Lokal İleri Prostat Kanserinde Sistemik Tedavi

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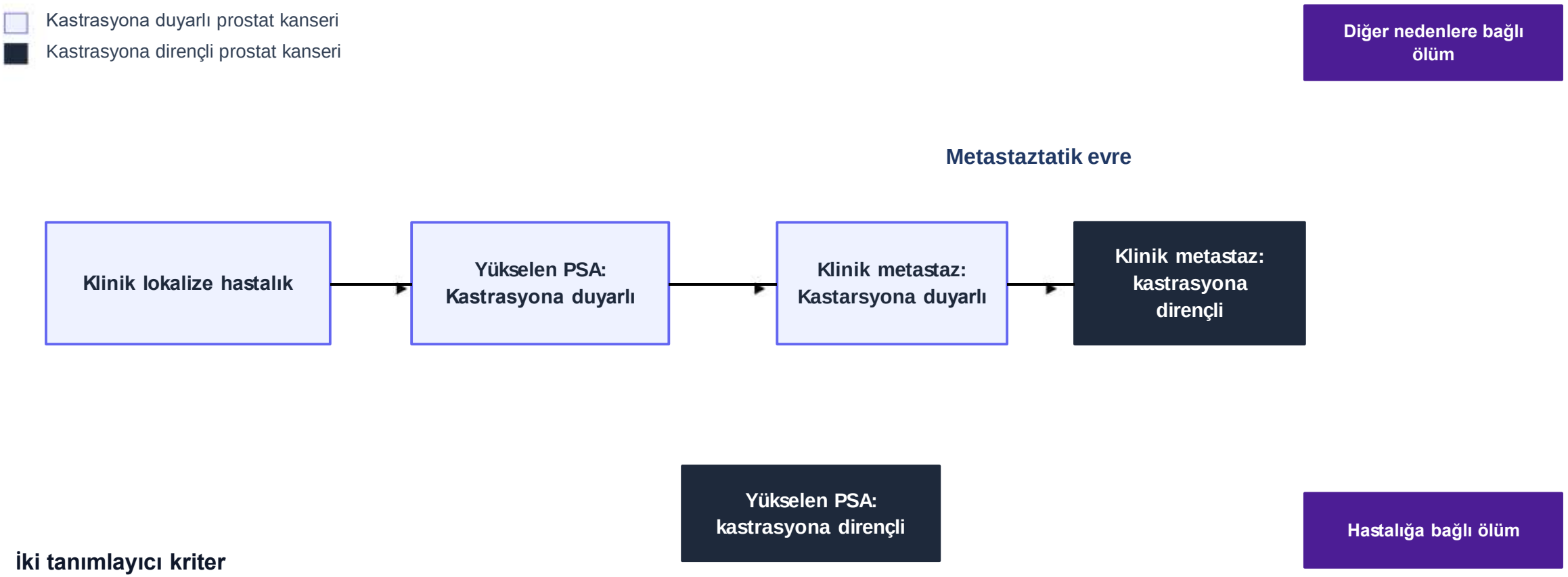
Ders Planı

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

Prostat kanserinin seyri

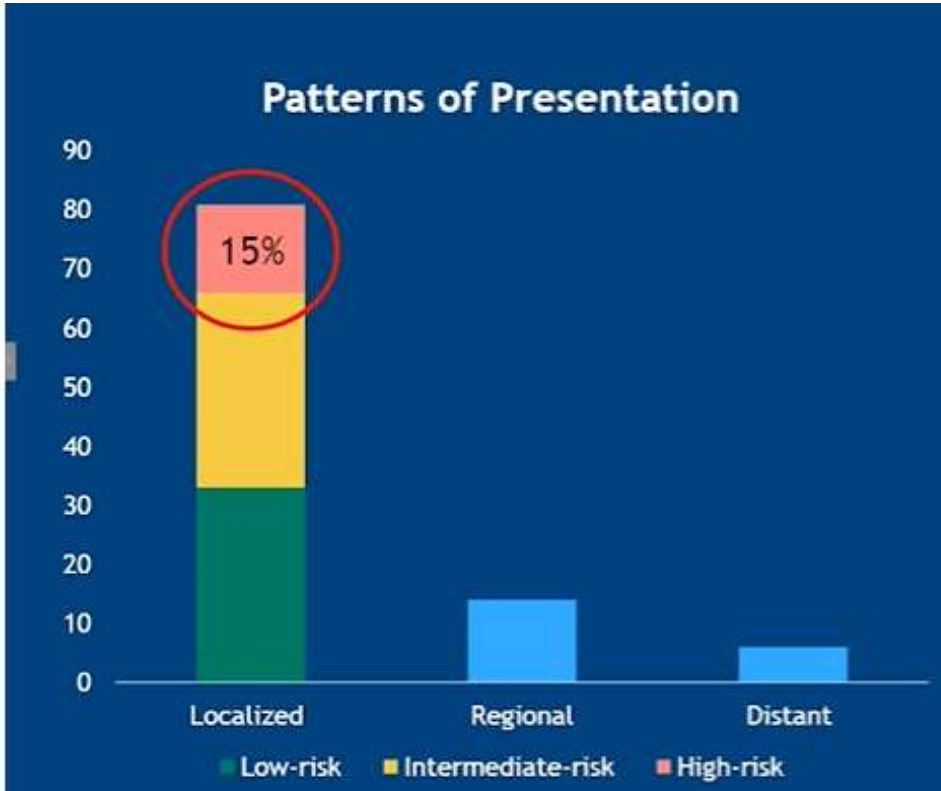


İki tanımlayıcı kriter

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

Scher HI ve ark. J Clin Oncol. 2008;26:1148-1159'dan uyarlanmıştır.

Lokalize Yüksek Riskli Prostat Kanseri



Increased Mortality in High-Risk Prostate Cancer

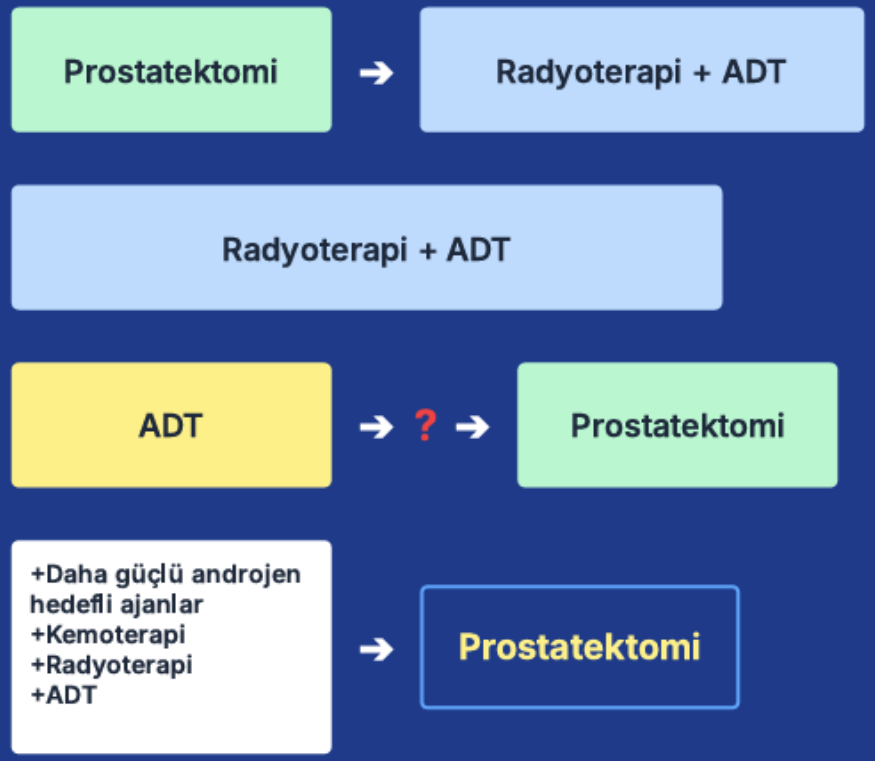
High-Risk Feature	15-Year PCSM
PSA > 20 ng/mL	22%
Gleason 8-10	34%
cT3	38%
High-risk Disease*	19%

PCSM=Prostate cancer specific mortality; PSA=Prostate specific antigen. *Defined by D'Amico criteria: PSA > 20 ng/mL, Gleason 8-10, or cT2c-T3.

Cooperberg, JCO, 2010; Eggener, J Urol, 2011

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

ADT: Androjen Deprivasyon Tedavisi

Neoadjuvan Tedavi Gerekçesi

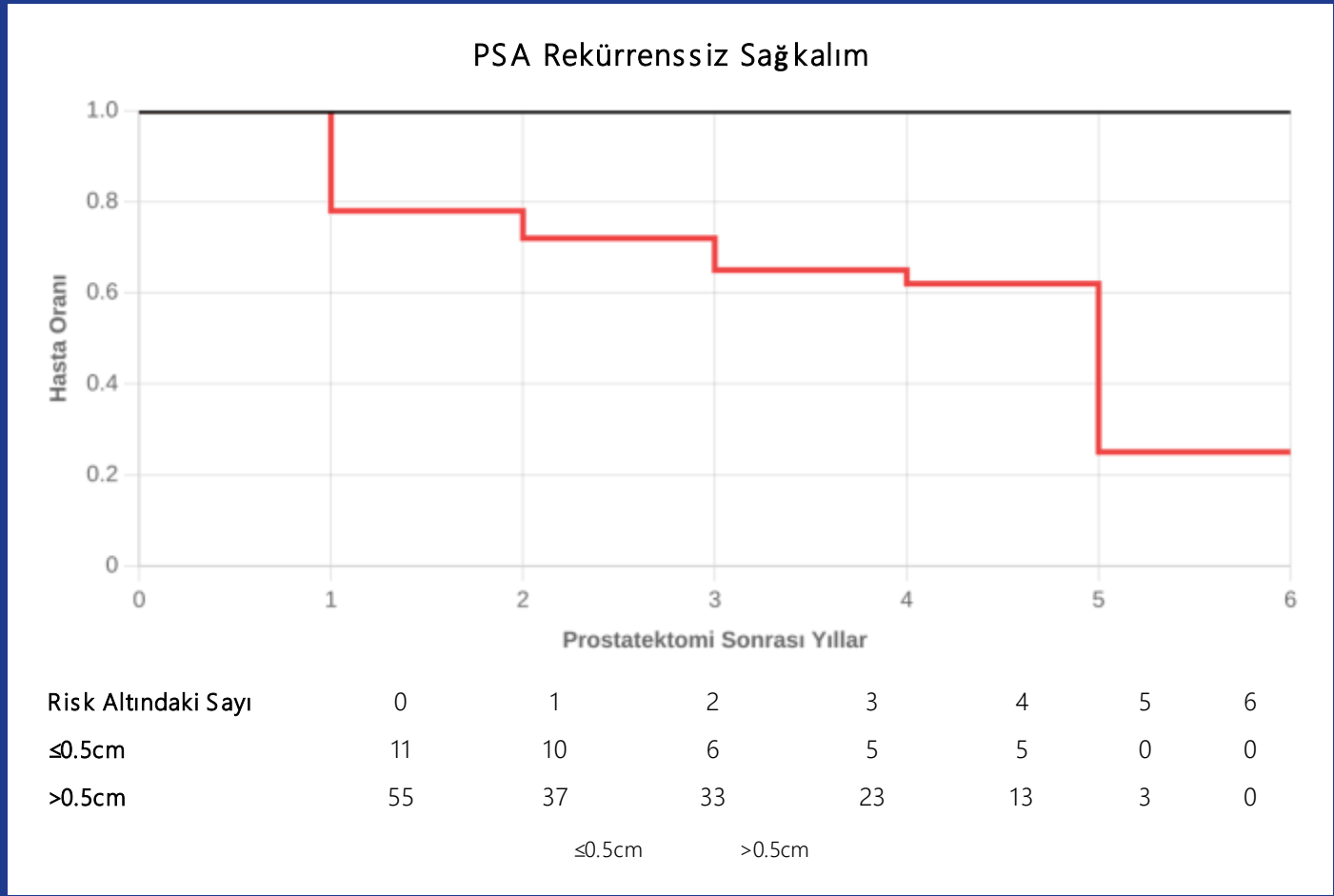
Patolojik Yanıtın PSA Rekürrensi ile Korelasyonu

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



Risk Altındaki Sayı	0	1	2	3	4	5	6
≤0.5cm	11	10	6	5	5	0	0
>0.5cm	55	37	33	23	13	3	0

≤0.5cm >0.5cm

McKay et al, PCPD, 2018

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 cm3 to a mean of 0.8 ng/ml and 29.5 cm3, respectively.
Van Poppel	1995	Leuven,	65	Stages T2b and T3 prostate cancer	Estramustine +	For T2b tumors, a significant decrease in
		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).

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

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

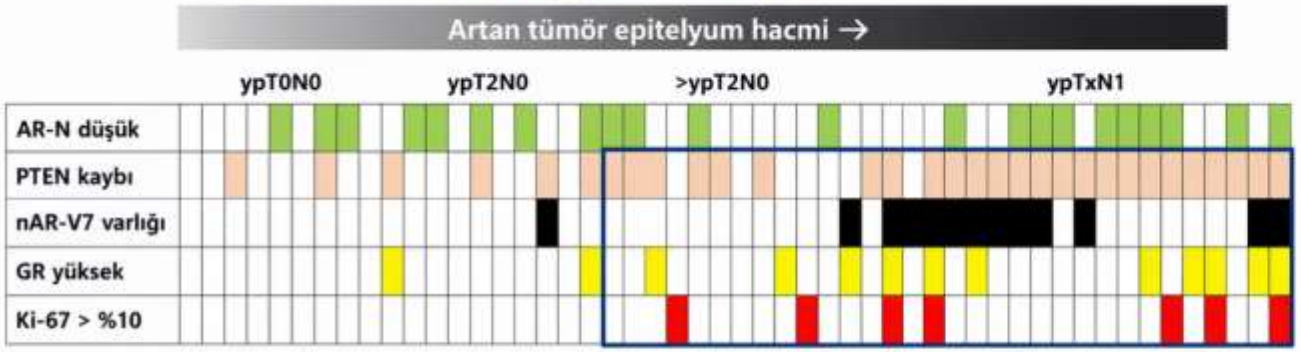
Yeni Nesil AR Yolağı İnhibitörleri ile Neoadjuvan Tedavi

Neoadjuvan Yeni Nesil AR Yolağı İnhibitörleri

BULGULAR

- Tümör hacmi ve tümör hücreselliği anlamlı derecede değişkenlik göstermiştir.
- ≥ypT2N0 varlığı Gleason skoru ile korele bulunmamış; ancak **önceden tanımlanmış moleküler imza, PTEN ekspresyonu** ve **kribriform/intraduktal yayılımın 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.

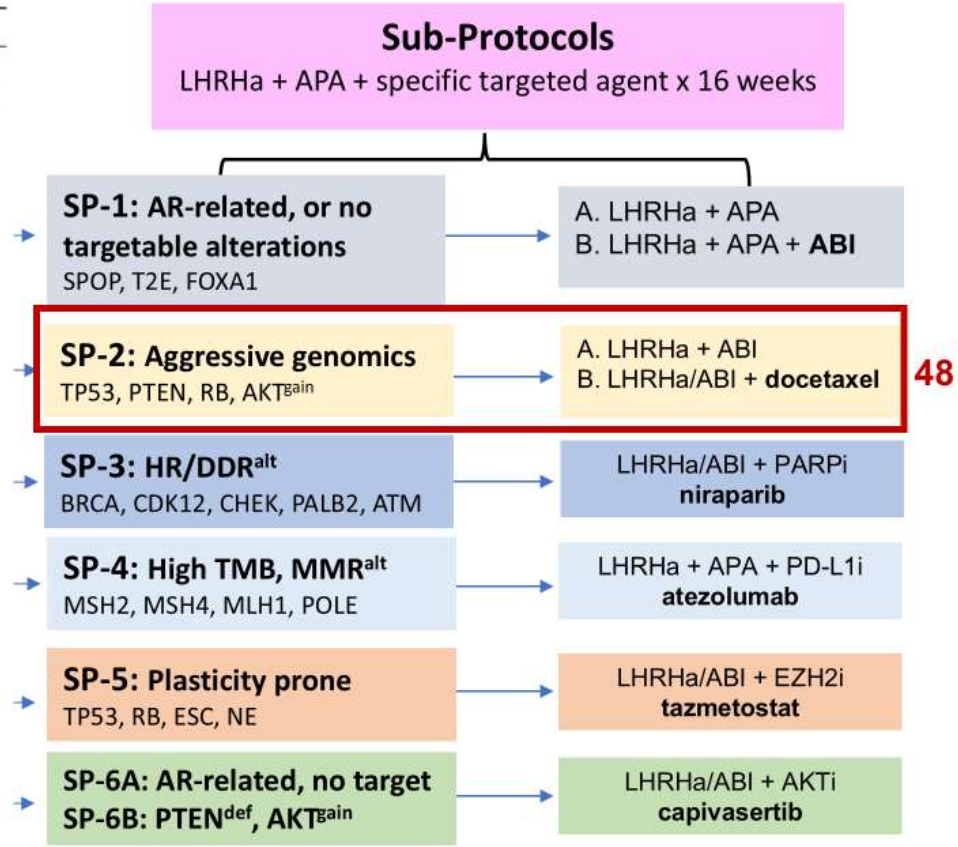
Belirteç		Patoloji Evresi >ypT2N0 N (%)	Patoloji Evresi ≤ypT2N0 N (%)	Fisher kesin testi p-değeri
AR-N	Düşük	13 (%42)	9 (%47)	0.77
	Yüksek	18 (%58)	10 (%53)	
PTEN	Kayıp	24 (%77)	7 (%37)	**0.007**
	İntakt	7 (%23)	12 (%63)	
nARV7	Nükleer yokluğu	19 (%61)	**18 (%95)**	**0.009**
	Varlığı	12 (%39)	**1 (%5)**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

AR-N: Androjen Reseptörü – Nükleer, nAR-V7: Nükleer Androjen Reseptör Varyant 7, GR: Glukokortikoid Reseptör, Ki-67: Proliferasyon belirteci

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)
	$10 \leq$ PSA < 20	8 (33.3)	6 (25.0)	72 (30.8)
	$20 \leq$ PSA < 40	5 (20.8)	3 (12.5)	45 (19.2)
	$40 \leq$ 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

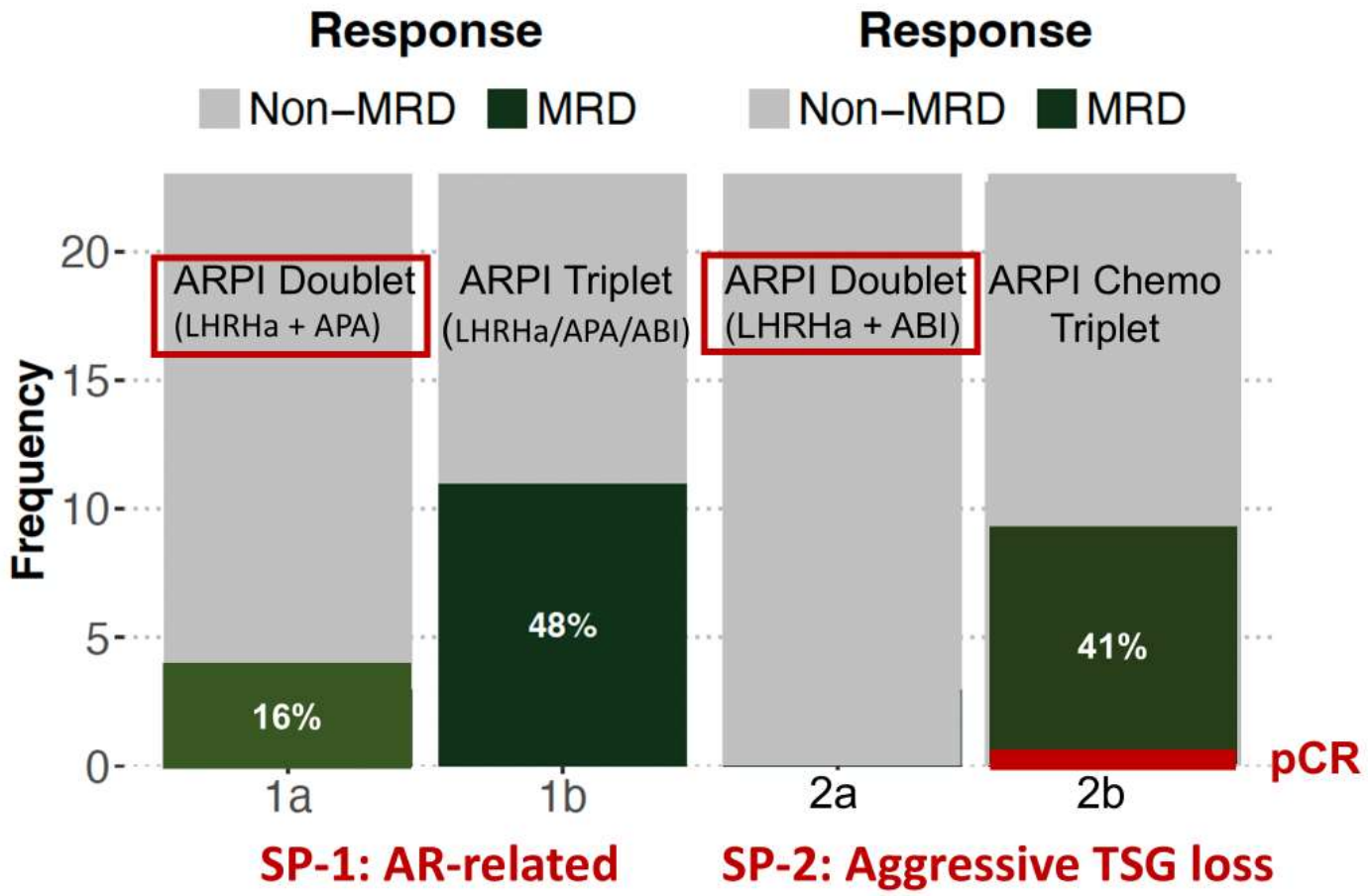
Yeni Nesil AR Yolağı İnhibitörleri ile Neoadjuvan Tedavi

