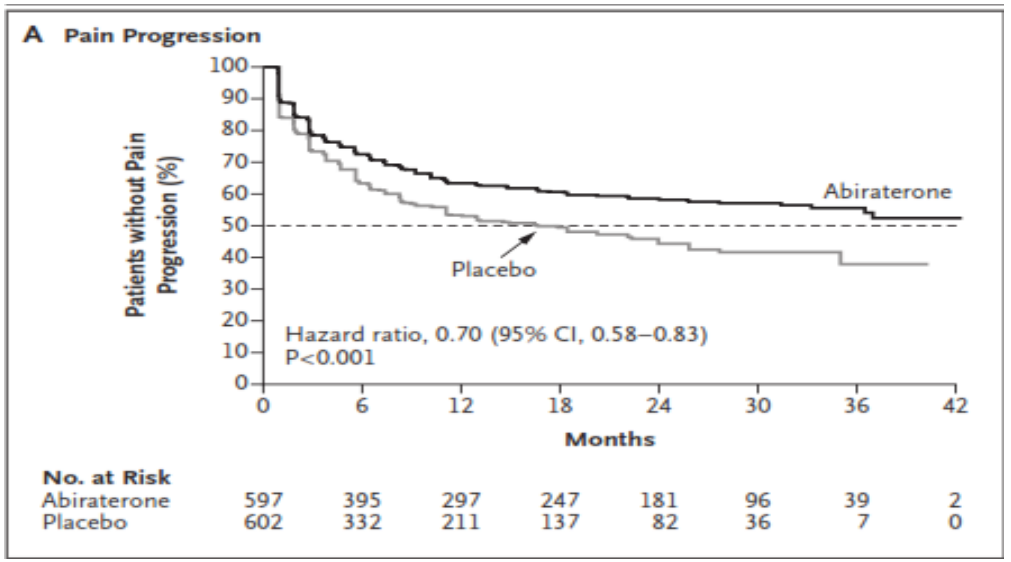


Table 1. Prespecified Secondary and Exploratory Efficacy End Points.*

End Point	Abiraterone Group (N=597)	Placebo Group (N=602)	Hazard Ratio (95% CI)	P Value†
Secondary end points				
Median time to pain progression (mo)	NR	16.6	0.70 (0.58–0.83)	<0.001
Median time to PSA progression (mo)	33.2	7.4	0.30 (0.26–0.35)	<0.001
Median time to next symptomatic skeletal event (mo)	NR	NR	0.70 (0.54–0.92)	0.009
Median time to chemotherapy (mo)	NR	38.9	0.44 (0.35–0.56)	<0.001
Median time to subsequent prostate cancer therapy (mo)	NR	21.6	0.42 (0.35–0.50)	<0.001
Exploratory end point				
Patients with a PSA response (%)‡	91	67	1.36 (1.28–1.45)	<0.001

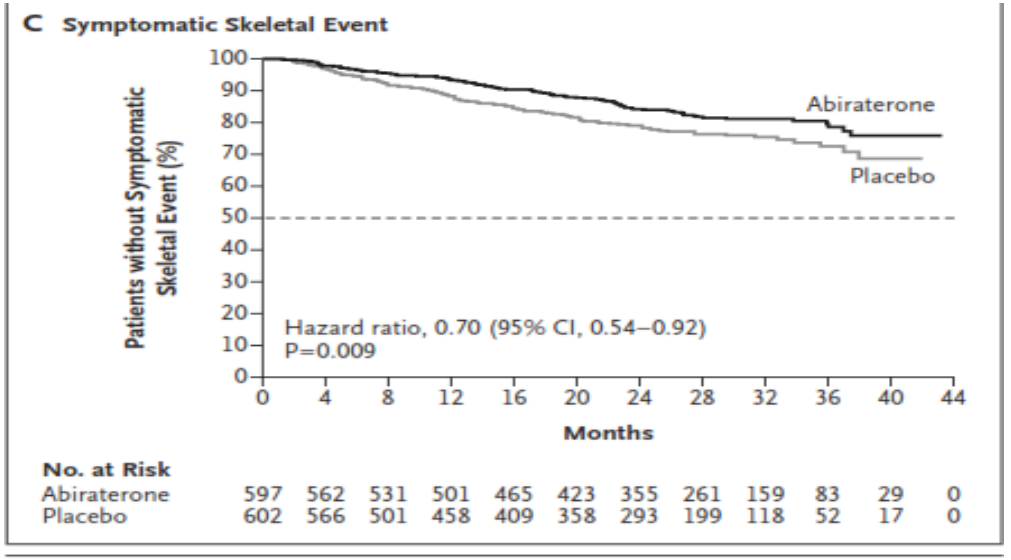


Table 2. Adverse Events.*

Adverse Event	Abiraterone Group (N=597)			Placebo Group (N=602)		
	number of patients (percent)					
Any adverse event	558 (93)			557 (93)		
Grade 3 or 4 adverse event	374 (63)			287 (48)		
Any serious adverse event	165 (28)			146 (24)		
Any adverse event leading to treatment discontinuation	73 (12)			61 (10)		
Adverse event leading to death	28 (5)			24 (4)		
	All Grades	Grade 3	Grade 4	All Grades	Grade 3	Grade 4
Graded adverse events†						
Hypertension	219 (37)	121 (20)	0	133 (22)	59 (10)	1 (<1)
Hypokalemia	122 (20)	57 (10)	5 (1)	22 (4)	7 (1)	1 (<1)
ALT increased	98 (16)	31 (5)	2 (<1)	77 (13)	8 (1)	0
Hyperglycemia	75 (13)	26 (4)	1 (<1)	68 (11)	18 (3)	0
AST increased	87 (15)	25 (4)	1 (<1)	68 (11)	9 (1)	0
Bone pain	74 (12)	20 (3)	0	88 (15)	17 (3)	0
Cardiac disorder						
Any	74 (12)	15 (3)	5 (1)	47 (8)	6 (1)	0
Atrial fibrillation	8 (1)	2 (<1)	0	2 (<1)	1 (<1)	0
Anemia	54 (9)	12 (2)	3 (1)	85 (14)	26 (4)	1 (<1)
Back pain	110 (18)	14 (2)	0	123 (20)	19 (3)	0
Fatigue	77 (13)	10 (2)	0	86 (14)	14 (2)	0
Spinal-cord compression	14 (2)	12 (2)	0	12 (2)	7 (1)	3 (<1)

Supported by Janssen Research and Development.

Disclosure forms provided by the authors are available with the full text of this article at NEJM.org.

We thank the patients who volunteered to participate in this trial and the investigators and trial staff who cared for them; Giri Sulur, Ph.D., Jason Martin, Ph.D., and Kris Deprince, M.D., for their clinical support; Arturo Molina, M.D., and Julie Larsen, Pharm.D., for their overall support and intellectual guidance; Justin Li, Ph.D., for trial-design support; Susan Li, Ph.D., for data-analysis support; and Ira Mills, Ph.D., of PAREXEL, for providing editorial assistance.

