

Lokal İleri Prostat Kanserinde Sistemik Tedavi

Dr. Deniz Tural

Ko Üniversitesi Hastanesi Tıbbi Onkoloji

Ders Planı

- ☐ Neoadjuvan sistemik tedaviler
- ☐ PSA persistent ve nüksü olan hastalarda tedavi
- ☐ Adjuvan tedaviler
- ☐ Kombinasyon tedavileri
- ☐ Sonuç

Prostat kanserinin seyri

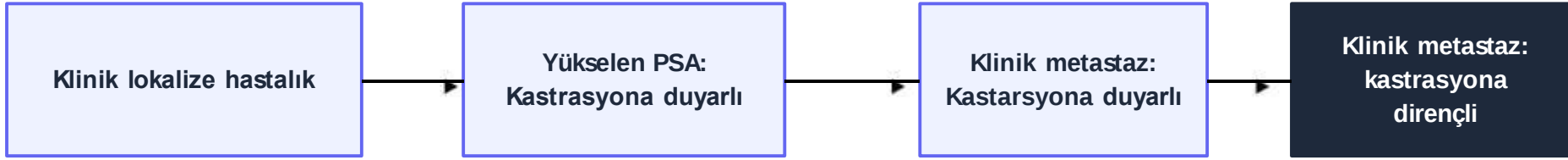


Kastrasyona duyarlı prostat kanseri

Kastrasyona dirençli prostat kanseri

Diğer nedenlere bağlı ölüm

Metastaz evre



Yükselen PSA:
kastrasyona dirençli

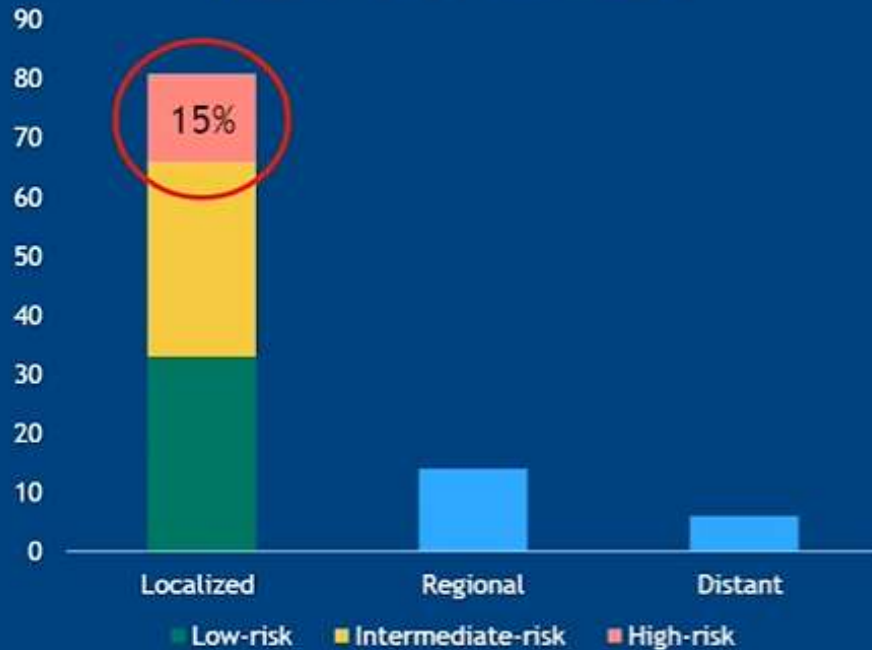
Hastalığa bağlı ölüm

İki tanımlayıcı kriter

- Kastrat testosteron seviyelerinde (<50 ng/dL) yükselen PSA
- Radyografik olarak tanımlanabilir metastaz yokluğu

Lokalize Yüksek Riskli Prostat Kanseri

Patterns of Presentation

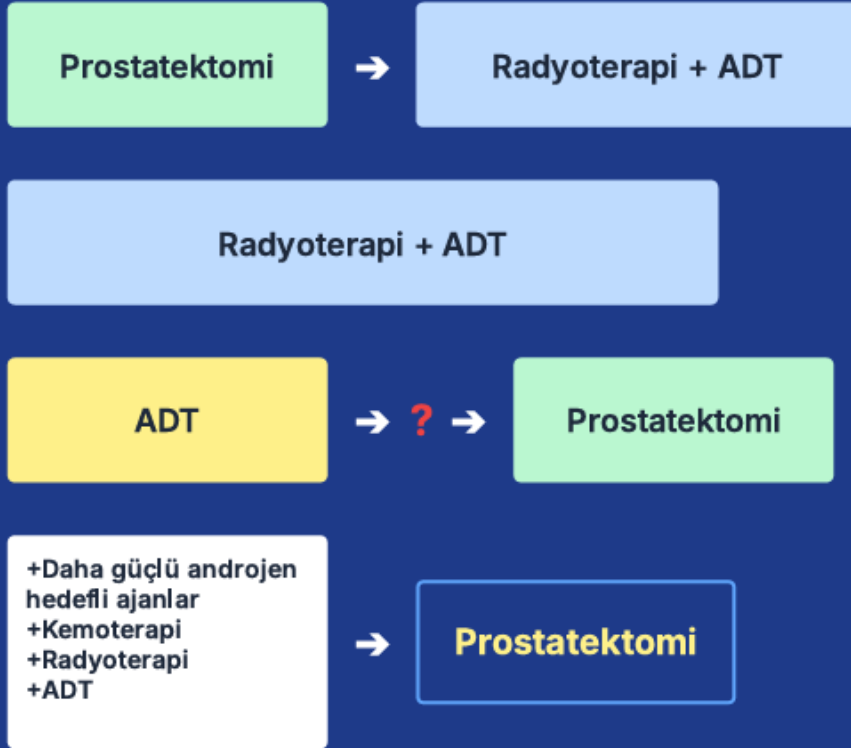


Increased Mortality in High-Risk Prostate Cancer

High-Risk Feature	15-Year PCSM
PSA > 20 ng/mL	22%
Gleason 8-10	34%
cT3	38%
High-risk Disease*	19%

Lokalize Yüksek Riskli Prostat Kanseri

Yüksek Riskli Prostat Kanserinde Tedavi Paradigmaları



Neoadjuvan Tedavi

- Uzun süreli sağkalımı iyileştirdiği gösterilen meme, rektum, mesane ve diğer kanser türlerinde standart bakım (standard of care) uygulamasıdır.
- Lokal hastalığın evresini düşürerek (down-stage) cerrahi rezeksiyonu kolaylaştırabilir.
- Cerrahi sonrası tedavi ihtiyacını azaltabilir veya geciktirebilir.
- Tedaviye yanıtın *in vivo* değerlendirilmesine olanak sağlar.

Pertrelli et al, Eur Urology, 2014
Berger et al, JCO, 2005
Mass et al, Lancet Oncology, 2010
Cortazar et al, Lancet Oncology, 2014
McKay et al, Drugs, 2012

Neoadjuvan Tedavi Gerekçesi

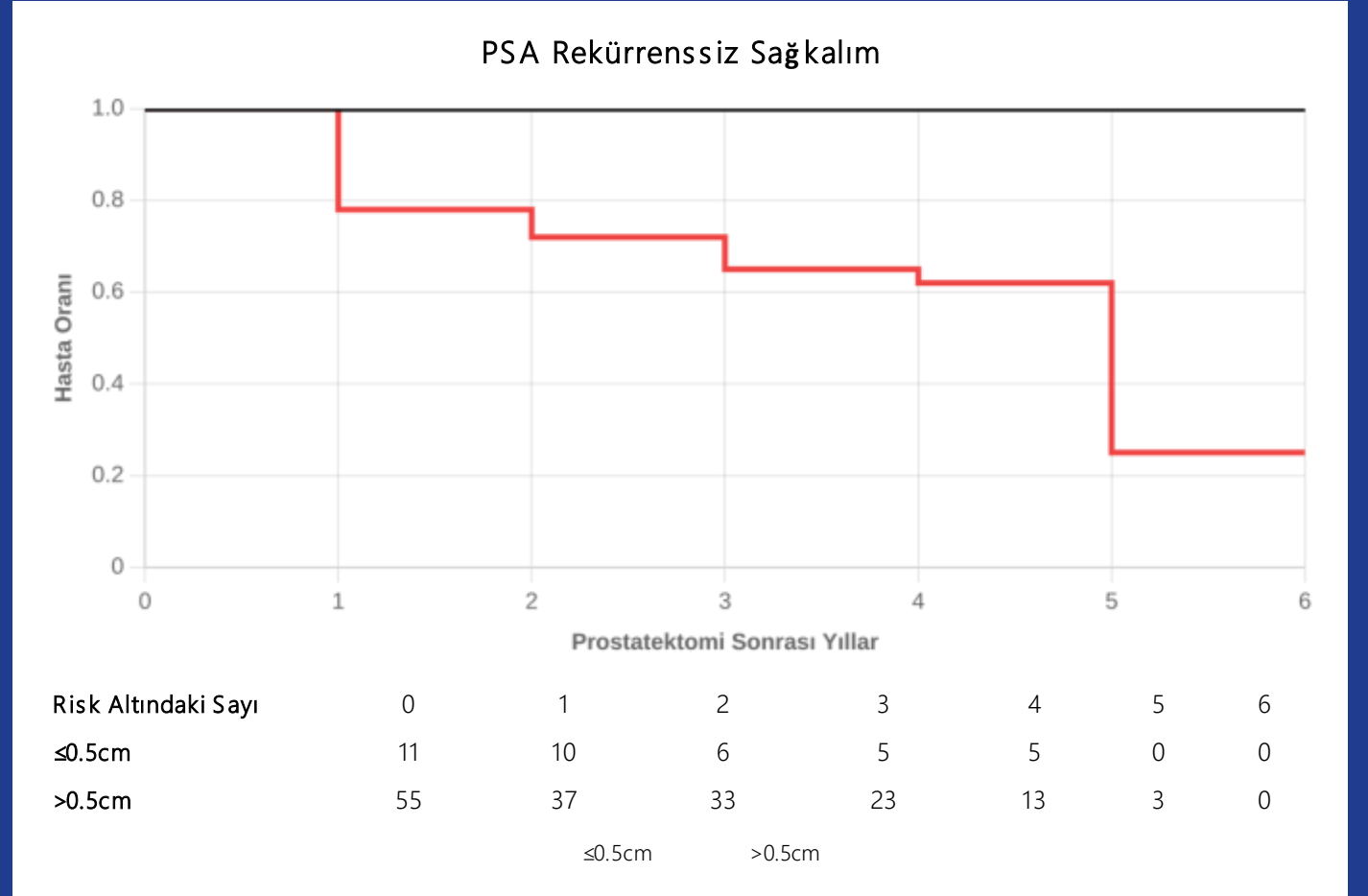
Patolojik Yanıtın PSA Rekürrensi ile Korelasyonu

Üç güncel neoadjuvan çalışmanın havuzlanmış analizi (n=72)

Medyan takip süresi 3.4 yıl

Radikal prostatektomi sırasında pCR veya MRD gözlenen hastalarda rekürrens saptanmamıştır.

pCR: Patolojik tam yanıt; MRD: Minimum rezidüel hastalık



Lokal İleri Yüksek Riskli Prostat Kanserinde ADT ile Neoadjuvan Tedavi

Neoadjuvant therapy with Convention Androgen Deprivation therapy agents

Author	Year	Location	n	Abbreviated inclusion criteria	Agent (Duration)	Primary endpoint results
Labrie (26)	1993	Québec, Canada	77	Early stage prostate cancer	Leuprolide + Flutamide (3 Months)	Cancer-positive margins were reduced from 38.5% in control patients to 13.0% in men who received neoadjuvant combination (p = 0.006).
Debruyne (27)	1994	Nijmegen, Netherlands	65	cT2-3, N0, M0 stages of prostate cancer	Goserelin + Flutamide (3 Months)	Serum PSA levels and prostatic volume decreased from a mean of 12.8 ng/ml and 42.8 cm ³ to a mean of 0.8 ng/ml and 29.5 cm ³ , respectively.
Van Poopel	1995	Leuven	65	Stages T2b and T3 prostate cancer	Estramustine +	For T2b tumors, a significant decrease in

ADT ile cerrahi sınır oranlarında iyileşme ve downstaging sağlanmakla birlikte, biyokimyasal progresyonsuz sağkalım (BPFS) ve genel sağkalım (OS) üzerine anlamlı katkı gösterilmemiştir

		Canada			months vs 8 months)	group (0.052 vs 0.12mc/L, P<0.001). Surgical margins favored 8 month ADT group (12% vs 23%, p=0.01).
Selli (34)	2002	Pisa, Italy	265	Surgically resectable clinical stage (T2-T3, N0, M0) prostatic cancer	Goserelin, Bicalutamide (3/6 Months)	PSA progression: significant differences between treatment groups.
Prezioso (35)	2004	Naples, Italy	91	Prostatic cancer clinical stage T2b or less	Leuprolide, Cyproterone (3 Months)	Neoadjuvant group: 31% of patients had a decrease in tumor and prostate volume.
Gravina (36)	2007	L'Aquila, Italy	61	Prostate cancer clinical Stage T2-T3a	Bicalutamide (4 Months)	Neoadjuvant treatment had a reduction of positive surgical margins (13.1% versus 34.5%, P = 0.011).

Yeni Nesil AR Yolağı İnhibitörleri ile Neoadjuvan Tedavi

Neoadjuvan Yeni Nesil AR-yolağı İnhibitörleri Güçlü Neoadjuvan Tedaviden Elde Edilen Patolojik Yanıtlar

Son 10 yılda gerçekleştirilen bir dizi neoadjuvan çalışma
Güçlü neoadjuvan hormon tedavisini değerlendiren Faz 2 biyobelirteç entegreli çalışmalar

	NeoAbi (n=58)	NeoEnza (n=40)	NeoAbiEnza (n=75)
Kollar (Arms)	12h Abi vs. 24h Abi	Enza vs. EDL	EL vs. APEL
TY (CR)	%4 vs. %10	%0 vs. %4	%8 vs. %12
MRH (MRD)*	%0 vs. %14	%0 vs. %13	%11 vs. %18
TY + MRH (CR + MRD)	%4 vs. %24	%0 vs. %17	%19 vs. %30

Abi: Abirateron; Enza: Enzalutamid; EDL: Enzalutamid, dutasterid, löprolid; APEL: Abirateron, prednizon, enzalutamid, löprolid; EL: Enzalutamid, löprolid.
TY (CR): Tam yanıt; MRH (MRD): Minimum rezidüel hastalık. *MRH, en büyük kesit boyutu ≤ 0.3 -0.5 cm olan rezidüel tümör olarak tanımlanmıştır.

Taplin et al, JCO, 2014
Montgomery et al, CCR, 2016
McKay et al, JCO, 2019

Yeni Nesil AR Yolağı İnhibitörleri ile Neoadjuvan Tedavi

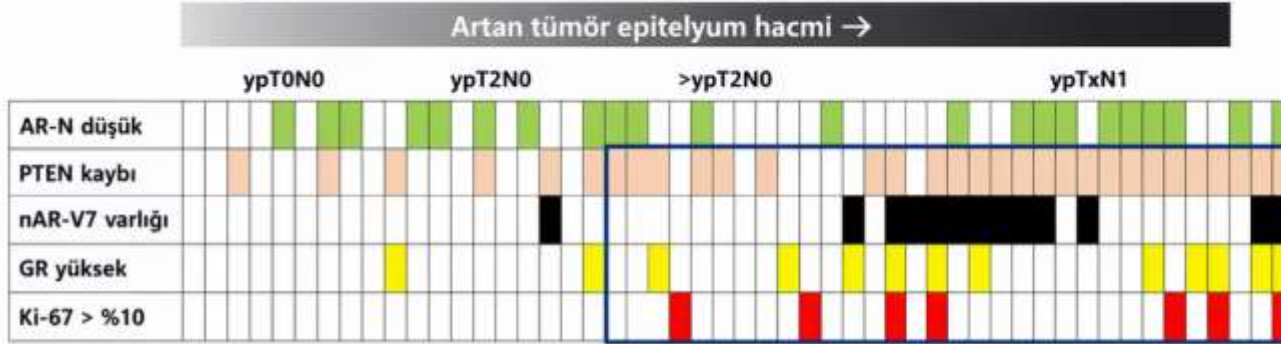
Neoadjuvan Yeni Nesil AR Yolağı İnhibitörleri



BULGULAR

- Tümör hacmi ve tümör hücreliliği anlamlı derecede değişkenlik göstermiştir.
- ≥ypT2N0 varlığı Gleason skoru ile korele bulunmamış; ancak **önceden tanımlanmış moleküler imza, PTEN ekspresyonu ve kribriiform/intraduktal yayılımının olmaması** ile anlamlı korelasyon göstermiştir.
- Dört belirteçten oluşan aday imza (**PTEN kaybı, nAR-V7 varlığı, glukokortikoid reseptör [GR] yüksekliği veya Ki-67 >%10**) tedavi direncini öngördürücü bulunmuştur.

Tedavi Öncesi Tümör Özellikleri ile Tedavi Yanıtı Arasındaki İlişki (Tek Değişkenli Analizler)



Tanısal Biyopsi Belirteçleri

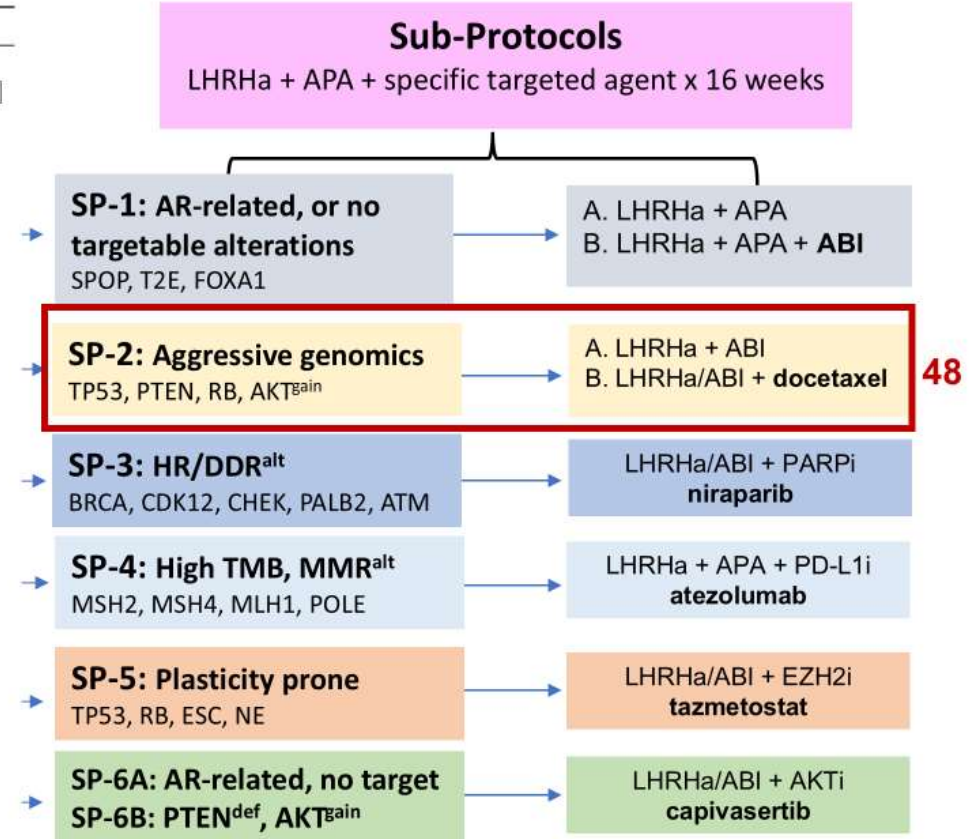
- ✓ PTEN kaybı, persistan kanserlerde zenginleşmiştir.
- ✓ Nükleer AR-V7 varlığı, GR yüksekliği (> %10) ve Ki-67 > %10, persistan kanser ile koreledir.

