Kastrasyona Duyarlı Metastatik Prostat Kanserinde Yoğun Tedavi

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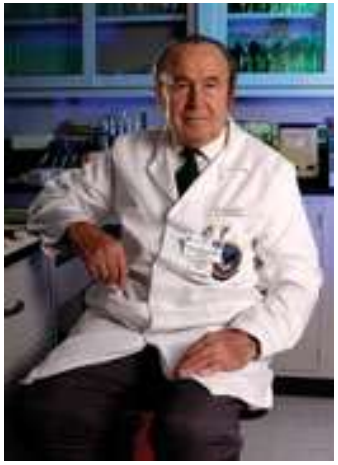
Ders Planı

- ❑ Giriş
- ❑ Tedavi kararında etkili faktörler
- ❑ Dosetaksel hangi hasta grubuna eklenmeli
- ❑ Diğer doz yoğun kombinasyonlar
- ❑ Genomik analize göre tedaviyi yoğunlaştırmak
- ❑ Gelecek perspektif
- ❑ Sonuç

Kastrasyona Duyarlı Metastatik Prostat Kanseri ADT Tedavisi

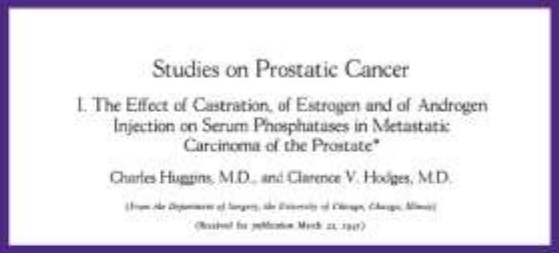


- Charles Brenton Huggins(1901-1997)
- 1927'de Chicago Üniversitesinde Üroloji kliniğinde akademik kadro aldı
- Köpeklerde yaptığı deneylerle, prostat hücrelerinin büyümesinde testosteron hormonuna bağımlı olduğunu tespit etti
- Prostat kanseri olanlarda orişektomi ile tümörün küçüldüğünü belirledi.
- Bu çalışmalarıyla 1966 Nobel ödülü aldı
- Dr. Andrew V. Schally LHRH analoğu keşfi ile 1977 Nobel ödülü alıyor

Kastrasyona Duyarlı Metastatik Prostat Kanseri ADT Tedavisi

Historical Perspective: Androgens & Prostate Cancer

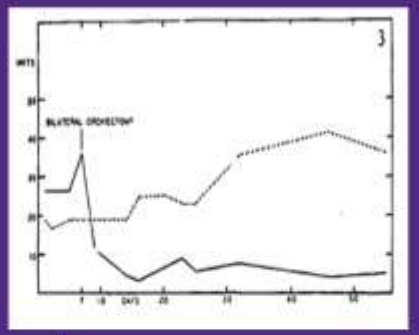
C. Huggins
1966 Nobel Prize



Studies on Prostatic Cancer

I. The Effect of Castration, of Estrogen and of Androgen Injection on Serum Phosphatases in Metastatic Carcinoma of the Prostate*

Charles Huggins, M.D., and Clarence V. Hodges, M.D.



Cancer Res 1941;1:293-297

- **Seminal Observation**: PCa is an androgen driven/dependent disease & surgical or medical castration can induce significant regressions of PC.
  - *Role of acid phosphatase as a biomarker*
- >90% of patients initially respond to androgen deprivation therapy (ADT), however, most will progress to castration resistance with a median survival of about 4 years.

Tedavi Kararında Etkili Faktörler

Hastalıkla İlişkili Faktörler

1- Yüksek volüm/Düşük volüm

2- Denovo/metakron metastaz

3-Metastaz bölgesi

4-Gleason skoru

5-Primer tümörün genetik profil

Klinik Faktörler

1-Semptomatik olması

2-ECOG PS

3-Ek hastalıklar

4-Başka hastalıklar için aldığı tedaviler

5-Hastalık için daha önce aldığı tedaviler

Başlanacak tedavi ile ilgili faktörler

1-Uygulama şekli

2-Etki etme mekanizması

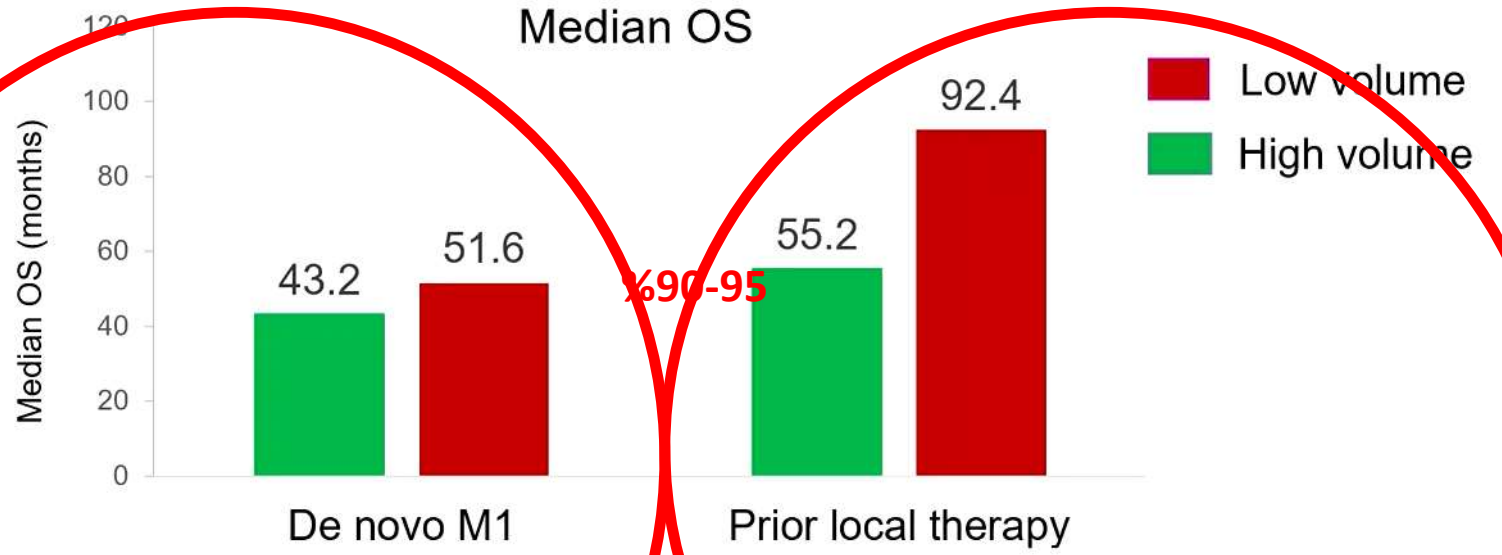
3- Yan etkileri

4-İlaç etkileşimi

5-Tedavi maliyeti

Tanı Anında Metastatik Hastalık Agresif Seyirli

De Novo mHNPC is associated with a worse prognosis



Retrospective analysis of 436 consecutive patients with M1 HSPC treated with ADT between 1990 and 2013 at the Dana-Farber Institute

Francini E, et al. The Prostate 2018;78:889-95.

2021 ESMO congress

OUDARD Stéphane

%90-95

%5-10

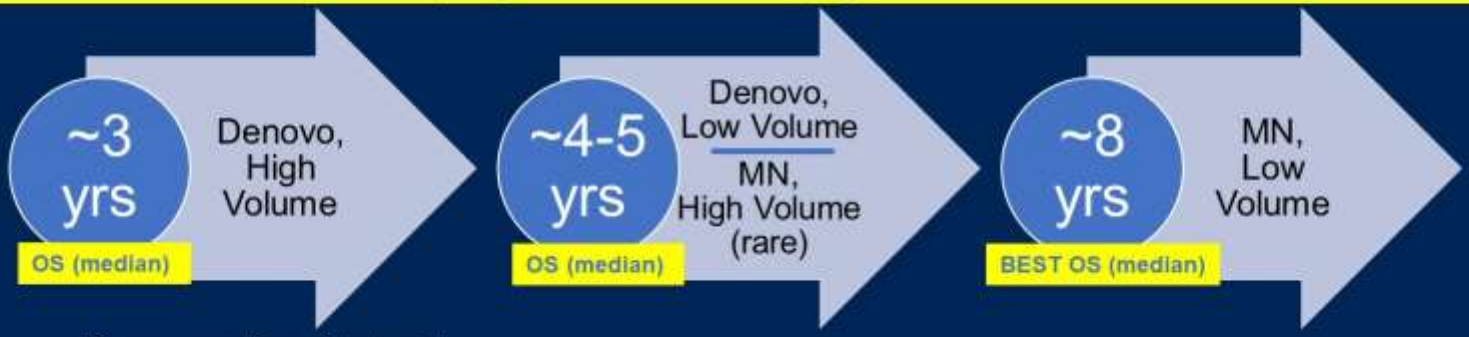
%90-95

TANI ANINDA METASTATİK VE YÜKSEK VOLÜMLÜ HASTALIK AGRESİF SEYİRLİ

Metastatic HSPC Trials – Clinical Risk Groups

	CHAARTED N= 790	STAMPEDE, M1 N= 1086	LATITUDE N=1199	STAMPEDE, M1 N=999	ENZAMET N=1125	TITAN N=1052
ADT + *(NSAA)	DOC	DOC	ABI	ABI	ENZA*	APA
PRIMARY ENDPOINT, OS HR (95%, CI)	0.72 (0.59-0.89)	0.81 (0.69-0.95)	0.66 (0.56-0.78)	0.61 (0.49-0.75)	0.67 (0.52-0.86)	0.65 (0.53-0.79)

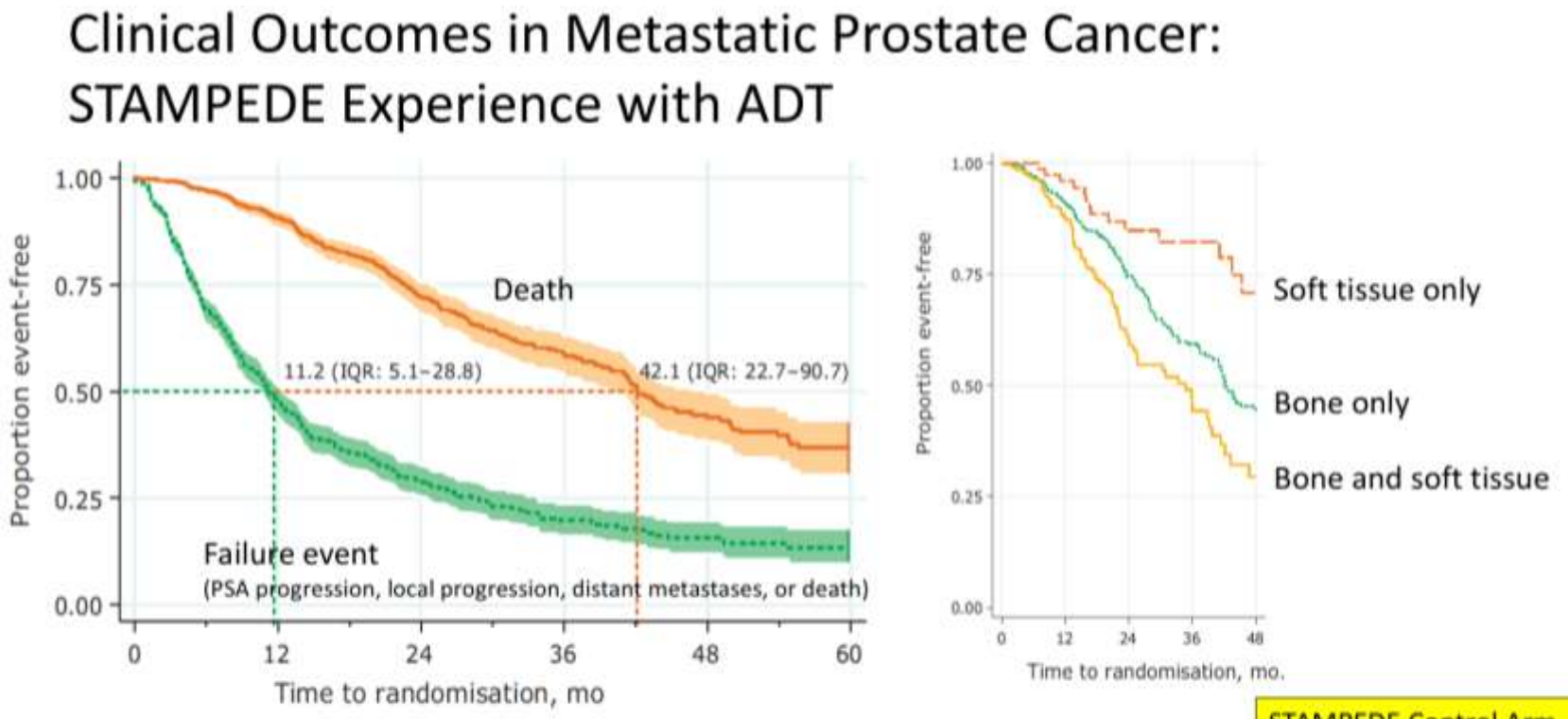
Can clinical prognostic factors help guide treatment selection?



Denovo = new diagnosis/untreated
MN = metachronous diagnosis/previously treated

Modified from :Francini et al, Prostate, 2018; Gravis et al, Eur Urol, 2018

ADT alan hastalarda metastaz bölgesine göre sağkalım



STAMPEDE Control Arm
- Metastatic disease
- Accrued 10/2005-1/2014
- N=917

James ND *et al* (2015) Eur Urol 67: 1028-1038

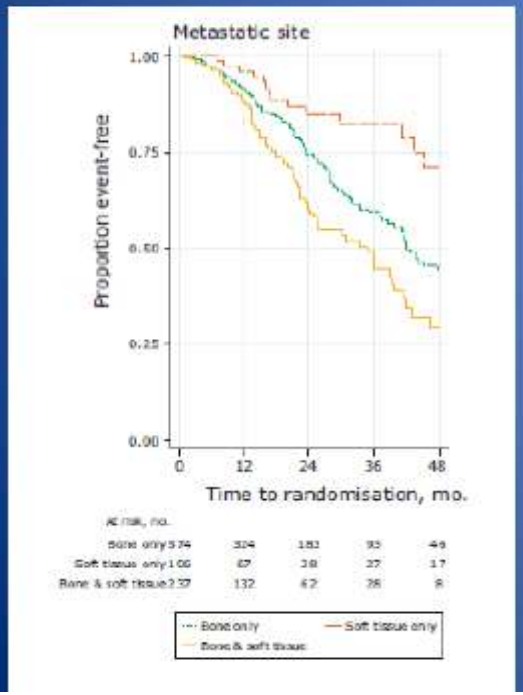
Yalnız ADT alanlarda 5-yıllık sağkalım %30-40. Non-regional lenf nodu iyi prognoz ile ilişkili

Metastaz bölgesine göre hastalık seyri farklı

Survival with Newly Diagnosed Metastatic Prostate Cancer in the "Docetaxel Era": Data from 917 Patients in the Control Arm of the STAMPEDE Trial (MRC PR08, CRUK/06/019)

Nicholas David James [a,], Melissa R. Spears [b], Noel W. Clarke [c], David P. Dearnaley [d,e], Johann S. De Bono [d,e], Joanna Gale [f], John Hetherington [g], Peter J. Hoskin [h], Robert J. Jones [i], Robert Laing [j], Jason F. Lester [k], Duncan McLaren [l], Christopher C. Parker [d,e], Mahesh K.B. Parmar [b], Alastair W.S. Ritchie [b], J. Martin Russell [m], Räto T. Strebel [n], George N. Thalmann [o], Malcolm D. Mason [k], Matthew R. Sydes [b]*

EUROPEAN UROLOGY 67 (2015) 1028–1038



STAMPEDE ÇALIŞMASI; 917 KONTROL KOLUNDE(ADT alan) BULUNAN M1 HASTALARIN SONUÇLARI

Hastaların %62 yalnız kemik ve %26 kemik+yumuşka doku met.(lenf nodu metastazı)

2 Yıllık sağkalım; yumuşak doku met.%85

Kemik met.%75

Yumuşak doku+kemik met.%60

2yılık FFS; yumuşak dokuda %54, kemik met %28 , yumuşak doku+kemik met.%18

Kastrasyona Duyarlı Metastatik Prostat Kanseri Tedavisinin Seyri

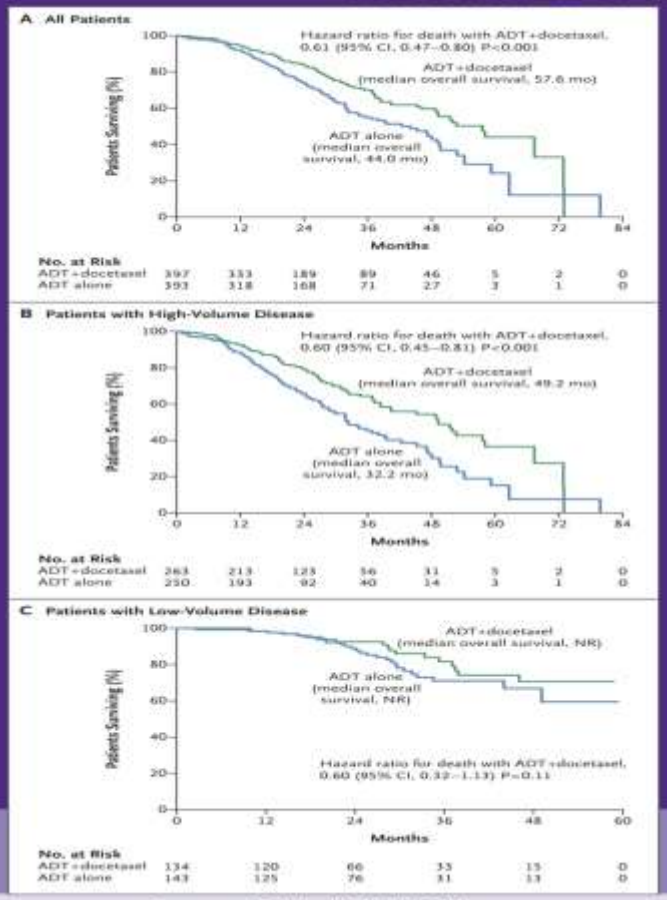
Sağkalımı artıran kanıt düzeyi yüksek çalışmalar

Studies	Intervention	Control	Comments
GETUG-AFU 15 CHAARTED STAMPEDE-C	Docetaxel + ADT	ADT	Benefit in high-volume subgroup
LATITUDE STAMPEDE-G	Abiraterone + ADT	ADT	Similar benefits by risk group
ARCHES ENZAMET	Enzalutamide + ADT	ADT	Similar benefits by risk group
TITAN	Apalutamide + ADT	ADT	Similar benefits by risk group
ARASENS	Darolutamide + ADT + docetaxel	ADT + docetaxel	Similar benefits for recurrent and de novo metastatic disease
PEACE-1	Abiraterone +ADT + docetaxel (+/- prostate radiation)	ADT + docetaxel (+/- prostate radiation)	Subgroup analysis

Gravis et al Lancet Oncol 2013; Sweeney et al NEJM 2015; James N et al Lancet 2015; Attard G et al Lancet Oncol 2023; Fizazi K et al NEJM 2017; James et al NEJM 2017; Armstrong et al JCO 2021; Davis et al NEJM 2019; Chi KN et al NEJM 2019; Smith MR et al NEJM 2022; Fizazi K et al Lancet 2022

Hastalık Volümü Dosetaksel Tedavi Etkinliği için Prediktif

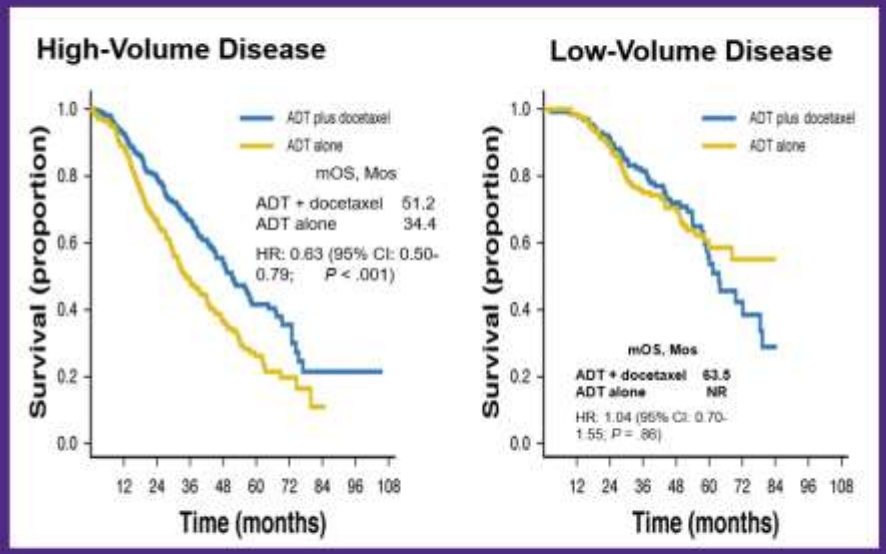
CHAARTED: ADT +/- Docetaxel in mHSPC



Sweeney CJ et al. NEJM 2015

(N = 790, Median follow-up 53.7m)

Long-Term Follow-up: High-Volume vs Low-Volume Disease

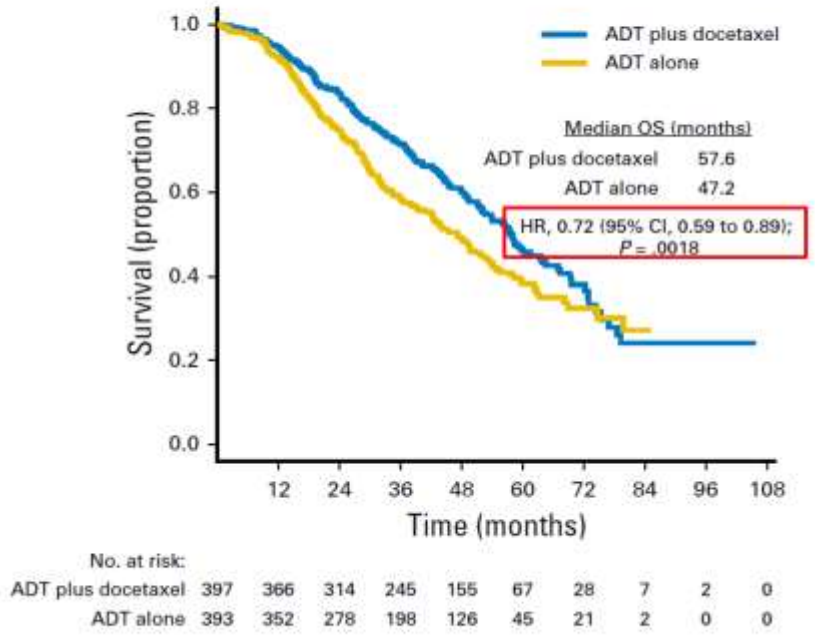


Kyriakopoulos CE, et al. J Clin Oncol. 2018

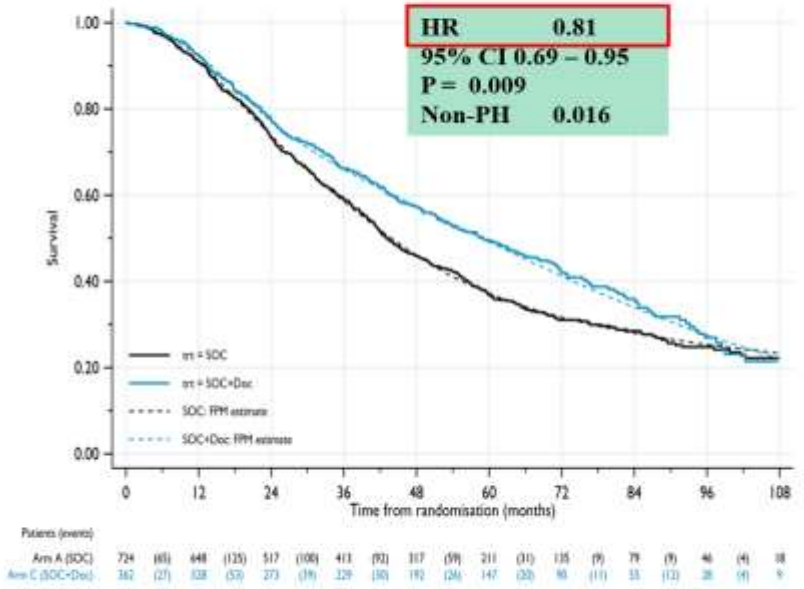
Yüksek volümlü hastalığı olanlar; viseral organ metastazı olan yada ≥4 kemik lezyonu olan ve en az ≥1 vertebra, pelvis dışı kemiklerde metastaz olmalı

Hastalık Volümü Dosetaksel Tedavi Etkinliği için Prediktif

CHAARTED and STAMPEDE: Lower OS benefit of docetaxel in long-term analysis



Kyriakopoulos CE, J Clin Oncol 2018



Clarke N, Ann Oncol. 2019

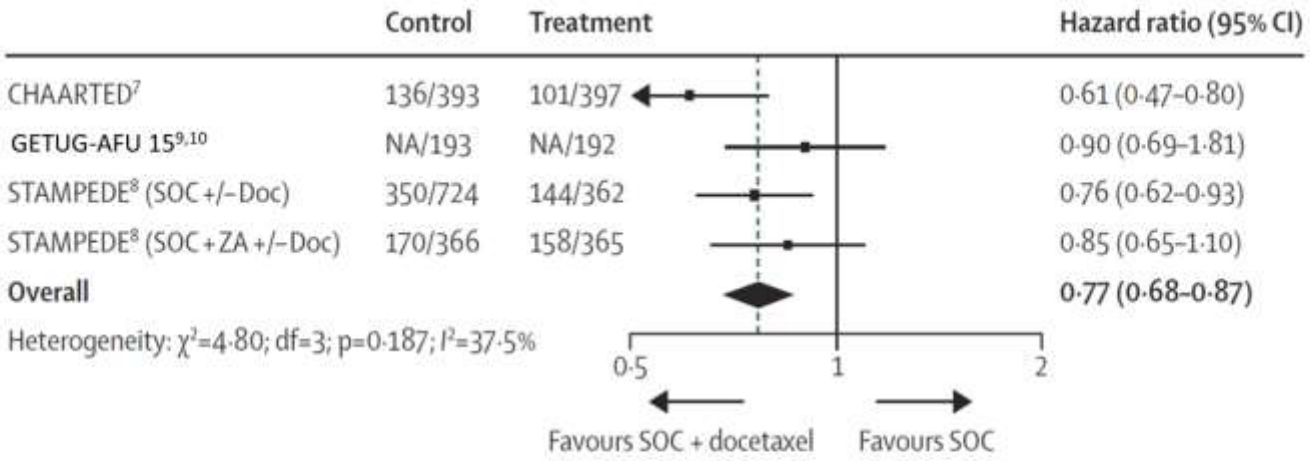
STAMPEDE tüm hastalar de novo metastatik ve %41 high volüm, CHAARTED çalışmasında de novo metastaz oranı %72 ve %66 high volüm