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

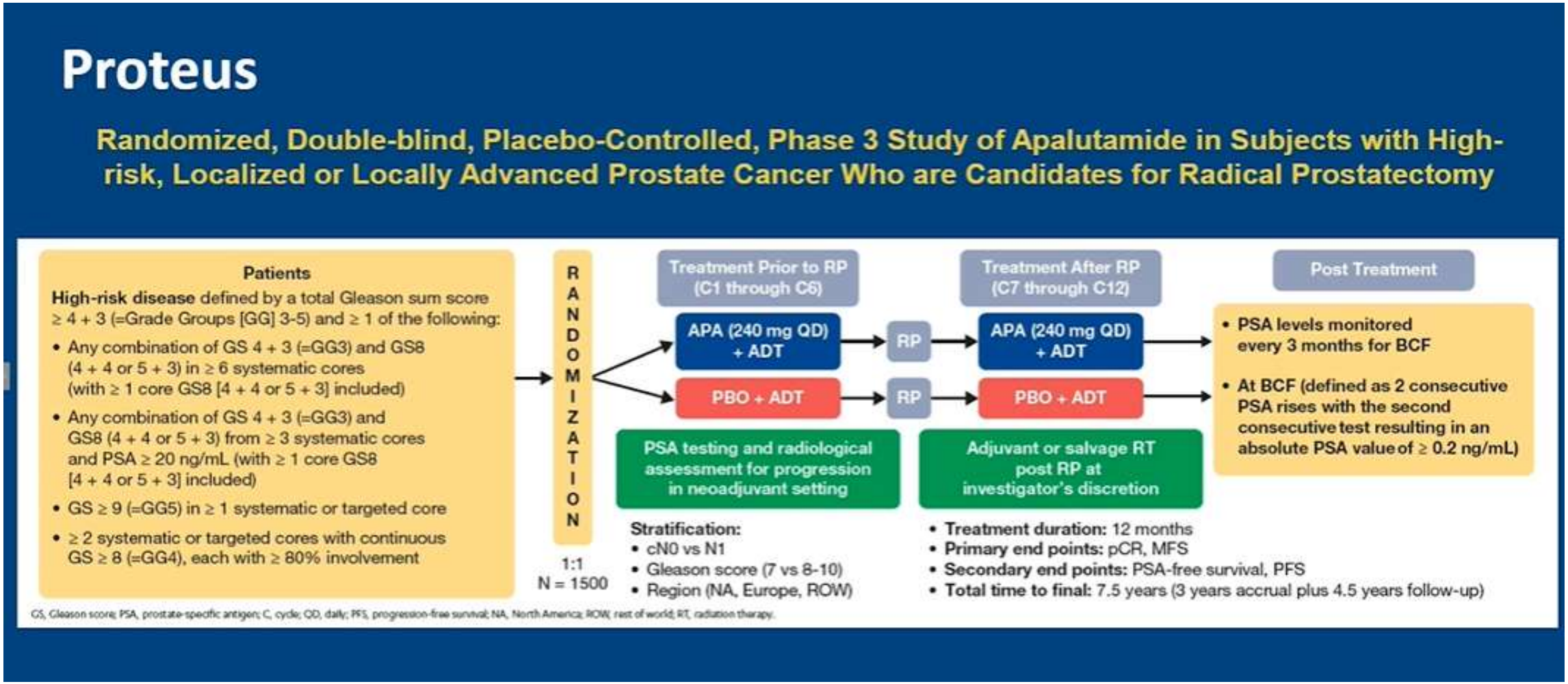
SP-1: MRD rate higher in ARPI triplet than doublet

- **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



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

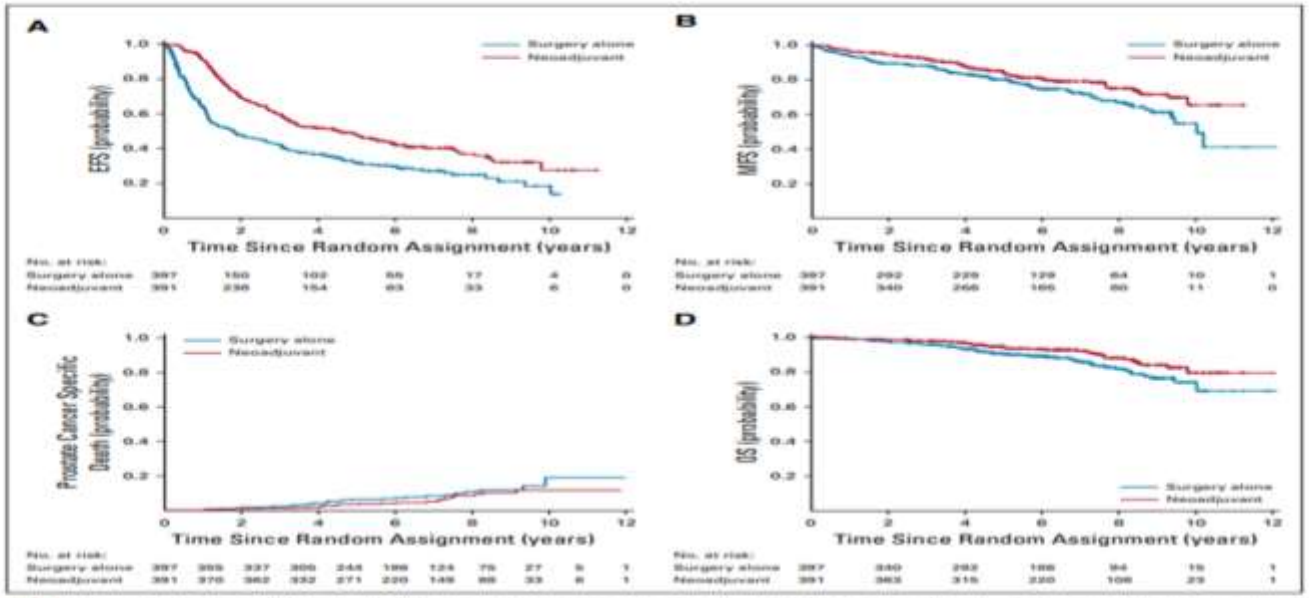


FIG 3. (A) Event-free survival (EFS) or the likelihood of not requiring additional treatment after radical prostatectomy in men treated with neoadjuvant chemohormonal therapy plus radical prostatectomy (designated neoadjuvant) versus radical prostatectomy alone (designated surgery alone). An event is 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**

Eastham J et al, JCO 2020

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

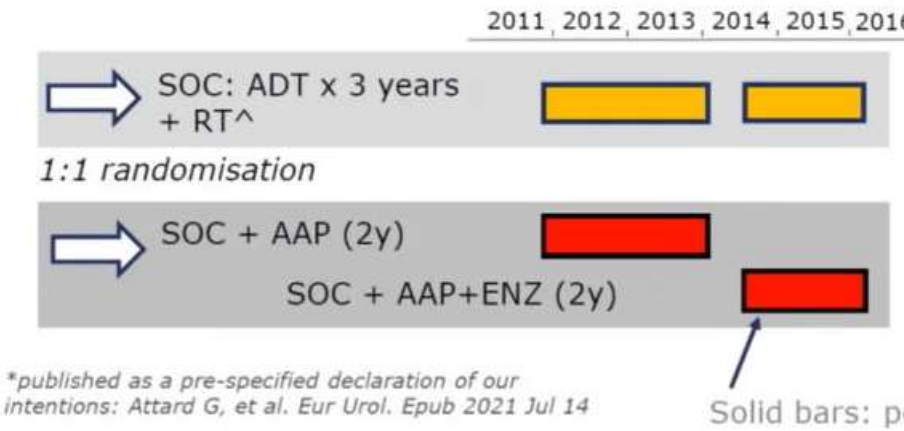
Abiraterone acetate and prednisolone with or without enzalutamide for high-risk non-metastatic prostate cancer: a meta-analysis of primary results from two randomised controlled phase 3 trials of the STAMPEDE platform protocol

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 ± 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

- 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 N0M0 and suggested in N+ disease

Attard al. Lancet. 2022 Jan

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

Patient characteristics

- Randomised groups were well balanced (**N=1974**)

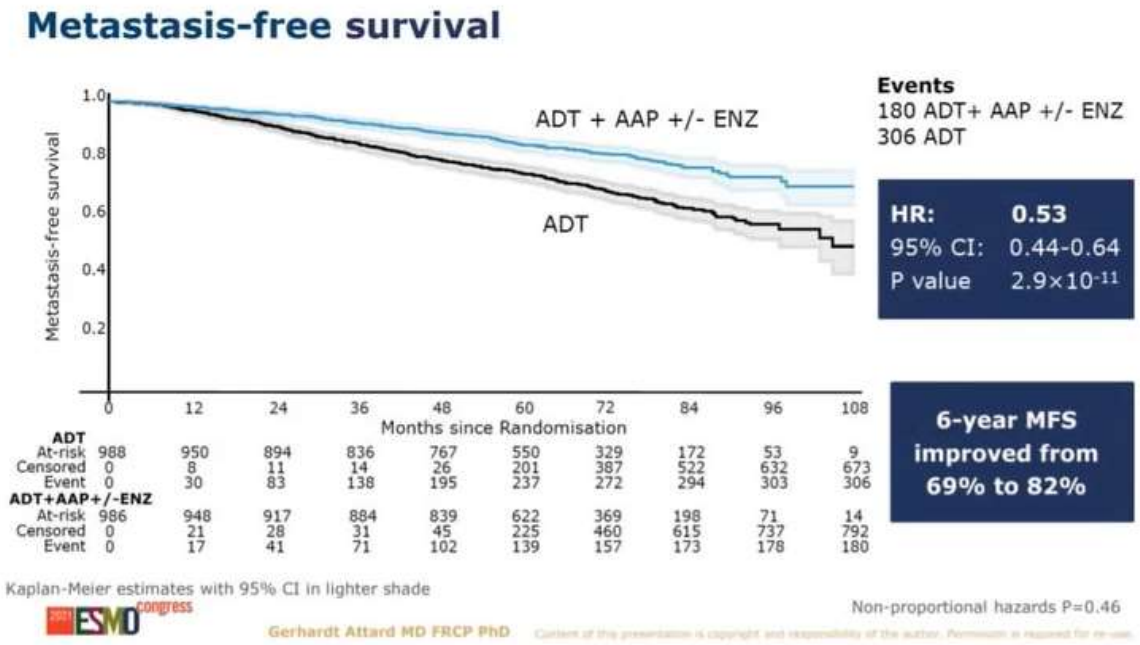
- Median age = 68 years
- Median PSA = 34 ng/ml
- N1 = 39%
- 3% relapsing after prior treatment

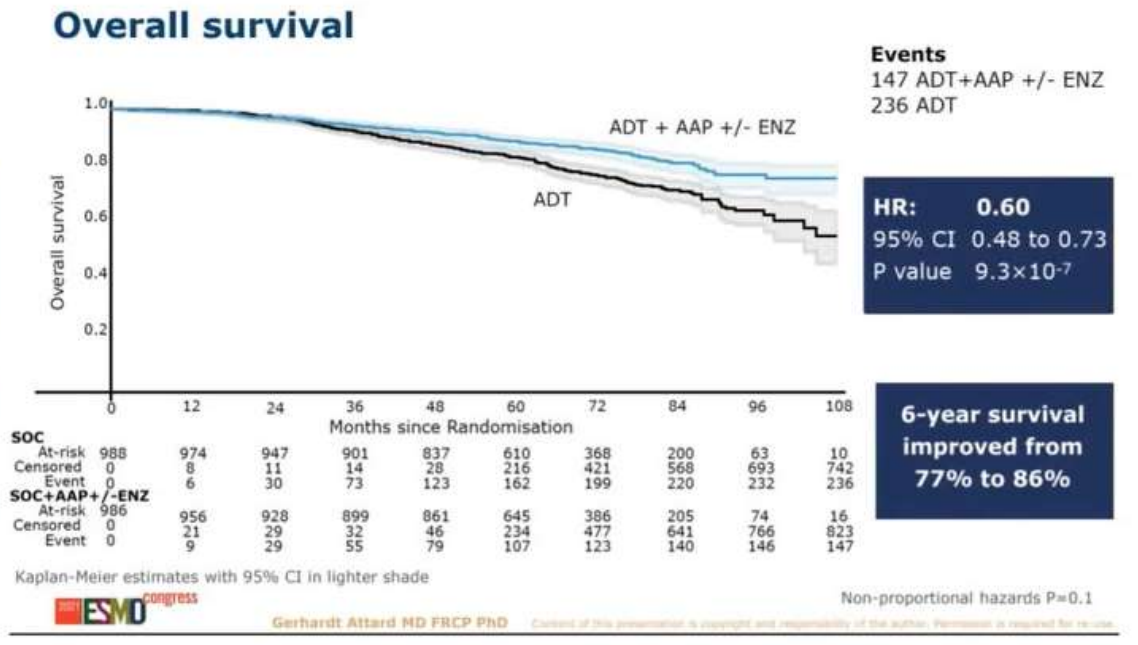
- Planned for local radiotherapy:
  - 99% newly-diagnosed, N0
  - 71% newly-diagnosed, N1
  - 7% previously-treated patients

- Median follow-up = 72 months
  (85 months AAP comparison & 60 months AAP+ENZ comparison)

Attard al. Lancet. 2022 Jan

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



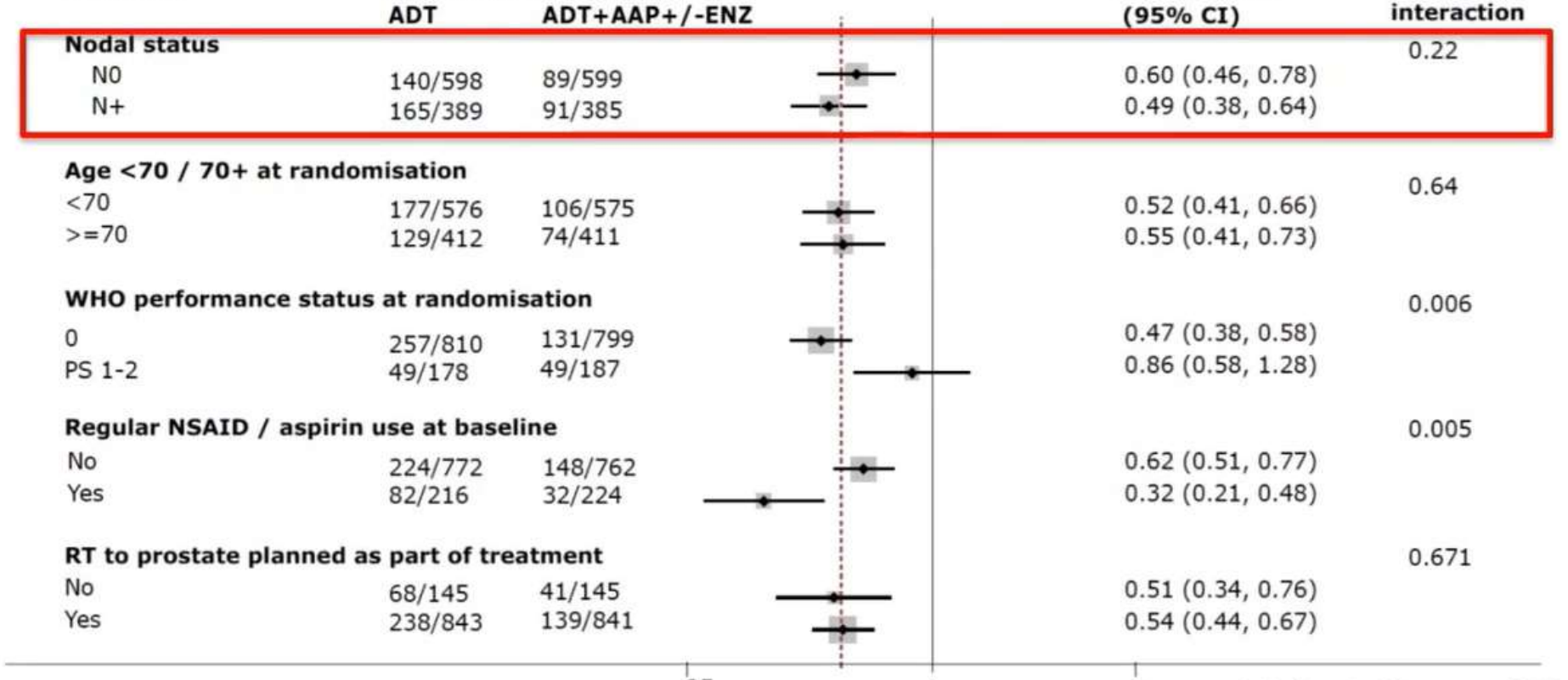


Attard al. Lancet. 2022 Jan

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

Metastasis-free survival: Subgroup analysis

Subgroup	*N events/N patients* ADT	ADT+AAP+/-ENZ	Hazard Ratio (95% CI)	P value for interaction
Nodal status				0.22
N0	140/598	89/599	0.60 (0.46, 0.78)	
N+	165/389	91/385	0.49 (0.38, 0.64)	
Age <70 / 70+ at randomisation				0.64
<70	177/576	106/575	0.52 (0.41, 0.66)	
>=70	129/412	74/411	0.55 (0.41, 0.73)	
WHO performance status at randomisation				0.006
0	257/810	131/799	0.47 (0.38, 0.58)	
PS 1-2	49/178	49/187	0.86 (0.58, 1.28)	
Regular NSAID / aspirin use at baseline				0.005
No	224/772	148/762	0.62 (0.51, 0.77)	
Yes	82/216	32/224	0.32 (0.21, 0.48)	
RT to prostate planned as part of treatment				0.671
No	68/145	41/145	0.51 (0.34, 0.76)	
Yes	238/843	139/841	0.54 (0.44, 0.67)	