Belirteç	Patoloji Evresi		Fisher kesin testi p-değeri
	>ypT2N0 N (%)	≤ypT2N0 N (%)	
AR-N Düşük Yüksek	13 (%42) 18 (%58)	9 (%47) 10 (%53)	0.77
PTEN Kayıp İntakt	24 (%77) 7 (%23)	7 (%37) 12 (%63)	0.007
nARV7 Nükleer yokluğu Varlığı	19 (%61) 12 (%39)	18 (%95) 1 (%5)	0.009
GR Düşük Yüksek	20 (%65) 11 (%35)	17 (%89) 2 (%11)	0.091
Ki67 ≤%10 >%10	24 (%77) 7 (%23)	19 (%100) 0 (%0)	0.035
Klinik Evre cT2 cT3/4	6 (%16) 32 (%84)	11 (%44) 14 (%56)	0.02
Biyopsi Gleason 7 8-10	10 (%26) 28 (%73)	8 (%32) 17 (%68)	0.77
Tanısal PSA (ng/mL) >10	26 (%68)	16 (%64)	0.23

Yeni Nesil AR Yolağı İnhibitörleri ile Neoadjuvan Tedavi

GUNS: Genomic Umbrella Neoadjuvant Study in High Risk PCA

		SP 2a	SP 2b	Cohort
n		24	24	234
Age, years (median [IQR])		64.00 [58.50, 69.00]	63.00 [58.00, 67.00]	65.00 [60.00, 71.00]
Race (%)				
	Asian	1 (4.2)	1 (4.2)	30 (12.8)
	Black or African American	1 (4.2)	2 (8.3)	13 (5.6)
	White	22 (91.7)	21 (87.5)	190 (81.2)
	Unknown			1 (0.4)
PSA, ng/mL (%)				
	< 10	6 (25.0)	8 (33.3)	76 (32.5)
	10 ≤ PSA < 20	8 (33.3)	6 (25.0)	72 (30.8)
	20 ≤ PSA < 40	5 (20.8)	3 (12.5)	45 (19.2)
	40 ≤ PSA < 80	5 (20.8)	5 (20.8)	37 (15.8)
	≥ 80		2 (8.3)	4 (1.7)
Grade group (%)				
	2	1 (4.2)	1 (4.2)	5 (2.1)
	3	3 (12.5)	4 (16.7)	21 (9.0)
	4	3 (12.5)	3 (12.5)	37 (15.8)
	5	17 (70.8)	16 (66.7)	171 (73.1)
IDC (%)				
	No	6 (33.3)	7 (46.7)	90 (60.4)
	Yes	12 (66.7)	8 (53.3)	59 (39.6)
Cribriform (%)				
	No	9 (50.0)	4 (26.7)	77 (52.0)
	Yes	9 (50.0)	11 (73.3)	71 (48.0)
cT stage (%)				
	T1	2 (8.3)	3 (12.5)	38 (16.2)
	T2	15 (62.5)	12 (50.0)	123 (52.6)
	T3	7 (29.2)	9 (37.5)	69 (29.5)
	T4			1 (0.4)
	TX			3 (1.3)
cN stage (%)				
	N0	20 (83.3)	17 (70.8)	211 (90.2)
	N1	4 (16.7)	7 (29.2)	21 (9.0)
	NX			2 (0.9)
Tempus xT (%)				
	No			32 (13.7)
	Yes	24 (100.0)	24 (100.0)	202 (86.3)
Tempus RNA-seq (%)				
	No	7 (29.2)	4 (16.7)	85 (36.3)
	Yes	17 (70.8)	20 (83.3)	149 (63.7)



NCT04812366

Yeni Nesil AR Yolağı İnhibitörleri ile Neoadjuvan Tedavi

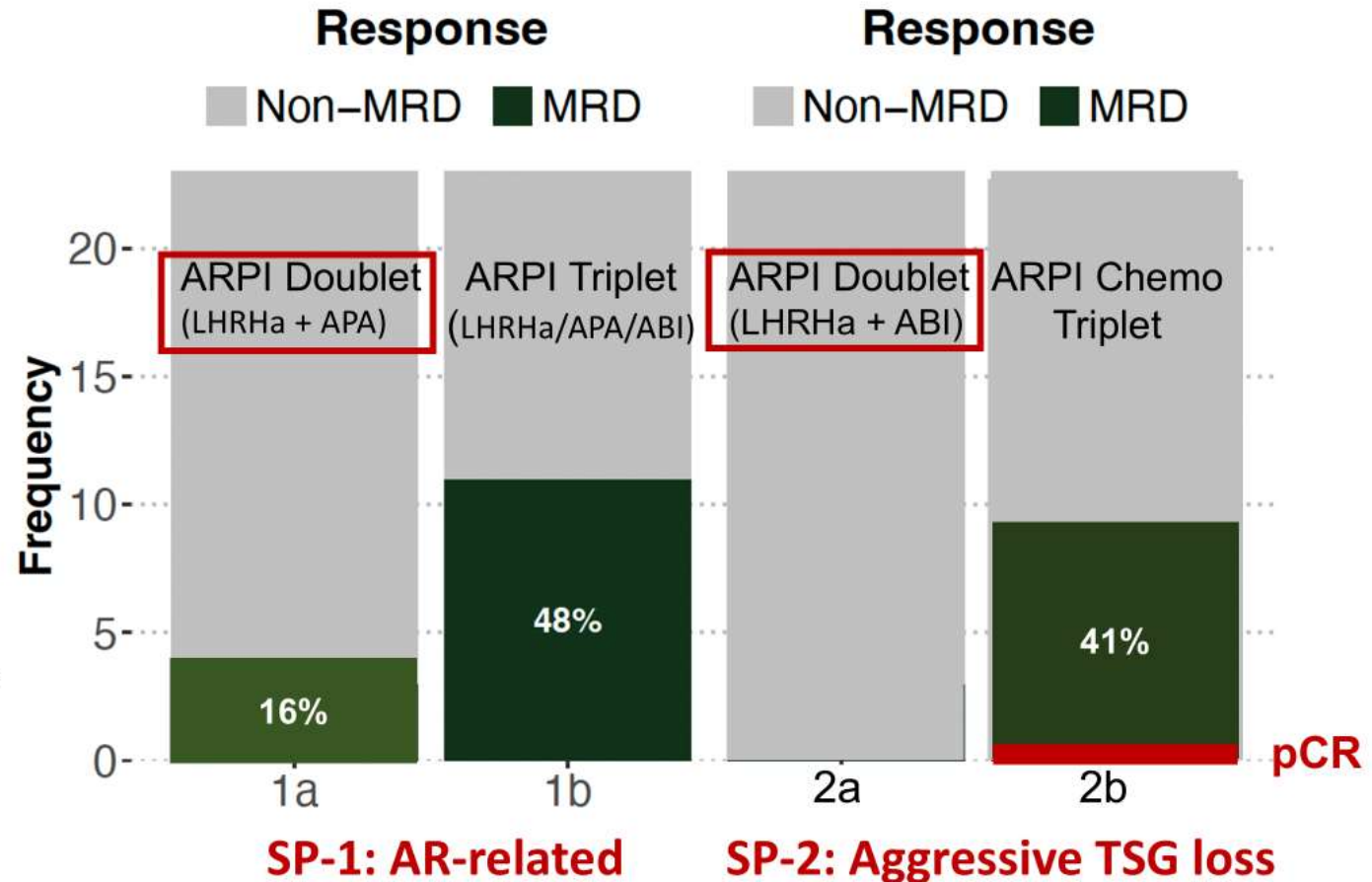
Pathologic Response in SP-1 and SP-2 Cancers in GUNS

SP-1: MRD rate higher in ARPI triplet than doublet

• **48% vs 16%, p=0.028**

- No pCR
- Degenerative scores higher in SP-1b vs SP-1a

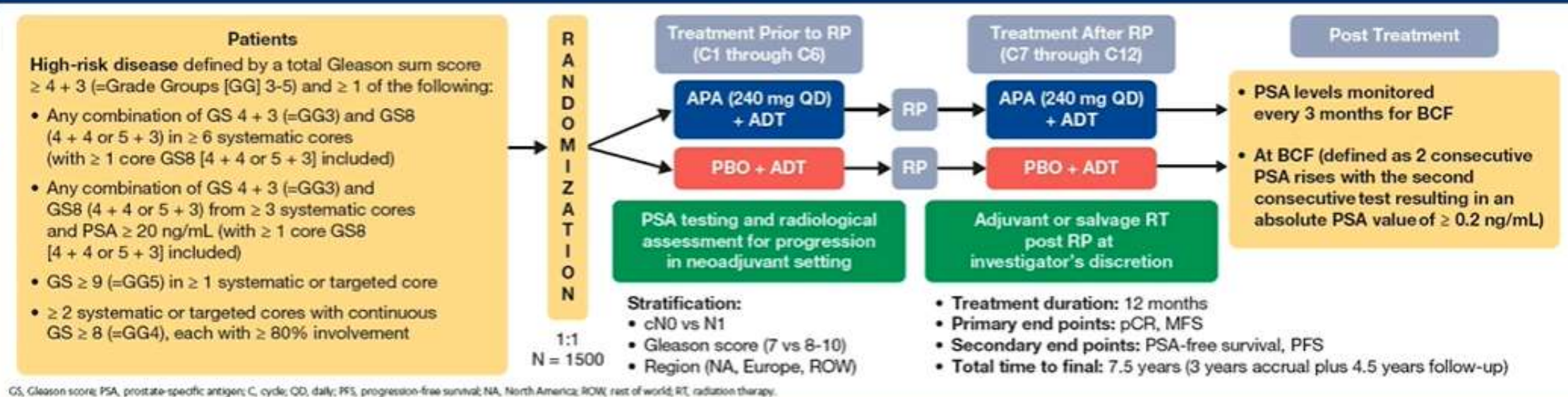
- MRD rate lowest in SP-2a treated with ARPI doublet



Yeni Nesil AR Yolağı İnhibitörleri ile Neoadjuvan Tedavi Devam Eden Çalışmalar

Proteus

Randomized, Double-blind, Placebo-Controlled, Phase 3 Study of Apalutamide in Subjects with High-risk, Localized or Locally Advanced Prostate Cancer Who are Candidates for Radical Prostatectomy



Lokal İleri Yüksek Riskli Prostat Kanserinde Neoadjuvan Kemoterapi ve Androjen Deprivasyon Tedavisi (ADT)

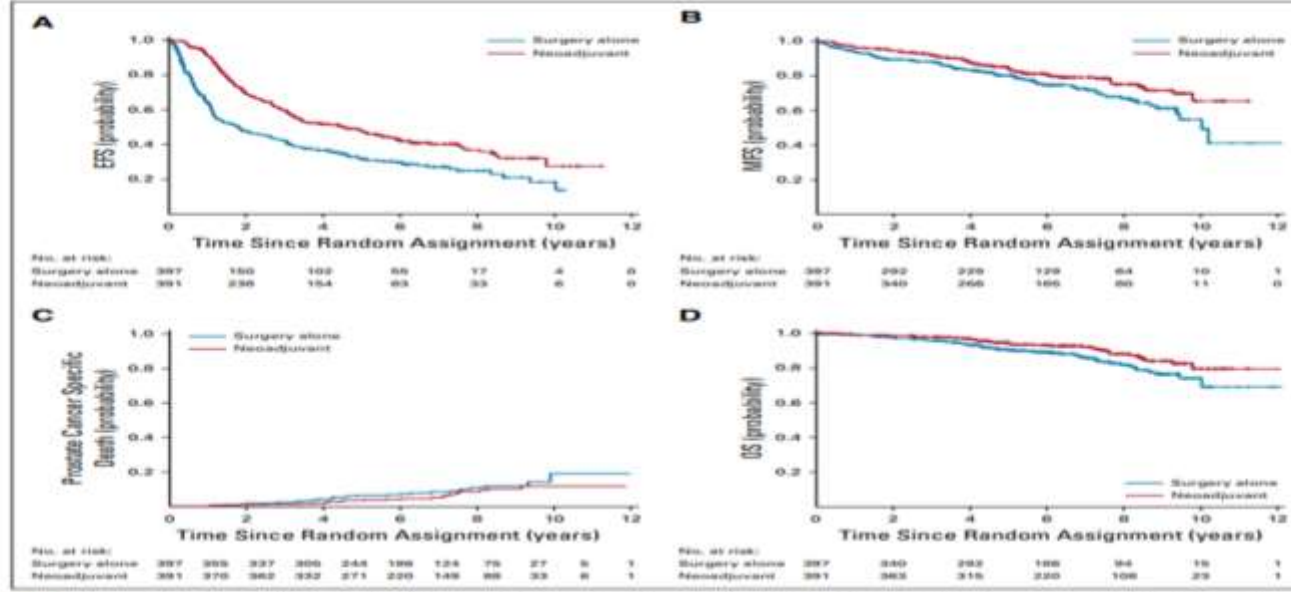


FIG 3. (A) Event-free survival (EFS) or the likelihood of not requiring additional treatment after radical prostatectomy in men treated with neoadjuvant chemohormonal therapy plus radical prostatectomy (designated neoadjuvant) versus radical prostatectomy alone (designated surgery alone). An event is defined as death, prostate-specific antigen progression, local or distant progression, initiation of androgen-deprivation therapy, and/or radiation therapy > 6 months after surgery. (B) Metastasis-free survival (MFS; the time from randomization to metastasis) in men treated with neoadjuvant chemohormonal therapy plus radical prostatectomy versus radical prostatectomy alone. (C) Prostate cancer-specific survival (the time from randomization to death from prostate cancer) in men treated with neoadjuvant chemohormonal therapy plus radical prostatectomy versus radical prostatectomy alone. Cause of death was assigned by the treating physician. (D) Overall survival (OS; the time from randomization to death) in men treated with neoadjuvant chemohormonal therapy plus radical prostatectomy versus radical prostatectomy alone.

Cancer and Leukemia Group B 90203 (Alliance): Radical Prostatectomy With or Without Neoadjuvant Chemohormonal Therapy in Localized, High-Risk Prostate Cancer

SONUÇ

- Neoadjuvan kemoterapi + ADT, EFS ve MFS üzerinde iyileşme eğilimi sağlar
- OS ve kansere özgü sağkalım üzerine etkisi sınırlı ve anlamlı düzeyde değil
- Rutin kullanım için veri yok

Definitif Radyoterapi + Androjen Deprivasyon Tedavisi + Yeni Nesil AR Yolağı İnhibitörleri

Abiraterone acetate and prednisolone with or without enzalutamide for high-risk non-metastatic prostate cancer: a meta-analysis of primary results from two randomised controlled phase 3 trials of the STAMPEDE platform protocol



In 2019, the reporting plan was amended to

- Split M1 and nonmetastatic patients, power the **primary endpoint on MFS**
- **Meta-analyze data** from the AAP $\pm$ enzalutamide + ADT vs ADT comparisons

Newly diagnosed

1. cN1

2. High risk cN0

≥ 2 of T3/4
GS 8-10
PSA ≥ 40

M0 with conventional imaging

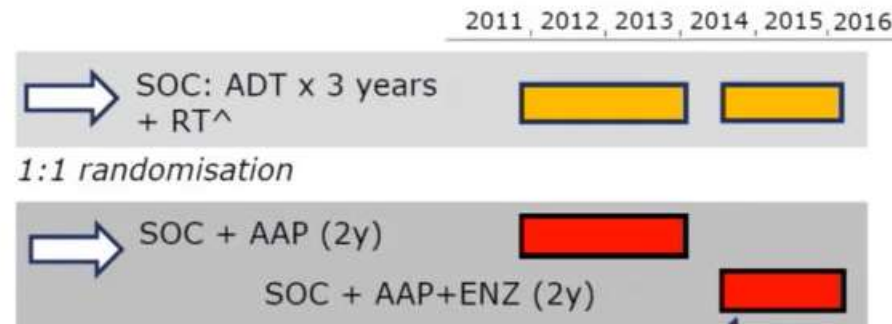
Relapsing disease (Prior RT/RP)

Any of the following

cN1

PSA ≥ 20

PSA ≥ 4 & DT <6m



**published as a pre-specified declaration of our intentions: Attard G, et al. Eur Urol. Epub 2021 Jul 14*

Solid bars: period of accrual

SOC, standard of care

- No overlapping controls
- Same protocol & eligibility criteria
- 2 years AAP+/-ENZ
- No evidence of OS benefit with AAP+/-ENZ in mCRPC ¹

RT was mandated in NOM0 and suggested in N+ disease

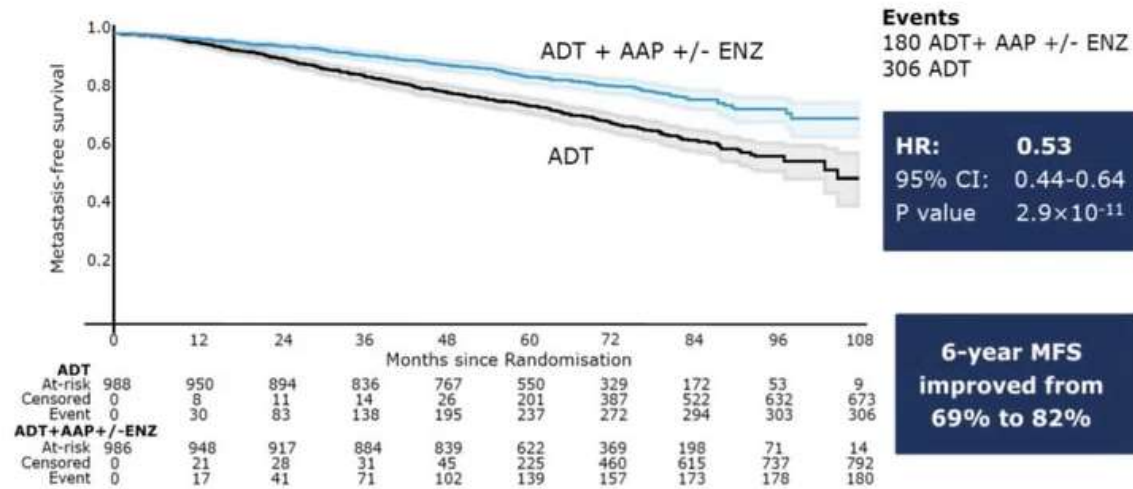
Definitif Radyoterapi + Androjen Deprivasyon Tedavisi + Yeni Nesil AR Yolağı İnhibitörleri

Patient characteristics

- Randomised groups were well balanced (**N=1974**)
- Median age = 68 years
- Median PSA = 34 ng/ml
- N1 = 39%
- 3% relapsing after prior treatment
- Planned for local radiotherapy: - 99% newly-diagnosed, N0
 - 71% newly-diagnosed, N1
 - 7% previously-treated patients
- Median follow-up = 72 months
(85 months AAP comparison & 60 months AAP+ENZ comparison)

Definitif Radyoterapi + Androjen Deprivasyon Tedavisi + Yeni Nesil AR Yolağı İnhibitörleri

Metastasis-free survival



Kaplan-Meier estimates with 95% CI in lighter shade

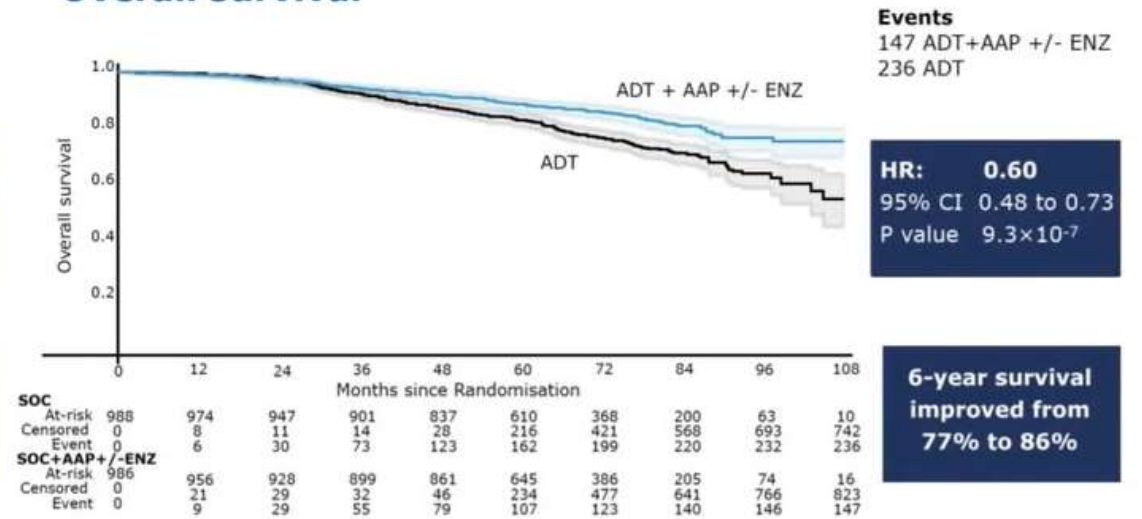


Gerhardt Attard MD FRCP PhD

Non-proportional hazards $P=0.46$

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Overall survival



Kaplan-Meier estimates with 95% CI in lighter shade



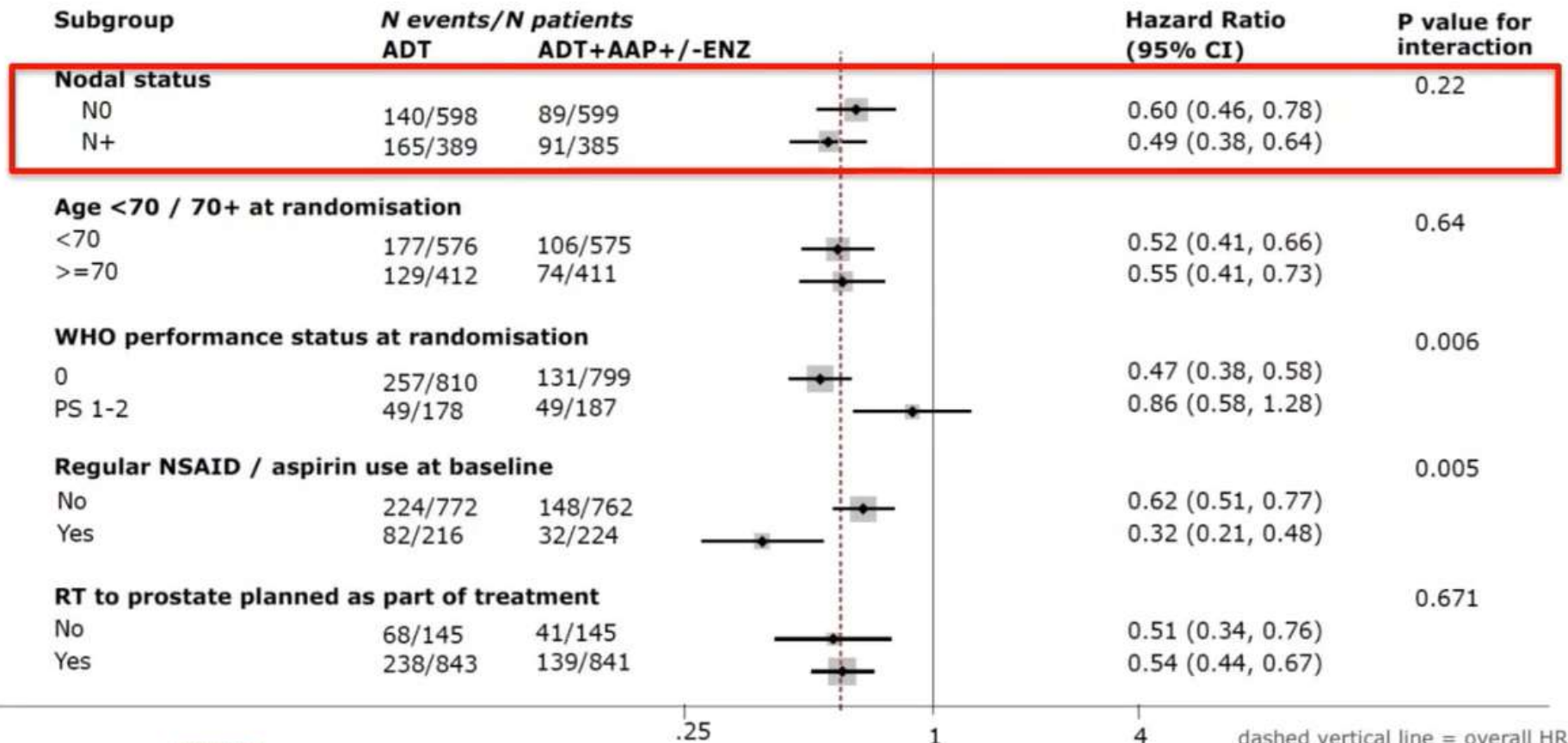
Gerhardt Attard MD FRCP PhD

Non-proportional hazards $P=0.1$

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Definitif Radyoterapi + Androjen Deprivasyon Tedavisi + Yeni Nesil AR Yolağı İnhibitörleri