Metastatik Kastrasyona Duyarlı Prostat Kanserinde Dosetaksel Etkinliği

Meta-Analysis of RCTs of Docetaxel in mCSPC

Overall Survival

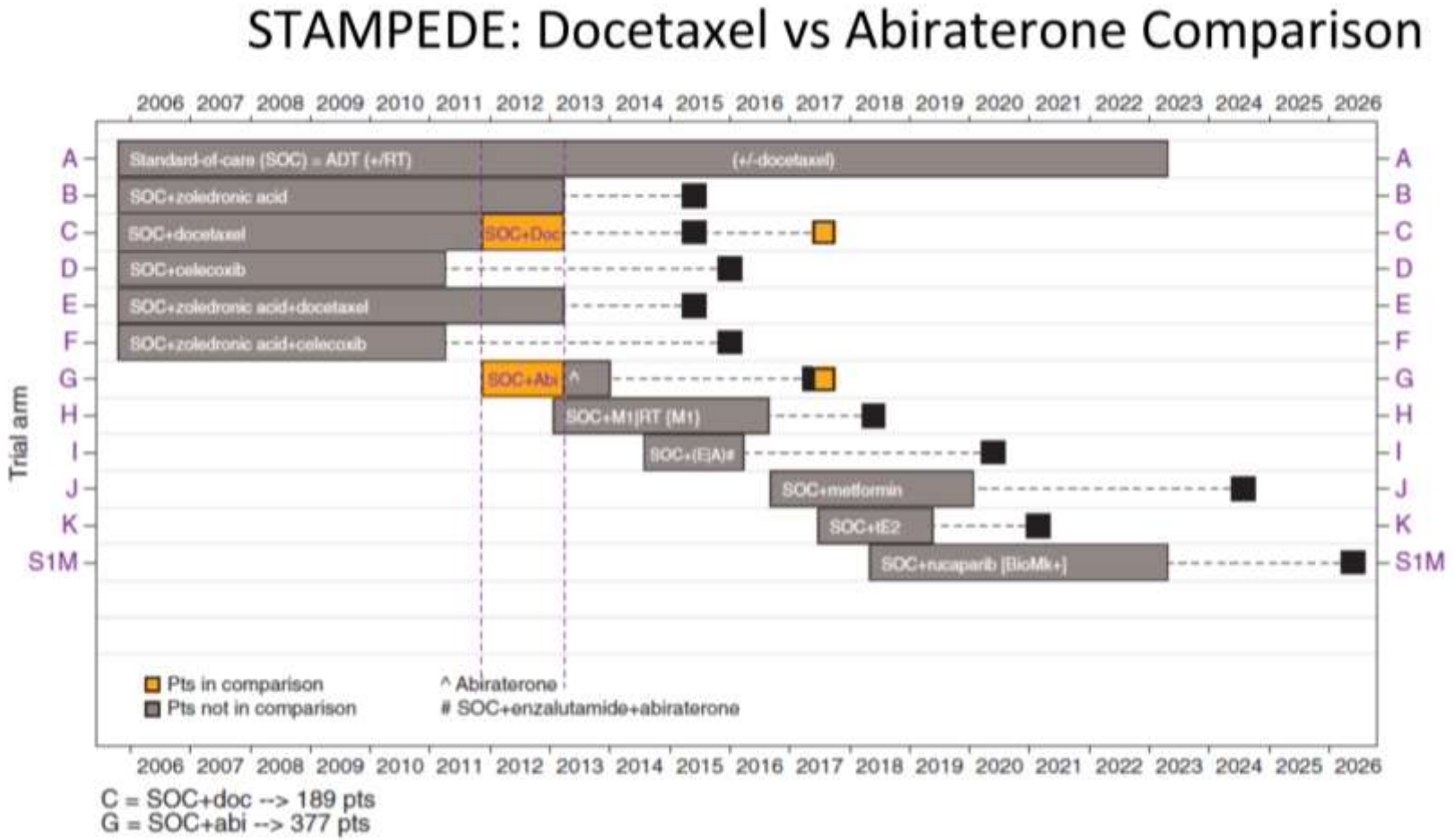
A



- Results based on 2993 men/2198 events
- 9% absolute improvement in survival at 4 years

Vale et al. Lancet Oncol 2016; 17(2):243-56

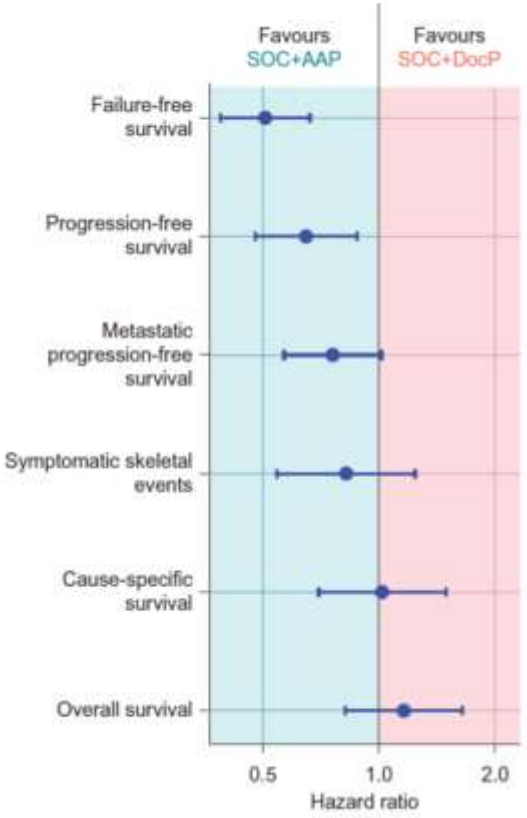
Kastrasyona Duyarlı Prostat Kanserinde Dosetaksel karşı Abiraterone

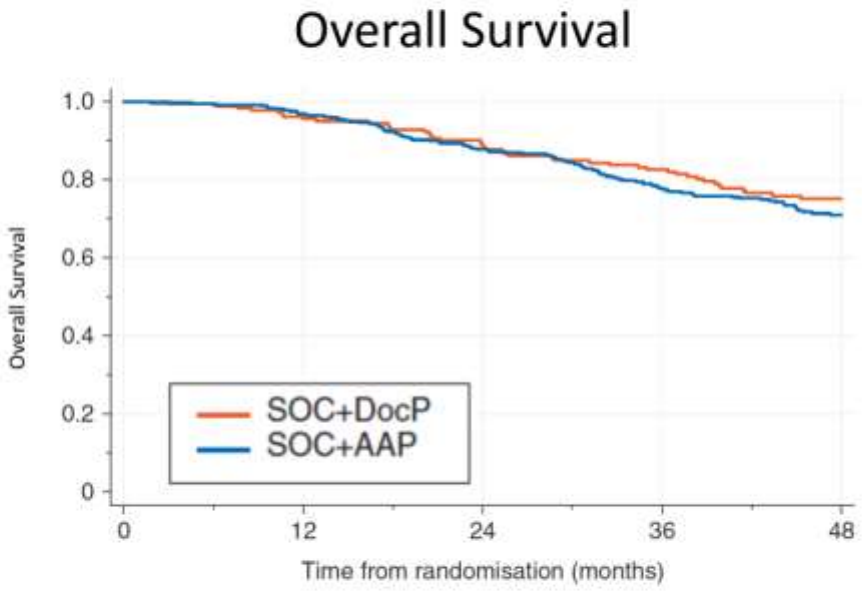


Sydes et al (2018) *Annals of Oncology* 29:1235-1248

Kastrasyona Duyarlı Prostat Kanserinde Dosetaksel karşı Abiraterone

STAMPEDE: Docetaxel vs Abiraterone Comparison

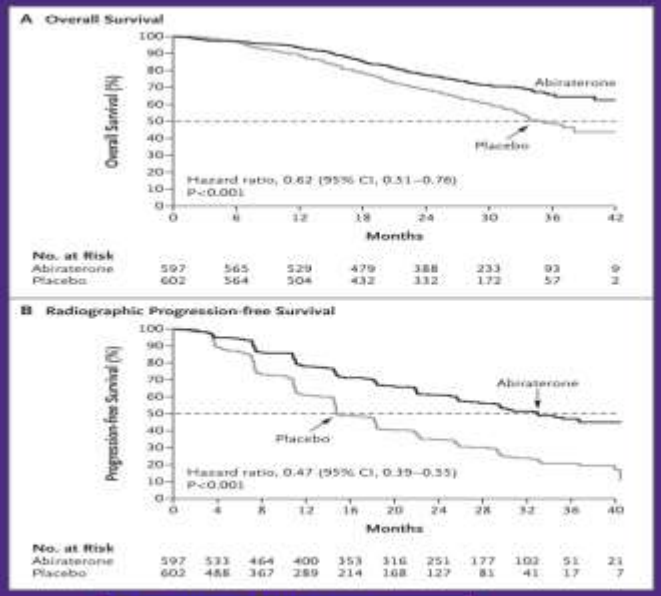




Sydes et al (2018) *Annals of Oncology* 29:1235-1248

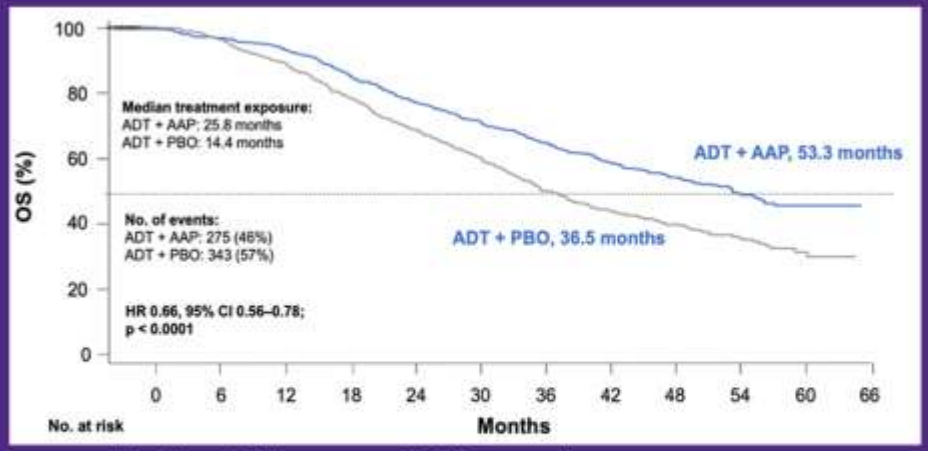
Kastrasyona Duyarlı Metastatik Prostat Kanseri Tedavisi

LATITUDE: ADT + Abiraterone/Prednisone or Placebo in Newly Diagnosed High-Risk mHSPC



OS rate at 3 years:
ADT + AA + P: 66%
ADT + placebos: 49%

Fizazi et al. NEJM 2017



- Median follow-up of 51.8 months
- 34% reduction in risk of death
- Median OS was significantly longer for abiraterone + ADT vs placebo + ADT
  - 53.3 months vs 36.5 months
  - HR = 0.66; $p < 0.0001$

Fizazi K et al. Lancet Oncol 2019;20(5):686-700

En az 2≥ kötü risk grubuna sahip hastalar dahil edilmiş; Gleason skoru≥8, 3≥ fazla kemik metastazı, Viseral metastaz

Dışlama kriterleri; Daha önce cerrahi, Radyoterapi ,Kemoterapi

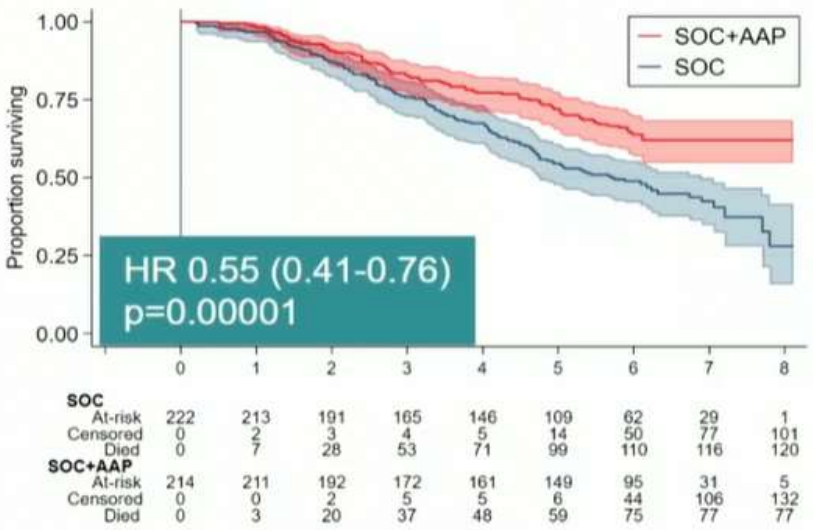
Metastatik hastalığa bağlı semptomu olanlarda RT ve Cerrahiye izin verilmiş

Yeni nesil androjen yolağı inhibitörleri riskten bağımsız etkili

VIRTUAL 2020 ESMO congress

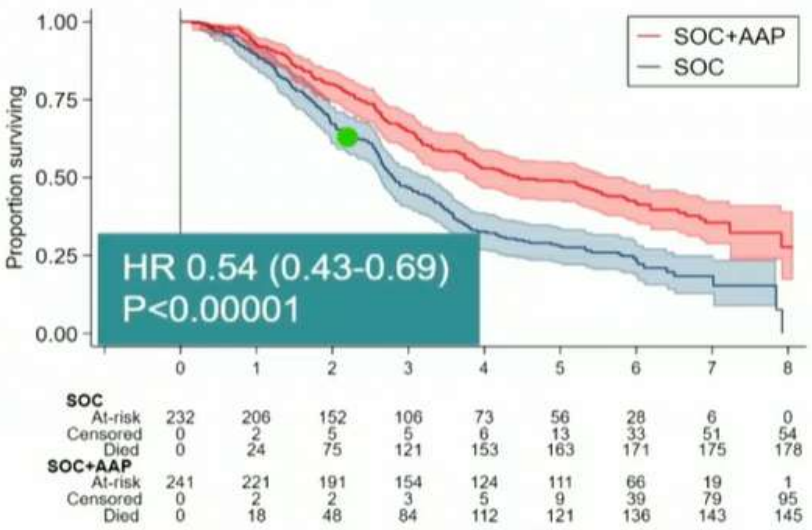
STAMPEDE: OS by risk group (LATITUDE)

Low risk



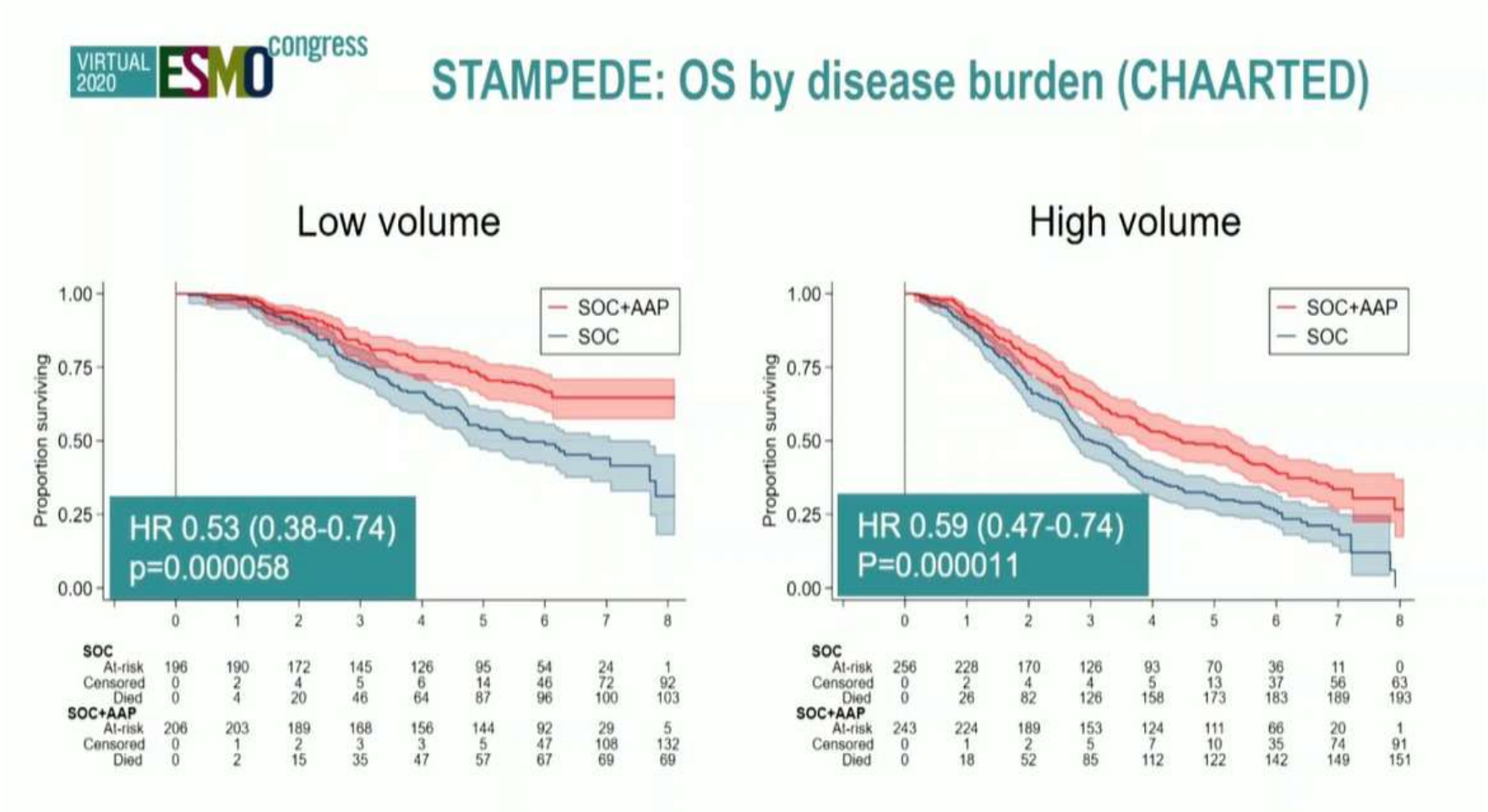
HR 0.66 (0.44-0.98)
p=0.041

High risk



HR 0.54 (0.41-0.70)
P<0.001

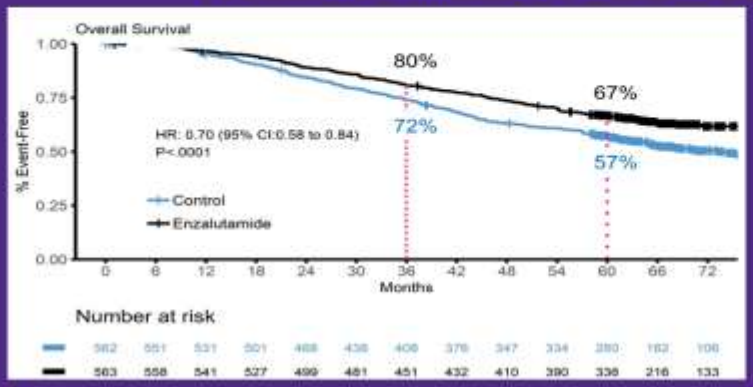
Yeni nesil androjen yolağı inhibitörleri tümör yükünden bağımsız etkili



Kastrasyona Duyarlı Metastatik Prostat Kanseri Tedavisi

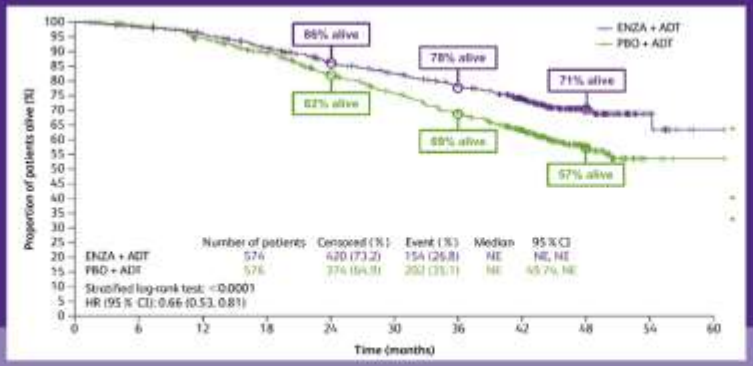
Final Overall Survival (OS) Analyses: Enzalutamide for Metastatic Hormone-Sensitive Prostate Cancer

ENZAMET[1]
Enzalutamide + testosterone suppression (TS)



- Median follow-up of 68.0 months
- 30% reduction in risk of death
- Median OS was significantly longer for enzalutamide + TS versus standard NSAA + TS
  - **Not reached vs 73.2 months**
  - **HR = 0.70; p < 0.0001**

ARCHES[2]
Enzalutamide + ADT

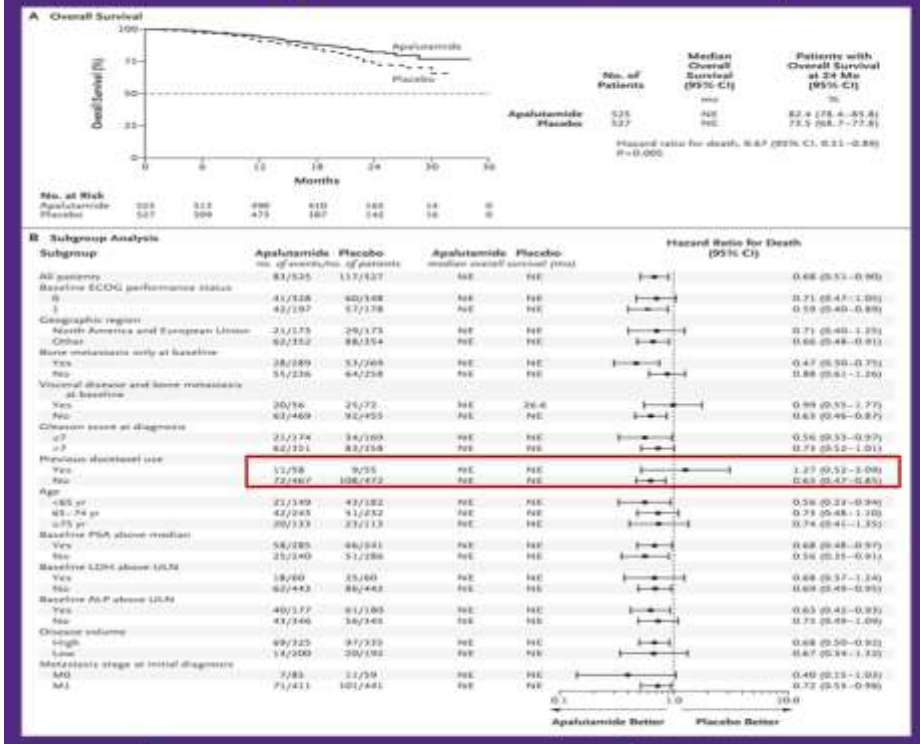


- Median follow-up of 44.6 months
- 34% reduction in risk of death
- Median OS was not reached for enzalutamide plus ADT, but was 47.7 months (95% CI, 43.3 to not evaluable) for placebo plus ADT.
  - **- HR = 0.66; p< 0.001**

1. Davis ID et al. ASCO 2022;Abstract LBA5004; 2. Armstrong AJ et al. J Clin Oncol 2022;40(15):1616-22.

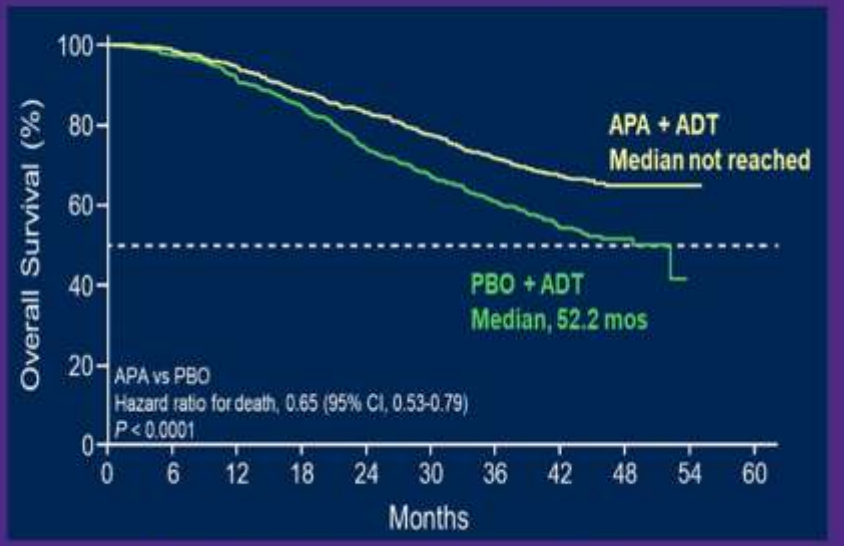
Kastrasyona Duyarlı Metastatik Prostat Kanseri Tedavisi