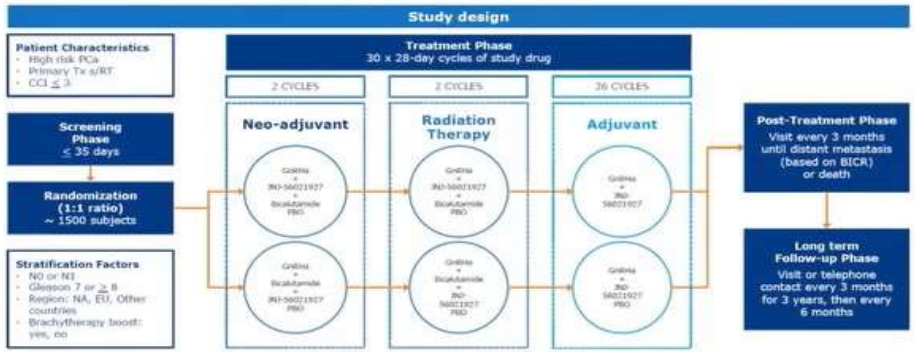
2021 ESMO congress

Gerhardt Attard MD FRCP PhD

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

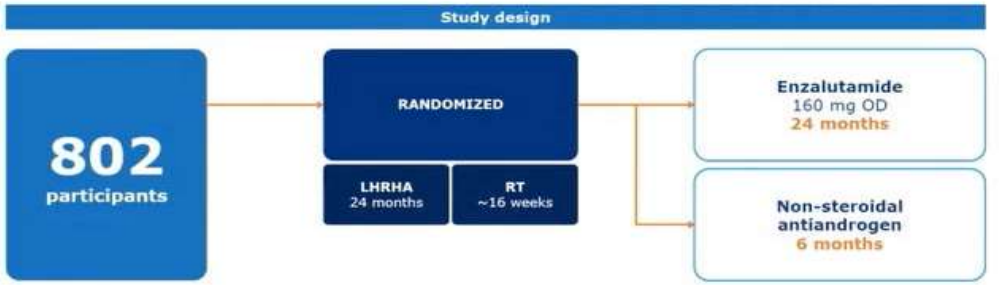
Apalutamide

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



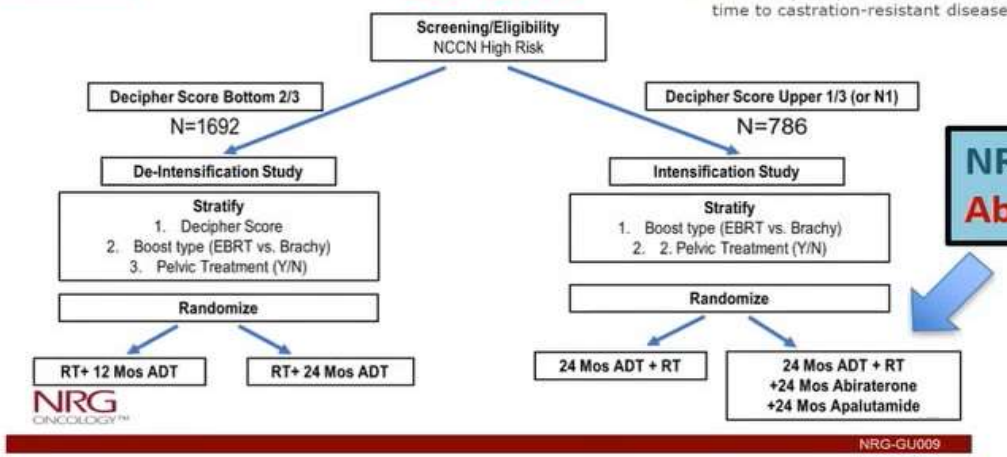
Enzalutamide

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

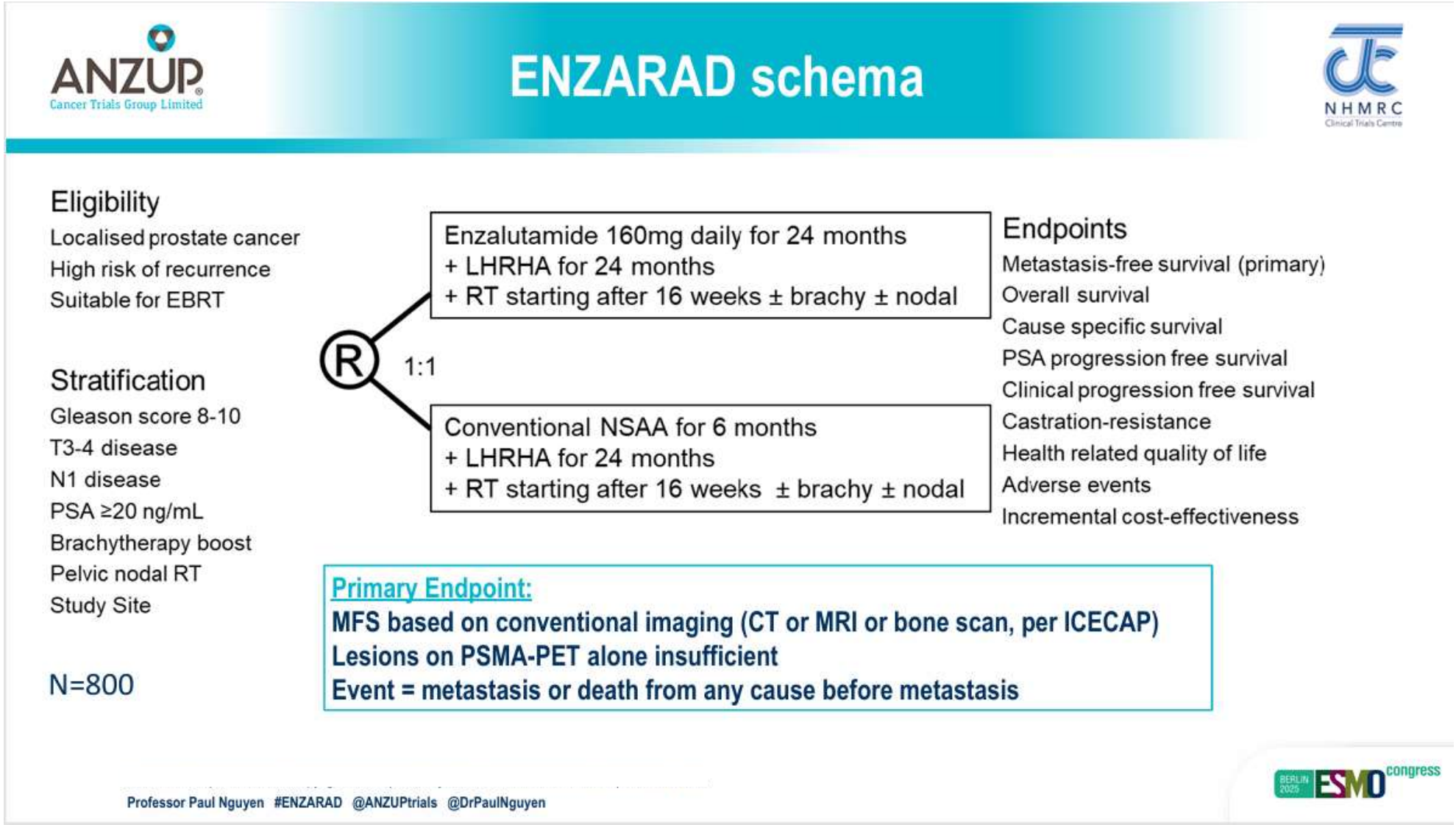
SCHEMA



NRG GU009
Abiraterone + Apalutamide

Clinical Trial Information:
NCT02531516; NCT02446444; NCT04513717

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

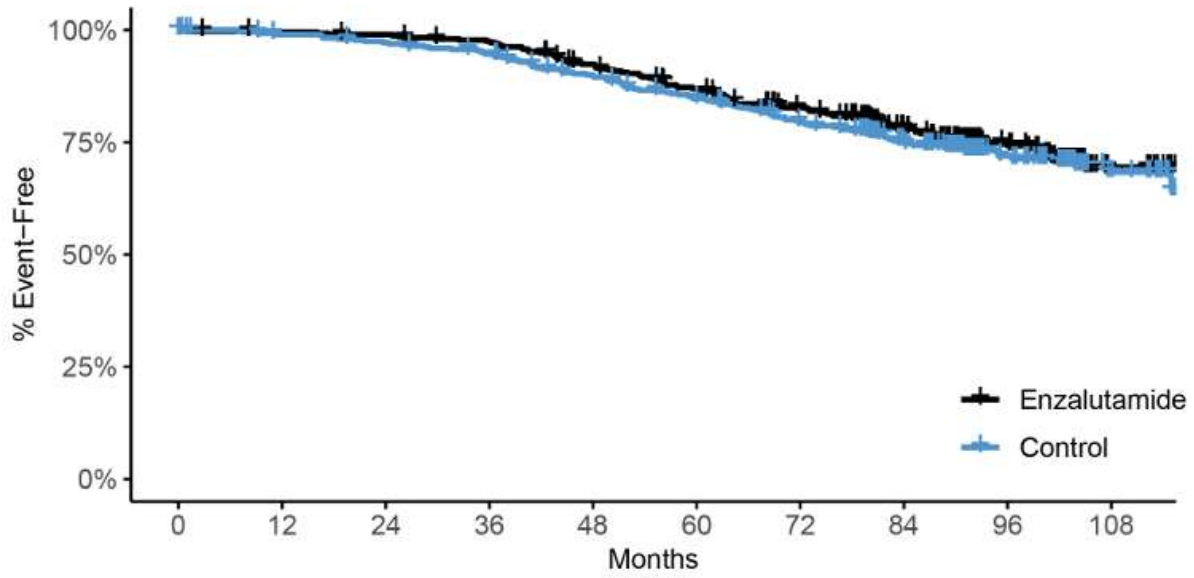


Definitif Radyoterapi + Androjen Deprivasyon Tedavisi + Yeni Nesil AR Yolağı İnhibitörleri

ANZUP Cancer Trials Group Limited

Primary endpoint: MFS by conventional imaging

NHMRC Clinical Trials Centre



	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)

Professor Paul Nguyen #ENZARAD @ANZUPtrials @DrPaulNguyen

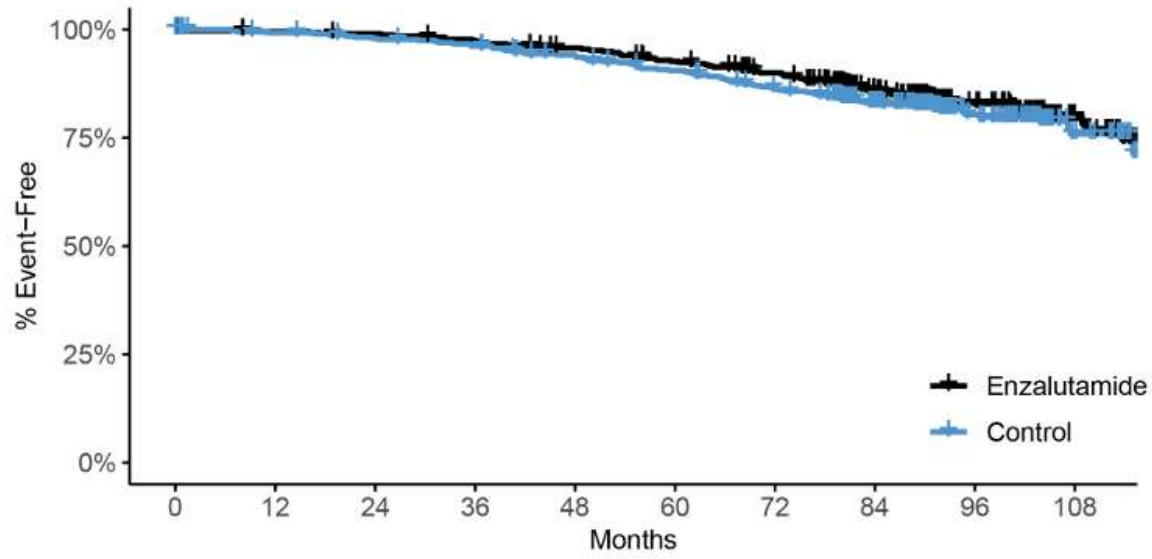
BERLIN 2025 ESMO congress

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

ANZUP Cancer Trials Group Limited

Overall Survival

NHMRC Clinical Trials Centre



	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)

Professor Paul Nguyen #ENZARAD @ANZUPtrials @DrPaulNguyen

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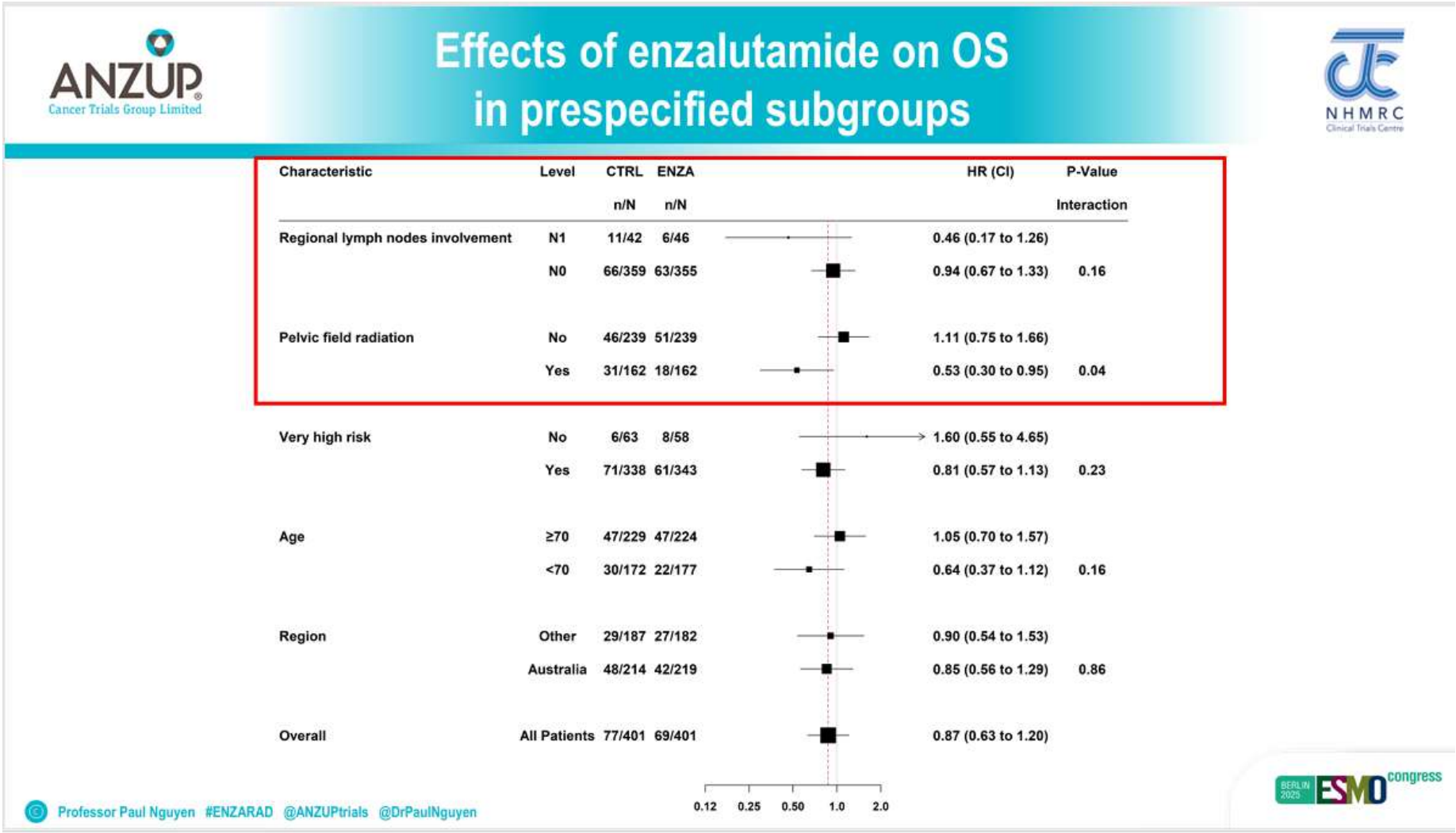
Definitif Radyoterapi + Androjen Deprivasyon Tedavisi + Yeni Nesil AR Yolağı İnhibitörleri



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

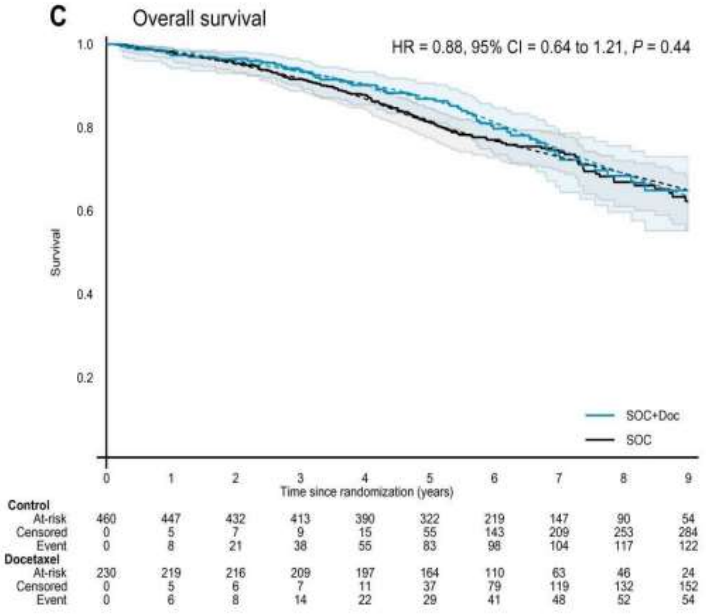
	STAMPEDE (abiraterone)	ENZARAD (enzalutamide)
HR for MFS in cN1	0.49	0.43
HR for MFS in all patients	0.53 (p<0.0001)	0.88 (p=.34)
cN1	39%	11%
Median PSA	35	14
Clinical T3-4	92%	47%
Received radiation	82%	100%
Gleason 8-10	79%	89%

Professor Paul Nguyen #ENZARAD @ANZUPtrials @DrPaulNguyen

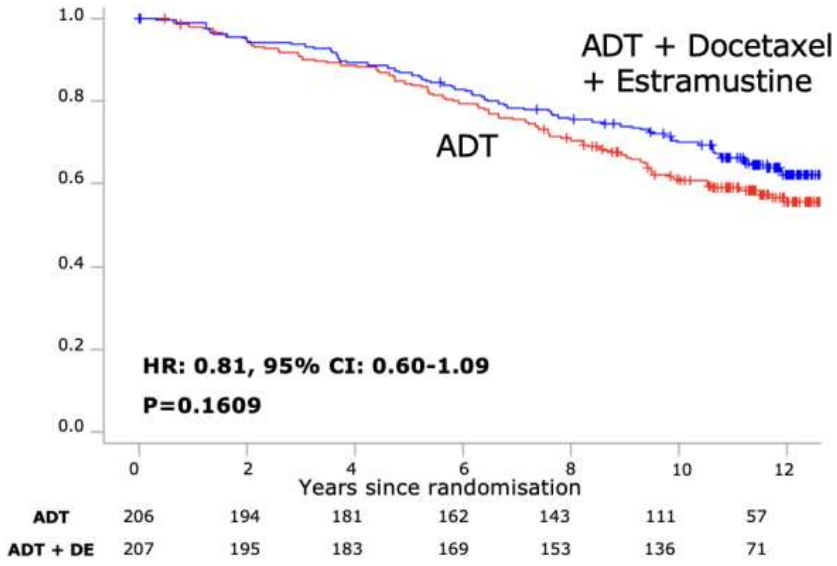
Yüksek Riskli Lokalize Prostat Kanserinde Definitif Radyoterapi (RT) + ADT ve Adjuvan Kemoterapi

Docetaxel in M0 prostate cancer: no MSF/OS benefit

STAMPEDE

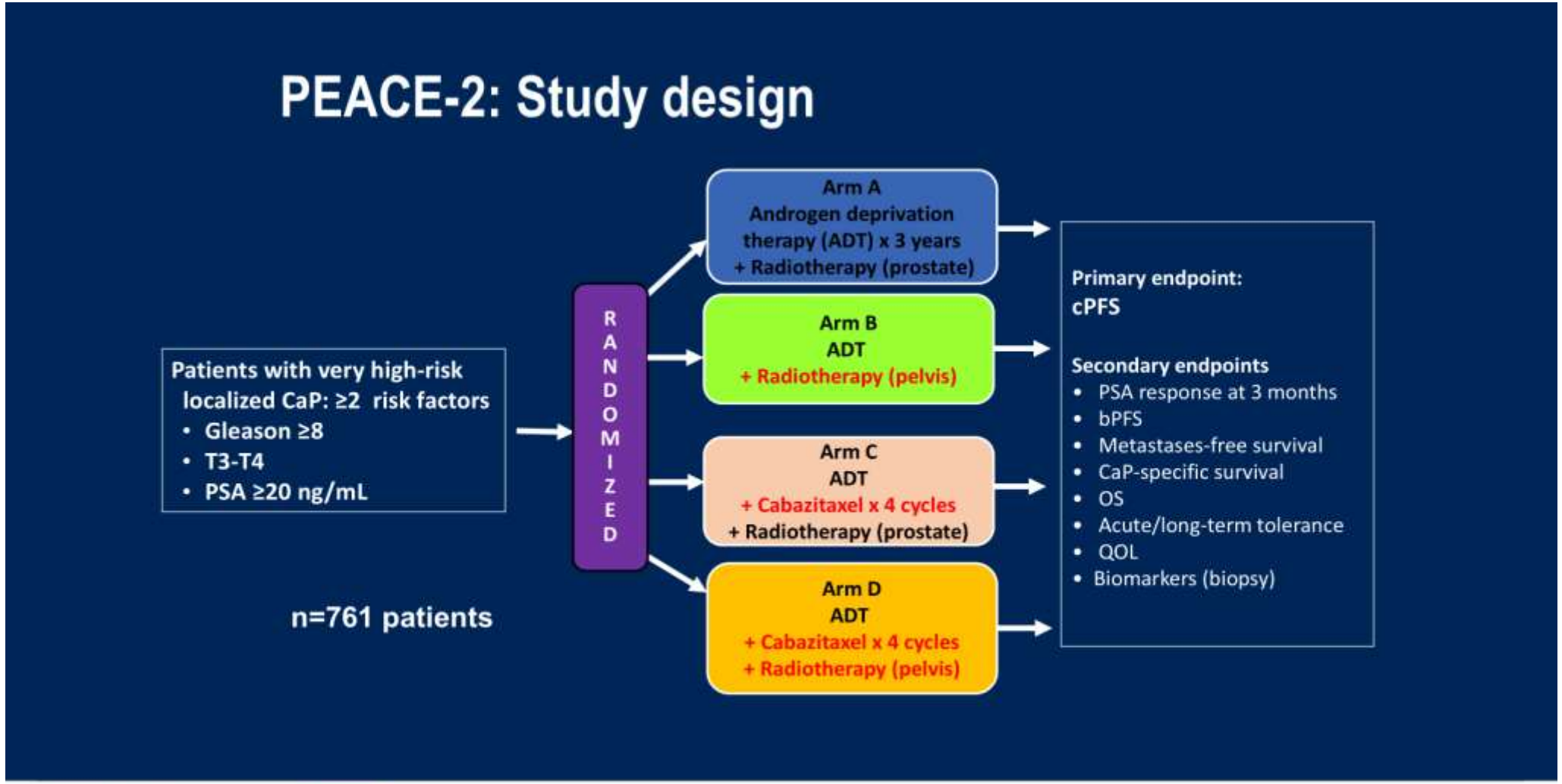


GETUG -12



James N, et al. JNCI Cancer Spectrum. 2022;6(4)
Fizazi et al. Lancet Oncol 2016;17(7):787-794

