Oligometastatik Prostat Kanseri

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Bakırköy Dr. Sadi Konuk Eğitim ve Araştırma Hastanesi
Tıbbi Onkoloji

Prostat Kanseri İnsidans ve Mortalite

	Common Types of Cancer	Estimated New Cases 2015	Estimated Deaths 2015
1.	Breast Cancer (Female)	231,840	40,290
2.	Lung and Bronchus Cancer	221,200	158,040
3.	**Prostate Cancer**	**220,800**	**27,540**
4.	Colon and Rectum Cancer	132,700	49,700
5.	Bladder Cancer	74,000	16,000
6.	Melanoma of the Skin	73,870	9,940
7.	Non-Hodgkin Lymphoma	71,850	19,790
8.	Thyroid Cancer	62,450	1,950
9.	Kidney and Renal Pelvis Cancer	61,560	14,080
10.	Endometrial Cancer	54,870	10,170

Prostate cancer represents 13.3% of all new cancer cases in the U.S.

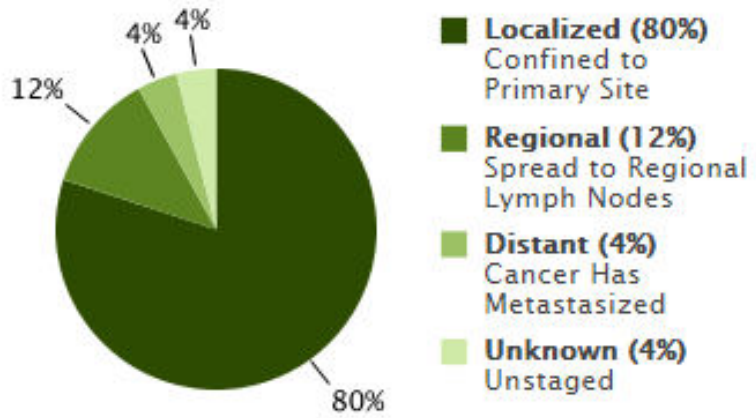
13.3%

In 2015, it is estimated that there will be 220,800 new cases of prostate cancer and an estimated 27,540 people will die of this disease.

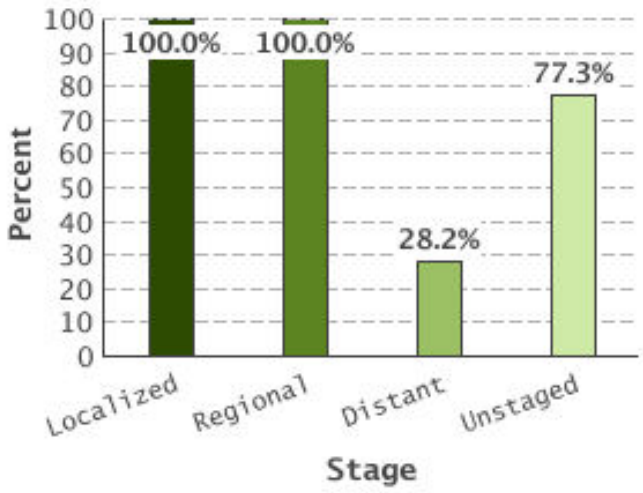
Prostat Kanseri İnsidans ve Mortalite

Percent of Cases & 5-Year Relative Survival by Stage at Diagnosis: Prostate Cancer

Percent of Cases by Stage

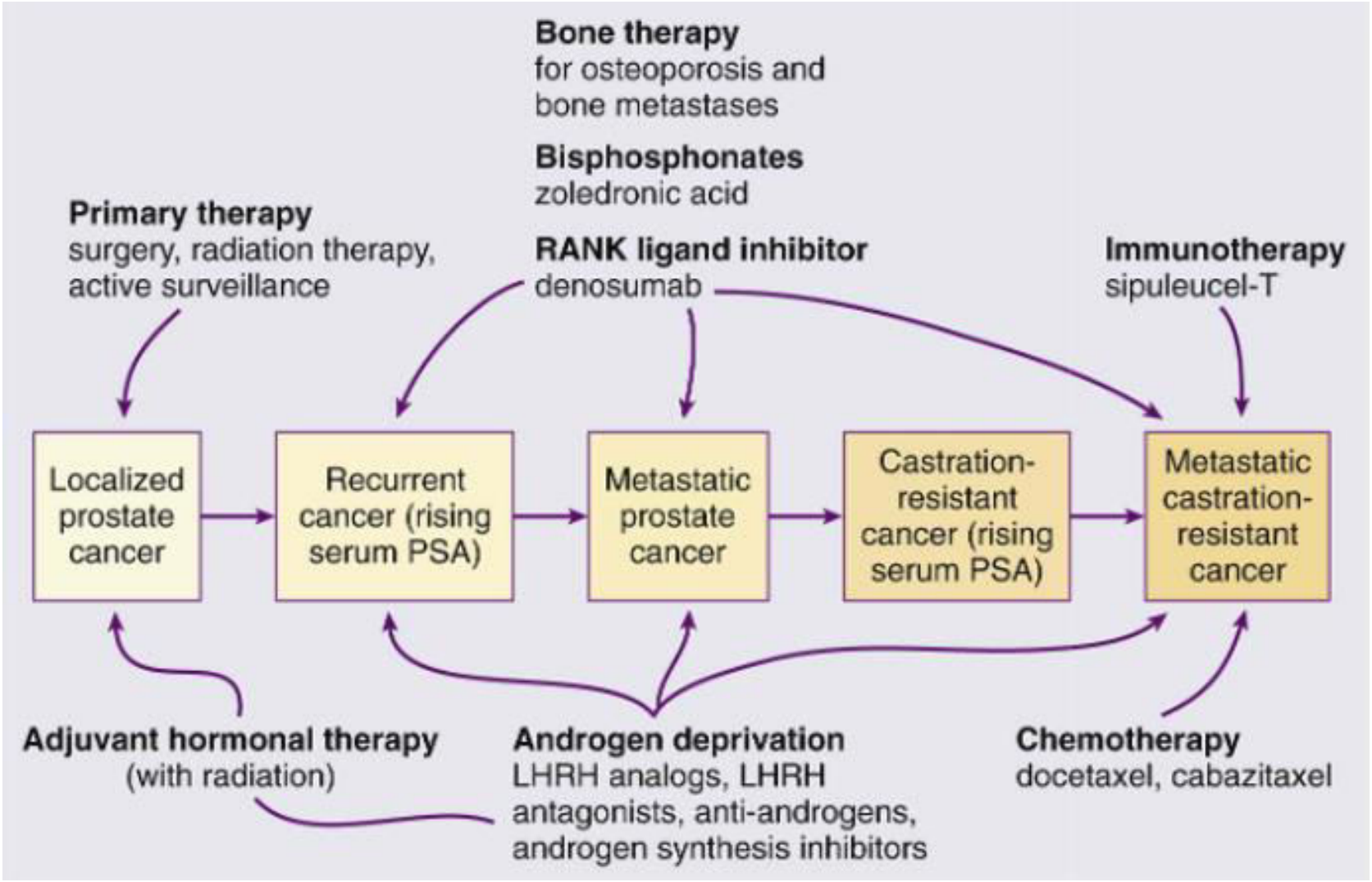


5-Year Relative Survival



SEER 18 2005-2011, All Races, Males by SEER Summary Stage 2000

Prostat Kanseri Tedavi Yaklaşımları



Şekil; Abeloff's Clinical Oncology, 10th edition

OLİGOMETASTATİK HASTALIK

Oligometastatik Hastalık[1]

Hellman ve arkadaşları tarafında 1995 yılında tanımlanmış

- Primer tümör tedavi edilmemiş
- Senkron metastaz saptanan
- metastaz bölgesi sayısı 5≤ olan hasta grubu

Oligorekürrens Hastalık[2]

Niibe ve arkadaşları tarafından 2010 yılında tanımlanmış

- Primer tümör tedavi edilmiş
- Metakron metastaz gelişen
- Metastaz bölgesi sayısı 5≤ olan hasta grubu

1. J Clin Oncol. 1995;13:8-10 2.Jpn J Clin Oncol 2010;40:107–111

OLİGOMETASTATİK HASTALIK

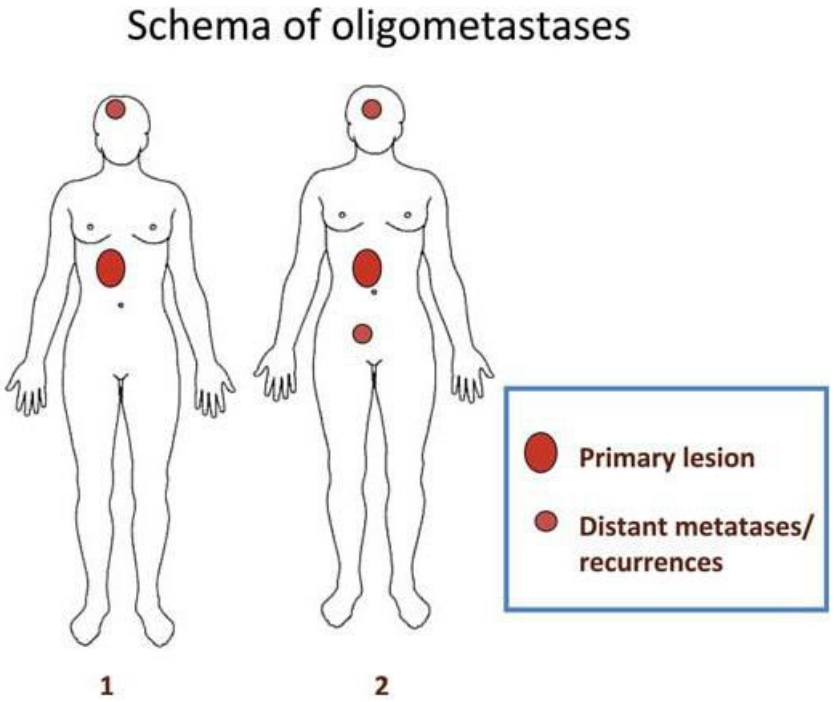


Figure 1. This is a schema of oligometastases. Schema 1 shows one distant metastasis/recurrence with a primary lesion. Schema 2 shows two distant metastases/recurrences with a primary lesion.

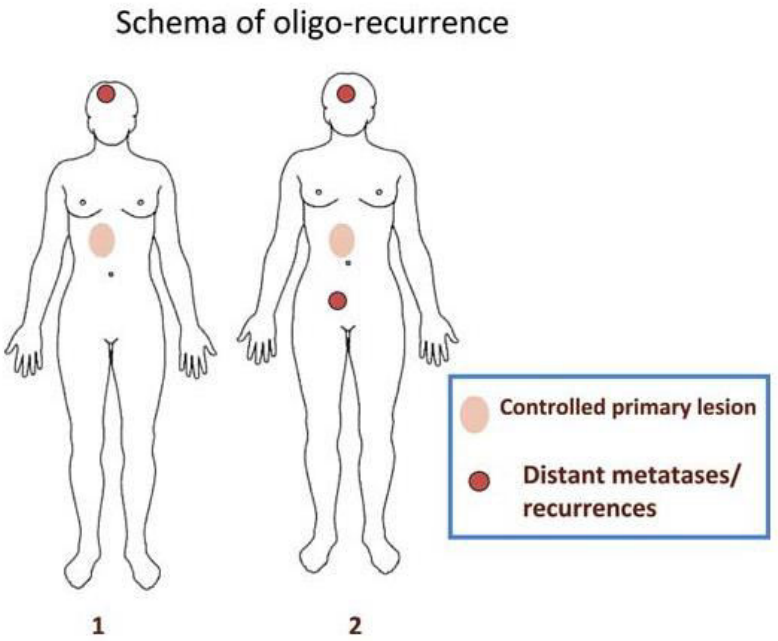


Figure 2. This is a schema of oligo-recurrence. Schema 1 shows one distant metastasis/recurrence with a controlled primary lesion. Schema 2 shows two distant metastases/recurrences with a controlled primary lesion. The biggest difference between oligometastases and oligo-recurrences lies in the uncontrolled or controlled primary lesion. Oligo-recurrence requires a controlled primary lesion.

Niiebe etal. Jpn J Clin Oncol 2010;40:107–111

OLİGOMETASTATİK HASTALIK NEDEN ?
NASIL? TEDAVİ

Amaç

- Progresyona kadar geçen süreyi uzatmak
- Tam kür elde etmek
- Tümör yükünü azaltmak
- Primer tümör odağından kaynaklanan yayılımı engellemek
- Obstrüktif üropatiyi engellemek

Tedavi

Primer ve metastik bölgeye yönelik olarak

- Cerrahi
- RT(SABRT vb)
- RFA

Oligometastatik Prostat Kanseri Tanımı

Study Group (ClinicalTrials.gov Identifier/ISRCTN Number)	Number of Metastases	Site of Metastases	Imaging Modality
University of Florida (NCT01859221)	NS	Any except brain or CNS	—
Sunnybrook Health Sciences Centre (NCT02563691)	≤ 5	Outside the prostate and pelvic LNs	—
Sidney Kimmel Comprehensive Cancer Center (NCT02489357)	≤ 4	Extrapelvic	—
Mayo Clinic (NCT01777802)	≤ 3	NS	—
Grupo de Investigación Clínica en Oncología Radioterapia (NCT02192788)	≤ 4	Bone, LN	—
University Hospital, Ghent (NCT01558427)	≤ 3	NS (N, M1a/b)	—
Technische Universität Dresden (NCT02264379)	≤ 5	NS	—
City of Hope Medical Center (NCT00544830)	≤ 5	NS (N1–3, M1)	—
Memorial Sloan Kettering Cancer Center (NCT02020070)	≤ 10	Bone, LN	—
Sidney Kimmel Comprehensive Cancer Center (ORIOLE) (NCT02680587)	≤ 3	Bone, LN	—
MD Anderson Cancer Center (NCT01751438)	NS	Any except brain or CNS	Bone scan, CT scan, and/or MRI
Martini-Klinik am UKE GmbH (NCT02454543)	≤ 5	Bone, LN	—
Oxford University Hospitals (ISRCTN15704862)	NS	Bone, LN	—
University Hospital, Ghent (NCT02138721)	NS	Any except brain or CNS	—

CNS = central nervous system; LN = lymph node; NR = not reported; NS = not specified.

Oligometastatik Prostat Kanseri Tanımı

Studies	n	Number of Metastases	Site of Metastases	Imaging Modality
Tabata et al[81]	35	≤ 5	Bone only; each site < 50% size of vertebral body	Bone scan
Ahmed et al[82]	17	≤ 5	NS	^{11}C-choline PET/CT, MRI, biopsy, CT, and ^{11}C-choline PET/CT + MRI
Berkovic et al[83]	24	≤ 3	Bone, LN	Bone scan + ^{18}F-FDG PET/CT, bone scan + ^{11}C-choline PET/CT
Schick et al[84]	50	≤ 4	NS	Bone scan + ^{18}F-choline PET/CT, bone scan + ^{11}C-acetate PET/CT
Decaestecker et al[85]	50	≤ 3	Bone, LN	^{18}F-FDG PET/CT, ^{18}F-choline PET/CT
Ost et al[66]	119	≤ 3	Any	^{18}F-FDG PET/CT, ^{18}F-choline PET/CT

FDG = fluorodeoxyglucose; LN = lymph node; NS = not specified; PET = positron emission tomography.

http://www.cancernetwork.com

OLİGOMETASTATİK HASTALIK

Metastatik bölge kanser hücre klonları

Copy number analysis indicates monoclonal origin of lethal metastatic prostate cancer

Wennuan Liu[1,9], Sari Laitinen[2,9], Sofia Khan[3], Mauno Vihinen[3], Jeanne Kowalski[4], Guoqiang Yu[5], Li Chen[5], Charles M Ewing[6], Mario A Eisenberger[7], Michael A Carducci[7], William G Nelson[7], Srinivasan Yegnasubramanian[7], Jun Luo[6,7], Yue Wang[5], Jianfeng Xu[1], William B Isaacs[6,7], Tapio Visakorpi[2] & G Steven Bova[6–8]

NATURE MEDICINE VOLUME 15 | NUMBER 5 | MAY 2009

30 hastada otopsi sonrası yapılan genetik incelemede, metastatik bölge klonları, primer tümör ile benzer özelikler göstermektedir.