Apalutamide for Metastatic, Castration-Sensitive Prostate Cancer



- 8% difference in OS at 2 years
- Reduced risk of death by 33%

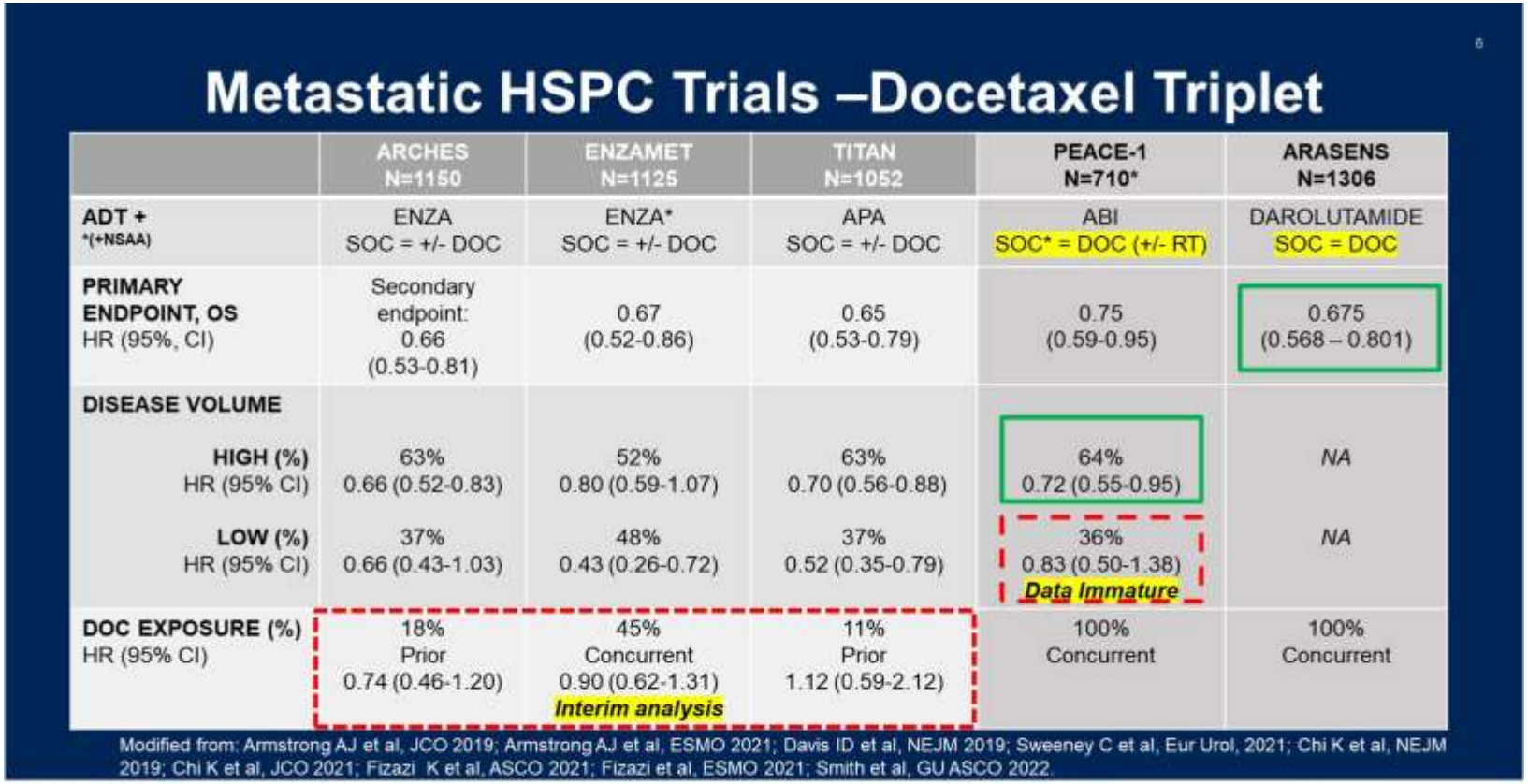
Chi KN et al.NEJM 2019



- Median follow-up of 44.0 months
  - 35% reduction in risk of death
- Median OS was significantly longer for apalutamide + ADT vs placebo + ADT:
  - Not reached vs 52.2 months
  - HR = 0.65; p < 0.0001

Chi KN et al. J Clin Oncol 2021

Kastrasyona Duyarlı Metastatik Prostat Kanseri Tedavisi



Metastatic HSPC Trials –Docetaxel Triplet

	ARCHES N=1150	ENZAMET N=1125	TITAN N=1052	PEACE-1 N=710*	ARASENS N=1306
ADT + *(+NSAA)	ENZA SOC = +/- DOC	ENZA* SOC = +/- DOC	APA SOC = +/- DOC	ABI SOC* = DOC (+/- RT)	DAROLUTAMIDE SOC = DOC
PRIMARY ENDPOINT, OS HR (95%, CI)	Secondary endpoint: 0.66 (0.53-0.81)	0.67 (0.52-0.86)	0.65 (0.53-0.79)	0.75 (0.59-0.95)	0.675 (0.568 – 0.801)
DISEASE VOLUME					
HIGH (%) HR (95% CI)	63% 0.66 (0.52-0.83)	52% 0.80 (0.59-1.07)	63% 0.70 (0.56-0.88)	64% 0.72 (0.55-0.95)	*NA*
LOW (%) HR (95% CI)	37% 0.66 (0.43-1.03)	48% 0.43 (0.26-0.72)	37% 0.52 (0.35-0.79)	36% 0.83 (0.50-1.38) ***Data Immature***	*NA*
DOC EXPOSURE (%) HR (95% CI)	18% Prior 0.74 (0.46-1.20)	45% Concurrent 0.90 (0.62-1.31) ***Interim analysis***	11% Prior 1.12 (0.59-2.12)	100% Concurrent	100% Concurrent

Modified from: Armstrong AJ et al, JCO 2019; Armstrong AJ et al, ESMO 2021; Davis ID et al, NEJM 2019; Sweeney C et al, Eur Urol, 2021; Chi K et al, NEJM 2019; Chi K et al, JCO 2021; Fizazi K et al, ASCO 2021; Fizazi et al, ESMO 2021; Smith et al, GU ASCO 2022.

ASCO Genitourinary Cancers Symposium #GU22 PRESENTED BY: Dana Rathkopf, MD

ASCO AMERICAN SOCIETY OF CLINICAL ONCOLOGY KNOWLEDGE CONQUERS CANCER

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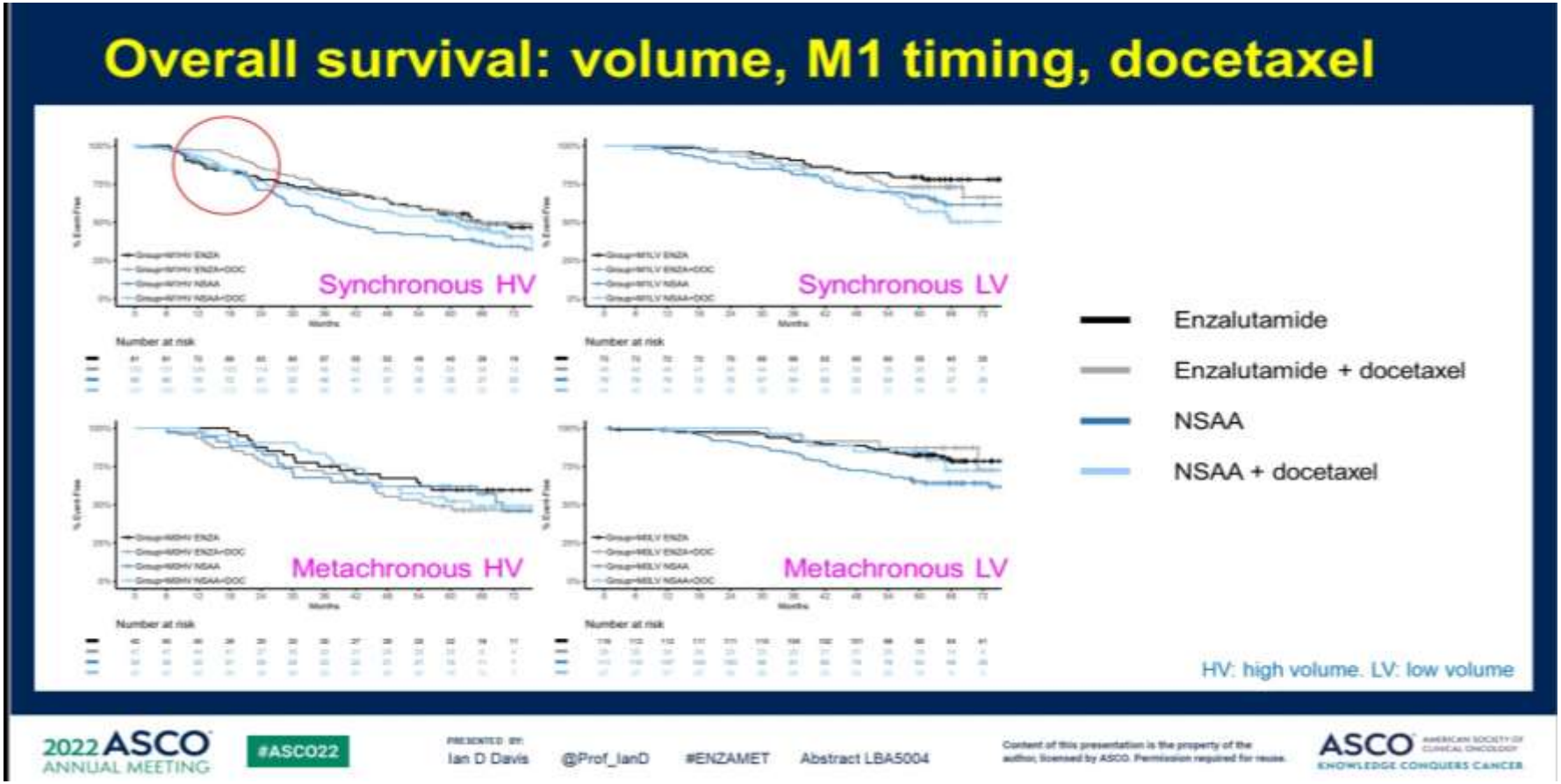
ENZAMET çalışması de novo yüksek volümde üçlü tedavi etkili



Kastrasyona Duyarlı Metastatik Prostat Kanseri Tedavisi

Metastatic HSPC Trials – Disease Volume

	CHAARTED N=790	STAMPEDE, M1 N=1086	LATITUDE N=1199	STAMPEDE, M1 N=1002	ENZAMET N=1125	TITAN N=1052
ADT + *(NSAA)	DOC	DOC	ABI	ABI	ENZA*	APA
Primary Endpoint, OS HR (95%, CI)	0.72 (0.59-0.89)	0.81 (0.69-0.95)	0.66 (0.56-0.78)	0.61 (0.49-0.75)	0.67 (0.52-0.86)	0.65 (0.53-0.79)
De novo, M1 (%) HR (95% CI)	73% 0.68 (0.54-0.85)	95%	100% 0.66 (0.56-0.78)	> 90%	72% 0.69 (0.52-0.91)	81% 0.68 (0.55-0.85)
Metachronous (%) HR (95% CI)	27% 0.97 (0.58-1.62)	NA	-	NA	28% 0.56 (0.29-1.06)	19% 0.39 (0.22-0.69)
Disease Volume						
HIGH (%) HR (95% CI)	65% 0.63 (0.50-0.79)	43% 0.81 (0.64-1.02)	100% 0.66 (0.56-0.78)	52% 0.54 (0.41-0.70)	52% 0.80 (0.59-1.07)	63% 0.70 (0.56-0.88)
LOW (%) HR (95% CI)	35% 1.04 (0.70-1.55)	33% 0.76 (0.54-1.07) CHAARTED criteria; 23% unassessed	-	48% 0.66 (0.44-0.98) LATITUDE criteria, n=901	48% 0.43 (0.26-0.72) CHAARTED criteria	37% 0.52 (0.35-0.79) CHAARTED criteria

HIGH VOLUME: CHAARTED- visceral mets and/or ≥ 4 bone mets at least one outside the vert/pelvis; LATITUDE- 2 of 3: GS ≥8, ≥3 lesions on bone scan, and visceral mets

Modified from: Sweeney C et al, NEJM 2015; Kyriakopoulos C et al, JCO 2018; James ND et al, Lancet 2015; Clarke NW et al, Ann Oncol 2019; Fizazi K et al, NEJM 2017; Fizazi K et al, Lancet Onc 2019; James ND et al, NEJM 2017; Hoyle AP et al, Eur Urol 2019; Davis ID et al, NEJM 2019; Sweeney C et al, Eur Urol, 2021; Chi K et al, NEJM 2019; Chi K et al, JCO 2021.

ENZAMET yüksek volüm hasta grubu uzun dönem alt grup analizi

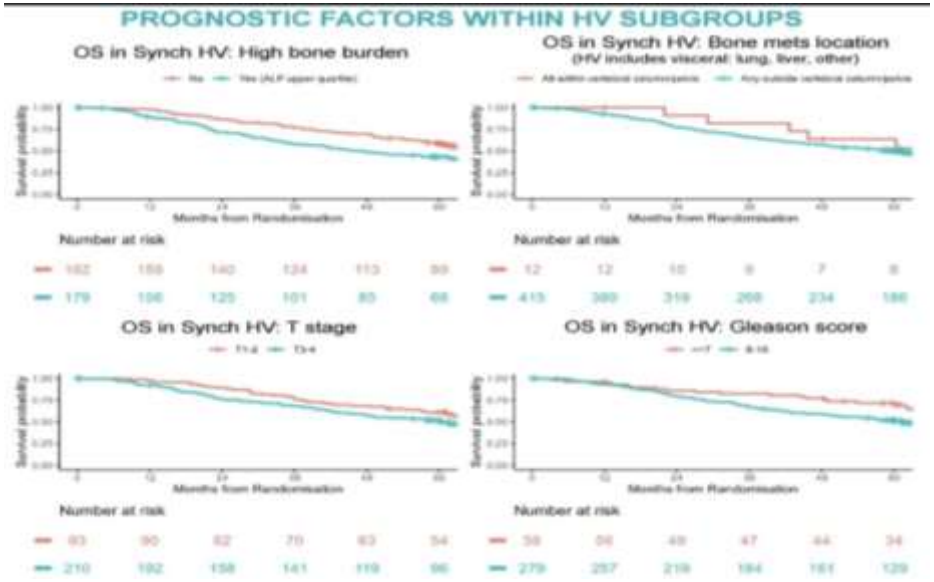


Fig 3. OS in Synch HV (TS+ENZA arm) by docetaxel x bone burden (docetaxel not randomised)

OUTCOMES OF LV SUBGROUP WITH ≥4 BONE METASTASES WITHIN VERTEBRAL BODIES AND PELVIS

Subgroup (treatments arms combined)	5-year OS (95% CI), %
HV (≥4 bone mets with ≥1 beyond vertebrae/pelvis + no visceral + BB high)	42 (34-49)
HV (≥4 bone mets with ≥1 beyond vertebrae/pelvis + no visceral + BB low)	58 (52-65)
LV (≥4 bone mets within vertebrae/pelvis)^	69 (57-84)

^within this group: 62% Synch, 38% Metach

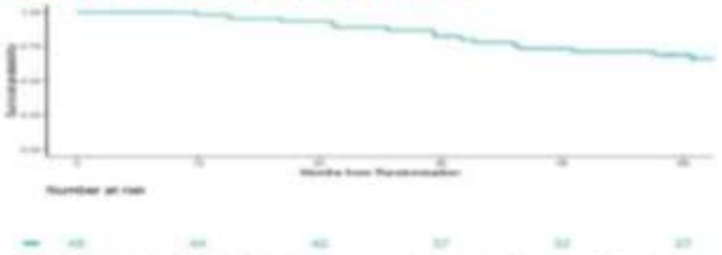


Fig 4. OS in LV with ≥4 bone mets (vertebrae/pelvis)

ESMO 2024: Clinical Prognostic Factors Within the High-Volume Subgroup of Metastatic Hormone Sensitive Prostate Cancer in ENZAMET (ANZUP 1304)

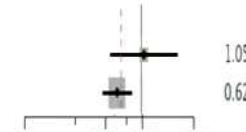
Yeni nesil androjen yolağı inhibitörleri viseral metastazda etkinliği düşük

Does type of metastasis matter in mHNPC?

Results from new hormonal treatments in mHNPC according visceral mets

ENZAMET

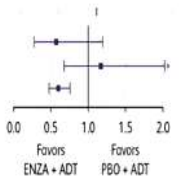
Subgroup	Enzalutamide (no. of events/total no.)	Standard Care (no. of events/total no.)	Hazard Ratio (95% CI)
Visceral metastases			
Yes	18/62	18/67	1.05 (0.54–2.02)
No	84/501	125/495	0.62 (0.47–0.82)



Enzalutamide Better Standard Care Better

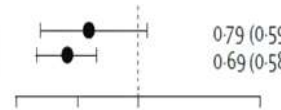
ARCHES

Subgroup	ENZA + ADT/PBO + ADT N (E)	Median (months)	HR (95% CI)
No previous use of ADT or orchiectomy	39 (10)/61 (23)	NR/NR	0.57 (0.27, 1.20)
Visceral metastases – yes	64 (28)/64 (24)	48.5/50.3	1.16 (0.67, 2.00)
Visceral metastases – no	510 (126)/512 (178)	NR/NR	0.60 (0.48, 0.76)



LATITUDE

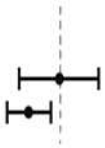
	Median (months) AA+P	Placebo+P	HR (95% CI)
Visceral disease at entry			
Yes	12·9	8·3	0·79 (0·59–1·05)
No	17·1	12·3	0·69 (0·58–0·82)



Favours AA+P Favours placebo+P

TITAN

Subgroup	Apalutamide Placebo (no. of events/no. of patients)		Apalutamide Placebo (median overall survival (mo))		
Visceral disease and bone metastasis at baseline					
Yes	20/56	25/72	NE	26.6	0.99 (0.55–1.77)
No	63/469	92/455	NE	NE	0.63 (0.46–0.87)
Gleason score at diagnosis					



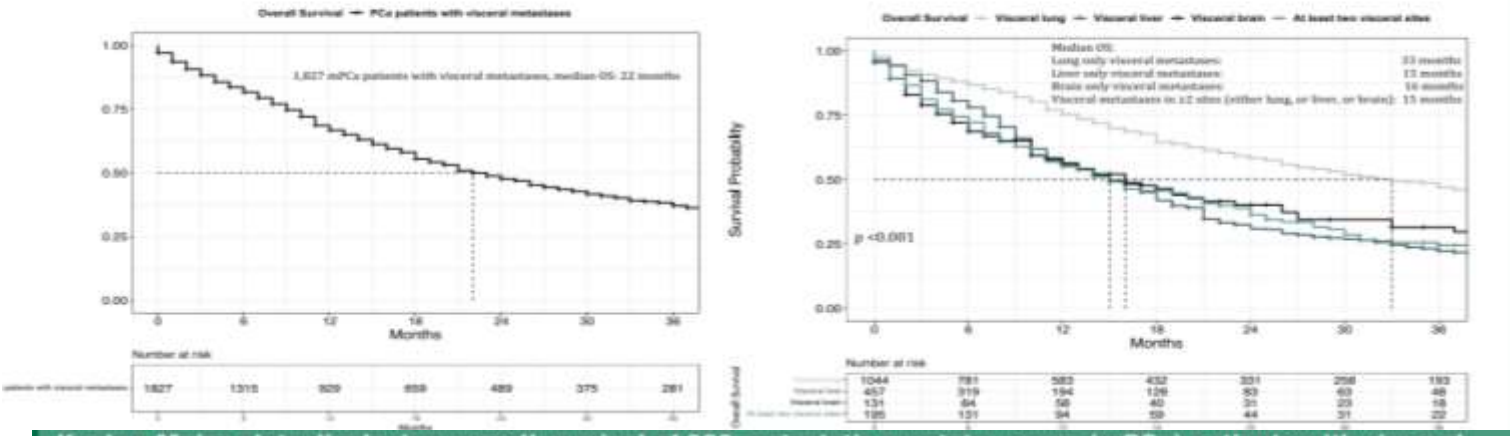
2021 ESMO congress

OUDARD Stéphane

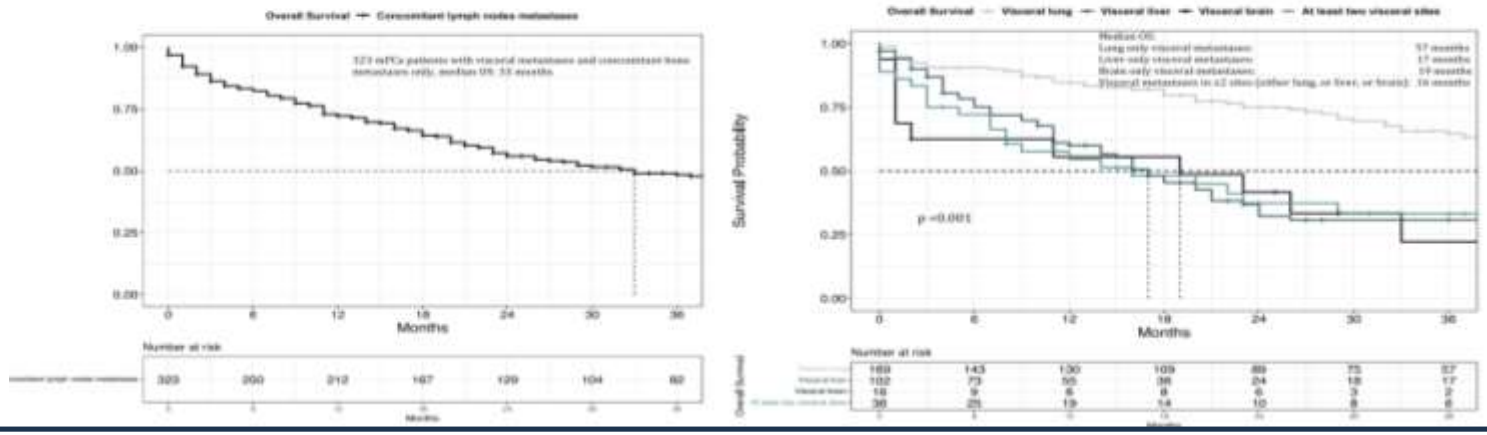
1. Davis I, et al. NEJM 2019;381:121-131 2. Armstrong A, et al. ESMO 2021 oral comm. abstract LBA25 3. Chi K, et al. NEJM 2019;381:13-24 4. Fizazi K, et al. Lancet Oncol. 2019 May;20(5):686-700.

Viseral metastaz tanımı

Kaplan-Meier plots displaying overall survival in 1827 metastatic prostate cancer (mPCa) patients with visceral metastases, regardless of presence of lymph node and/or bone metastases: (A) in the overall population; (B) according to location of visceral metastatic sites.



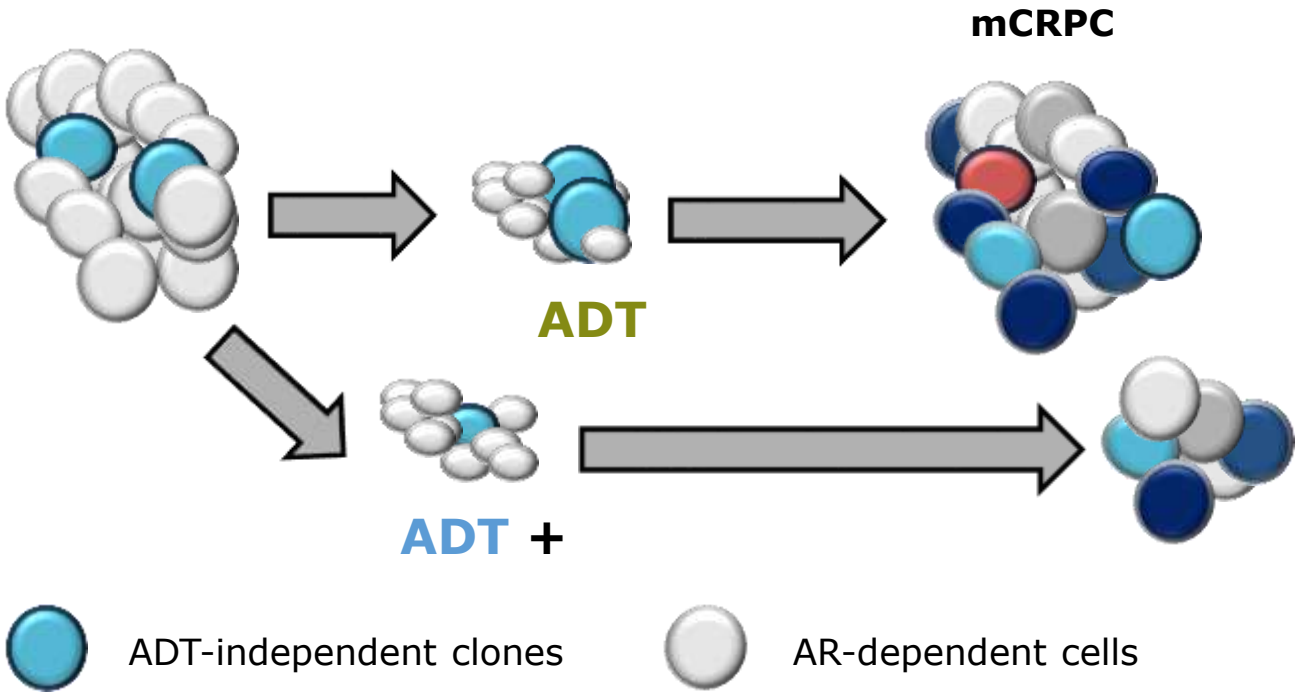
Kaplan-Meier plots displaying overall survival of 323 metastatic prostate cancer (mPCa) patients with visceral metastases with concomitant lymph node metastases only: (A) in the overall population; (B) according to location of visceral metastatic sites.