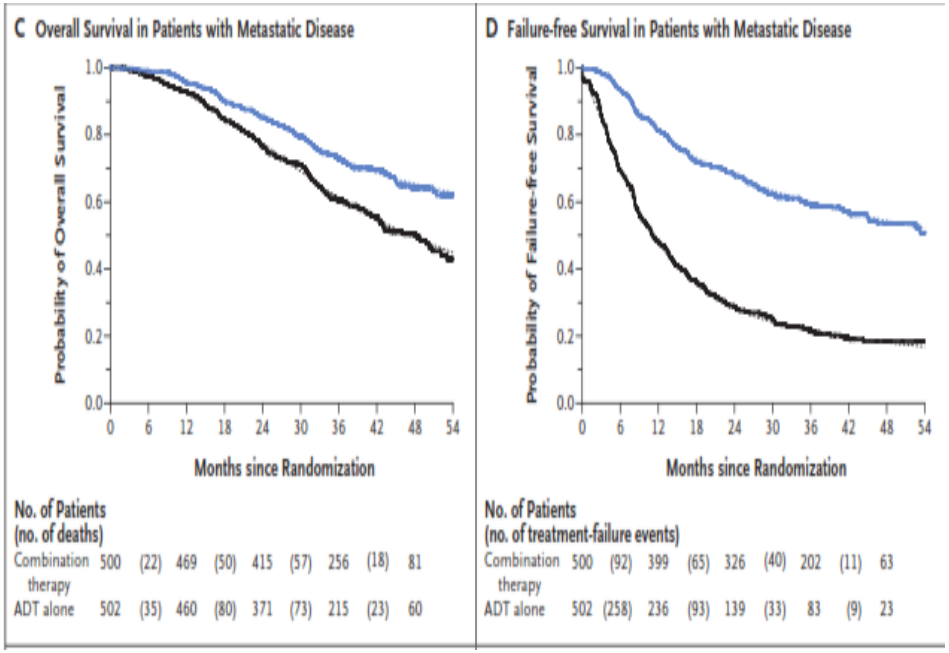
- ✓ Η προσθήκη αμπιρατερόνης και πρεδνιζόνης στον ανδρογονικό αποκλεισμό αυξάνει την ολική επιβίωση και τον χρόνο μέχρι την απεικονιστική πρόοδο της νόσου
- ✓ Τα παραπάνω στους ασθενείς που διαγιγνώσκονται για πρώτη φορά με μεταστατικό αλλά ευνουχο-ευαίσθητο καρκίνο του προστάτη
- ✓ Σαφής διαφορά στις επιπλοκές και μάλιστα στις σοβαρές επιπλοκές (Grade 4-5)

