Oligometastatik Prostat Kanseri

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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

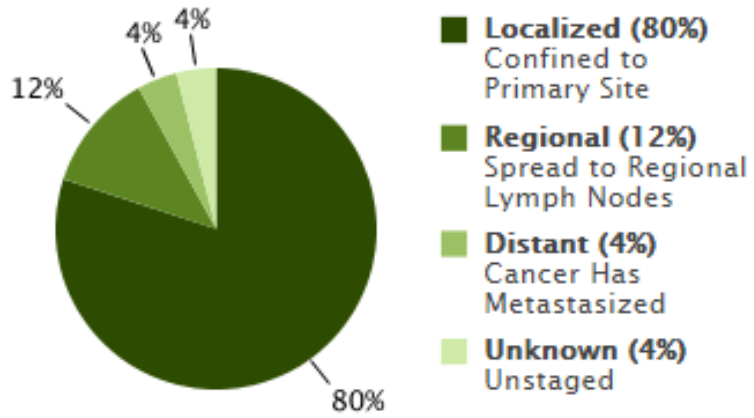
Prostate cancer represents 13.3% of all new cancer cases in the U.S.

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.

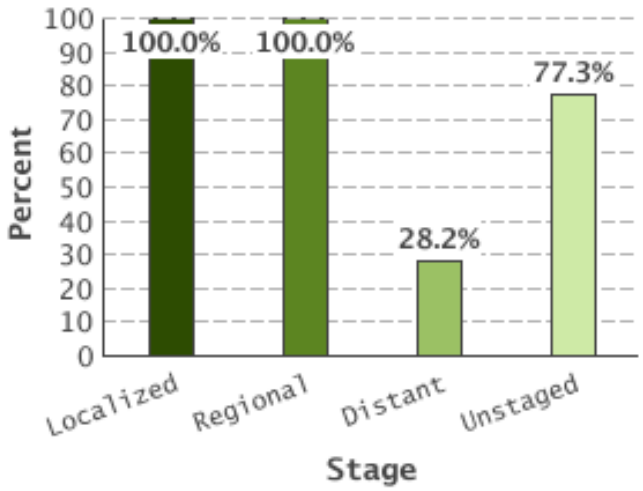
Prostat Kanseri İnsidans ve Mortalite

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

Percent of Cases by Stage

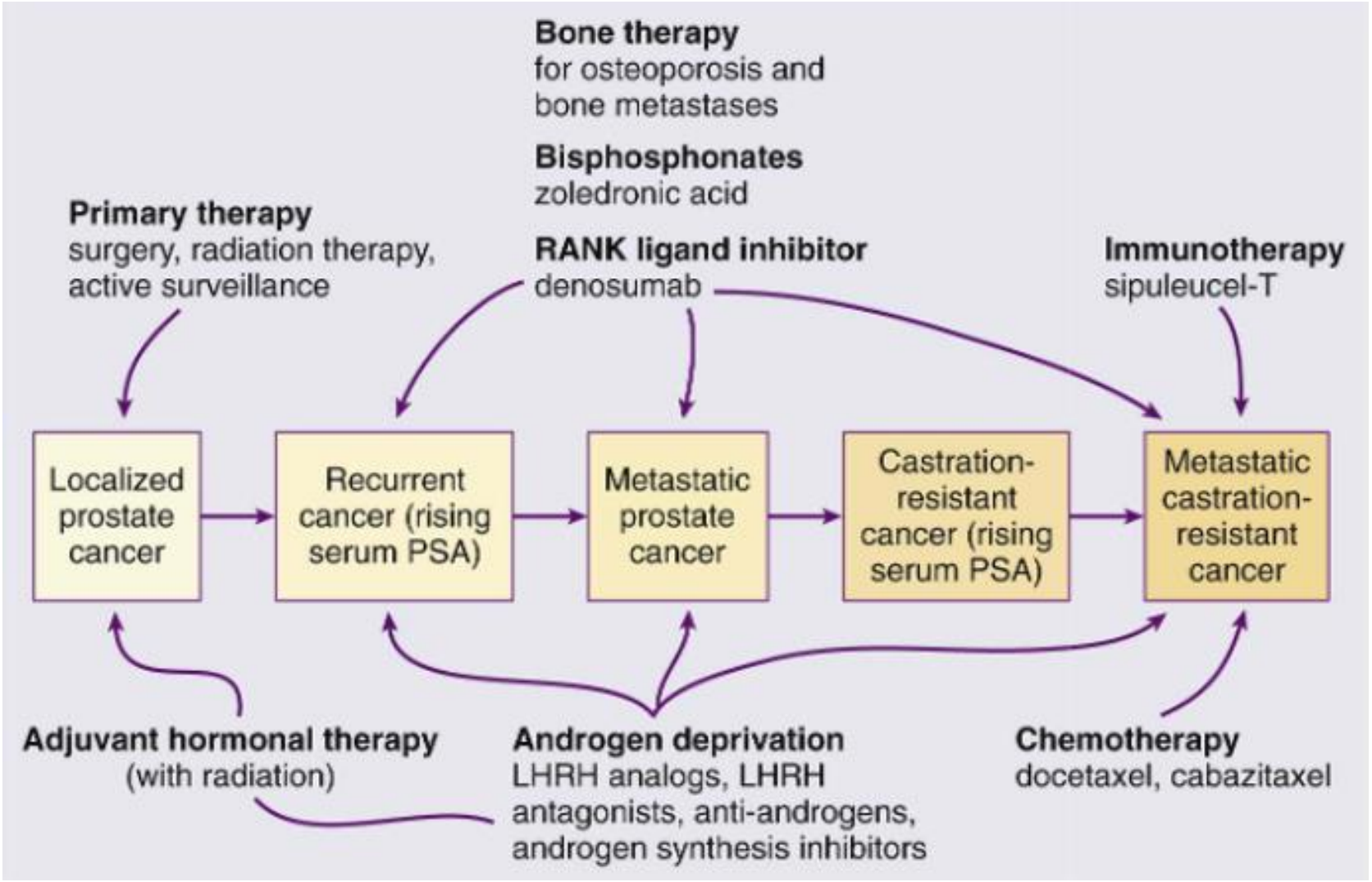


5-Year Relative Survival



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

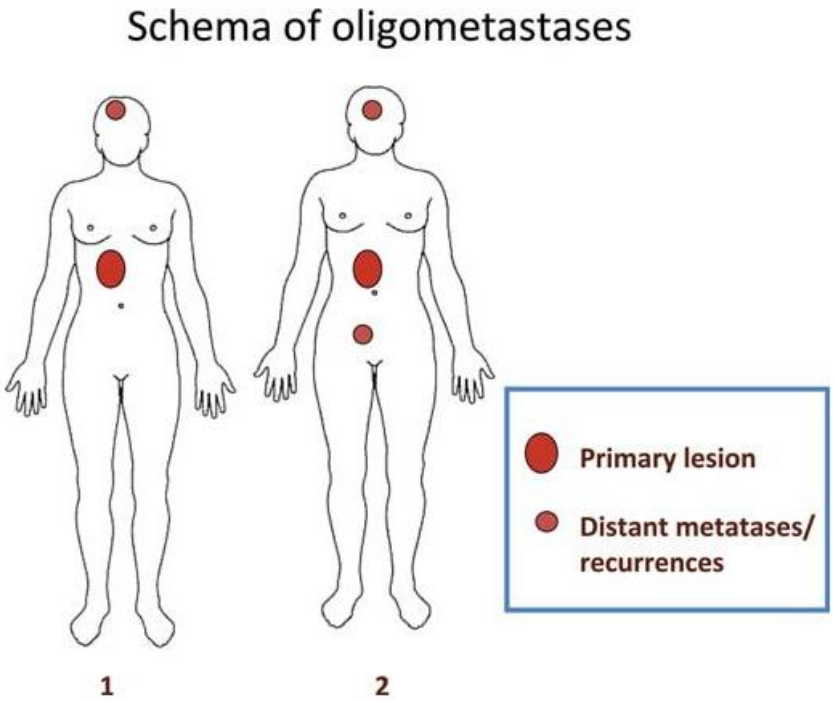


Figure 1. This is a schema of oligometastases. Schema 1 shows one distant metastasis/recurrence with a primary lesion. Schema 2 shows two distant metastases/recurrences with a primary lesion.

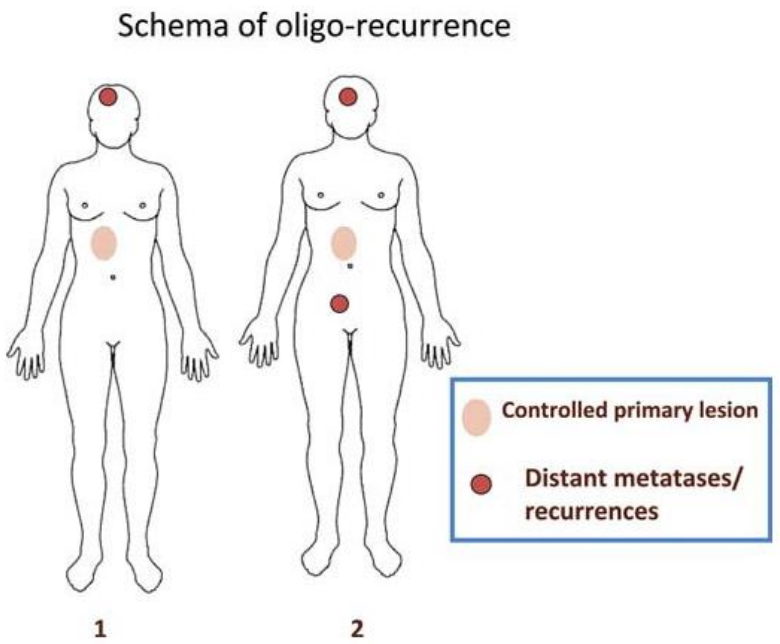


Figure 2. This is a schema of oligo-recurrence. Schema 1 shows one distant metastasis/recurrence with a controlled primary lesion. Schema 2 shows two distant metastases/recurrences with a controlled primary lesion. The biggest difference between oligometastases and oligo-recurrences lies in the uncontrolled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

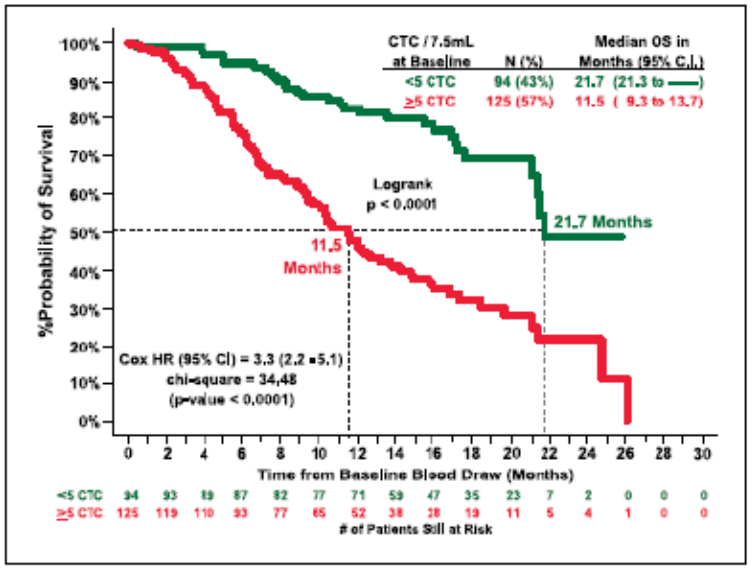
OLİGOMETASTATİK HASTALIK

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



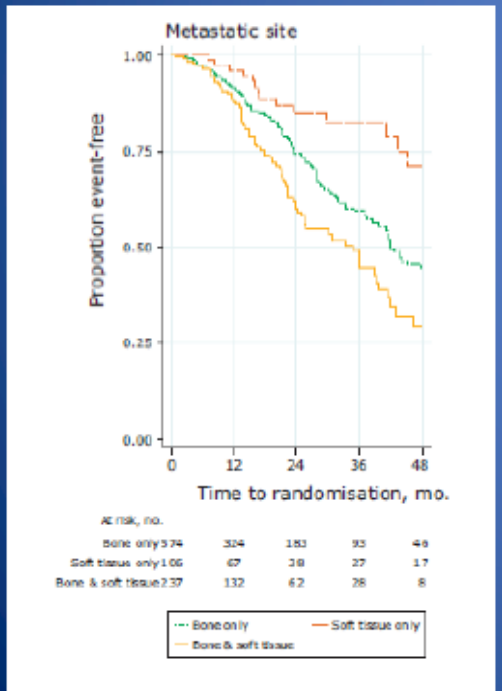
231 prosta kanserli hasta CTC düzeyi düşük olanların prognozu daha iyi