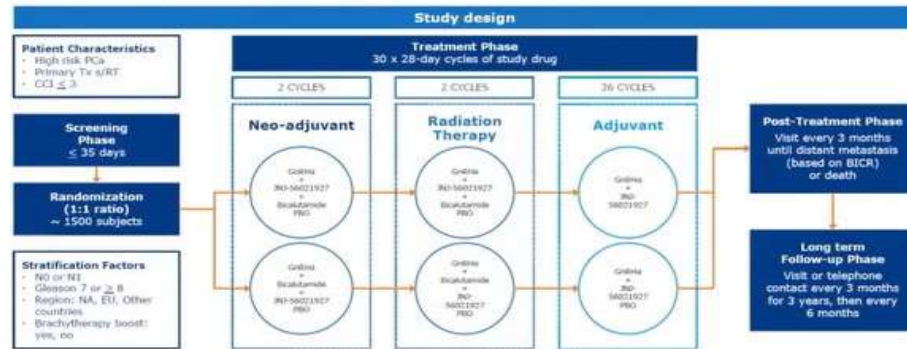
Metastasis-free survival: Subgroup analysis



Definitif Radyoterapi + Androjen Deprivasyon Tedavisi + Yeni Nesil AR Yolağı İnhibitörleri

Apalutamide

ATLAS: Apalutamide in high-risk, localized or locally advanced PC patients receiving primary RT



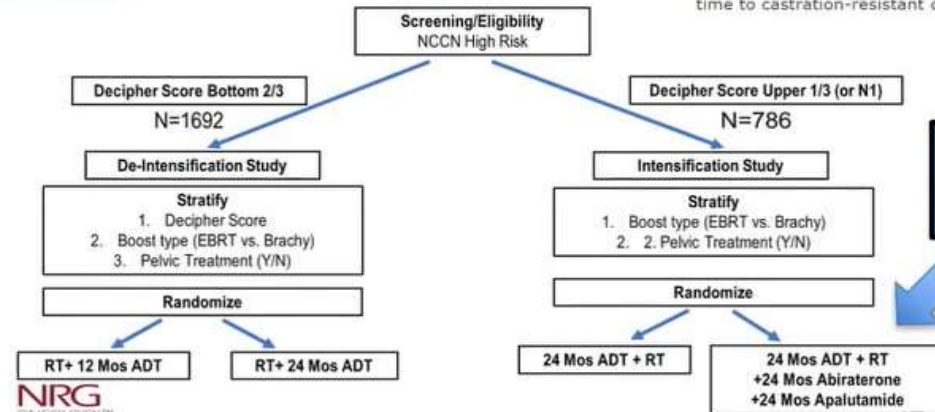
Enzalutamide

ENZARAD: Enzalutamide in ADT with RT for high-risk, clinically localized PC



- Primary endpoint is OS
- Secondary endpoints include CSS, PSA PFS, clinical PFS, time to subsequent hormonal therapy, time to castration-resistant disease (PCWG2 criteria), MFS, AEs and HRQOL

SCHEMA



NRG GU009

Abiraterone + Apalutamide

Clinical Trial Information:

NCT02531516; NCT02446444; NCT04513717

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Definitif Radyoterapi + Androjen Deprivasyon Tedavisi + Yeni Nesil AR Yolağı İnhibitörleri



ENZARAD schema



Eligibility

Localised prostate cancer
High risk of recurrence
Suitable for EBRT

Stratification

Gleason score 8-10
T3-4 disease
N1 disease
PSA ≥ 20 ng/mL
Brachytherapy boost
Pelvic nodal RT
Study Site

N=800

(R)

1:1

Enzalutamide 160mg daily for 24 months
+ LHRHA for 24 months
+ RT starting after 16 weeks $\pm$ brachy $\pm$ nodal

Conventional NSAA for 6 months
+ LHRHA for 24 months
+ RT starting after 16 weeks $\pm$ brachy $\pm$ nodal

Endpoints

Metastasis-free survival (primary)
Overall survival
Cause specific survival
PSA progression free survival
Clinical progression free survival
Castration-resistance
Health related quality of life
Adverse events
Incremental cost-effectiveness

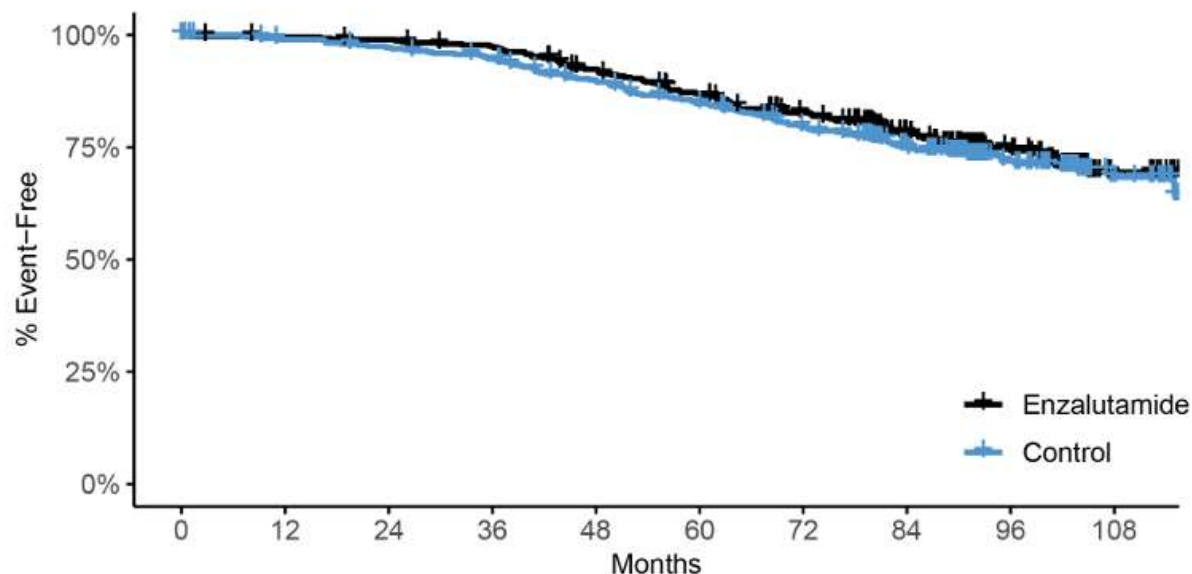
Primary Endpoint:

MFS based on conventional imaging (CT or MRI or bone scan, per ICECAP)
Lesions on PSMA-PET alone insufficient
Event = metastasis or death from any cause before metastasis

Definitif Radyoterapi + Androjen Deprivasyon Tedavisi + Yeni Nesil AR Yolağı İnhibitörleri



Primary endpoint:
MFS by conventional imaging



	events/N	MFS 8y
ENZA	98/401	74%
NSAA	109/401	72%

HR = 0.88 (95% CI 0.67, 1.15)
2p = 0.34 (log-rank test)

Median FU = 8 years

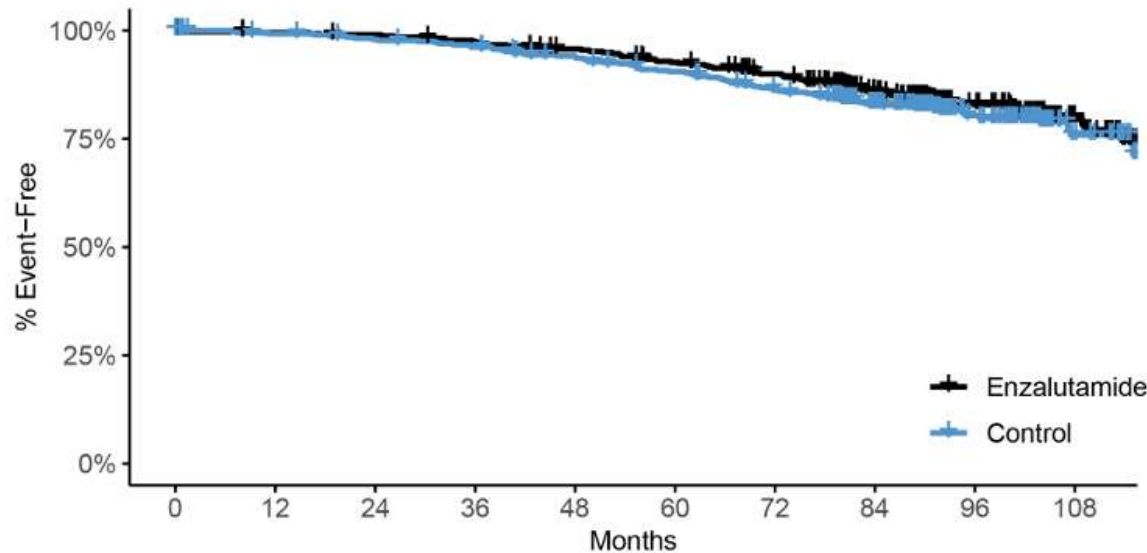
Number at risk (number censored)

401 (2)	395 (4)	392 (5)	384 (7)	359 (12)	334 (16)	306 (28)	226 (93)	117 (192)	36 (267)
401 (2)	390 (7)	382 (8)	370 (10)	345 (16)	323 (19)	297 (26)	221 (86)	113 (187)	47 (249)

Definitif Radyoterapi + Androjen Deprivasyon Tedavisi + Yeni Nesil AR Yolağı İnhibitörleri



Overall Survival



	events/N	OS 8y
ENZA	69/401	83%
NSAA	77/401	80%

HR = 0.87 (0.63, 1.20)
2p = 0.40 (log-rank test)

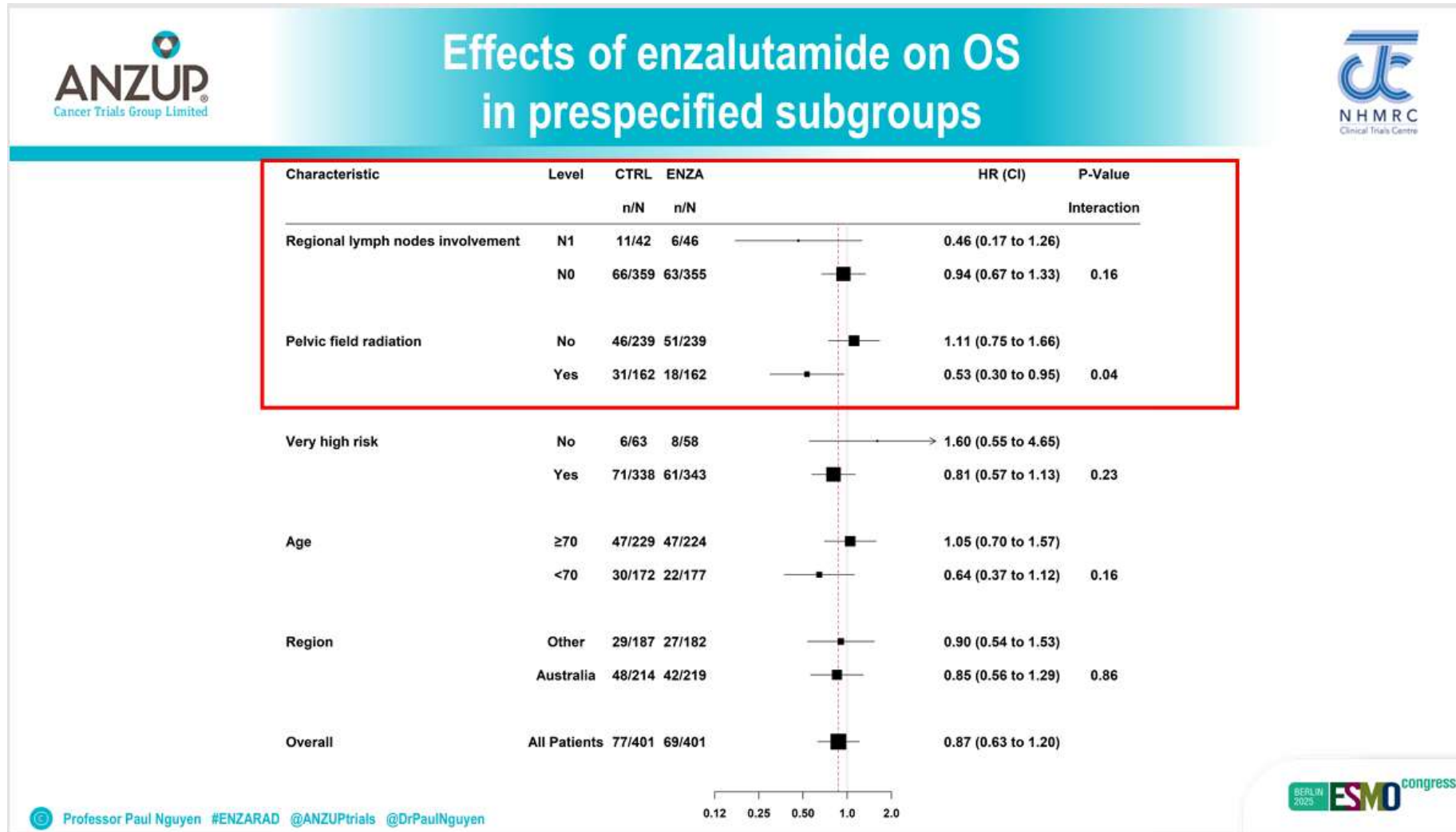
Number at risk (number censored)

401 (0)	395 (4)	392 (5)	385 (6)	374 (10)	359 (13)	339 (23)	256 (92)	136 (204)	49 (287)
401 (1)	392 (6)	385 (8)	377 (9)	362 (15)	346 (18)	326 (23)	249 (88)	128 (203)	49 (278)

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Professor Paul Nguyen #ENZARAD @ANZUPtrials @DrPaulNguyen

Definitif Radyoterapi + Androjen Deprivasyon Tedavisi + Yeni Nesil AR Yolağı İnhibitörleri



Definitif Radyoterapi + Androjen Deprivasyon Tedavisi + Yeni Nesil AR Yolağı İnhibitörleri

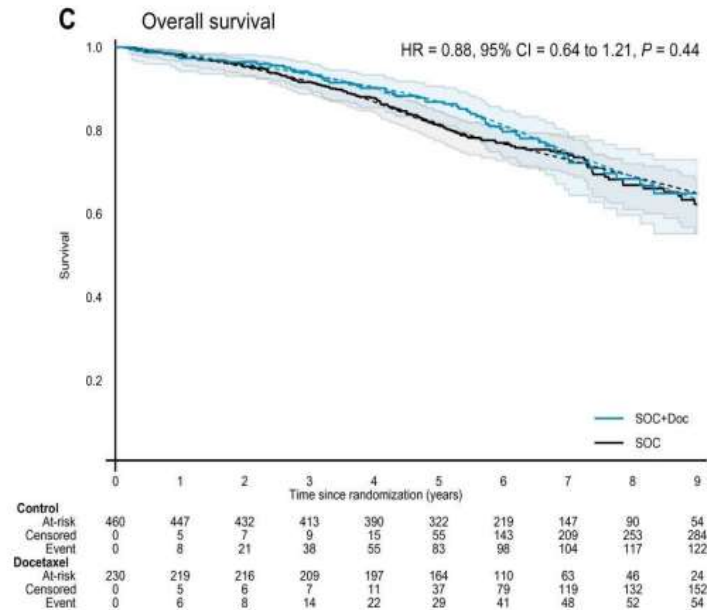
ENZARAD Benefit in cN1 is consistent with STAMPEDE but ENZARAD enrolled more favorable risk patients

	STAMPEDE (abiraterone)	ENZARAD (enzalutamide)
HR for MFS in cN1	0.49	0.43
HR for MFS in all patients	0.53 (p<0.0001)	0.88 (p=.34)
cN1	39%	11%
Median PSA	35	14
Clinical T3-4	92%	47%
Received radiation	82%	100%
Gleason 8-10	79%	89%

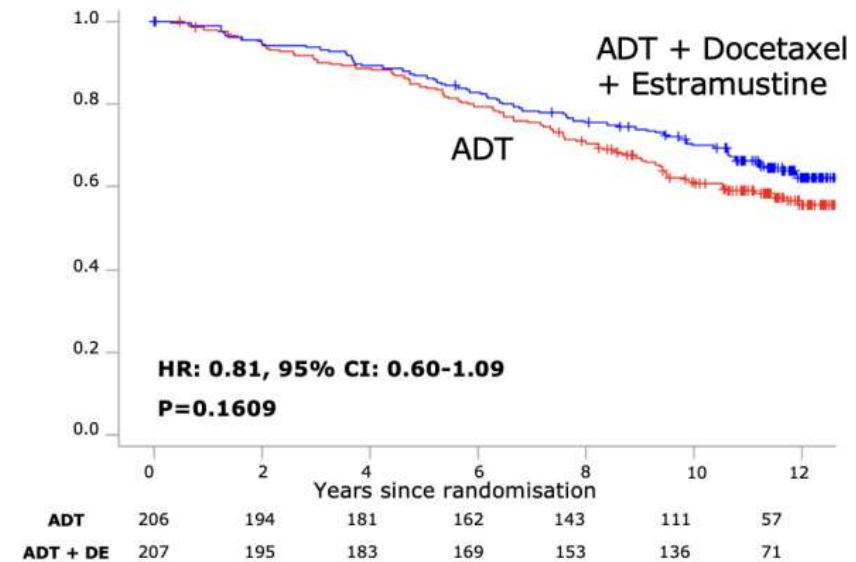
Yüksek Riskli Lokalize Prostat Kanserinde Definitif Radyoterapi (RT) + ADT ve Adjuvan Kemoterapi

Docetaxel in M0 prostate cancer: no MSF/OS benefit

STAMPEDE

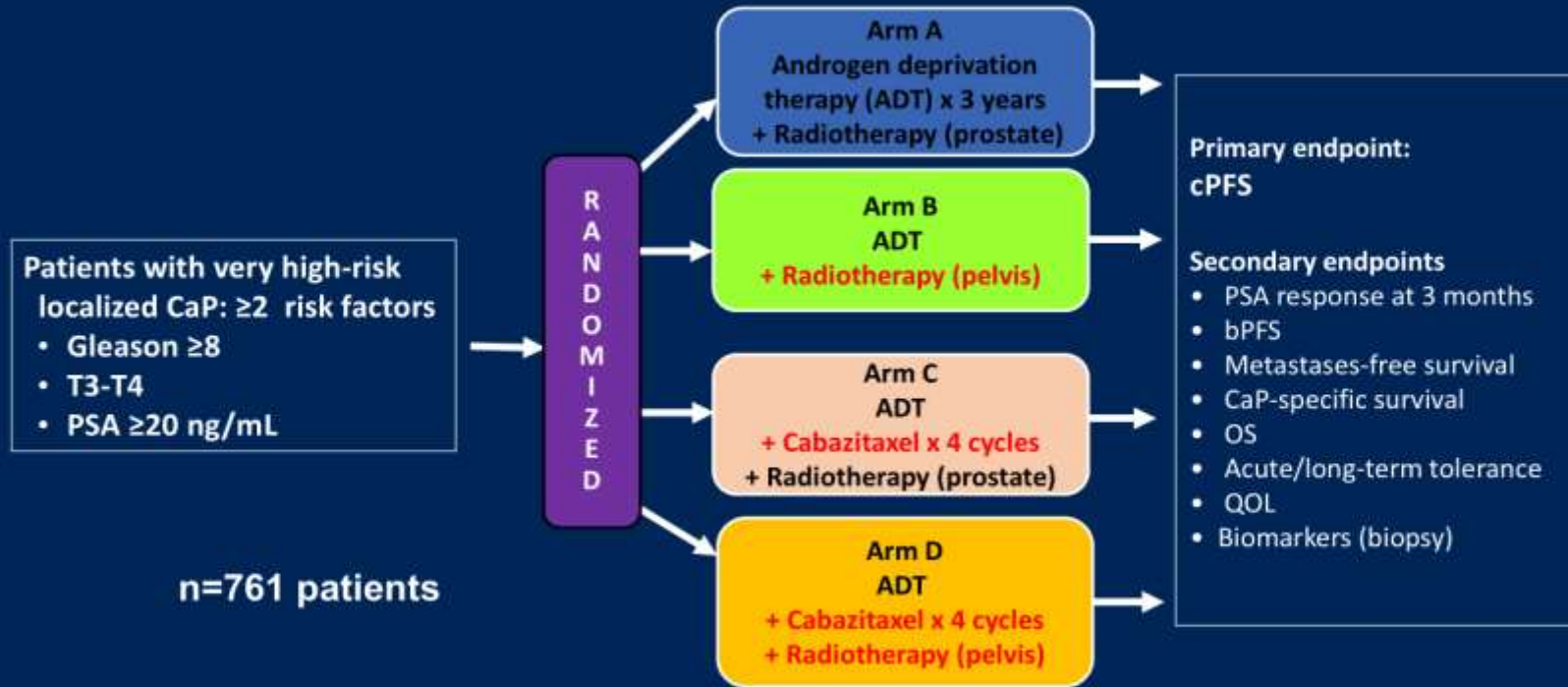


GETUG -12



Yüksek Riskli Lokalize Prostat Kanserinde Definitif Radyoterapi (RT) + ADT ve Adjuvan Kemoterapi

PEACE-2: Study design



Yüksek Riskli Lokalize Prostat Kanserinde Definitif Radyoterapi (RT) + ADT ve Adjuvan Kemoterapi

30

PEACE-2: Treatments

- Androgen Deprivation Therapy (ADT): 3 years
 - LHRH agonist
 - LHRH antagonist
- Radiotherapy:
 - 74-78 Gy with 2 Gy fractions, IMRT mandatory
 - Started 3 months after ADT initiation
 - If pelvic RT: 46-50 Gy
- Cabazitaxel: 20-25 mg/m²/3w x 4 cycles, G-CSF recommended

Yüksek Riskli Lokalize Prostat Kanserinde Definitif Radyoterapi (RT) + ADT ve Adjuvan Kemoterapi

