Generalitat de Catalunya
Departament de Salut

ICO
Institut Català d'Oncologia

Pròstata en estadi IV:

Tractament del primari i impacte dels nous tractaments sistèmics

À. Roselló (ICO-Girona)

XXVI CONGRÉS GOCO
16 de Novembre de 2018

Å **Standard of care**:

- Deprivación androgènica +/- QT
- Deprivación androgènica +/- Abiraterone

Addition of docetaxel or bisphosphonates to standard of care in men with localised or metastatic, hormone-sensitive prostate cancer: a systematic review and meta-analyses of aggregate data

Claire L Vale, Sarah Burdett*, Larysa H M Rydzewska, Laurence Albiges, Noel W Clarke, David Fisher, Karim Fizazi, Gwenaelle Gravis, Nicholas D James, Malcolm D Mason, Mahesh K B Parmar, Christopher J Sweeney, Matthew R Sydes, Bertrand Tombal, Jayne F Tierney, for the STOpCaP Steering Group*

Docetaxel

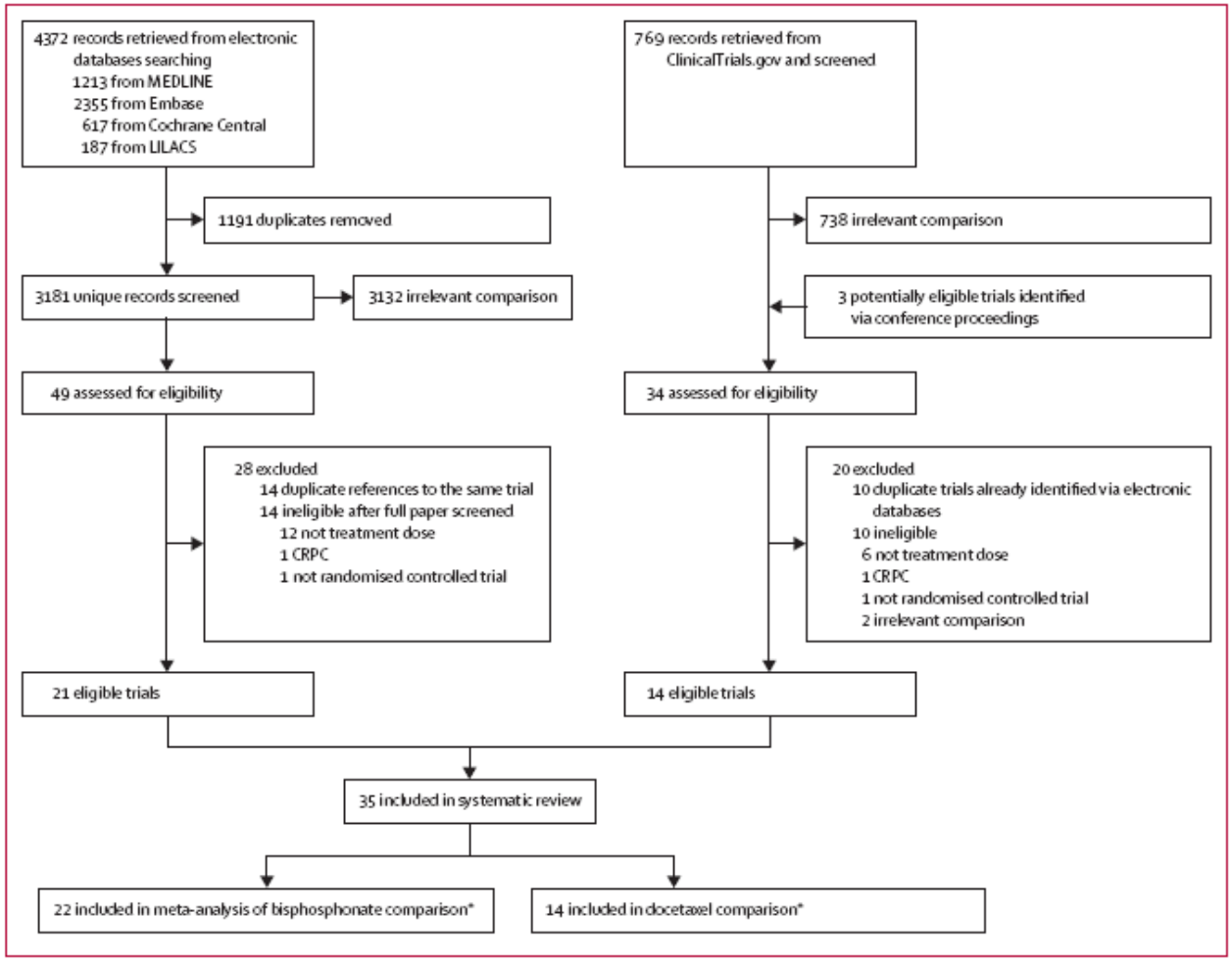


Figure 1: Study flow chart
CRPC=castrate-resistant prostate cancer. *One trial (STAMPEDE)[1] is eligible to be included in both docetaxel and bisphosphonate comparisons.