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

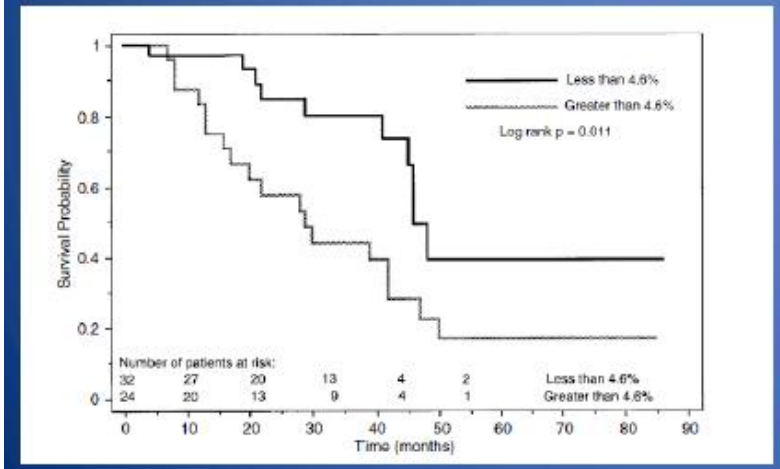
OLİGOMETASTATİK HASTALIK

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



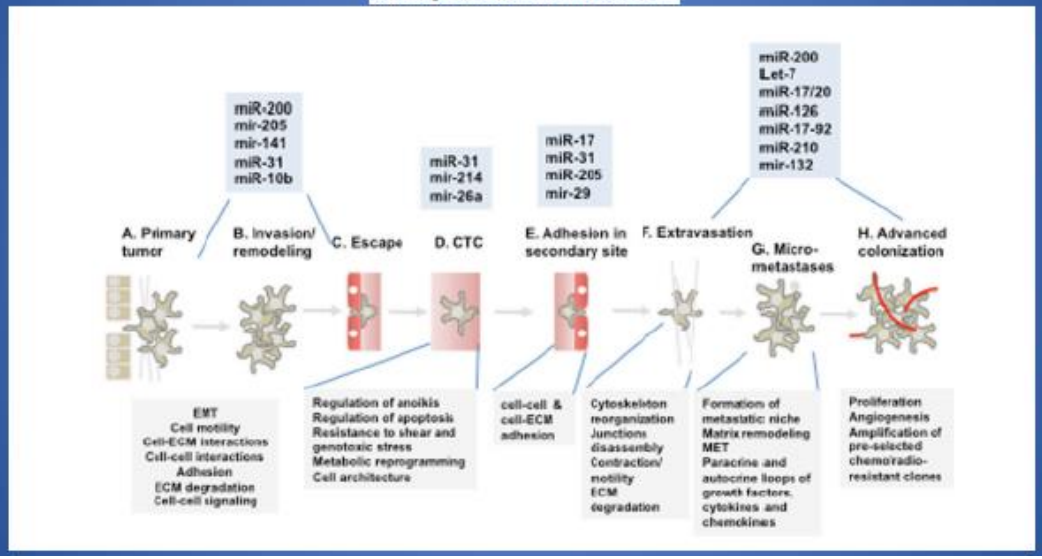
Kemik metastazı olan 56 prostat kanserli hastanın verileri retrospektif incelenen çalışmaya göre; PABS disease specific survival üzerine etkili bağımsız bir risk faktörüdür

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.

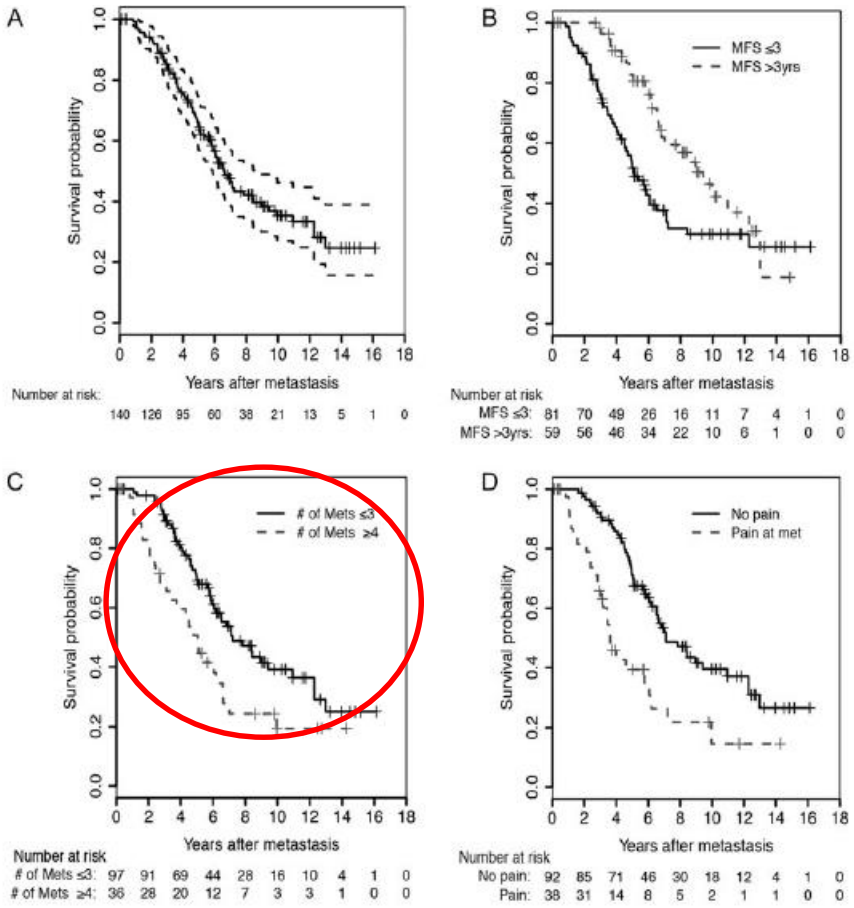
Tanı Anında Tümör Yükü Sağkalım İle İlişkili

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]*

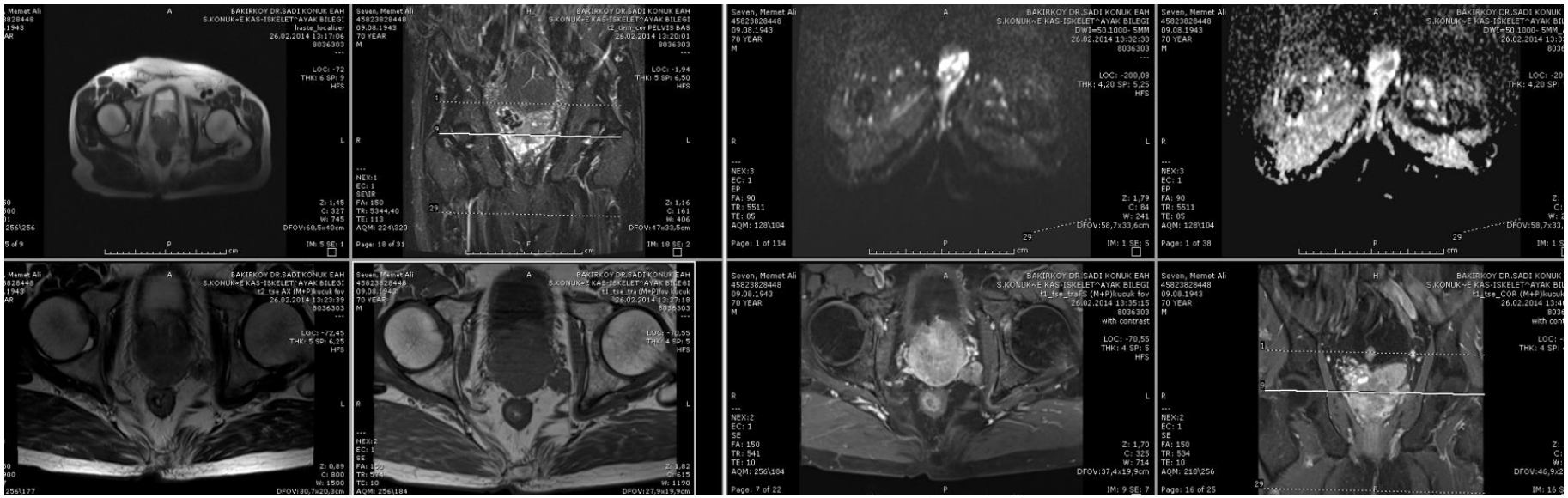
[1]*Sidney Kimmel Comprehensive Cancer Center;* [2]*Brady Urological Institute, Johns Hopkins University, Baltimore, USA*



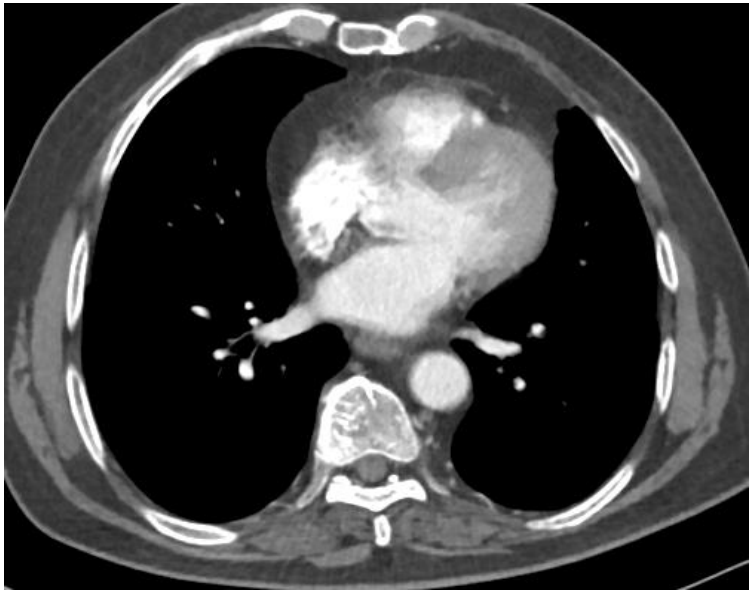
Vaka Sunumu

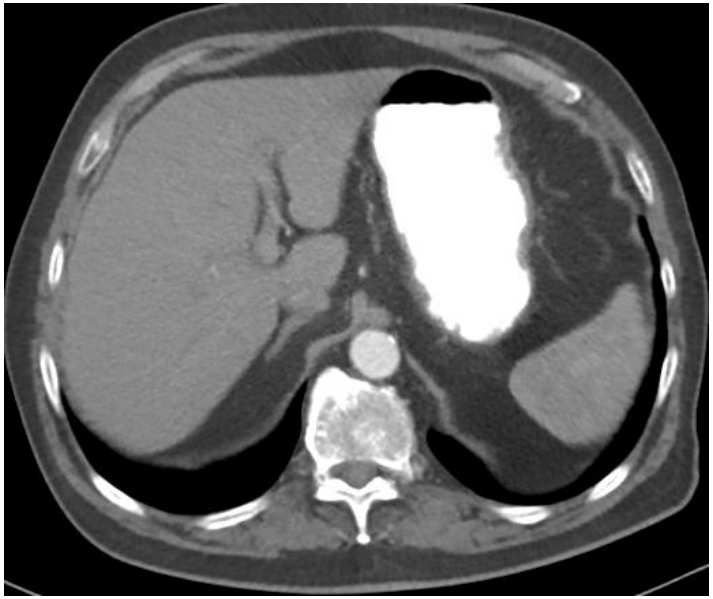
- 73 yaşında erkek hasta
- Bilinen hastalık öyküsü; KAH
- Aile öyküsü yok
- Sürekli kullandığı ilaç; Ecoprine 100 mg/gün
- Operasyon öyküsü yok
- 35 yıl paket sigara içmiş
- 11/2013 tarihinde ; idrar yaparken zorlanma şikayeti ile başvurmuş
- PSA : 37 ng/ml