32

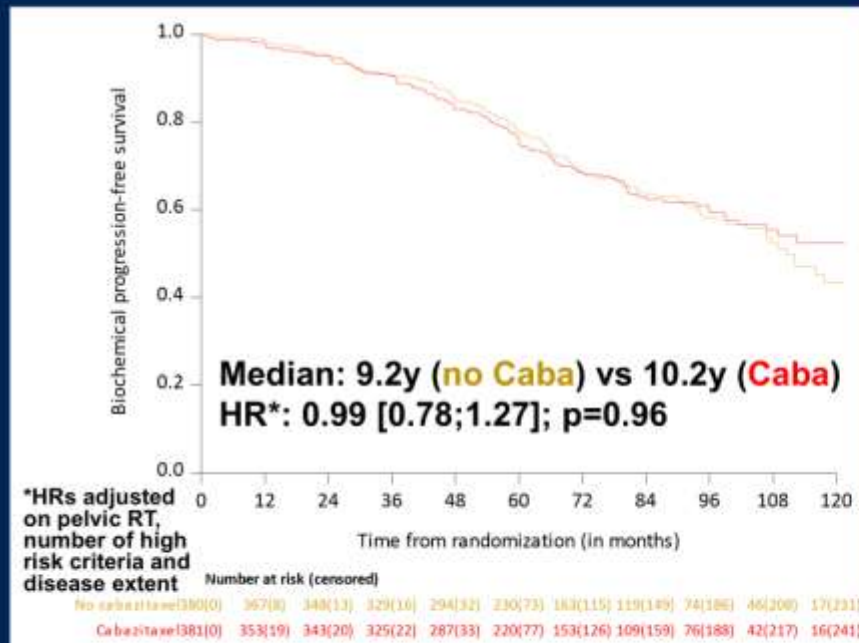
PEACE-2: Patients characteristics

	ADT-Prostate RT (n=189)	ADT-RT Pelvis (n=191)	ADT-RT + Caba (n=191)	ADT-RT Pelvis + Caba (n=190)
Median [IQR] age (years)	67 [61-71]	67 [61-70]	67 [62-70]	66 [62-71]
T3-T4	166 (88%)	168 (88%)	174 (91%)	176 (93%)
Gleason score 8-10	145 (77%)	143 (75%)	156 (82%)	142 (75%)
Median [IQR] PSA (ng/mL)	22 [9-38]	23 [9-43]	19 [9-33]	22 [9-42]
Risk factors:				
2	149 (79%)	150 (79%)	150 (79%)	150 (79%)
3	40 (21%)	41 (21%)	41 (21%)	40 (21%)

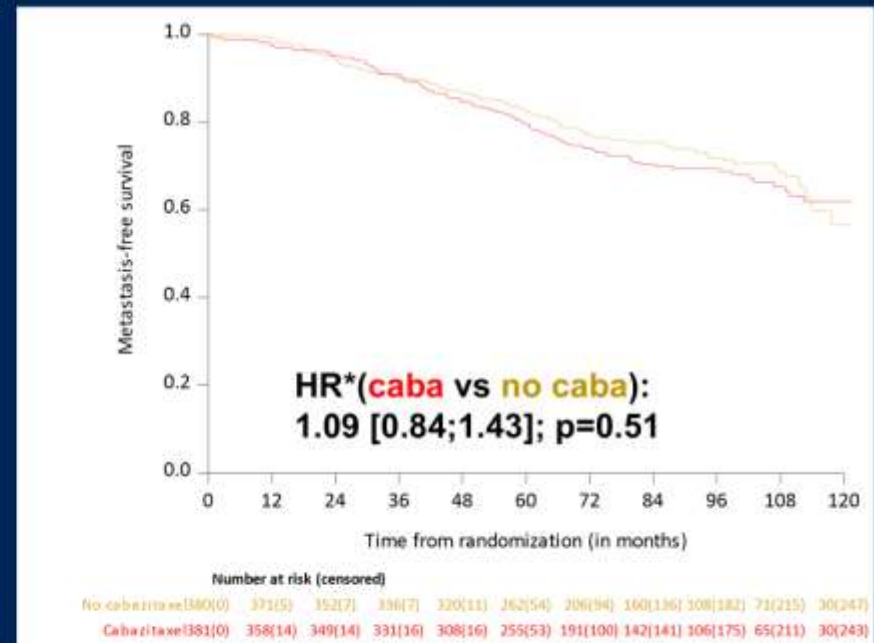
Yüksek Riskli Lokalize Prostat Kanserinde Definitif Radyoterapi (RT) + ADT ve Adjuvan Kemoterapi

PEACE-2: Secondary endpoints

Biochemical-PFS

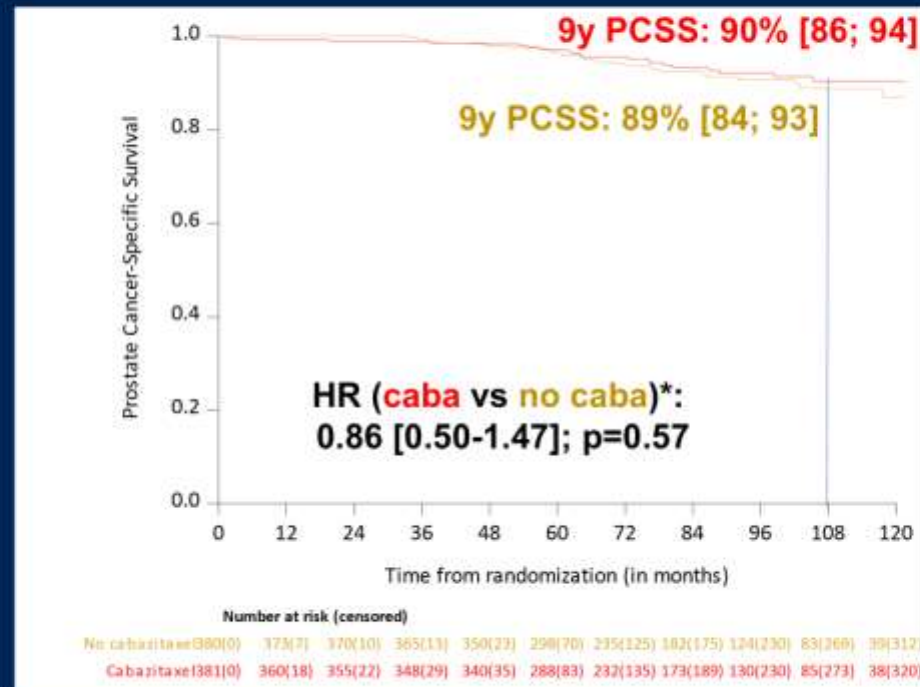


MFS



Yüksek Riskli Lokalize Prostat Kanserinde Definitif Radyoterapi (RT) + ADT ve Adjuvan Kemoterapi

PEACE-2: Prostate cancer Specific Survival



*HR adjusted on pelvic RT, number of high risk criteria and disease extent

Biyokimyasal Rekürens

Tanım

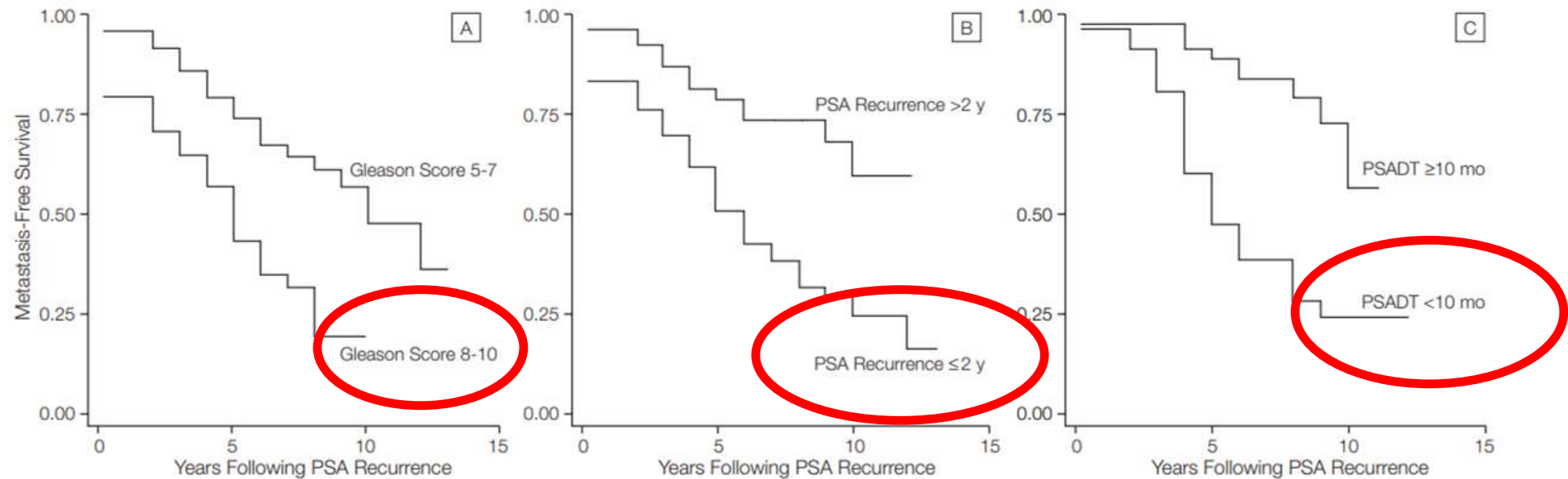
- ☐ ❶ Biyokimyasal Rekürens ; Daha önceleri EUA tanımlaması, Prostatektomi sonrası PSA değeri nadir düzeye düşen hastalarda PSA değerinin artarak ≥ 0.2 ng/ml olarak ölçülmesi ve bunun birkaç ölçümle doğrulanması
- ☐ ❷ NCCN tanımlaması; Prostatektomi sonrası PSA değeri nadir düzeye düşen hastalarda PSA değerinin artarak ≥ 0.1 ng/ml olarak ölçülmesi ve bunun birkaç ölçümle doğrulanması
- ☐ ❷ Primer tedavi olarak radyoterapi alan hastalarda PSA değerinin ≥ 2 ng/ml olarak ölçülmesi
- ☐ Biyokimyasal Rekürens, Prostatektomi ve Radyoterapi sonrası risk grubuna göre 27–53%.
- ☐ Biyokimyasal Rekürens olan hastaların hepsinde metastaz görülmez. Bu nedenle risk skorlamasına göre yüksek grupta olanlar erken ya da salvage tedavi almalıdır.

❶ Van den Broeck T, et al. Biochemical Recurrence in Prostate Cancer: The European Association of Urology Prostate Cancer Guidelines Panel Recommendations. Eur Urol Focus 2019)

❷ Schaeffer E, Srinivas S, Antonarakis ES, et al. NCCN guidelines: prostate cancer, version 3.2023

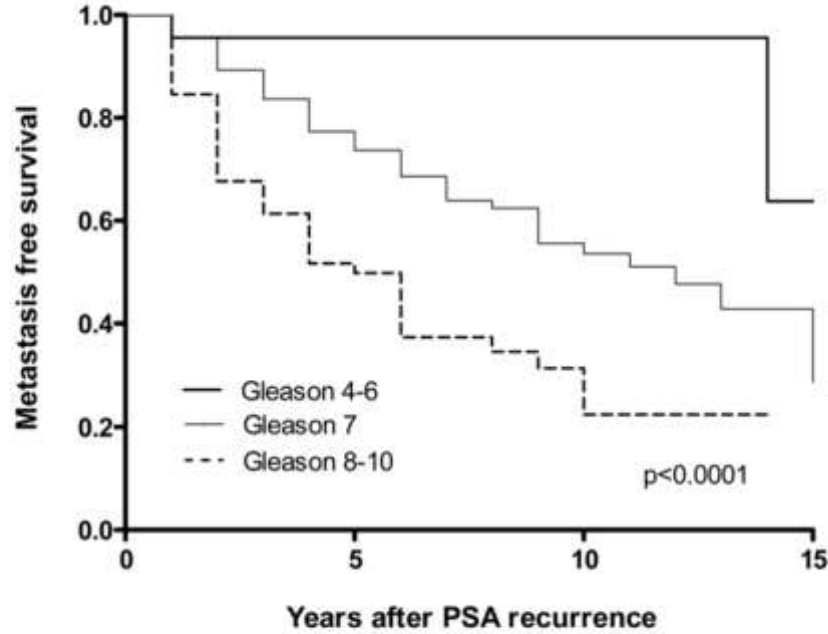
Biyokimyasal Rekürens ve PSA Persistansı Metastaz riski

Figure 3. Actuarial Likelihood of Metastasis-Free Survival in 304 Men With Prostate-Specific (PSA) Antigen Elevation After Radical Prostatectomy

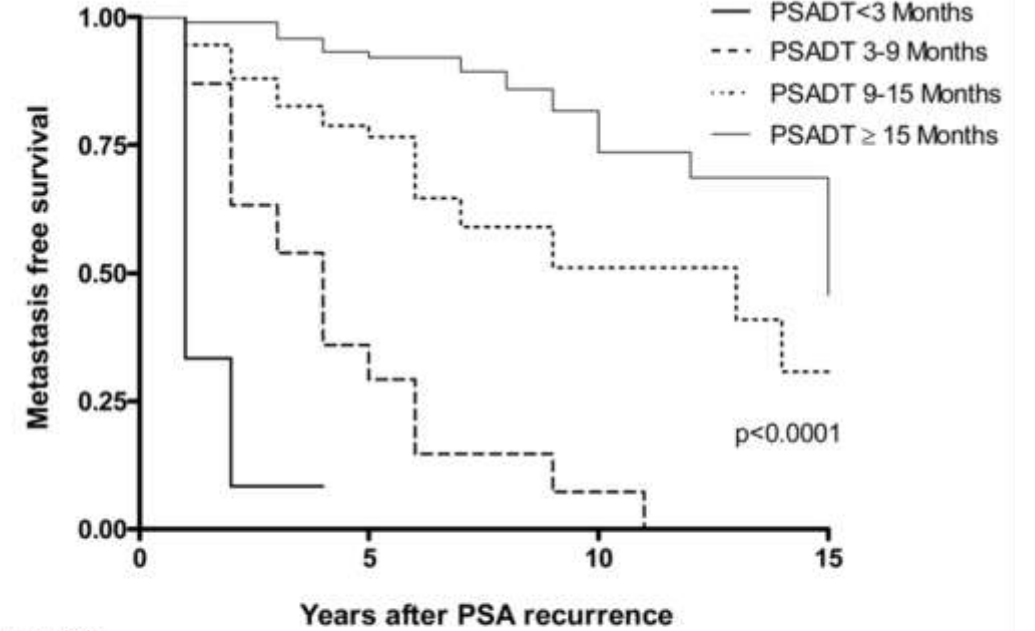


A, Based on Gleason scores in the radical prostatectomy specimen ($P < .001$). B, Based on years until initial biochemical recurrence ($P < .001$). C, Based on prostate-specific antigen doubling time (PSADT) ($P < .001$).

Biyokimyasal Rekürens Metastaz riski



Number at risk				
Gleason score 4-6	88	26	6	1
Gleason score 7	239	85	29	3
Gleason score 8-10	123	28	7	0



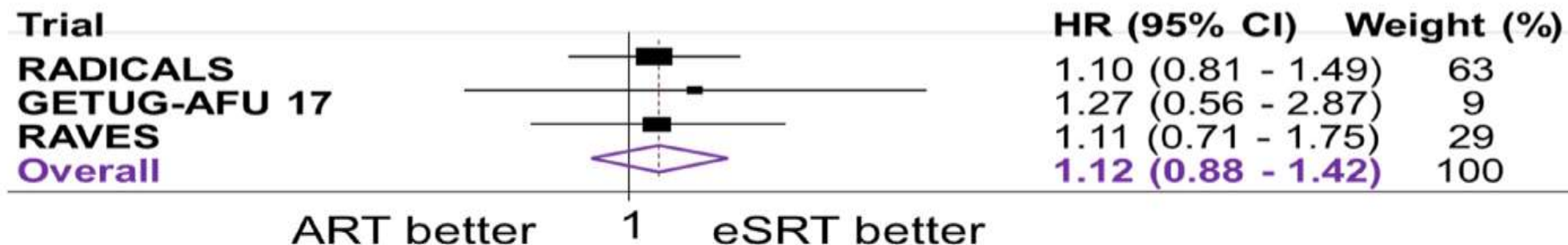
Number at risk				
PSADT < 3 Month	46	0	0	0
PSADT 3-9 Month	106	16	2	0
PSADT 9-15 Month	86	37	11	1
PSADT ≥ 15 Month	212	86	30	3

Cerrahi sonrası medyan 8 yıl takip süresinde, 450 biyokimyasal nüks gelişen ve herhangi bir salvage tedavi almayan hastanın 134'de metastaz görüldü(%29.8).

Radikal Prostatektomi sonrası Adjuvan RT vs Salvage RT

Three Randomized Trials Suggest *Most* Patients Should Get Salvage Radiation, Not Adjuvant

ARTISTIC Meta-Analysis (Vale CL, Lancet Oncology 2020)



Radikal Prostatektomi sonrası Adjuvan RT > Salvage RT

Den, JCO 2015: Decipher May Identify Men Who Benefit Most from Adjuvant RT

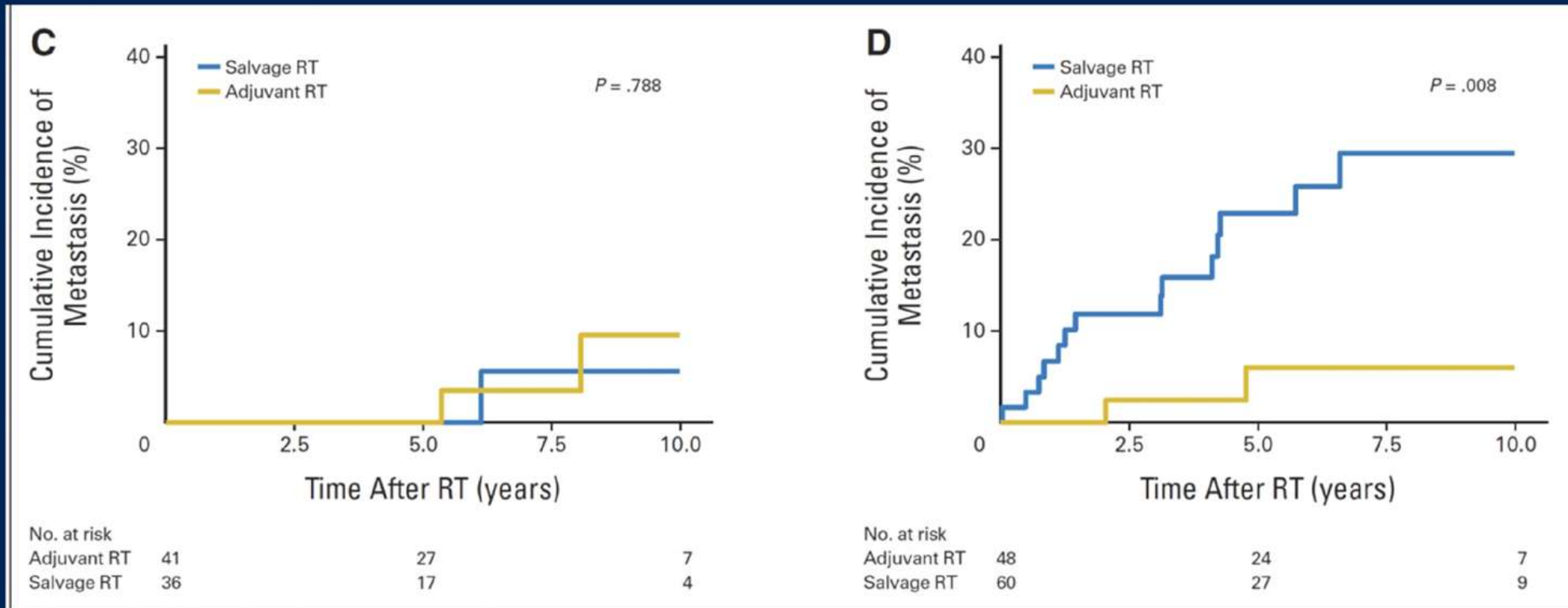
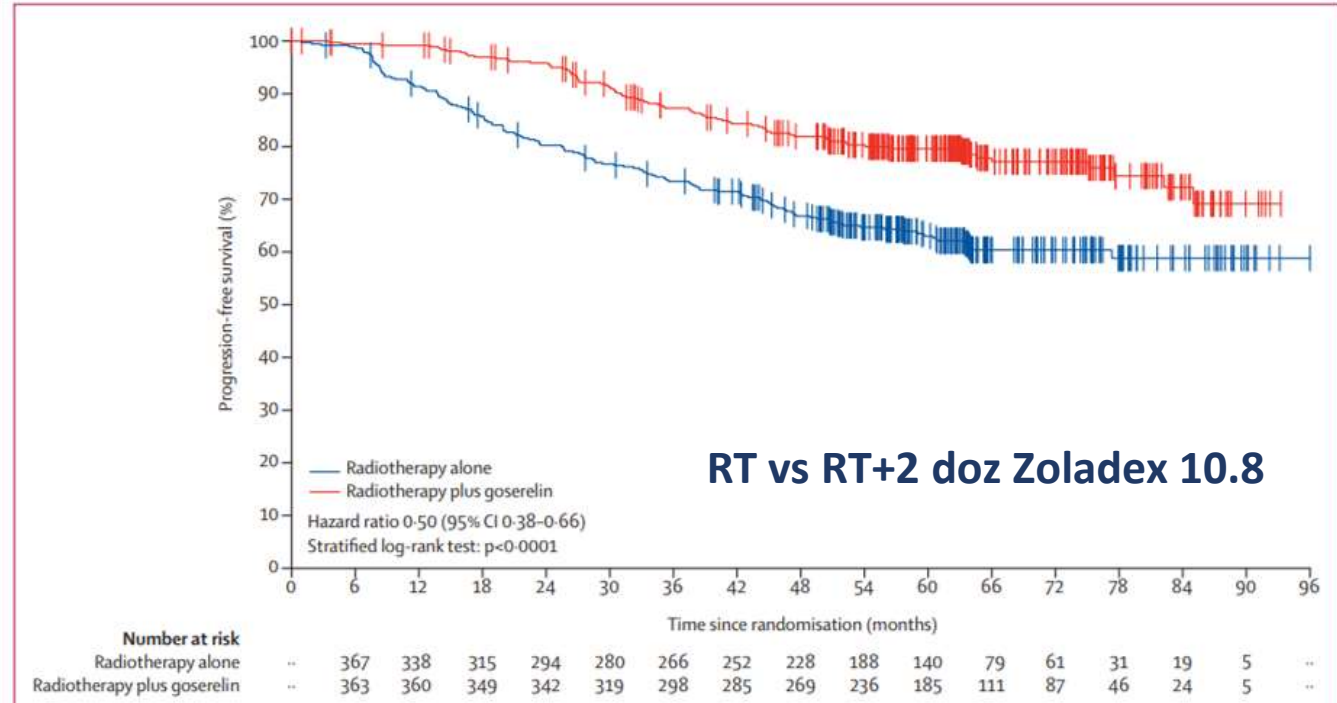


Fig 3. Cumulative incidence curves to evaluate benefit from adjuvant radiotherapy (RT) versus salvage RT stratified by (A and B) Cancer of the Prostate Risk Assessment Postsurgical (CAPRA-S) score and (C and D) genomic classifier (GC).