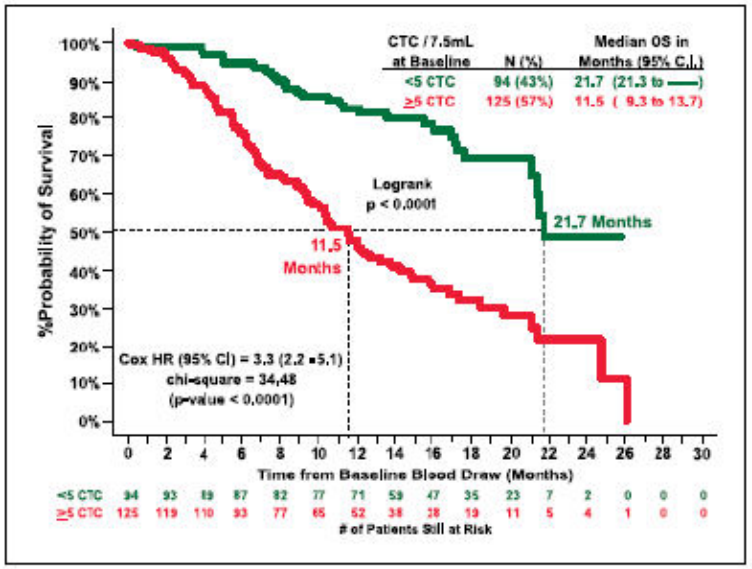
OLİGOMETASTATİK HASTALIK

Circulating Tumour Cells

Circulating Tumor Cells Predict Survival Benefit from Treatment in Metastatic Castration-Resistant Prostate Cancer

Johann S. de Bono,[1] Howard I. Scher,[2] R. Bruce Montgomery,[3] Christopher Parker,[1] M. Craig Miller,[4] Henk Tissing,[4] Gerald V. Doyle,[4] Leon WW.M. Terstappen,[4] Kenneth J. Pienta,[5] and Derek Raghavan[6]

Clin Cancer Res 2008;14(19) October 1, 2008



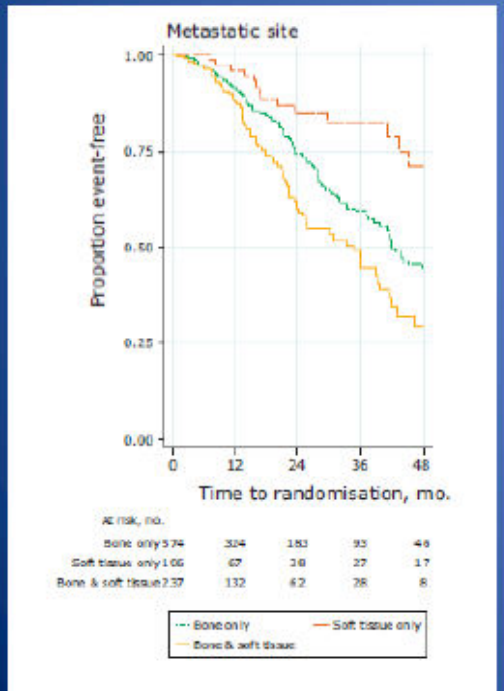
231 prosta kanserli hasta CTC düzeyi düşük olanların prognozu daha iyi

OLİGOMETASTATİK HASTALIK

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

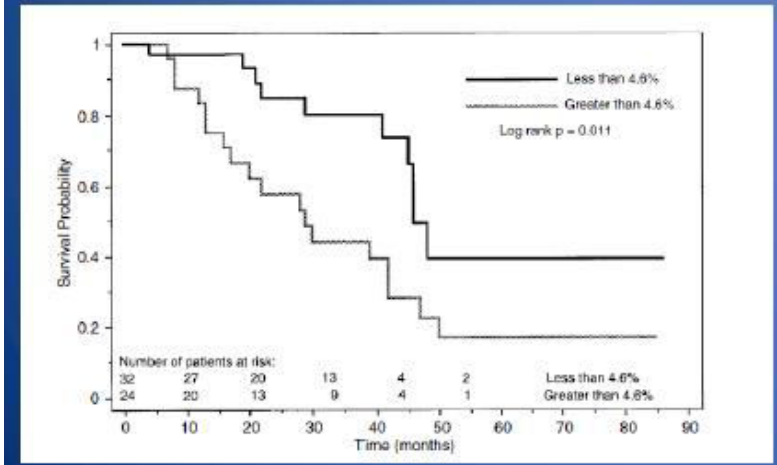
OLİGOMETASTATİK HASTALIK

Percentage of the positive area of bone metastasis is an independent predictor of disease death in advanced prostate cancer

M Noguchi[a,1], H Kikuchi[1], M Ishibashi[2] and S Noda[1]

[1]Department of Urology, 67 Asahi-machi, Kurume University School of Medicine, Kurume, Fukuoka, Japan; [2]Division of Nuclear Medicine and Department of Radiology, 67 Asahi-machi, Kurume University School of Medicine, Kurume, Fukuoka, Japan

British Journal of Cancer (2003) 88, 195–201



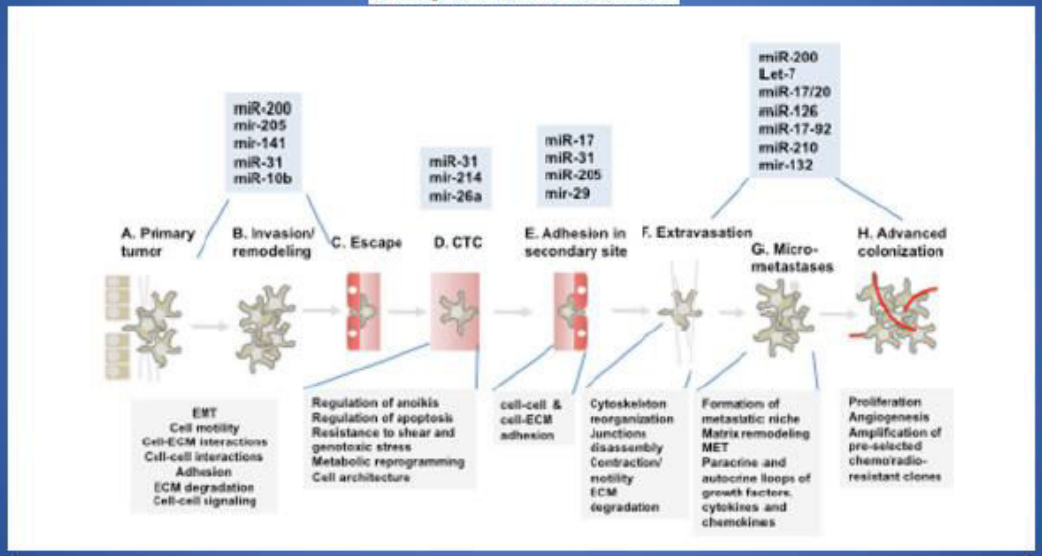
- Retrospective analysis of 56 men with bone mets
- %PABS is an independent predictor of disease-specific survival

OLİGOMETASTATİK HASTALIK

Towards a molecular basis of oligometastatic disease: potential role of micro-RNAs

Abhineet Uppal · Mark K. Ferguson · Mitchell C. Posner · Samuel Hellman · Nikolai N. Khodarev · Ralph R. Weichselbaum

Clin Exp Metastasis (2014) 31:735–748



34 hastanın, 42 tümör örneğinde 39 miRNA belirteciyle yapılan çalışmada, oligometastaz ve polimetastatik hastalığın bir birinden farklı olduğu saptanmıştır.

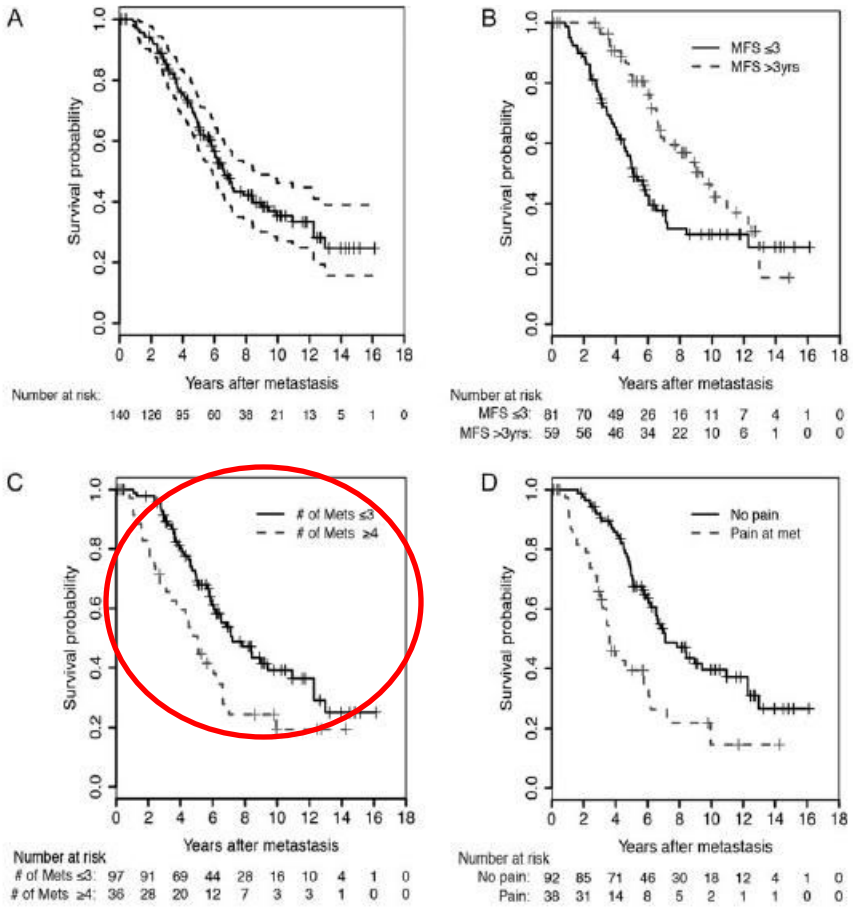
Tanı Anında Tümör Yükü Sağkalım İle İlişkili

Annals of Oncology 24: 2881–2886, 2013
doi:10.1093/annonc/mdt335
Published online 14 August 2013

Metastasis-free survival is associated with overall survival in men with PSA-recurrent prostate cancer treated with deferred androgen deprivation therapy

M. T. Schweizer[1], X. C. Zhou[1], H. Wang[1], T. Yang[1], F. Shaukat[1], A. W. Partin[2], M. A. Eisenberger[1] & E. S. Antonarakis[1]*

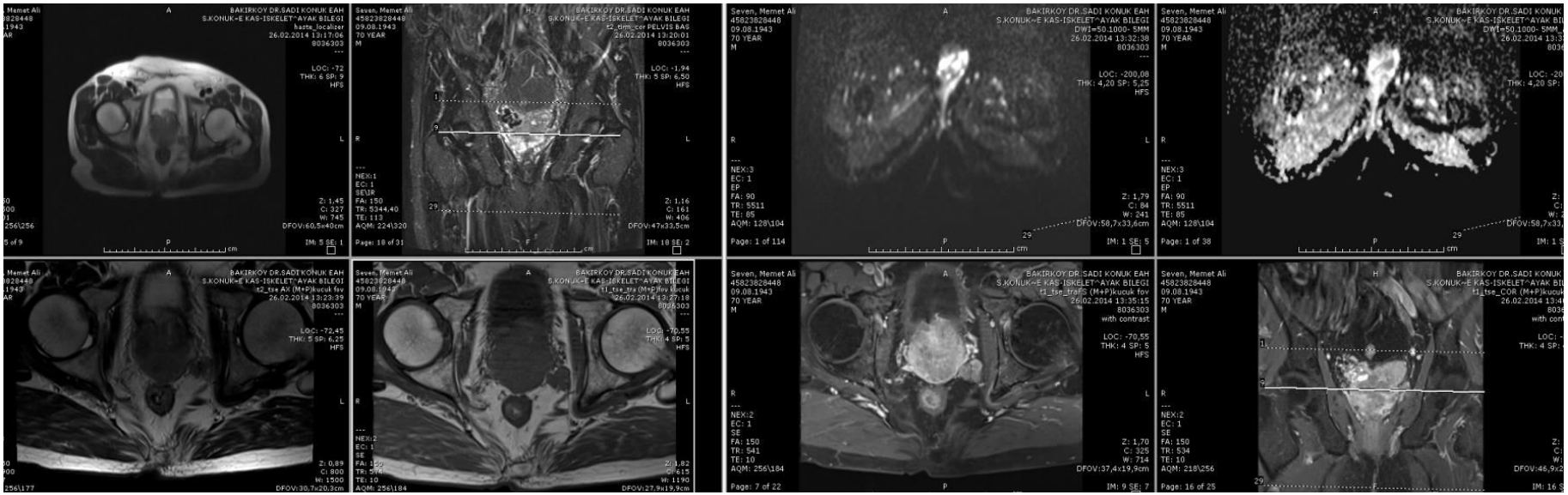
[1]*Sidney Kimmel Comprehensive Cancer Center;* [2]*Brady Urological Institute, Johns Hopkins University, Baltimore, USA*



Vaka Sunumu

- 73 yaşında erkek hasta
- Bilinen hastalık öyküsü; KAH
- Aile öyküsü yok
- Sürekli kullandığı ilaç; Ecoprine 100 mg/gün
- Operasyon öyküsü yok
- 35 yıl paket sigara içmiş
- 11/2013 tarihinde ; idrar yaparken zorlanma şikayeti ile başvurmuş
- PSA : 37 ng/ml