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



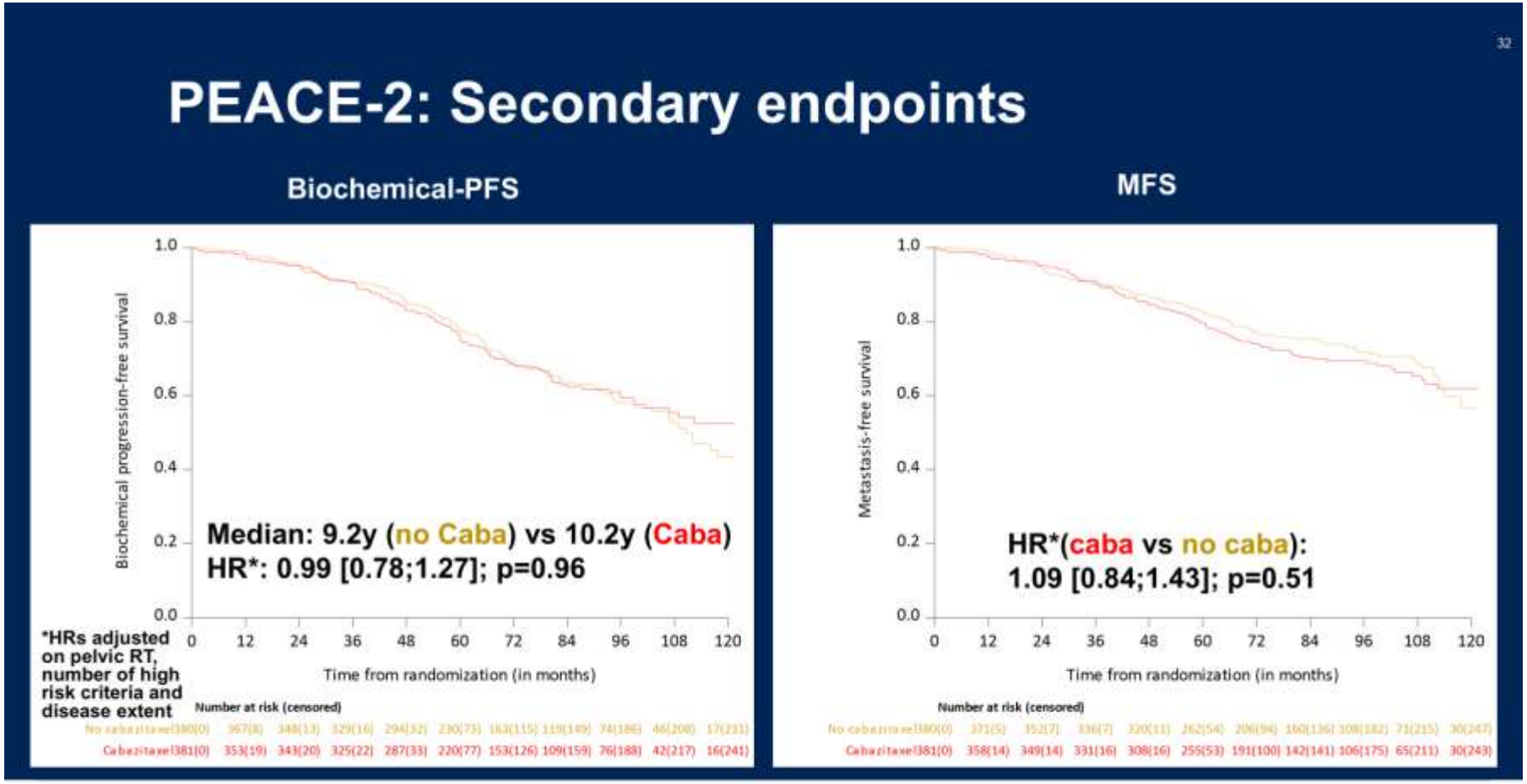
Yüksek Riskli Lokalize Prostat Kanserinde Definitif Radyoterapi (RT) + ADT ve Adjuvan Kemoterapi

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

PEACE-2: Patients characteristics

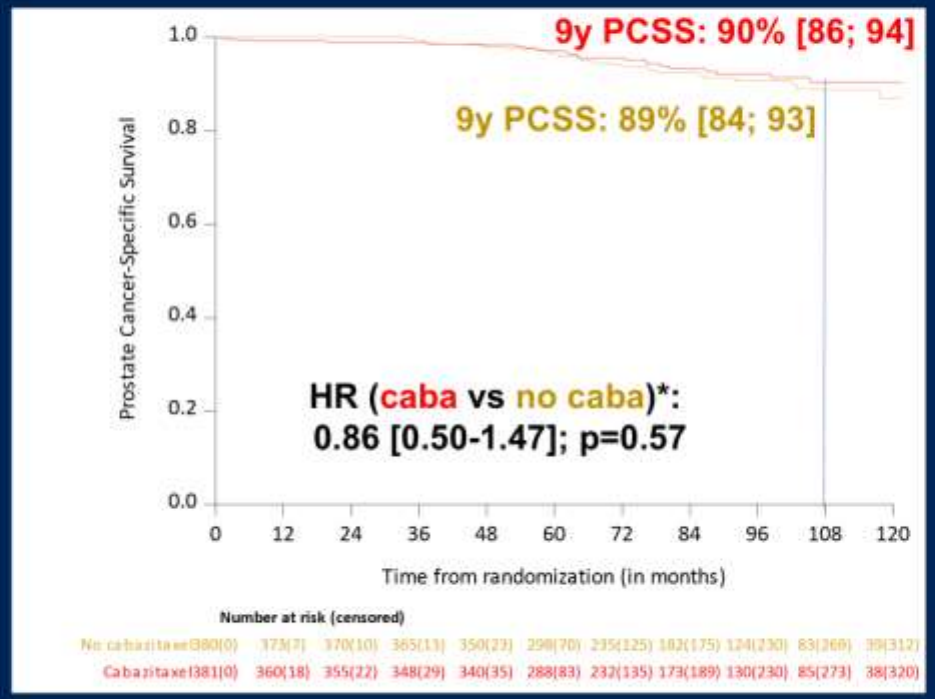
	ADT-Prostate RT (n=189)	ADT-RT Pelvis (n=191)	ADT-RT + Caba (n=191)	ADT-RT Pelvis + Caba (n=190)
Median [IQR] age (years)	67 [61-71]	67 [61-70]	67 [62-70]	66 [62-71]
T3-T4	166 (88%)	168 (88%)	174 (91%)	176 (93%)
Gleason score 8-10	145 (77%)	143 (75%)	156 (82%)	142 (75%)
Median [IQR] PSA (ng/mL)	22 [9-38]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

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



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%.

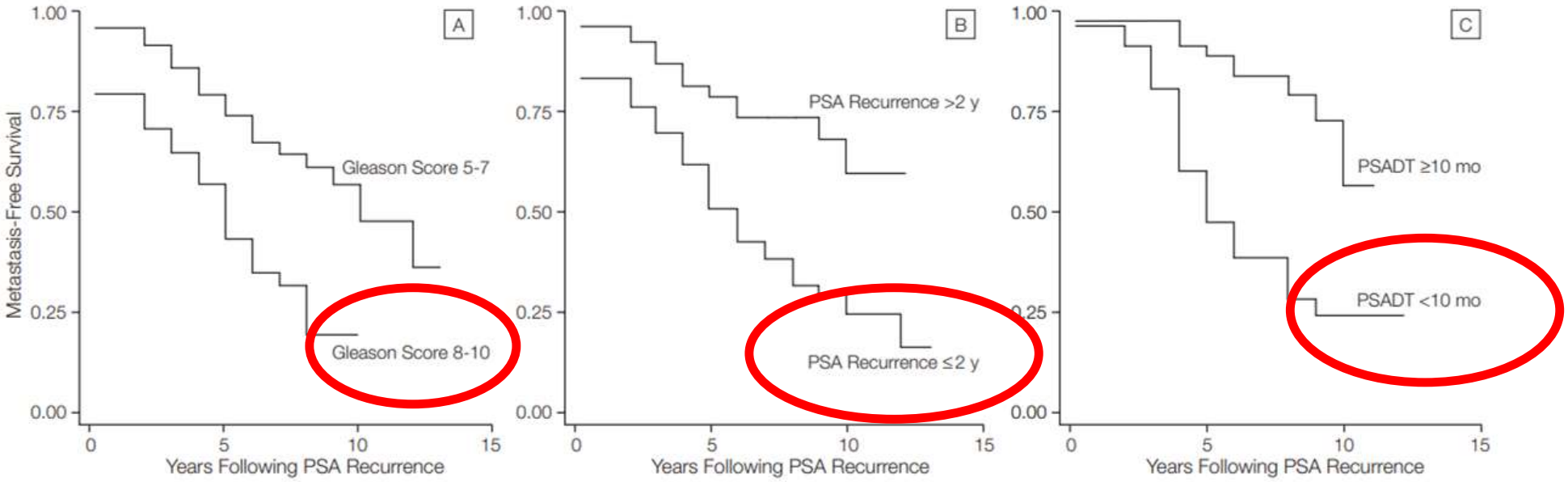
- Biyokimyasal Rekürens olan hastaların hepsinde metastaz görülmez. Bu nedenle risk skorlamasına göre yüksek grupta olanlar erken ya da salvage tedavi almalıdır.

❶ Van den Broeck T, et al. Biochemical Recurrence in Prostate Cancer: The European Association o fUrology 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

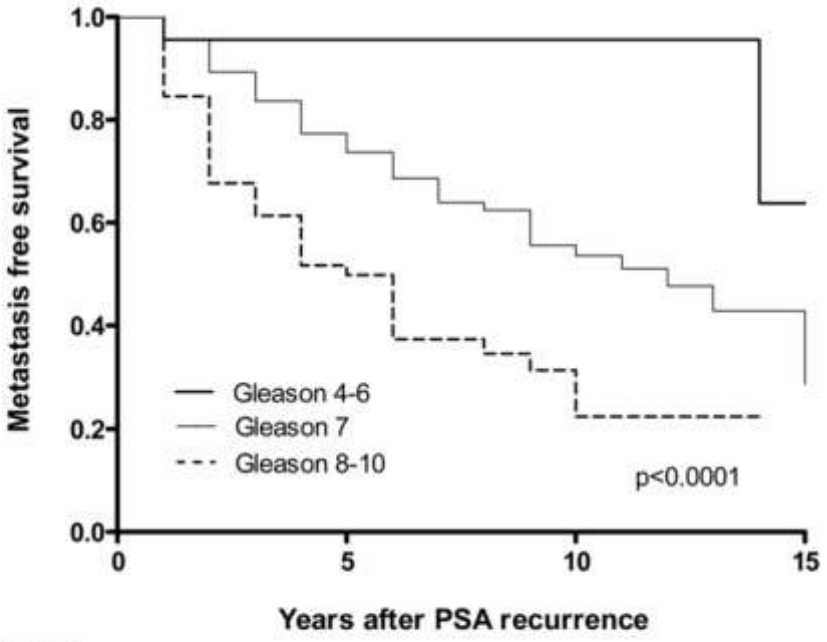
Biyokimyasal Rekürens ve PSA Persistansı Metastaz riski

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

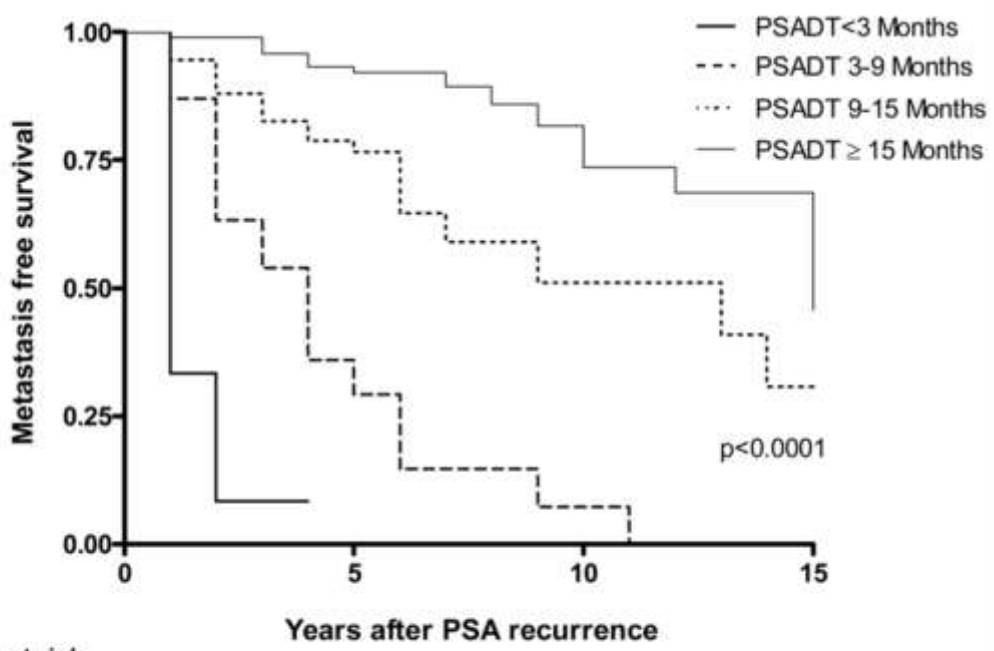


A, Based on Gleason scores in the radical prostatectomy specimen ($P<.001$). B, Based on years until initial biochemical recurrence ($P<.001$). C, Based on prostate-specific antigen doubling time (PSADT) ($P<.001$).

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

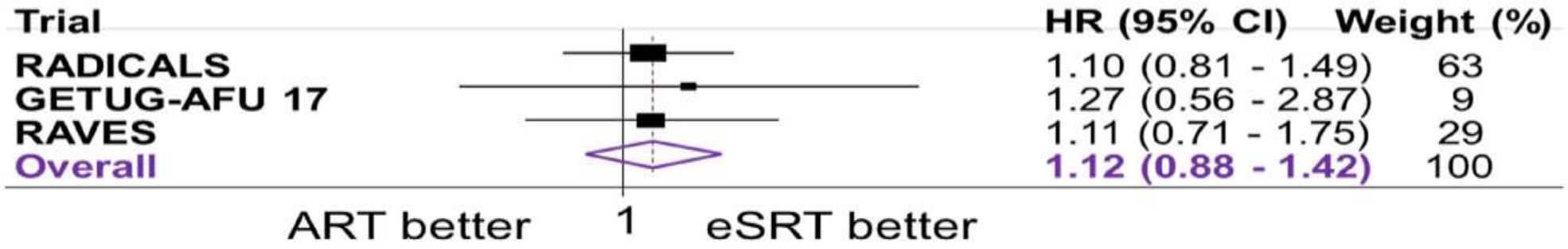
Cerrahi sonrası mediyan 8 yıl takip süresinde, 450 biyokimyasal nüks gelişen ve herhangi bir salvage tedavi almayan hastanın 134'de metastaz görüldü(%29.8).

Emmanuel S. Antonarakis, BJU Int. 2012

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

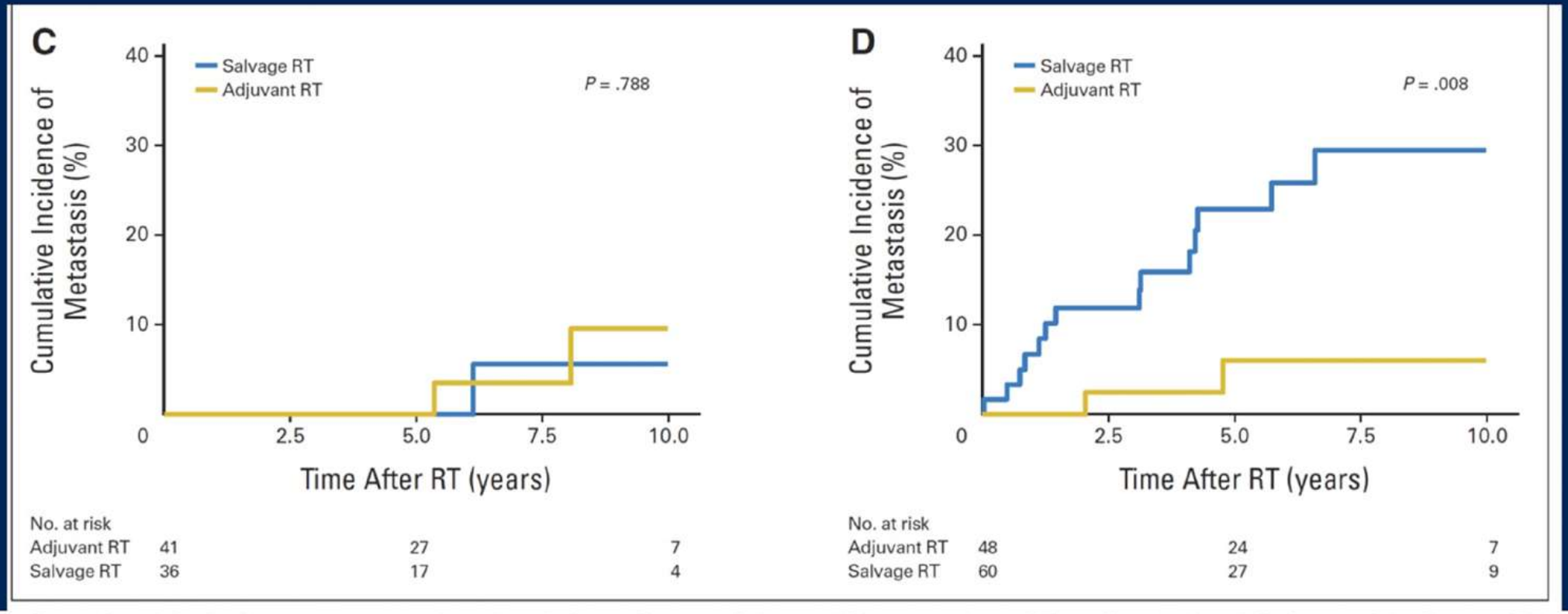
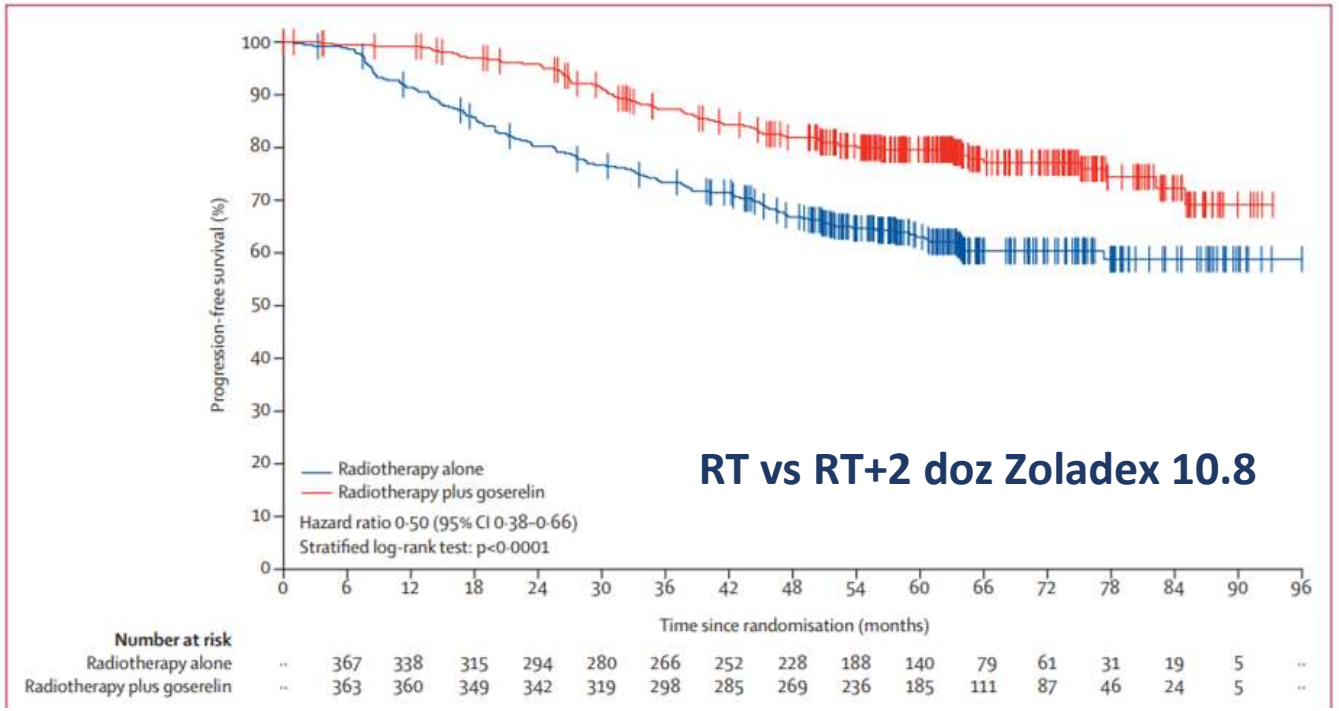


Fig 3. Cumulative incidence curves to evaluate benefit from adjuvant radiotherapy (RT) versus salvage RT stratified by (A and B) Cancer of the Prostate Risk Assessment Postsurgical (CAPRA-S) score and (C and D) genomic classifier (GC).