Akciğer+/-lenf met(kemik met olmadan) mOS; 57 ay, Karaciğer ve beyin met; 15 ve 19 ay

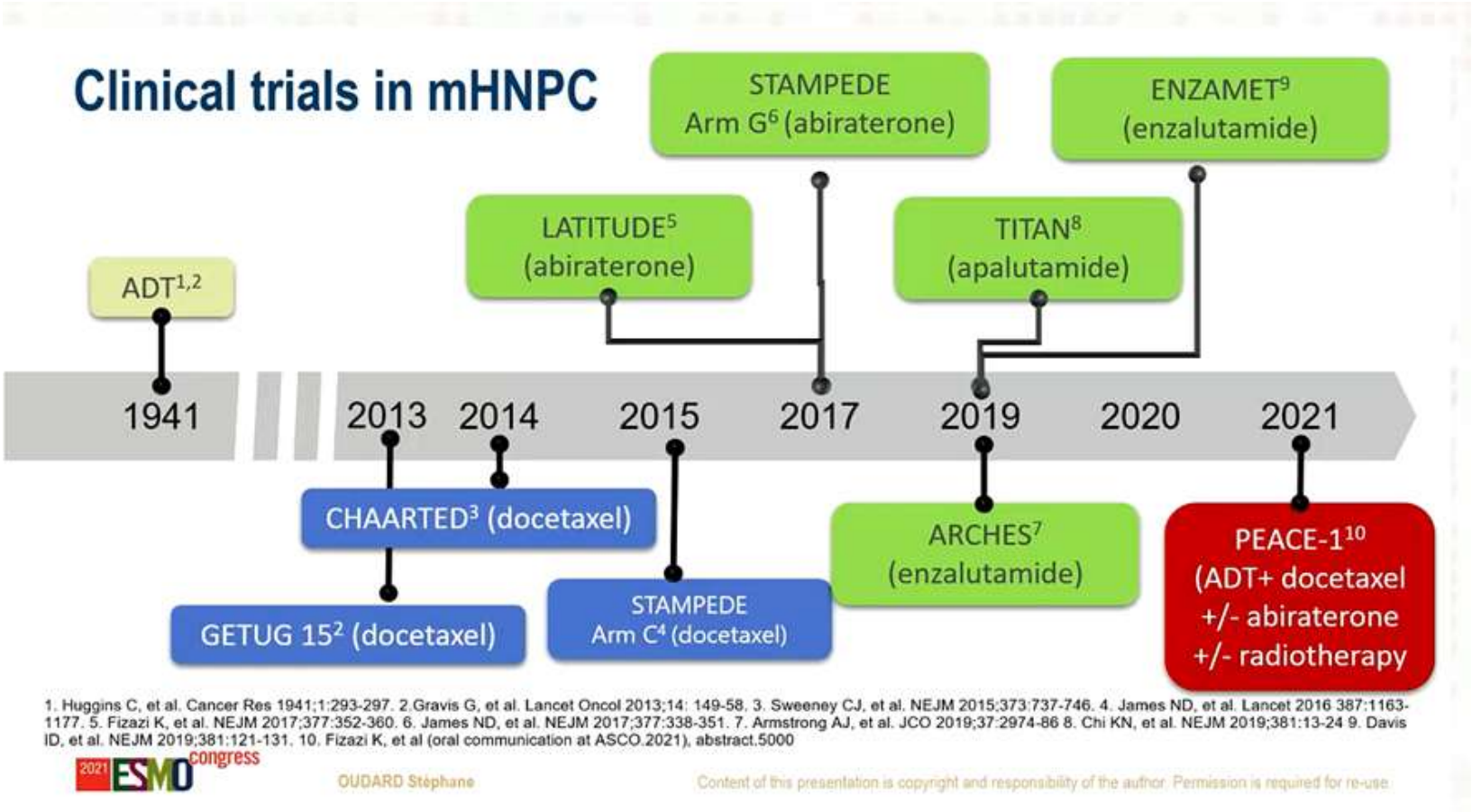
Tappero S, at al. Clinical Genitourinary Cancer 2023

Kastrasyona Duyarlı Metastatik Prostat Kanseri Daha Yoğun Tedavisi



Role of Effective Systemic Therapy

Kastrasyona Duyarlı Metastatik Prostat Kanseri Tedavisi

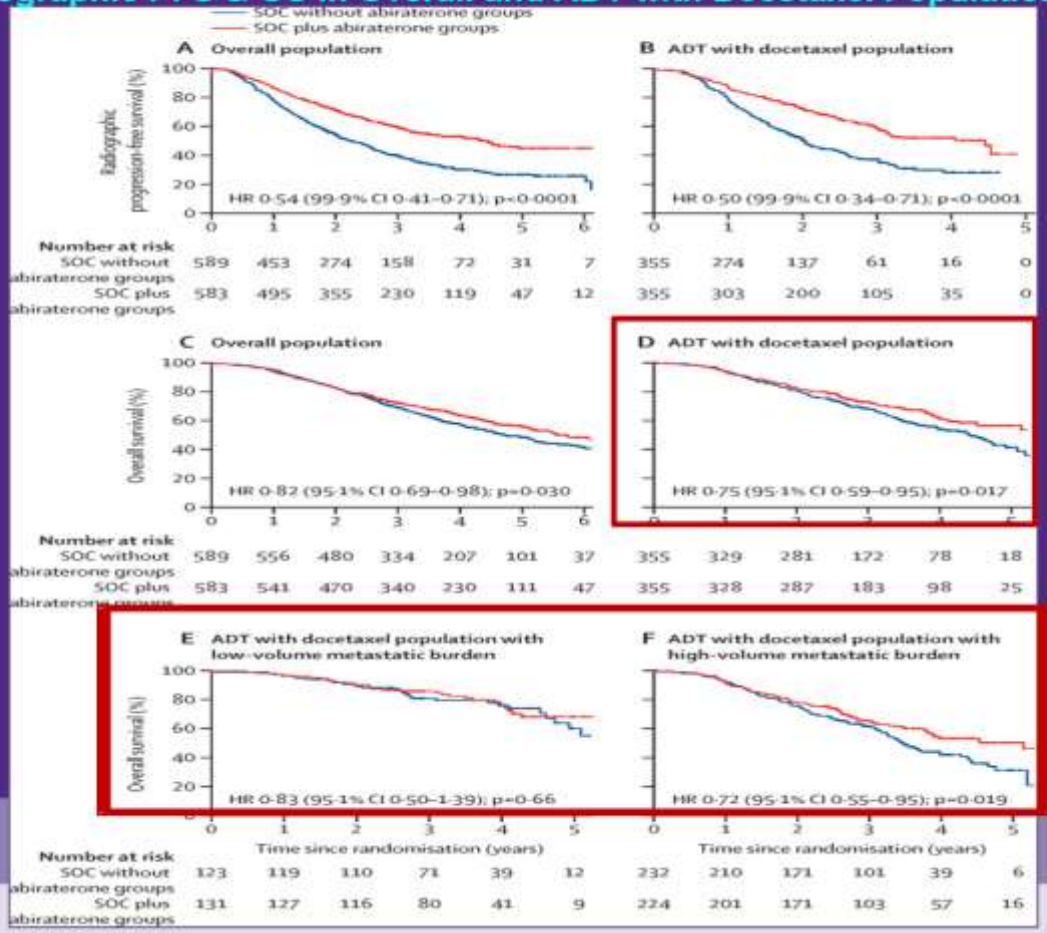


1. Huggins C, et al. Cancer Res 1941;1:293-297. 2.Gravis G, et al. Lancet Oncol 2013;14: 149-58. 3. Sweeney CJ, et al. NEJM 2015;373:737-746. 4. James ND, et al. Lancet 2016 387:1163-1177. 5. Fizazi K, et al. NEJM 2017;377:352-360. 6. James ND, et al. NEJM 2017;377:338-351. 7. Armstrong AJ, et al. JCO 2019;37:2974-86 8. Chi KN, et al. NEJM 2019;381:13-24 9. Davis ID, et al. NEJM 2019;381:121-131. 10. Fizazi K, et al (oral communication at ASCO.2021), abstract.5000

Kastrasyona Duyarlı Metastatik Prostat Kanseri Üçlü Kombinasyon

Triplet #1: PEACE-1: ADT + Abiraterone/Prednisone in De Novo mHSPC

Radiographic PFS & OS in Overall and ADT with Docetaxel Population



Fizazi et al:
Lancet 2022

Kastrasyona Duyarlı Metastatik Prostat Kanseri Tedavisi

PEACE-1: Adverse Events

	ADT with Docetaxel		ADT without Docetaxel	
	SOC + Abi (+/- RT)	SOC (+/- RT)	SOC + Abi (+/- RT)	SOC (+/- RT)
Any AE	346 (100%)	349 (100%)	226 (100%)	233 (99%)
Severe (grade >3)	217 (63%)	181 (52%)	149 (66%)	97 (41%)
Fatal (grade 5)	7 (2%)	3 (1%)	8 (4%)	5 (2%)
Frequent severe AEs				
Hypertension	76 (22%)	45 (13%)	66 (29%)	38 (16%)
Neutropenia	34 (10%)	32 (9%)	0	0
Hepatotoxicity	20 (6%)	2 (1%)	14 (6%)	3 (1%)
Febrile Neutropenia	18 (5%)	19 (5%)	2 (1%)	1 (<1%)
Fatigue	10 (3%)	15 (4%)	3 (1%)	0
Peripheral neuropathy	4 (1%)	6 (2%)	1 (<1%)	0

Fizazi et al, Lancet, 2022

Kastrasyona Duyarlı Metastatik Prostat Kanseri Tedavisi

ASCO Genitourinary Cancers Symposium

Efficacy and safety of abiraterone acetate plus prednisone and androgen deprivation therapy +/- docetaxel in older patients (≥ 70 years), with *de novo* metastatic castration sensitive prostate cancer, compared to younger patients (< 70 years), in the PEACE-1 trial Abst#20

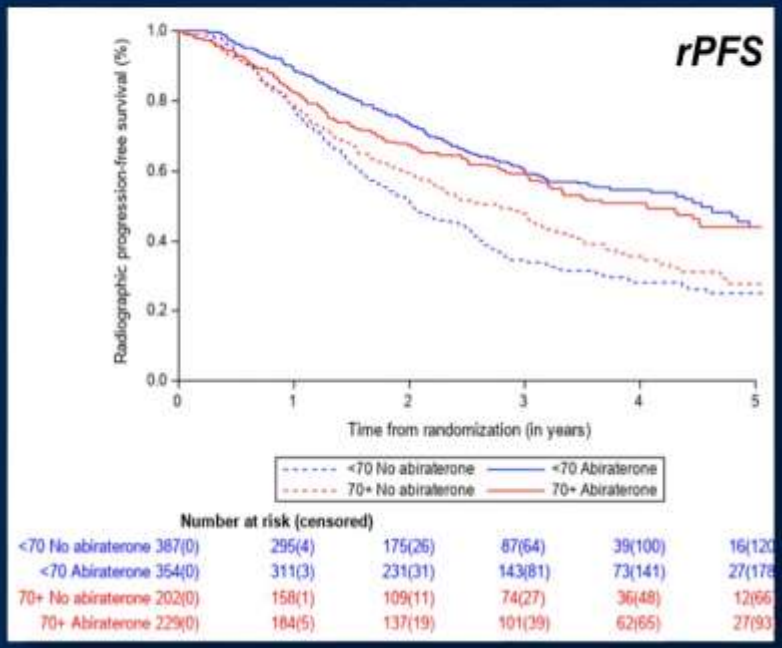
Mourey L[1], Boyle H[2], Roubaud G[3], McDermott R[5], Supiot S[6], Tombal B[7], Flechon A[2], Berthold D[8], Ronchin P[9], Kacso G[10], Berdah J-F[11], Calabro F[12], Gravis G[13], Palumbo S[14], Gil T[15], Vie B[16], Ribault H[17], Fizazi K[18], Foulon S[18], Carles J[19].

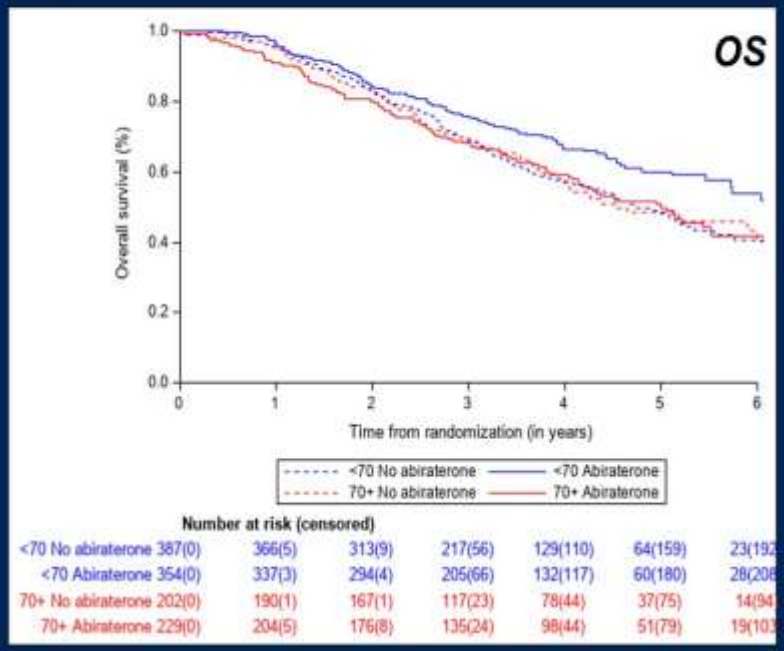
[1]Institut Universitaire du Cancer-Oncopole, Toulouse, France; [2]Centre Leon Bérard, Lyon, France; [3]Institut Bergonié, Bordeaux, France; [5]St. Vincent's University Hospital, Dublin, Ireland; [6]Institut de Cancerologie de l'Ouest-Rene Gauducheau, Nantes, France; [7]Cliniques Universitaires Saint-Luc, Brussels, Belgium; [8]Centre Hospitalier Universitaire Vaudois, Lausanne, Switzerland; [9]Centre Azuréen d'Oncologie, Mougins, France; [10]Iuliu Hatieganu University Cluj Napoca, Romania; [11]Clinique Sainte Marguerite, Toulon, France; [12]San Camillo and Forlanini Hospitals, Rome, Italy; [13]Institut Paoli-Calmettes, Marseille, France; [14]Pôle Hospitalier Jolimont, La Louvière, Belgium; [15]Institut Jules Bordet, Brussels, Belgium;[16] Centre Armoricain Radiothérapie Imagerie Oncologie, Plerin, France; [17]Unicancer, [18]Institut Gustave Roussy, Villejuif, France; [19]Vall d'Hebron University Hospital, Barcelona, Spain

Üçlü Kombinasyonda Yaş Sınırlaması

Results (1)

Overall population





Age ≥ 70: HR 0.65, 95%CI (0.42-1.01)
Age <70: HR 0.49, 95%CI (0.35-0.69)
p-value of the interaction test 0.08

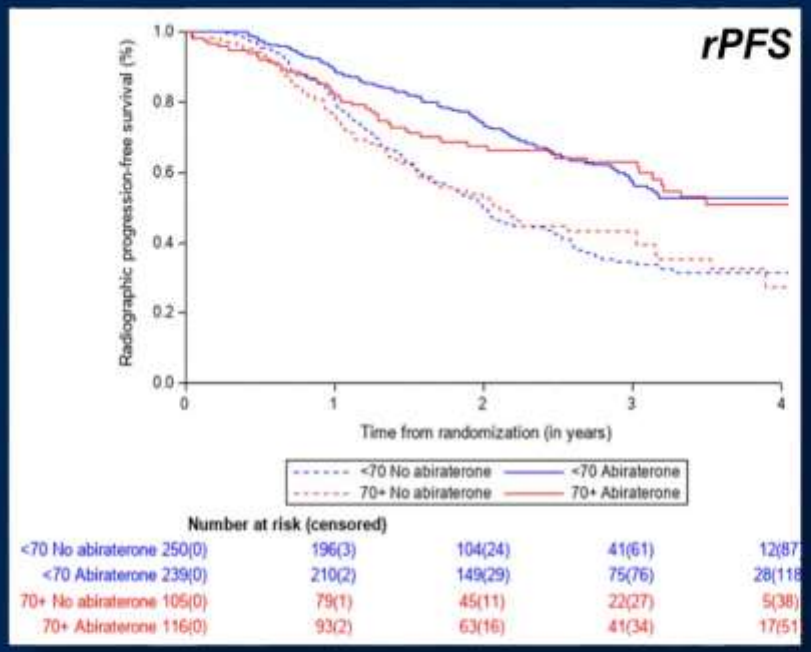
Age ≥ 70: HR 0.95, 95%CI (0.72-1.25)
Age <70: HR 0.73, 95%CI (0.58-0.92)
p-value of the interaction test 0.15

Benefit of AA+P on rPFS and OS may decrease with age

Üçlü Kombinasyonda Yaş Sınırlaması

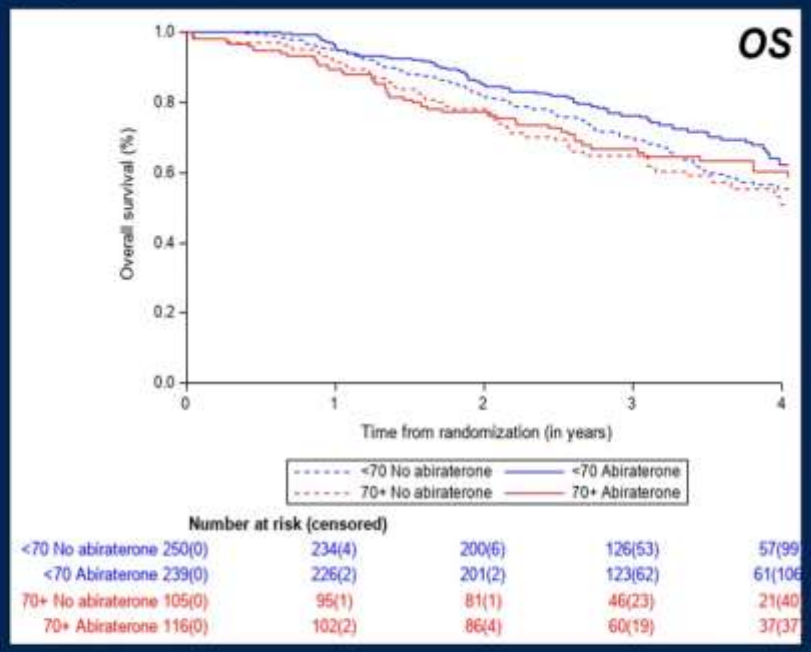
Results (2)

Docetaxel population



Number at risk (censored)

<70 No abiraterone 250(0)	196(3)	104(24)	41(61)	12(87)
<70 Abiraterone 239(0)	210(2)	149(29)	75(76)	28(118)
70+ No abiraterone 105(0)	79(1)	45(11)	22(27)	5(38)
70+ Abiraterone 116(0)	93(2)	63(16)	41(34)	17(51)



Number at risk (censored)

<70 No abiraterone 250(0)	234(4)	200(6)	126(53)	57(99)
<70 Abiraterone 239(0)	226(2)	201(2)	123(62)	61(106)
70+ No abiraterone 105(0)	95(1)	81(1)	46(23)	21(40)
70+ Abiraterone 116(0)	102(2)	86(4)	60(19)	37(37)

Age ≥ 70: HR 0.55, 95%CI (0.29-1.04)
Age < 70: HR 0.50, 95%CI (0.33-0.78)
p-value of the interaction test 0.67

Age ≥ 70: HR 0.80, 95%CI (0.53-1.2)
Age < 70: HR 0.71, 95%CI (0.52-0.95)
p-value of the interaction test 0.63

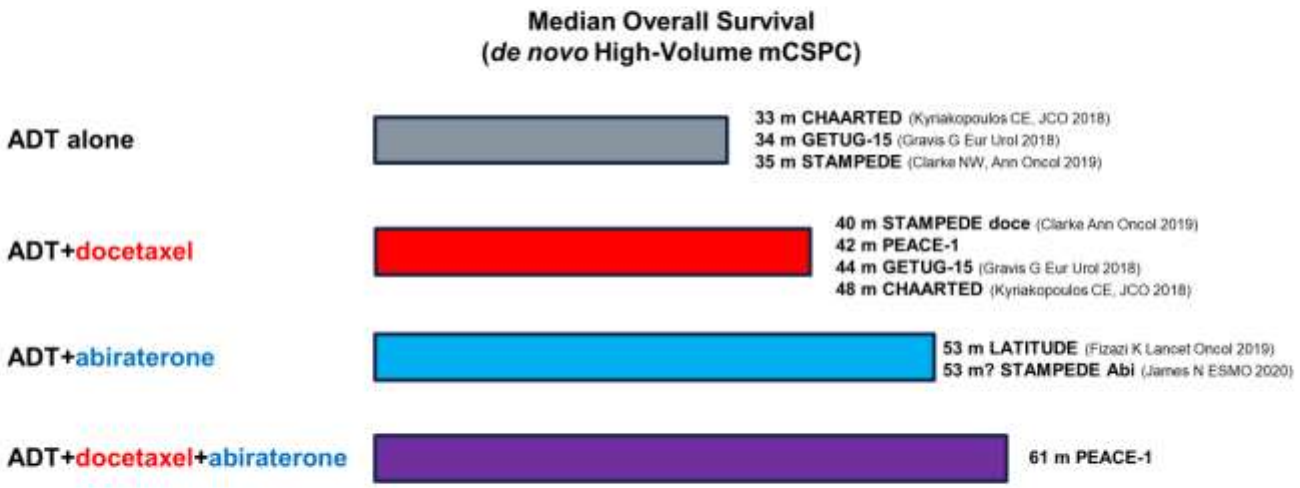
- rPFS benefit of AA+P was comparable in older and younger patients
- OS benefit difficult to assess (insufficient number of older patients/events)

Kastrasyona Duyarlı Metastatik Prostat Kanseri Üçlü Kombinasyon

GUSTAVE ROUSSY

Triplet PEACE-1 OS results in the context of recent data

unicancer

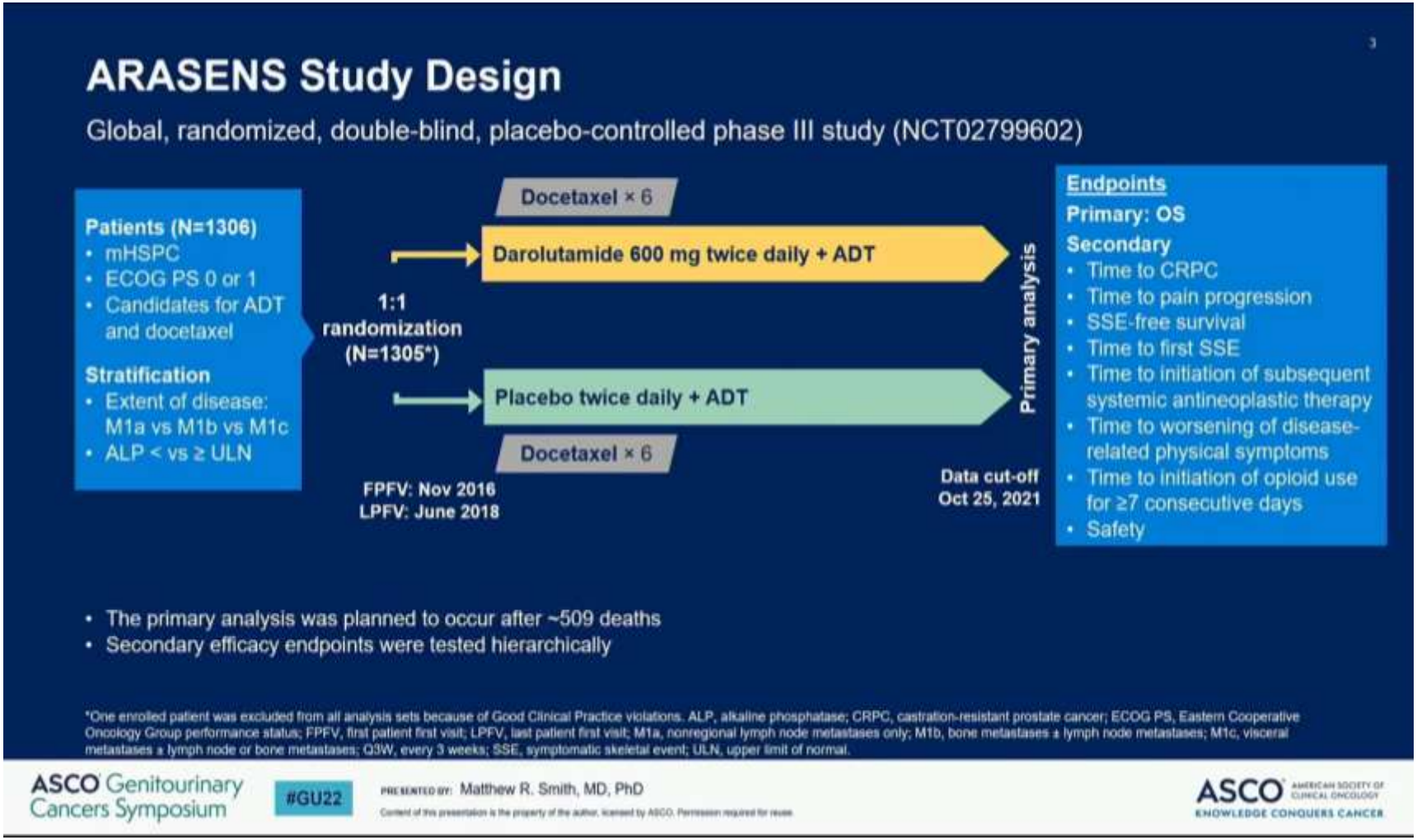


2021 ESMO congress

Karim Fizazi

Con

Kastrasyona Duyarlı Metastatik Prostat Kanseri Üçlü Kombinasyon



Kastrasyona Duyarlı Metastatik Prostat Kanseri Üçlü Kombinasyon

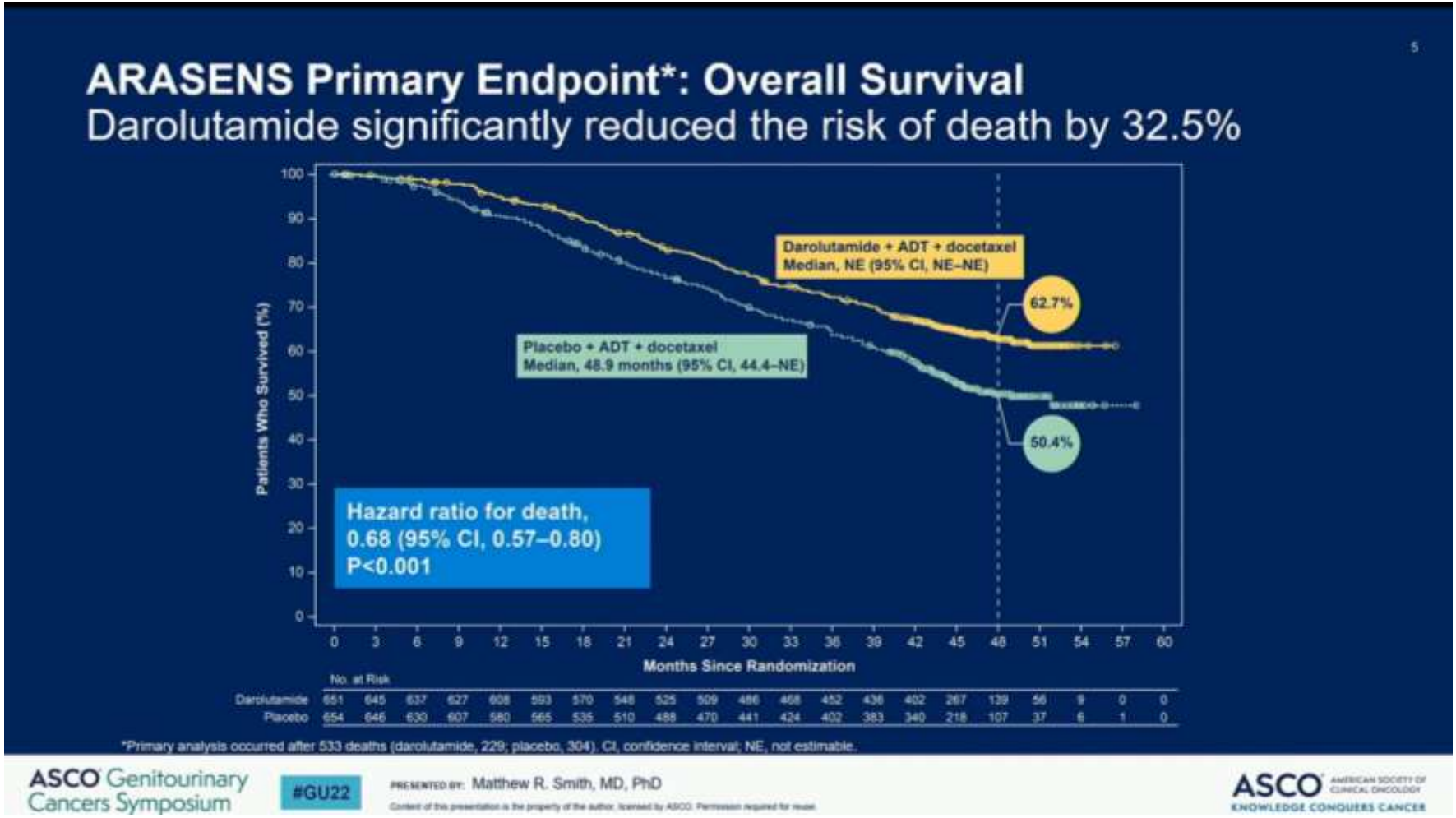
Baseline Demographics and Disease Characteristics