Docetaxel

	Accrual period	Number of patients	Control	Treatment	Metastatic status	Median age (range)	Gleason score of 8–10 (%)	Performance status of 0–1 (%)	Median follow-up (survival)	Treatment on progression (control group only)
Docetaxel trials										
GETUG-12[35,36]	November, 2002–December, 2006	413	ADT (goserelin 10·8 mg every 3 months for 3 years)	ADT plus docetaxel (70 mg/m² for four cycles) plus estramustine	M0	63 (46–77)	42%	Unknown	7 years, 6 months	Not reported
TAX 3501[37]	December, 2005–September, 2007	228	ADT (leuprolide 22·5 mg every 3 months for 18 months)	ADT plus docetaxel (75 mg/m² every 3 weeks for six cycles)	M0	61·9*	52%	Unknown	3 years, 3 months	Not reported
RTOG 0521[38]	December, 2005–August, 2009	612	ADT (LHRH agonist plus oral anti-androgen plus RT)	ADT plus docetaxel (75 mg/m² every 3 weeks for six cycles) plus prednisone	M0	66 (unknown)	84%	Unknown	6 years	Not reported
STAMPEDE (standard of care with or without docetaxel)[9]	September, 2005–March, 2013	1776	ADT (plus radiotherapy for M0 patients)	ADT plus docetaxel (75 mg/m² every 3 weeks for six cycles) plus predisone	M0 and M1	65 (40–82)	70%	99%	3 years, 6 months	40% received docetaxel (49% received life-extending treatments)
STAMPEDE (standard of care plus zoledronic acid with or without docetaxel)[9]	September, 2005–March, 2013	1186	ADT (plus radiotherapy for M0 patients) plus zoledronic acid (4 mg every 3–4 weeks for 2 years)	ADT (plus radiotherapy for M0 patients) + zoledronic acid (4 mg for 3–4 weeks for 2 years) plus docetaxel (75 mg/m² every 3 weeks for six cycles)	M0 and M1	66 (42–84)	71%	99%	3 years, 6 months	36% received docetaxel (45% received life-extending treatments)
GETUG-15[9,10]	October, 2004–December, 2008	385	ADT (LHRH agonist or surgical castration or combined androgen blockade)	ADT plus docetaxel (75 mg/m² every 3 weeks for up to nine cycles)	M1	63·5 (57–70)	56%	100%	6 years, 11 months	62% received docetaxel
CHAARTED[7]	July, 2006–November, 2012	790	ADT (LHRH agonist or LHRH antagonist) or surgical castration	ADT plus docetaxel (75 mg/m² every 3 weeks for six cycles)	M1	64 (36–91)	61%	98%	2 years, 5 months	147 (51%) of 287 men received docetaxel (104 of 287 men received abiratarone or enzalutamide)