02/2014 Alt Batın-Pelvik MR

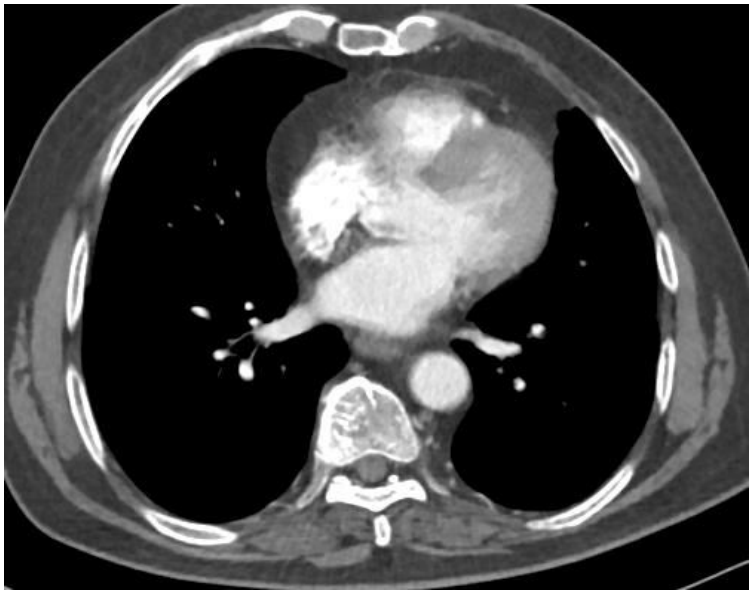


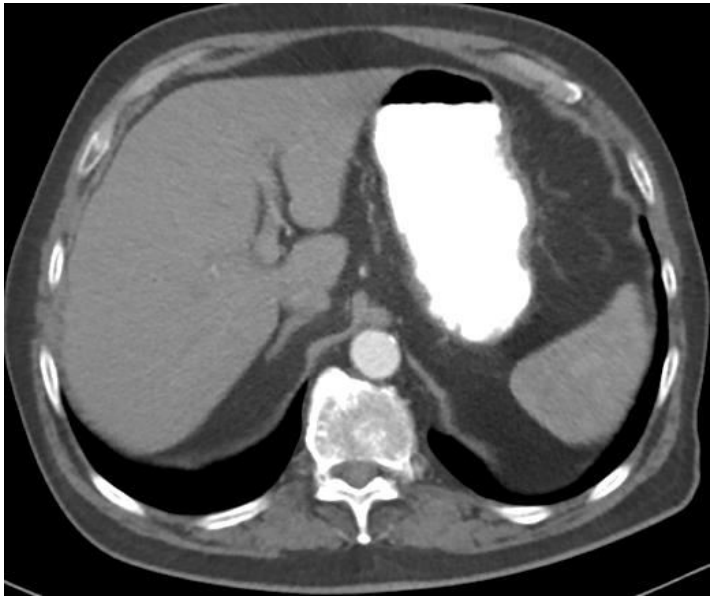
02/2014 Alt Batın-Pelvik MR

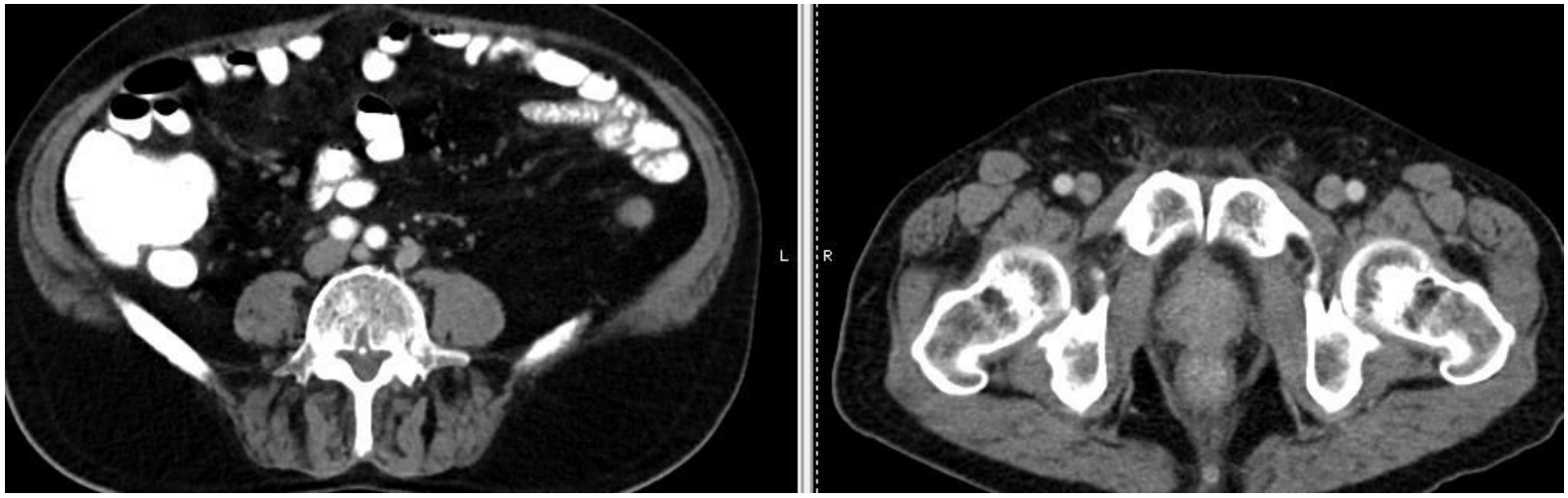
HİZMET ADI : Mr Diğer

Kontrastlı - Nonkontrast Prostat mrg tetkiki
Klinik bilgi:
Teknik: endorektal coıl kullanılarak t2a tse aksial, sagittal ve koronal sekanslar alındı.
Bulgular:
Mesane küçük görünümdedir. Mesane trabekülasyonunda artış saptandı.
Prostat transvers çapı 54,7mm, ön-arka çapı 49mm, kranio-kaudal çapı 42mm ölçüldü. T2 görüntülerde prostat gland heterojen yapıda izlendi. ADC haritasında prostat posterior kesimde periferik zonda, transvers çapı 44,7mm, ön-arka çapı 31,6mm olan lezyon izlenmektedir. Bu görünüm prostat tümörü şeklinde değerlendirilmiştir.
Kontrastlı incelemede prostat gland heterojen kontrast tutulumu göstermektedir. Bu düzeyde prostat ile seminal vezikül arasındaki yağlı plan obliteredir. Prostat gland muhtemelen sol seminal veziküle invazyon göstermektedir. Prostatın hemen sol lateral kesimi komşuluğunda, ADC haritasında hipointens görünümde, kontrastlı incelemede kontrast tutulumu gösteren, yaklaşık 24x20mm boyutunda konglemere lenf nodu ile uyumlu görünüm saptandı.
Sağda seminal veziküller düzeyinde T1 görüntülerde belirgin hiperintens, T2 görüntülerde hafif hipointens, yağ baskılı T2 görüntülerde hipointensite ile karakterize hemoraji ile uyumlu olabilecek görünüm saptandı.
Aksial kesitlerde sağda asetabulum posterior kesimi düzeyinde, sol femur başı inferioru düzeyinde, T1 görüntülerde hipointens, T2 görüntülerde sağ asetabulumdaki net olarak seçilememekle birlikte, sol femur başı düzeyindeki hafif hiperintens, kontrastlı incelemede her ikisinde de kontrast tutulumunun izlendiği 2 adet kemik lezyonu saptandı. Bu görünümler ilk planda metastazı düşündürmektedir. Gerekirse ileri inceleme önerilir.
Solda pelvis superiorunda, iliak damar komşuluğunda, uzun çapı 11,2mm olan lenf nodu izlendi.

02/2014 Toraks-Batın BT







02/2014 Toraks-Batın BT

Oral ve IV Kontrastlı Üst ve Alt Abdominal BT İncelemesinde:

Görüntü alanına giren torakal kesitlerde T10 vertebra korepsudan santral yerleşimli milimetrik sklerotik dansite artışı izlenmektedir.

İlaveten T10 vertebra korpusu sağ yarımından sağ pedinkülüne doğru uzanım gösteren sklerotik dansite artışı izlenmektedir. PET BT ile ek değerlendirme önerilir.

Karaciğer kontur ve boyutları normal, parankim dansitesi homojendir. **Karaciğer sol lob segment 4 te yakalşık 8mm ebadında kalsifikasyon izlenmektedir.**

Portal ve hepatik venler normal görünümdedir. İntrahepatik safra yolları ve koledok normaldir.

Safra kesesi lümeni ve duvar yapısı normaldir.

Pankreas baş ve gövde proksimali normal görünümdedir.

Dalak boyut ve parankim dansitesi normal görünümdedir.

Bilateral böbrek kontur, boyut ve parankim dansiteleri normaldir.

Bilateral surrenal lojları normaldir.

Abdominal aortada ve dalları normaldir.

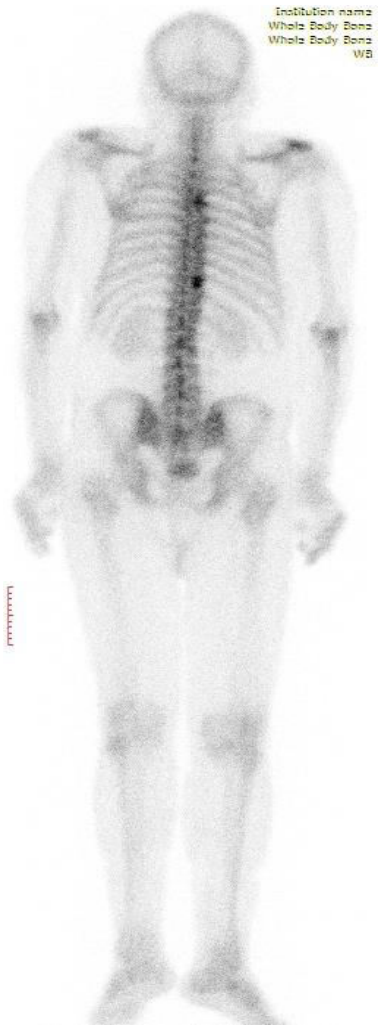
Sol ana iliak arter komşuluğunda , sol derin iliak arter komşuluğunda , sol obduratör zincirde büyüğü yaklaşık 8* 13.5mm ebatlerında multipl LAP kitleleri izlenmektedir.

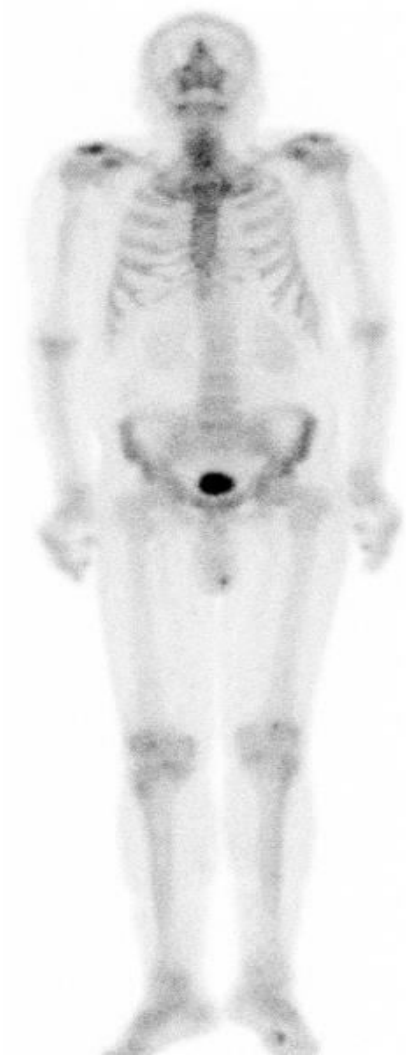
Batında serbest sıvı ve kitle izlenmemiştir.

Mesane duvar ve lümen görünümü normaldir.

Prostat bezi boyutları normaldir.

02/2014 TVS





02/2014 TVS

HİZMET ADI : Tüm Vücut Kemik Sintigrafisi

TÜM VÜCUT KEMİK SİNTİGRAFİSİ

Tc99m-MDP İV enjeksiyonundan 4 saat sonra alınan tüm vücut, statik ve SPECT görüntülemede ;

Th 5. ve 10. vertebra sağ yarısında fokal artmış aktivite tutulumu izlenmektedir. Dejeneratif değişiklik Metastaz Radyolojik verifikasyonu uygun olur.

Sol ayak 1. falanksta öncelikle travmaya sekonder olduğu düşünülen hafif artmış aktivite tutulumu mevcuttur.

İskelet sistemi diğer alanlarında normal sınırlarda tutulum izlenmektedir.

02/2014 Prostat Biyopsisi

Klinik Bulguları :
Klinik Tanı : PSA : 34
Materyal Alım Şekli : TRU - CUT
Materyal Cinsi : PROSTAT

RAPOR BİLGİLERİ
– Patoloji Sonucu –
Makroskopik Bulgular : 1 - SOL FARLATERAL KAYITLI ; 1.3X0.1 CM ÖLÇÜLERİNDE DOKU ÖRNEĞİNİN TAMAMI 1K.
2 - SOL DORSOLATERAL KAYITLI : 1.3X0.1 CM ÖLÇÜLERİNDE DOKU ÖRNEĞİNİN TAMAMI 1K.
3 - SOL MEDİAL KAYITLI : 1.5X0.1 CM ÖLÇÜLERİNDE DOKU ÖRNEĞİNİN TAMAMI 1K.
4 - SOL BAZİS KAYITLI : 1.2X0.1 CM ÖLÇÜLERİNDE DOKU ÖRNEĞİNİN TAMAMI 1K.
5 - SOL APEKS KAYITLI : 0.5X0.1 CM ÖLÇÜLERİNDE DOKU ÖRNEĞİNİN TAMAMI 1K.
6 - SAĞ FARLATERAL KAYITLI : DOKU İZLENMEDİ
7 - SAĞ DORSOLATERAL KAYITLI : 1X0.1 CM ÖLÇÜLERİNDE DOKU ÖRNEĞİNİN TAMAMI 1K.
8 - SAĞ MEDİAL KAYITLI : 0.3X0.1 CM ÖLÇÜLERİNDE DOKU ÖRNEĞİNİN TAMAMI 1K.
9 - SAĞ BAZİS KAYITLI : 1X0.1 CM ÖLÇÜLERİNDE DOKU ÖRNEĞİNİN TAMAMI 1K.
10 - SAĞ APEKS KAYITLI : 1X0.1 CM ÖLÇÜLERİNDE DOKU ÖRNEĞİNİN TAMAMI 1K.

Mikroskopik Bulgular :

Tanı : 1-3-4-5-7-8-9-10) PROSTAT İĞNE BİYOPSİLERİ;
PROSTATİK ASİNER ADENOKARSİNOM

- TÜMÖRÜN HİSTOLOJİK GRADE: PRİMER PATERN: 4
SEKONDER PATERN: 5
GLEASON SKOR: 9

- OLGUDAN ALINAN 9 ADET PROSTAT İĞNE BİYOPSİ ÖRNEKLERİNİN YAKLAŞIK %60-70' İ TÜMÖR İLE İNFİLTREDİR.
- TÜMÖRDE PERİNÖRAL İNVAZYON: MEVCUT
- TÜMÖRDE LENFOVASKÜLER İNVAZYON: SAPTANMADI

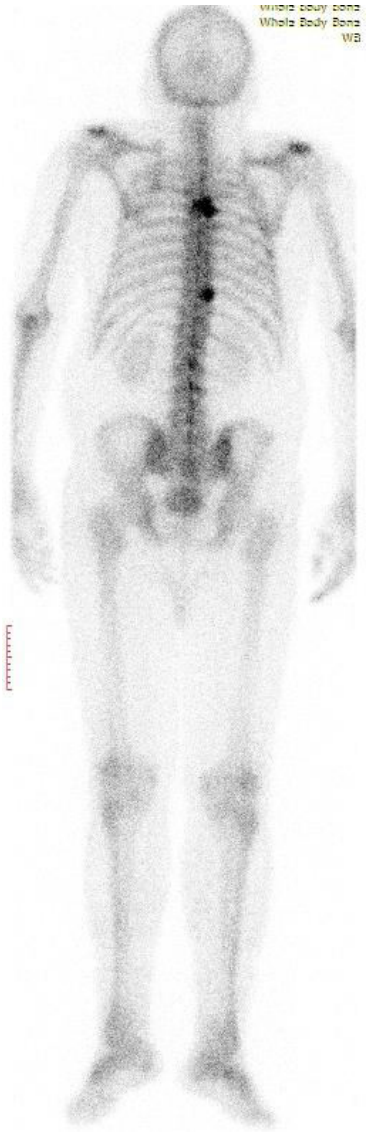
5-7-9) PROSTAT : İĞNE BİYOPSİ ÖRNEKLERİ : BENİGN PROSTAT DOKULARI

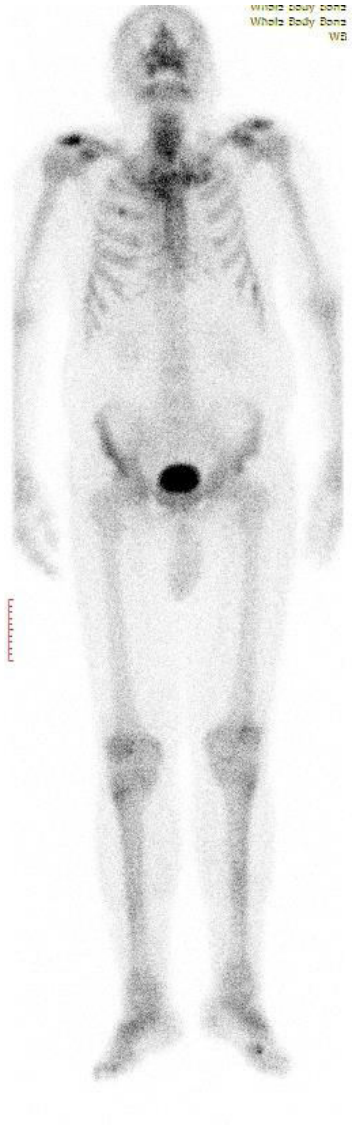
02/2014 Tedavi Başlanıyor

Hormona duyarlı metastatik prostat ca

- Bikalutamid 50mg/gün(14 gün)
- Leuprolid asetat 22.5

01/2015 TVS


Whole Body Bone
Whole Body Bone
WB


Whole Body Bone
Whole Body Bone
WB

01/2015 Tedavi Planı

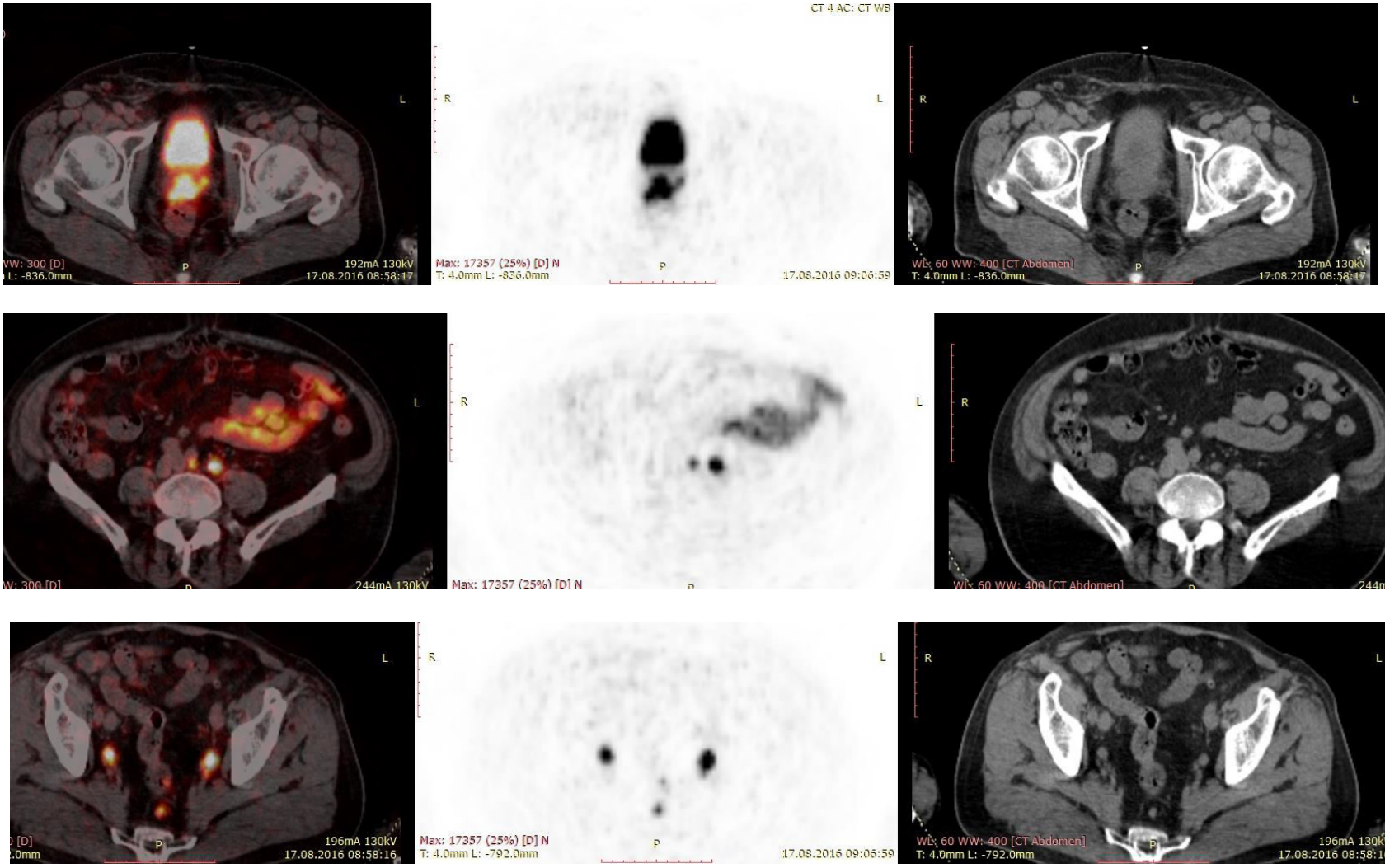
Sırt bölgesinde ağrı dışında şikayeti yok