Patient demographics and disease characteristics		Darolutamide + ADT + docetaxel (n=651)	Placebo + ADT + docetaxel (n=654*)
Age, median (range), y		67 (41–89)	67 (42–86)
Region, n (%)	North American	125 (19.2)	119 (18.2)
	Asia Pacific	229 (35.2)	244 (37.3)
	Rest of World	297 (45.6)	291 (44.5)
EGOG performance status, n (%)	0/1	466 (71.6)/185 (28.4)	462 (70.6)/190 (29.1)
Gleason score ≥8 at initial diagnosis, n (%)		505 (77.6)	516 (78.9)
Metastatic stage at initial diagnosis, n (%)	M1	558 (85.7)	566 (86.5)
	M0	86 (13.2)	82 (12.5)
	Mx	7 (1.1)	6 (0.9)
Metastatic stage at screening, n (%)	M1a	23 (3.5)	16 (2.4)
	M1b	517 (79.4)	520 (79.5)
	M1c	111 (17.1)	118 (18.0)
Serum PSA, median (range), ng/mL†		30.3 (0.0–9219.0)	24.2 (0.0–11,947.0)
Serum ALP, median (range), U/L†		148 (40–4885)	140 (36–7680)
ALP stratification, n (%)†	≥ULN	361 (55.5)	363 (55.5)

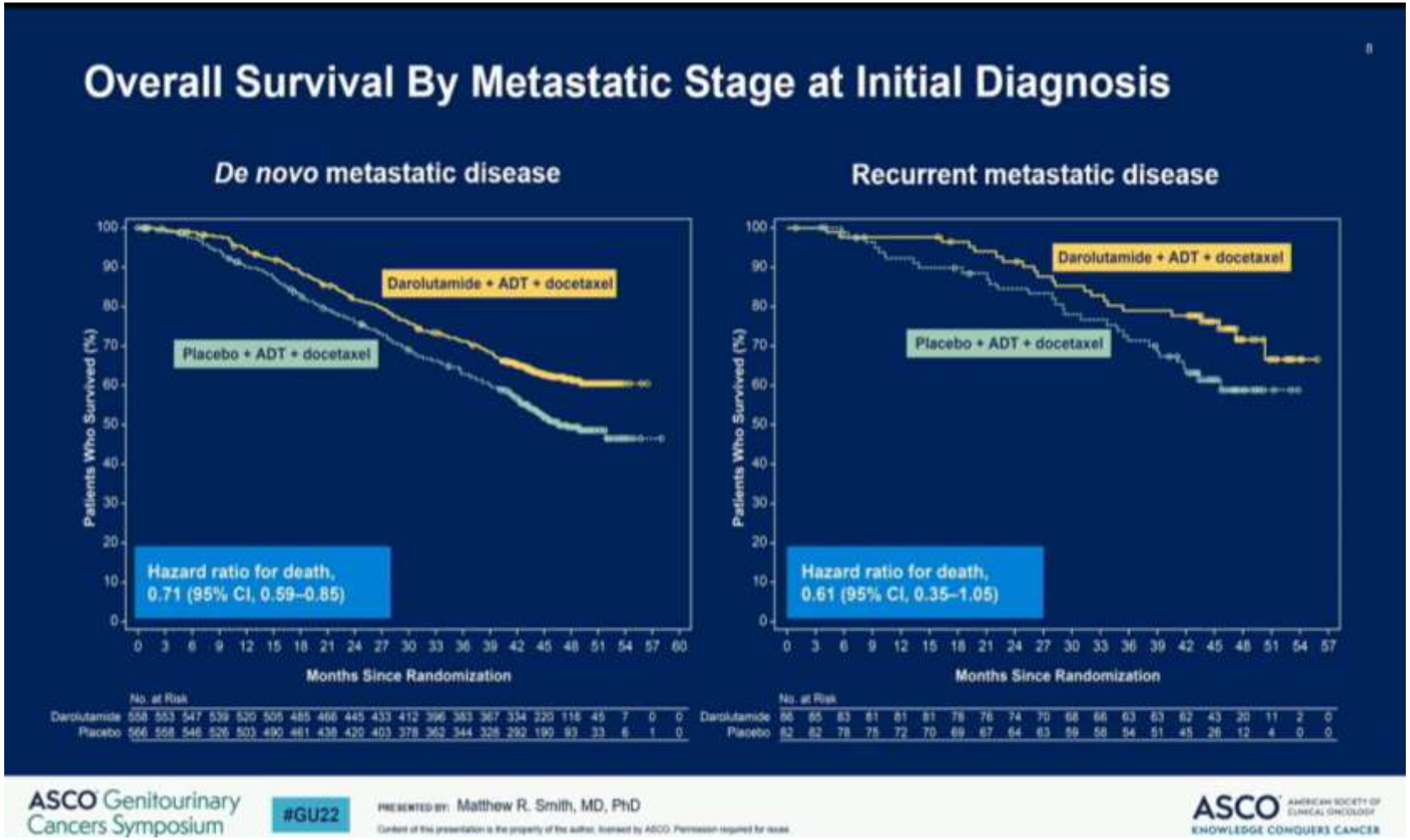
*One patient randomized to placebo but who received darolutamide was included in the placebo group for the full analysis set. †Centrally assessed; samples were collected while patients were receiving ADT.
PSA, prostate-specific antigen.

PRESENTED BY: Matthew R. Smith, MD, PhD

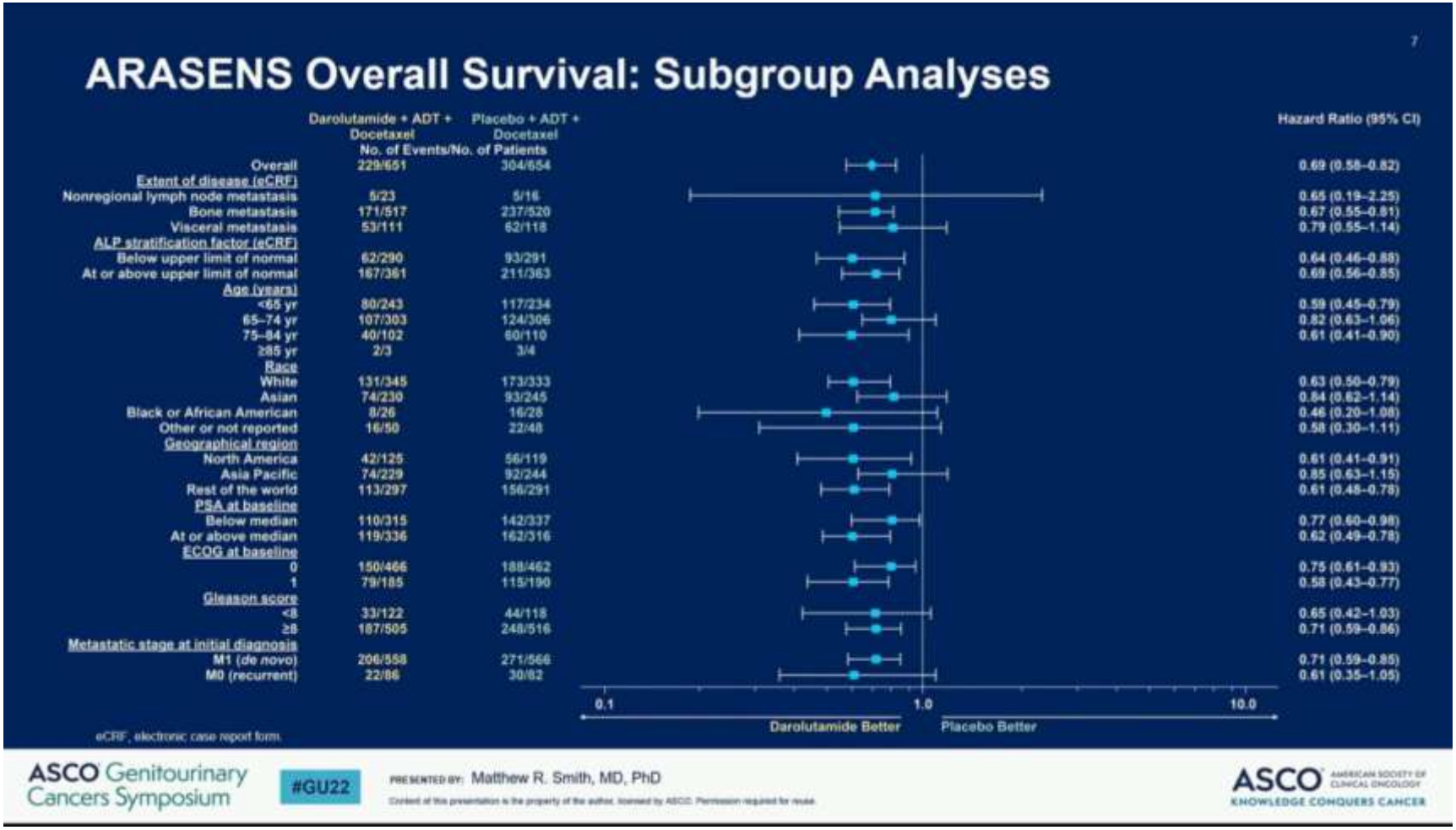
Kastrasyona Duyarlı Metastatik Prostat Kanseri Üçlü Kombinasyon



Kastrasyona Duyarlı Metastatik Prostat Kanseri
Üçlü Kombinasyon



Kastrasyona Duyarlı Metastatik Prostat Kanseri Üçlü Kombinasyon



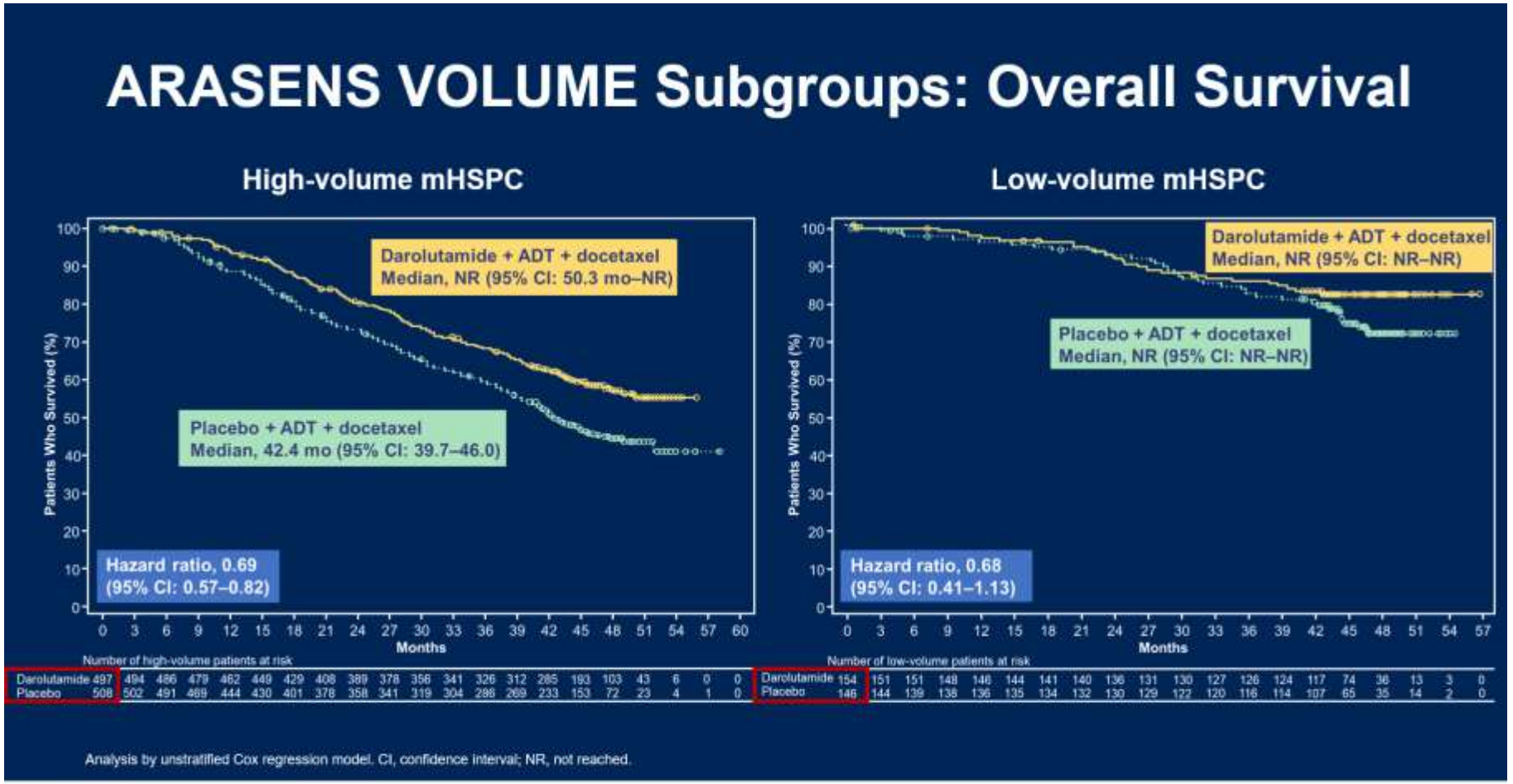
Kastrasyona Duyarlı Metastatik Prostat Kanseri
Üçlü Kombinasyon

Adverse Events of Special Interest for AR Pathway Inhibitors

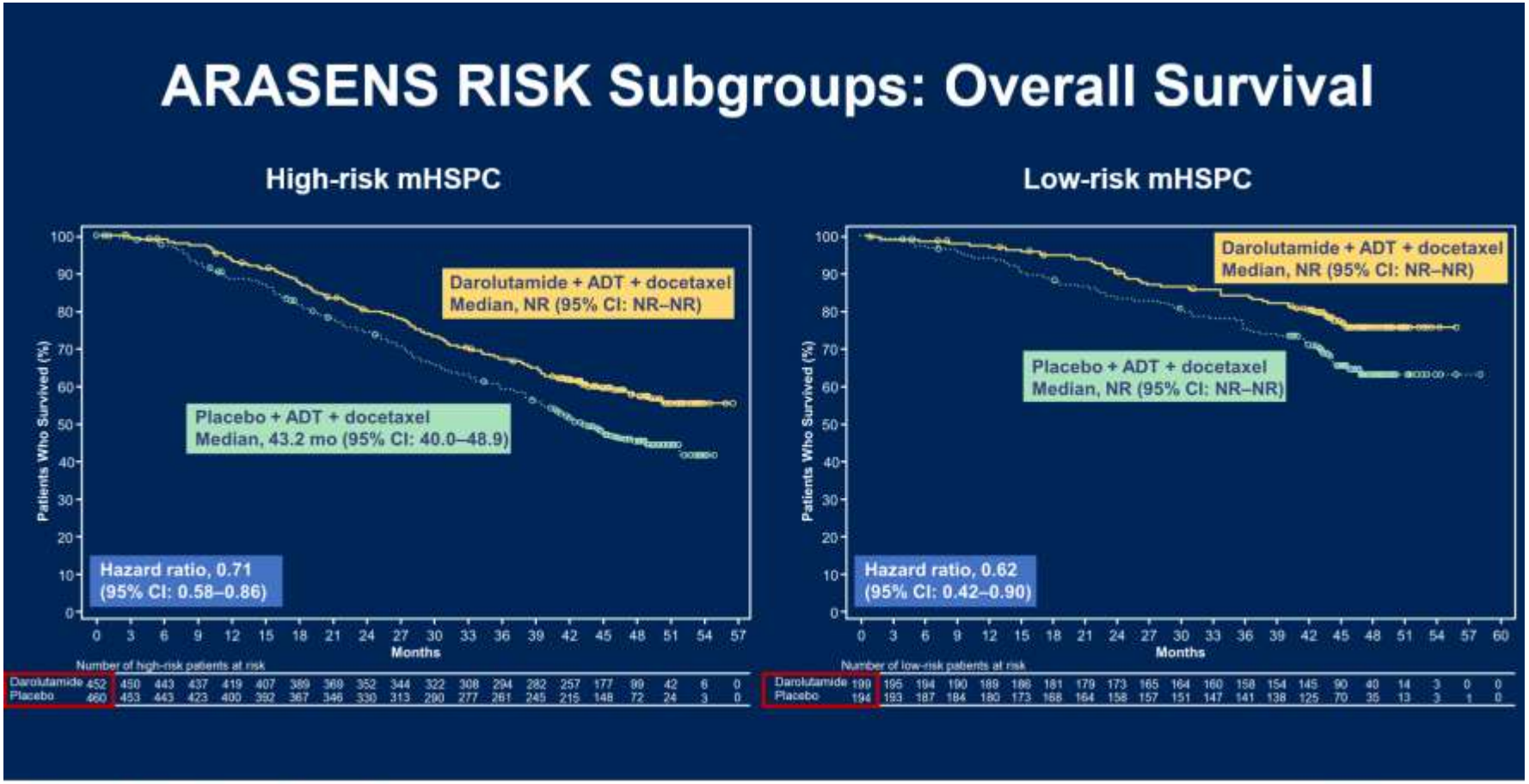
AEs associated with AR pathway inhibitor therapy	Darolutamide + ADT + docetaxel (n=652)		Placebo + ADT + docetaxel (n=650)	
	Patients, n (%)	EAIR/100 PY*	Patients, n (%)	EAIR/100 PY*
Fatigue	216 (33.1)	12.5	214 (32.9)	17.8
Bone fracture	49 (7.5)	2.8	33 (5.1)	2.7
Falls	43 (6.6)	2.5	30 (4.6)	2.5
Rash†	108 (16.6)	6.2	88 (13.5)	7.3
Diabetes mellitus and hyperglycemia‡	99 (15.2)	5.7	93 (14.3)	7.7
Weight decreased	22 (3.4)	1.3	35 (5.4)	2.9
Vasodilatation and flushing	133 (20.4)	7.7	141 (21.7)	11.7
Breast disorders/gynecomastia‡	21 (3.2)	1.2	10 (1.5)	0.8
Hypertension‡	89 (13.7)	5.1	60 (9.2)	5.0
Cardiac disorder‡	71 (10.9)	4.1	76 (11.7)	6.3
Cerebral ischemia	8 (1.2)	0.5	8 (1.2)	0.7
Mental impairment disorder‡	23 (3.5)	1.3	15 (2.3)	1.2
Depressed mood disorder‡	21 (3.2)	1.2	24 (3.7)	2.0
Seizure	4 (0.6)	0.2	1 (0.2)	0.1

*EAIR is the number of patients with a given AE divided by the total darolutamide/placebo treatment duration of all patients in years and expressed in 100 PY. †This category combines the following MedDRA terms: rash, maculopapular rash, drug eruption, pruritic rash, erythematous rash, macular rash, papular rash, follicular rash, pustular rash, and vesicular rash. ‡This category is a MedDRA High-Level Group Term. EAIR, exposure-adjusted incidence rate; PY, patient year.

Kastrasyona Duyarlı Metastatik Prostat Kanseri Tedavisi



Kastrasyona Duyarlı Metastatik Prostat Kanseri
Üçlü Kombinasyon



Kastrasyona Duyarlı Metastatik Prostat Kanseri Tedavisi

	ENZAMET (N=1125)	PEACE-1 (N=1173)	ARASENS (N=1306)
Agent | comparator	Enzalutamide | NSAA	2x2: SoC; abiraterone; RT; both. RT arms collapsed for analysis.	ADT + docetaxel + darolutamide / placebo
Docetaxel	45% (concurrent)	60% (concurrent)	100% (concurrent)
Primary endpoint: HR (CI)	OS: 0.70 (0.58-0.84)	rPFS: 0.50 (0.40-0.62) OS: 0.82 (0.69-0.98)	OS: 0.68 (0.57-0.80)
Relevant "triplet" outcome	Med OS: NR vs 73.2mo 3yr OS: 80% vs 72% 5yr OS: 67% vs 57%	Med rPFS: 4.5 vs 2.0yr Med OS: 5.7 vs 4.7yr	Improved OS Improved secondary endpoints Similar toxicity
Prior ADT	Up to 3mo	Up to 3mo	Up to 12 weeks
Anti-androgen with ADT	Both arms	No	Experimental arm only
Synchronous M1	67%	100%	86%
Visceral metastases	11%	11%	17%
Volume/burden of disease (high | low)	53% | 47%	57% | 43%	77% high volume, 70% high risk

Viseral metastazı olanlarda dörtlü kombinasyon

Early results from CASCARA: A phase 2 study of cabazitaxel/carboplatin plus abiraterone in high-volume metastatic castrate-sensitive prostate cancer (mCSPC).

Background: Best treatment of mCSPC involves doublet therapy (ADT + novel hormonal agent) or triplet therapy (ADT + novel hormone + docetaxel); however, opportunity remains for further improvement. Studies show that homologous recombination repair (HRR) gene mutations are enriched in metastatic prostate cancer, and may portend resistance to docetaxel. CASCARA tested quadruplet therapy (ADT + cabazitaxel/carboplatin + abiraterone) in high-volume mCSPC, aiming to enhance PSA responses and decrease progression at 1 year. **Methods:** This phase 2 study enrolled 61 mCSPC patients with high-volume disease who received ADT plus cabazitaxel (20 mg/m^2 q21d x 6) and carboplatin (AUC=4 q21d x 6) followed by abiraterone (1000 mg, plus prednisone 5 mg). Primary endpoint was freedom from PSA/radiographic progression at 1 year. Other endpoints included PSA_{50} response, freedom from PSA progression, and safety. Archival biopsies were retrospectively evaluated for HRR (*BRCA1/2*, *ATM*, *CHEK2*, *CDK12*, *BRIP1*, *RAD51B*) mutations at a CLIA-certified lab. A sample size of 61 was determined using a Simon two-stage design (stage 1: 32 men, stage 2: 29 men) with a null hypothesis of a 1-year PSA/radiographic progression-free rate of 0.80 against a one-sided alternative of 0.92. **Results:** From 11/2019 to 06/2022, 61 men enrolled at 7 sites. Median age was 64 (range, 45–76) years; 21% were African American. Median baseline PSA was 8.9 (range, 0.1–1021) ng/mL. 44% of men had ECOG=1. 91% had Gleason sum 8–10. Prevalence of DNA alterations (50 evaluable pts) was 18% for HRR mutations, 38% for *TP53* muts, 22% for *ERG* fusions, 10% for *SPOP* muts. Freedom from PSA/radiographic progression at 1 year was 77% (95% CI, 63–87%), and freedom from PSA progression at 1 year was 81% (95% CI, 67–90%). The PSA_{50} rate response was 97%. PSA ≤0.2 ng/mL at month-7, a surrogate for survival in other mCSPC studies, was 61%; PSA ≤4 ng/mL at month-7 was 82%. Outcomes according to mutation status are shown. AEs included 7% grade (Gr)-3/4 myelosuppression, 8% Gr-3/4 infections, 10% Gr-3 GI disorders, and 3% Gr-3 fatigue. There were 4 treatment-related discontinuations. **Conclusions:** Quadruplet therapy with ADT + cabazitaxel/carboplatin + abiraterone was well tolerated. At 1 year, 77% of pts were progression-free. PSA ≤0.2 ng/mL at month-7 was 61%, exceeding the historical month-7 PSA ≤0.2 ng/mL rate of 45% in CHAARTED–docetaxel arm. Further exploration of this quadruplet strategy in randomized phase III studies is warranted. Clinical trial information: NCT03934840. Research Sponsor: Sanofi-Genzyme.