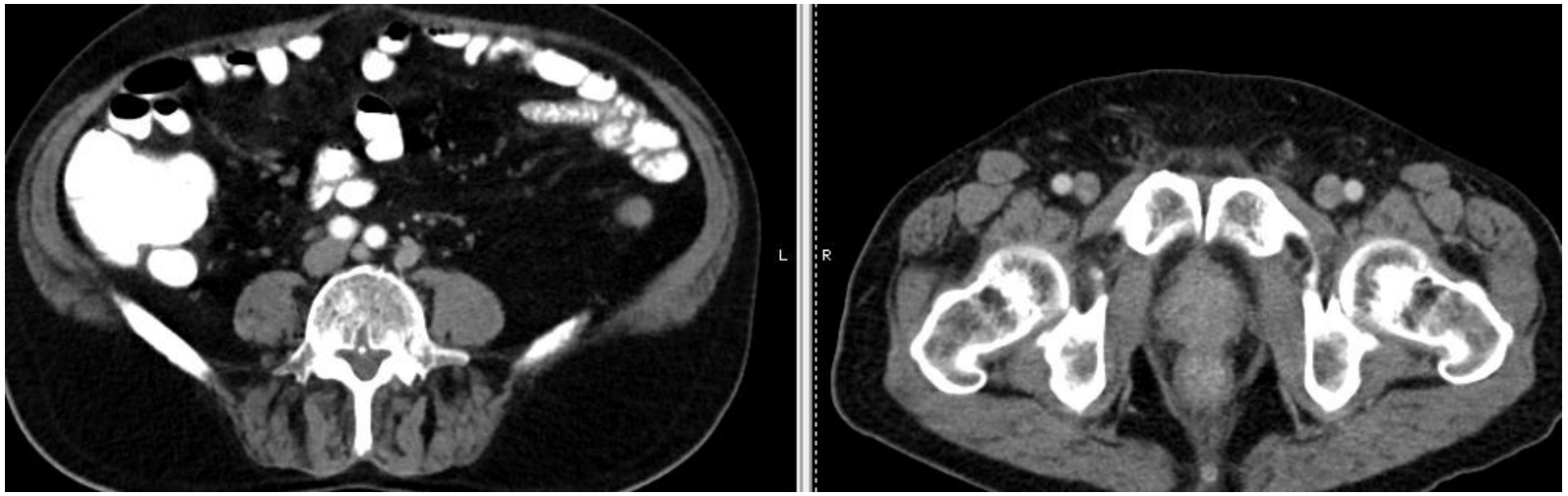
02/2014 Alt Batın-Pelvik MR



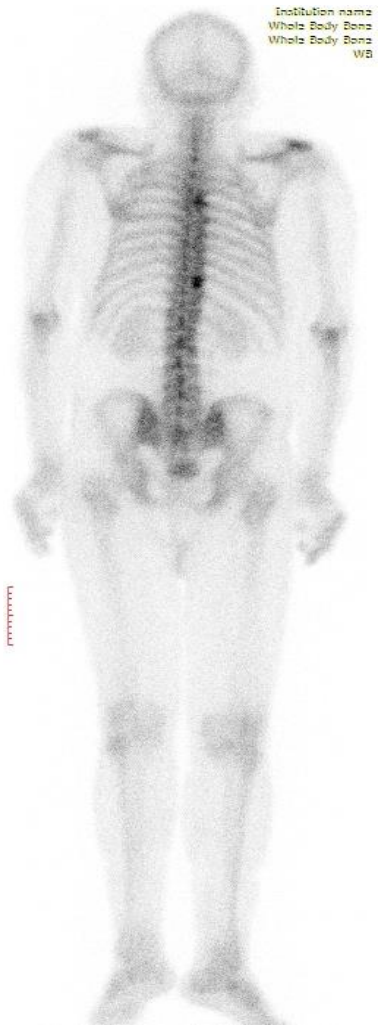
02/2014 Toraks-Batın BT

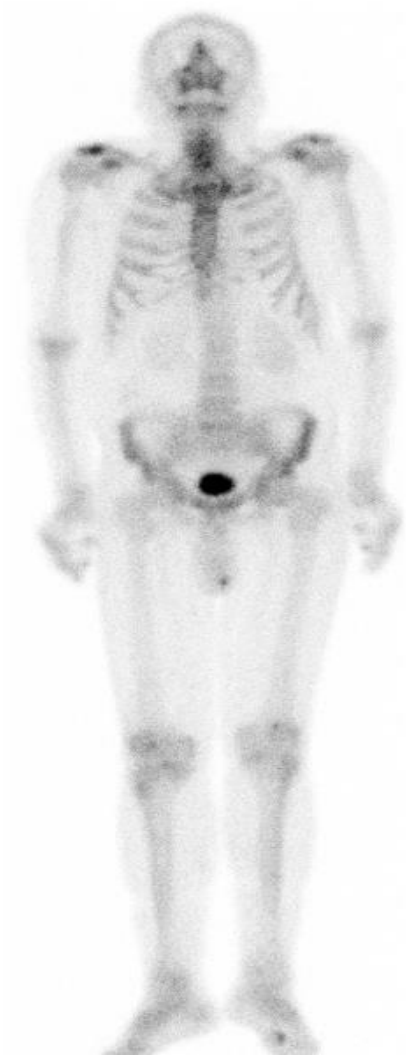






02/2014 TVS





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

Evreleme Nasıl Yapılmalı

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

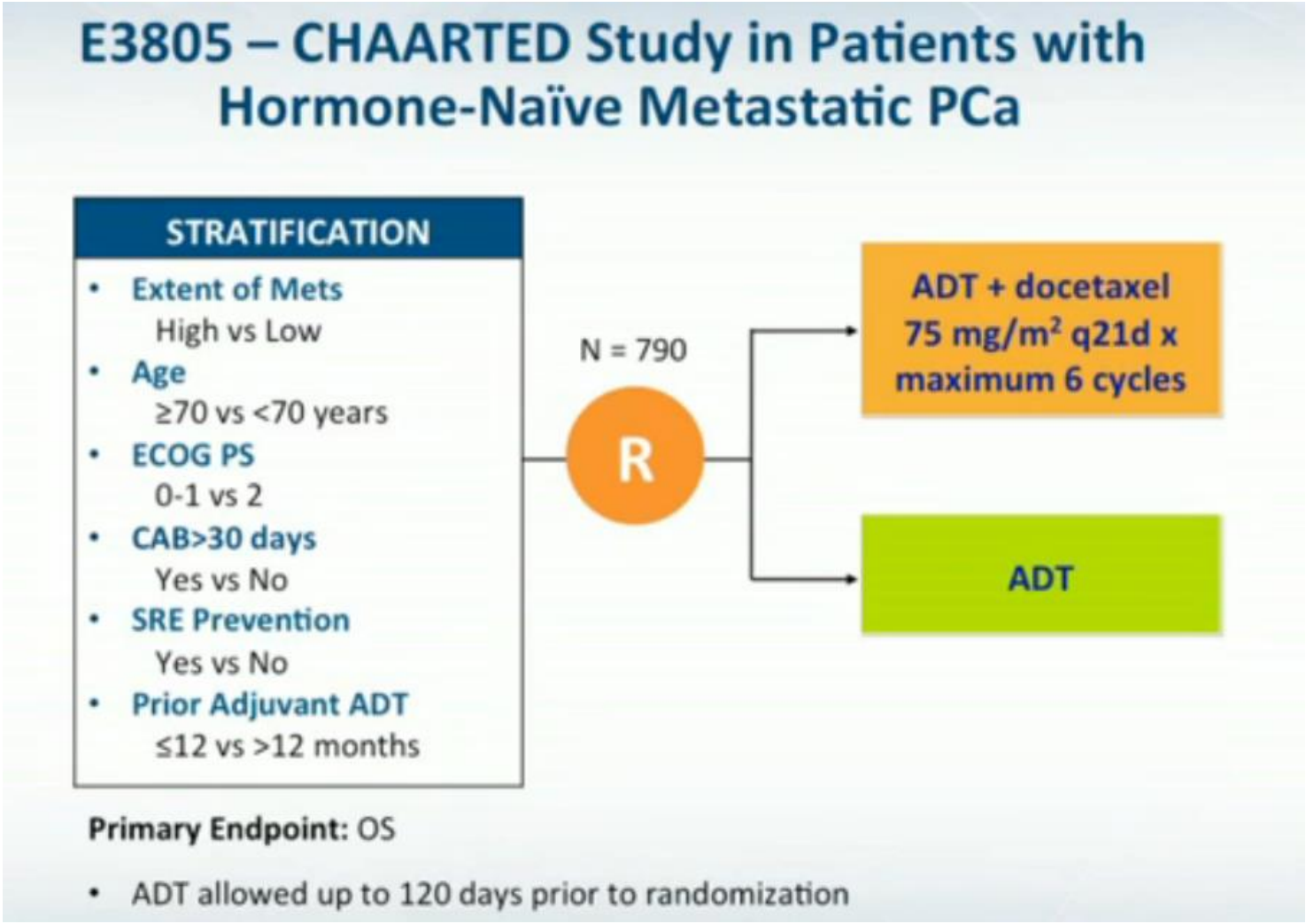
Kemik, viseral ve lenf nodu metastazı ve doğru evreleme için

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

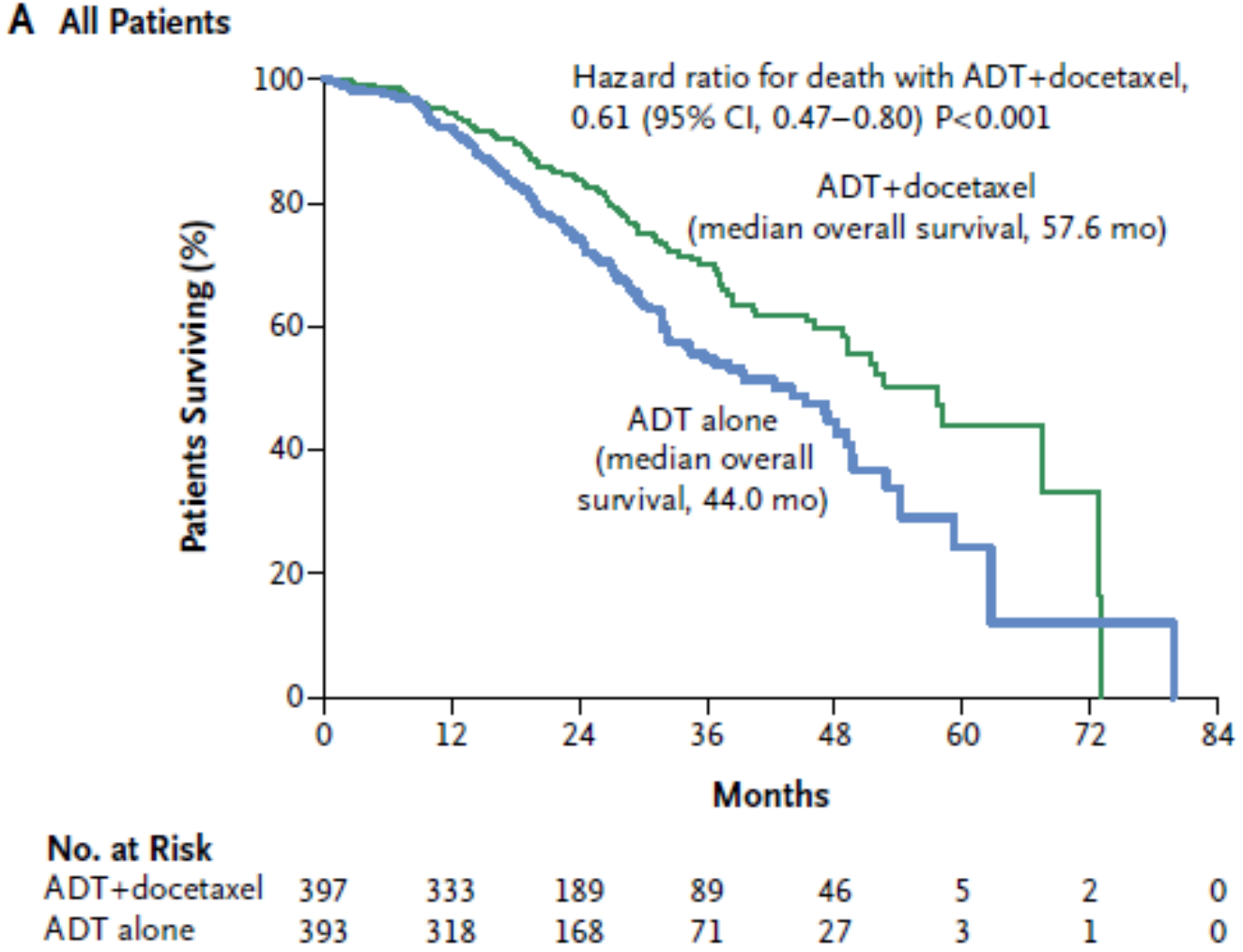
1. Heidenreich A. EAU guidelines on prostate cancer. Part I. Eur Urol. 2014
2. Heidenreich A. EAU guidelines on prostate cancer. Part II. Eur Urol. 2014
3. Mohler JL. Prostate cancer. Version 1.2016. J Natl Compr Canc Netw. 2016