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)

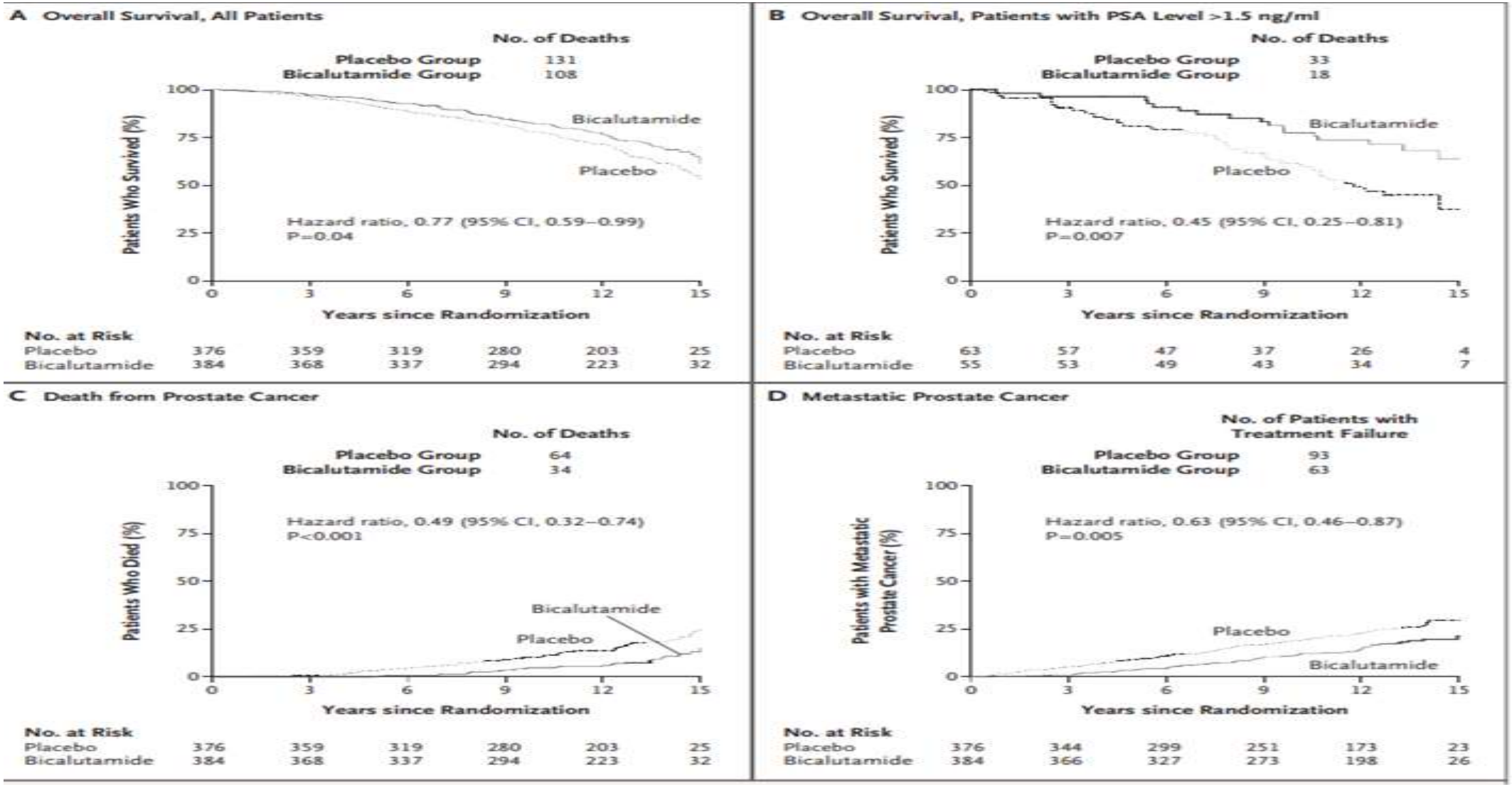


RT vs RT+2 doz Zoladex 10.8

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

GETUG-AFU 16, Lancet Oncol 2016

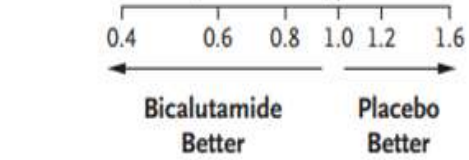
Biyokimyasal Rekürrens ve PSA Persistansında RT + 2 Yıl Bikalutamid (150 mg/gün) – RTOG 9601



RTOG 9601, N Engl J Med 2017

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

Subgroup	No. of Patients (%)	Bicalutamide Group	Placebo Group	Hazard Ratio (95% CI)	P Value
		12-yr overall survival rate (%)			
Overall	760 (100.0)	76.3	71.3	0.77 (0.59–0.99)	0.04
Gleason score					
2–6	214 (28.2)	79.5	79.2	0.95 (0.57–1.59)	0.84
7	413 (54.5)	78.5	70.9	0.69 (0.49–0.98)	0.04
8–10	131 (17.3)	63.9	58.4	0.76 (0.44–1.30)	0.32
PSA level at trial entry					
<0.7 ng/ml	405 (53.3)	76.8	80.7	1.13 (0.77–1.65)	0.53
0.7–1.5 ng/ml	237 (31.2)	77.0	67.5	0.61 (0.39–0.95)	0.03
>1.5 ngl/ml	118 (15.5)	73.5	48.9	0.45 (0.25–0.81)	0.007
Positive surgical margin					
No	191 (25.1)	73.5	72.9	0.87 (0.53–1.41)	0.56
Yes	569 (74.9)	77.3	70.7	0.73 (0.54–0.98)	0.04

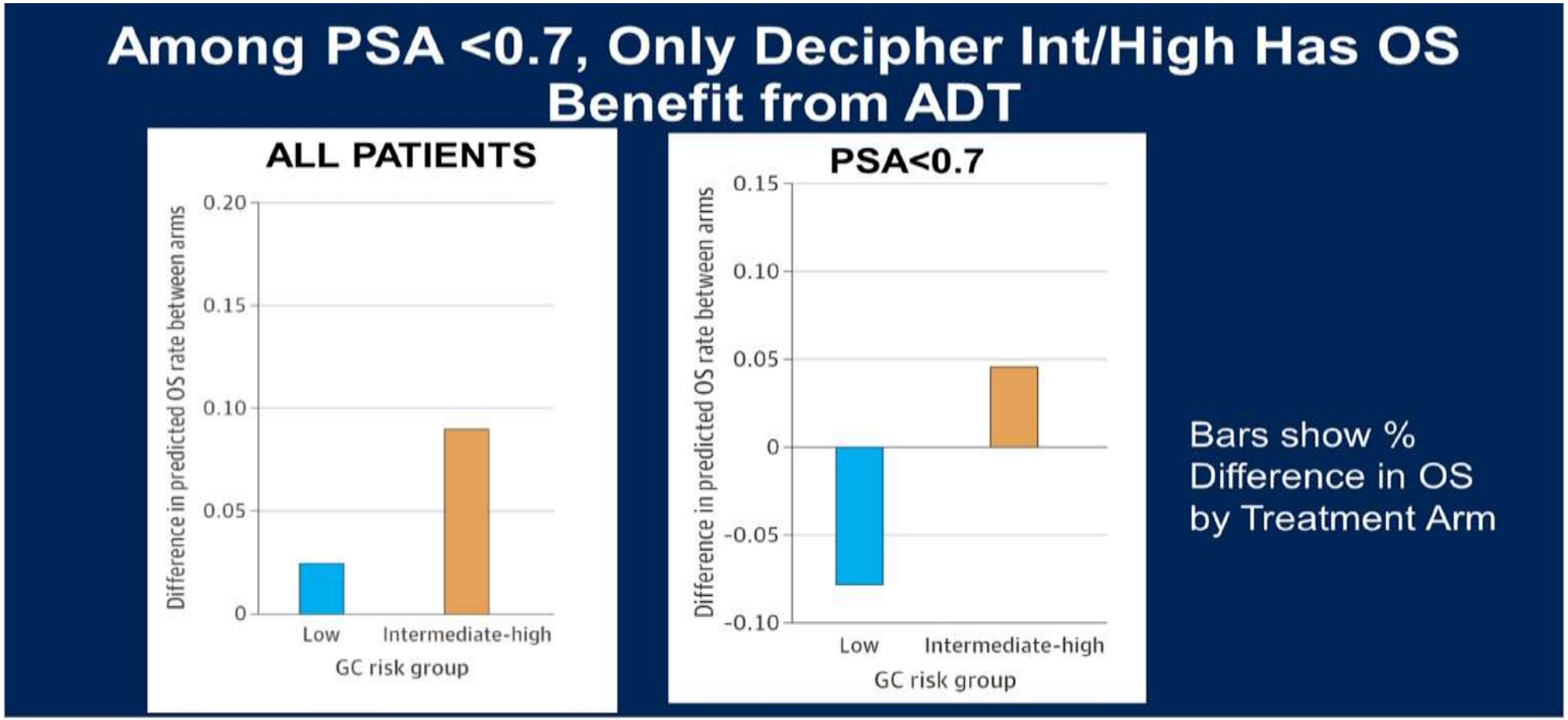


Bikalutamid grubundaki hastaların %69,7'sinde jinekomasti gelişmiştir.

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

RTOG 9601, N Engl J Med 2017

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



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

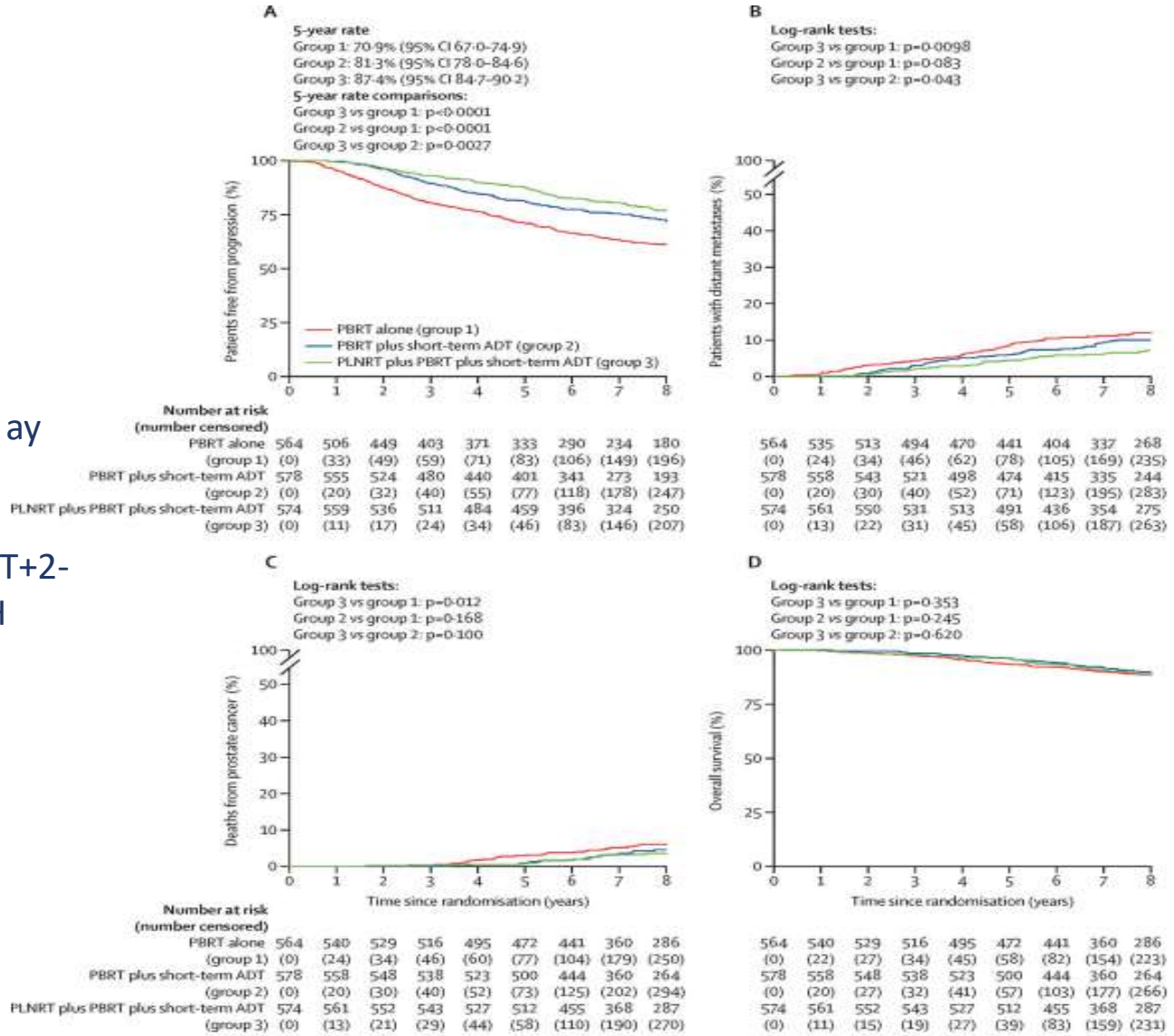


Figure 2:
Kaplan-Meier estimates and cumulative incidence curves: (A) Freedom from progression,

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

RTOG 0534 SPPORT, Lancet. 2022

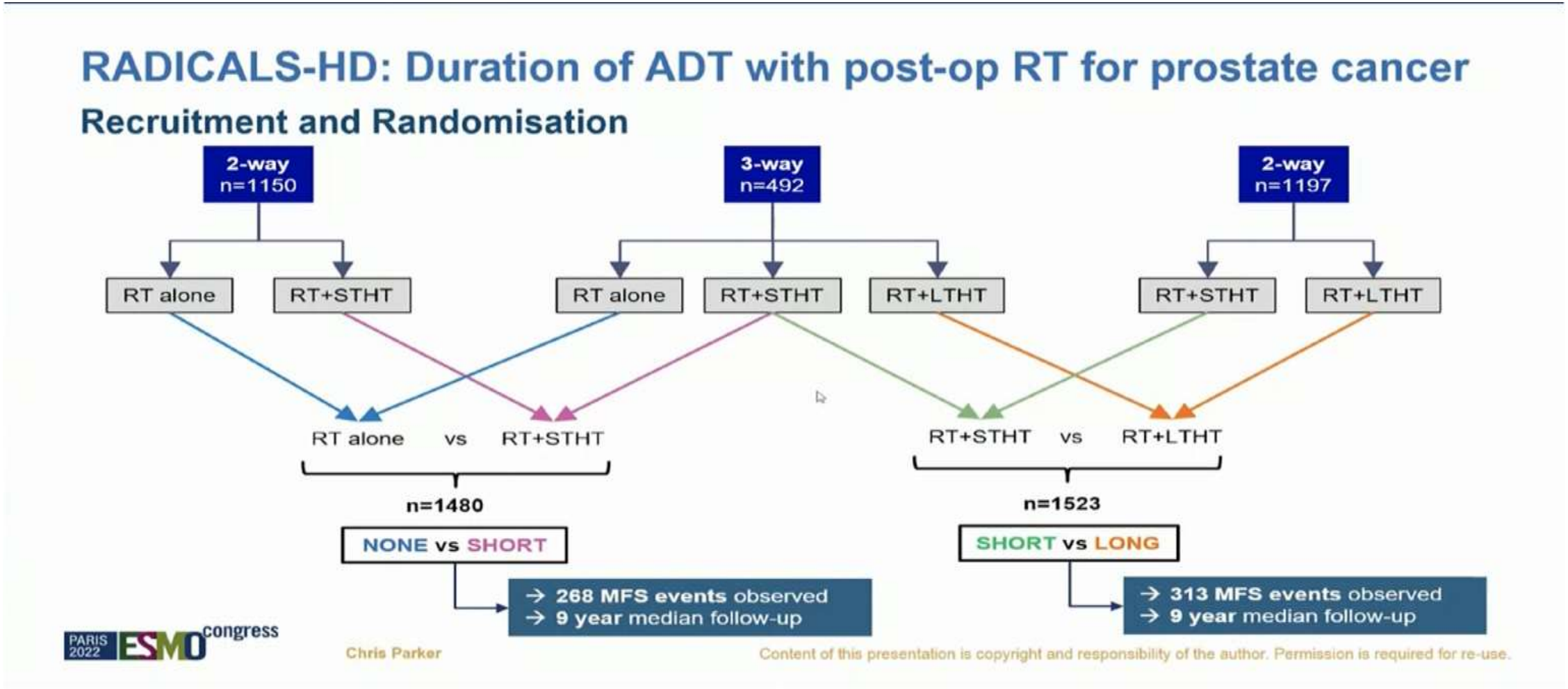
PSMA PET-CT negatif yüksek riskli hastalarda pelvik RT

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)

Management of Patients with Advanced Prostate Cancer. Report from the 2024 Advanced Prostate Cancer Consensus Conference (APCCC), Eur Urol (2024).

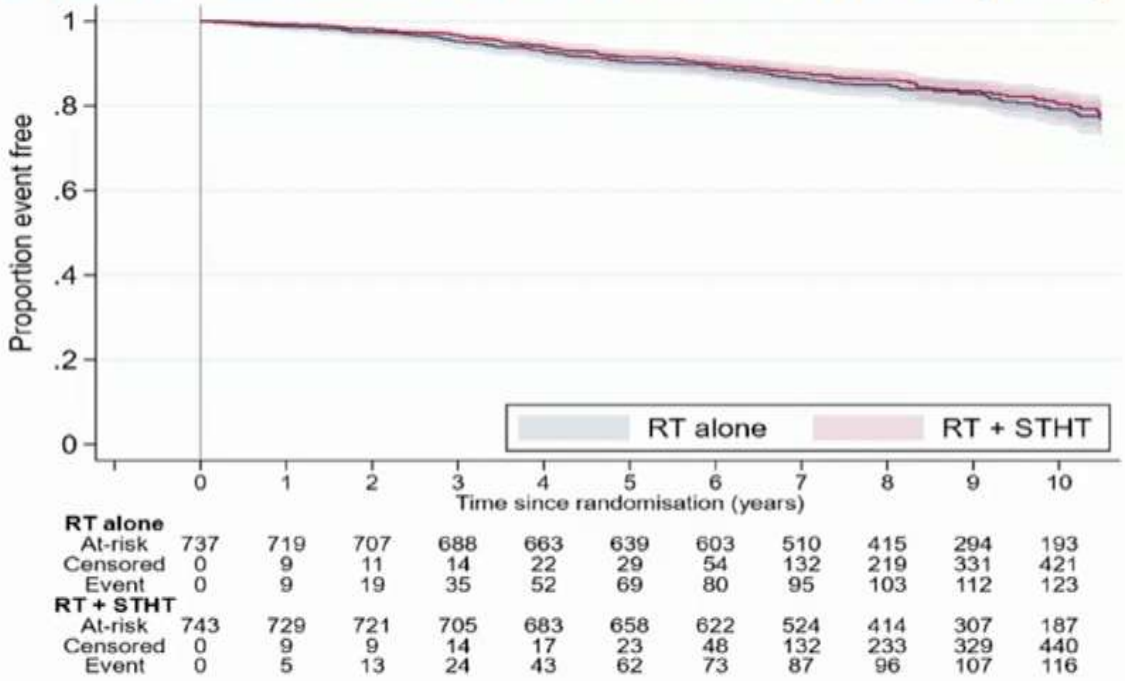
Biyokimyasal Rekürens ve PSA Persistansı RT+uzun dönem ADT



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)



RT alone										
At-risk	737	719	707	688	663	639	603	510	415	294	193
Censored	0	9	11	14	22	29	54	132	219	331	421
Event	0	9	19	35	52	69	80	95	103	112	123
RT + STHT										
At-risk	743	729	721	705	683	658	622	524	414	307	187
Censored	0	9	9	14	17	23	48	132	233	329	440
Event	0	5	13	24	43	62	73	87	96	107	116

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

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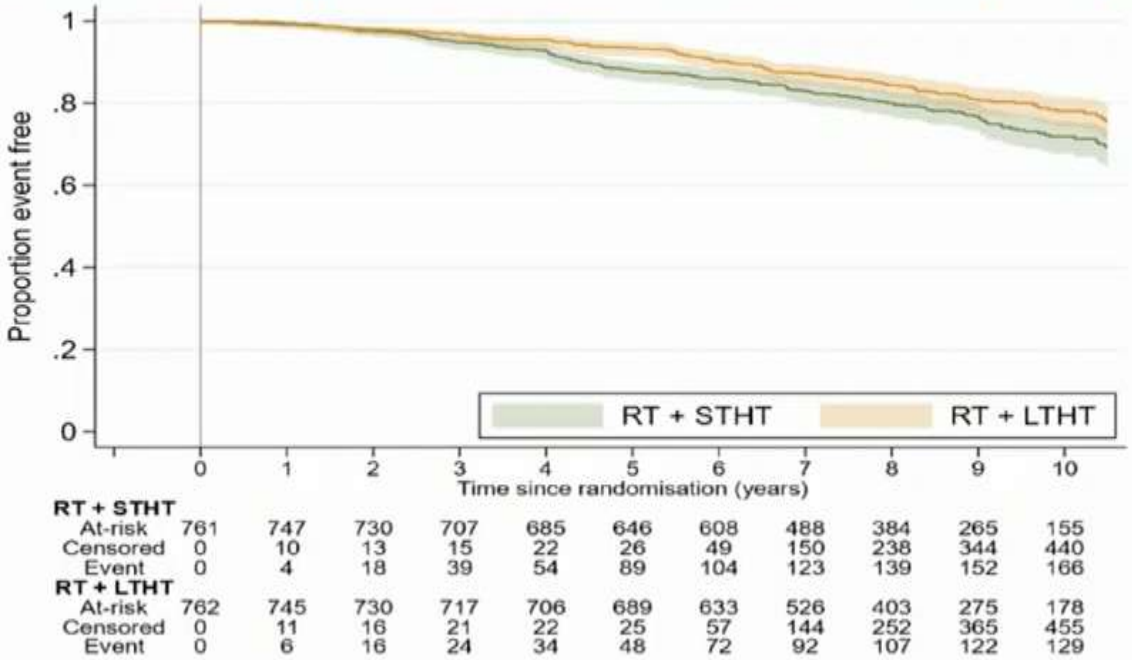
Biyokimyasal Rekürens ve PSA Persistansı
RT+uzun dönem ADT

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

Short vs Long: Metastases-Free Survival (MFS)