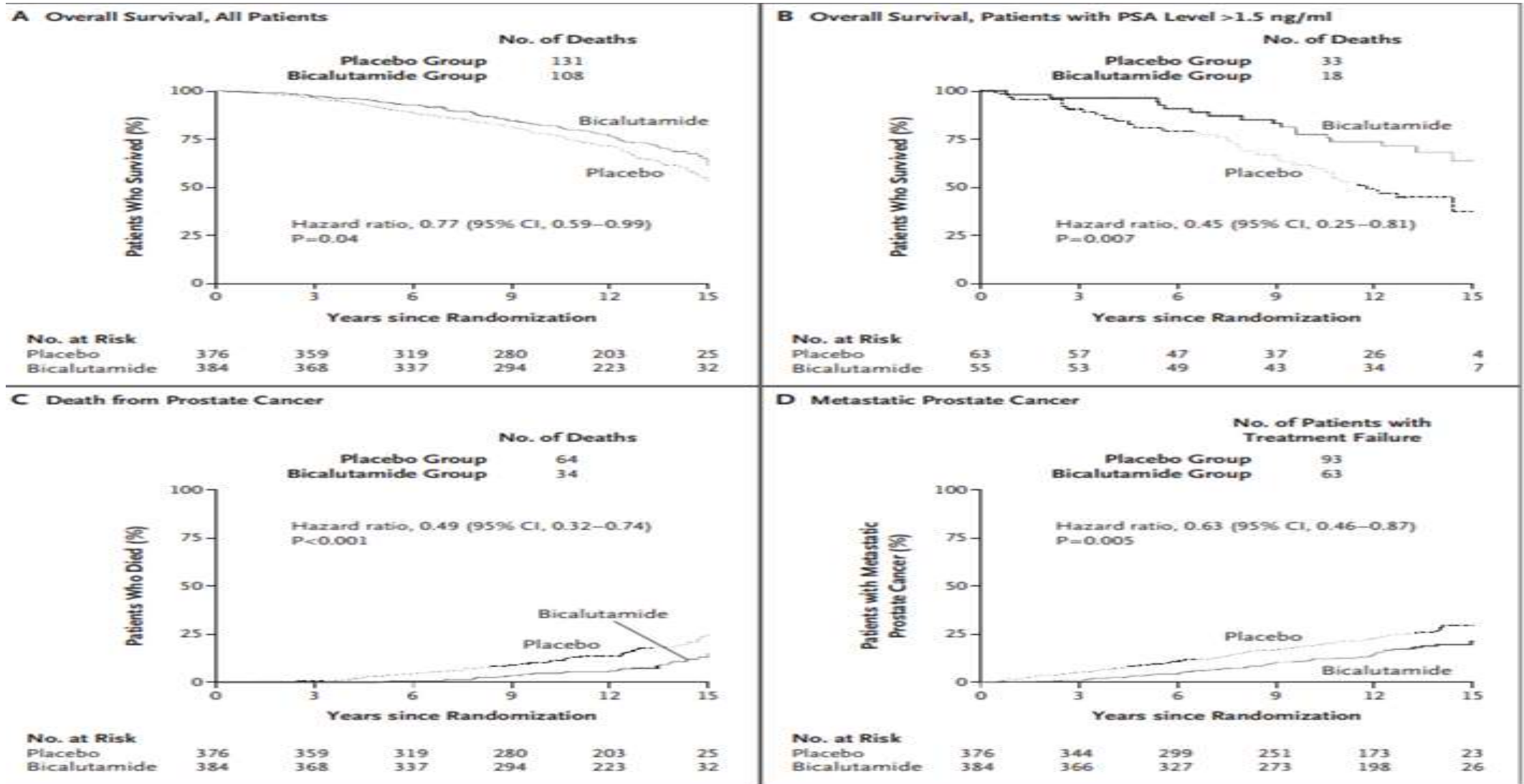
Biyokimyasal Rekürrens ve PSA Persistansında Prostat ± Pelvis Radyoterapisi (RT) + ADT

	Radiotherapy alone (n=373)	Radiotherapy and goserelin (n=369)
Age (years)	67 (52-85)	67 (49-80)
Gleason score		
<8	332 (89%)	329 (89%)
≥8	41 (11%)	40 (11%)
Pathological tumour stage (TNM 2005)		
pT2a	37 (10%)	29 (8%)
pT2b	76 (20%)	75 (20%)
pT2c	88 (24%)	92 (25%)
pT3a	121 (32%)	127 (34%)
pT3b	50 (13%)	44 (12%)
pT4 bladder neck involvement	0	1 (<1%)
Missing	1 (<1%)	1 (<1%)
Pathological node involvement (TNM 2005)		
pN0	274 (74%)	273 (74%)
pNX	99 (27%)	96 (26%)
Positive surgical margins	196 (53%)	175 (47%)
Seminal vesicle involvement	318 (85%)	312 (85%)
PSA doubling time >6 months	276 (74%)	270 (73%)
ECOG performance status		
0	345 (92%)	329 (89%)
1	13 (4%)	22 (6%)
Missing	15 (4%)	18 (5%)
PSA at baseline randomisation (µg/L), median (IQR)*	0.30 (0.20-0.50)	0.30 (0.20-0.50)
Time between surgery and relapse (months), median (IQR)*	29.99 (19-52)	33.98 (21-53)
Presurgery PSA (µg/L), median (IQR)†	8.10 (6-12)	8.35 (6-12)

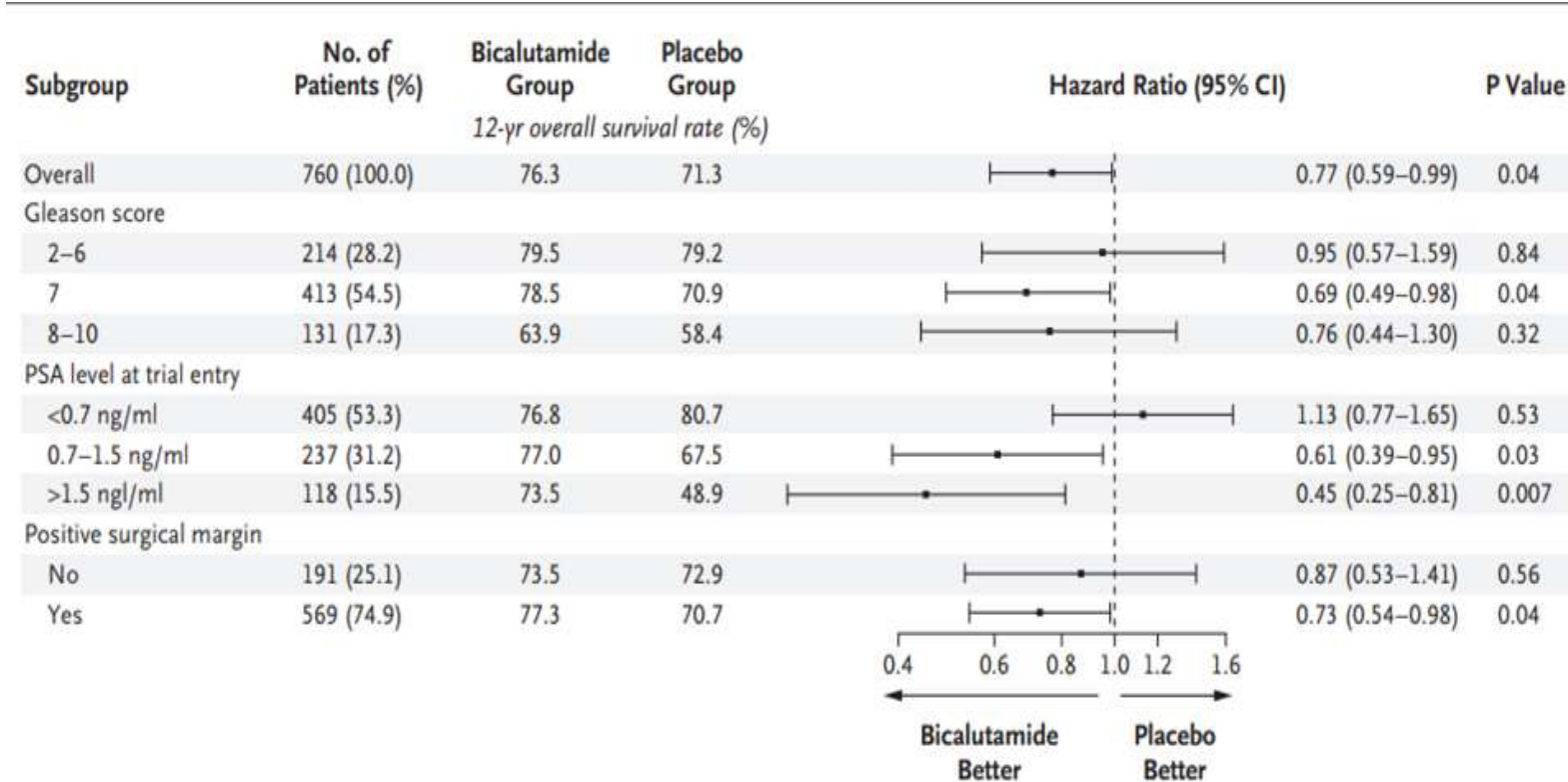


5 yılda biyokimyasal veya klinik progresyonsuz sağkalım: %80'e karşı %62 (%57-67); HR: 0,50; p<0,0001

Biyokimyasal Rekürrens ve PSA Persistansında RT + 2 Yıl Bicalutamid (150 mg/gün) – RTOG 9601



Biyokimyasal Rekürrens ve PSA Persistansında RT + 2 Yıl Bikalutamid (150 mg/gün) – RTOG 9601

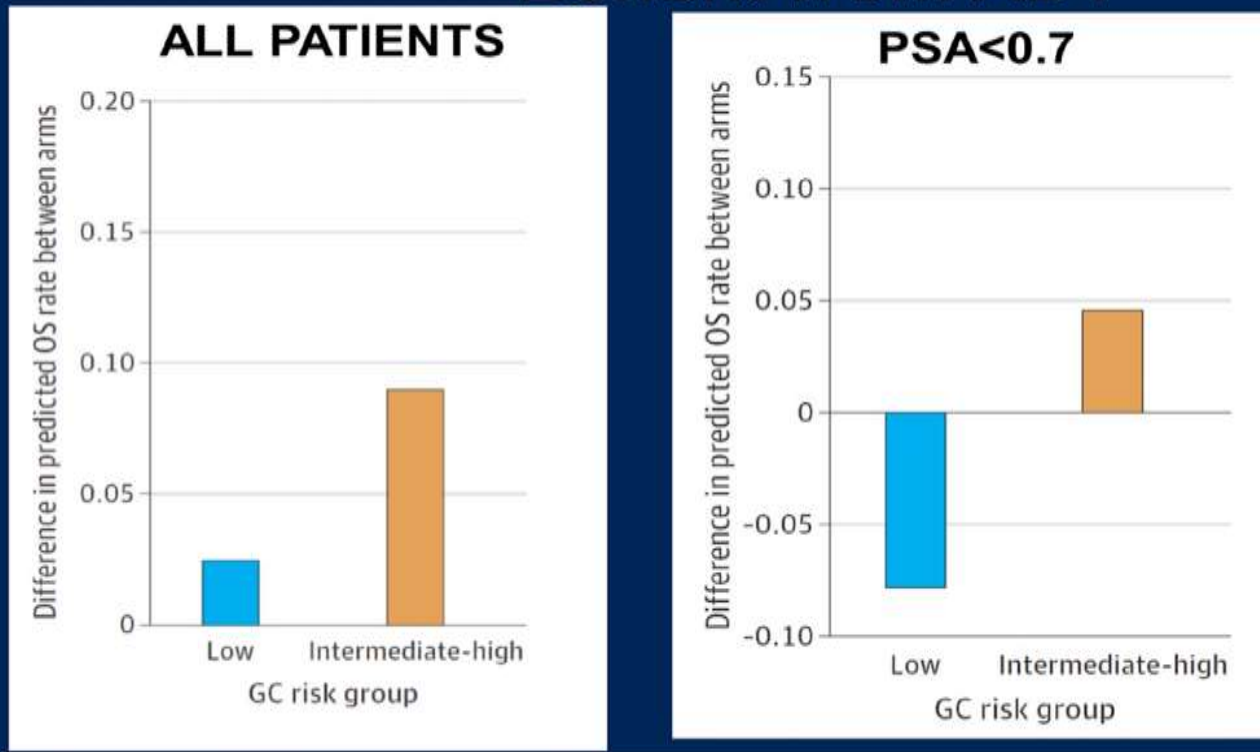


Bikalutamid grubundaki hastaların %69,7'sinde jinekomasti gelişmiştir.

Advers olay olarak bildirilen kardiyovasküler ölüm oranı, bikalutamid grubunda plasebo grubuna kıyasla anlamlı olarak daha yüksek bulunmamıştır.

Biyokimyasal Rekürrens ve PSA Persistansında RT + 2 Yıl Bikalutamid (150 mg/gün) – RTOG 9601

Among PSA <0.7, Only Decipher Int/High Has OS Benefit from ADT



Bars show % Difference in OS by Treatment Arm

Biyokimyasal Rekürens ve PSA Persistansı

Prostat+pelvis RT+ADT Sonuçları

1-PBRT

2-PBRT+4-6 ay
LHRH

3-PBRT+PLNRT+2-
4 ay LHRH

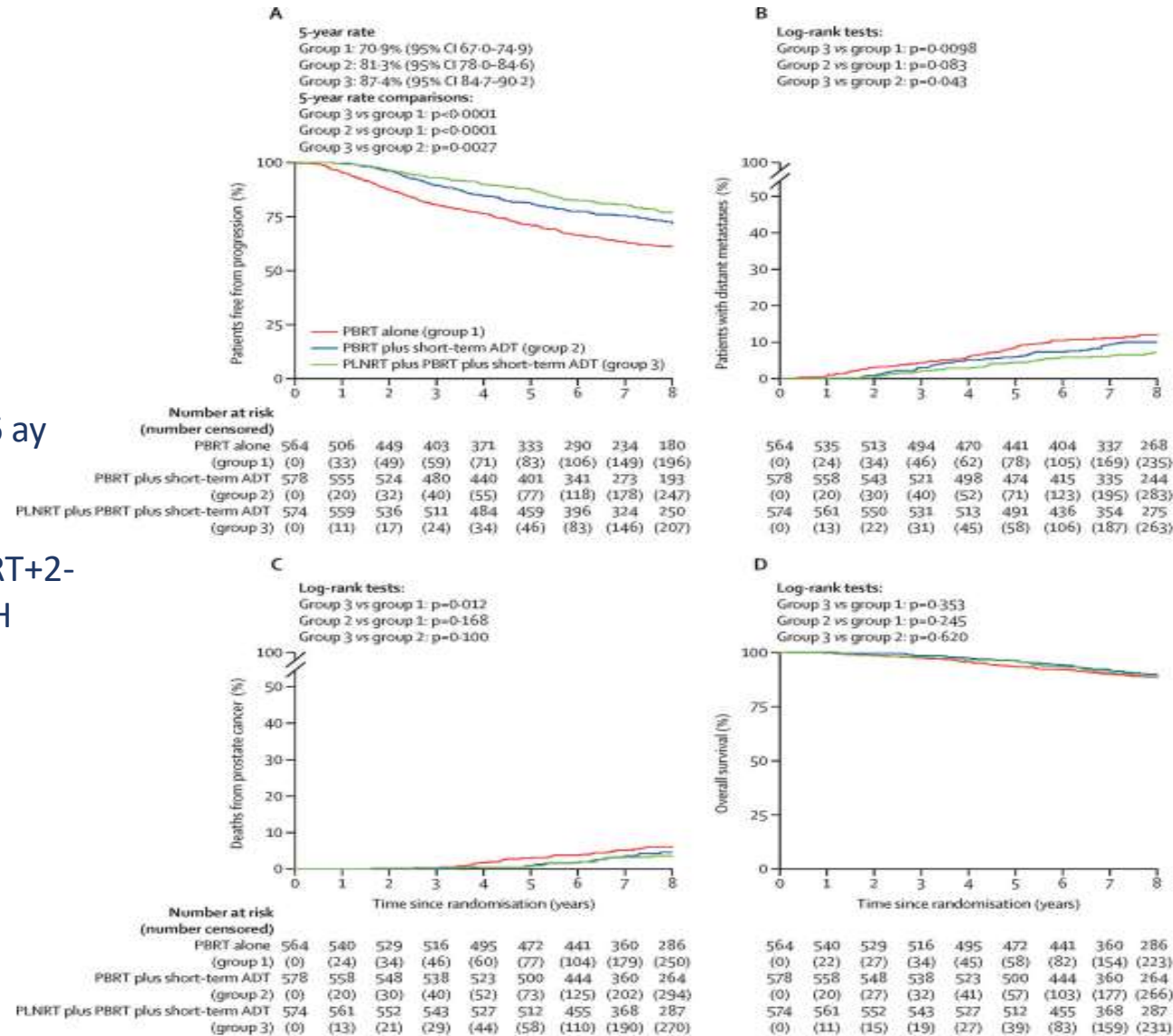


Figure 2:
Kaplan-Meier estimates and cumulative incidence curves: (A) Freedom from progression,

pT2/pT3

Overall, about 15% had pT3b disease, 53% had pT2 disease, 50% had positive margins, and 17% had Gleason score ≥ 8 disease. Pelvic lymphadenectomy was done in 65%, with a median number of lymph nodes removed of 6. The median PSA at protocol registration was 0.35 and 25% had a value of 0.2 or less.

The 5 yr FFP rates for all 1716 eligible patients were 71%, 81% and 87% for Arms 1, 2 and 3, respectively

Acute grade 2+ and 3+ adverse events increased significantly from Arm 1 to Arm 2 to Arm 3; however, only significant late grade 2+ blood/bone marrow events were attributable to the use of PLNRT

PSMA PET-CT negatif yüksek riskli hastalarda pelvik RT

In patients with high-risk localised/locally advanced prostate cancer undergoing RT to the prostate, who have had a PSMA PET and are cN0, do you recommend radiation therapy to the pelvic nodes

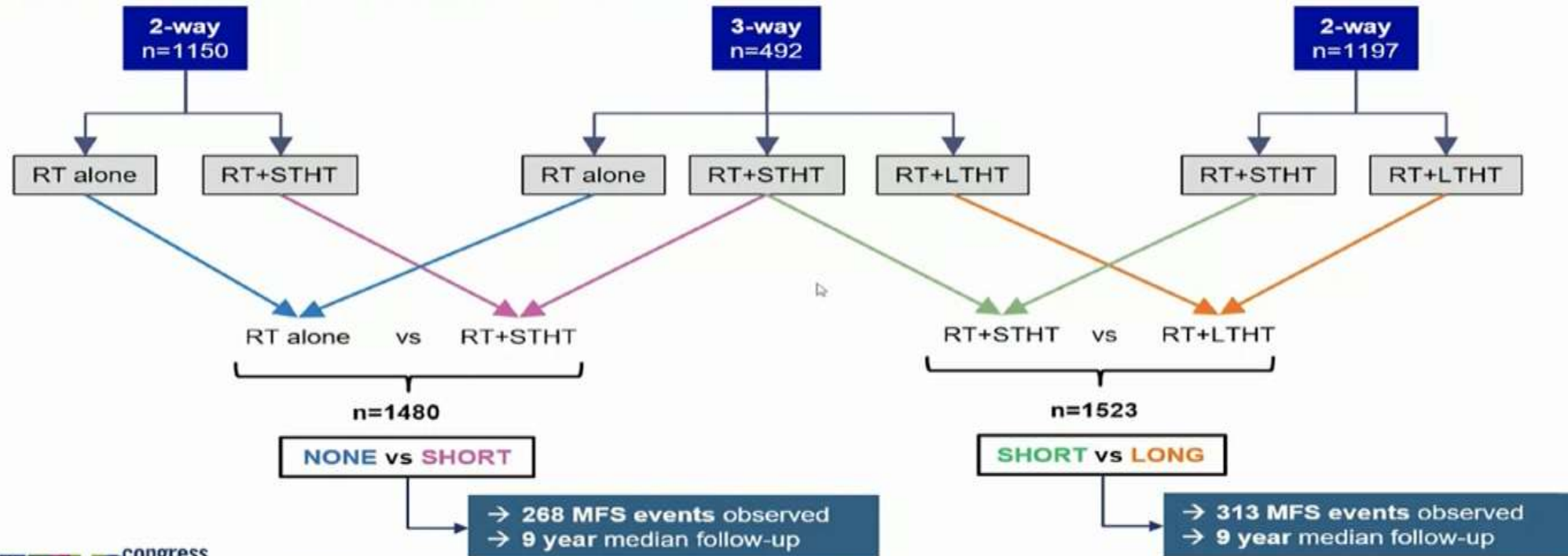
- ☐ **Yes, in the majority of patients: 56% (50 votes)**
- ☐ Yes, but only in selected patients based on risk factors: 21% (19 votes)
- ☐ No: 23% (21 votes)
- ☐ Abstain/unqualified to answer (16 votes)

Biyokimyasal Rekürens ve PSA Persistansı

RT+uzun dönem ADT

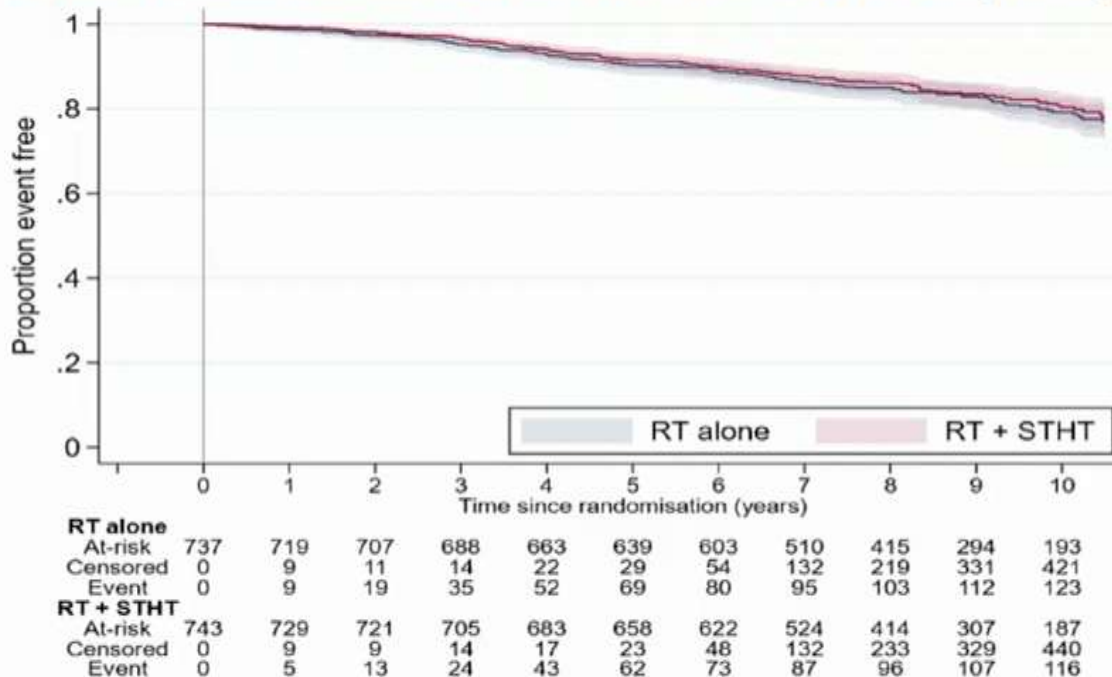
RADICALS-HD: Duration of ADT with post-op RT for prostate cancer