Docetaxel

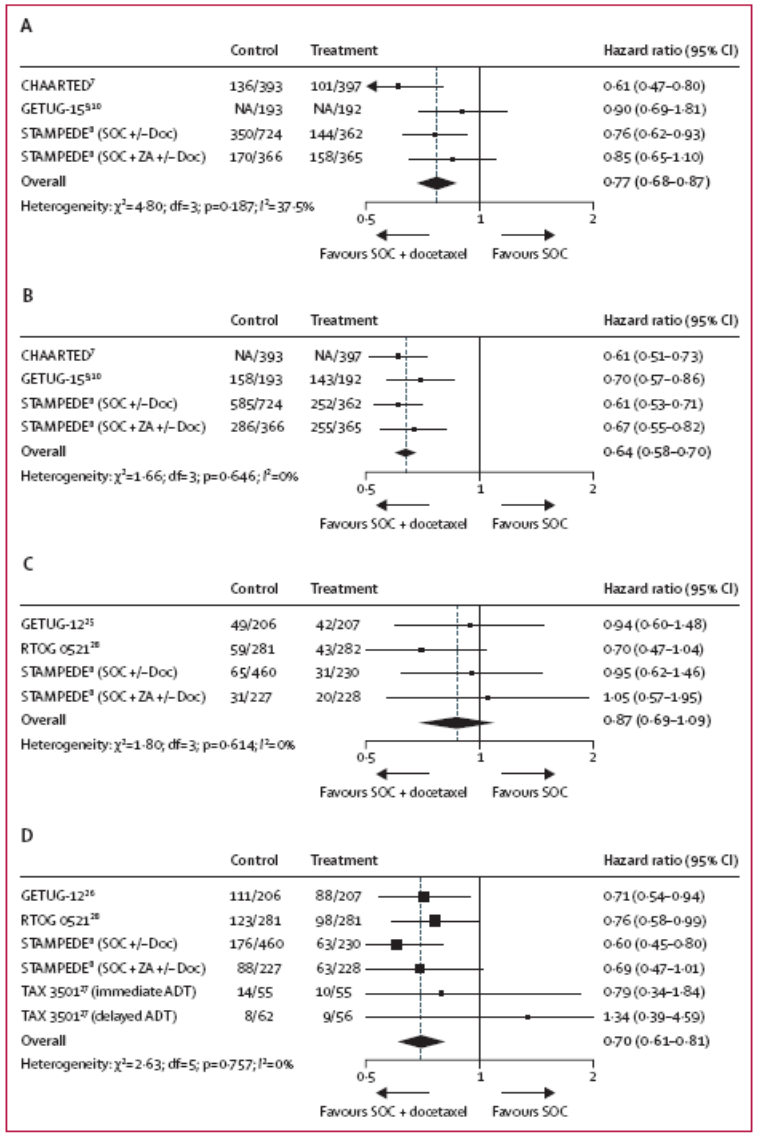


Figure 2: Effect of addition of docetaxel to standard of care on survival and failure-free survival
(A) Effect of the addition of docetaxel on survival in men with M1 disease. (B) Effect of the addition of docetaxel on failure-free survival in men with M1 disease. (C) Effect of the addition of docetaxel on survival in men with M0 disease. (D) Effect of the addition of docetaxel on failure-free survival in men with M0 disease. NA=event numbers by group not available. SOC=standard of care.

- M1
  - HR: 0.77 (0.68-0.87)
  - ↑absolut 9% OS a 4 anys (95% CI 5-14)
  - (49% vs 40%)
- HR: 0.64 (0.58-0.70)
  - ↑absolut 16% FFS a 4 anys (95% CI 12-19)
  - (36% vs 20%)
- M0
  - HR: 0.87 (0.69-1.09)
  - No diferències en OS
- HR: 0.70 (0.61-0.81)
  - ↑absolut 8% FFS a 4 anys (95% CI 5-10)
  - (78% vs 70%)