ECOG PS 1

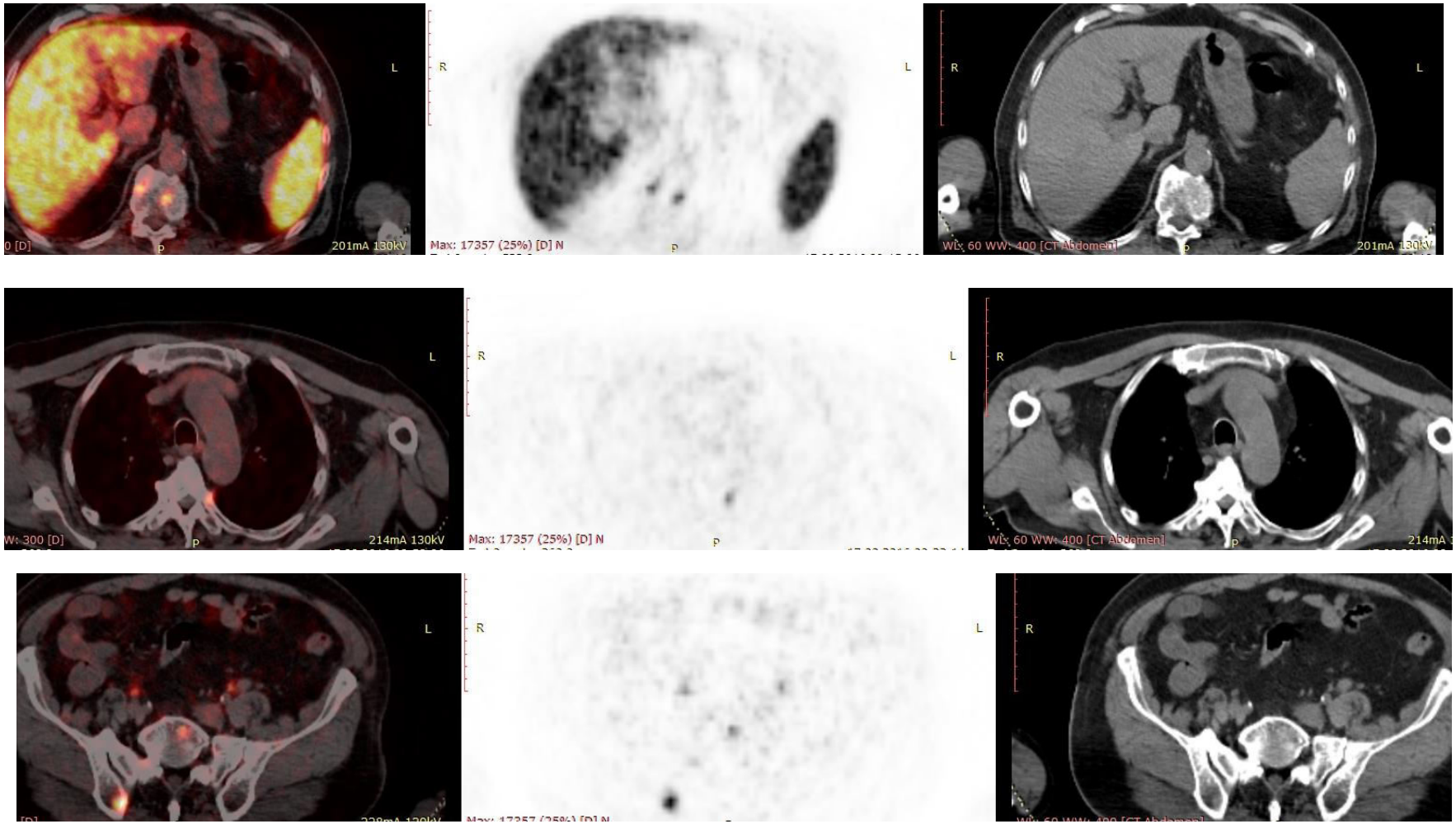
PSA?

- ❑ Bikalutamid 50mg/gün
- ❑ Leuprolid asetat 22.5
- ❑ Zoledronik asid 4 mg?
- ❑ Palyatif RT?

08/2016 Ga-68 PSMA PET/BT



08/2016 Ga-68 PSMA PET/BT



09/2016 Tedavi Planlaması

Çekim saati:8:56, Pozisyon sayısı:9 Pozisyon süresi:4 Dk,Çekim kapsama alanı: Pelvis Bölgesi, Geç Çekim saati: :, Pozisyon süresi: Dk, Pozisyon sayısı: ,BT parametreleri: mAs, Çekim alanı: Verteks
Serum PSA düzeyi:13,77 , Gleason skoru:4+5

BULGULAR:

Prostat apeksinden başlayarak bazise kadar uzanan santral yerleşimli multifokal görünümlü yoğun PSMA tutan nodüler odaklar izlenmektedir. Ayrıca presakral yağlı dokuda, bilateral internal iliak, bilateral common iliak ve bilateral distal paraaortik lenfatik istasyonlarda en büyüğünün boyutu 1.5 cm'ye ulaşan yoğun PSMA tutulum ile karakterize multipl lenfadenomegaliler izlenmiştir. Geri kalan infradiafragmatik - supradiafragmatik lenfatik istasyonlarda patolojik düzeyde PSMA tutan başka bir lenf nodu seçilememiştir.

Visseral organlarda fizyolojik sınırlarda radyofarmosötik dağılımı izlenmiştir.

İskelette muhtelif servikal, dorsal ve lomber vertebralarda, sol 4. kosta vertebral bileşkede, sol 8. kosta lateralinde, sol 11. kosta posteriorunda ve sağ iliak kemik posterior bölümünde intramedüller yerleşimli litik yapıda yoğun PSMA tutan multipl odaklar izlenmektedir.

Sonuç:

-Prostat lojunda nüks tümöral proses ile uyumlu yoğun PSMA tutulum odakları; muhtelif abdominopelvik lenfatik lojlarda metastatik karakterde yoğun PSMA tutan lenf nodları; iskelette yoğun PSMA tutulumu ile karakterize büyük çoğunluğu intramedüller yerleşimli yaygın metastatik odaklar saptanan Ga-68 PSMA PET/BT çalışması.

09/2016 PSA düzeyi

	Parametre Adı	Sonuc	Birim	Normal Değerler		Önceki Sonuc
↑	Glukoz	205	mg/dL	74	106	Grafik.
	Üre	45	mg/dL	16.6	48.5	Grafik.
	Ürik Asit	4.2	mg/dL	3,4	7	Grafik.
↑	Kreatinin	1.36	mg/dL	0.7	1.2	Grafik.
	eGFR	51.26	mL/min/1.7			Grafik.
CKD-EPI formülü kullanilarak hesaplanmistir.						
	AST	17	U/L	0	40	Grafik.
	ALT	10	IU/L	0	41	Grafik.
	GGT	20	U/L	5	36	Grafik.
↑	LDH	221	U/L	135	214	Grafik.
	ALP	57	U/L	40	120	Grafik.
	Total Protein	7	g/dL	6.4	8.3	Grafik.
	Albumin	4.18	g/dL	3.5	5.2	Grafik.
↑	Direkt Bilirubin	0.25	mg/dL	0	0,2	Grafik.
	Total Bilirubin	0.7	mg/dL	0	1,2	Grafik.
	İndirekt Bilirubin	0.45	mg/dL	0	1,2	Grafik.
	Kalsiyum	8.9	mg/dL	8.6	10.2	Grafik.
	Sodyum	142.4	mmol/L	136	145	Grafik.
	Potasyum	4.48	mmol/L	3.5	5.1	Grafik.
↓	Total Testosteron	0.38	ng/mL	1.32	8.92	Grafik.
↑	PSA	45.76	ng/mL	0	4	Grafik.

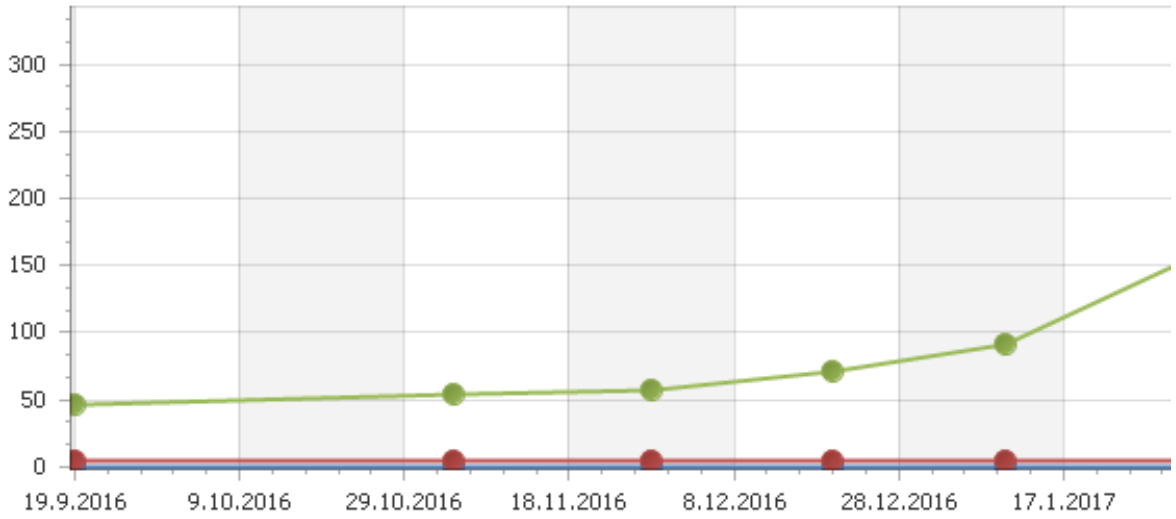
09/2016 Tedavi Değişikliği Yapılıyor

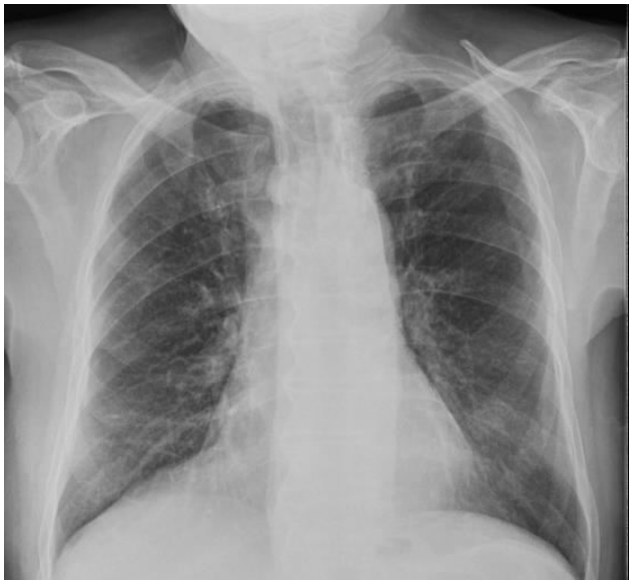
- ❑ Dositaksel
- ❑ Deltakortile 2x5 mg
- ❑ Zolendronik asid 4 mg
- ❑ Leuprolide acetate 22.5
- ❑ Palyatif RT

02/207 Tedaviye Yanıt Değerlendirmesi

- ❑ 6 kür KT sonrası nefes darlığı şikayeti başlıyor
- ❑ Günlük aktivitelerini yaparken zorlanma
- ❑ Sık kan transfüzyon ihtiyacı
- ❑ ECOG P2
- ❑ PSA düzeyinde artma
- ❑ Dış merkez BT akciğere yeni nodüller lezyonlar

02/207 Tedaviye Yanıt Değerlendirmesi

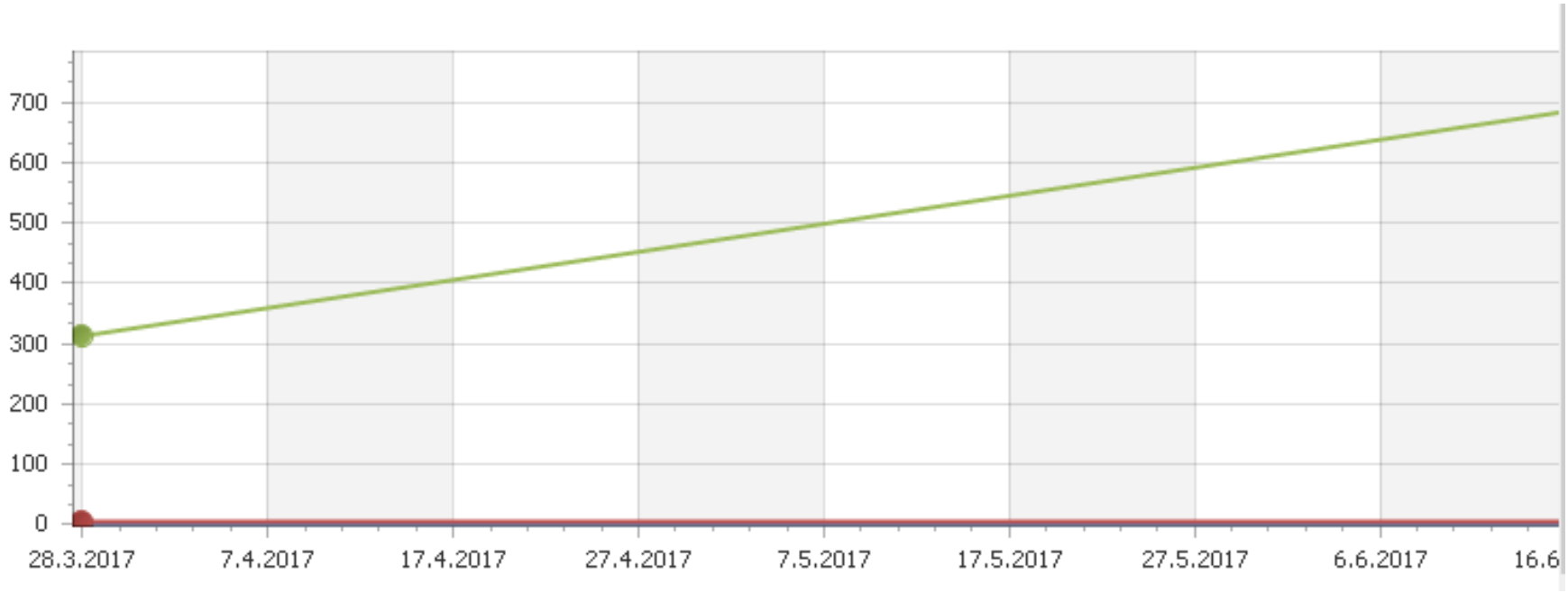




03/2017 Tarihinde Tedavi Değişikliği

- Enzalutamide(Xtandi) 160 mg/gün
- Zolendronik asid 4 mg
- Leuprolide acetate 22.5

Tedaviye Yanıt



Evreleme Nasıl Yapılmalı ?