PSA≤0.2 oranı %61

Charles J. Ryan, ASCO GU 2023

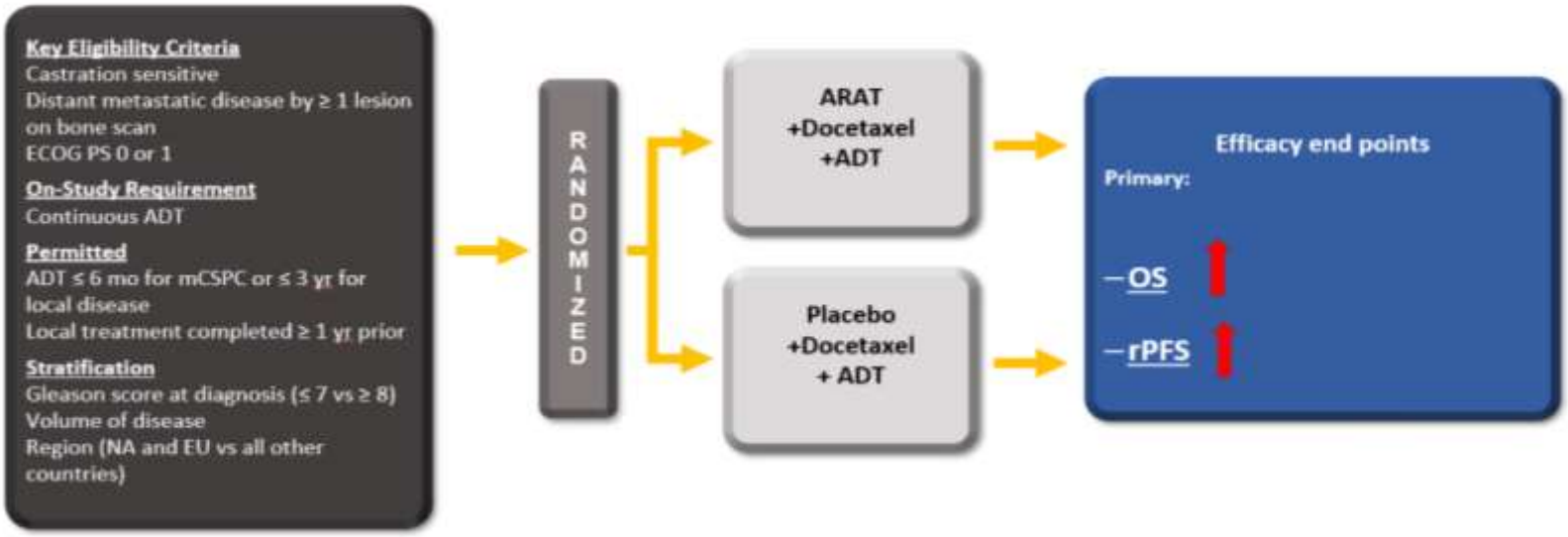
Viseral metastazı olanlarda dörtlü kombinasyon

	HRR status N (%)	*TP53* status N (%)	*ERG* fusion N (%)	*SPOP* status N (%)
Freedom from PSA/radiographic progression at 1 yr	HRRm – 6 (67%) HRRwt – 34 (83%)	*TP53*m – 14 (77%) *TP53*wt – 26 (84%)	*ERG*m – 11 (100%) *ERG*wt – 29 (74%)	*SPOP*m – 5 (100%) *SPOP*wt – 35 (78%)
PSA ≤0.2 ng/mL at month 7	HRRm – 3 (38%) HRRwt – 27 (66%)	*TP53*m – 12 (67%) *TP53*wt – 18 (60%)	*ERG*m – 9 (82%) *ERG*wt – 21 (55%)	*SPOP*m – 4 (100%) *SPOP*wt – 26 (58%)

Charles J. Ryan, ASCO GU 2023

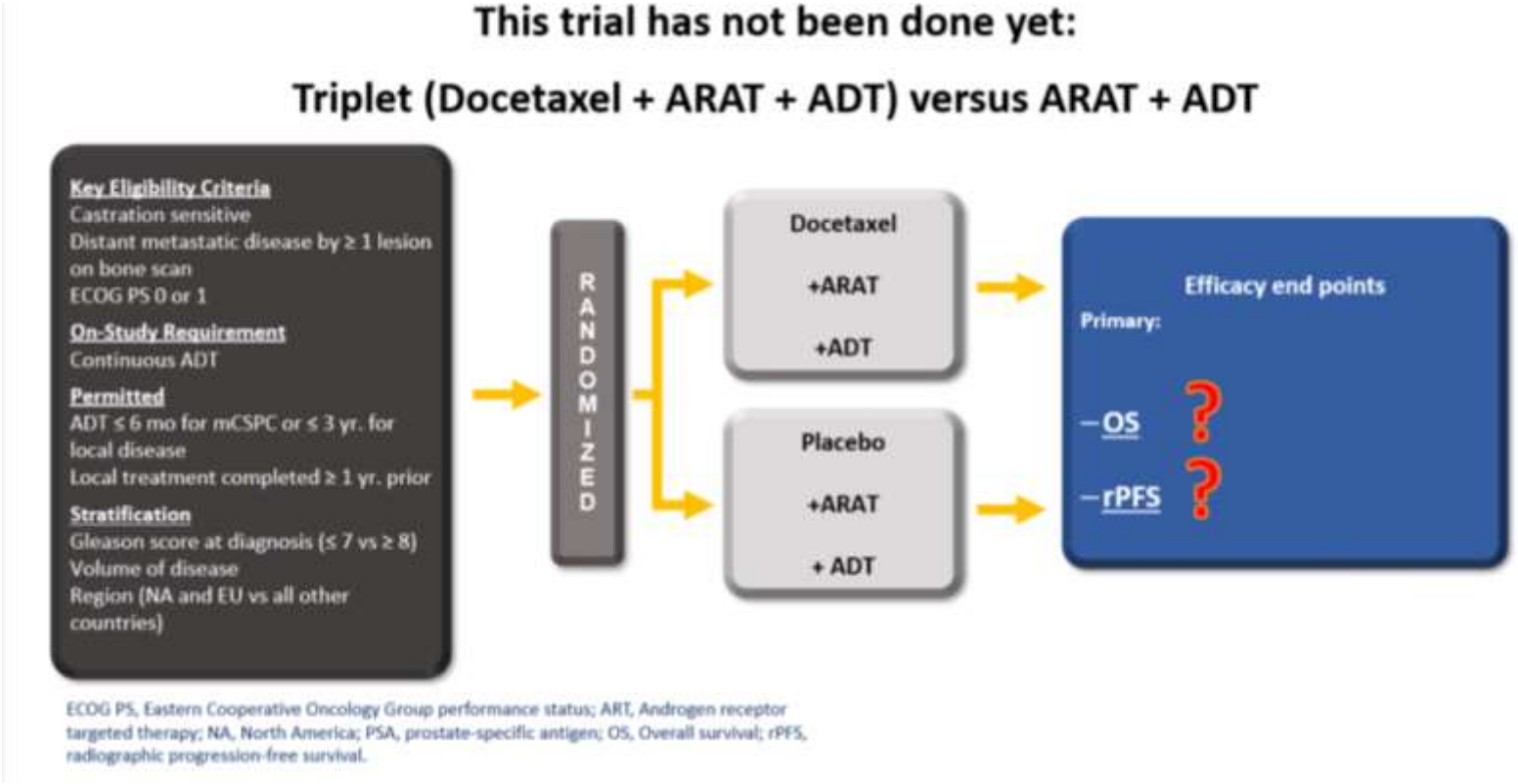
Evre IV Kastrasyona Duyarlı Prostat Kanseri
Üçlü Kombinasyonlar

Phase III Trial: Triplets (ARAT+ Docetaxel + ADT) vs. Docetaxel + ADT



ECOG PS, Eastern Cooperative Oncology Group performance status; ART, Androgen receptor targeted therapy; NA, North America; PSA, prostate-specific antigen; OS, Overall survival; rPFS, radiographic progression-free survival.

Evre IV Kastrasyona Duyarlı Prostat Kanseri
Üçlü Kombinasyonlar



ECOG PS, Eastern Cooperative Oncology Group performance status; ART, Androgen receptor targeted therapy; NA, North America; PSA, prostate-specific antigen; OS, Overall survival; rPFS, radiographic progression-free survival.

Kastrasyona Duyarlı Prostat Kanseri Tedavi sonrası PSA değeri Sağkalım İlişkisi

Overall Survival after Androgen Deprivation in New Metastatic Prostate Cancer

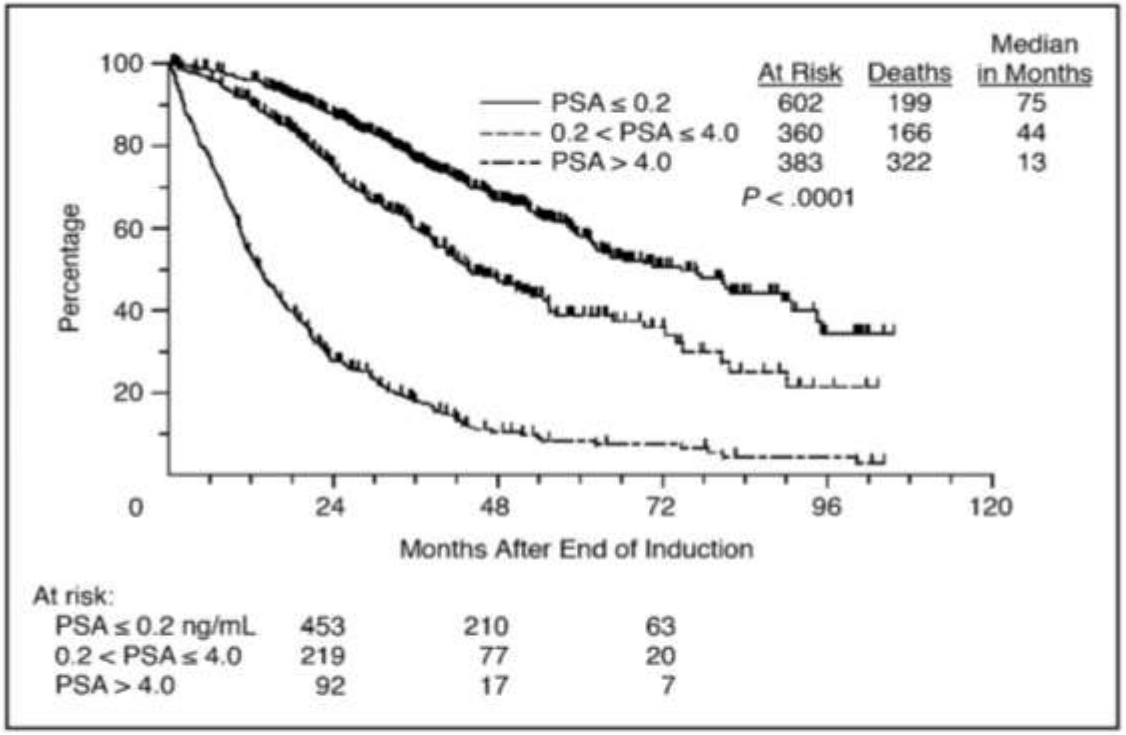
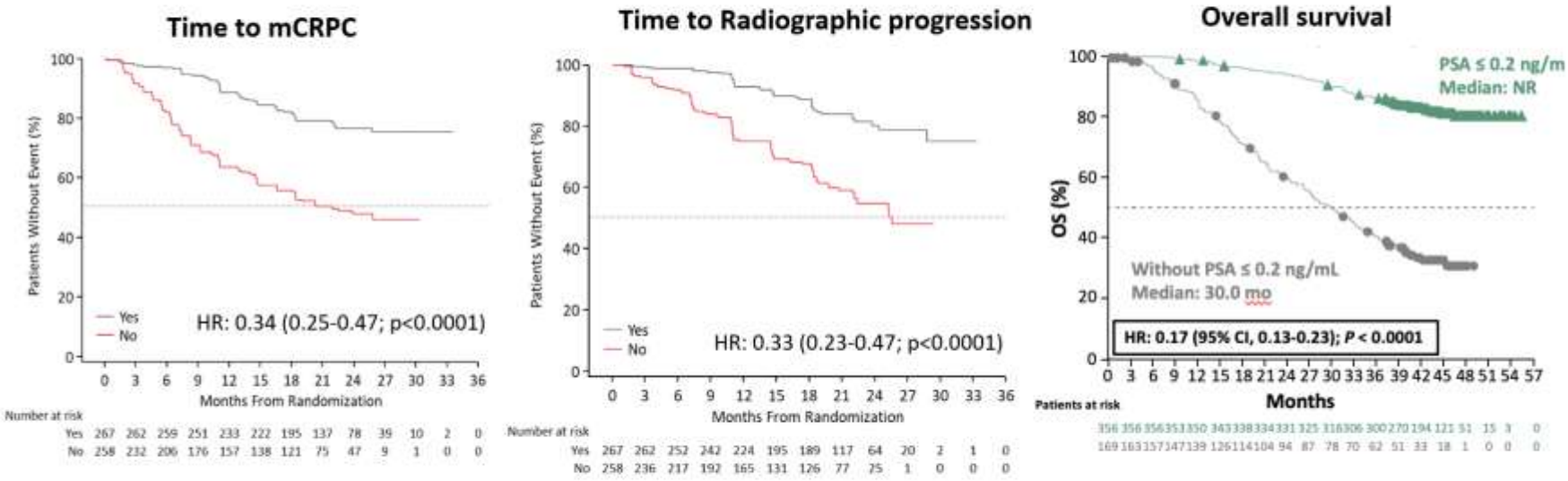


Fig 2. Overall survival by prostate-specific antigen (PSA, ng/mL) status at end of induction
Maha Hussain: Journal of Clinical Oncology 2006; 24 3984-3990.

Courtesy of Simon Chowdhury, MD, PhD

Kastrasyona Duyarlı Metastatik Prostat Kanseri Nadir PSA Uzun Sağkalımı Gösterir

Patients who achieved reduction of PSA ≤0.2 ng/mL by 3 months



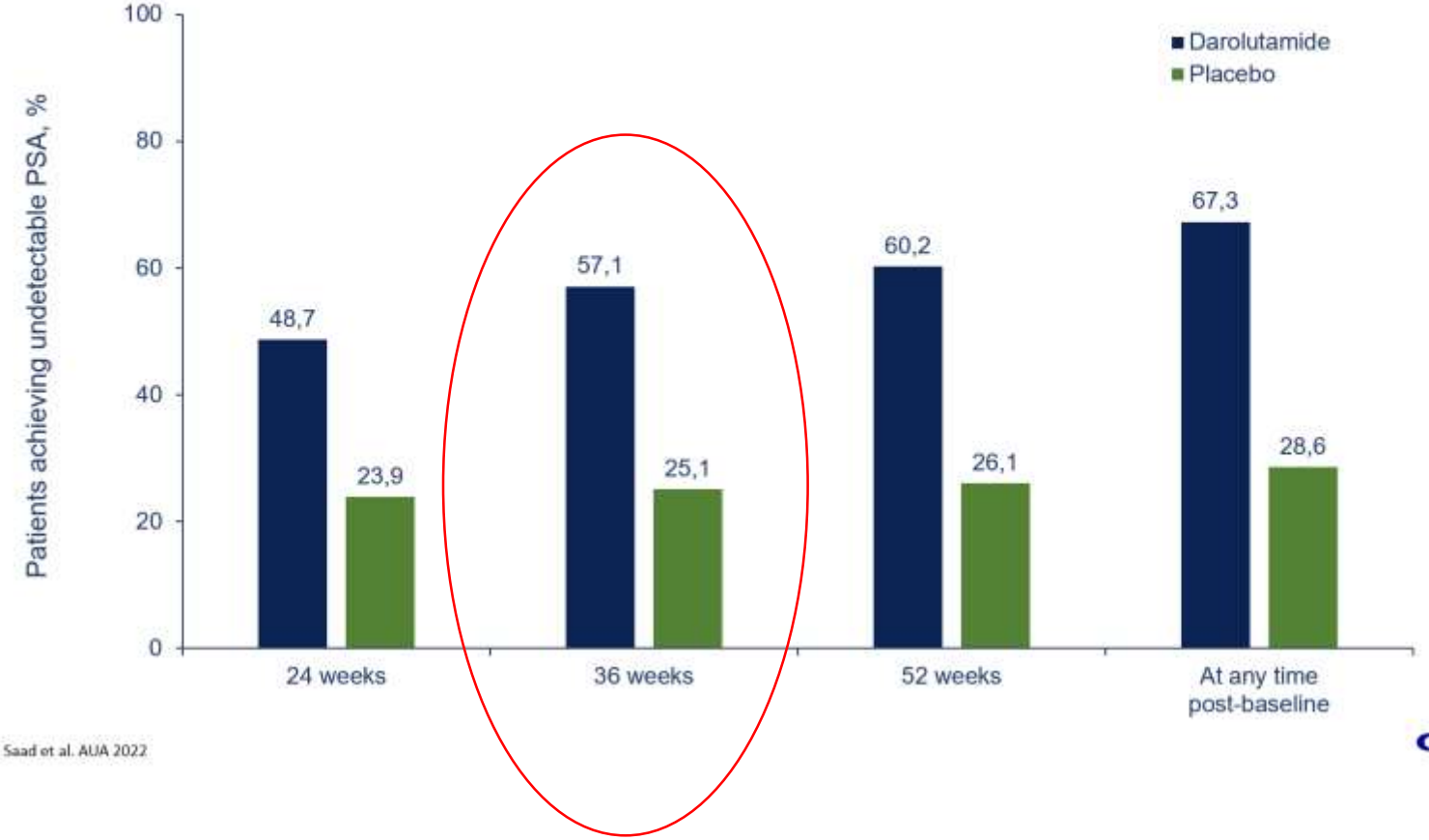
Data from the TITAN study: Chi K et al. N Engl J Med. 2019 Jul 4;381(1):13-24.

Chi KN, et al. Oral presentation at AUA Annual Meeting (Virtual), September 10-13, 2021

CHUM

Kastrasyona Duyarlı Metastatik Prostat Kanseri Tedavisi

Objective: Undetectable (≤0.2) PSA Levels



Saad et al. AUA 2022

CHUM

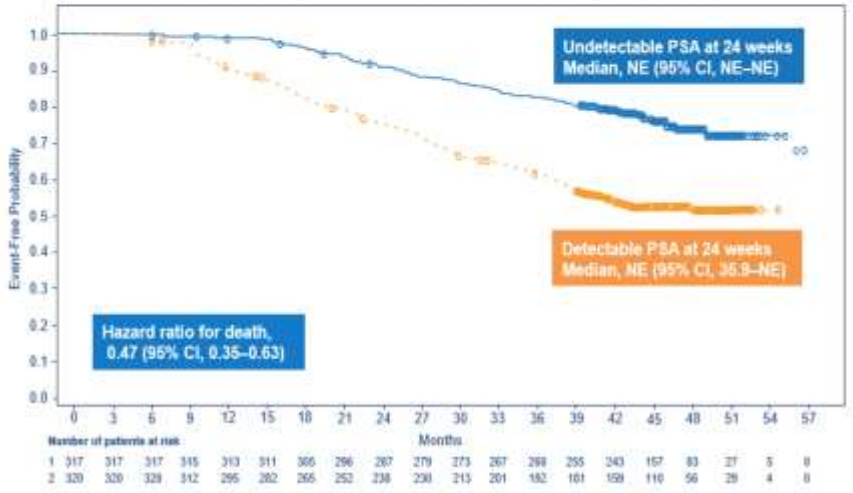
Kastrasyona Duyarlı Metastatik Prostat Kanseri Tedavisi

Results: Overall Survival

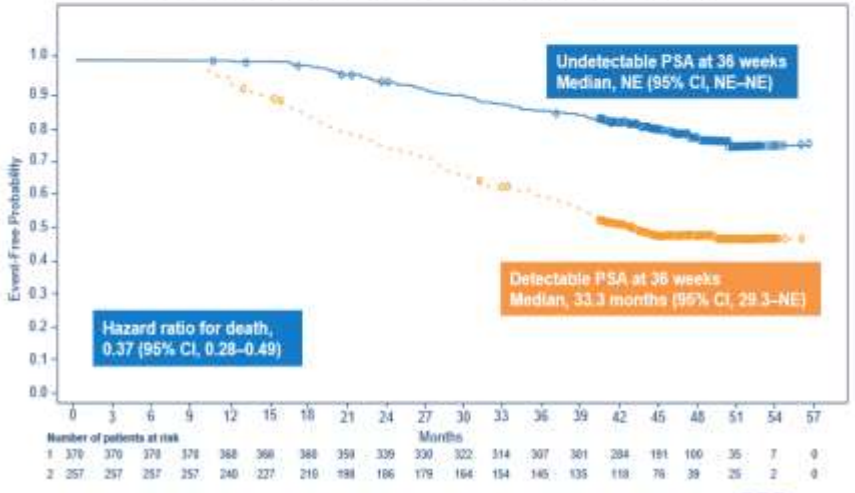
Undetectable PSA at 24 and 36 weeks was associated with a 53% and 63% reduction in the risk of death

Darolutamide + ADT + docetaxel

Undetectable vs detectable PSA at 24 weeks



Undetectable vs detectable PSA at 36 weeks

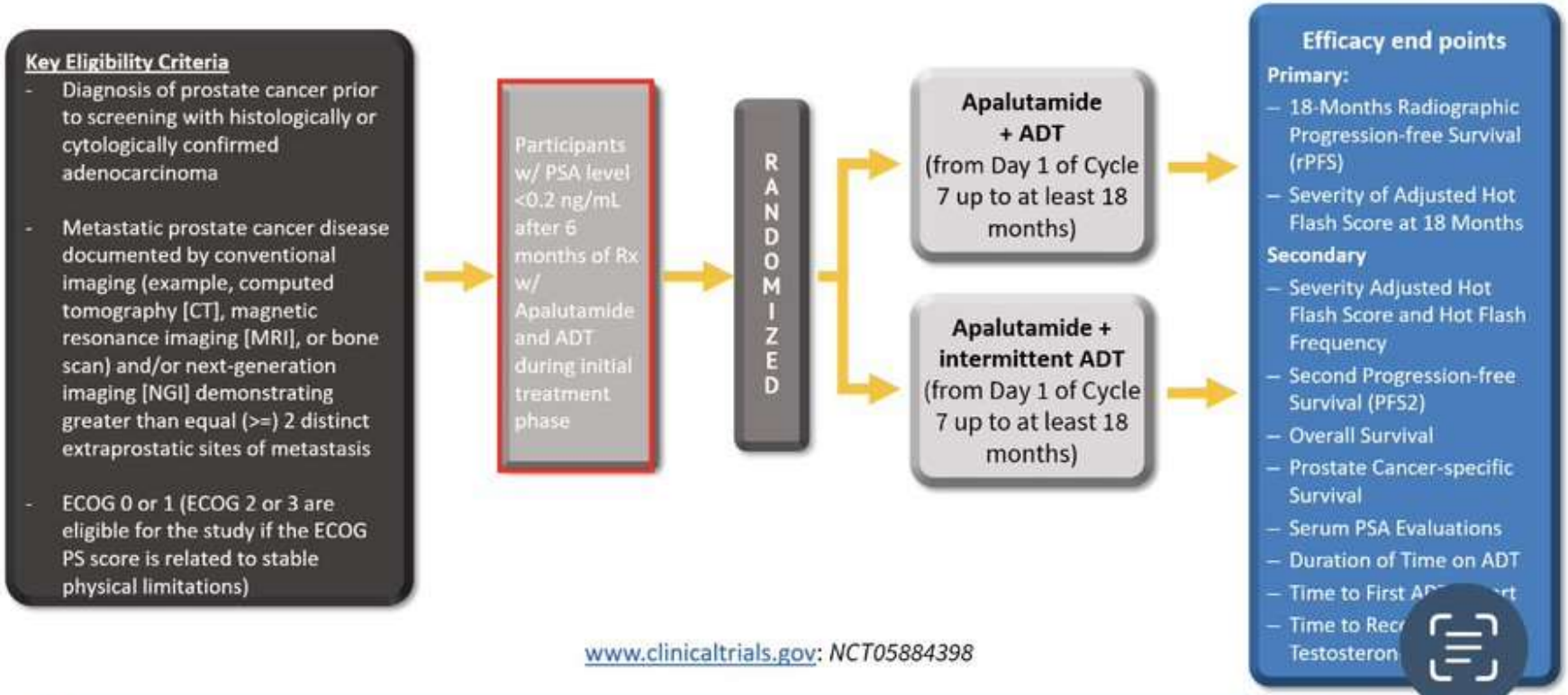


Saad et al. AUA 2022

CHUM

Gelecek Perspektif

LIBERTAS Trial: Phase 3 Trial Design



www.clinicaltrials.gov: *NCT05884398*

Prostat kanserinde genomik profil

Recent insights into the molecular landscape of advanced PC have identified the following potentially actionable targets:

Molecular alteration	Frequency of expression in advanced PC*
High levels of PSMA expression	**(>80%)[1–5]**
AR pathway mutations/alterations	(63%–71%)[6]
PTEN-PI3K-AKT pathway alterations	(49%)[6]
Cell cycle (CDK) pathway alterations	(21%)[6]
DNA repair pathway alterations	(19%–23%)[6]
WNT pathway alterations	(18%)[6]
MSI-H, dMMR	(~3–5%)[7,8]

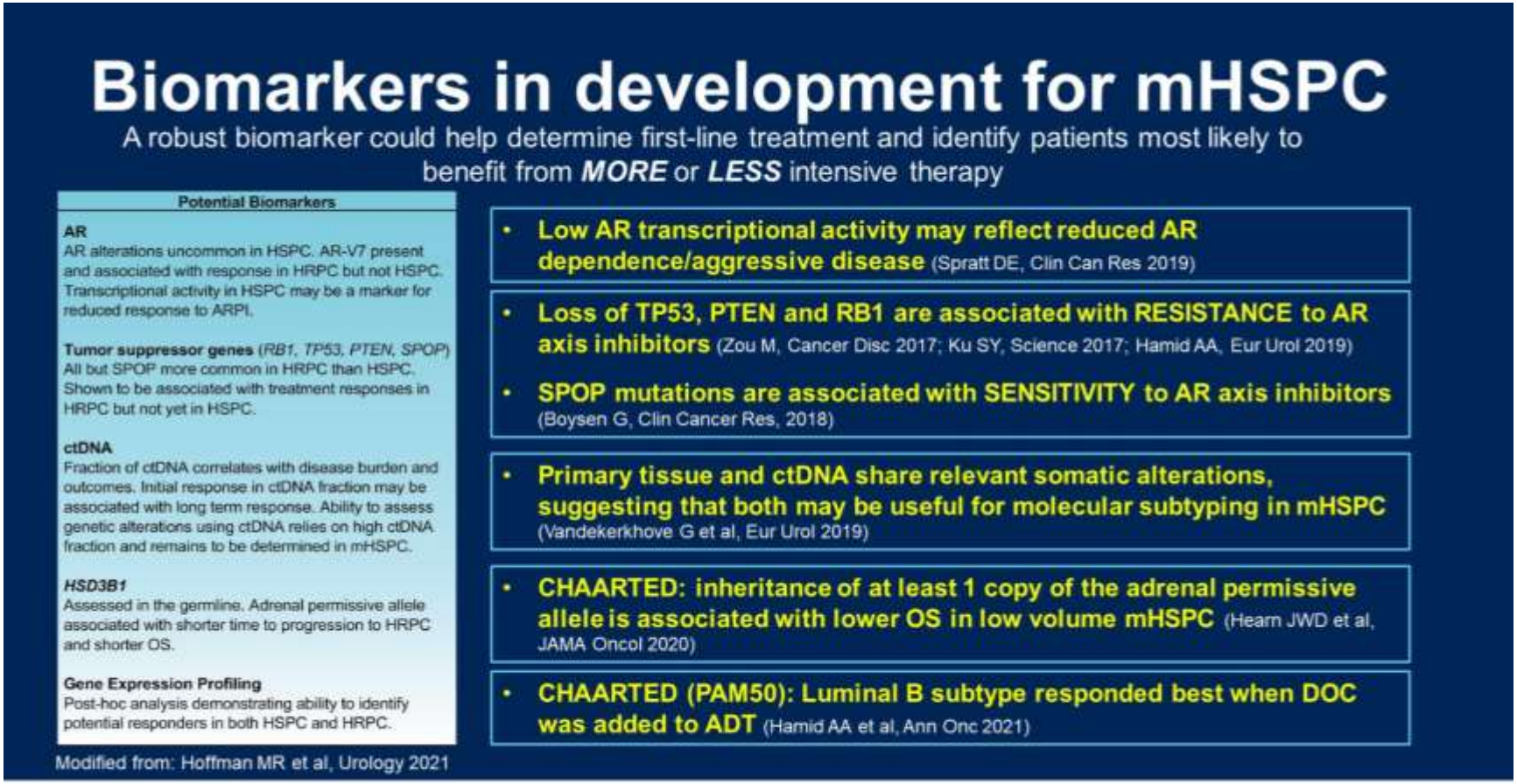
PSMA appears to be the most broadly applicable potential biomarker and actionable target in advanced PC[1–6]

**Each figure represents 10% of patients with advanced PC.*

1. Hope TA, et al. J Nucl Med. 2017;58(12):1956–1961; 2. Hupe MC, et al. Front Oncol. 2018;8:623; 3. Pomykala KL, et al. J Nucl Med. 2020;61(3):405–411; 4. Minner S, et al. Prostate. 2011;71(3):281–288; 5. Bostwick DG, et al. Cancer. 1998;82(11):2256–2261; 6. Robinson D, et al. Cell. 2015;161(5):1215–1228; 7. Abida W, et al. JAMA Oncol. 2019; 5(4):471-478; 8. Lindh C, et al. APMIS. 2019; 127(8):554-560.