The NEW ENGLAND JOURNAL of MEDICINE

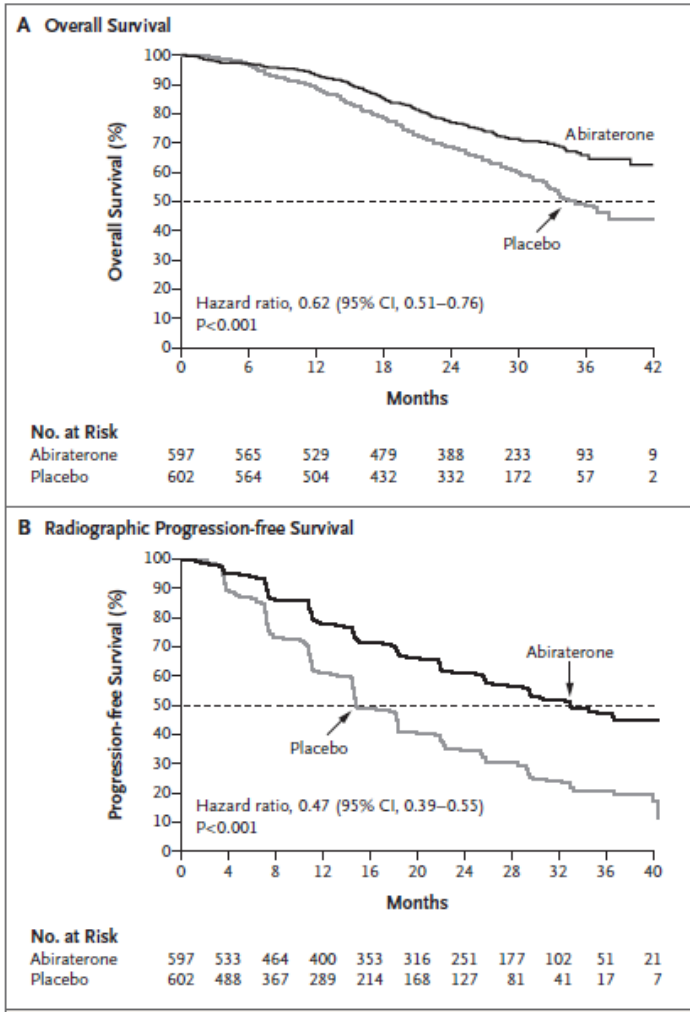
ORIGINAL ARTICLE

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*

LATITUDE

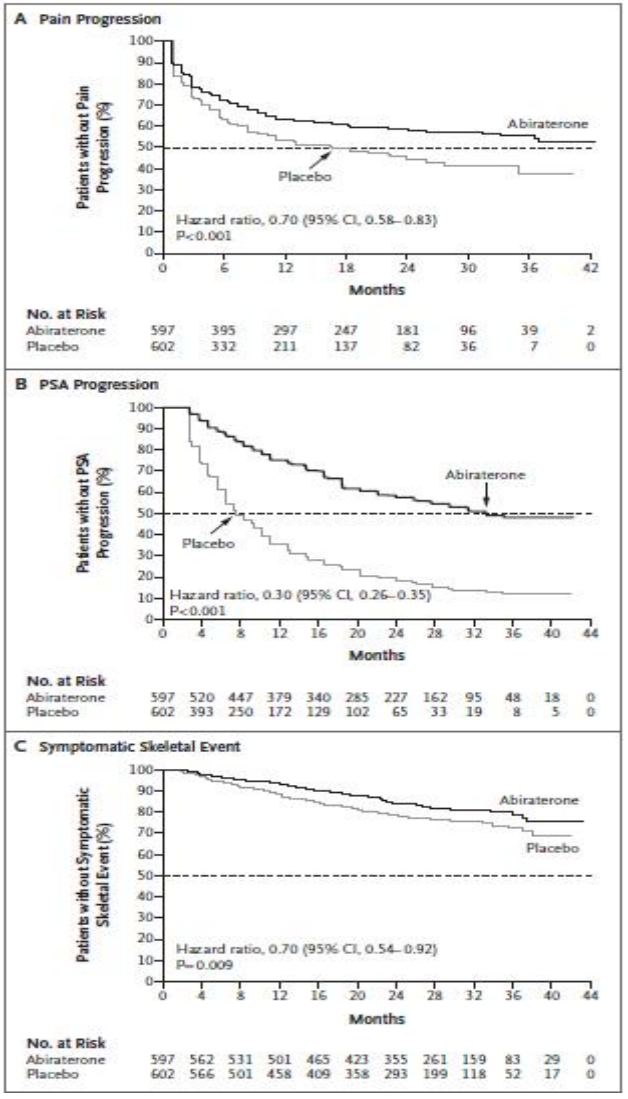
	ADT plus abiraterone acetate and prednisone group (n=597)	ADT plus placebos group (n=602)
Median age, years (range)	68 (38-89)	67 (33-92)
Gleason score at initial diagnosis		
<7	4 (1%)	1 (<1%)
7	9 (2%)	15 (2%)
≥8	584 (98%)	586 (97%)
ECOG performance status at baseline		
0	326 (55%)	331 (55%)
1	245 (41%)	255 (42%)
2	26 (4%)	16 (3%)
Patients with ≥3 bone metastases at screening	586 (98%)	585 (97%)
Extent of disease		
Number of patients	596	600
Bone	580 (97%)	585 (98%)
Liver	32 (5%)	30 (5%)
Lungs	73 (12%)	72 (12%)
Node	283 (47%)	287 (48%)
Prostate mass	151 (25%)	154 (26%)
Viscera	18 (3%)	13 (2%)
Soft tissue	9 (2%)	15 (3%)
Other	2 (<1%)	0
Baseline BPI-SF scores		
Number of patients	570	579
Worst pain in the past 24 h	2·2 (2·5)	2·2 (2·4)
Least pain in the past 24 h	1·2 (1·7)	1·2 (1·8)
Average pain in the past 24 h	1·8 (1·9)	1·9 (1·9)
Pain at time of survey	1·4 (1·9)	1·3 (1·9)
Percentage of pain relief in the past 24 h with use of medication*	35·8 (40·5)	37·5 (41·4)
Pain interference subscale score	1·5 (2·0)	1·5 (2·0)