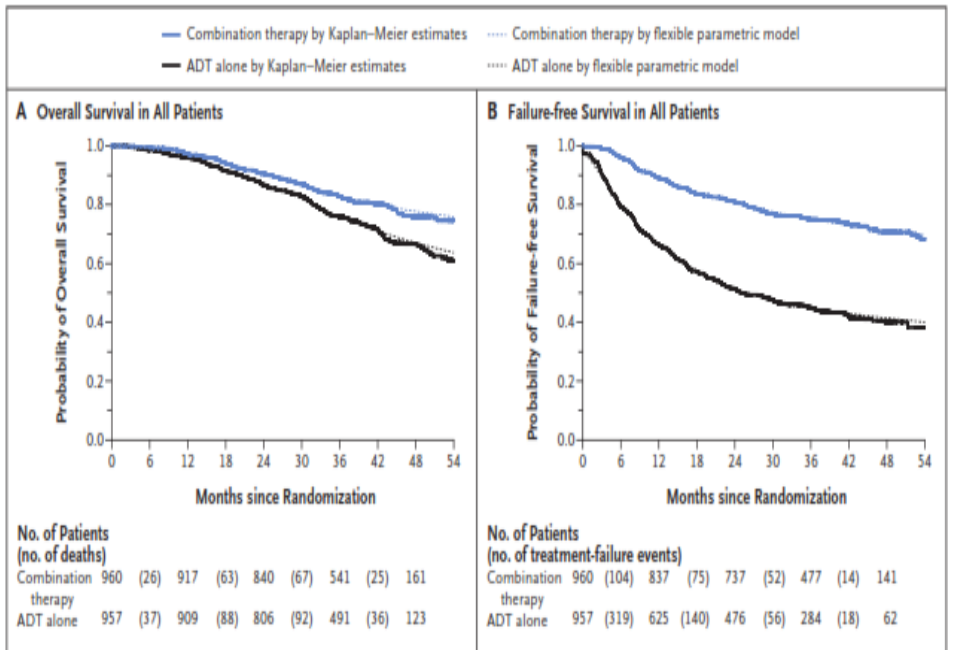
The NEW ENGLAND JOURNAL of MEDICINE

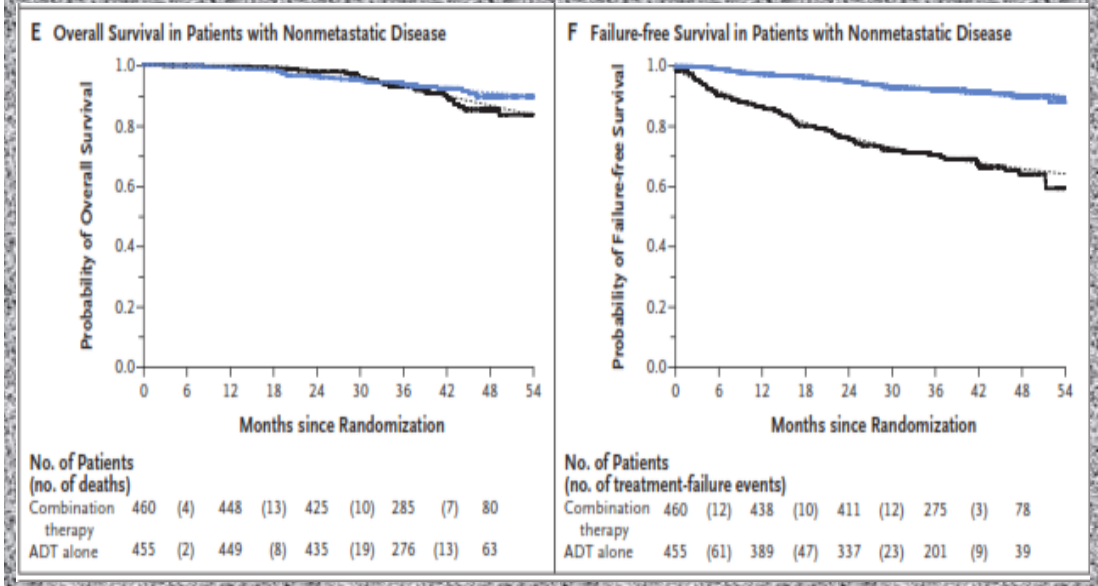
ORIGINAL ARTICLE

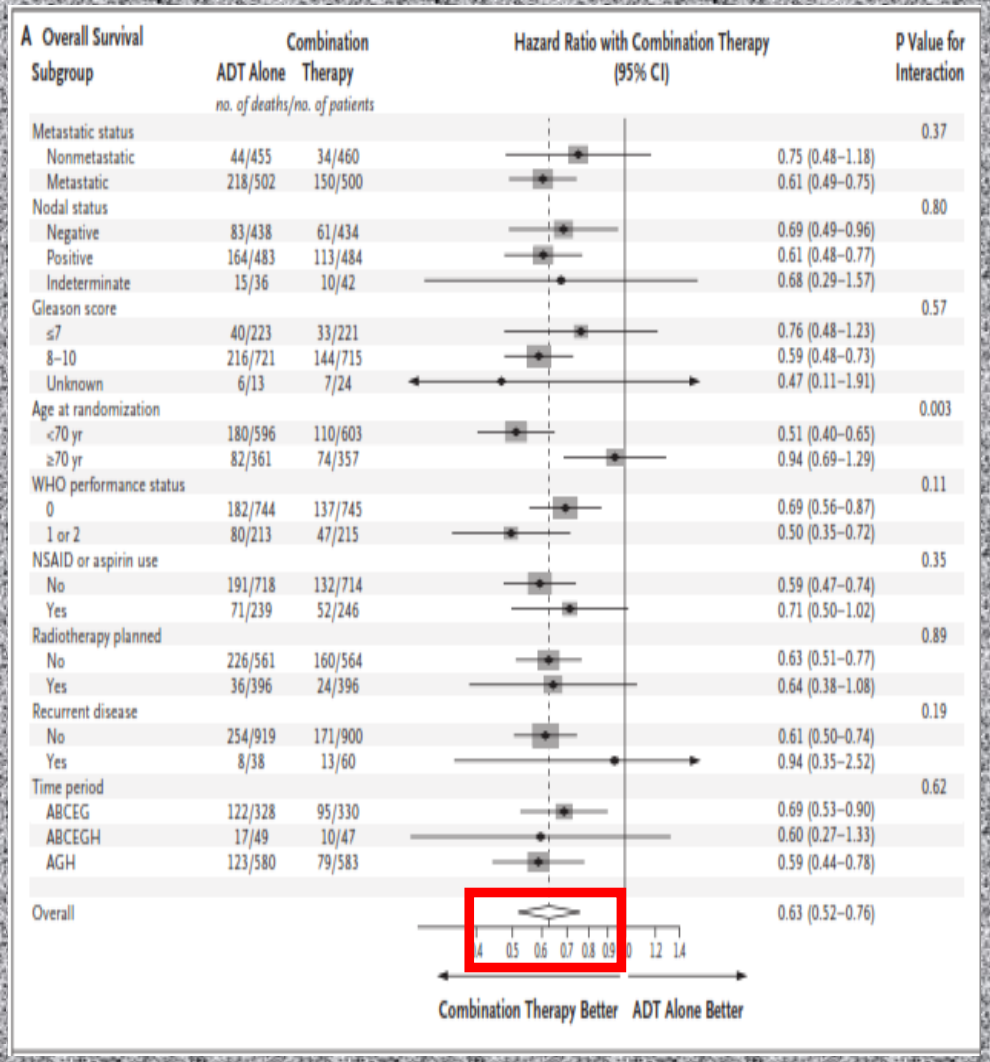
Abiraterone for Prostate Cancer Not Previously Treated with Hormone Therapy

N.D. James, J.S. de Bono, M.R. Spears, N.W. Clarke, M.D. Mason, D.P. Dearnaley, A.W.S. Ritchie, C.L. Amos, C. Gilson, R.J. Jones, D. Matheson, R. Millman, G. Attard, S. Chowdhury, W.R. Cross, S. Gillessen, C.C. Parker, J.M. Russell, D.R. Berthold, C. Brawley, F. Adab, S. Aung, A.J. Birtle, J. Bowen, S. Brock, P. Chakraborti, C. Ferguson, J. Gale, E. Gray, M. Hingorani, P.J. Hoskin, J.F. Lester, Z.I. Malik, F. McKinna, N. McPhail, J. Money-Kyrle, J. O'Sullivan, O. Parikh, A. Protheroe, A. Robinson, N.N. Srihari, C. Thomas, J. Wagstaff, J. Wylie, A. Zarkar, M.K.B. Parmar, and M.R. Sydes, for the STAMPEDE Investigators*


C Overall Survival in Patients with Metastatic Disease
Probability of Overall Survival
1.0
0.8
0.6
0.4
0.2
0.0
0 6 12 18 24 30 36 42 48 54
Months since Randomization
No. of Patients
(no. of deaths)
Combination therapy 500 (22) 469 (50) 415 (57) 256 (18) 81
ADT alone 502 (35) 460 (80) 371 (73) 215 (23) 60
D Failure-free Survival in Patients with Metastatic Disease
Probability of Failure-free Survival
1.0
0.8
0.6
0.4
0.2
0.0
0 6 12 18 24 30 36 42 48 54
Months since Randomization
No. of Patients
(no. of treatment-failure events)
Combination therapy 500 (92) 399 (65) 326 (40) 202 (11) 63
ADT alone 502 (258) 236 (93) 139 (33) 83 (9) 23


Combination therapy by Kaplan–Meier estimates
Combination therapy by flexible parametric model
ADT alone by Kaplan–Meier estimates
ADT alone by flexible parametric model
A Overall Survival in All Patients
Probability of Overall Survival
1.0
0.8
0.6
0.4
0.2
0.0
0 6 12 18 24 30 36 42 48 54
Months since Randomization
No. of Patients
(no. of deaths)
Combination therapy 960 (26) 917 (63) 840 (67) 541 (25) 161
ADT alone 957 (37) 909 (88) 806 (92) 491 (36) 123
B Failure-free Survival in All Patients
Probability of Failure-free Survival
1.0
0.8
0.6
0.4
0.2
0.0
0 6 12 18 24 30 36 42 48 54
Months since Randomization
No. of Patients
(no. of treatment-failure events)
Combination therapy 960 (104) 837 (75) 737 (52) 477 (14) 141
ADT alone 957 (319) 625 (140) 476 (56) 284 (18) 62


E Overall Survival in Patients with Nonmetastatic Disease
Probability of Overall Survival
1.0
0.8
0.6
0.4
0.2
0.0
0 6 12 18 24 30 36 42 48 54
Months since Randomization
No. of Patients
(no. of deaths)
Combination therapy 460 (4) 448 (13) 425 (10) 285 (7) 80
ADT alone 455 (2) 449 (8) 435 (19) 276 (13) 63
F Failure-free Survival in Patients with Nonmetastatic Disease
Probability of Failure-free Survival
1.0
0.8
0.6
0.4
0.2
0.0
0 6 12 18 24 30 36 42 48 54
Months since Randomization
No. of Patients
(no. of treatment-failure events)
Combination therapy 460 (12) 438 (10) 411 (12) 275 (3) 78
ADT alone 455 (61) 389 (47) 337 (23) 201 (9) 39