Hormon Duyarlı Metastatik Prostat Kanseri

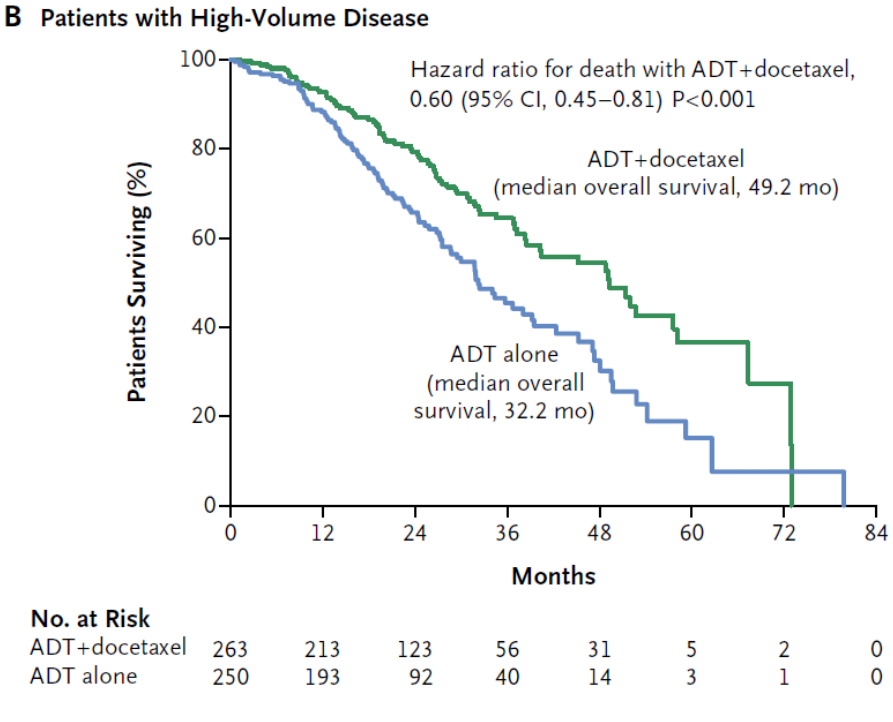
ADT + Erken Dönem Kemoterapi

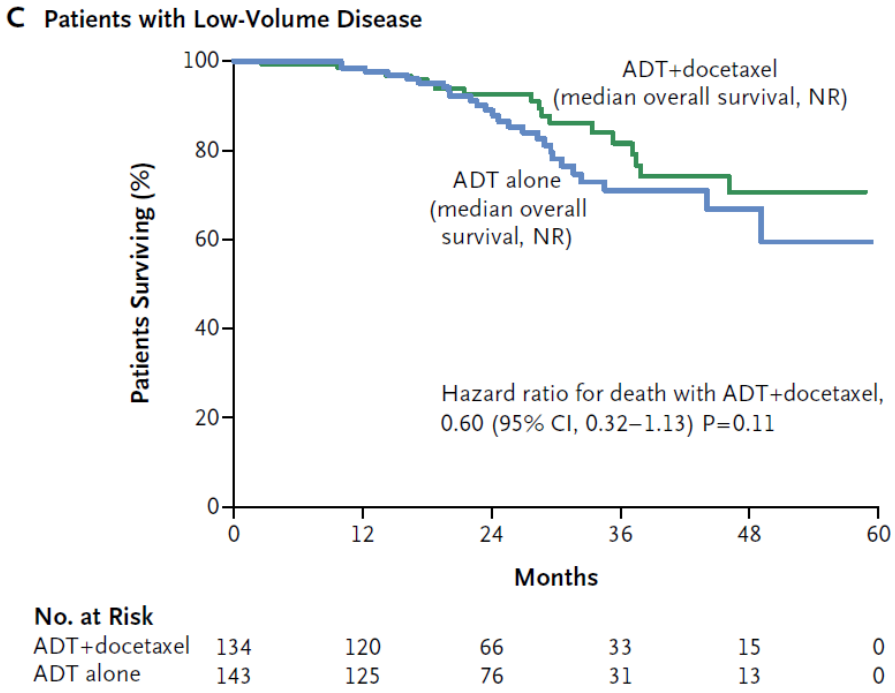


ADT + Erken Dönem Kemoterapi



ADT + Erken Dönem Kemoterapi

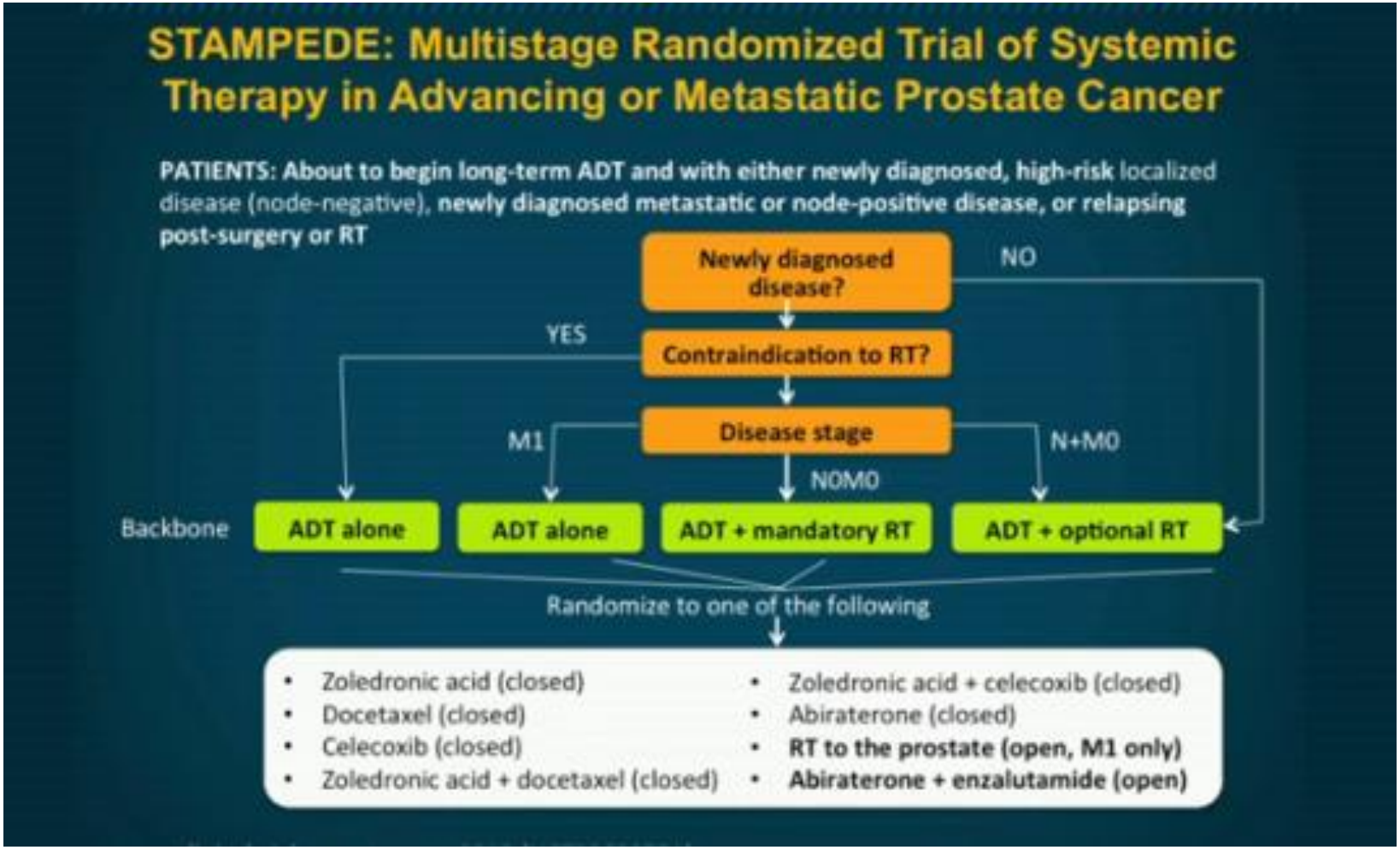




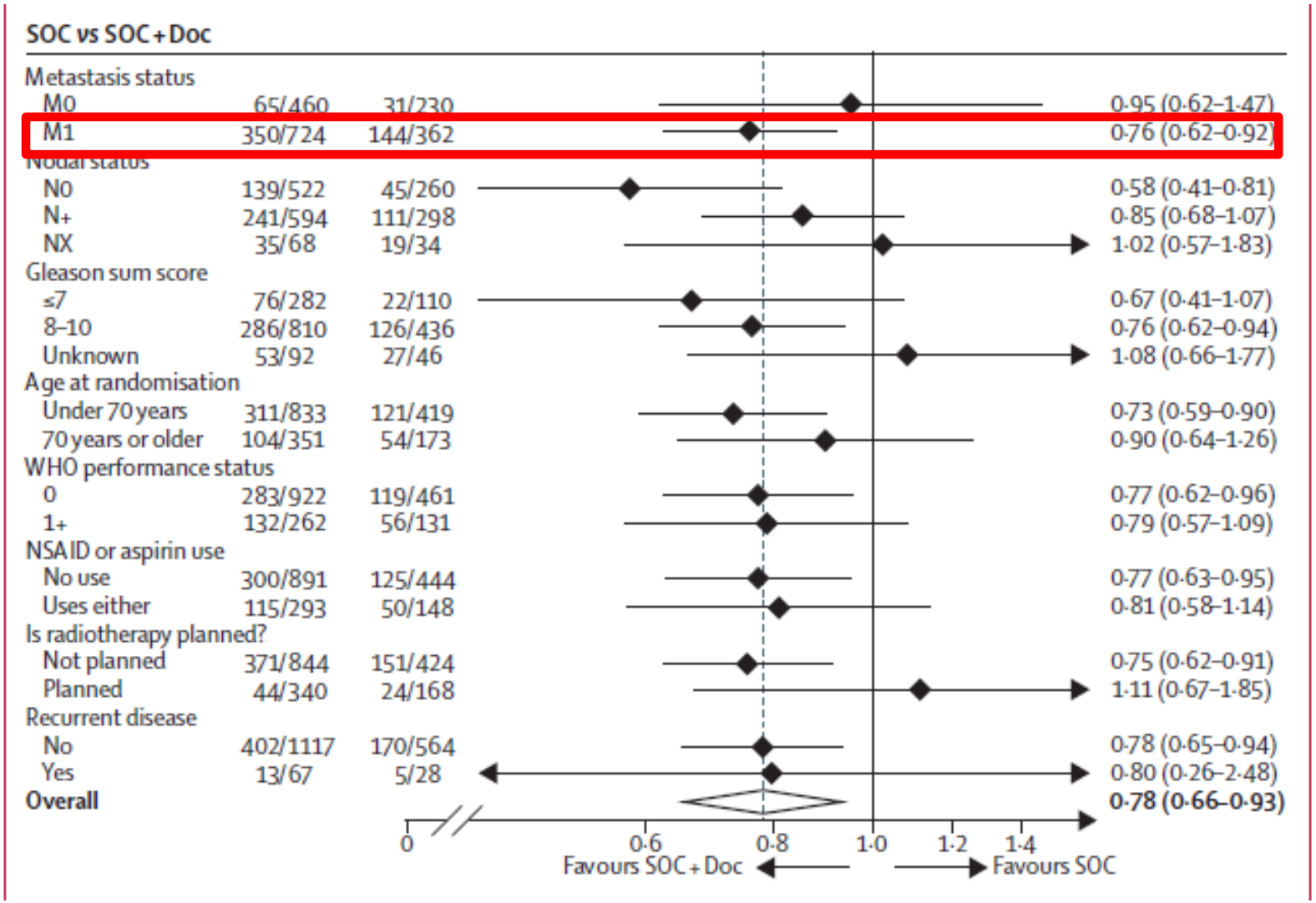
Yüksek volümlü hastalığı olanlar; viseral organ metastazı olan yada ≥4 kemik lezyonu olan ve en az ≥1 vertebra, pelvis dışı kemiklerde metastaz olmalı