Recruitment and Randomisation



Biyokimyasal Rekürens ve PSA Persistansı RT+uzun dönem ADT

RADICALS-HD: Duration of ADT with post-op RT for prostate cancer None vs Short: Metastases-Free Survival (MFS)



NONE vs SHORT		
	RT alone (n=737)	RT+STHT (n=743)
Events	142	126
HR (95%CI)	0.89 (0.69 to 1.14)	
P-value	0.35	
10yr event free	79%	80%

Note: HR < 1 favour RT+STHT
Note: predicted 10yr MFS = 80%

29% Received *Adjuvant RT*

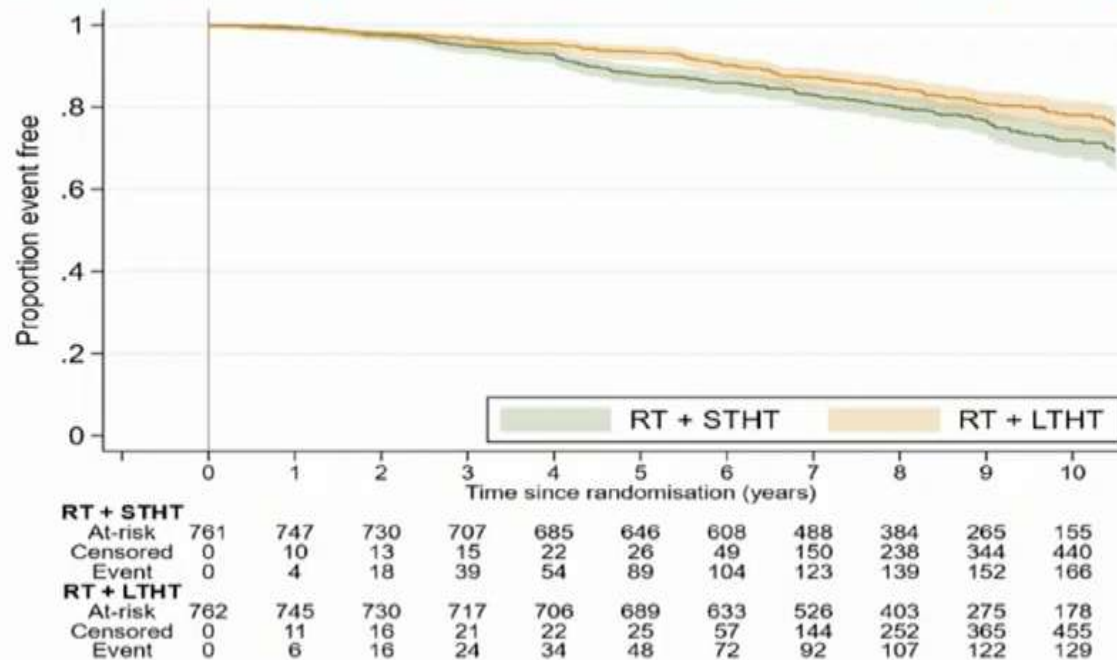
11% Gleason 8-10

Biyokimyasal Rekürens ve PSA Persistansı

RT+uzun dönem ADT

RADICALS-HD: Duration of ADT with post-op RT for prostate cancer

Short vs Long: Metastases-Free Survival (MFS)



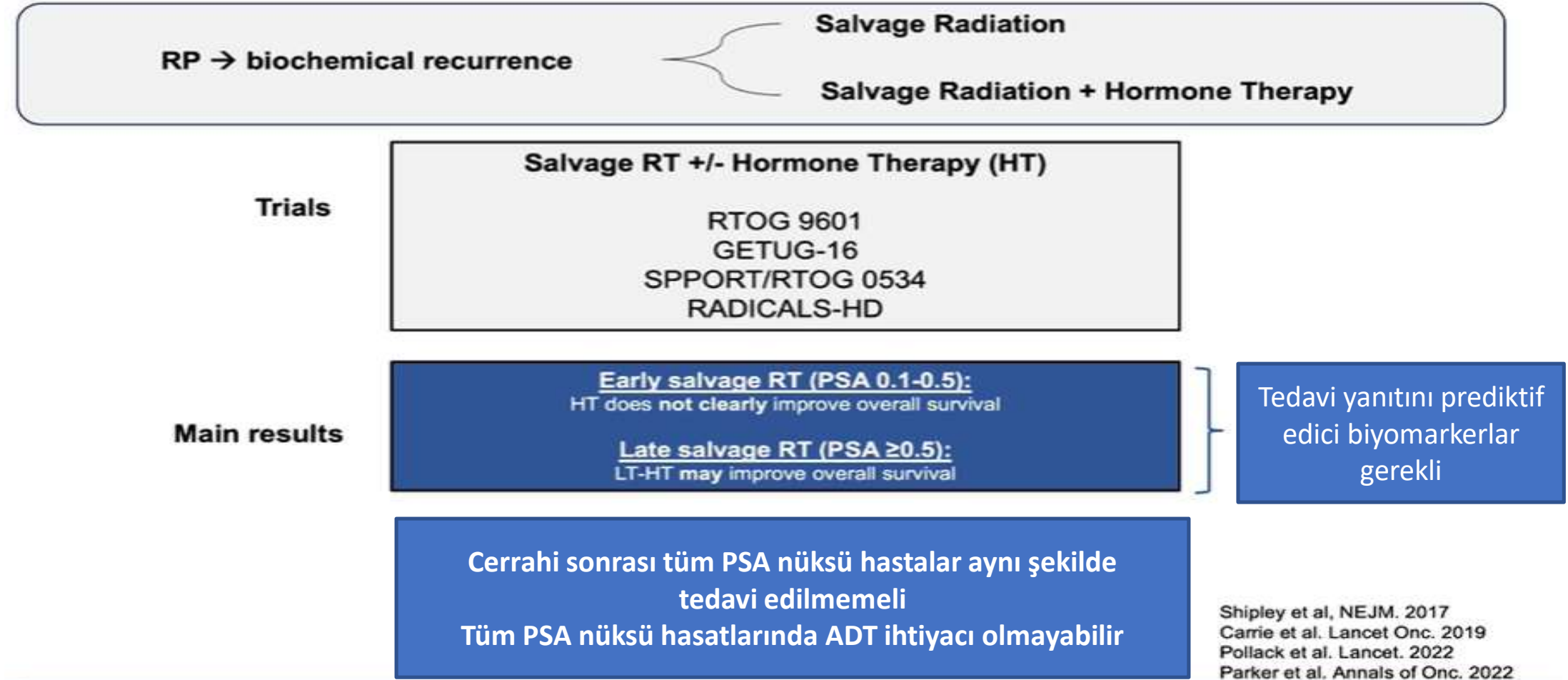
	SHORT vs LONG	
	RT+STHT (n=761)	RT+LTHT (n=762)
Events	174	139
HR (95%CI)	0.77 (0.61 to 0.97)	
P-value	0.03	
10yr event free	72%	78%

Note: HR < 1 favour RT+LTHT
Note: predicted 10yr MFS = 75%

43% Received *Adjuvant RT*

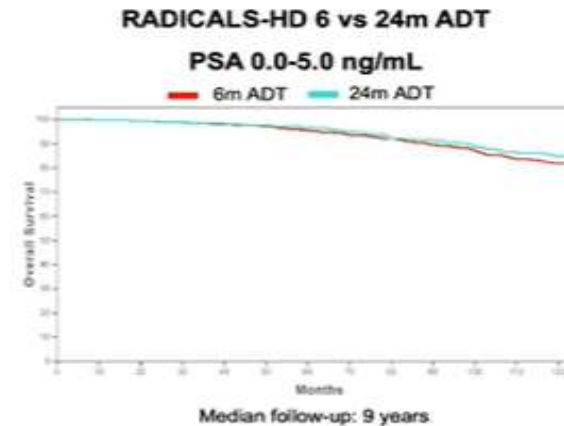
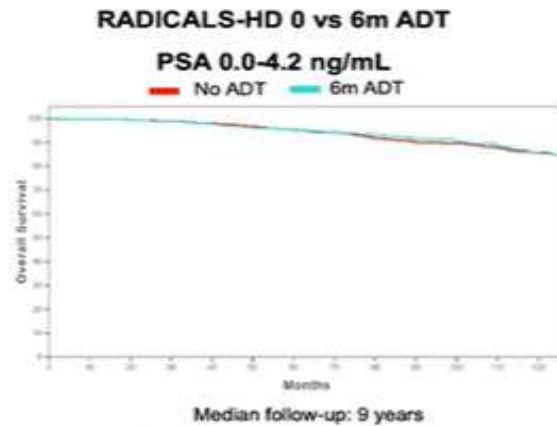
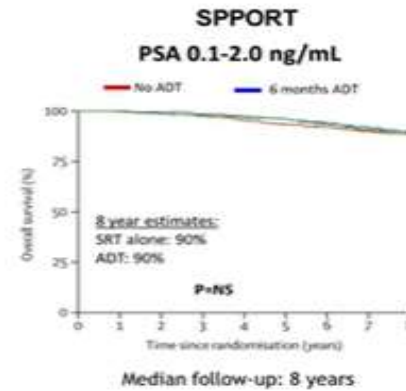
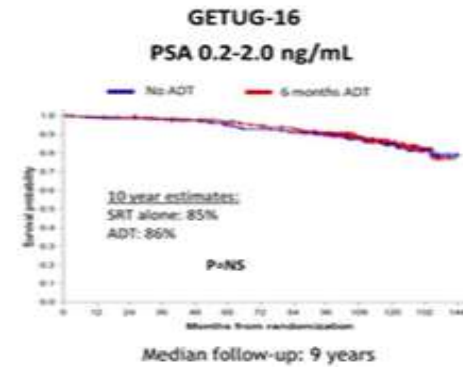
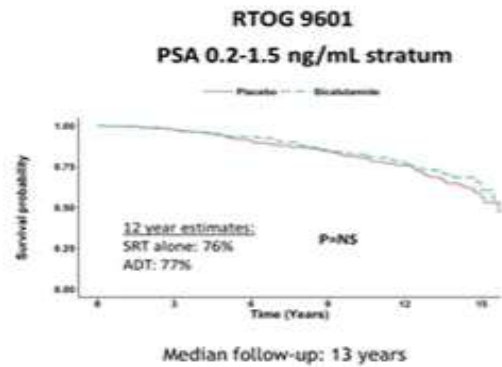
28% Gleason 8-10

Biyokimyasal Rekürens ve PSA Persistansı



ADT+RT ile artmış MFS , Tüm popülasyonda OS faydası yok

Consistent Results in >5,000 patients: Lack of Overall Survival Benefit



Shipley et al, NEJM. 2017
Carrie et al. Lancet Onc. 2019
Pollack et al. Lancet. 2022
Parker et al. Annals of Onc. 2022

İzole PSA nüksünde hangi hastalara sistemik tedavi

Risk group	Characteristics
BCR after radical prostatectomy	
Low-risk BCR	PSA-DT >1 yr and pGS <8 (ISUP grade <4)
High-risk BCR	PSA-DT ≤1 yr or pGS 8–10 (ISUP grade 4–5)
BCR after radiation therapy	
Low-risk BCR	IBF > 18 mo and bGS <8 (ISUP grade <4)
High-risk BCR	IBF ≤ 18 mo or bGS 8–10 (ISUP grade 4–5)
BCR = biochemical recurrence; PSA-DT = prostate-specific antigen doubling time; pGS = pathological Gleason score; ISUP = International Society of Urological Pathology; IBF = interval from primary therapy to biochemical failure; bGS = biopsy Gleason score.	

+Tedavi öncesi PSA(≥0.5 ng/dl

Biyokimyasal Rekürens ve PSA Persistansı Doz Yoğun Tedavi

FORMULA 509 Schema

Patients With Recurrent Prostate Cancer After Prostatectomy

Stratify

1. PSA >0.5 vs. ≤0.5
2. pN1 vs. pN0

R
A
N
D
O
M
I
Z
E

Salvage Radiation
with **6 mo GnRH Agonist and
bicalutamide**

Salvage Radiation
with **6 mo GnRH Agonist,
Abiraterone Acetate plus
Prednisone, and Apalutamide**

N=345

Primary outcome: Progression-free survival

Secondary outcomes: Metastasis-free survival, Physician-reported toxicity,
Patient-reported toxicity



Biyokimyasal Rekürens ve PSA Persistansı Doz Yoğun Tedavi

Patient Characteristics

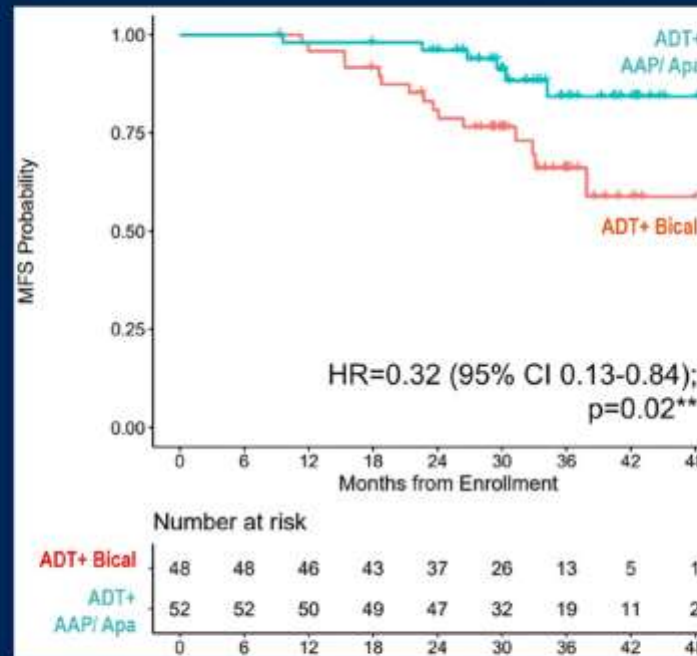
	ADT + Bical (N=172)	ADT + AAP/Apa (N=173)	Overall (N=345)
Age at Enrollment			
Mean (SD)	64.2 (6.8)	63.2 (7.4)	63.7 (7.1)
Median (Range)	65.0 (47.1 – 78.9)	63.0 (43.6 – 81.8)	64.7 (43.6 – 81.8)
Race			
Asian	2 (1.2%)	4 (2.3%)	6 (1.7%)
Black	18 (10.5%)	13 (7.5%)	31 (9.0%)
White	146 (84.9%)	150 (86.7%)	296 (85.8%)
More than one race	3 (1.7%)	2 (1.2%)	5 (1.5%)
Other	3 (1.7%)	4 (2.3%)	7 (2.0%)
Gleason Score			
6	2 (1.2%)	2 (1.1%)	4 (1.2%)
7	86 (50.0%)	96 (55.5%)	182 (52.7%)
8	17 (9.9%)	20 (11.6%)	37 (10.7%)
9	67 (38.9%)	54 (31.2%)	121 (35.1%)
10	0 (0%)	1 (0.6%)	1 (0.3%)
PSA at Enrollment			
Mean (SD)	0.9 (1.7)	0.8 (1.6)	0.9 (1.6)
Median (Range)	0.3 (0 – 11.58)	0.3 (0.1 – 9.1)	0.3 (0 – 11.58)
Pathologic Nodal Status			
pN0	123 (71.5%)	123 (71.1%)	246 (71.3%)
pN1	49 (28.5%)	50 (28.9%)	99 (28.7%)

- Median age 65
- 35% Gleason 9
- Median PSA 0.3
- 31% PSA >0.5
- 29% pN1



Biyokimyasal Rekürens ve PSA Persistansı Doz Yoğun Tedavi

MFS Benefit Among PSA >0.5 (n=100)



3 year MFS
84.3% vs. 66.1%

Absolute improvement
18.2% at 3 years

NNT = 5

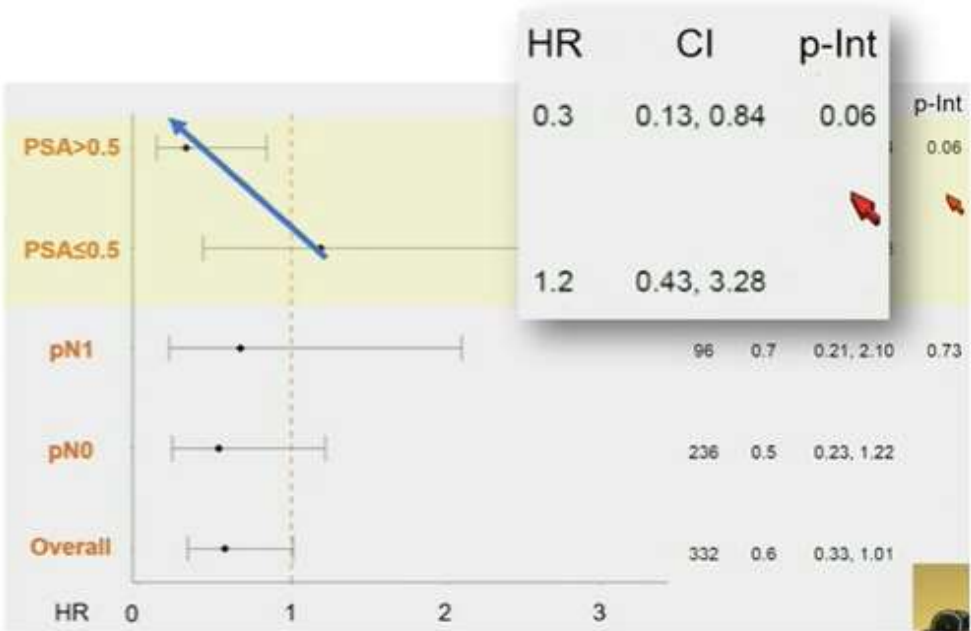
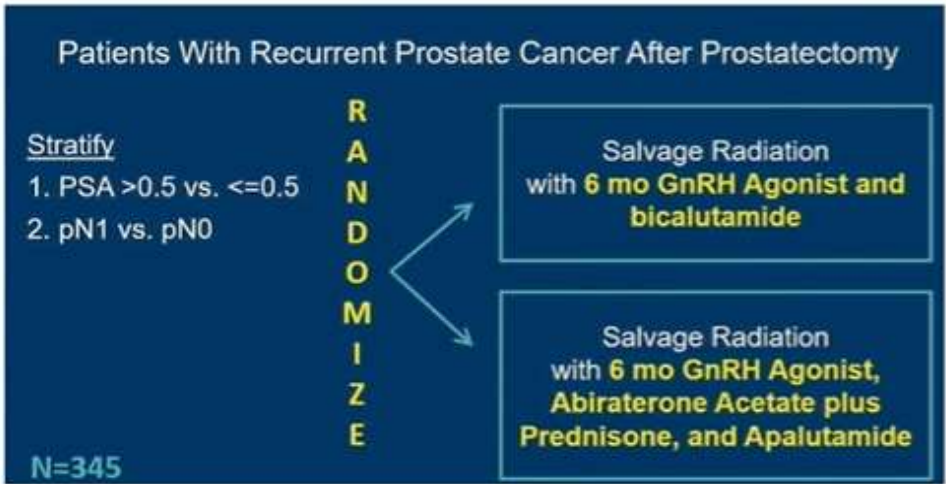
**two-sided



Tedavi öncesi PSA düzeyi kombine tedaviler için prediktif

Differential Benefit by pre-SRT PSA

Formula-509



Biyokimyasal Rekürens ve PSA Persistansı Doz Yoğun Tedavi

PARIS
2022 ESMO congress

PRESTO: A Phase 3 Open- Label Study of Androgen Annihilation in Patients with High-Risk Biochemically Relapsed Prostate Cancer (AFT-19)