RT + STHT											
At-risk	761	747	730	707	685	646	608	488	384	265	155
Censored	0	10	13	15	22	26	49	150	238	344	440
Event	0	4	18	39	54	89	104	123	139	152	166
RT + LTHT											
At-risk	762	745	730	717	706	689	633	526	403	275	178
Censored	0	11	16	21	22	25	57	144	252	365	455
Event	0	6	16	24	34	48	72	92	107	122	129

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

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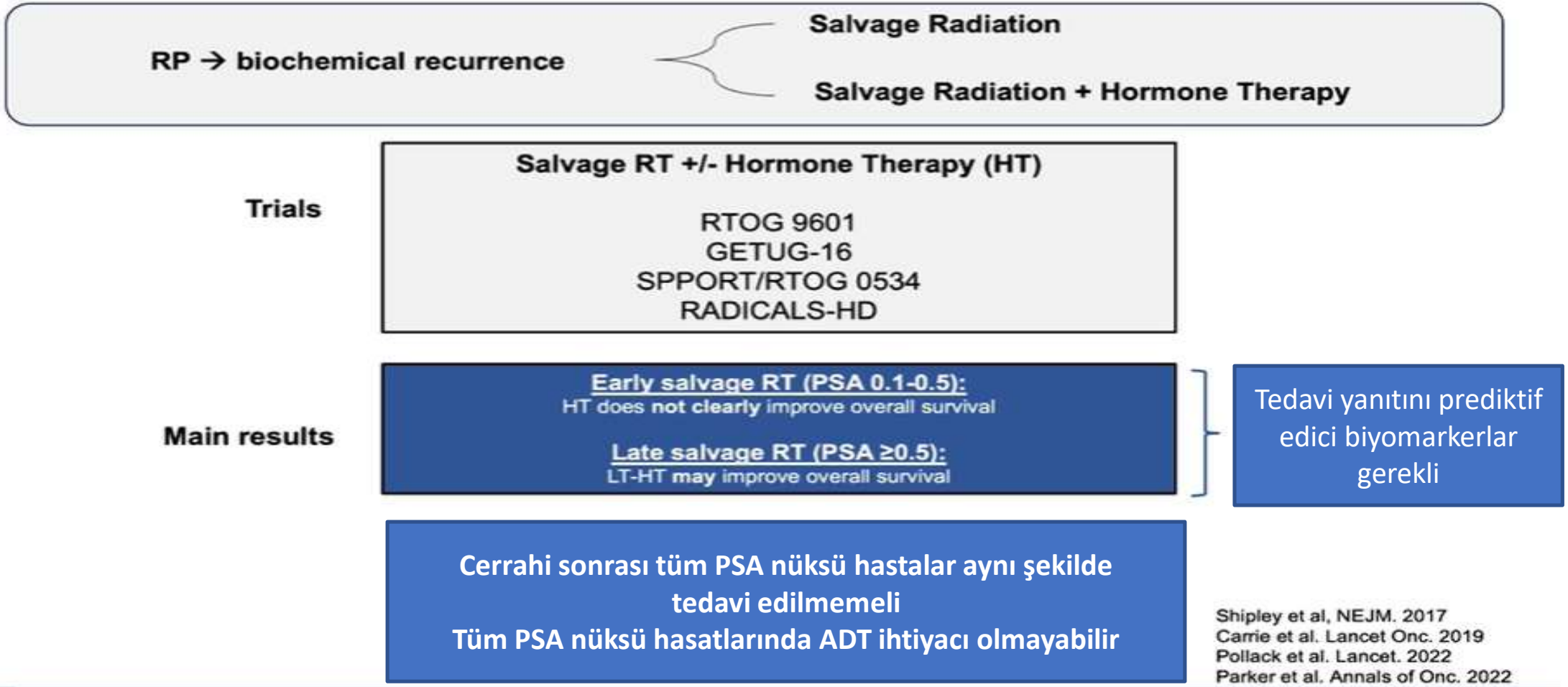
Biyokimyasal Rekürens ve PSA Persistansı

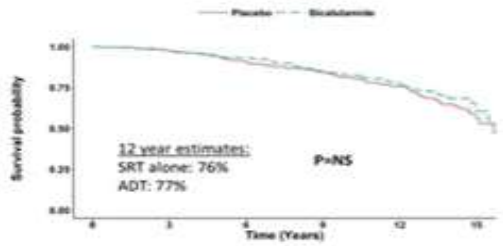


ADT+RT ile artmış MFS , Tüm popülasyonda OS faydası yok

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

RTOG 9601

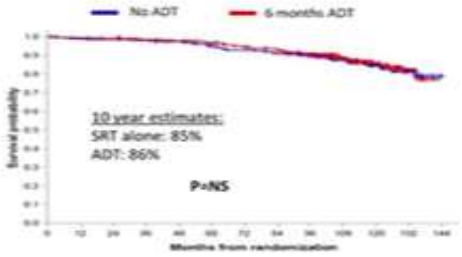
PSA 0.2-1.5 ng/mL stratum



Median follow-up: 13 years

GETUG-16

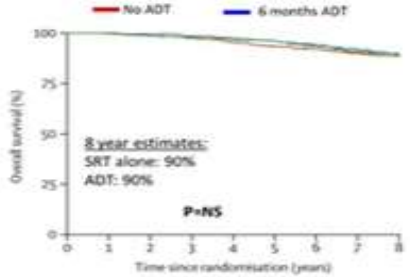
PSA 0.2-2.0 ng/mL



Median follow-up: 9 years

SPPORT

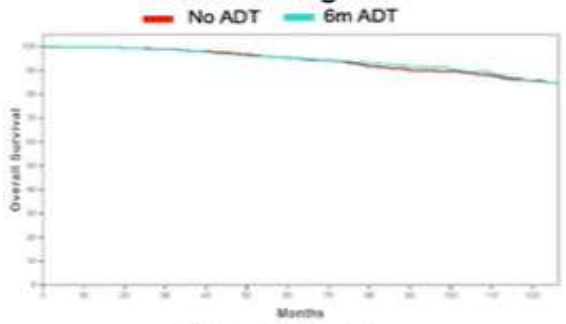
PSA 0.1-2.0 ng/mL



Median follow-up: 8 years

RADICALS-HD 0 vs 6m ADT

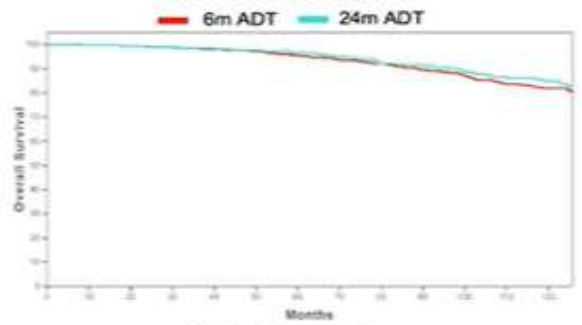
PSA 0.0-4.2 ng/mL



Median follow-up: 9 years

RADICALS-HD 6 vs 24m ADT

PSA 0.0-5.0 ng/mL



Median follow-up: 9 years

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

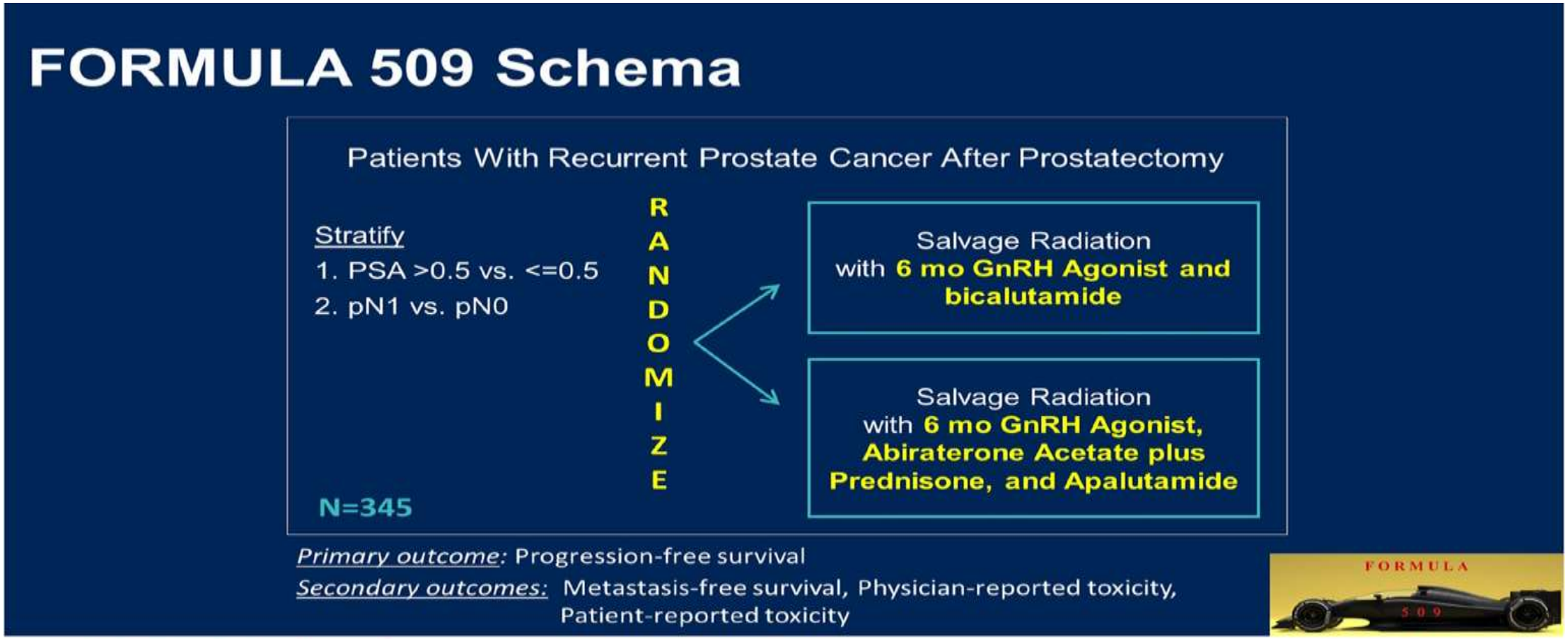
İzole PSA nüksünde hangi hastalara sistemik tedavi

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



Biyokimyasal Rekürens ve PSA Persistansı Doz Yoğun Tedavi

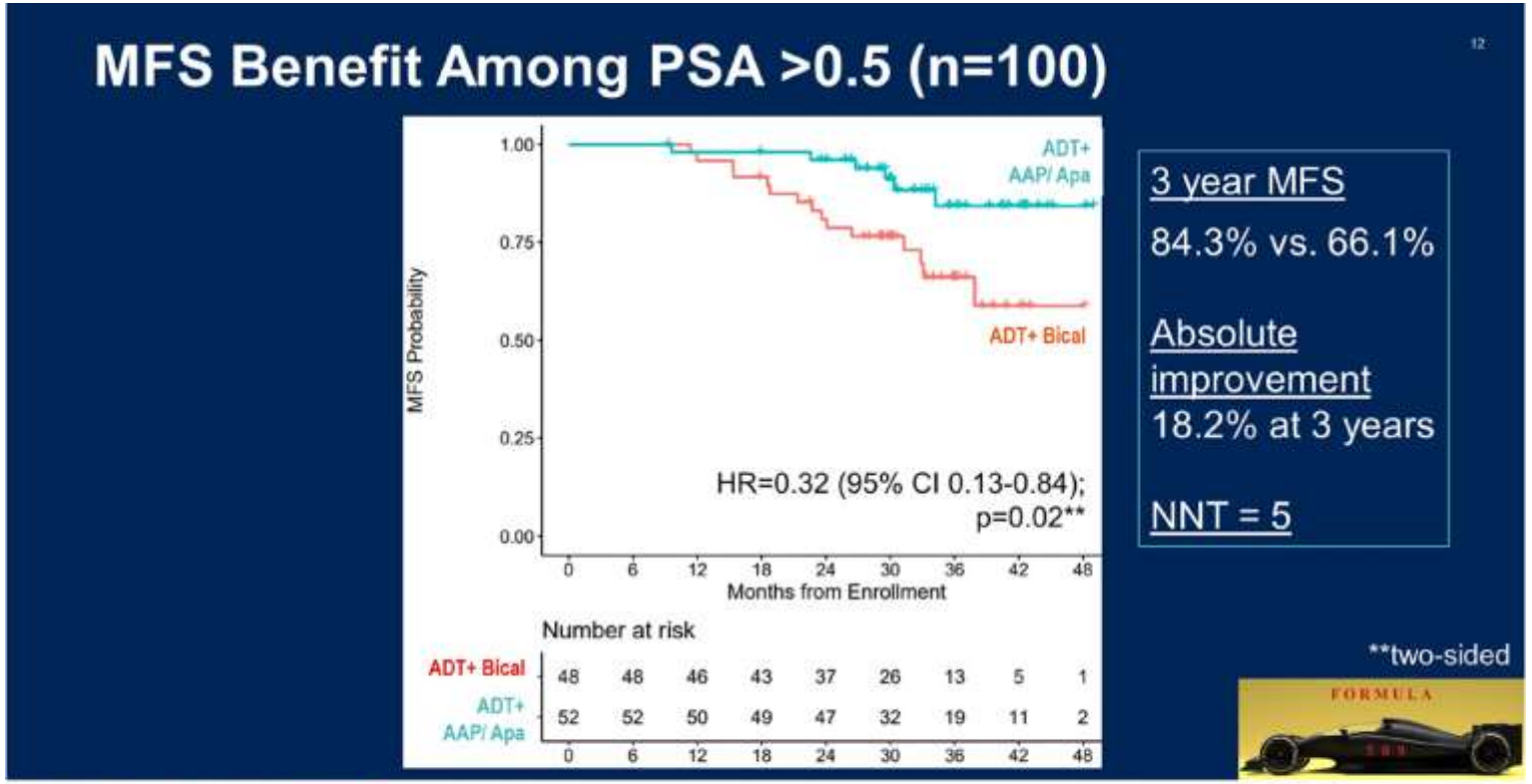
Patient Characteristics

	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

PRESENTED BY: Paul Nguyen, MD

Biyokimyasal Rekürens ve PSA Persistansı Doz Yoğun Tedavi



Tedavi öncesi PSA düzeyi kombine tedaviler için prediktif

Differential Benefit by pre-SRT PSA

Formula-509

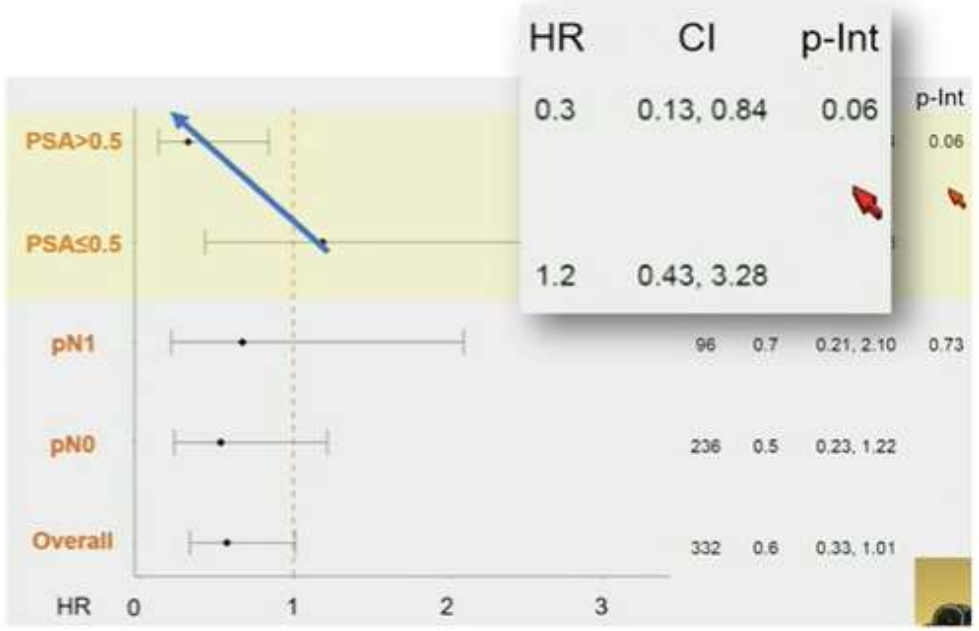
Patients With Recurrent Prostate Cancer After Prostatectomy

Stratify
1. PSA >0.5 vs. <=0.5
2. pN1 vs. pN0

RANDOMIZE

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

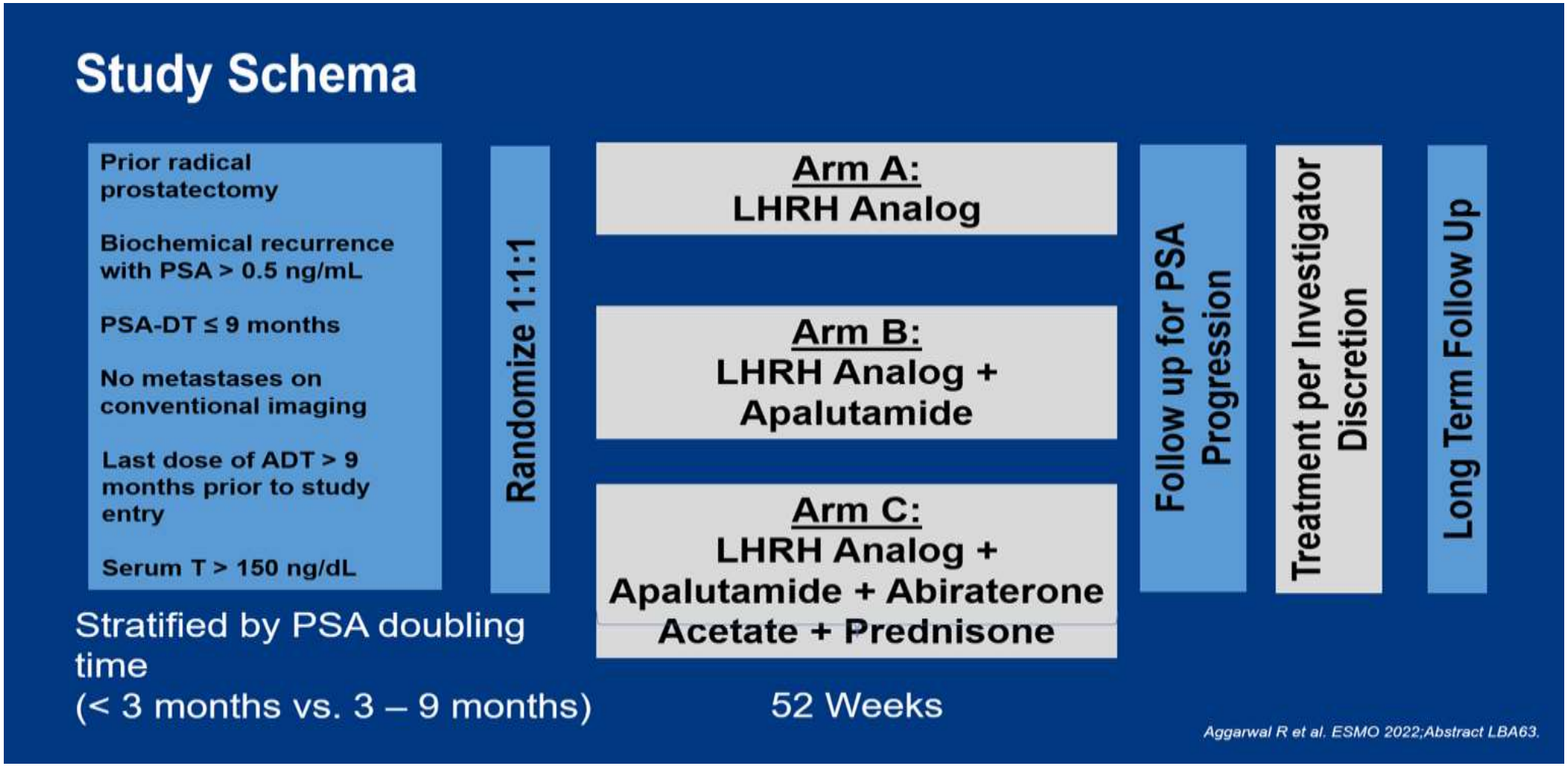
N=345



Nguyen P et al. ASCO GU 2023

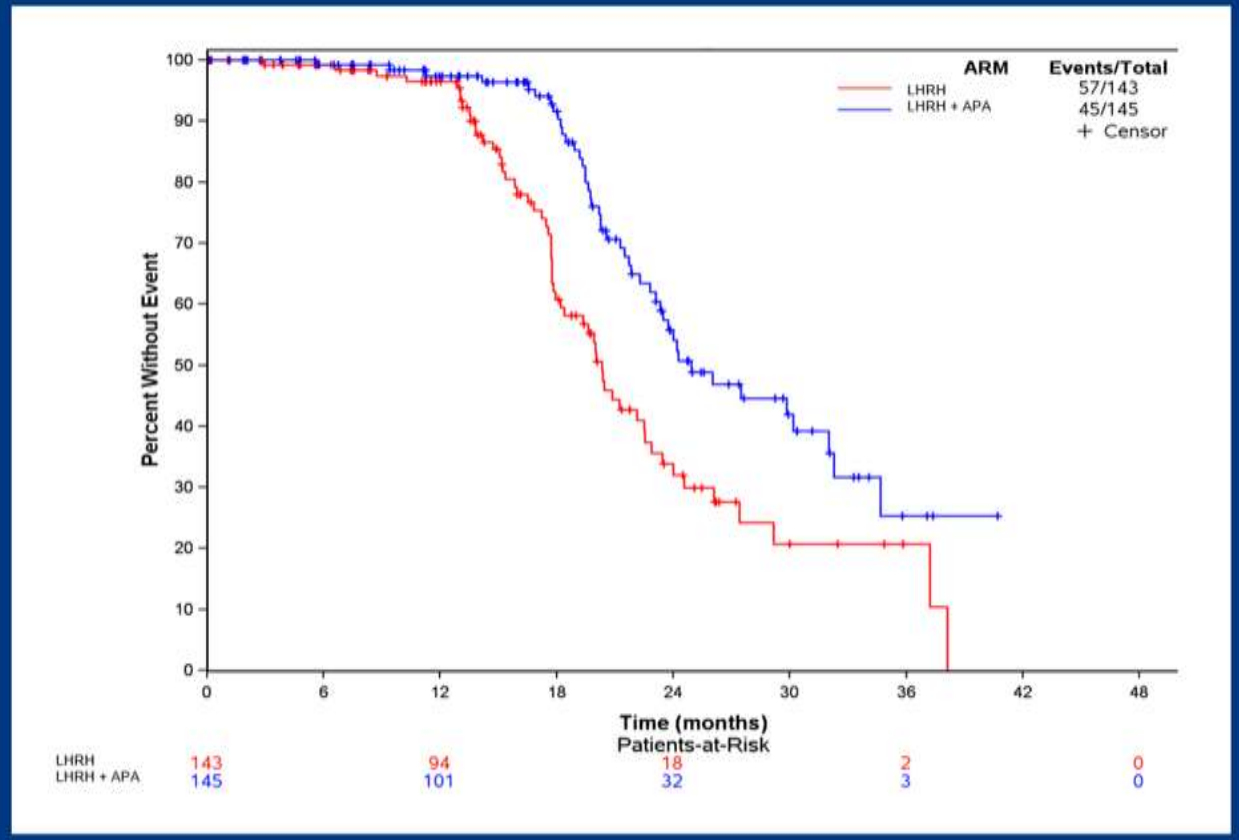
Biyokimyasal Rekürens ve PSA Persistansı Doz Yoğun Tedavi