Hormon Duyarlı Metastatik Prostat Kanseri

ADT + Erken Dönem Kemoterapi

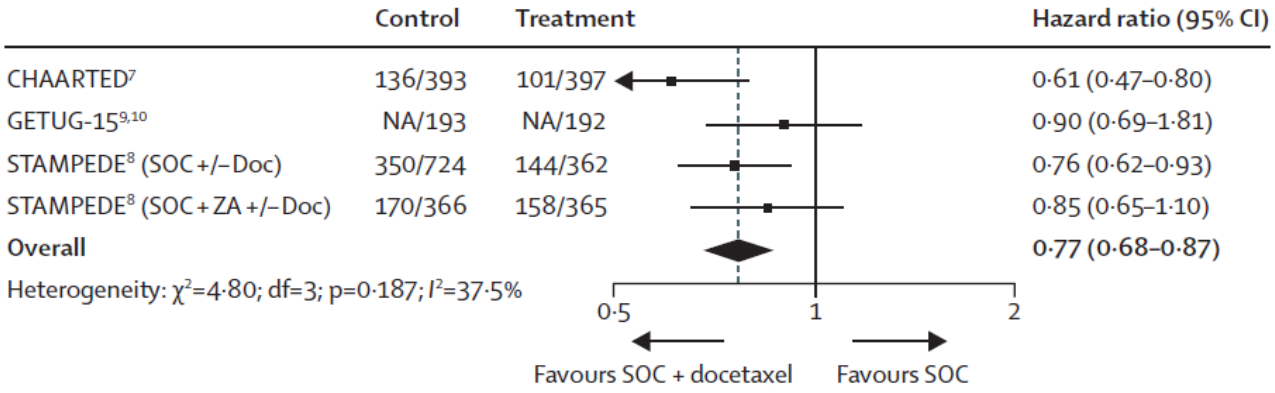


ADT + Erken Dönem Kemoterapi

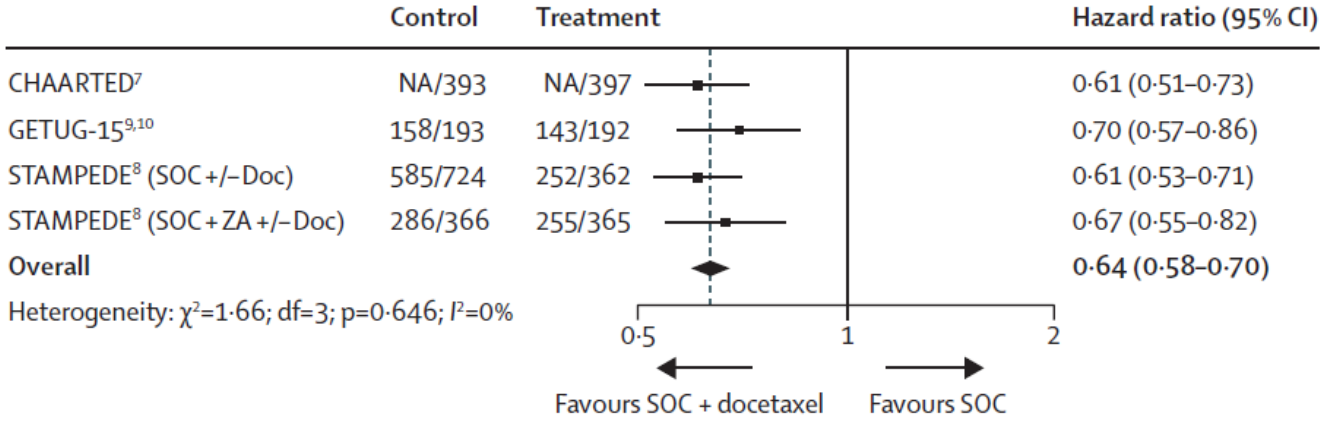


Hormon Duyarlı Metastatik Prostat Kanseri

Metaanaliz; ADT + Erken Dönem Kemoterapi



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



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

Hormon Duyarlı Metastatik Prostat Kanseri

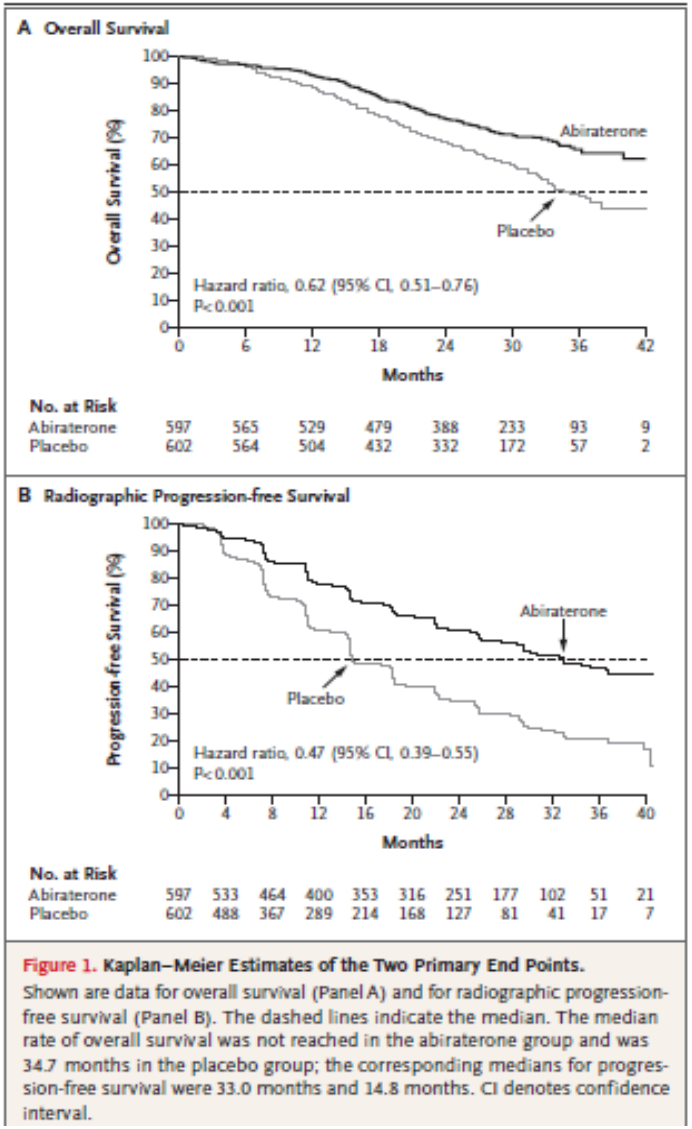


Figure 1. Kaplan–Meier Estimates of the Two Primary End Points.
Shown are data for overall survival (Panel A) and for radiographic progression-free survival (Panel B). The dashed lines indicate the median. The median rate of overall survival was not reached in the abiraterone group and was 34.7 months 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

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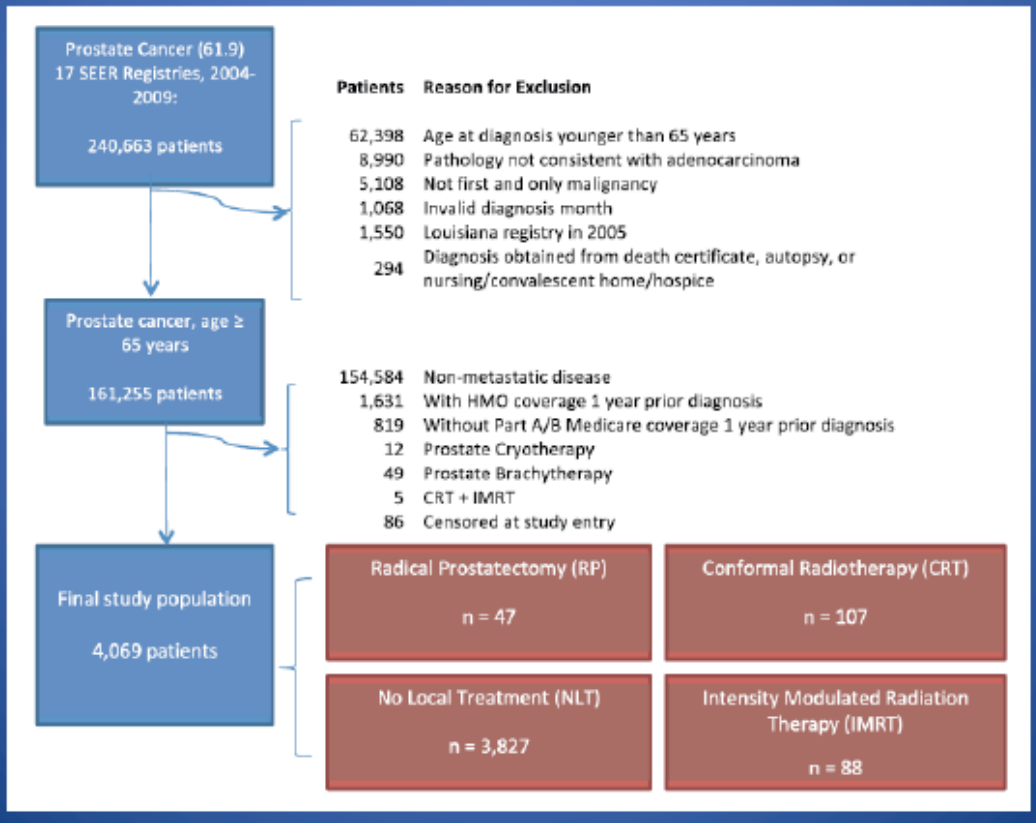
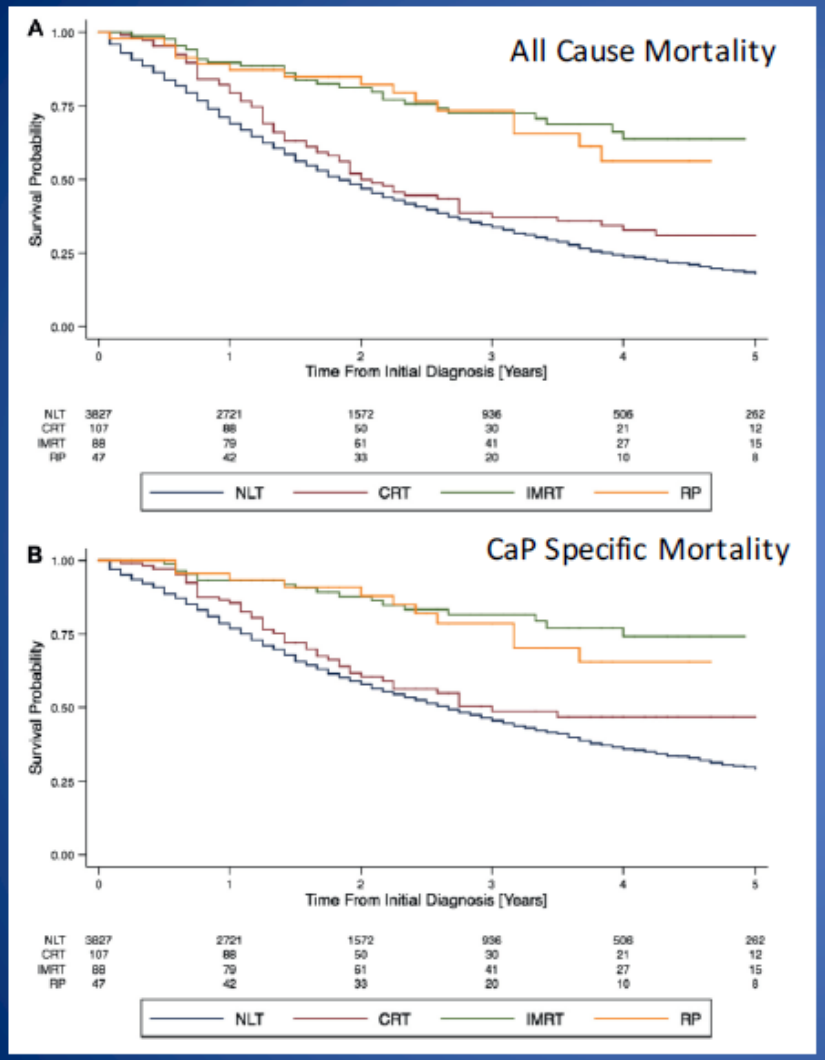


Oligometastatik Prostat Kanseri Retrospektif veri Sonuçları



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

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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 ca hangi hasta grubu lokal tedaviden yarar görebilir

- 70 yaşından genç olan
- Tanı anında PSA değeri 20 ng/mL altında olan
- Klinik T4'den küçük evrede olanlar
- Yüksek Gleason skoruna sahip olmaya(8<)
- Sınırlı sayıda kemik metastazı olan(<4)
- Bulk lenfadenopatisi olmayan
- 6 aylık ADT sonrası PSA değeri nadir yada 1 ng/mL düşük olanlar

Culp SH, et al. Might men diagnosed with metastatic prostate cancer benefit from definitive treatment of the primary tumor? A SEER-based study. Eur Urol. 2014;65:1058-66.