AKT, protein kinase B; AR, androgen receptor; CDK, cyclin-dependent kinase; PC, prostate cancer; PI3K, phosphoinositide 3-kinase; PSMA, prostate-specific membrane antigen; PTEN, phosphatase and tensin homolog; WNT, wingless int-1.

Gelecek Perspektif



Gelecek Perspektif

Biomarker	Details	Sensitivity	Trials in mHSPC (BM selected)
DNA repair	BRCA1, BRCA2, PALB2	PARPi	ProBIO
	HRRm	PARPi-ARPI	TALAPRO-3, EvoPAR-01, AMPLITUDE
	MMR-d/MSI-H	ICI	NCT04126070, NCT03879122
PI3K	PTEN	PI3Ki	CAPITELLO-281
	PIK3CA, AKT1	PI3Ki	
Cell-cycle	RB1 or RB1/TP53 doublet, high Ki67	Platinum (doublet)	
	Cyclin D1, intact RB1, CDK2NA, low Ki67	CDK4/6i	CYCLONE-3
TMPRSS2-ERG / ERG	ERG alter microtubule (dynamics)	Taxanes (triplet)	ProBIO
TSG	Compound mutation in TP53, PTEN, RB1	Taxanes (triplet)	-
SPOP	Role in AR regulation	ARPI	-
RNA	Decipher, GC Q4	Taxanes	STAMPEDE
	PAM50: Luminal B	Taxanes	STAMPEDE
ctDNA%	Low ctDNA%	ICI, PSMA-RLT	-
	High ctDNA%	Taxanes (triplet)	-

Gelecek Perspektif

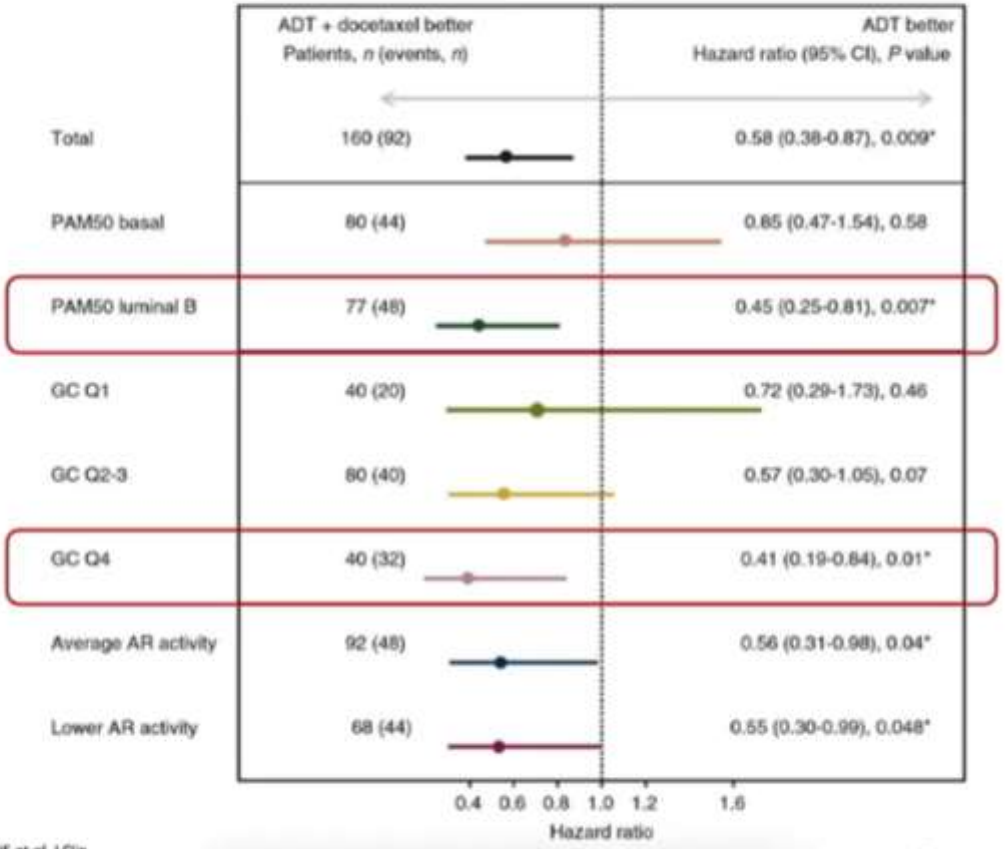
Decipher as a Prognostic Tool - Evolution from GRID Signatures

Hypotheses and analyses plan

- 59 signatures derived from pan-transcriptome data
- CHAARTED biomarker cohort (N=160) used as training set[1]

Pre-defined statistical analyses plan

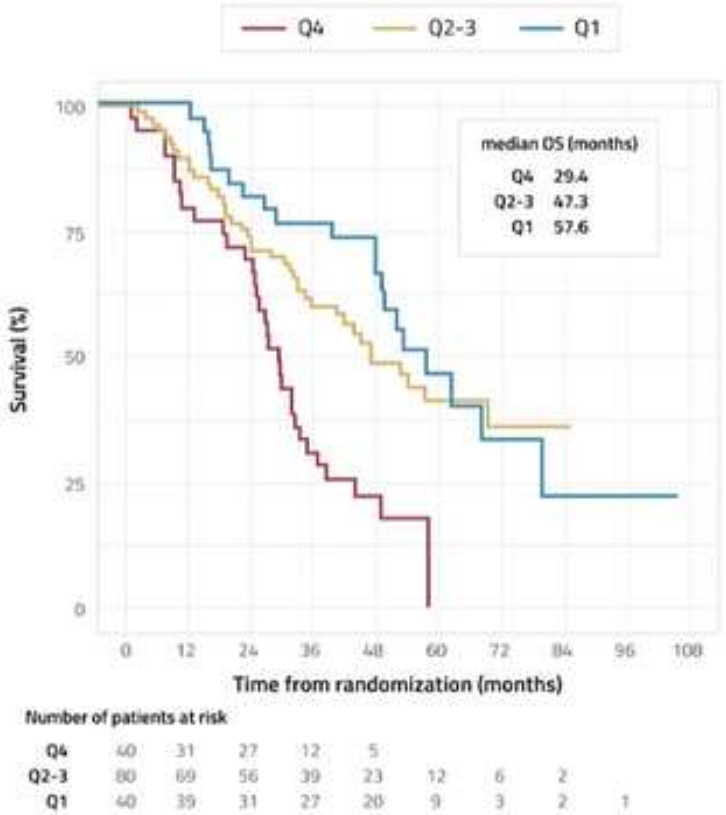
- 4 signatures identified for predictive testing **Decipher**[2], **PAM50**[3], **PSC**[4], and **AR-A**[5]



1. Hamid A ... Sweeney C. *et al.* Ann Oncol. 2021; 2. Nguyen P *et al.* Int J Radiat Oncol Biol Phys. 2023; 3. Parker JS *et al.* J Clin Oncol. 2009; 4. Weiner AB *et al.* Cancer; 2023 5. Spratt D et al. Clin Cancer Res 2019
Adapted from: Emily Grist, et al. Decipher mRNA score for prediction of survival benefit from docetaxel at start of androgen deprivation therapy (ADT) for advanced prostate cancer (PC): An ancillary study of the STAMPEDE docetaxel trials. ESMO. 13-17 September 2024; Barcelona, Spain.

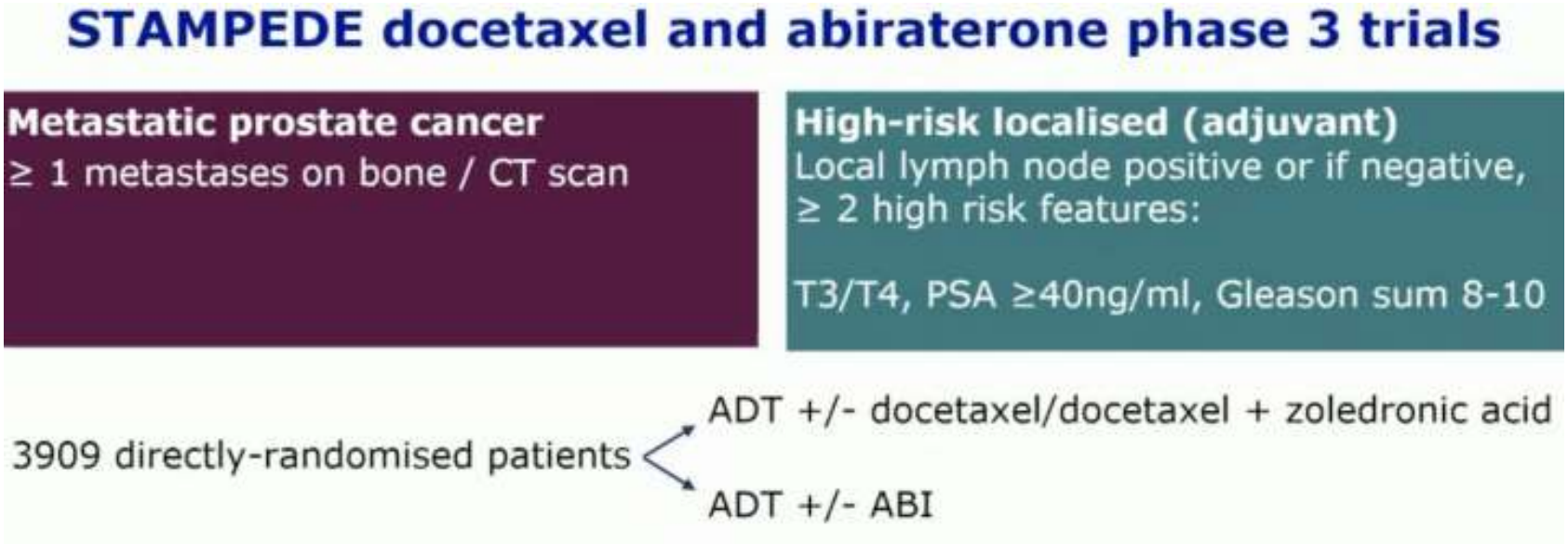
Gelecek Perspektif

Overall Survival in CHAARTED Stratified by Decipher Genomic Classifier Quartiles



Adapted based on data from: Anis Hamid, et al. Transcriptional profiling of primary prostate tumor in metastatic hormone-sensitive prostate cancer and association with clinical outcomes: correlative analysis of the E3805 CHAARTED trial. Annals of Oncology, 2021;32(9): 1157-1166. DOI: 10.1016/j.annonc.2021.06.003.

Gelecek Perspektif; klinik bulgulara gen ve genomik verilerin eklenmesi



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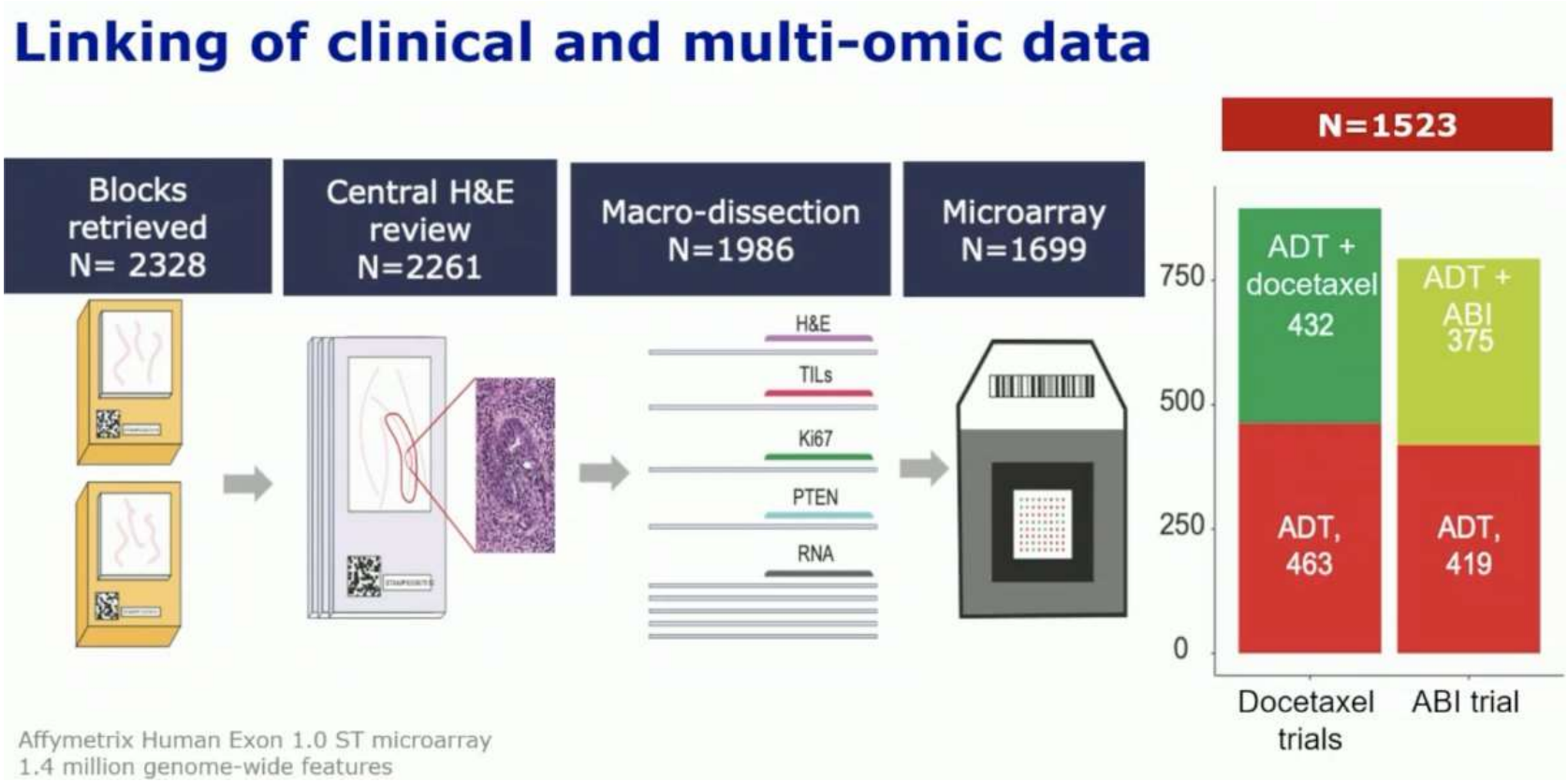


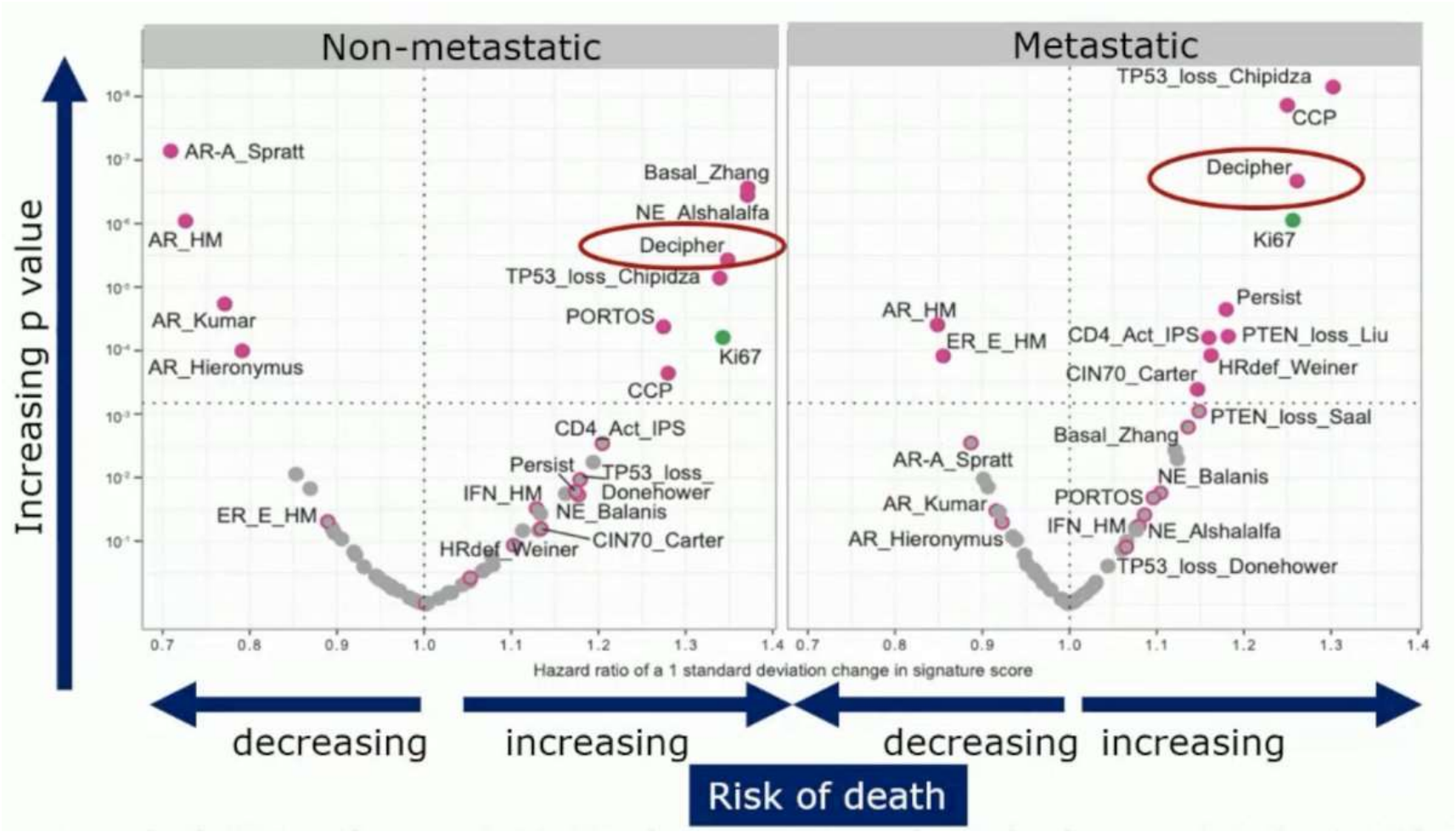
Gelecek Perspektif; klinik bulgulara gen ve genomik verilerin eklenmesi

Clinical qualification of transcriptome signatures for advanced prostate cancer starting androgen deprivation therapy with or without abiraterone acetate and prednisolone: an ancillary study of the STAMPEDE trial

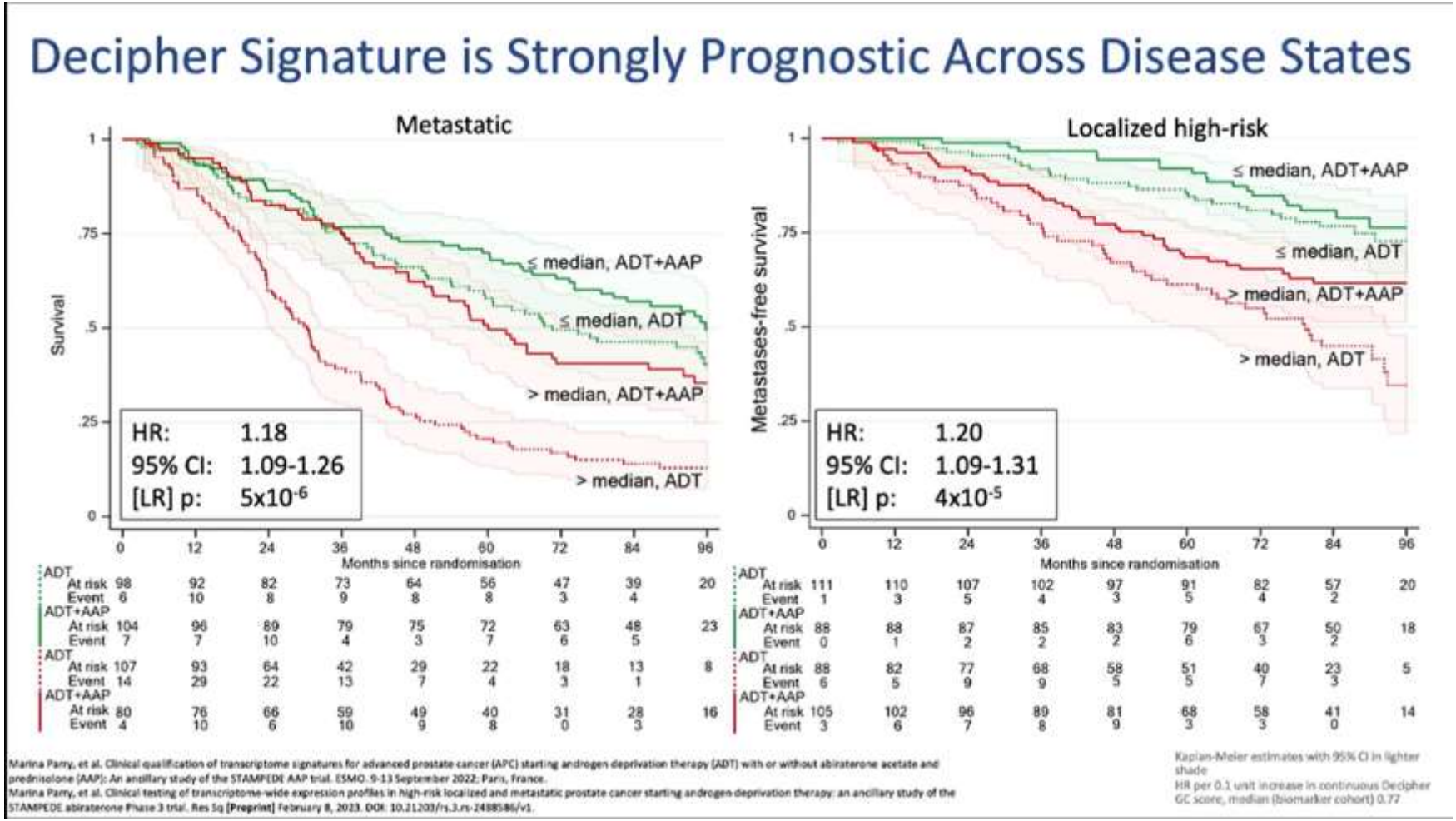
Marina Parry, Emily Grist, Christopher Brawley, James Proudfoot, Larissa Mendes, Sharan Lall, Alex Hoyle, Ashwin Sachdeva, Yang Liu, Claire Amos, Matthew Sydes, Robert Jones, Max Parmar, Felix Feng, Christopher Sweeney, Noel Clarke, Elai Davicioni, Nick James, Louise Brown, Gerhardt Attard **on behalf of the STAMPEDE investigators**

Marina Parry, et al. Clinical qualification of transcriptome signatures for advanced prostate cancer (APC) starting androgen deprivation therapy (ADT) with or without abiraterone acetate and prednisolone (AAP): An ancillary study of the STAMPEDE AAP trial. ESMO. 9-13 September 2022; Paris, France.
Marina Parry, et al. Clinical testing of transcriptome-wide expression profiles in high-risk localized and metastatic prostate cancer starting androgen deprivation therapy: an ancillary study of the STAMPEDE abiraterone Phase 3 trial. Res Sq **[Preprint]** February 8, 2023. DOI: 10.21203/rs.3.rs-2488586/v1.