Biyokimyasal Rekürens ve PSA Persistansı Doz Yoğun Tedavi



Biyokimyasal Rekürens ve PSA Persistansı Doz Yoğun Tedavi

Arm B: ADT + apalutamide vs. ADT monotherapy



Median follow up 21.5 months

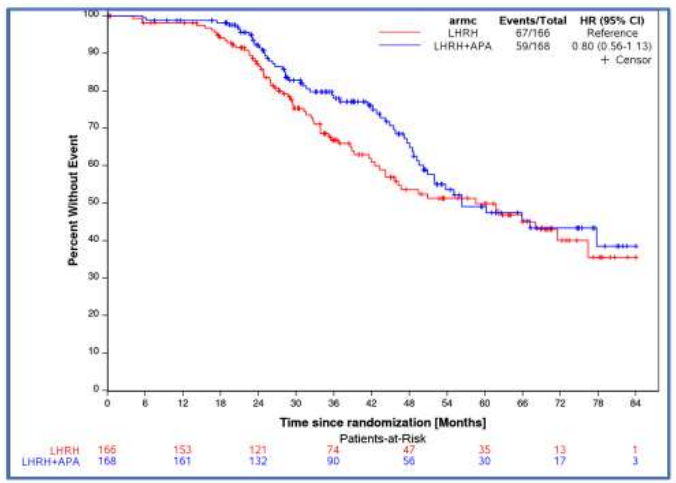
102 PSA PFS events

Median PSA progression-free survival

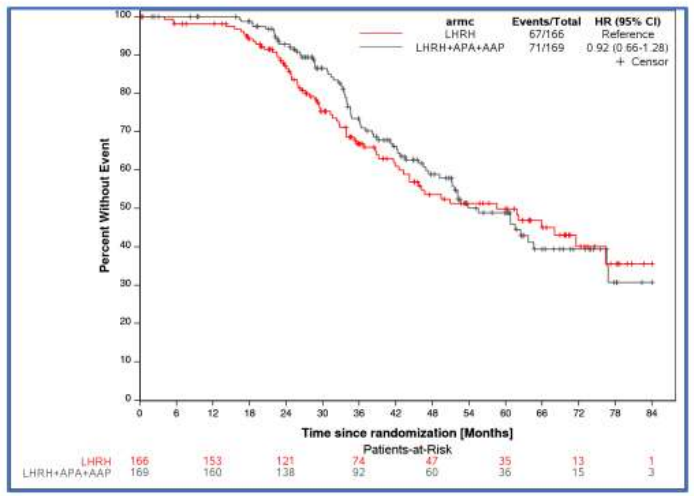
- ADT + APA = 24.9 months (95% CI: 23.3 – 32.3)
- ADT alone = 20.3 months (95% CI: 18.2 – 22.9)
- **Hazard ratio 0.52 (95% CI: 0.35 – 0.77)**
- One-sided p-value = 0.00047)

Aggarwal R et al. ESMO 2022;Abstract LBA63.

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)**

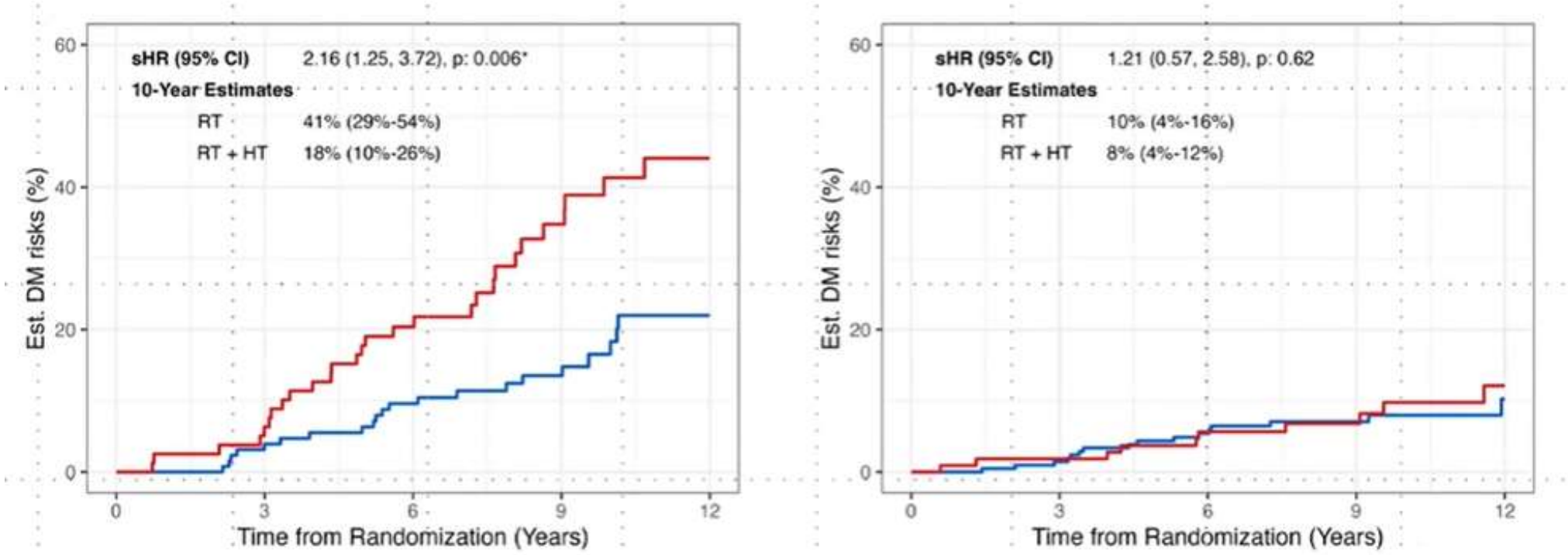
Not practice changing

Presenter: Dr. Constance Thibault

Sistemik tedaviler için yeni prediktif markerlar

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

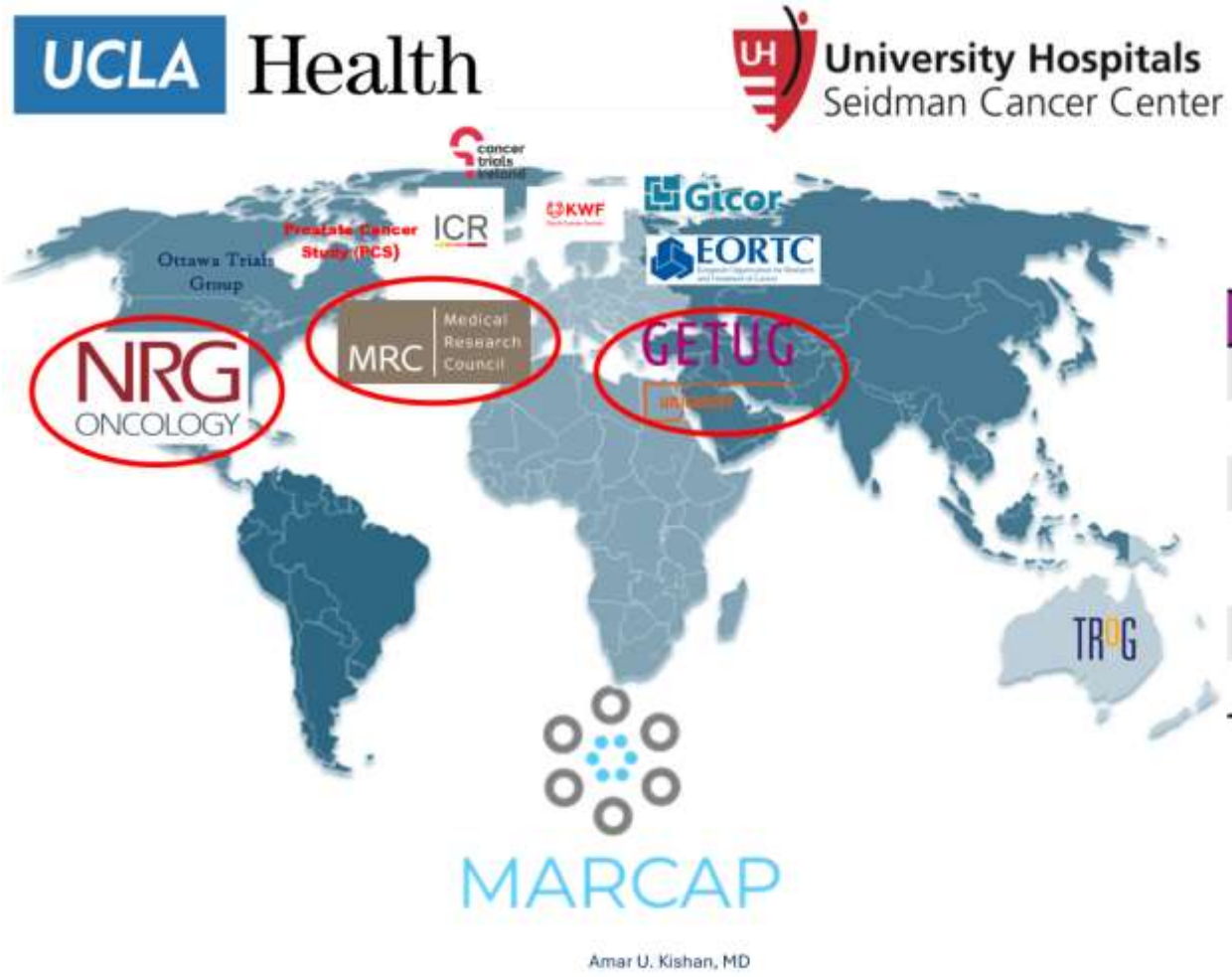
Role of IPD Meta-Analyses

- 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 **P**ost-**O**perative **S**alvage or Adjuvant Radioth**E**rapy and Ant**I**-An**D**rogen Therapy for Men with Pr**O**state Ca**N**cer (**POSEIDON**) IPD meta-analysis of all published randomized trials

MARCAP

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

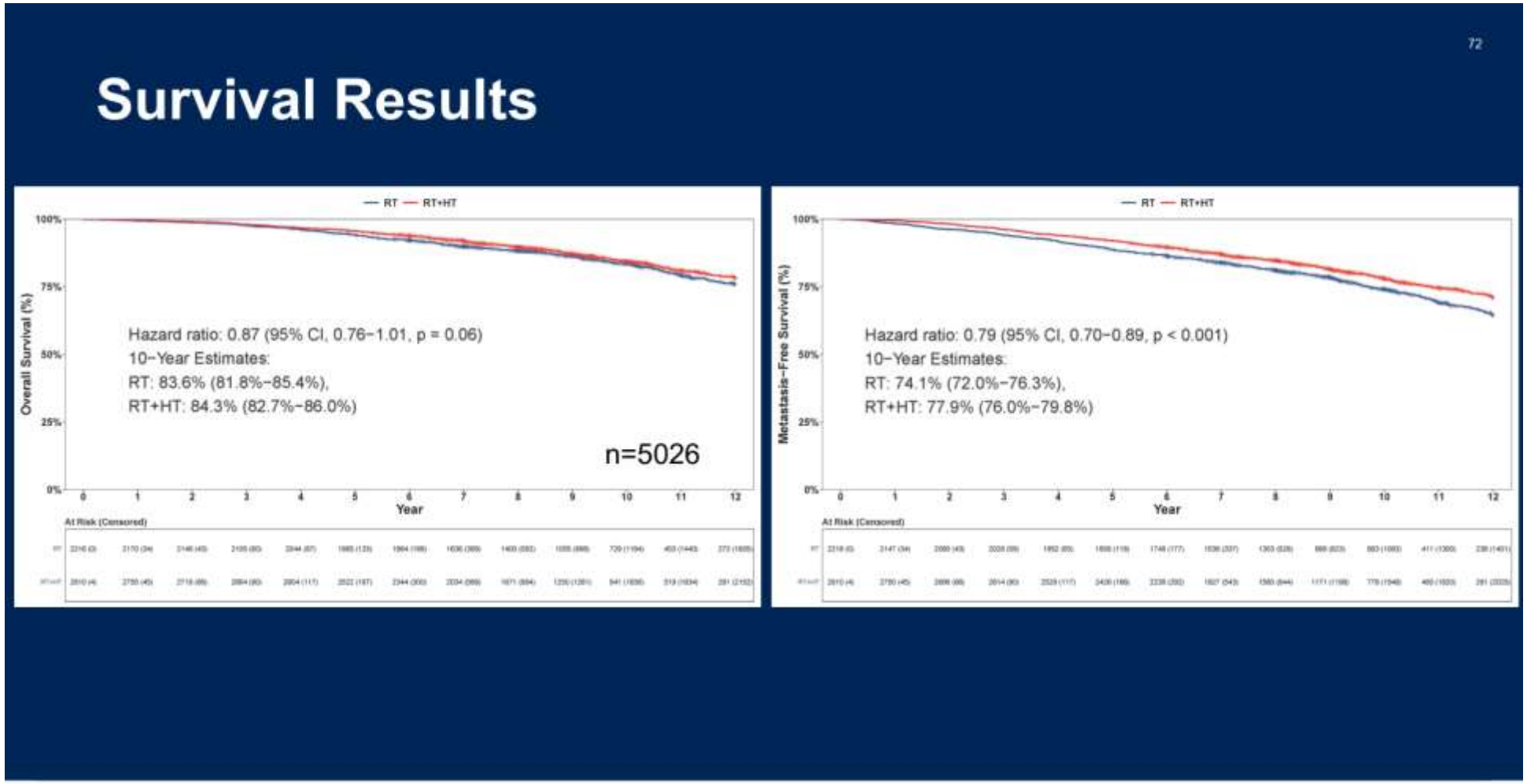


Included Trials
RTOG 9601: RT vs RT+LT-HT
GETUG-16: RT vs RT+ST-HT
RADICALS: RT vs. RT+ST-HT
RADICALS: RT vs. RT+ST-HT vs. RT+LT-HT
RADICALS: RT+ST-T vs. RT+LT-HT
RTOG 0534: RT vs. RT+ST-HT*

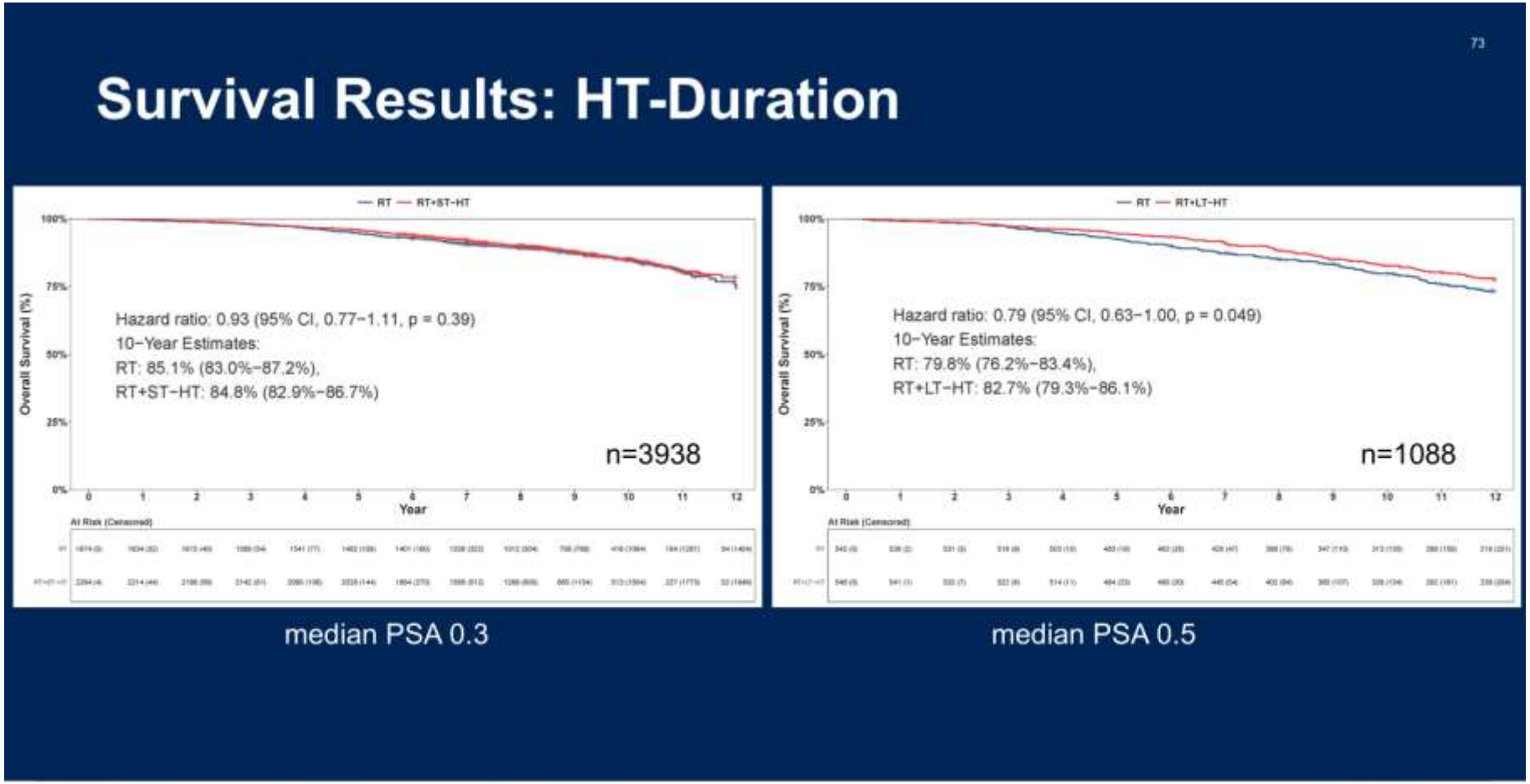
Prostat Kanserinde Post-Operatif Radyoterapi ve Anti-Androjen Tedavisi: POSEIDON Bireysel Hasta Verileri Meta-Analizi

	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%)

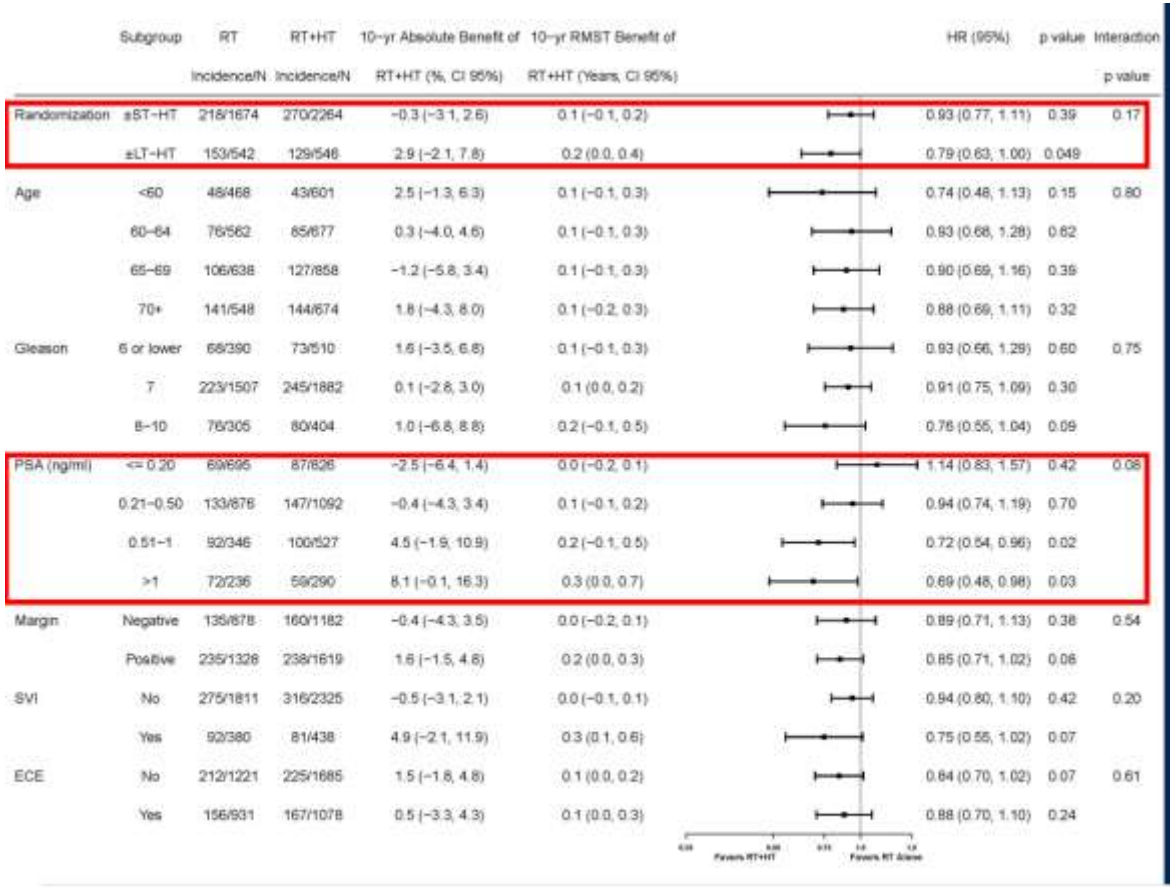
Prostat Kanserinde Post-Operatif Radyoterapi ve Anti-Androjen Tedavisi: POSEIDON Bireysel Hasta Verileri Meta-Analizi