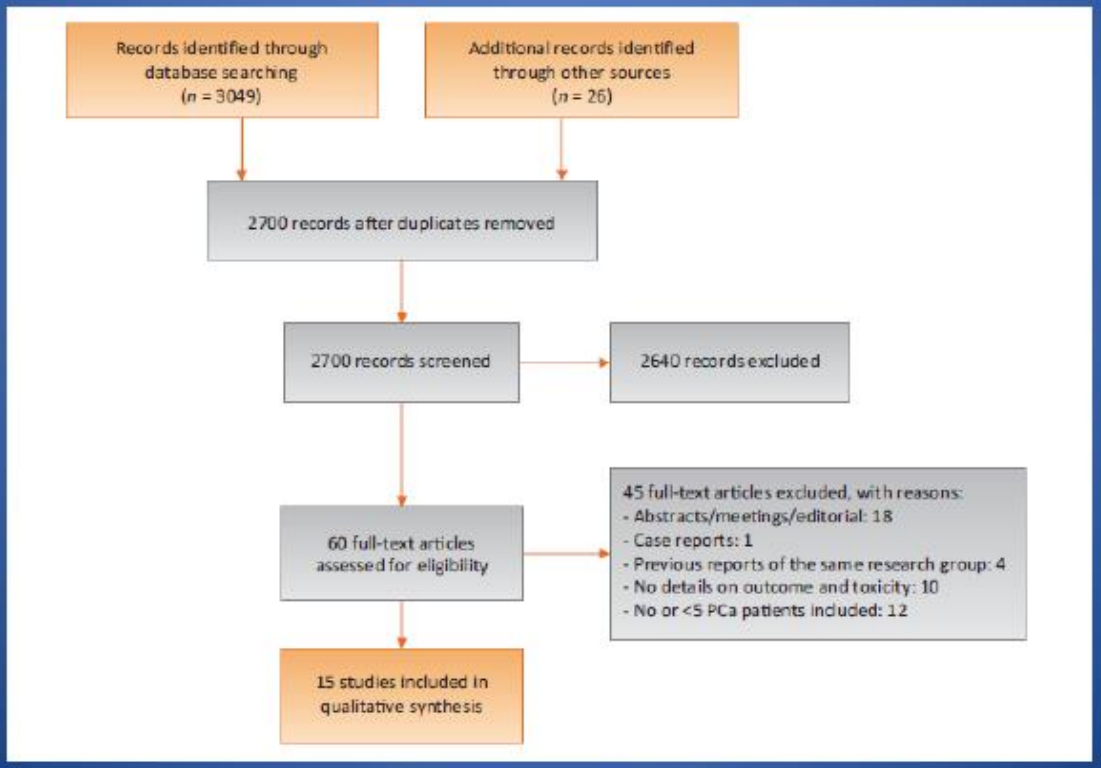
Heidenreich A, Pfister D, Porres D. Cytoreductive radical prostatectomy in patients with prostate cancer and low volume skeletal metastases: results of a feasibility and case-control study. J Urol. 2015;193:832-8.

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.

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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.

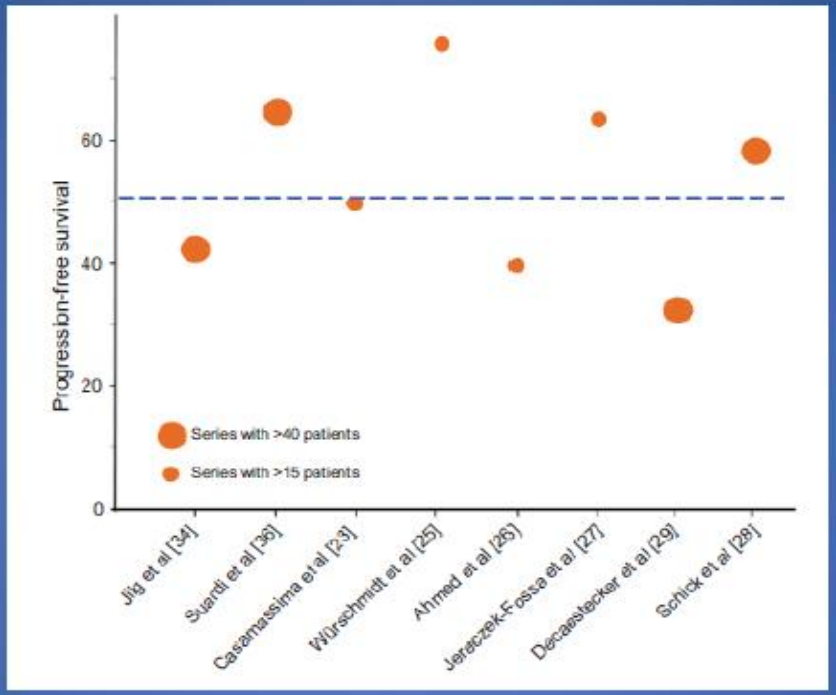
Complication type	Muacevic et al. [24] (*n* = 40), no. (%)	Würschmidt et al.* [25] (*n* = 15), no. (%)	Ahmed et al. [26] (*n* = 17), no. (%)	Jereczek-Fossa et al. [27] (*n* = 19), no. (%)	Decaestecker et al. [29] (*n* = 50), no. (%)	Total (*n* = 141), no. (%)
Grade 1						
Bone pain	0 (0)	0 (0)	0 (0)	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.

Oligometastatik Prostat Kanseri Retrospektif veri Sonuçları



15 ve üzeri hasta sayısı olan çalışmalar analize dahil edildiğinde; 3 yılık ortalama PFS tüm çalışmalarda yaklaşık %50 bulunmuş

EUROPEAN UROLOGY 67 (2015) 852–863

Oligometastatik Prostat Kanseri Prospektif Faz II Çalışma Sonuçları

VOLUME 36 · NUMBER 5 · FEBRUARY 10, 2018

JOURNAL OF CLINICAL ONCOLOGY

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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Clinical trial information: NCT01558427.

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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

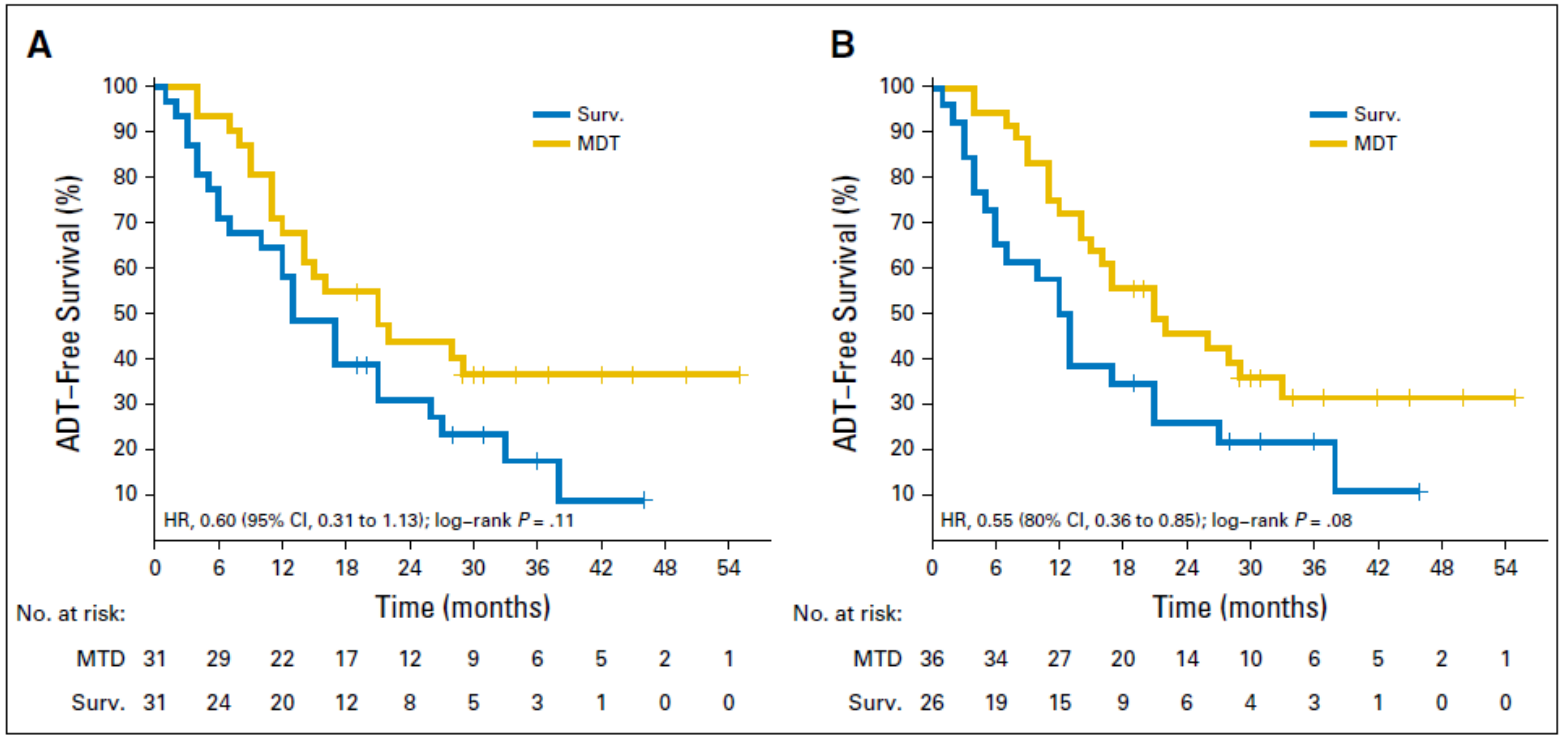

Fig 2. Kaplan-Meier plot comparing androgen deprivation therapy (ADT)–free survival of surveillance versus metastasis-directed therapy (MDT) for (A) the intention-to-treat analysis and (B) the per-protocol analysis. HR, hazard ratio; Surv., surveillance.

Oligometastatik Prostat Kanseri Prospektif Faz II Çalışma Sonuçları

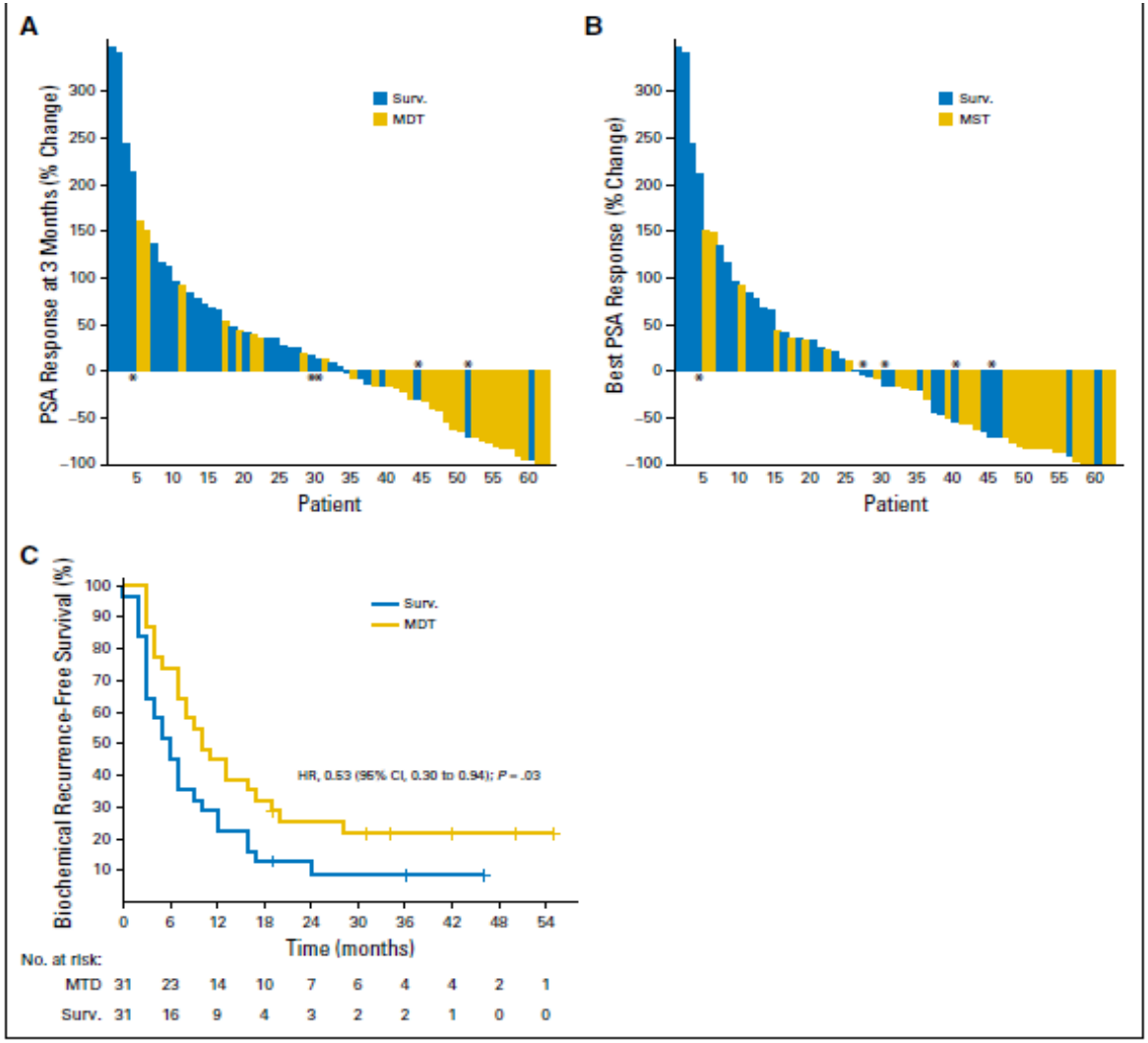

Fig 4. Waterfall plot of (A) the percentage change in prostate-specific antigen (PSA) after 3 months and (B) the best response. (C) Kaplan-Meier plot comparing biochemical recurrence-free survival of Surv versus MDT in the intention-to-treat analysis. (*) Indicates patients who were randomly assigned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