Rahul Aggarwal, on behalf of the Alliance
AFT-19 Study Investigators

Paris, France
11 SEP 2022



Biyokimyasal Rekürens ve PSA Persistansı Doz Yoğun Tedavi

Study Schema

Prior radical
prostatectomy

Biochemical recurrence
with PSA > 0.5 ng/mL

PSA-DT ≤ 9 months

No metastases on
conventional imaging

Last dose of ADT > 9
months prior to study
entry

Serum T > 150 ng/dL

Randomize 1:1:1

Arm A:
LHRH Analog

Arm B:
LHRH Analog +
Apalutamide

Arm C:
LHRH Analog +
Apalutamide + Abiraterone
Acetate + Prednisone

Follow up for PSA
Progression

Treatment per Investigator
Discretion

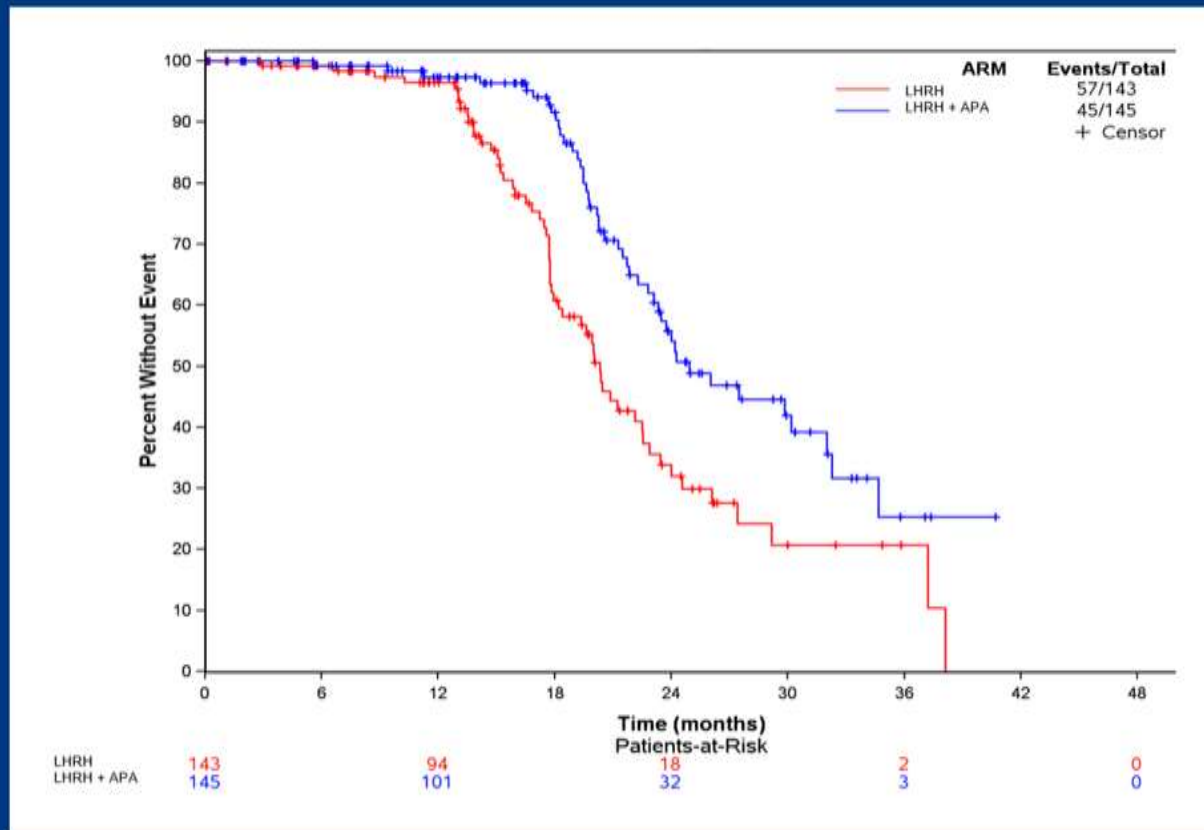
Long Term Follow Up

Stratified by PSA doubling
time
(< 3 months vs. 3 – 9 months)

52 Weeks

Biyokimyasal Rekürens ve PSA Persistansı Doz Yoğun Tedavi

Arm B: ADT + apalutamide vs. ADT monotherapy



Median follow up 21.5 months

102 PSA PFS events

Median PSA progression-free survival

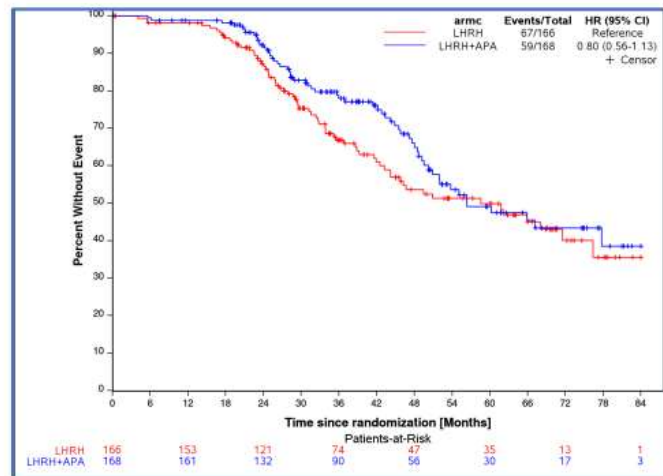
ADT + APA = 24.9 months
(95% CI: 23.3 – 32.3)

ADT alone = 20.3 months
(95% CI: 18.2 – 22.9)

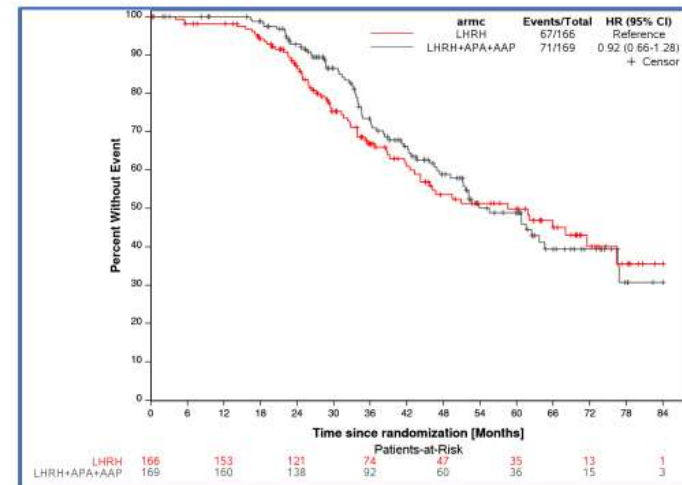
**Hazard ratio 0.52 (95%
CI: 0.35 – 0.77)**

One-sided p-value =
0.00047)

PRESTO study: secondary endpoints



- MFS events: 38% of patients randomized
- HR = 0.80 (95% CI: 0.56 – 1.13)



- MFS events: 41% of patients randomized
- HR = 0.92 (95% CI: 0.56 – 1.13)

Not practice changing

Presenter: Dr. Constance Thibault

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Sistemik tedaviler için yeni prediktif markerlar



ROGEL CANCER CENTER
MICHIGAN MEDICINE

NRG
ONCOLOGY
Advancing Research. Improving Lives.™

University Hospitals
Seidman Cancer Center
Cleveland | Ohio

AI prognostic biomarker for recurrent prostate cancer after prostatectomy: development and validation using deep learning on digital histopathology from NRG/RTOG-0534 and NRG/RTOG-9601

Todd M. Morgan, Yi Ren, Siyi Tang, Wouter Zwerink, Emmalyn Chen, Akinori Mitani, Huei-Chung Huang, Jeffry P. Simko, Sandy DeVries, William U. Shipley, Alan Pollack, David Bowes, André-Guy Martin, Alexander G. Balogh, Jeff M. Michalski, Michael J. Greenberg, Jason A. Efstathiou, Jean-Paul Bahary, Ashley E. Ross, Andre Esteva, Timothy N. Showalter, Paul L. Nguyen, Karen E. Hoffman, Joseph P. Rodgers, Felix Y. Feng, Daniel E. Spratt

AUA 2024
MAY 3-6
San Antonio

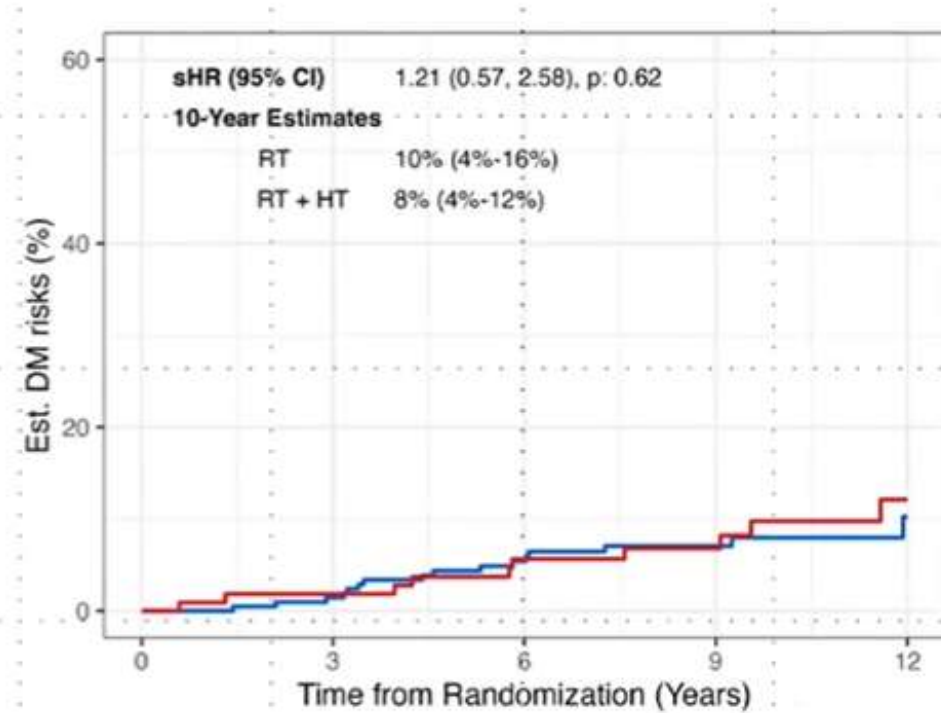
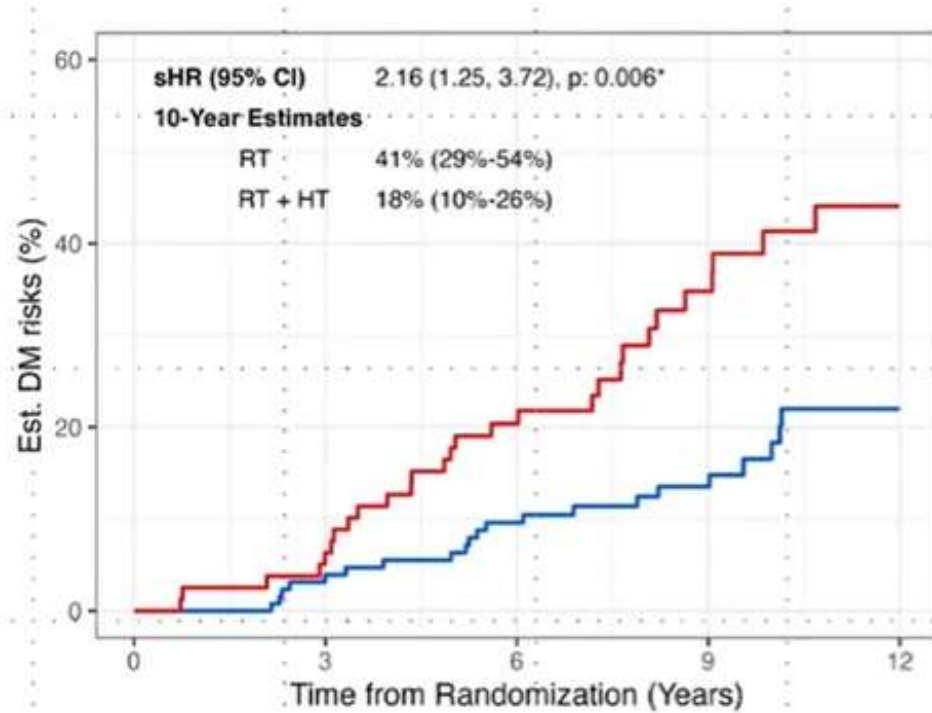
 @wandering_gu
@DrSpratticus
@NRGOnc

NCI National Clinical Trials Network
A National Cancer Institute program

NCI Community Oncology Research Program
A program of the National Cancer Institute of the National Institutes of Health

Sistemik tedaviler için yeni prediktif markerlar

New Artera Multi-modal AI model:



Prostat Kanserinde Post-Operatif Radyoterapi ve Anti-Androjen Tedavisi: POSEIDON Bireysel Hasta Verileri Meta-Analizi

Role of IPD Meta-Analyses

- An individual patient data (IPD) meta-analysis allows a more granular evaluation of potential interaction thresholds, non-linear associations, and subgroup-specific effects
- We launched the Post-Operative Salvage or Adjuvant RadiothErapy and AntI-AnDrogen Therapy for Men with PrOstate CaNcer (**POSEIDON**) IPD meta-analysis of all published randomized trials



Prostat Kanserinde Post-Operatif Radyoterapi ve Anti-Androjen Tedavisi: POSEIDON Bireysel Hasta Verileri Meta-Analizi

UCLA Health

University Hospitals
Seidman Cancer Center



Included Trials

RTOG 9601: RT vs RT+LT-HT

GETUG-16: RT vs RT+ST-HT

RADICALS: RT vs. RT+ST-HT

RADICALS: RT vs. RT+ST-HT vs.
RT+LT-HT

RADICALS: RT+ST-T vs. RT+LT-HT

RTOG 0534: RT vs. RT+ST-HT*

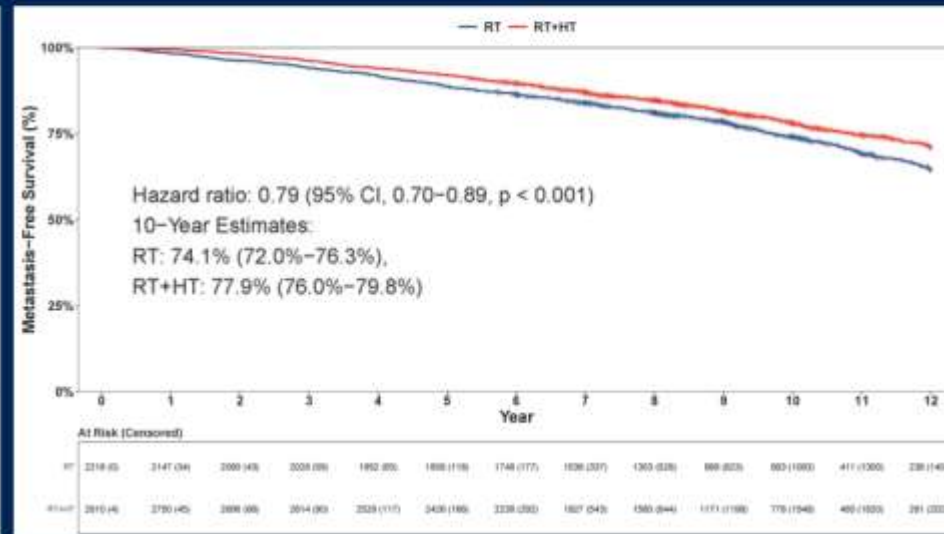
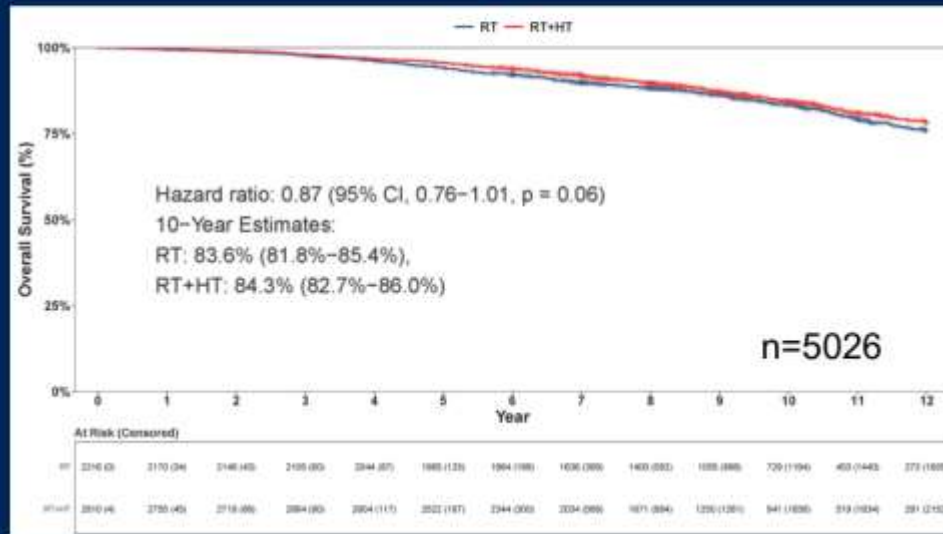
Prostat Kanserinde Post-Operatif Radyoterapi ve Anti-Androjen Tedavisi: POSEIDON Bireysel Hasta Verileri Meta-Analizi

	HT Use		Short-Term HT Use (ST-HT)		Long-Term HT Use (LT-HT)	
	RT alone	RT+HT	RT alone	RT+ST-HT	RT alone	RT+LT-HT
n	2,216	2,810	1,674	2,264	542	546
Follow-up (median, IQR), years	9.10 (7.30-10.97)		8.80 (7.13-10.10)		12.34 (9.37-13.86)	
Age						
<65	1030 (46.5%)	1278 (45.5%)	760 (45.1%)	1032 (45.6%)	270 (49.8%)	246 (45.1%)
65-69	638 (28.8%)	858 (30.5%)	494 (29.5%)	691 (30.5%)	144 (26.6%)	167 (30.6%)
≥70	548 (24.7%)	674 (24.0%)	420 (25.1%)	541 (23.9%)	128 (23.6%)	133 (24.4%)
PSA (median, IQR) ng/mL	0.3 (0.2, 0.6)	0.3 (0.2, 0.6)	0.3 (0.2, 0.5)	0.3 (0.2, 0.5)	0.5 (0.3, 0.9)	0.5 (0.3, 0.9)
Pathologic Gleason Score						
6	390 (17.6%)	510 (18.1%)	270 (16.1%)	384 (17.0%)	120 (22.7%)	126 (23.7%)
7	1,507 (68.0%)	1,882 (67.0%)	1,188 (71.0%)	1,562 (69.0%)	319 (60.4%)	320 (60.2%)
8-10	305 (13.8%)	404 (14.4%)	216 (12.9%)	318 (14.0%)	89 (16.9%)	86 (16.2%)
Positive Margins	1,328 (60.2%)	1,619 (57.8%)	938 (56.4%)	1,225 (54.3%)	390 (72.0%)	394 (72.2%)
Seminal Vesicle Invasion	380 (17.3%)	483 (15.9%)	250 (15.1%)	341 (15.3%)	130 (24.3%)	97 (18.2%)
Extracapsular Extension	931 (43.3%)	1078 (37.0%)	697 (43.0%)	837 (37.6%)	234 (44.1%)	241 (44.7%)

Prostat Kanserinde Post-Operatif Radyoterapi ve Anti-Androjen Tedavisi: POSEIDON Bireysel Hasta Verileri Meta-Analizi

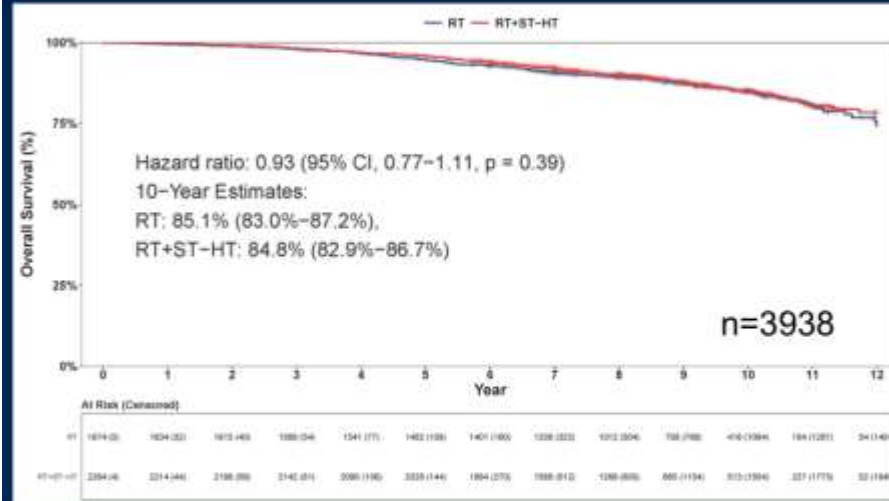
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Survival Results

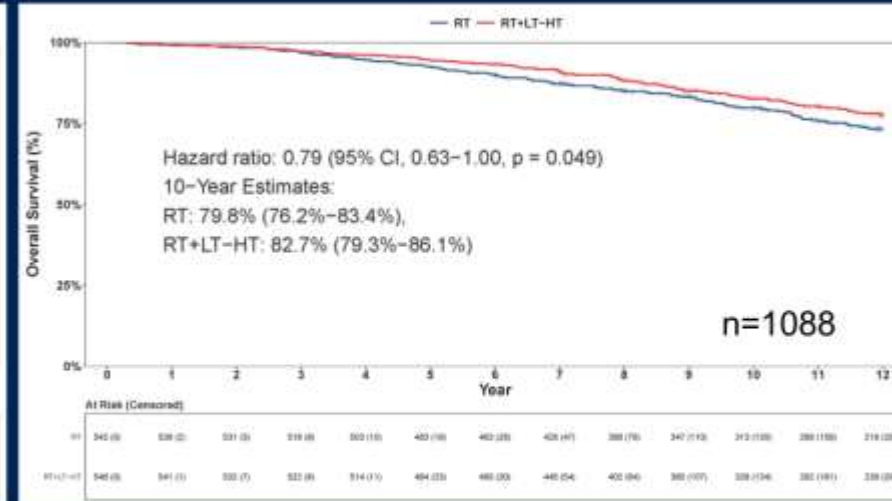


Prostat Kanserinde Post-Operatif Radyoterapi ve Anti-Androjen Tedavisi: POSEIDON Bireysel Hasta Verileri Meta-Analizi

Survival Results: HT-Duration

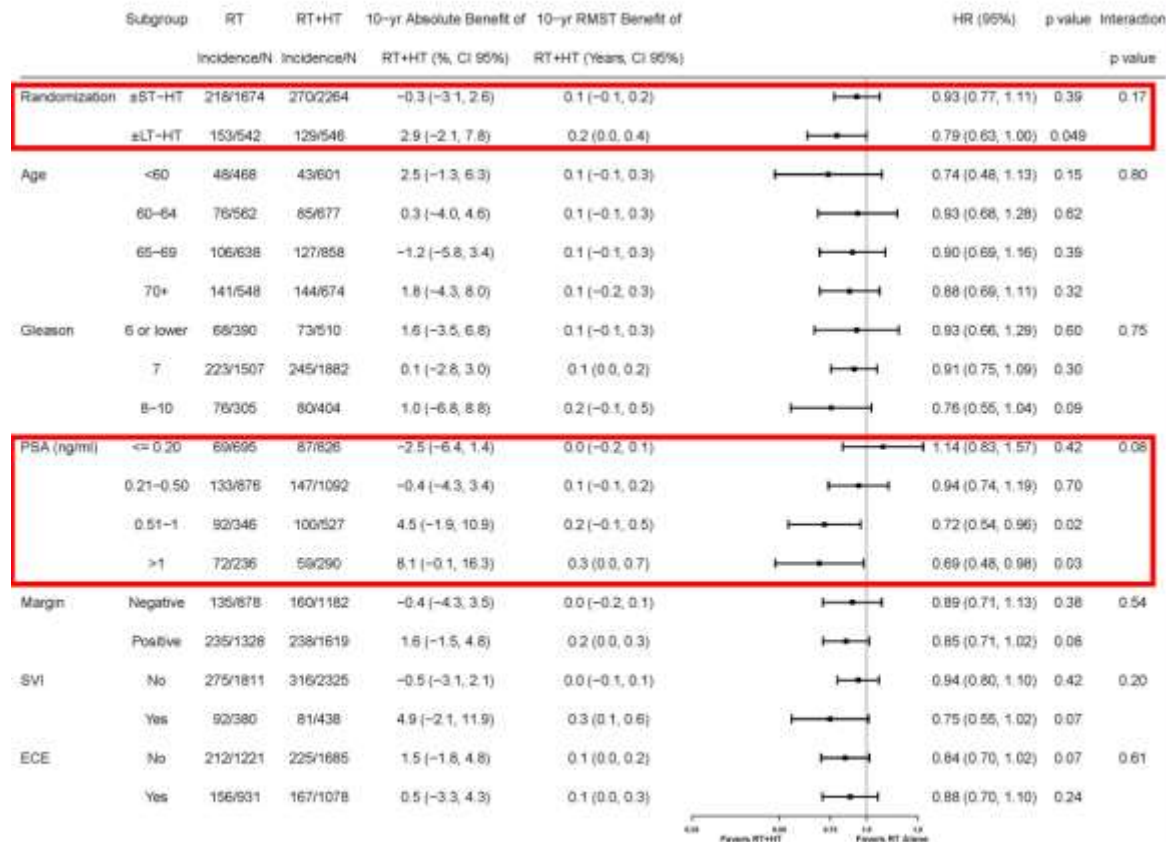


median PSA 0.3



median PSA 0.5

Prostat Kanserinde Post-Operatif Radyoterapi ve Anti-Androjen Tedavisi: POSEIDON Bireysel Hasta Verileri Meta-Analizi