A Overall Survival
Subgroup
ADT Alone
Combination Therapy
no. of deaths/no. of patients
Hazard Ratio with Combination Therapy (95% CI)
P Value for Interaction
Metastatic status 0.37
Nonmetastatic 44/455 34/460 0.75 (0.48–1.18)
Metastatic 218/502 150/500 0.61 (0.49–0.75)
Nodal status 0.80
Negative 83/438 61/434 0.69 (0.49–0.96)
Positive 164/483 113/484 0.61 (0.48–0.77)
Indeterminate 15/36 10/42 0.68 (0.29–1.57)
Gleason score 0.57
≤7 40/223 33/221 0.76 (0.48–1.23)
8–10 216/721 144/715 0.59 (0.48–0.73)
Unknown 6/13 7/24 0.47 (0.11–1.91)
Age at randomization 0.003
<70 yr 180/596 110/603 0.51 (0.40–0.65)
≥70 yr 82/361 74/357 0.94 (0.69–1.29)
WHO performance status 0.11
0 182/744 137/745 0.69 (0.56–0.87)
1 or 2 80/213 47/215 0.50 (0.35–0.72)
NSAID or aspirin use 0.35
No 191/718 132/714 0.59 (0.47–0.74)
Yes 71/239 52/246 0.71 (0.50–1.02)
Radiotherapy planned 0.89
No 226/561 160/564 0.63 (0.51–0.77)
Yes 36/396 24/396 0.64 (0.38–1.08)
Recurrent disease 0.19
No 254/919 171/900 0.61 (0.50–0.74)
Yes 8/38 13/60 0.94 (0.35–2.52)
Time period 0.62
ABCEG 122/328 95/330 0.69 (0.53–0.90)
ABCEGH 17/49 10/47 0.60 (0.27–1.33)
AGH 123/580 79/583 0.59 (0.44–0.78)
Overall 0.63 (0.52–0.76)
.4 0.5 0.6 0.7 0.8 0.9 1.0 1.2 1.4
Combination Therapy Better
ADT Alone Better

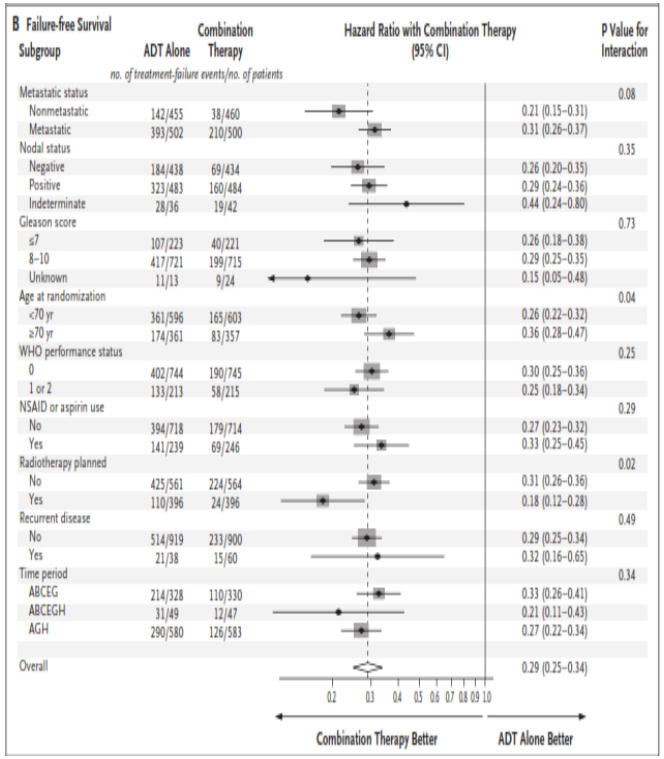
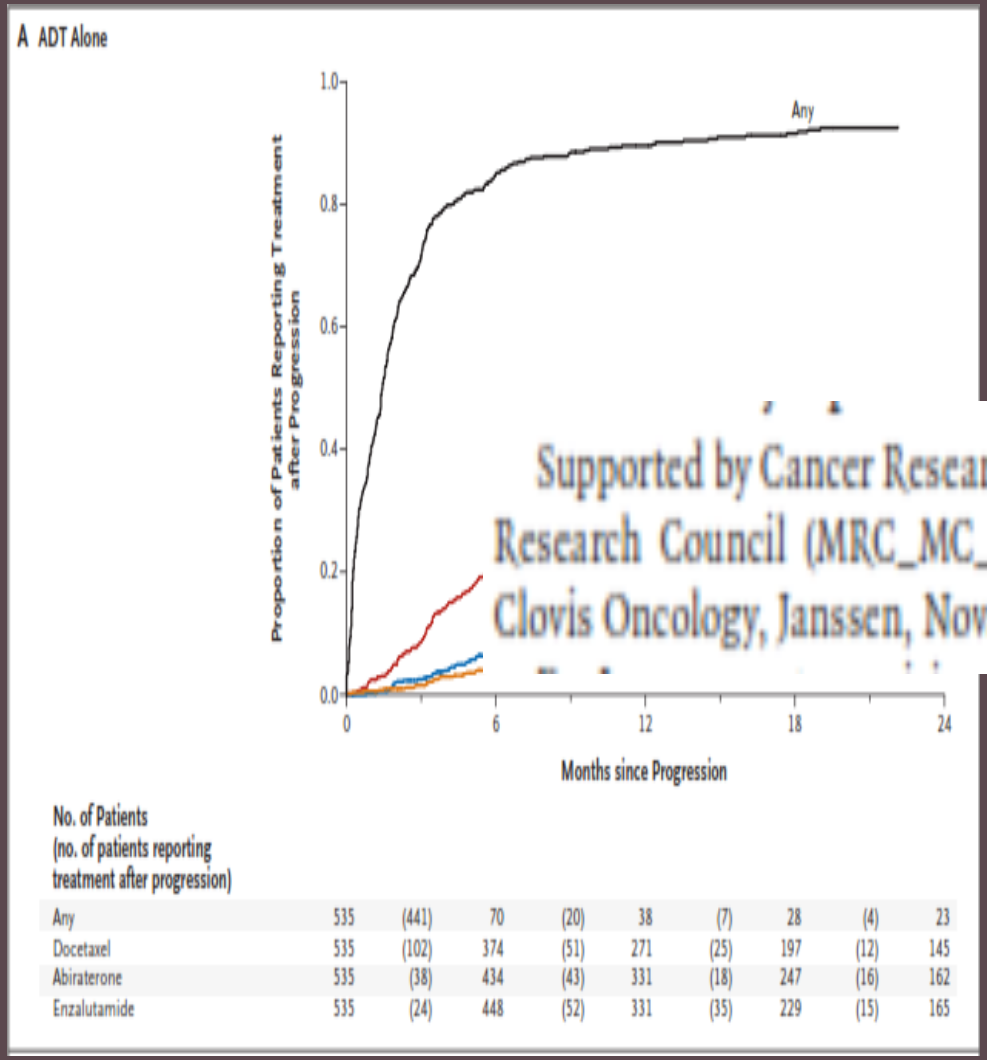