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



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



Subgroup		RT Incidence/N	RT+HT Incidence/N	10-yr Absolute Benefit of RT+HT (%, CI 95%)	10-yr RMST Benefit of RT+HT (Years, CI 95%)	HR (95%)	p value	Interaction p value
Randomization	±ST-HT	218/1674	270/2264	−0.3 (−3.1, 2.6)	0.1 (−0.1, 0.2)	0.93 (0.77, 1.11)	0.39	0.17
	±LT-HT	153/542	129/546	2.9 (−2.1, 7.8)	0.2 (0.0, 0.4)	0.79 (0.63, 1.00)	0.049	
Age	<60	48/468	43/601	2.5 (−1.3, 6.3)	0.1 (−0.1, 0.3)	0.74 (0.48, 1.13)	0.15	0.80
	60–64	76/562	85/677	0.3 (−4.0, 4.6)	0.1 (−0.1, 0.3)	0.93 (0.68, 1.28)	0.62	
	65–69	106/638	127/858	−1.2 (−5.8, 3.4)	0.1 (−0.1, 0.3)	0.90 (0.69, 1.16)	0.39	
	70+	141/548	144/674	1.8 (−4.3, 8.0)	0.1 (−0.2, 0.3)	0.88 (0.69, 1.11)	0.32	
Gleason	6 or lower	68/390	73/510	1.6 (−3.5, 6.8)	0.1 (−0.1, 0.3)	0.93 (0.66, 1.29)	0.60	0.75
	7	223/1507	245/1882	0.1 (−2.8, 3.0)	0.1 (0.0, 0.2)	0.91 (0.75, 1.09)	0.30	
	8–10	76/305	80/404	1.0 (−6.8, 8.8)	0.2 (−0.1, 0.5)	0.76 (0.55, 1.04)	0.09	
PSA (ng/ml)	<= 0.20	69/695	87/826	−2.5 (−6.4, 1.4)	0.0 (−0.2, 0.1)	1.14 (0.83, 1.57)	0.42	0.08
	0.21–0.50	133/878	147/1092	−0.4 (−4.3, 3.4)	0.1 (−0.1, 0.2)	0.94 (0.74, 1.19)	0.70	
	0.51–1	92/346	100/527	4.5 (−1.9, 10.9)	0.2 (−0.1, 0.5)	0.72 (0.54, 0.96)	0.02	
	>1	72/236	59/290	8.1 (−0.1, 16.3)	0.3 (0.0, 0.7)	0.69 (0.48, 0.98)	0.03	
Margin	Negative	135/878	160/1182	−0.4 (−4.3, 3.5)	0.0 (−0.2, 0.1)	0.89 (0.71, 1.13)	0.38	0.54
	Positive	235/1328	238/1619	1.6 (−1.5, 4.6)	0.2 (0.0, 0.3)	0.85 (0.71, 1.02)	0.08	
SVI	No	275/1811	316/2325	−0.5 (−3.1, 2.1)	0.0 (−0.1, 0.1)	0.94 (0.80, 1.10)	0.42	0.20
	Yes	92/380	81/438	4.9 (−2.1, 11.9)	0.3 (0.1, 0.6)	0.75 (0.55, 1.02)	0.07	
ECE	No	212/1221	225/1685	1.5 (−1.8, 4.8)	0.1 (0.0, 0.2)	0.84 (0.70, 1.02)	0.07	0.61
	Yes	156/931	167/1078	0.5 (−3.3, 4.3)	0.1 (0.0, 0.3)	0.88 (0.70, 1.10)	0.24	

74

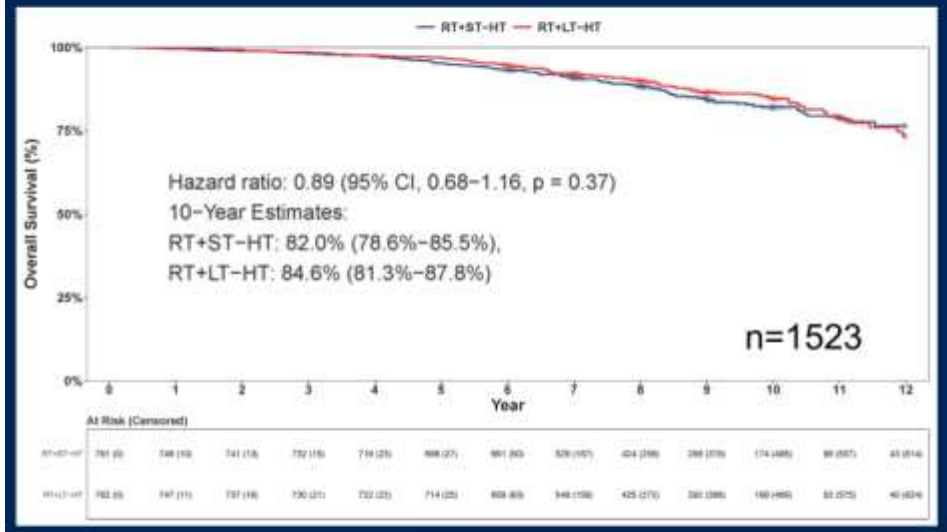
No significant interaction between impact of HT on OS and its duration

Trend towards significant impact of pre-PORT PSA

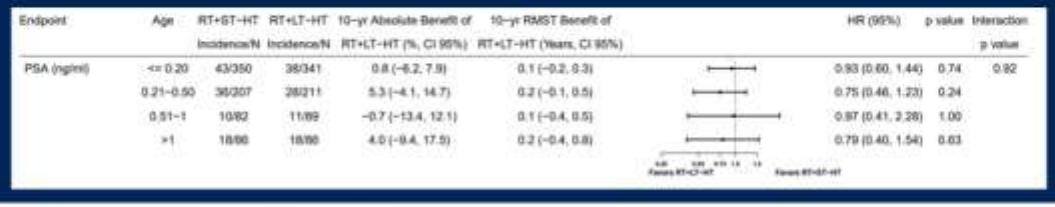
Multivariate model adjusted for age, pGS, and pT stage was significant for PSA at a cutpoint of 0.5 ng/mL (p=0.03)

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

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)



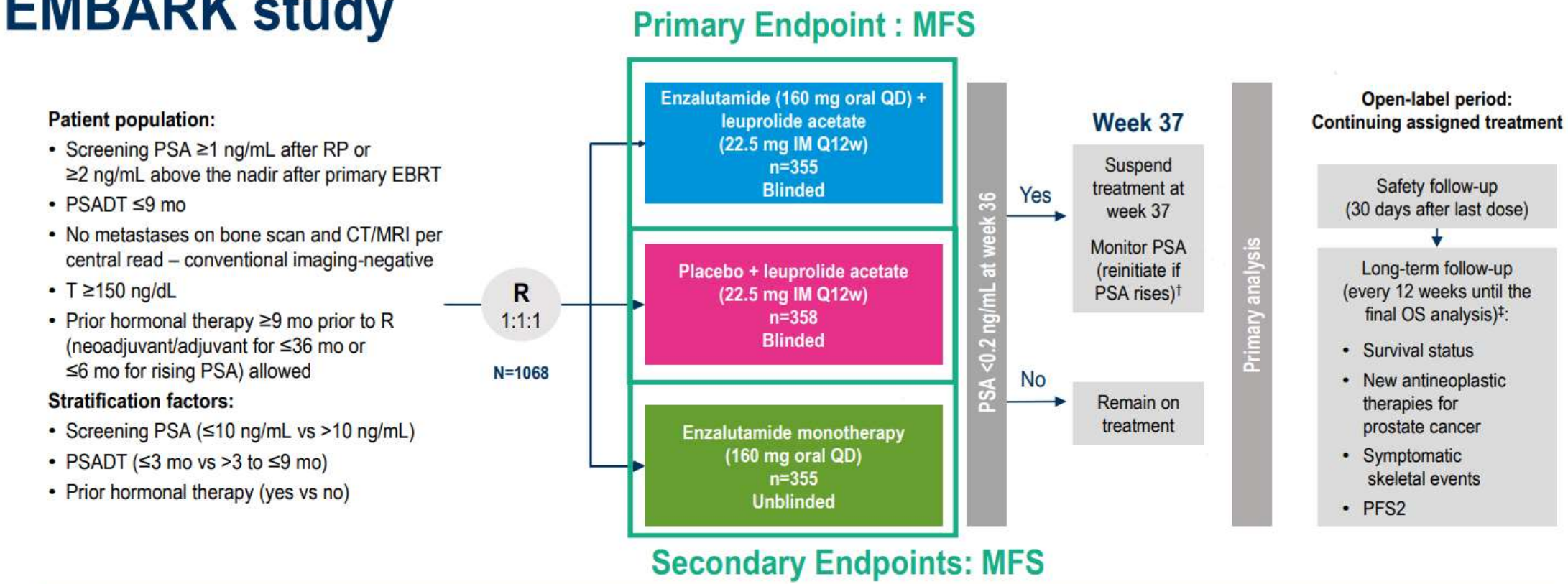
The Key ~~Un~~Answered Questions

- **Who needs HT with PORT? <u>Only patients with pre-PORT PSA >0.5 ng/ml</u>**
  - **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? <u>For most patients, ST-HT is sufficient</u>**
  - **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

EMBARK study



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

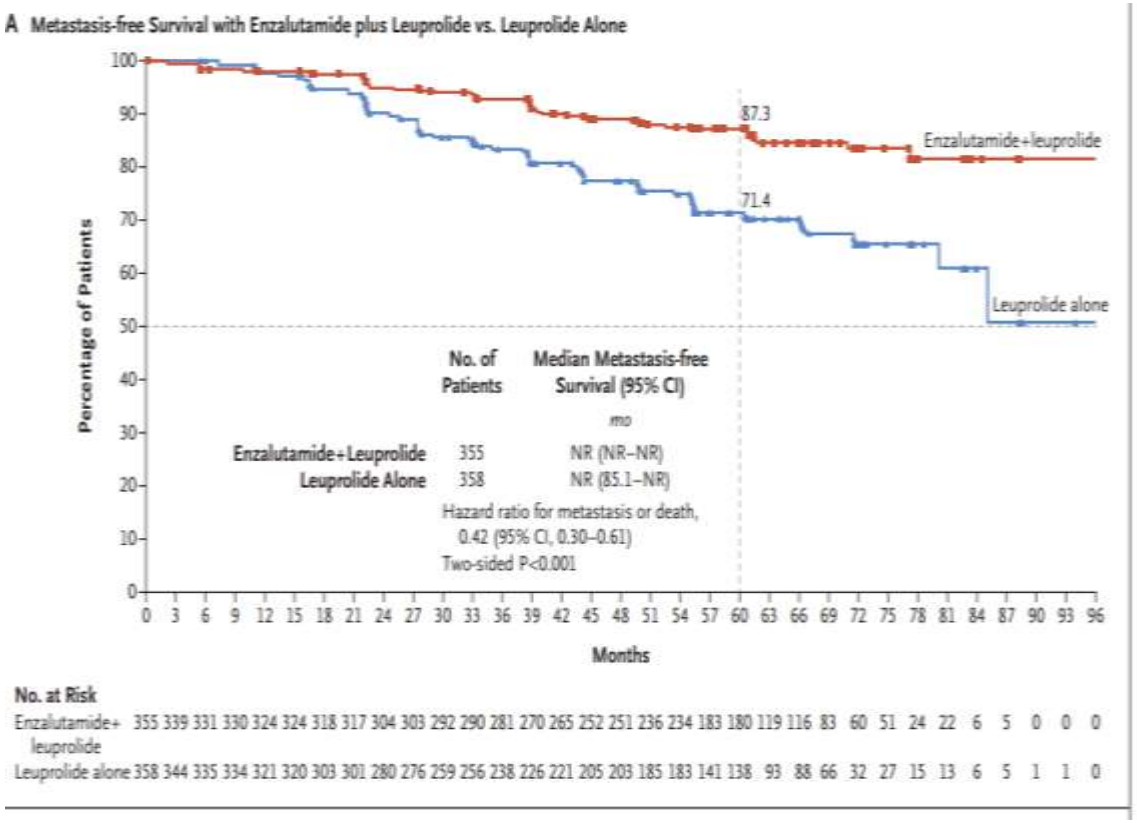
Improved Survival with Enzalutamide in Biochemically Recurrent Prostate Cancer

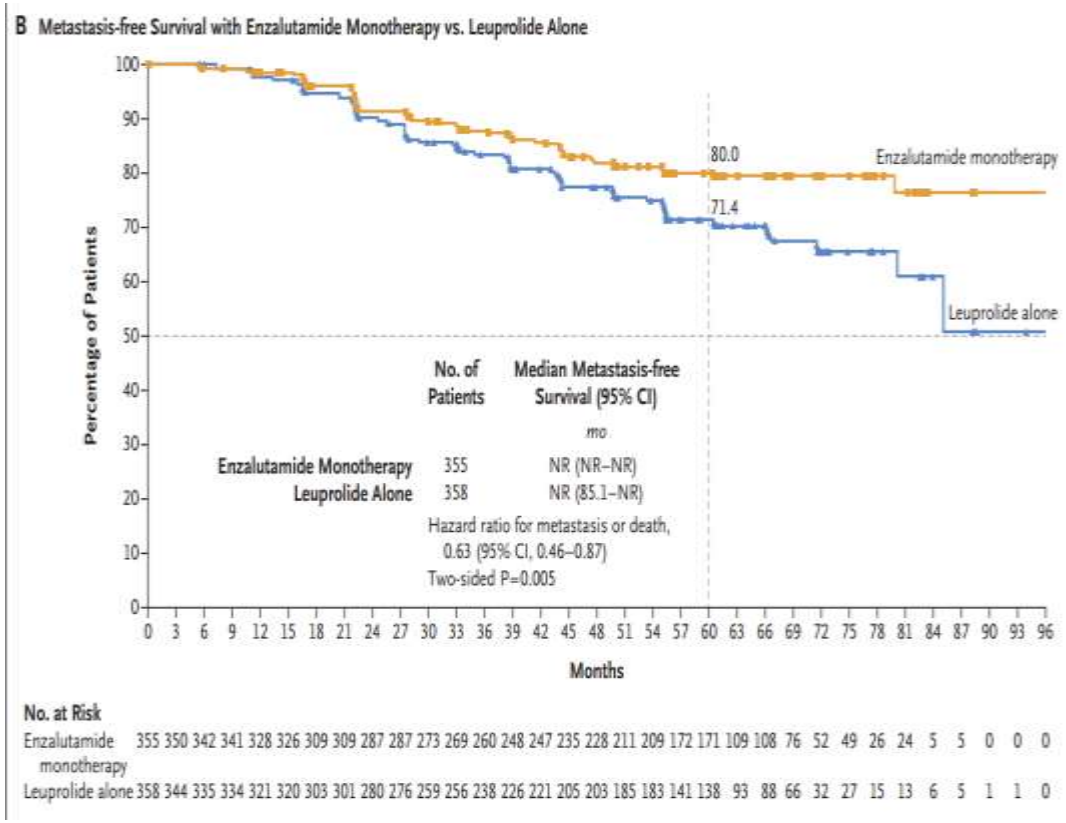
Neal D. Shore, M.D.,[1] Murilo de Almeida Luz, M.D.,[2] Ugo De Giorgi, M.D., Ph.D.,[3] Martin Gleave, M.D.,[4] Geoffrey T. Gotto, M.D., M.P.H.,[5] Christopher M. Pieczonka, M.D.,[6] Gabriel P. Haas, M.D.,[7] Choung-Soo Kim, M.D.,[8] Miguel Ramirez-Backhaus, M.D.,[9] Antti Rannikko, M.D., Ph.D.,[10,11] Matko Kalac, M.D., Ph.D.,[12] Swetha Sridharan, M.B., B.S.,[13] Matt Rosales, Ph.D.,[3] Yiyun Tang, Ph.D.,[14] Ronald F. Tutrone, Jr., M.D.,[15] Balaji Venugopal, M.B., B.S., M.D.,[16,17] Arnauld 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)

PRESENTED BY: Marc Dall'Era, MD and Yun Rose Li, MD, PhD

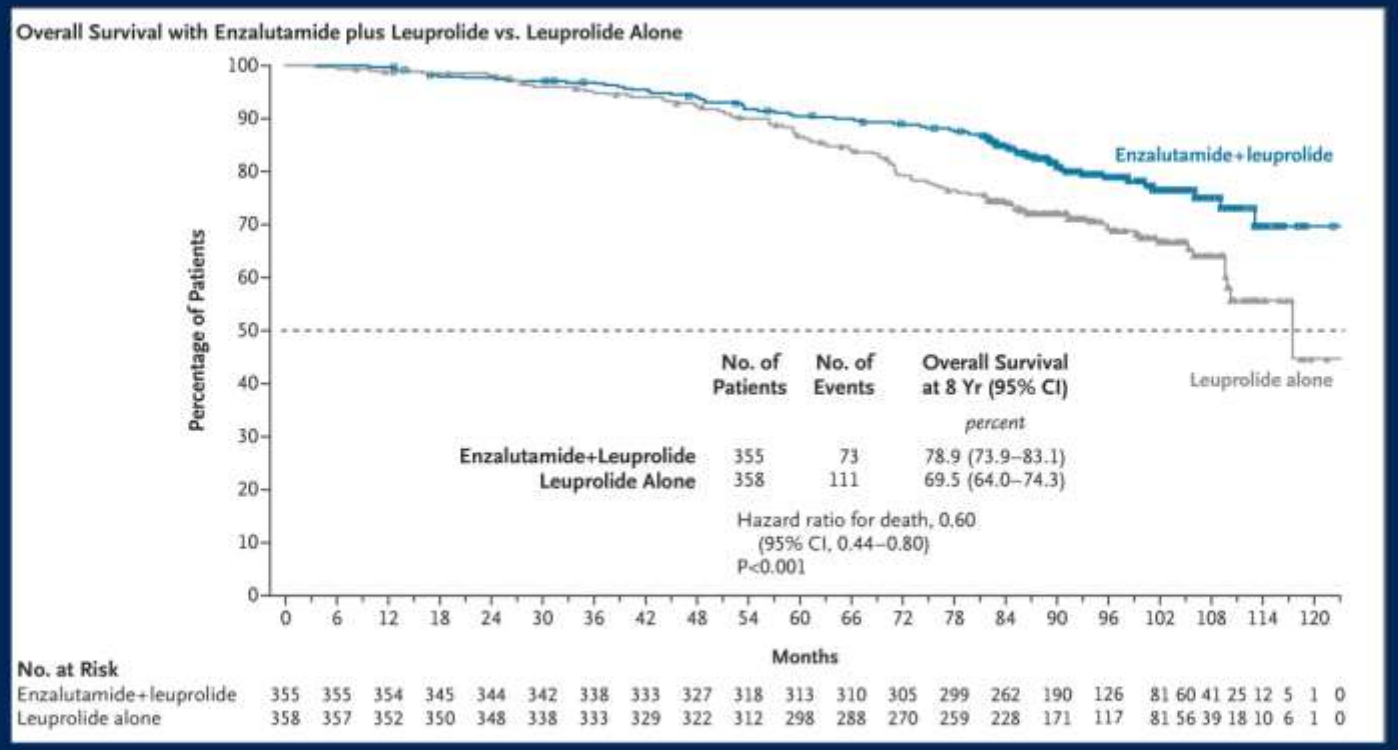
Biyokimyasal Rekürrens ve PSA Persistansı: Doz Yoğun Tedavi Yaklaşımı





S.J. Freedland, N Engl J Med 2023

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
- ❑ Özelikle 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 ≤ olanlarda tedavi düşünülmelidir
- Salvage RT ve ADT (6ay)düşünülmelidir
- Uzun dönem 24 ay adjuvan ADT(pT3≥ ve gleason skoru ≥8) ve pelvik lenf nodu pozitif
- Pelvik RT nüks riski yüksek hastalarda düşünülebilir(Gleason≥8, ≥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