- European Association of Urology(EUA)[1–2]
- National Comprehensive CancerNetwork(NCCN)[3]

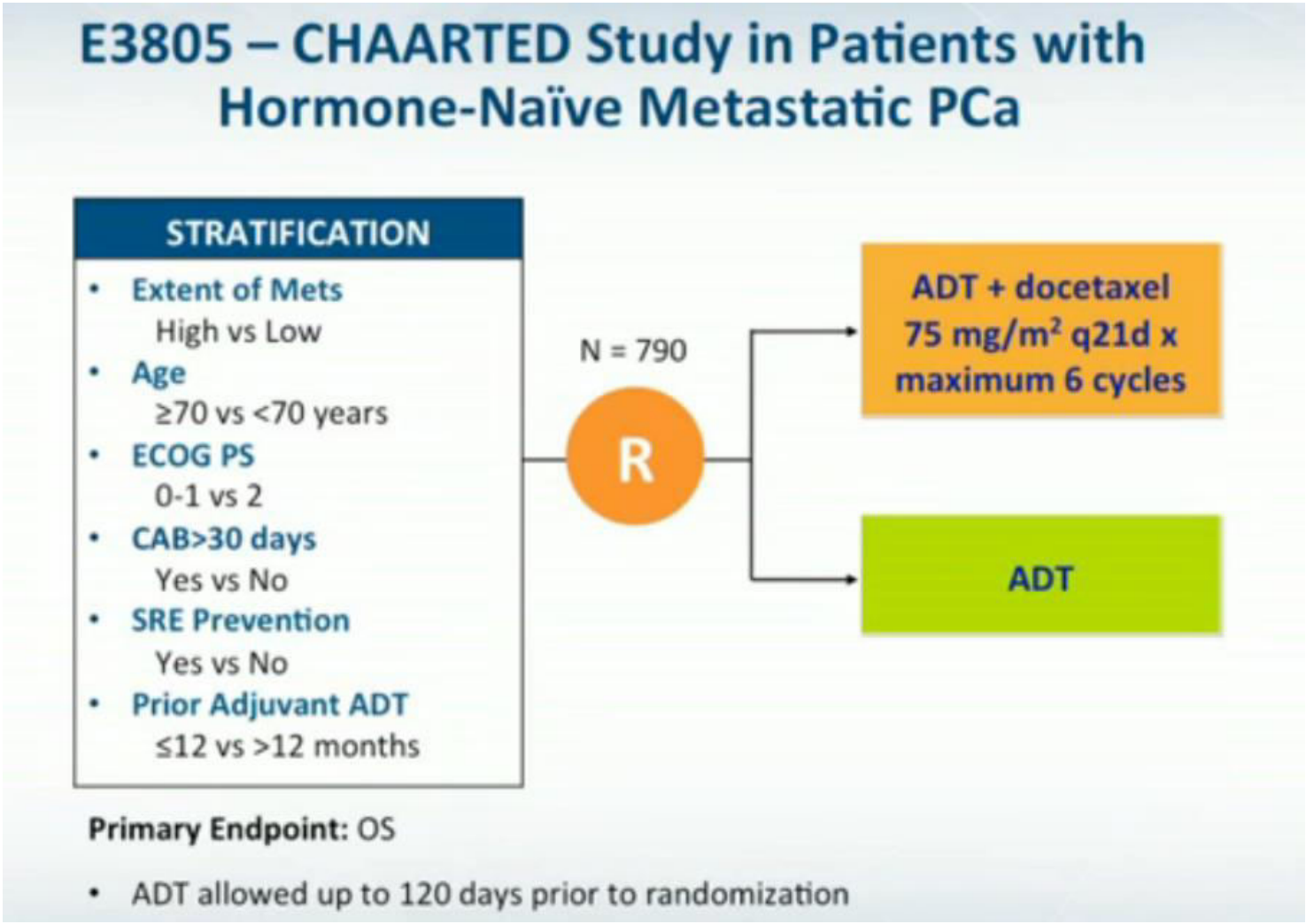
Kemik, viseral ve lenf nodu metastazı ve doğru evreleme için

- Bilgisayarlı Tomografi(BT)/ Manyetik Rezonans(MR)
- ^{99m}Tc- metilen difosfonat kemik sintigrafisi

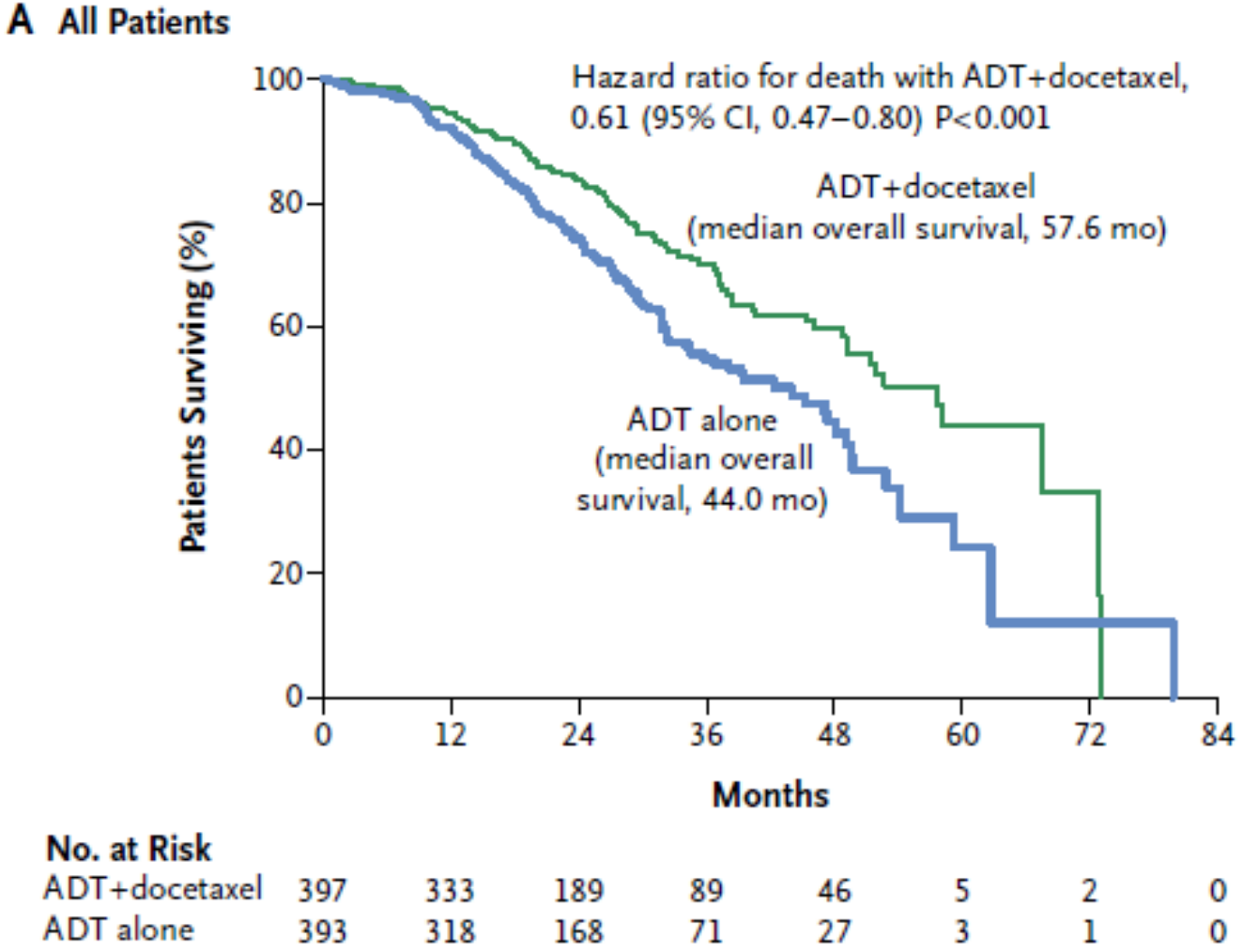
1. Heidenreich A. EAU guidelines on prostate cancer. Part I. Eur Urol. 2014
2. Heidenreich A. EAU guidelines on prostate cancer. Part II. Eur Urol. 2014
3. Mohler JL. Prostate cancer. Version 1.2016. J Natl Compr Canc Netw. 2016

Hormon Duyarlı Metastatik Prostat Kanseri

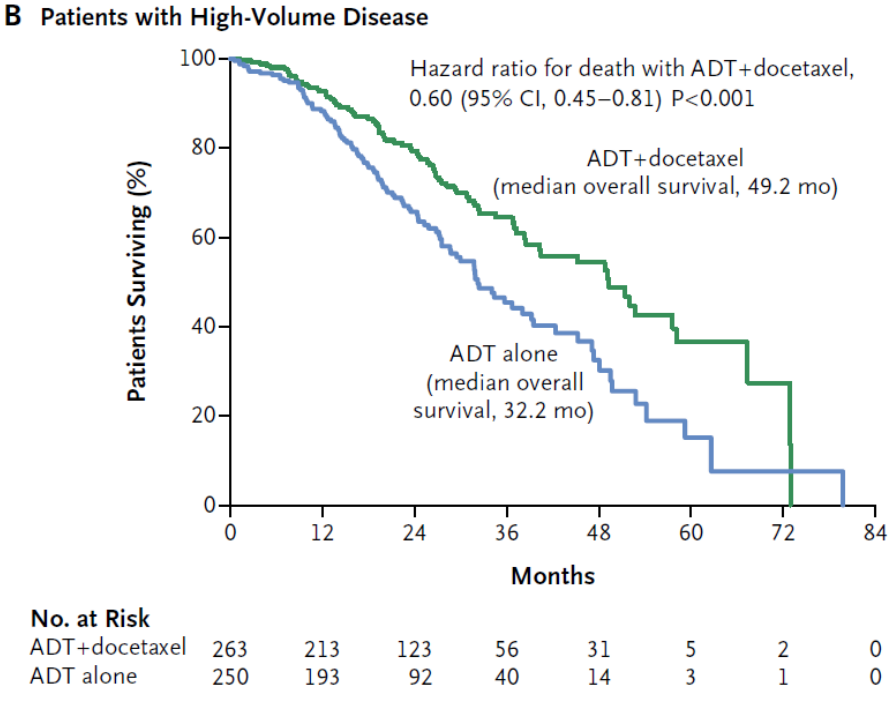
ADT + Erken Dönem Kemoterapi

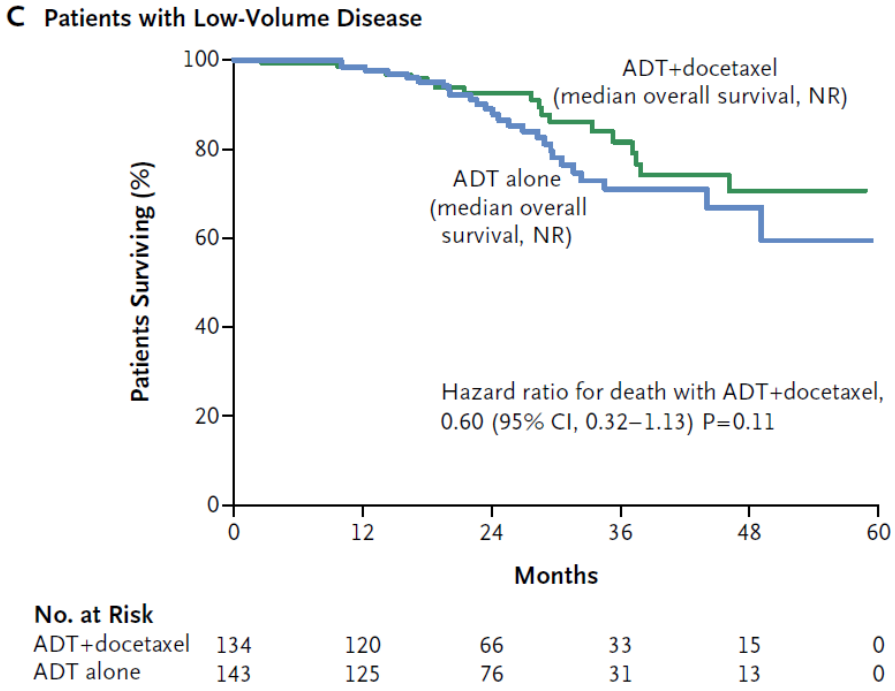


ADT + Erken Dönem Kemoterapi



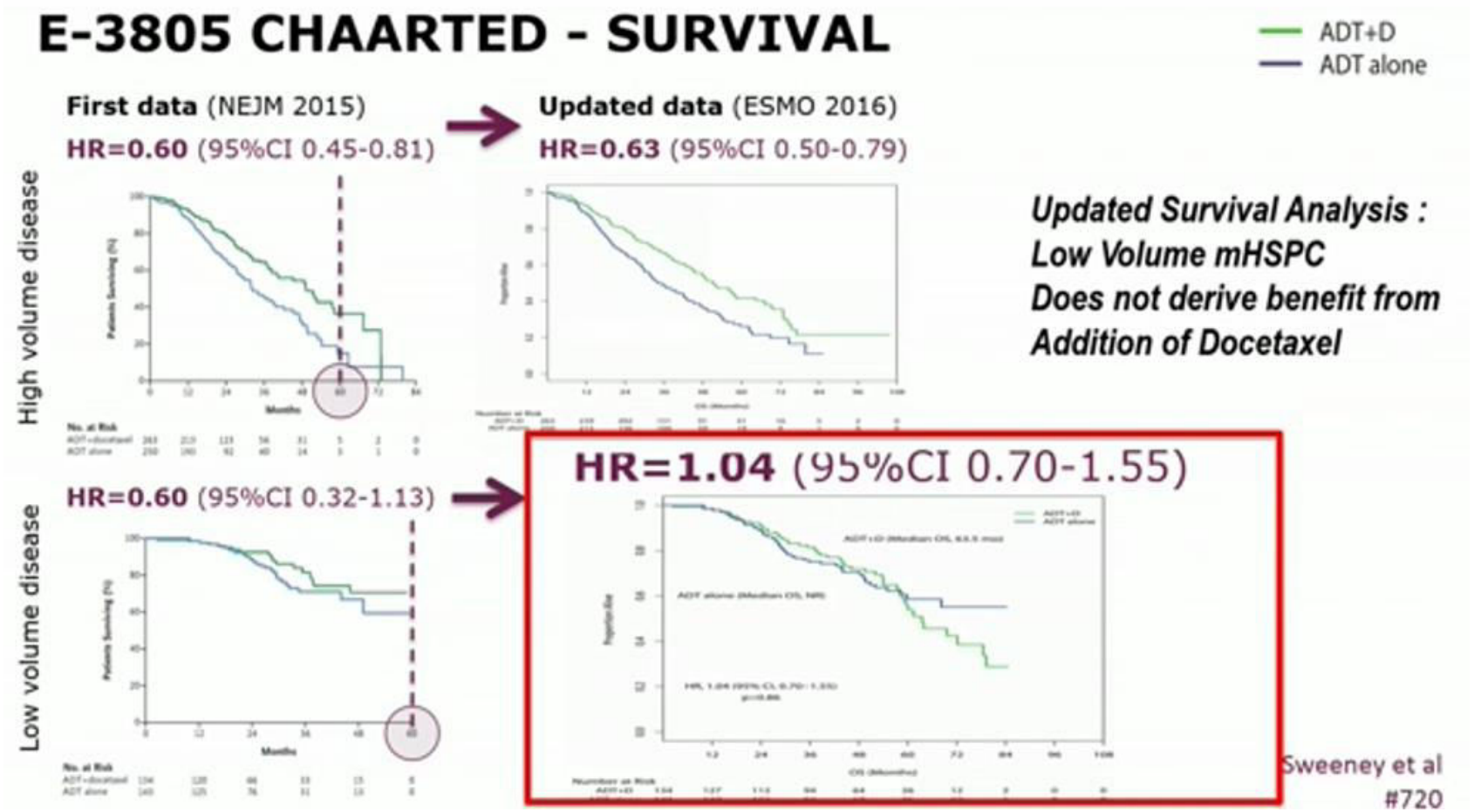
ADT + Erken Dönem Kemoterapi





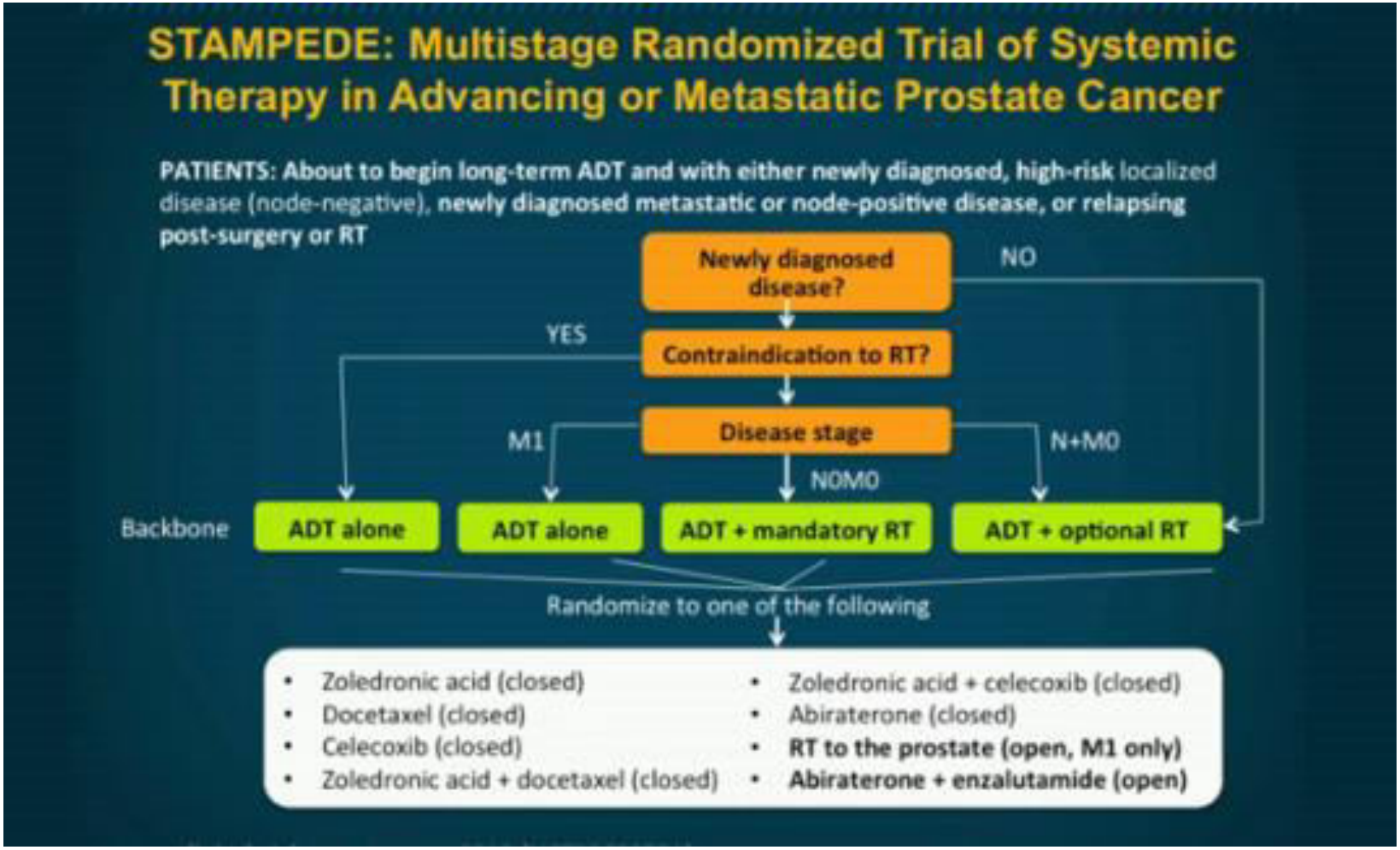
Yüksek volümlü hastalığı olanlar; viseral organ metastazı olan yada ≥4 kemik lezyonu olan ve en az ≥1 vertebra, pelvis dışı kemiklerde metastaz olmalı