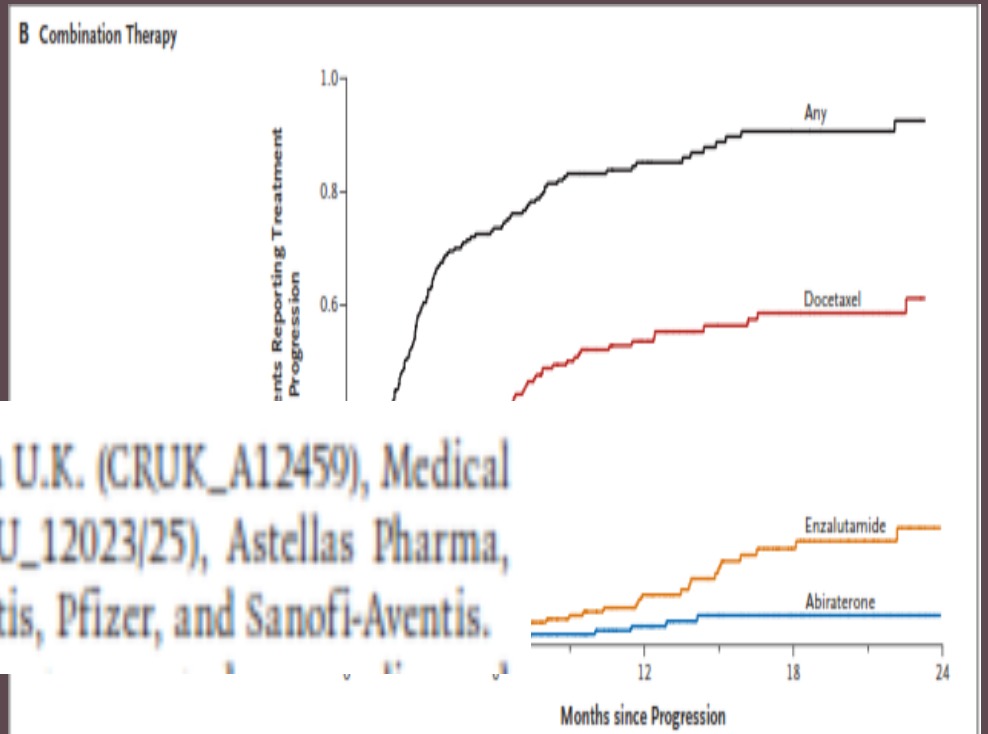
Table 2. Worst Adverse-Event Grade Reported during Entire Time in the Trial.*

Variable	ADT Alone	Combination Therapy
Safety population		
No. of patients	960	948
Patients with an adverse event — no. (%)		
Any grade	950 (99)	943 (99)
Grade 3–5	315 (33)	443 (47)
Grade 5 only†	3 (<1)	9 (1)
Grade 3–5 adverse events — no. (%)		
Endocrine disorders‡	133 (14)	129 (14)
Cardiovascular disorders	41 (4)	92 (10)
Hypertension	13 (1)	44 (5)
Myocardial infarction	9 (1)	10 (1)
Cardiac dysrhythmia	2 (<1)	14 (1)
Musculoskeletal disorders	46 (5)	68 (7)
Gastrointestinal disorders	40 (4)	49 (5)
Hepatic disorders	12 (1)	70 (7)
Increased ALT level	4 (<1)	53 (6)
Increased AST level	2 (<1)	10 (1)
General disorders	29 (3)	45 (5)
Fatigue	15 (2)	21 (2)
Edema	0	5 (1)
Respiratory disorders	23 (2)	44 (5)
Dyspnea	7 (1)	18 (2)
Laboratory abnormalities	21 (2)	34 (4)
Hypokalemia	3 (<1)	12 (1)

Το ποσοστό επιβίωσης ελεύθερο υποτροπής (στα 3 χρόνια) ήταν 75% για τον συνδυασμό και 45% για την ADT



No. of Patients (no. of patients reporting treatment after progression)									
Any	535	(441)	70	(20)	38	(7)	28	(4)	23
Docetaxel	535	(102)	374	(51)	271	(25)	197	(12)	145
Abiraterone	535	(38)	434	(43)	331	(18)	247	(16)	162
Enzalutamide	535	(24)	448	(52)	331	(35)	229	(15)	165



No. of Patients (no. of patients reporting treatment after progression)									
Any	248	(168)	51	(21)	21	(6)	9	(1)	2
Docetaxel	248	(83)	110	(25)	58	(5)	32	(1)	13
Abiraterone	248	(3)	179	(3)	122	(2)	71	(0)	32
Enzalutamide	248	(5)	179	(10)	116	(8)	62	(2)	25

Figure 3. Time until the Initiation of Second-Line Treatment after First Event of Radiologic, Clinical, or PSA Progression.

Supported by Cancer Research U.K. (CRUK_A12459), Medical Research Council (MRC_MC_UU_12023/25), Astellas Pharma, Clovis Oncology, Janssen, Novartis, Pfizer, and Sanofi-Aventis.

- ✓ Πληθυσμός ασθενών: τοπικά προχωρημένος ή μεταστατικός καρκίνος του προστάτη
- ✓ Θεραπευτικός χειρισμός: Ανδρογονικός αποκλεισμός με προσθήκη αμπιρατερόνης και πρεδνιζόνης
- ✓ Αποτελέσματα: Καλύτερα ποσοστά συνολικής επιβίωσης και επιβίωσης χωρίς απεικονιστική επιδείνωση
- ✓ Ο συνδυασμός παρουσίασε μικρότερο ποσοστό συμπτωματικών σκελετικών συμβαμάτων

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Systematic Review and Meta-Analysis

OPEN

Value of free/total prostate-specific antigen (f/t PSA) ratios for prostate cancer detection in patients with total serum prostate-specific antigen between 4 and 10ng/mL

A meta-analysis

Yan Huang, MD[a], Zhen-Zhen Li, MD[a], Ya-Liang Huang, MD[b], Hong-Jun Song, BD[c], You-Juan Wang, MD[a,*]

Πόσο χρήσιμος είναι στην καθημερινή μας πράξη;