Oligometastatik Prostat Kanseri Prospektif Faz III Çalışma Sonuçları

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European Association of Urology

Platinum Priority – Prostate Cancer
Editorial by XXX on pp. x–y of this issue

Effect on Survival of Androgen Deprivation Therapy Alone Compared to Androgen Deprivation Therapy Combined with Concurrent Radiation Therapy to the Prostate in Patients with Primary Bone Metastatic Prostate Cancer in a Prospective Randomised Clinical Trial: Data from the HORRAD Trial

Liselotte M.S. Boevé[a,b,], Maarten C.C.M. Hulshof[c], André N. Vis[b], Aeilko H. Zwinderman[d], Jos W.R. Twisk[e], Wim P.J. Witjes[f], Karl P.J. Delaere[g], R. Jeroen A. van Moorselaar[b], Paul C.M.S. Verhagen[h], George van Andel[a]*

[a] *Department of Urology, OLVG, Amsterdam, The Netherlands;* [b] *Department of Urology, VU university Medical Centre, Amsterdam, The Netherlands;* [c] *Department of Radiotherapy, Academic Medical Centre, Amsterdam, The Netherlands;* [d] *Department of Epidemiology and Biostatistics, Academic Medical Centre, Amsterdam, The Netherlands;* [e] *Department of Epidemiology and Biostatistics, VU university Medical Centre, Amsterdam, The Netherlands;* [f] *CuraTrial SMO & Research BV, Arnhem, The Netherlands;* [g] *Department of Urology, Zuyderland Medical Centre, Heerlen, The Netherlands;* [h] *Department of Urology, Erasmus Medical Centre, Rotterdam, The Netherlands*

Oligometastatik Prostat Kanseri Prospektif Faz III Çalışma Sonuçları

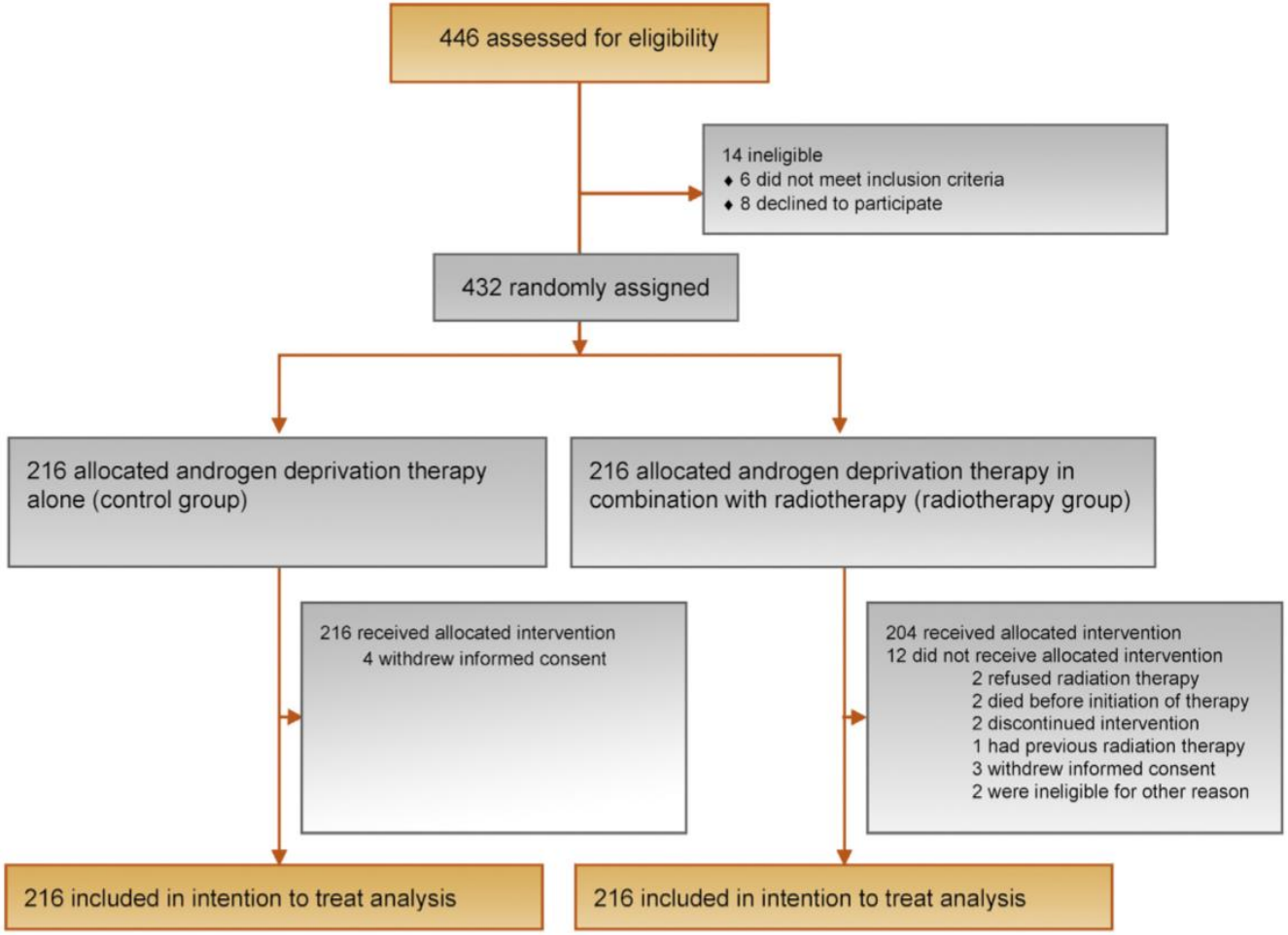
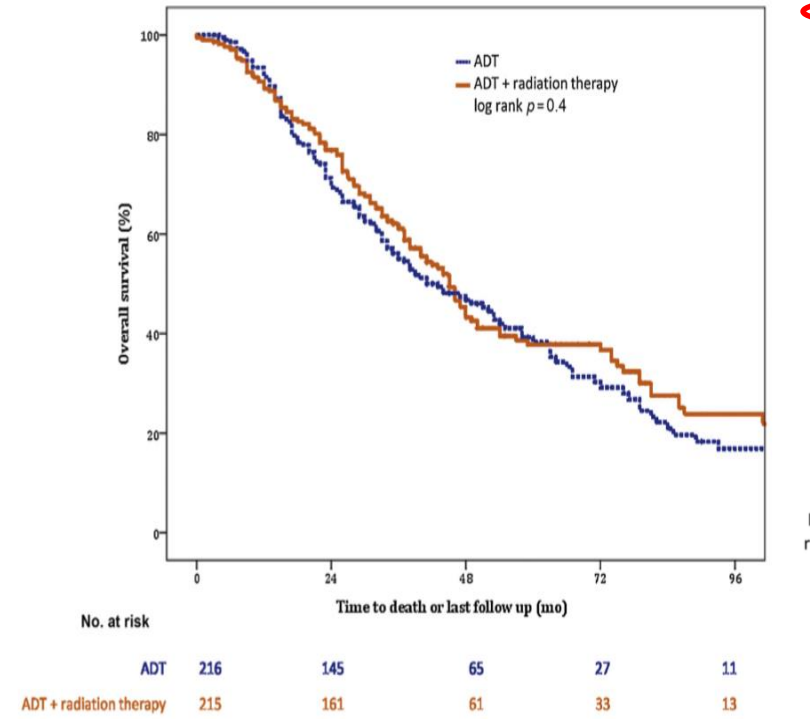
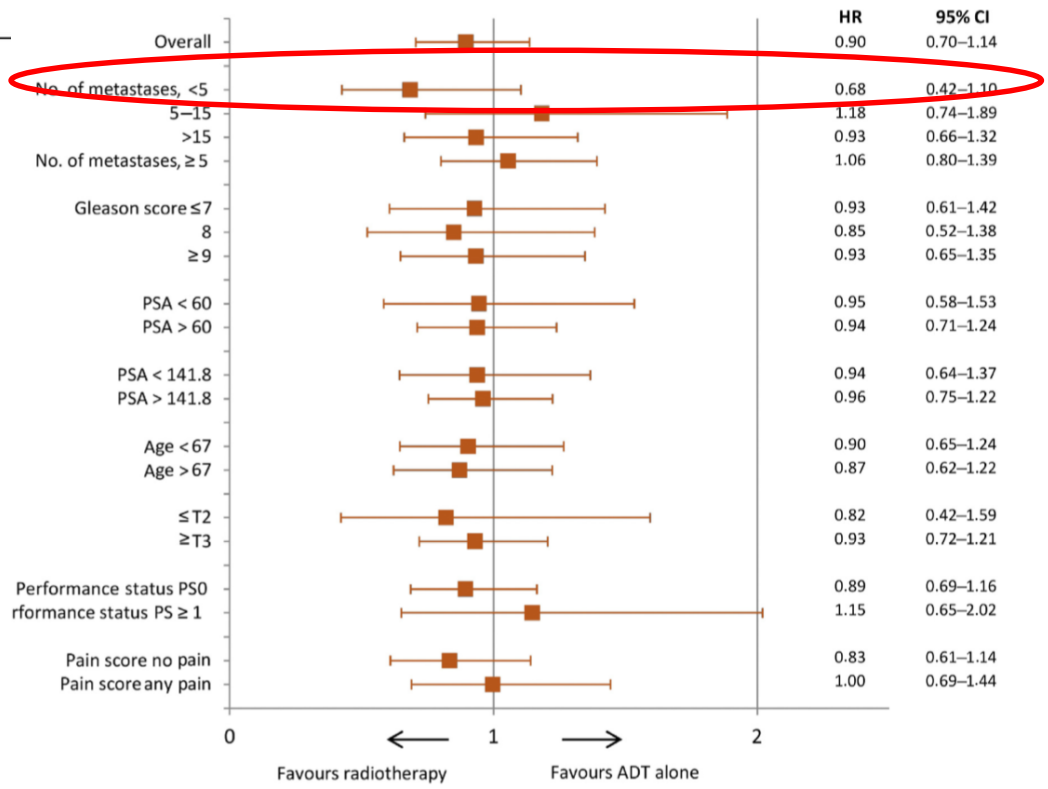


Fig. 1 – Trial profile.

Oligometastatik Prostat Kanseri
Prospektif Faz III Çalışma Sonuçları





Oligometastatik Prostat Kanseri Prospektif Faz III Çalışma Sonuçları

Radiotherapy to the primary tumour for newly diagnosed, metastatic prostate cancer (STAMPEDE): a randomised controlled phase 3 trial

Christopher C Parker, Nicholas D James, Christopher D Brawley, Noel W Clarke, Alex P Hoyle, Adnan Ali, Alastair W S Ritchie, Gerhardt Attard, Simon Chowdhury, William Cross, David P Dearnaley, Silke Gillessen, Clare Gilson, Robert J Jones, Ruth E Langley, Zafar I Malik, Malcolm D Mason, David Matheson, Robin Millman, J Martin Russell, George N Thalmann, Claire L Amos, Roberto Alonzi, Amit Bahl, Alison Birtle, Omar Din, Hassan Douis, Chinnamani Eswar, Joanna Gale, Melissa R Gannon, Sai Jonnada, Sara Khaksar, Jason F Lester, Joe M O'Sullivan, Omi A Parikh, Ian D Pedley, Delia M Pudney, Denise J Sheehan, Narayanan Nair Srihari, Anna T H Tran, Mahesh K B Parmar, Matthew R Sydes*, on behalf of the Systemic Therapy for Advanced or Metastatic Prostate cancer: Evaluation of Drug Efficacy (STAMPEDE) investigators†*

Summary

Background Based on previous findings, we hypothesised that radiotherapy to the prostate would improve overall survival in men with metastatic prostate cancer, and that the benefit would be greatest in patients with a low metastatic burden. We aimed to compare standard of care for metastatic prostate cancer, with and without radiotherapy.