ADT + Erken Dönem Kemoterapi
CHAARTED UZUN DÖNEM SONUÇLARI



Hormon Duyarlı Metastatik Prostat Kanseri

ADT + Erken Dönem Kemoterapi



ADT + Erken Dönem Kemoterapi

STAMPEDE: Docetaxel and/or Zoledronic Acid in Hormone-Naïve Metastatic PCa

First overall survival analysis of patients enrolled in the following 4 study arms:

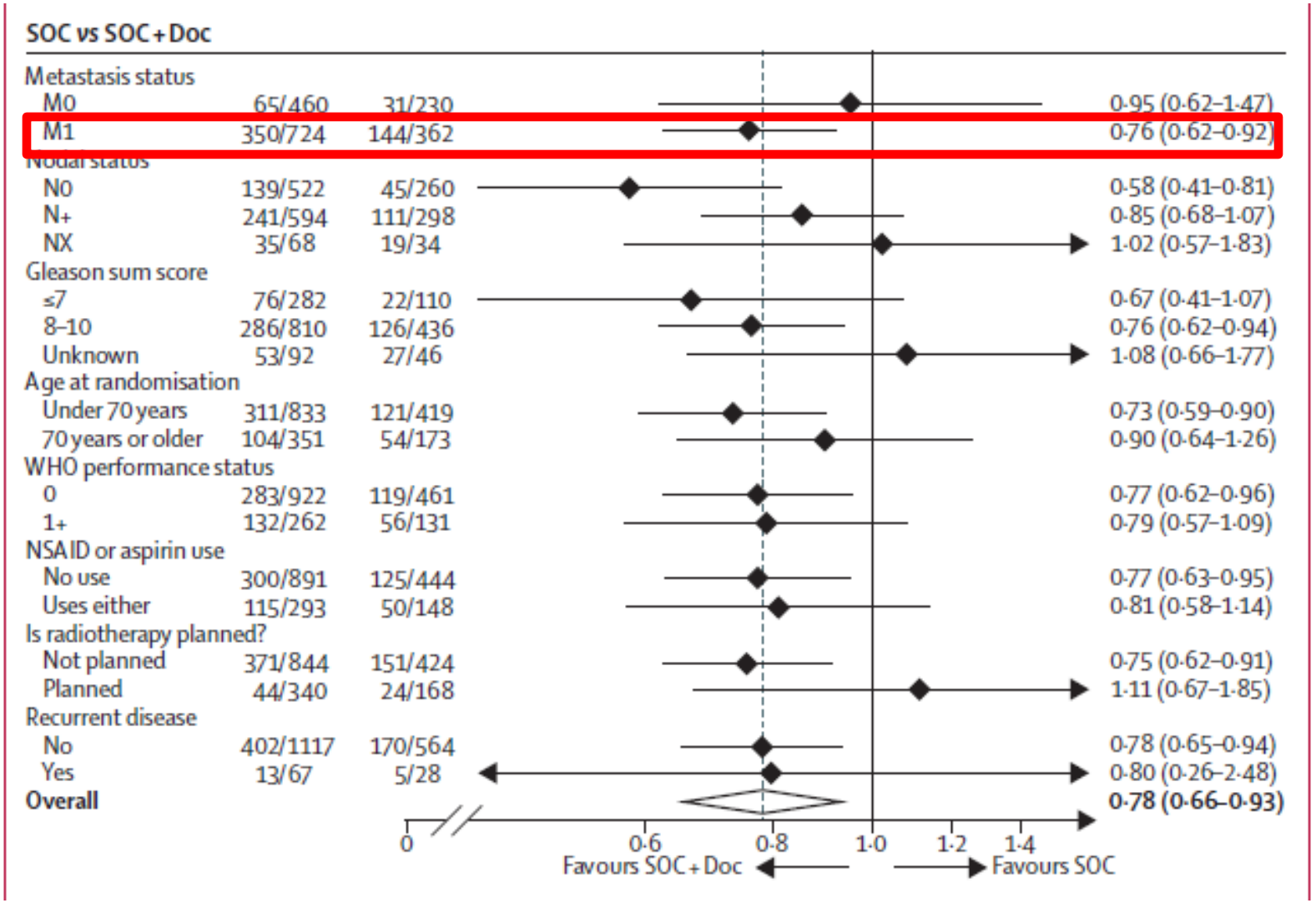
- Standard of care (SOC; n = 1,184)
- Docetaxel (Doc) + SOC (n = 592)
- Zoledronic acid (ZDA) + SOC (n = 593)
- Doc + ZDA + SOC (n = 593)

	SOC	Doc + SOC	ZDA + SOC	Doc + ZDA + SOC
Median overall survival	67 mo	77 mo	80 mo	72 mo
Hazard ratio (*p*-value)	**Ref***	**0.76 (0.003)**	**0.93 (0.44)**	**0.81 (0.02)**
Median failure-free survival	21 mo	37 mo	21 mo	37 mo
Hazard ratio (*p*-value)	**Ref***	**0.62 ($<0.1 \times 10^{-10}$)**	**0.93 (0.26)**	**0.62 ($<0.1 \times 10^{-10}$)**

* Pairwise comparisons to control SOC study arm were calculated for each research arm.

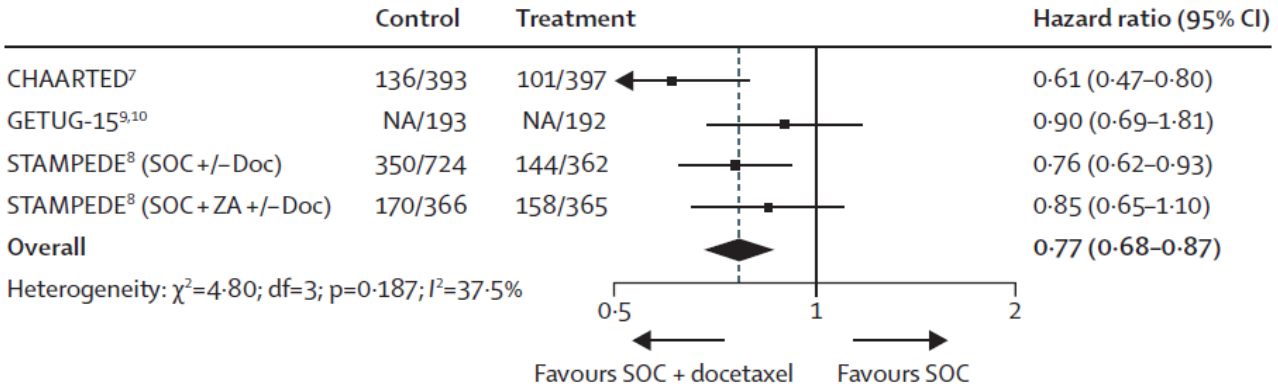
- **Docetaxel, and not ZDA, improves overall survival compared to SOC**
- **Docetaxel + ZDA improves survival but offers no obvious benefit over docetaxel alone**

ADT + Erken Dönem Kemoterapi

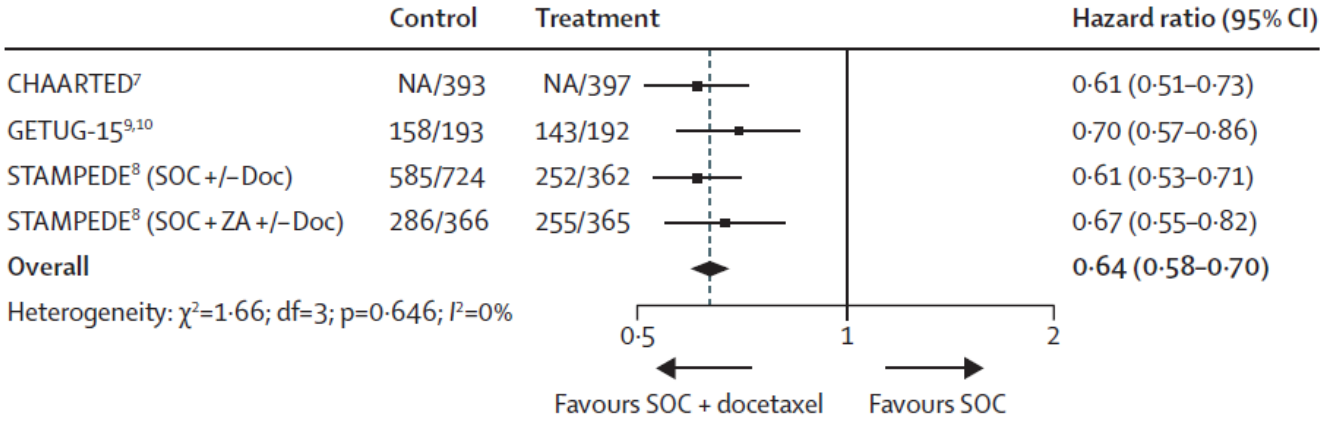


Hormon Duyarlı Metastatik Prostat Kanseri

Metaanaliz; ADT + Erken Dönem Kemoterapi



2992 hormona duyarlı metastatik prostat ca hastaya ADT +dositaksel eklenmesi ; 4-yıllık sağkalımı %9 artırıyor



2992 hormona duyarlı metastatik prostat ca hastaya ADT +dositaksel eklenmesi ; 4 yılık %16 nüksüz süreyi uzatıyor

Hormon Duyarlı Metastatik Prostat Kanseri

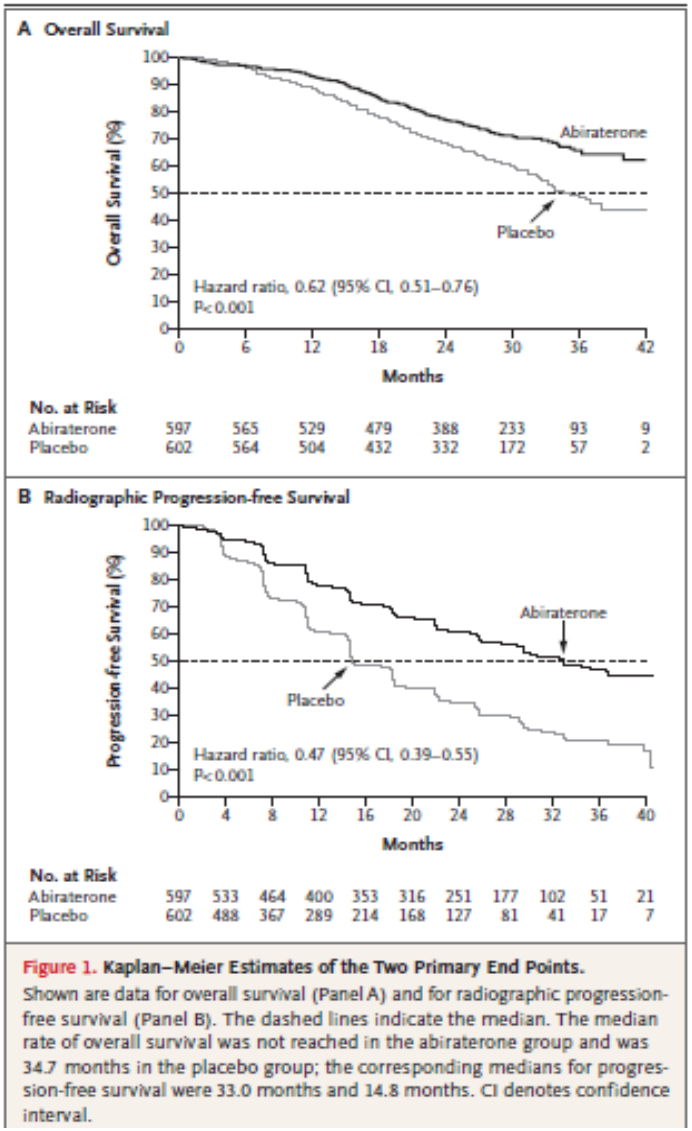


Figure 1. Kaplan–Meier Estimates of the Two Primary End Points.
Shown are data for overall survival (Panel A) and for radiographic progression-free survival (Panel B). The dashed lines indicate the median. The median rate of overall survival was not reached in the abiraterone group and was 34.7 months in the placebo group; the corresponding medians for progression-free survival were 33.0 months and 14.8 months. CI denotes confidence interval.

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Abiraterone plus Prednisone in Metastatic, Castration-Sensitive Prostate Cancer

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

ABSTRACT

BACKGROUND

Abiraterone acetate, a drug that blocks endogenous androgen synthesis, plus prednisone is indicated for metastatic castration-resistant prostate cancer. We evaluated the clinical benefit of abiraterone acetate plus prednisone with androgen-deprivation therapy in patients with newly diagnosed, metastatic, castration-sensitive prostate cancer.

From Gustave Roussy, University of Paris Sud, Villejuif, France (K.F.); Janssen Research and Development, Los Angeles (N.T.), Beerse, Belgium (P.D.P.), San Diego, CA (T.K.), and Raritan, NJ (Y.C.P.); Insti-

En az 2≥ kötü risk grubuna sahip hastalar dahil edilmiş

1. **Gleason skoru≥8**
2. **3≥ fazla kemik metastazı**
3. **Viseral metastaz**

Dışlama kriterleri

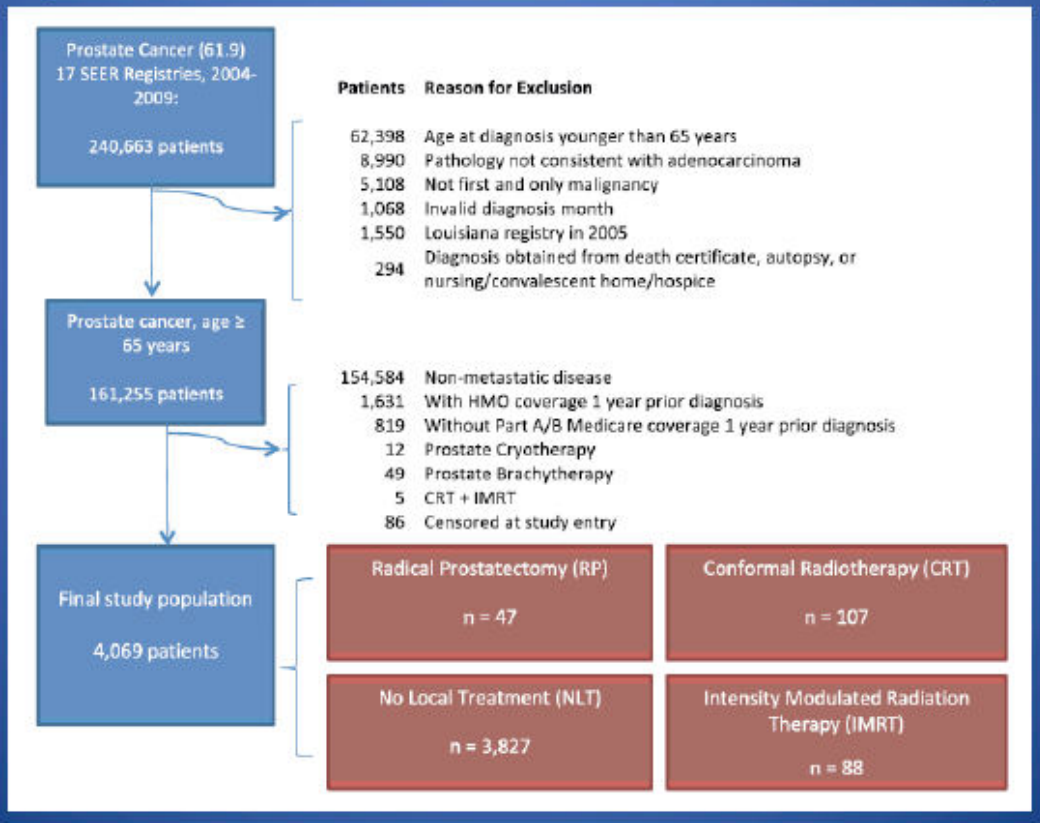
1. **Daha önce cerrahi**
2. **Radyoterapi**
3. **Kemoterapi**
4. **Metastik hastalığa bağlı semptomu olanlarda RT ve Cerrahiye izin verilmiş**