- 15 μελέτες
- >6500 ασθενείς
- Χαμηλό ρίσκο για bias
- Cut off value κυμαίνεται

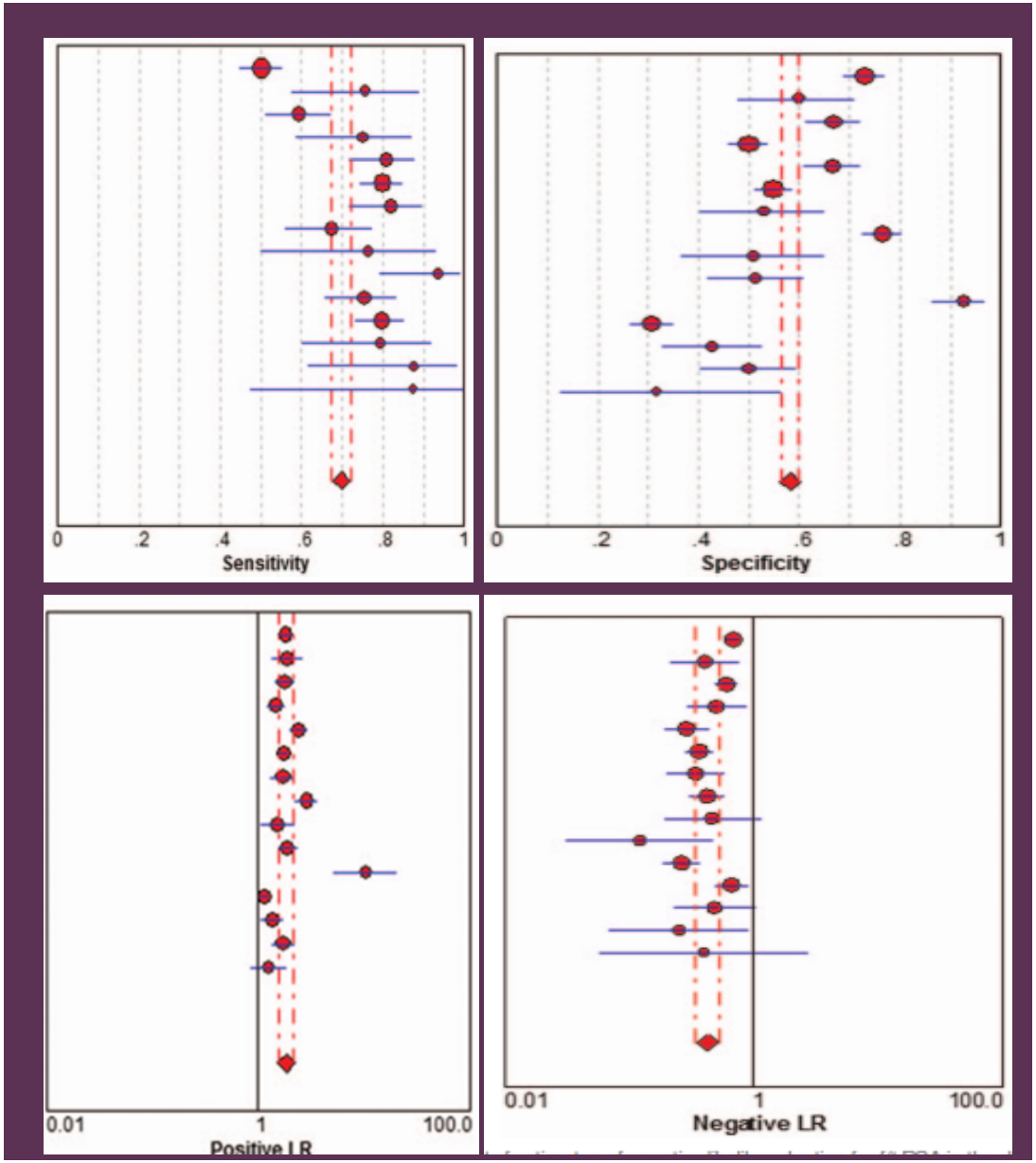
Table 1

Characteristics of studies included in the meta-analysis.

Author	Year	Sensitivity (%)	Specificity (%)	TP	FP	FN	TN	fPSA% cutoff	PSA level, ng/mL	Diagnosis standard
Takashi Kawahara	Japan (2015)	50.1	73.1	179	122	178	331	15%	4–10	Biopsy-confirmed diagnoses
Milkovic B	Serbia (2014)	76	60	25	30	8	45	20%	4–10	Biopsy-confirmed diagnoses
Bo Liu,	China (2014)	59.5	67	91	101	62	205	16%	4–10	Biopsy-confirmed diagnoses
Bulent Erol	Turkey (2014)	74	50	30	309	10	308	15%	4–10	Biopsy-confirmed diagnoses
C. Börgermann	Germany (2009)	80	66.7	80	94	19	189	20%	4–10	Biopsy-confirmed diagnoses
C. Börgermann	Germany (2009)	80	54.9	188	339	47	413	14%	4–10	Biopsy-confirmed diagnoses
Shingo Yamamoto	Japan (2008)	82	52.1	64	32	14	36	15%	4–10	Biopsy-confirmed diagnoses
Chi-Rei Yang	Taiwan (2005)	67.5	76.6	54	106	26	347	20%	4–10	Biopsy-confirmed diagnoses
Marcos D. Ferreira	Brazil (2005)	78.2	50	13	25	4	26	15%	4–10	Biopsy-confirmed diagnoses
Y Nakano	Japan (2005)	95	51.4	30	54	2	57	15%	4–10	Biopsy-confirmed diagnoses
Muhittin A. Serdar	Turkey (2002)	75	93	74	8	24	102	15%	4–10	Biopsy-confirmed diagnoses
M. Craig Miller	U.S. (2001)	79.5	30.8	142	304	36	134	25%	4–10	Biopsy-confirmed diagnoses
H Miyake	Japan (2001)	80	43	23	59	6	44	20%	4–10	Biopsy-confirmed diagnoses
Cem Özden Yeniyol	Turkey (2001)	87.5	50	14	57	2	57	18%	4–10	Biopsy-confirmed diagnoses
Bulbul MA	USA (2000)	87.5	31	7	13	1	6	20%	4–10	Biopsy-confirmed diagnoses

FN = false negative, FP = false positive, fPSA = free prostate-specific antigen, TN = true negative, TP = true positive.

- Ευαισθησία 0.7
- Ειδικότητα 0.58
- Λόγος θετικών (σε ασθενείς με την νόσο) προς θετικών (σε ασθενείς χωρίς την νόσο)= 4.81
- PLR =1.85 2πλάσια πιθανότητα οι ασθενείς με Pca να έχουν αυξημένο λόγο
- NLR= 0.42 42% πιθανότητα ασθενείς με Pca να έχουν χαμηλό λόγο



Ακατάλληλος δείκτης (για PSA 4-10)
Μη ύπαρξη standard cut off value

Table 3

Meta-regression of the diagnostic accuracy of f/t PSA.

Covariate	No. of studies	Coefficient	RDOR (95% CI)	P
Cutoff value				
0.15			.43)	.5392
<0.15 or>				
Ethnicity				
Caucasian			.76)	.4186
Asian				
Study design				
retrospectiv			.93)	.2514
prospective				
Publication yea				
After 2007			.56)	.2893
Before 200	8			

PSA = prostate-specific antigen, RDOR = relative DOR.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what's new?