Gelecek Perspektif; klinik bulgulara gen ve genomik verilerin eklenmesi

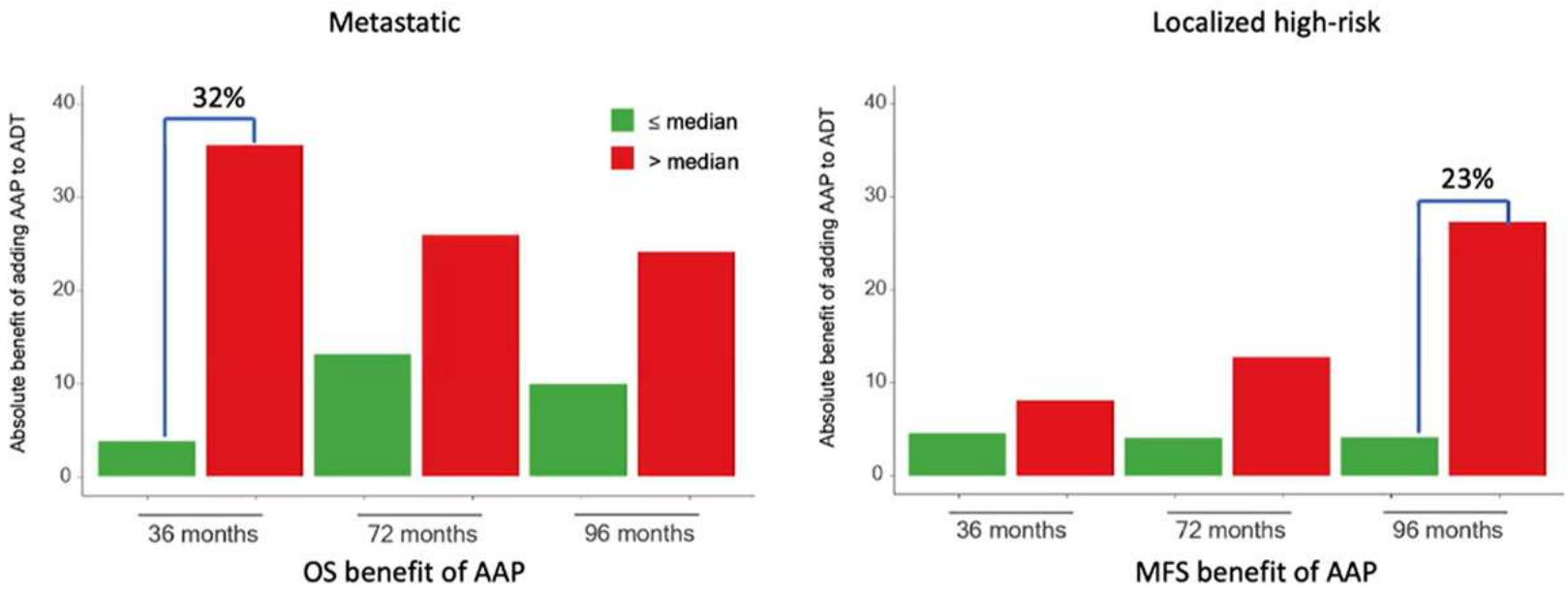


Gelecek Perspektif; klinik bulgulara gen ve genomik verilerin eklenmesi



Gelecek Perspektif; klinik bulgulara gen ve genomik verilerin eklenmesi

Absolute Benefit of Adding AAP to ADT Varies by Decipher Score



Event rate calculated using flexible parametric modelling adjusted for baseline characteristics

Marina Parry, et al. Clinical qualification of transcriptome signatures for advanced prostate cancer (APC) starting androgen deprivation therapy (ADT) with or without abiraterone acetate and prednisolone (AAP): An ancillary study of the STAMPEDE AAP trial. ESMO. 9-13 September 2022; Paris, France.
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Decipher mRNA score for prediction of survival benefit from docetaxel at start of androgen deprivation therapy for advanced prostate cancer: an ancillary study of the STAMPEDE docetaxel trials

Emily Grist, Peter Dutey-Magni, Larissa Mendes, Marina A. Parry, Ashwin Sachdeva, James Proudfoot, Anis A. Hamid, Claire L. Amos, William R. Cross, Silke Gillessen, Daniel M. Berney, Matthew R. Sydes, Mahesh K.B. Parmar, Felix Y. Feng, Noel W. Clarke, Elai Davicioni, Christopher J. Sweeney, Nicholas D. James, Louise C. Brown, Gerhardt Attard on behalf of the STAMPEDE Investigators

ClinicalTrials.gov number, NCT00268476 & Current Controlled Trials number, ISRCTN78818544 Trial conducted by Medical Research Council Trials Unit at University College London, U.K.

105 UK trial sites participated in this study

Emily Grist, et al. Decipher mRNA score for prediction of survival benefit from docetaxel at start of androgen deprivation therapy (ADT) for advanced prostate cancer (PC): An ancillary study of the STAMPEDE docetaxel trials. ESMO. 13-17 September 2024; Barcelona, Spain.

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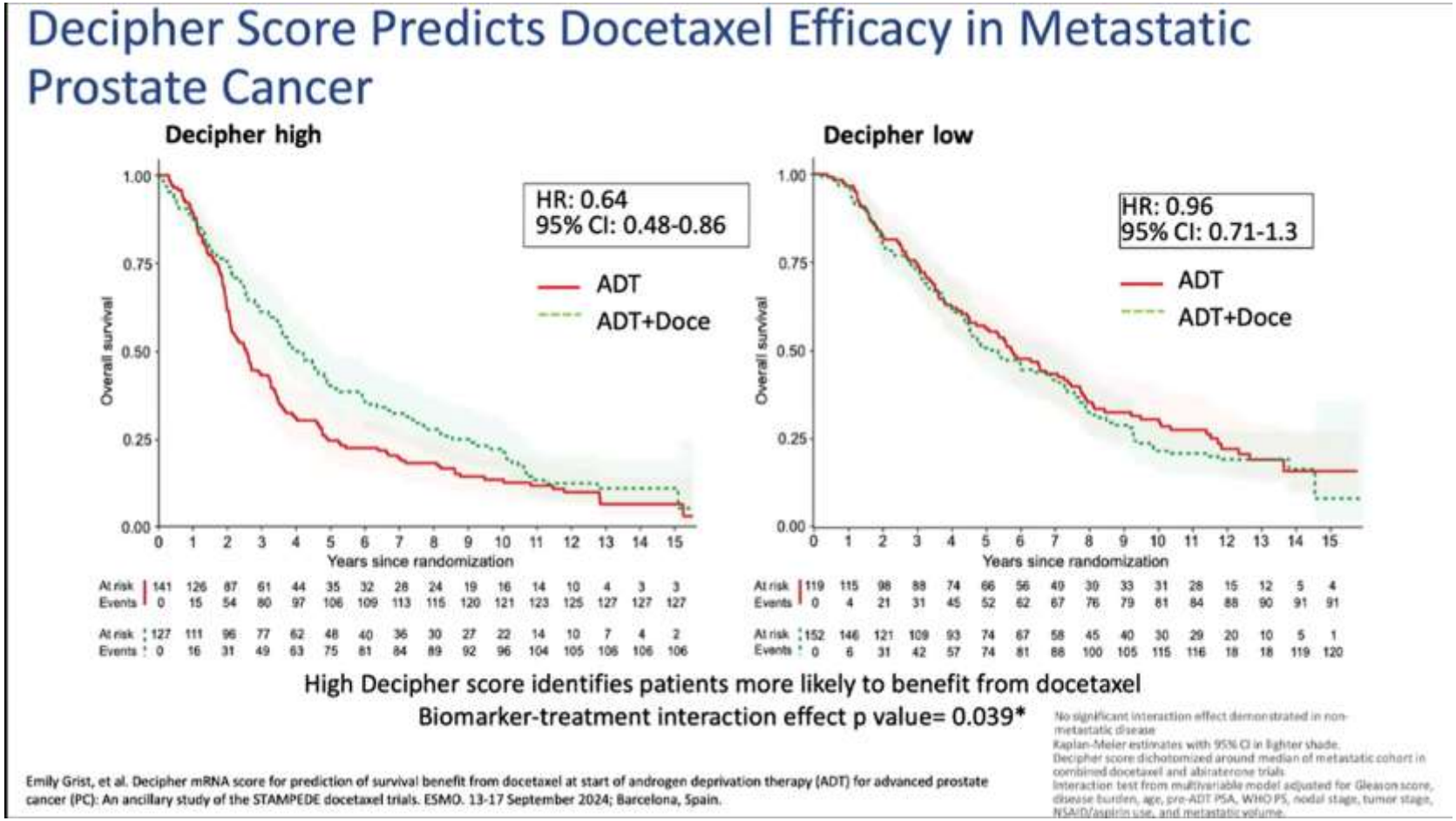

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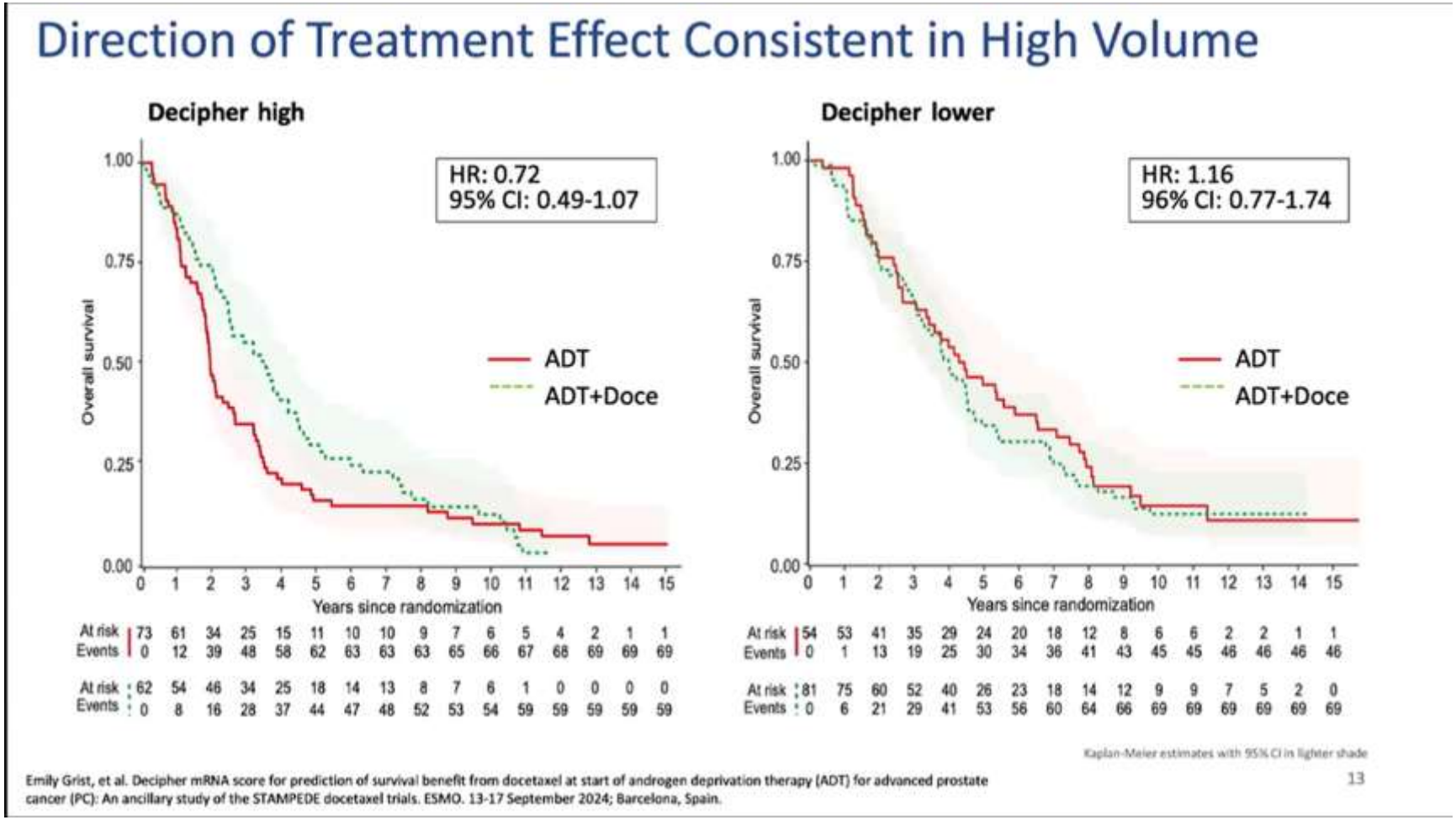
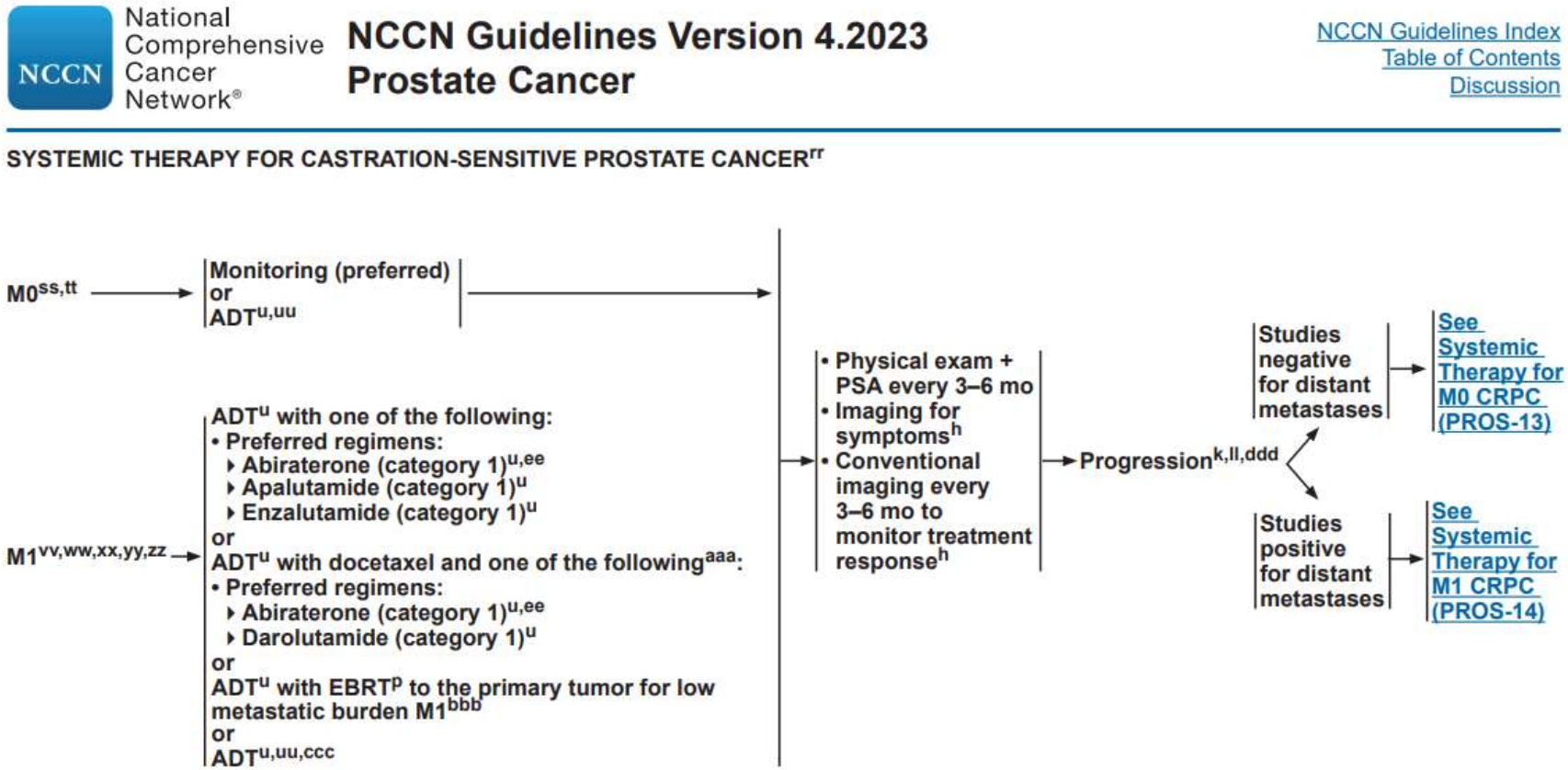


Diğer Doz Yoğun Seçenekler

Name/Sponsor	ARTA	3rd agent	Design (n)
AMPLITUDE	Abiraterone	Niraparib	Randomized, HRR+ (788)
TALAPRO-3	Enzalutamide	Talazoparib	Randomized HRR+ (550)
City of Hope PCF	Abiraterone	Talazoparib	Single arm, Unselected (70)
PSMAddition	Lu177-PSMA-617	Any ARTA	Randomized, PSMA PET + (1126)
KEYNOTE-991	Enzalutamide	Pembrolizumab	Randomized (1232)
NCT03951831	n/a (ADT + Doce)	Cemiplimab	Single arm (20)
MSKCC	Abi/Enza	Atezolizumab	SBRT, Single arm (44)
CABIOS	Abiraterone	Cabozantinib, Nivolumab	Single arm (22)
CASCARA (U Minn)	Abiraterone	Cabazi + Carbo	Single arm (60)
Capitello-281	Abiraterone	Capivasertib	Randomized, PTEN def (1000)
CYCLONE-3	Abiraterone	Abemaciclib	Randomized, unselected (900)

Metastatik Kastrasyona Duyarlı Prostat Kanseri Tedavi



Metastatik Kastrasyona Duyarlı Prostat Kanseri Tedavi

National Comprehensive Cancer Network®

NCCN Guidelines Version 1.2025
Prostate Cancer

NCCN Guidelines Index
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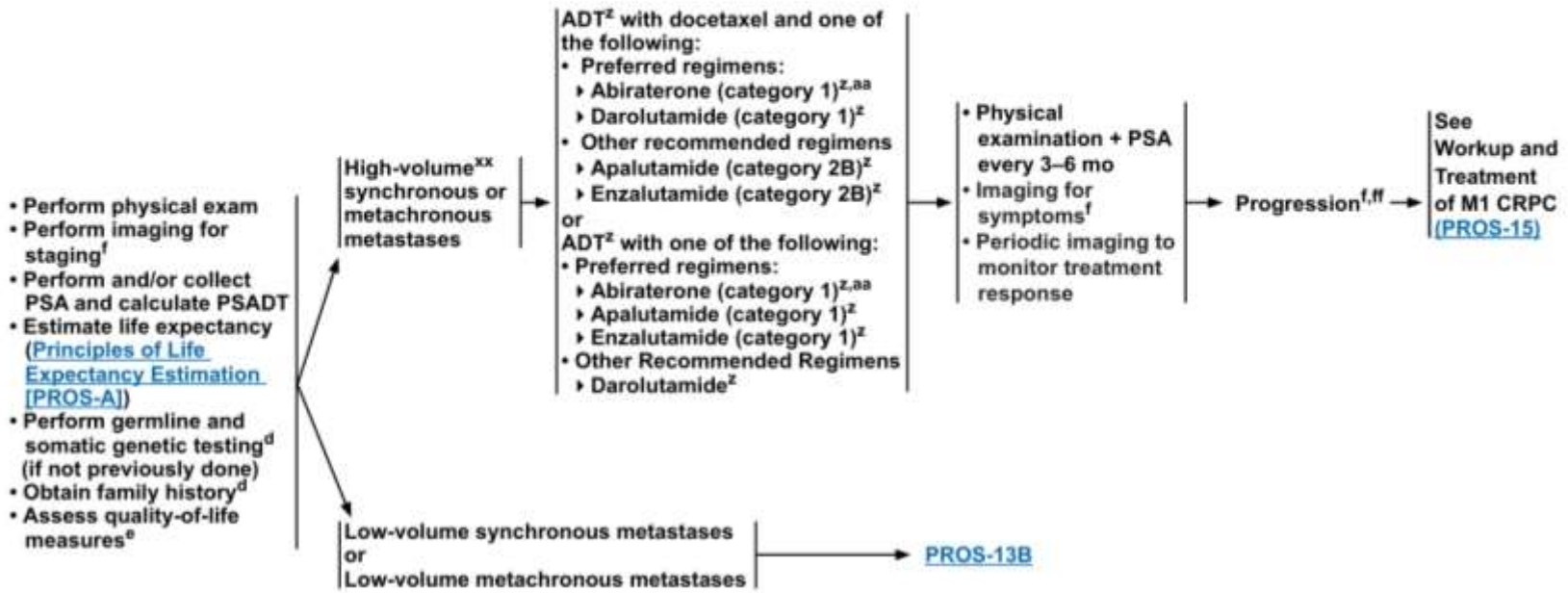
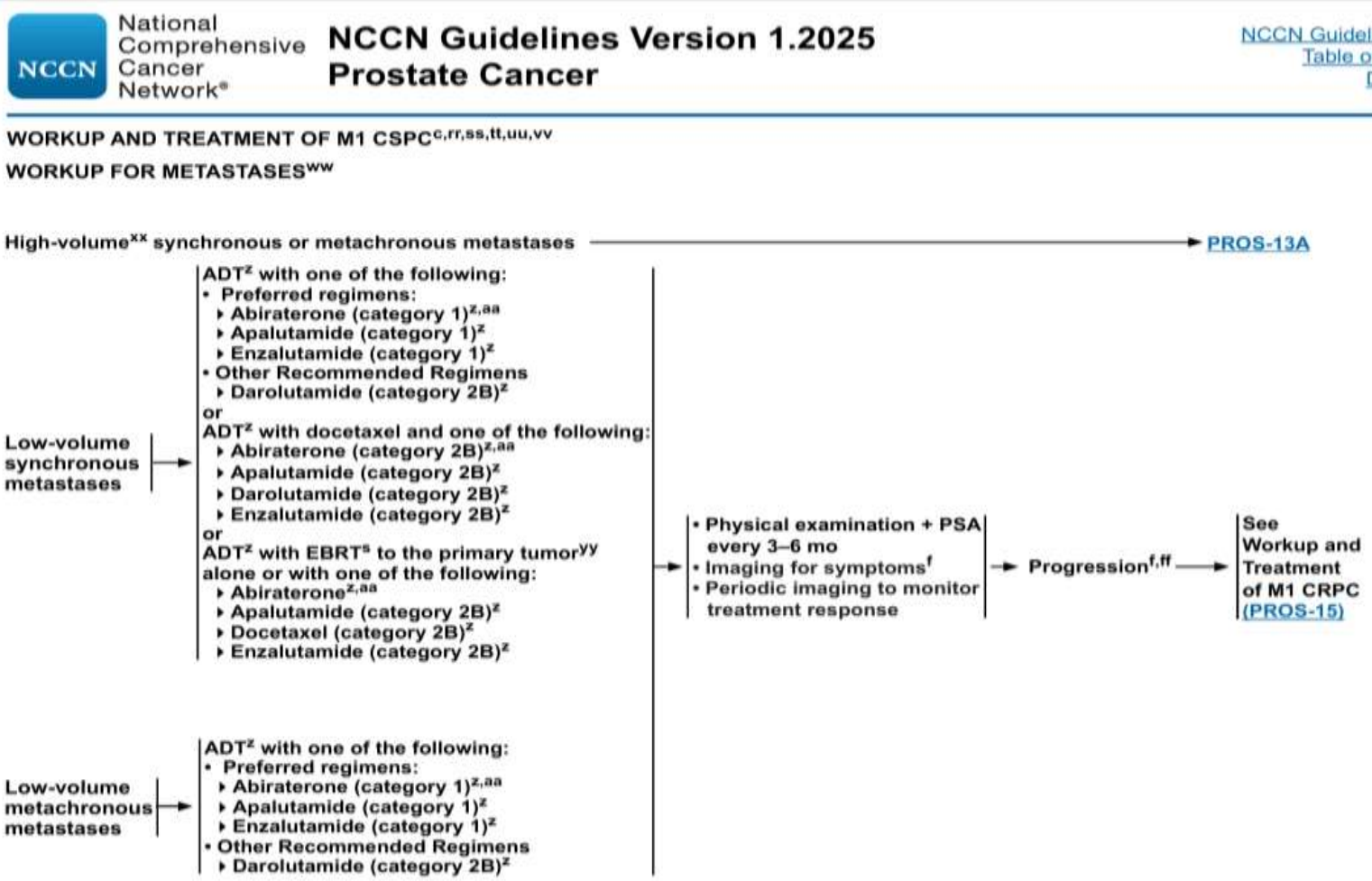
Discussion

WORKUP AND TREATMENT OF M1 CSPC[c,rr,ss,tt,uu,vv]

WORKUP FOR METASTASES[ww]



Metastatik Kastrasyona Duyarlı Prostat Kanseri Tedavi



Tedavi Kararında Etkili Faktörler

Hastalıkla İlişkili Faktörler

1- Yüksek volüm/Düşük volüm

2- Denovo/metakron metastaz

3-Metastaz bölgesi

4-Gleason skoru

5-Primer tümörün genetik profil

Klinik Faktörler

1-Semptomatik olması

2-ECOG PS

3-Ek hastalıklar

4-Başka hastalıklar için aldığı tedaviler

5-Hastalık için daha önce aldığı tedaviler

Başlanacak tedavi ile ilgili faktörler

1-Uygulama şekli

2-Etki etme mekanizması

3- Yan etkileri

4-İlaç etkileşimi

5-Tedavi maliyeti

Sonuç

- ADT+yeni nesil androjen yolağı inhibitörü/ ADT+yeni nesil androjen yolağı+dosetaksel karşılaştırması yok
- Üçlü tedavi

Viseral metastaz, de novo, yüksek volüm, genç, yaşam beklentisi uzun hastalarda ön planda düşünülebilir

Karaciğer metastazı gibi kötü seyirli hastalarda dörtlü kombinasyon? Daha çok veriye ihtiyaç var

- İkili kombinasyon

CHARTED kriterlerine göre düşük volüm, metakron metastaz, non-regioneal lenf nodu, akciğer metastazı olan hastalarda ikili kombinasyon düşünülebilir

- Yeni nesil androjen yolağı inhibitörü, hastanın ek hastalığı, ilaç etkileşimi ve yan etki profiline göre seçilmesi önerilir
- Genomik profilleme tedavi seçiminde etkili olacak.
- Gelecek dönem PSA yanıtına göre tedavi yoğunluğunda azaltma ya da yoğunluğunu artırma bir seçenek olabilir