Oligometastatik Prostat Kanseri Retrospektif Veri Sonuçları

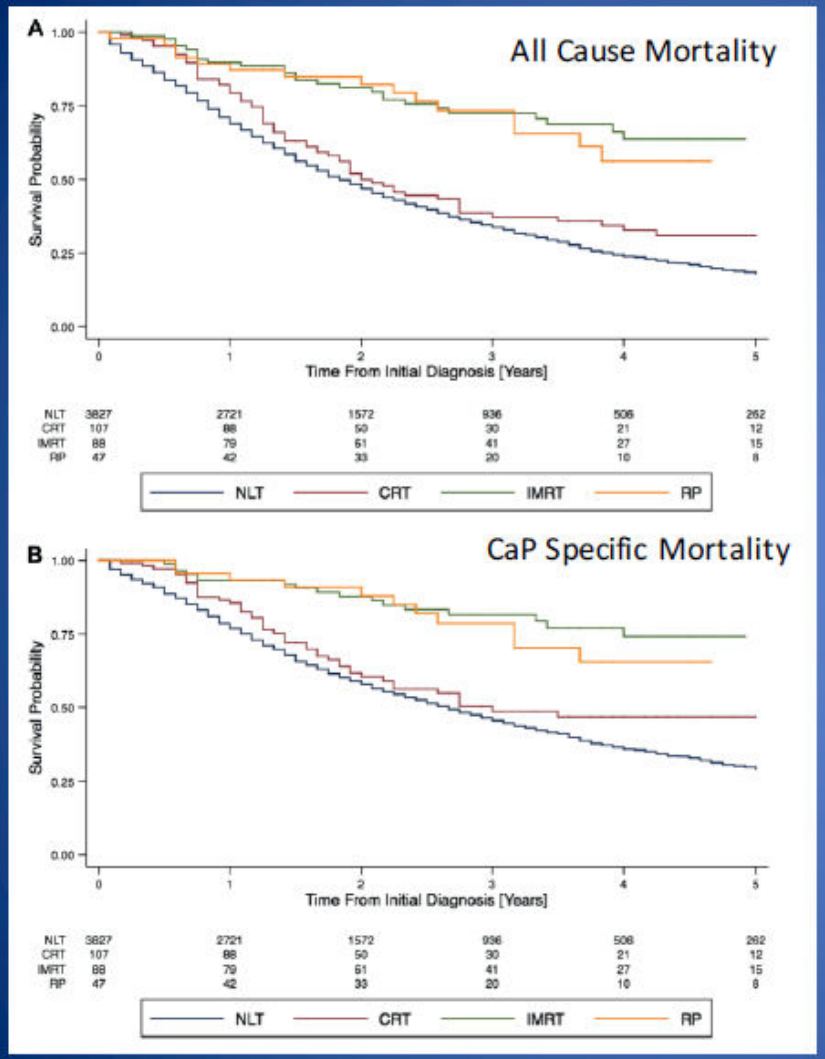
Radical Prostatectomy or External Beam Radiation Therapy vs No Local Therapy for Survival Benefit in Metastatic Prostate Cancer: A SEER-Medicare Analysis

Raj Satkunasivam,* Andre E. Kim, Mihir Desai, Mike M. Nguyen, David I. Quinn, Leslie Ballas, Juan Pablo Lewinger, Mariana C. Stern, Ann S. Hamilton, Monish Aron and Inderbir S. Gill

0022-5347/15/1942-0378/0
THE JOURNAL OF UROLOGY®
http://dx.doi.org/10.1016/j.juro.2015.02.084
Vol. 194, 378-385, August 2015
Printed in U.S.A.



Oligometastatik Prostat Kanseri Retrospektif Veri Sonuçları



Tüm nedenlere bağlı ölüm oranı; RP %52 ve IMRT %62 daha düşük bulunmuş. CRT ve Tedavi edilmeyen grup benzer bulunmuş. PCa bağlı mortalite; RP %57 ve IMRT %55 daha düşük saptanmış

0022-5347/15/1942-0378/0
THE JOURNAL OF UROLOGY®
Vol. 194, 378-385, August 2015
Printed in U.S.A.

Oligometastatik Prostat Kanseri Retrospektif SEER Veri Sonuçları

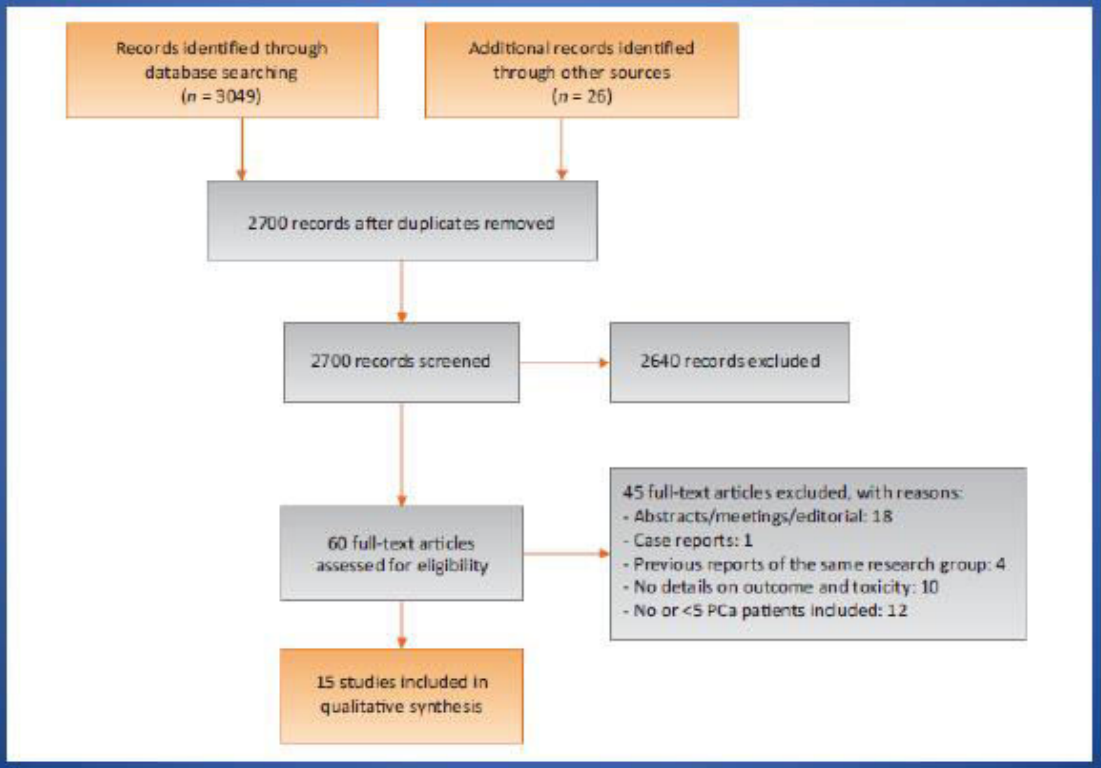
	RP	IMRT	CRT	NLT	*p-value*
	47	88	107	3827	
Year of Diagnosis – N (%)					
2004	6 (13)	12 (14)	21 (20)	709 (19)	0.2
2005	5 (11)	9 (10)	26 (24)	692 (18)	
2006	7 (15)	14 (16)	21 (20)	667 (17)	
2007	11 (23)	21 (24)	16 (15)	619 (16)	
2008	10 (21)	18 (20)	14 (13)	580 (15)	
2009	8 (17)	14 (16)	9 (8)	560 (15)	
Age at Diagnosis					
Mean (SD)	73.0 (6.0)	74.2 (6.1)	76.4 (6.3)	78.2 (7.2)	< 0.001
Race – N (%)					
NHW	38 (81)	75 (85)	81 (76)	2925 (76)	0.5
AA	7 (15)	9 (10)	13 (12)	608 (16)	
Hisp	0 (0)	2 (2)	3 (3)	95 (2)	
Asian	2 (4)	1 (1)	6 (6)	103 (3)	
Other/Unknown	0 (0)	1 (1)	4 (4)	96 (3)	
Marital Status – N (%)					
Single	2 (4)	10 (11)	6 (6)	408 (11)	0.1
Married	35 (74)	60 (68)	68 (64)	2248 (59)	
Separated/divorced/widowed/domestic partners	9 (19)	12 (14)	27 (25)	933 (24)	
Unknown	1 (2)	6 (7)	6 (6)	238 (6)	
PSA – N (%)					
< 10 ng/ml	25 (53)	35 (40)	9 (8)	401 (10)	< 0.001
10-19 ng/ml	6 (13)	16 (18)	20 (19)	449 (12)	
20-29 ng/ml	3 (6)	10 (11)	9 (8)	286 (7)	
> 30 ng/ml	6 (13)	17 (19)	55 (51)	2127 (56)	
Unknown	7 (15)	10 (11)	14 (13)	564 (15)	
PSA (Continuous)					
Mean (SD)	181 (263)	282 (338)	531 (369)	590 (380)	< 0.001
Gleason Score – N (%)					
≤6	5 (11)	10 (11)	8 (7)	167 (4)	< 0.001
7	22 (47)	24 (27)	22 (21)	569 (15)	
≥8	19 (40)	43 (49)	59 (55)	2042 (53)	
Unknown	1 (2)	11 (13)	18 (17)	1049 (27)	

Oligometastatik Prostat Kanseri Retrospektif Veri Sonuçları(Review)

Metastasis-directed Therapy of Regional and Distant Recurrences After Curative Treatment of Prostate Cancer: A Systematic Review of the Literature

Piet Ost [a,], Alberto Bossi [b], Karel Decaestecker [c], Gert De Meerleer [a], Gianluca Giannarini [d], R. Jeffrey Karnes [e], Mack Roach III [f], Alberto Briganti [g]*

EUROPEAN UROLOGY 67 (2015) 852–863



Oligometastatik Prostat Kanseri Retrospektif Veri Sonuçları

Table 1 – Full-text publications of metastasis-directed therapy for oligometastatic prostate cancer recurrence included in the systematic review

Study	No. of patients	Site of metastasis: node/bone/visceral	Median time to metastatic recurrence, mo	Median PSA at time of metastasis	Staging method	Type of MDT	Median follow-up, mo	Median PFS	Adjuvant ADT (%)	Median duration ADT	Prophylactic nodal radiotherapy (%)
Casamassima et al. [23]	25	25/0/0	11.8–36.7	5.65	Choline PET/CT	SBRT	29	24 mo	None	NA	7 (28)
Muacevic et al. [24]	40	0/40/0	NR	5.4	Choline PET/CT	SBRT	14*	NR	27 (68)	NR	NA
Würschmidt et al. [25]	15	15/0/0	NR	1.79	Choline PET/CT	NRT	28	Median not reached: 3-yr PFS: 75%	NR	NR	15 (100)
Ahmed et al. [26]	17	1/15/1	50.4	2.1	Choline PET/CT ($n = 9$), MRI ($n = 6$), CT ($n = 1$), and biopsy ($n = 1$)	SBRT	6	12 mo	15 (88)	NR	NA
Jereczek-Fossa et al. [27]	19	18/1/0	66	1.77 (pelvic nodes); 10.7 (M1)	Choline PET/CT	SBRT	17	Median not reached; 30-mo PFS: 63.5%	19 (100)	12–17 mo	None
Schick et al. [28]	50	33/15/2	15.6	6.7	Choline PET/CT and bone scintigraphy	SBRT ($n = 14$) NRT ($n = 36$)	31	Median not reached; 3-yr PFS: 58.6%	49 (98)	12 mo	25 (50)
Decaestecker et al. [29]	50	27/22/1	57.6	3.8	Choline ($n = 18$) or FDG ($n = 32$) PET/CT	SBRT	25	19 mo	35 (70)	1 mo	None
Picchio et al. [30]	83	83/0/0	NR	2.6	Choline PET/CT	HRT	22	NR	58 (70)	NR	77 (93)
Rinnab et al. [31]	15	15/0/0	NR	1.98	Choline PET/CT	LND	13.7*	NR	11 (73)	NR	1 (7)
Schilling et al. [32]	10	10/0/0	NR	8.75	Choline PET/CT	LND	11*	NR	6 (60)	NR	None
Winter et al. [33]	6	6/0/0	NR	2.04	Choline PET/CT	LND	24 mo	NR	None	NA	None
Busch et al. [37]	6	6/0/0	Mean: 79.9	37.6*	Choline ($n = 3$), MRI ($n = 1$), CT ($n = 2$)	LND	NR	15.5 mo	6 (100)	Lifelong ADT	None
Jilg et al. [34]	47	47/0/0	62	11.1*	Choline PET/CT	LND	35.5	27 mo**	34 (65)	NR	27 (52)
Martini et al. [35]	8	8/0/0	NR	1.62	Choline PET/CT	LND	NR	NR	None	NA	None
Suardi et al. [36]	59	59/0/0	NR	2.0	Choline PET/CT	LND	76.6	60 mo**	24 (41)	24 mo	21 (36)

ADT = androgen-deprivation therapy; CT = computed tomography; FDG = fluorodeoxyglucose; HRT = hypofractionated radiotherapy; LND = lymph node dissection; MDT = metastasis-directed therapy; MRI = magnetic resonance imaging; NA = not applicable; NR = not reported; NRT = normofractionated radiotherapy; PET/CT = positron emission tomography with coregistered computed tomography; PFS = progression-free survival; PSA = prostate-specific antigen; SBRT = stereotactic body radiotherapy.

* Mean numbers reported instead of median.

** Median estimated from curves.

EUROPEAN UROLOGY 67 (2015) 852–863

Oligometastatik Prostat Kanseri Retrospektif Veri Sonuçları

Table 4 – Complications associated with metastasis-directed therapy for oligometastatic prostate cancer recurrence: (a) complications associated with radiotherapy according to Common Terminology Criteria for Adverse Events; (b) complications associated with salvage lymph node dissection according to the Clavien-Dindo classification

a.

Complication type	Muacevic et al. [24] (*n* = 40), no. (%)	Würschmidt et al.* [25] (*n* = 15), no. (%)	Ahmed et al. [26] (*n* = 17), no. (%)	Jereczek-Fossa et al. [27] (*n* = 19), no. (%)	Decaestecker et al. [29] (*n* = 50), no. (%)	Total (*n* = 141), no. (%)
Grade 1						
Bone pain	0 (0)	0 (0)	0 (0)	0 (0)	3 (6)	3 (2)
Asymptomatic fracture	1 (2.5)	0 (0)	0 (0)	0 (0)	1 (2)	2 (1.4)
Fatigue	0 (0)	0 (0)	0 (0)	0 (0)	1 (2)	1 (0.7)
Rectal toxicity	0 (0)	0 (0)	0 (0)	0 (0)	2 (4)	2 (1.4)
Urinary toxicity	0 (0)	0 (0)	0 (0)	2 (11)	0 (0)	2 (1.4)
Grade 2						
Nausea requiring antiemetics	5 (12.5)	0 (0)	0 (0)	0 (0)	0 (0)	5 (3.5)
Rectal toxicity	0 (0)	2 (13.3)	0 (0)	1 (5)	2 (4)	5 (3.5)
Urinary toxicity	0 (0)	0 (0)	0 (0)	1 (5)	1 (2)	2 (1.4)
Grade 3						
Urinary toxicity	0 (0)	0 (0)	0 (0)	1 (5)	0 (0)	1 (0.7)

b.

Complication type	Rinnab et al. [31] (*n* = 15), no. (%)	Busch et al. [37] (*n* = 6), no. (%)	Jilg et al. [34] (*n* = 47), no. (%)	Suardi et al. [36] (*n* = 59), no. (%)	Total (*n* = 127), no. (%)
Grade 1					
Lymphorrhea	0 (0)	0 (0)	4 (7.7)	12 (20.3)	16 (12.5)
Fever	0 (0)	0 (0)	3 (5.8)	18 (30.5)	21 (16.5)
Temporary weakness of the hip flexor	0 (0)	0 (0)	1 (1.9)	0 (0)	1 (0.8)
Wound dehiscence	0 (0)	0 (0)	3 (5.8)	0 (0)	3 (2.3)
Grade 2					
Deep vein thrombosis	0 (0)	0 (0)	0 (0)	1 (1.7)	1 (0.8)
Ileus	1 (7)	0 (0)	0 (0)	12 (20.3)	13 (10.2)
Grade 3a					
Lymphocele requiring drainage	1 (7)	0 (0)	2 (3.9)	7 (11.2)	10 (7.8)
Wound dehiscence	0 (0)	0 (0)	0 (0)	3 (5.1)	3 (2.3)
Hydronephrosis requiring stenting	1 (7)	0 (0)	0 (0)	0 (0)	1 (0.8)
Grade 3b					
Lymphocele requiring surgical drainage	0 (0)	0 (0)	0 (0)	1 (1.7)	1 (0.8)

* One patient experienced a grade 4 toxicity: bladder shrinkage requiring cystectomy with urinary derivation. This patient received radiotherapy to the prostate gland and metastatic nodes for a recurrence in the seminal vesicle and iliac nodes after previous brachytherapy to the prostate.