Med Oncol (2017)34:133
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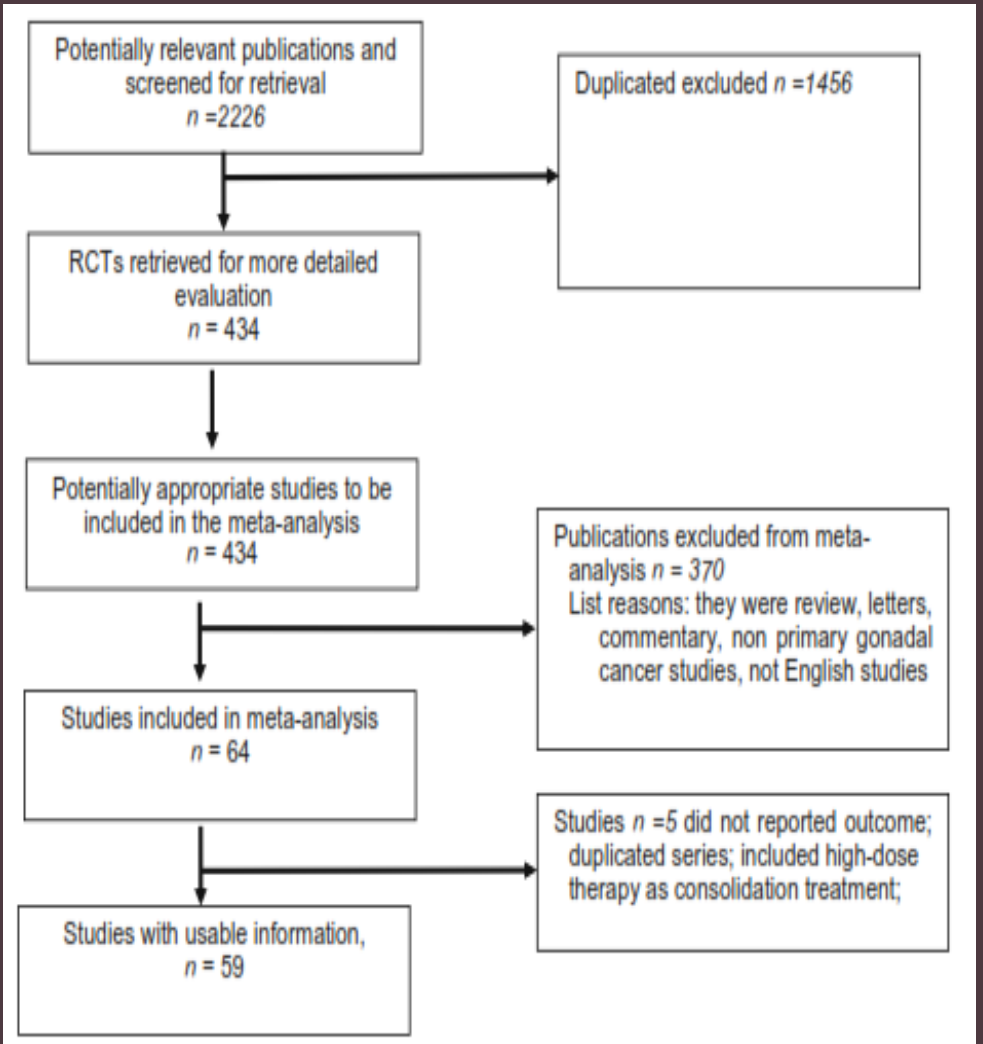
REVIEW ARTICLE

Salvage treatment for testicular cancer with standard- or high-dose chemotherapy: a systematic review of 59 studies

Fausto Petrelli[1] · Andrea Coinu[2] · Giovanni Rosti[3] · Paolo Pedrazzoli[3] · Sandro Barni[1]



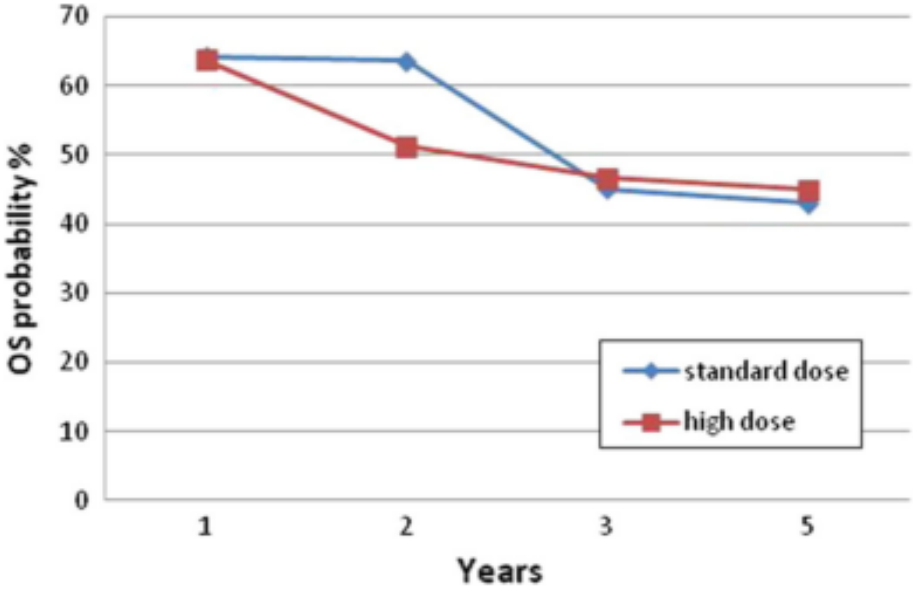


Table 3 Clinical outcomes in studies

Outcome	Standard-dose chemotherapy	High-dose chemotherapy	*P* value (Chi-square test)
Pooled ORR (%)	51.6	62.4	0.026
Median OS (months)	14.8	24.09	0.09 (*T* test)
Pooled mean 1-year OS (%)	64.2	63.7	0.9
Pooled mean 2-year OS (%)	63.6	51.2	0.4
Pooled mean 3-year OS (%)	45.1	46.7	0.75
Pooled mean 5-year OS (%)	43	45	0.6

OS overall survival, *ORR* overall response rate

>4000 ασθενείς

- Δεν φαίνεται να προσφέρει μεγαλύτερη συνολική επιβίωση
- Αντίθετα αυξάνει την θνησιμότητα την σχετιζόμενη με την θεραπεία
- Στα 2 ή 3 χρόνια μόνο 50% των ασθενών παραμένουν εν ζωή
- Δεν συμπεριελήφθησαν RCTs
- Μη σεμινωματώδεις όγκοι

Title: Pathologic Risk Factors for Metastatic Disease in Post-Pubertal Patients with Clinical Stage I Testicular Stromal Tumors

Author: Kyle O. Rove, Paul D. Maroni, Carrye R. Cost, Diane L. Fairclough, Gianluca Giannarini, Anne K. Harris, Kris Ann P. Schultz, Nicholas G. Cost

A. Demographic and clinical variables		
Number of patients	292 (% of Total N)	
Median age (range)	37 years	(Range = 12–76)
Median tumor size, largest diameter	1.5 cm	(Range = 0.5–13)
Primary RPLND	25	8.6%
Positive lymph nodes at RPLND	2	8.0%
Patients with OMD	27	9.2%
Location of first site of metastasis		
Retroperitoneum	22	81.5%
Lungs	4	14.8%
Inguinal lymph nodes	1	3.7%
Death	19/292	8.5%
Death from disease	15/292	5.1%
Overall survival in patients with OMD	12/27	44.4%
Median Follow Up	47 mo	(Range = 1–249 mo)