No significant interaction between impact of HT on OS and its duration

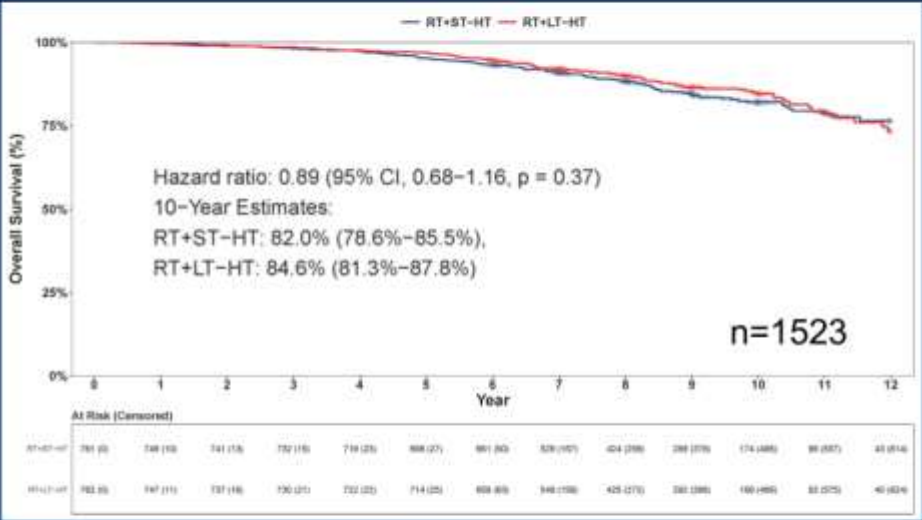
Trend towards significant impact of pre-PORT PSA

Multivariate model adjusted for age, pGS, and pT stage was significant for PSA at a cutpoint of 0.5 ng/mL (p=0.03)

Prostat Kanserinde Post-Operatif Radyoterapi ve Anti-Androjen Tedavisi: POSEIDON Bireysel Hasta Verileri Meta-Analizi

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Exploratory Analysis: HT-Prolongation



PSA Stratum	NNT
≤0.2	125 (-16, 13)
0.21-0.5	19 (-24, 7)
0.51-1.0	-149 (-7, 8)
>1.0	25 (-11, 6)

Endpoint	Age	RT+ST-HT Incidence/N	RT+LT-HT Incidence/N	10-yr Absolute Benefit of RT+LT-HT (%; CI 95%)	10-yr RMST Benefit of RT+LT-HT (Years; CI 95%)	HR (95%)	p value	Interaction p value
PSA (ng/ml)	≤0.20	43/350	38/341	0.8 (-6.2, 7.8)	0.1 (-0.2, 0.3)	0.93 (0.60, 1.44)	0.74	0.92
	0.21-0.50	36/207	28/211	5.3 (-4.1, 14.7)	0.2 (-0.1, 0.5)	0.75 (0.46, 1.23)	0.24	
	0.51-1	10/82	11/89	-0.7 (-13.4, 12.1)	0.1 (-0.4, 0.5)	0.97 (0.41, 2.28)	1.00	
	>1	18/86	18/86	4.0 (-9.4, 17.5)	0.2 (-0.4, 0.8)	0.79 (0.40, 1.54)	0.63	

The Key UnAnswered Questions

- Who needs HT with PORT? Only patients with pre-PORT PSA >0.5 ng/ml
 - Significant interaction between HT effect and pre-PORT PSA
 - Spline analyses overall showed no significant effect
- How long does HT with PORT need to be? For most patients, ST-HT is sufficient
 - No significant interaction between HT effect and HT duration
 - Exploratory analyses suggests minimal benefit to HT prolongation

Biyokimyasal Rekürrens ve PSA Persistansı: Doz Yoğun Tedavi Yaklaşımı

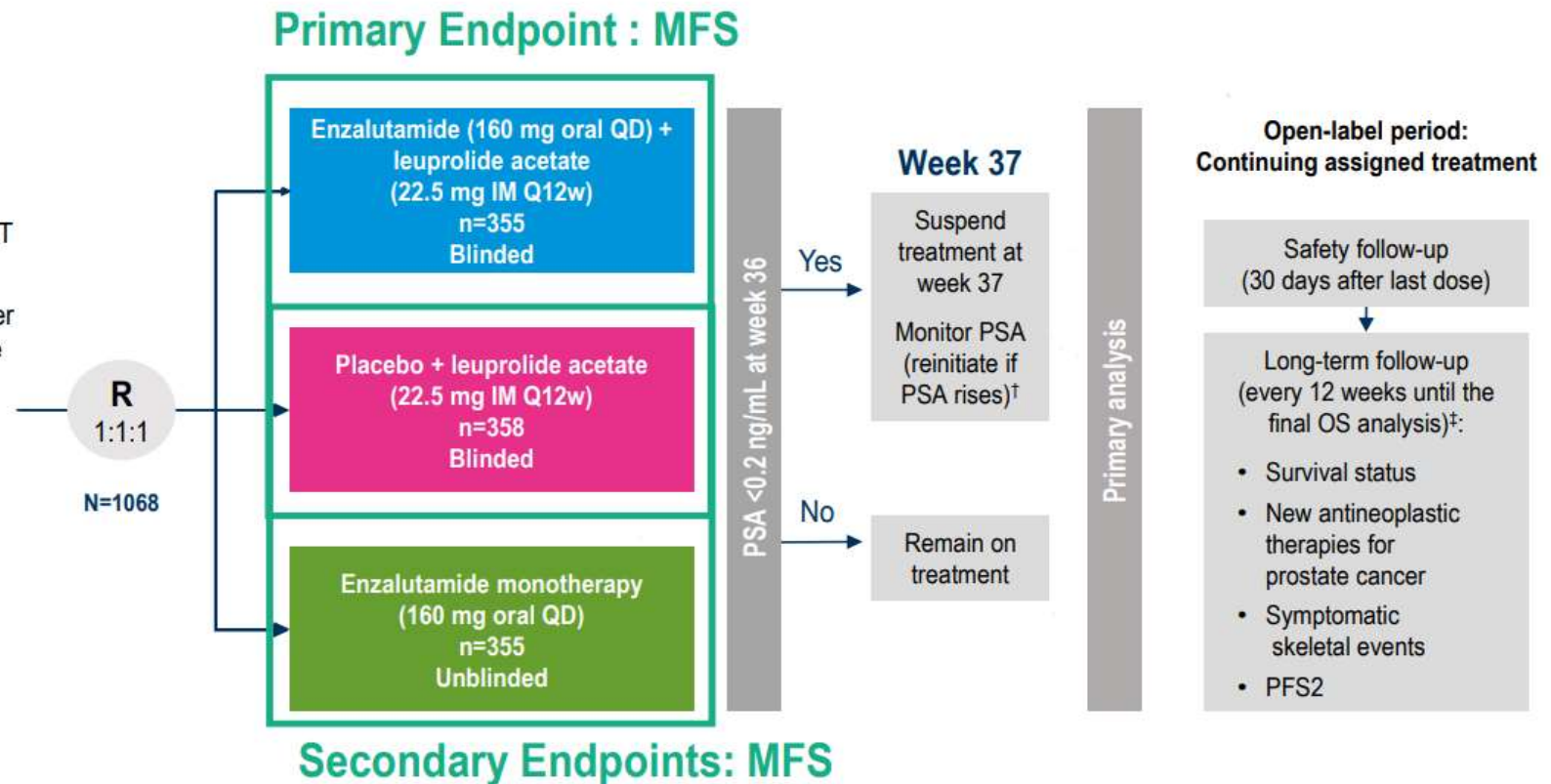
EMBARC study

Patient population:

- Screening PSA ≥ 1 ng/mL after RP or ≥ 2 ng/mL above the nadir after primary EBRT
- PSADT ≤ 9 mo
- No metastases on bone scan and CT/MRI per central read – conventional imaging-negative
- T ≥ 150 ng/dL
- Prior hormonal therapy ≥ 9 mo prior to R (neoadjuvant/adjuvant for ≤ 36 mo or ≤ 6 mo for rising PSA) allowed

Stratification factors:

- Screening PSA (≤ 10 ng/mL vs >10 ng/mL)
- PSADT (≤ 3 mo vs >3 to ≤ 9 mo)
- Prior hormonal therapy (yes vs no)



Primary endpoint: MFS by BICR for enzalutamide + leuprolide vs leuprolide alone

Key secondary endpoints: MFS by BICR for enzalutamide monotherapy vs leuprolide alone, time to PSA progression, time to first use of new antineoplastic therapy, OS

Other secondary endpoints included: Time to first symptomatic skeletal event, safety

Exploratory endpoint: PFS2

Biyokimyasal Rekürrens ve PSA Persistansı: Doz Yoğun Tedavi Yaklaşımı

THE NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Improved Survival with Enzalutamide in Biochemically Recurrent Prostate Cancer

Neal D. Shore, M.D.,¹ Murilo de Almeida Luz, M.D.,²
Ugo De Giorgi, M.D., Ph.D.,³ Martin Gleave, M.D.,⁴
Geoffrey T. Gotto, M.D., M.P.H.,⁵ Christopher M. Pieczonka, M.D.,⁶
Gabriel P. Haas, M.D.,⁷ Choung-Soo Kim, M.D.,⁸ Miguel Ramirez-Backhaus, M.D.,⁹
Antti Rannikko, M.D., Ph.D.,^{10,11} Matko Kalac, M.D., Ph.D.,¹²
Swetha Sridharan, M.B., B.S.,¹³ Matt Rosales, Ph.D.,⁷ Yiyun Tang, Ph.D.,¹⁴
Ronald F. Tutrone, Jr., M.D.,¹⁵ Balaji Venugopal, M.B., B.S., M.D.,^{16,17}
Arnaud Villers, M.D., Ph.D.,¹⁸ Henry H. Woo, M.B., B.S., D.Med.Sc.,^{19,20}
Fong Wang, M.D., Ph.D.,¹⁴ and Stephen J. Freedland, M.D.,^{21,22}

Previous hormonal therapy — no. (%)

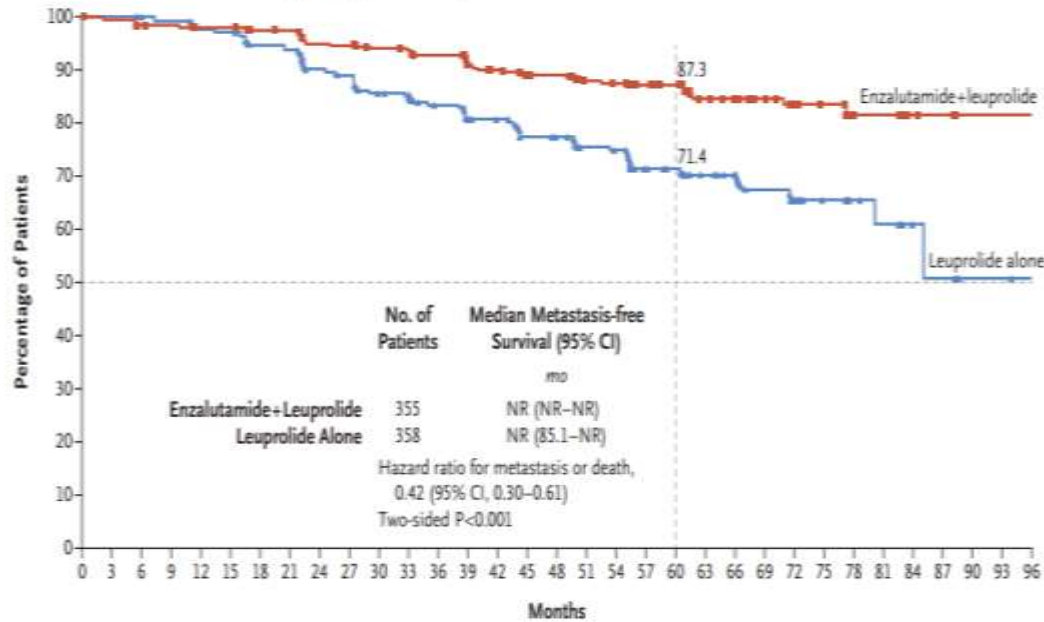
Yes	107 (30.1)	113 (31.6)
No	248 (69.9)	245 (68.4)

Primary definitive therapy — no. (%)

Prostatectomy alone	90 (25.4)	75 (20.9)
Radiation therapy alone	86 (24.2)	104 (29.1)
Prostatectomy and radiation therapy	179 (50.4)	179 (50.0)

Biyokimyasal Rekürrens ve PSA Persistansı: Doz Yoğun Tedavi Yaklaşımı

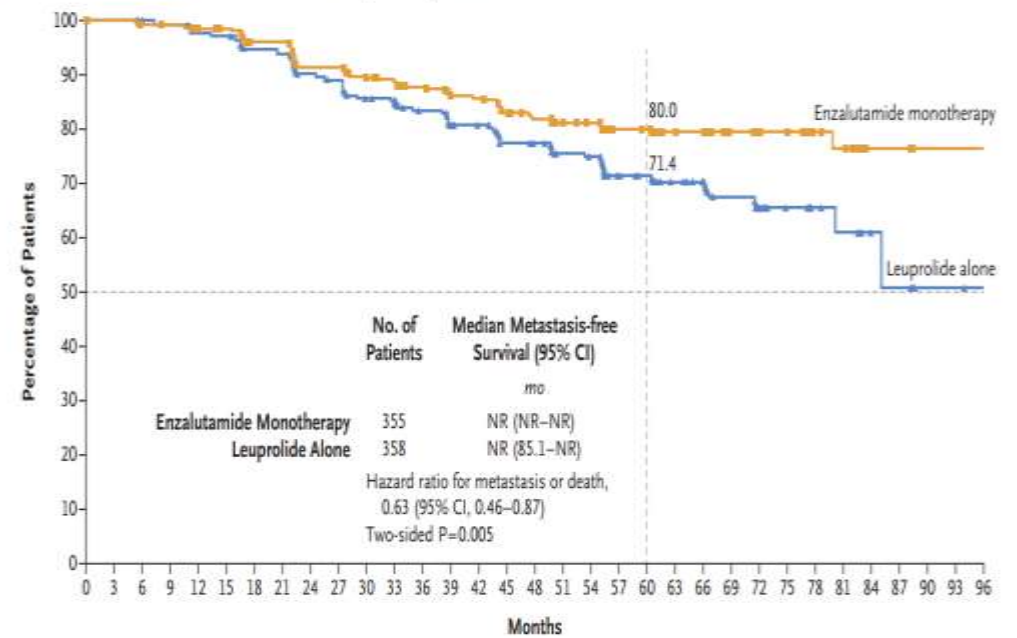
A Metastasis-free Survival with Enzalutamide plus Leuprolide vs. Leuprolide Alone



No. at Risk

Enzalutamide+leuprolide	355	339	331	330	324	324	318	317	304	303	292	290	281	270	265	252	251	236	234	183	180	119	116	83	60	51	24	22	6	5	0	0	0
Leuprolide alone	358	344	335	334	321	320	303	301	280	276	259	256	238	226	221	205	203	185	183	141	138	93	88	66	32	27	15	13	6	5	1	1	0

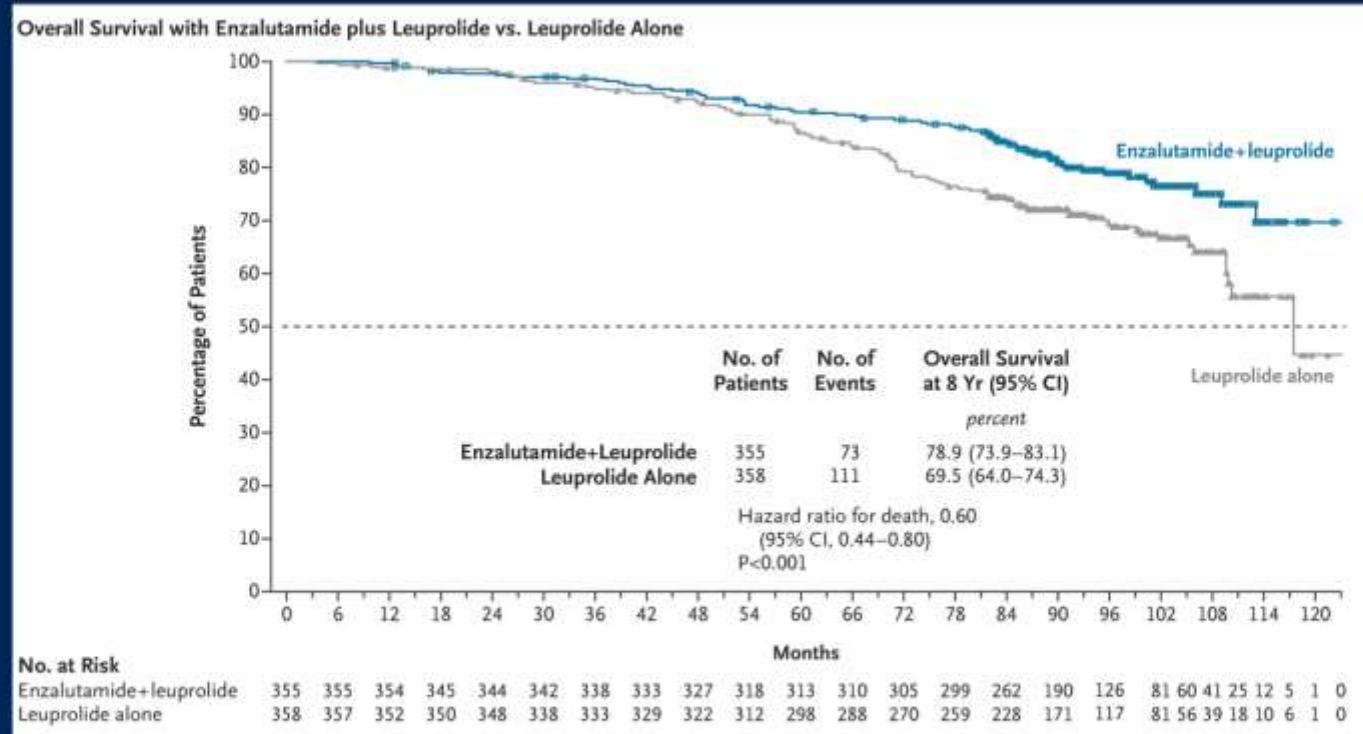
B Metastasis-free Survival with Enzalutamide Monotherapy vs. Leuprolide Alone



No. at Risk

Enzalutamide monotherapy	355	350	342	341	328	326	309	309	287	287	273	269	260	248	247	235	228	211	209	172	171	109	108	76	52	49	26	24	5	5	0	0	0
Leuprolide alone	358	344	335	334	321	320	303	301	280	276	259	256	238	226	221	205	203	185	183	141	138	93	88	66	32	27	15	13	6	5	1	1	0

Biyokimyasal Rekürrens ve PSA Persistansı: Doz Yoğun Tedavi Yaklaşımı



Özet

- ❑ Neoadjuvan tedavi özel durumlar dışında rutin olarak önerilmez
- ❑ Yeni nesil AR-yolak inhibitörleriyle bir grup hastada iyi sonuçlar elde edilmiştir
- ❑ Özellikle lokalize yüksek riskli prostat kanserinde karşılanmamış bir tedavi ihtiyacı vardır
- ❑ Bu grup hastalarda sistemik tedavinin etkin olduğu adjuvan çalışmalarda gösterilmiştir
- ❑ Çok sayıda devam eden çalışmalar mevcuttur
- ❑ Neoadjuvan tedavi ilerleyen zamanlarda daha çok gündemimize girecek

Özet

- ☐Biyokimyasal Rekürens ve PSA Persistansı olan hastada PSMA PET/CT ile evreleme yapılmalıdır.
- ☐Prostatektomi sonrası Biyokimyasal Rekürens olan gleason skoru ≥ 8 ya da PSA double time değeri 12ay $\leq$ olanlarda tedavi düşünülmelidir
- ☐Salvage RT ve ADT (6ay)düşünülmelidir
- ☐Uzun dönem 24 ay adjuvan ADT(pT3 $\geq$ ve gleason skoru ≥ 8) ve pelvik lenf nodu pozitif
- ☐Pelvik RT nüks riski yüksek hastalarda düşünülebilir(Gleason ≥ 8 , $\geq$ pT3, cerrahi sınır pozitifliği) ve pelvik lenf nodu+
- ☐Enzalutamide , double time ≤ 9 ay, RP sonrası PSA >1 ng/ml ve Radyoterapi sonrası 2 ng/ml

Özet

- ❑ RT sonrası Biyokimyasal Rekürens olan hastalarda
- ❑ PSA değeri ≥ 2 ng/ml olan hastalar için, PSA double time ≤ 9 ay olanlarda enzalutamide önerilebilir
- ❑ Enzalutamide ulaşamıyorsa, intermittent ADT önerilir
- ❑ Sistemik tedavi(ADT ve yeni nesil AR yolağı inhibitörü); Tedavi öncesi PSA değeri, primer tümör gleason skoru, PSA double time, Decipher Skoru, AI risk skorlaması yol gösterici
- ❑ ADT 6 ay vs. 24 ay; pelvik lenf nodu pozitif hastalarda uzun dönem ADT