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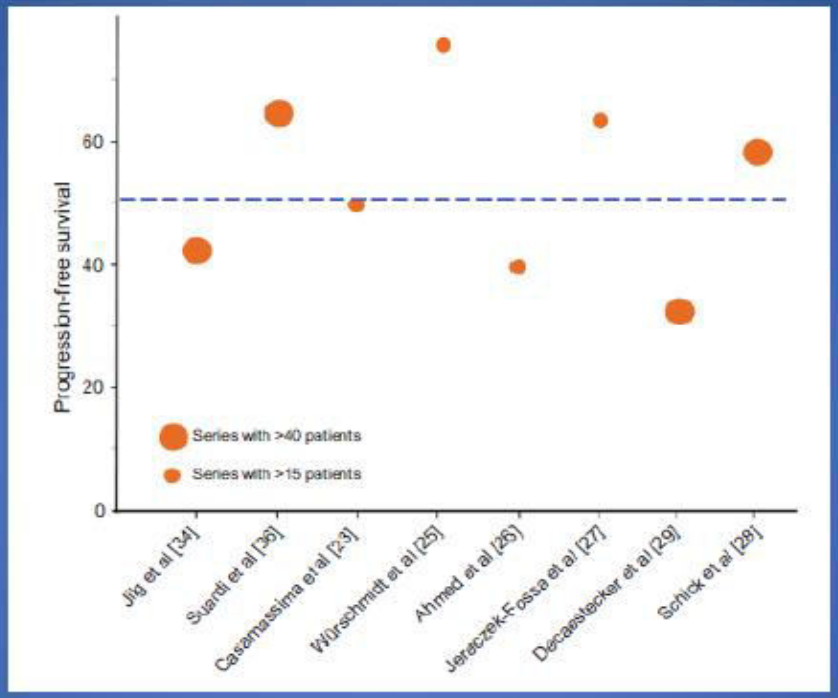

- Studies with >15 pts included in analysis
- Mean PFS of 50% from all studies at 3yrs

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Oligometastatik Prostat Kanseri Prospektif Faz II Çalışma Sonuçları

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ORIGINAL REPORT

Surveillance or Metastasis-Directed Therapy for Oligometastatic Prostate Cancer Recurrence: A Prospective, Randomized, Multicenter Phase II Trial

Piet Ost, Dries Reynders, Karel Decaestecker, Valérie Fonteyne, Nicolaas Lumen, Aurélie De Bruycker, Bieke Lambert, Louke Delrue, Renée Bultijnck, Tom Claeys, Els Goetghebeur, Geert Villeirs, Kathia De Man, Filip Ameye, Ignace Billiet, Steven Joniau, Friedl Vanhaverbeke, and Gert De Meerleer

Author affiliations and support information (if applicable) appear at the end of this article.

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0732-183X/18/3605w-446w/$20.00

A B S T R A C T

Purpose

Retrospective studies suggest that metastasis-directed therapy (MDT) for oligorecurrent prostate cancer (PCa) improves progression-free survival. We aimed to assess the benefit of MDT in a randomized phase II trial.

Patients and Methods

In this multicenter, randomized, phase II study, patients with asymptomatic PCa were eligible if they had had a biochemical recurrence after primary PCa treatment with curative intent, three or fewer extracranial metastatic lesions on choline positron emission tomography–computed tomography, and serum testosterone levels > 50 ng/mL. Patients were randomly assigned (1:1) to either surveillance or MDT of all detected lesions (surgery or stereotactic body radiotherapy). Surveillance was performed with prostate-specific antigen (PSA) follow-up every 3 months, with repeated imaging at PSA progression or clinical suspicion for progression. Random assignment was balanced dynamically on the basis of two factors: PSA doubling time (≤ 3 *v* > 3 months) and nodal versus nonnodal metastases. The primary end point was androgen deprivation therapy (ADT)–free survival. ADT was started at symptomatic progression, progression to more than three metastases, or local progression of known metastases.

Oligometastatik Prostat Kanseri Prospektif Faz II Çalışma Sonuçları

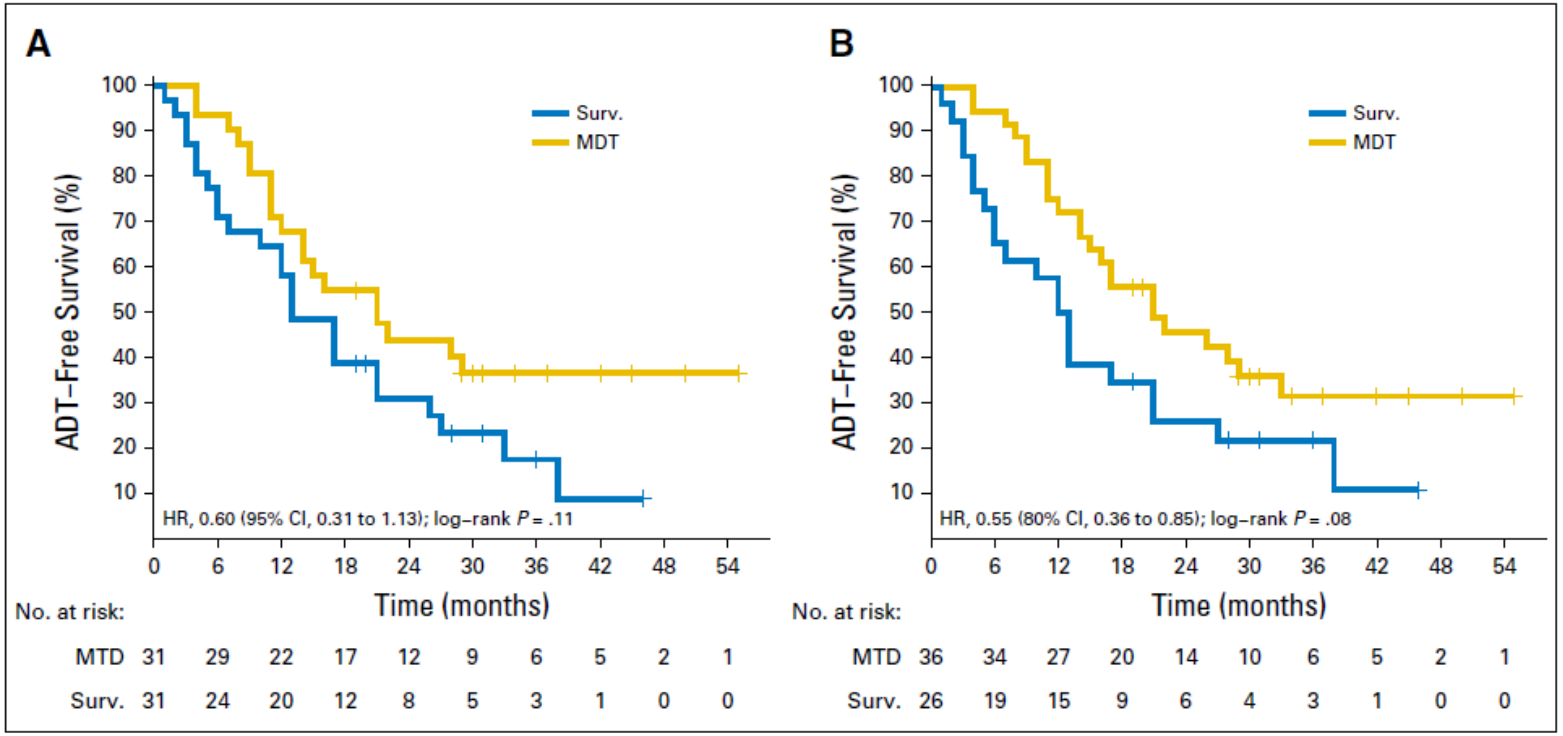

Fig 2. Kaplan-Meier plot comparing androgen deprivation therapy (ADT)–free survival of surveillance versus metastasis-directed therapy (MDT) for (A) the intention-to-treat analysis and (B) the per-protocol analysis. HR, hazard ratio; Surv., surveillance.

Oligometastatik Prostat Kanseri Prospektif Faz II Çalışma Sonuçları

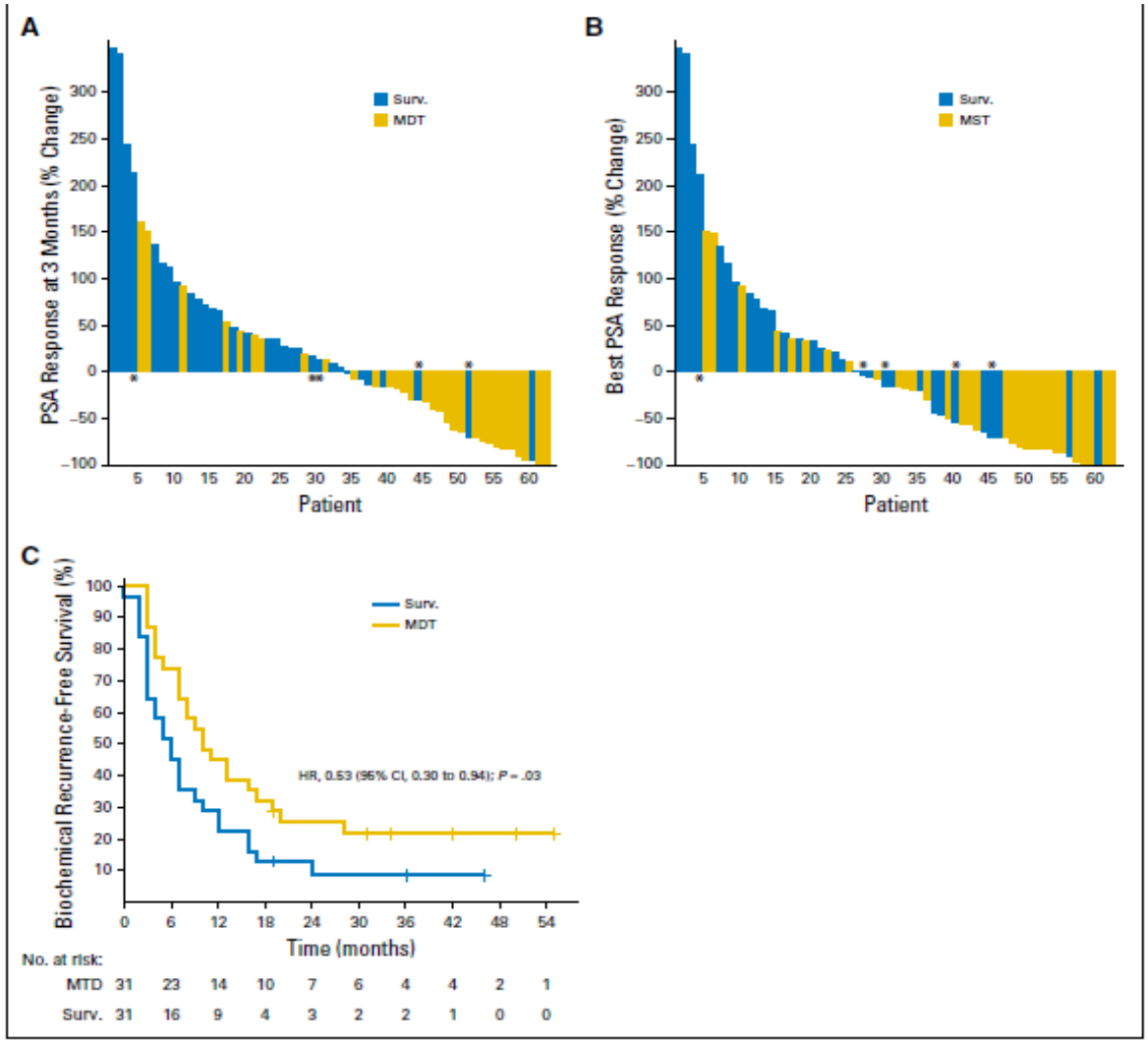

Fig 4. Waterfall plot of (A) the percentage change in prostate-specific antigen (PSA) after 3 months and (B) the best response. (C) Kaplan-Meier plot comparing biochemical recurrence-free survival of Surv versus MDT in the intention-to-treat analysis. (*) Indicates patients who were randomly assigned to the surveillance (Surv) arm but who were treated with metastasis-directed therapy (MDT). HR, hazard ratio.

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CTG NCT# / site	Condition	Name	Purpose	Algorithm	Primary Outcome/ Endpoint
01558427 UHosp, Ghent [169]	Prostate oligometastases	Salvage treatment of active clinical surveillance for OMPC: PhII RCT	To determine if salvage treatment of OMPC with either surgery or RT might postpone the start of ADT	Surgery -OR- RT, Which delays ADT?	ADT-free survival
02020070 MSKCC [170]	Prostate oligometastases	Ipilimumab, degarelix, + RP in castrate sensitive PC or ipilimumab + degarelix in biochemical recurrent castrate sensitive PC after RP	Assess safety + efficacy of combining HT + immunotherapy in non-castrate resistant PC. Cohort 1: ipilimumab + degarelix pre- and post- RP in newly diagnose OM castrate-sensitive disease. Cohort 2: post definitive local therapy with RP, but with biochemical recurrence	IT, LHRH antagonist + surgery -OR- IT, LHRH antagonist	Undetectable PSA at 12- and 20-mths with non-castrate testosterone.

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A Phase III of ADT + Docetaxel +/- Local RT +/- Abiraterone Acetate in Metastatic Hormone-naïve Prostate Cancer. (PEACE1)

The safety and scientific validity of this study is the responsibility of the study sponsor and investigators. Listing a study does not mean it has been evaluated by the U.S. Federal Government. Know the risks and potential benefits of clinical studies and talk to your health care provider before participating. Read our disclaimer for details.

ClinicalTrials.gov Identifier: NCT01957436

Recruitment Status : Recruiting
First Posted : October 8, 2013
Last Update Posted : December 13, 2017

See **Contacts and Locations**

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Collaborators:
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Metastatik Prostat Kanseri Tedavi Algoritması

National Comprehensive Cancer Network®

NCCN Guidelines Version 2.2017
Prostate Cancer

NCCN Guidelines Index
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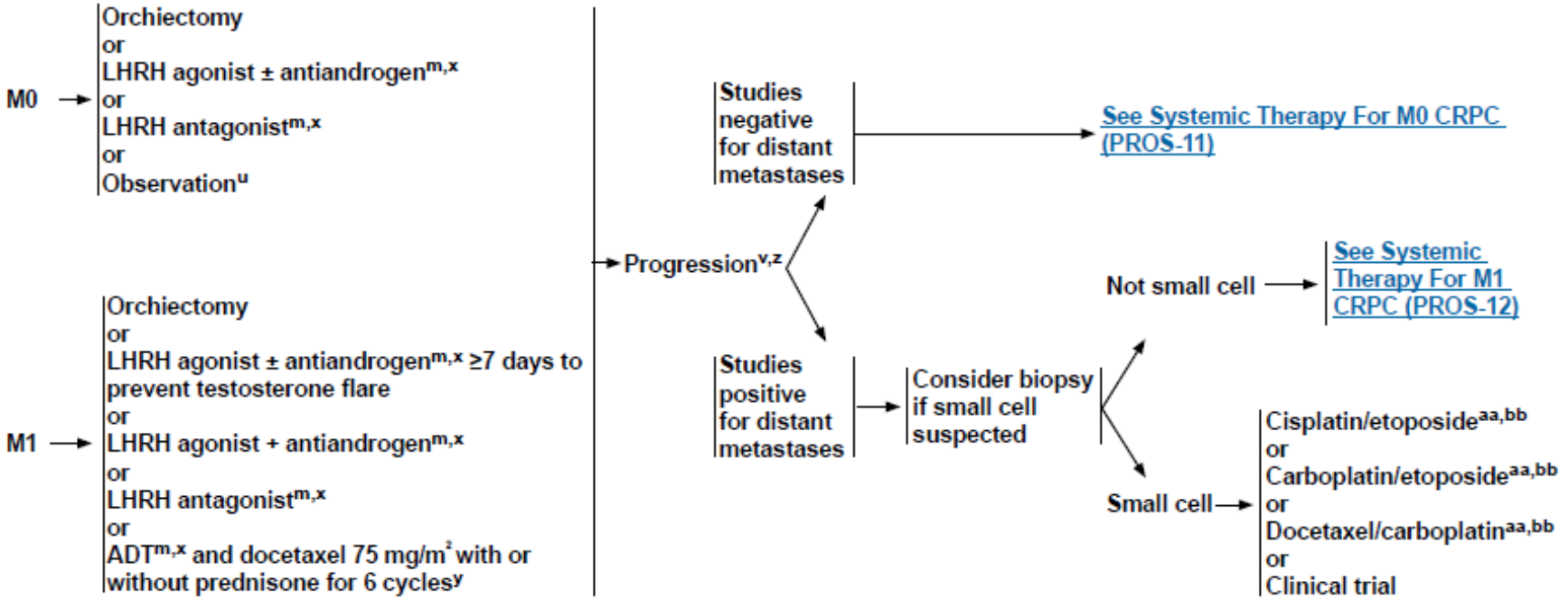
Discussion

SYSTEMIC THERAPY FOR PROGRESSIVE CASTRATION-NAIVE DISEASE[w]



Sonuç

- Retrospektif çalışmalarda pozitif sonuçlar mevcut
  - Bu grup hastalar daha indolent seyrediyor olabilir
  - Daha iyi risk grubunda ki hastalar dahil edilmiş olabilir
- Prospektif geniş kapsamlı çalışmaların sonuçlar beklenmektedir
- NCCN ve EAU kılavuzları rutin önermez
- Vaka bazlı, hastalar bilgilendirilerek uygulanabilir?