B. Tumor histology (when listed)	N	% of Total
Leydig cell tumor	169	69.8%
Sertoli cell tumors	51	21.1%
Classic SCT	20	8.3%
Large cell calcifying	14	5.8%
Sclerosing	17	7.0%
Granulosa cell tumor	14	5.8%
Mixed	3	1.2%
Undifferentiated	5	2.1%
Pathologic risk factors		
≥ 3 Mitoses per HPF	34/242	14.0%
Positive margins	7/230	3.0%
Rete testis invasion	8/230	3.5%
LVI	13/242	5.4%
Cellular atypia	32/242	13.2%
Necrosis	13/242	5.4%
Largest tumor diameter > 5 cm	21/240	8.8%

Pathologic risk factors				
≥ 3 mitoses per HPF	18/219 (8.2%)	16/23 (69.6%)	–	**< 0.001** ‡
Positive margins	2/210 (1.0%)	5/20 (25.0%)	–	**< 0.001** ‡
Rete testis invasion	4/210 (1.9%)	4/20 (20.0%)	–	**< 0.001** ‡
LVI	3/219 (1.4%)	10/23 (43.5%)	–	**< 0.001** ‡
Cellular atypia	21/219 (9.6%)	11/23 (47.8%)	–	**< 0.001** ‡
Necrosis	4/219 (1.8%)	9/23 (39.1%)	–	**< 0.001** ‡
Tumor diameter >5 cm	9/219 (4.1%)	12/21 (57.1%)	–	**< 0.001** ‡

C. Patients with # of risk factors			Patients with *n* or more risk factors		
	N	% of Total		N	% of Total
Zero risk factors	216	74.0%	Zero risk factors	216	74.0%
1 risk factor	37	12.7%	1 or more risk factor	76	26.0%
2 risk factors	15	5.1%	2 or more risk factors	39	13.4%
3 risk factors	14	4.8%	3 or more risk factors	25	8.6%
4 risk factors	5	1.7%	4 or more risk factors	10	3.4%
5 risk factors	3	1.0%	5 or more risk factors	5	1.7%
6 risk factors	2	0.7%			
			0–1 risk factors	253	86.6%
			2 or more risk factors	39	13.4%

Patients with *n* risk factors				
Number of patients	**Patients without OMD** 265 (N/265)	**Patients with OMD** 27 (N/27)	**Patients with # of pathologic RFs who have OMD**	**P-value**
Zero risk factors	214 (80.8%)	2 (7.4%)	2/216 (0.9%)	
1 risk factor	34 (12.8%)	3 (11.1%)	3/37 (8.1%)	
2 risk factors	8 (3.0%)	7 (25.9%)	7/15 (46.7%)	
3 risk factors	6 (2.3%)	8 (29.6%)	8/14 (57.1%)	**< 0.001** ‡
4 risk factors	3 (1.1%)	2 (7.4%)	2/5 (40.0%)	
5 risk factors	0 (0.0%)	3 (11.1%)	3/3 (100.0%)	
6 risk factors	0 (0.0%)	2 (7.4%)	2/2 (100.0%)	
Patients with *n* or more risk factors				
	Patients without OMD	**Patients with OMD**	**Patients with # of pathologic RFs who have OMD**	**P-value**
Number of patients	265 (N/265)	27 (N/27)		
1 or more risk factor	51 (19.2%)	25 (92.6%)	25/76 (32.9%)	
2 or more risk factors	17 (6.4%)	22 (81.5%)	22/39 (56.4%)	
3 or more risk factors	10 (3.8%)	15 (55.6%)	15/25 (60.0%)	**< 0.001** ‡
4 or more risk factors	3 (1.1%)	7 (25.9%)	7/10 (70.0%)	
5 or more risk factors	0 (0.0%)	5 (18.5%)	5/5 (100.0%)	

	5-year OMDFS (95% CI)	P-value	Univariate HR (95% CI, P-value)	Multivariate HR (95% CI, P-value)
< 40 vs. ≥ 40 years age	97.3% (93.9–100.0%) vs. 84.3% (76.5–92.1%)	**< 0.001 ‡**	**6.897 (2.326–20.447, p < 0.001)**	NS
< 50 vs. ≥ 50 years age	94.5% (90.8–98.2%) vs. 79.5% (65.8–93.2%)	**< 0.001 ‡**	**5.762 (2.523–13.162, p < 0.001)**	NS
Tumor Histology				
Leydig cell tumor	92.1% (87.4–96.8%)	**0.008 ‡**	1 (reference)	NS
Sertoli cell tumors				
Classic SCT	79.3% (60.7–97.9%)		**3.035 (1.073–8.588, p = 0.036)**	NS
Large cell calcifying	92.3% (77.8–100.0%)		NS	—
Sclerosing	100.0%		NS	—
Granulosa cell tumor	90.0% (71.4–100.0%)		NS	—
Mixed	100.0%		NS	—
Undifferentiated	71.1% (35.8–100.0%)		**6.762 (1.885–24.254, p = 0.003)**	NS
Pathologic risk factors				
≥ 3 mitoses per HPF	46.6% (26.0–67.2%)	**< 0.001 ‡**	**20.374 (8.338–49.781, p < 0.001)**	NS
Positive margins	42.9% (6.2–79.6%)	**< 0.001 ‡**	**15.555 (5.425–44.958, p < 0.001)**	NS
Rete testis invasion	Not Reached	**< 0.001 ‡**	**19.457 (5.924–63.907, p < 0.001)**	NS
LVI	21.1% (0–46.4%)	**< 0.001 ‡**	**23.541 (10.075–55.004, p < 0.001)**	**8.563 (1.788–41.013, p = 0.007)**
Cellular atypia	58.9% (36.6–81.2%)	**< 0.001 ‡**	**9.131 (3.945–21.134, p < 0.001)**	NS
Necrosis	49.2% (19.0–79.4%)	**< 0.001 ‡**	**17.234 (7.218–41.149, p < 0.001)**	NS
Largest tumor size > 5 cm	68.9% (41.1–89.7%)	**< 0.001 ‡**	**17.898 (7.262–44.107, p < 0.001)**	**10.951 (2.786–43.047, p = 0.001)**
Patients with *n* or more risk factors				
0 or 1 risk factors	98.3% (95% CI 96.3%–100.0%)	**< 0.001 ‡**	—	—
2 or more risk factors	48.1% (95% CI 29.9–66.3%)		—	—

- ✓ 10% των ασθενών με στρωματικό όγκο κλινικού σταδίου 1 θα αναπτύξουν μεταστατική νόσο
- ✓ Η αναγνώριση αυτών νωρίς θα μπορούσε δυνατικά να αλλάξει την πορεία της νόσου μέσω αλλαγής της αντιμετώπισής τους
- ✓ Τα δύο στοιχεία που φαίνεται να αποτελούν προγνωστικούς παράγοντες είναι η λεμφαγγειακή διήθηση και το μέγεθος του όγκου >5 cm


Patience
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