Methods We did a randomised controlled phase 3 trial at 117 hospitals in Switzerland and the UK. Eligible patients had newly diagnosed metastatic prostate cancer. We randomly allocated patients open-label in a 1:1 ratio to standard of care (control group) or standard of care and radiotherapy (radiotherapy group). Randomisation was stratified by hospital, age at randomisation, nodal involvement, WHO performance status, planned androgen deprivation therapy, planned docetaxel use (from December, 2015), and regular aspirin or non-steroidal anti-inflammatory drug use. Standard of care was lifelong androgen deprivation therapy, with up-front docetaxel permitted from December, 2015. Men allocated radiotherapy received either a daily (55 Gy in 20 fractions over 4 weeks) or weekly (36 Gy in six fractions over 6 weeks) schedule that was nominated before randomisation. The primary outcome was overall survival, measured as the number of deaths; this analysis had 90% power with a one-sided α of 2·5% for a hazard ratio (HR) of 0·75. Secondary outcomes were failure-free survival, progression-free survival, metastatic progression-free survival, prostate cancer-specific survival, and symptomatic local event-free survival. Analyses used Cox proportional hazards and flexible parametric models, adjusted for stratification factors. The primary outcome analysis was by intention to treat. Two prespecified subgroup analyses tested the effects of prostate radiotherapy by baseline metastatic burden

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*Contributed equally

†Listed at the end of the Article

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- ❑ YENİ TANI ALMIŞ METASTATİK PROSTAT CA
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- ❑ TÜM HASTALARA ADT YAPILMIŞ
- ❑ HASTALARIN 1/6 DOSETAKSEL ALMIŞ
- ❑ TÜM HASTALAR PRİMER TÜMÖR LOJUNA RT ALMIŞ

Oligometastatik Prostat Kanseri
Prospektif Faz III Çalışma Sonuçları

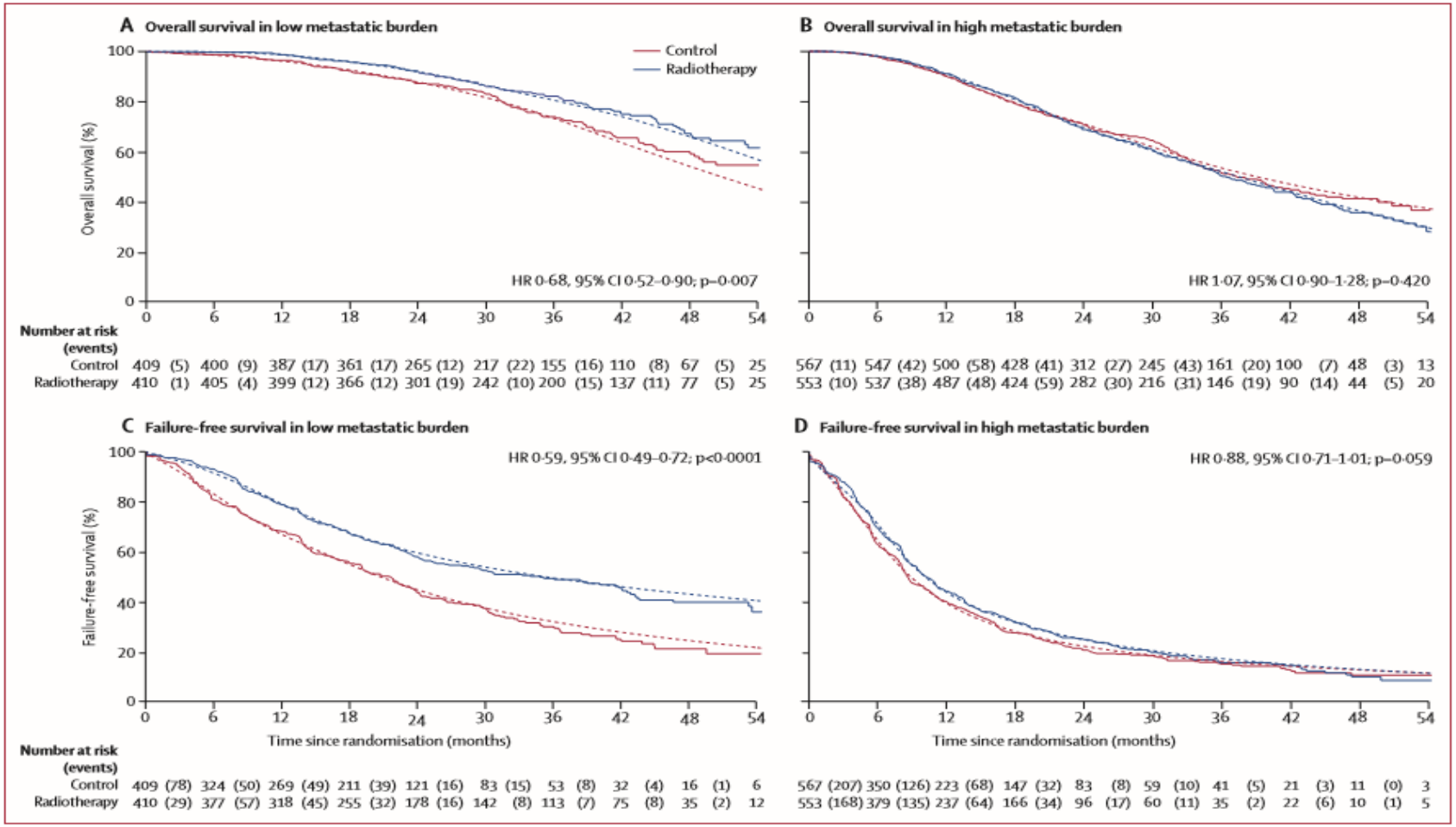

***Figure 4*: Overall survival and failure-free survival by treatment and metastatic burden**
HR=hazard ratio. Solid lines show the Kaplan-Meier analysis and dotted lines show the flexible parametric model.

Oligometastatik Prostat Kanseri Prospektif Faz III Çalışma Sonuçları

	Adjusted hazard ratio (95% CI)	Survival at 3 years*		Restricted mean survival time (months)*		
		Control	Radiotherapy	Control	Radiotherapy	Difference (95% CI)
Overall survival						
All patients	0·92 (0·80–1·06)	62%	65%	41·6	42·5	1·0 (–0·6 to 2·5)
Low metastatic burden	0·68 (0·52–0·90)	73%	81%	45·4	49·1	3·6 (1·0 to 6·2)
High metastatic burden	1·07 (0·90–1·28)	54%	53%	38·8	37·6	–1·2 (–3·5 to 1·1)
Failure-free survival						
All patients	0·76 (0·68–0·84)	23%	32%	21·4	26·2	4·8 (2·8 to 6·7)
Low metastatic burden	0·59 (0·49–0·72)	33%	50%	27·4	36·1	8·6 (5·6 to 11·7)
High metastatic burden	0·88 (0·77–1·01)	17%	18%	17·3	18·8	1·5 (–0·7 to 3·6)
Progression-free survival						
All patients	0·96 (0·85–1·08)	44%	44%	32·4	33·1	0·7 (–0·9 to 2·3)
Low metastatic burden	0·78 (0·63–0·98)	58%	63%	39·4	42·9	3·5 (0·4 to 6·7)
High metastatic burden	1·09 (0·94–1·26)	35%	30%	28·0	26·2	–1·8 (–4·3 to 0·8)
Metastatic progression-free survival						
All patients	0·97 (0·86–1·10)	47%	47%	33·9	34·4	0·4 (–1·5 to 2·4)
Low metastatic burden	0·80 (0·63–1·01)	62%	67%	41·1	44·2	3·1 (0·2 to 6·0)
High metastatic burden	1·10 (0·95–1·28)	37%	33%	29·3	27·3	–2·0 (–4·7 to 0·7)
Prostate cancer-specific survival						
All patients†	0·93 (0·80–1·09)	66%	69%	43·9	44·6	0·7 (–1·1 to 2·5)
Low metastatic burden	0·65 (0·47–0·90)	79%	86%	48·6	51·8	3·3 (1·0 to 5·5)
High metastatic burden	1·10 (0·92–1·32)	58%	56%	40·6	39·0	–1·6 (–3·9 to 0·7)
Symptomatic local event-free survival						
All patients	1·07 (0·93–1·22)	57%	55%	38·2	37·2	–1·1 (–3·1 to 0·9)
Low metastatic burden	0·82 (0·64–1·05)	65%	72%	41·6	44·0	2·4 (–0·7 to 5·4)
High metastatic burden	1·23 (1·05–1·46)	50%	43%	35·8	32·2	–3·6 (–6·2 to –1·0)

Hazard ratio and restricted mean survival time differences are for radiotherapy relative to control. *Survival probabilities and restricted mean survival time estimates are taken from flexible parametric models (t-star, 59 months). †Competing risks analysis, sub-hazard ratio 0·94, 95% CI 0·81–1·10; p=0·431.

Table 2: **Summary of estimated treatment effect for main outcome measures, for all patients and by metastatic burden**

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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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Save this study

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**

Sponsor:
UNICANCER

Collaborators:
Janssen-Cilag Ltd.
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Metastatik Prostat Kanseri Tedavi Algoritması

National Comprehensive Cancer Network®

NCCN Guidelines Version 2.2017
Prostate Cancer

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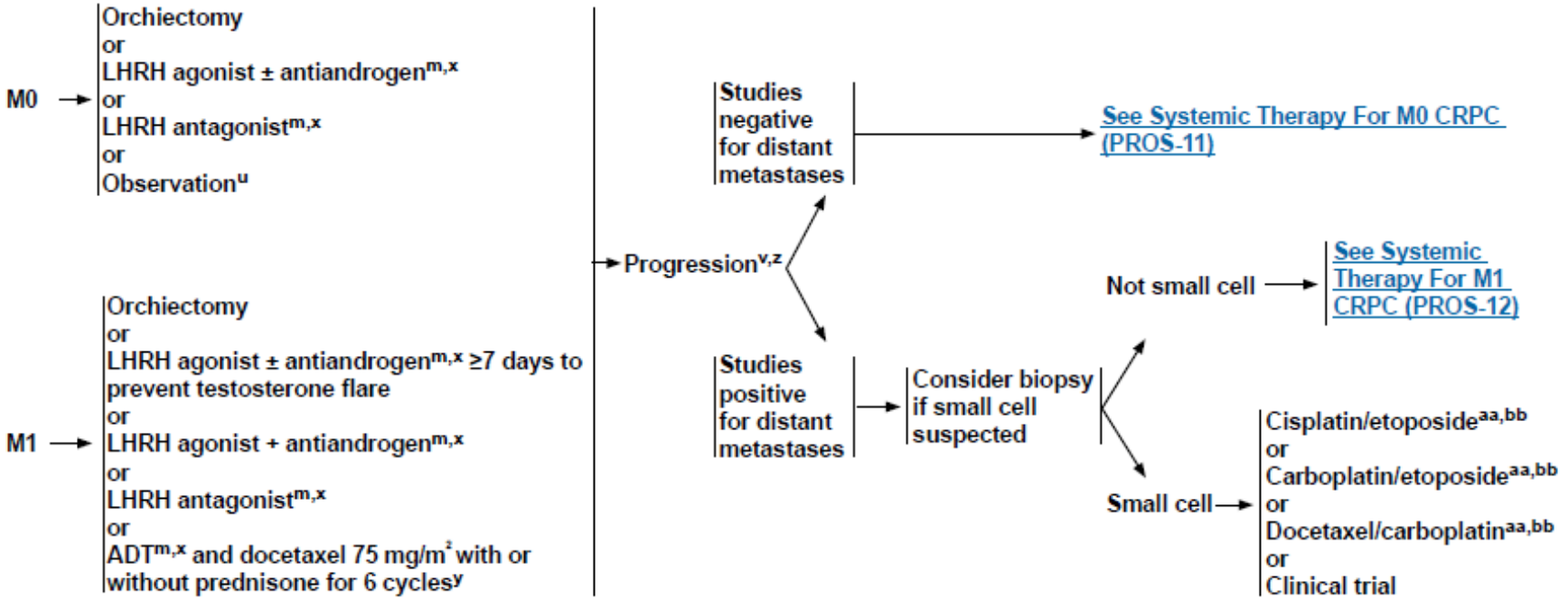
SYSTEMIC THERAPY FOR PROGRESSIVE CASTRATION-NAIVE DISEASE[w]



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