LATITUDE

Table 1. Prespecified Secondary and Exploratory Efficacy End Points.*

End Point	Abiraterone Group (N=597)	Placebo Group (N=602)	Hazard Ratio (95% CI)	P Value†
Secondary end points				
Median time to pain progression (mo)	NR	16.6	0.70 (0.58–0.83)	<0.001
Median time to PSA progression (mo)	33.2	7.4	0.30 (0.26–0.35)	<0.001
Median time to next symptomatic skeletal event (mo)	NR	NR	0.70 (0.54–0.92)	0.009
Median time to chemotherapy (mo)	NR	38.9	0.44 (0.35–0.56)	<0.001
Median time to subsequent prostate cancer therapy (mo)	NR	21.6	0.42 (0.35–0.50)	<0.001
Exploratory end point				
Patients with a PSA response (%)‡	91	67	1.36 (1.28–1.45)	<0.001



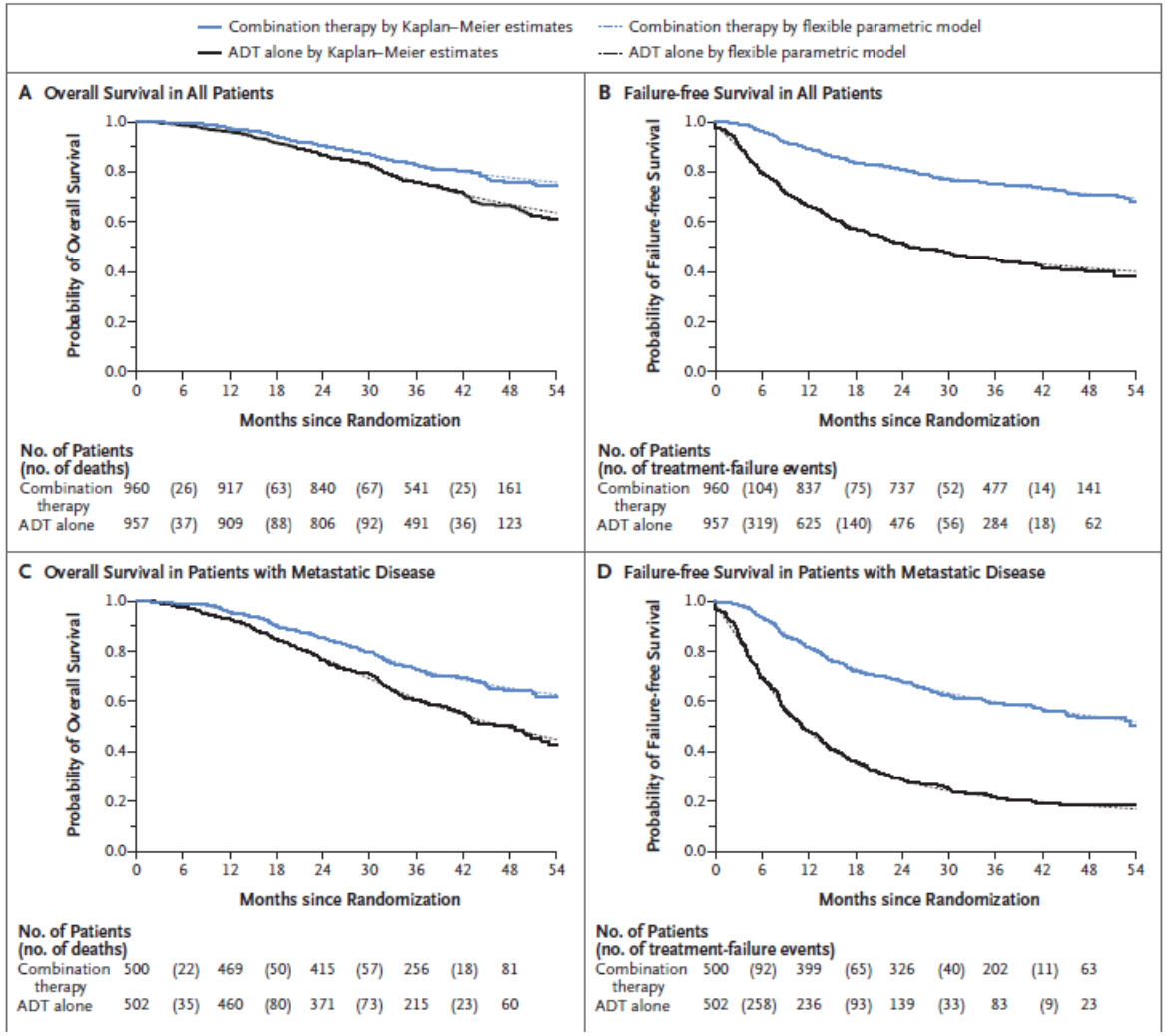
The NEW ENGLAND JOURNAL of MEDICINE

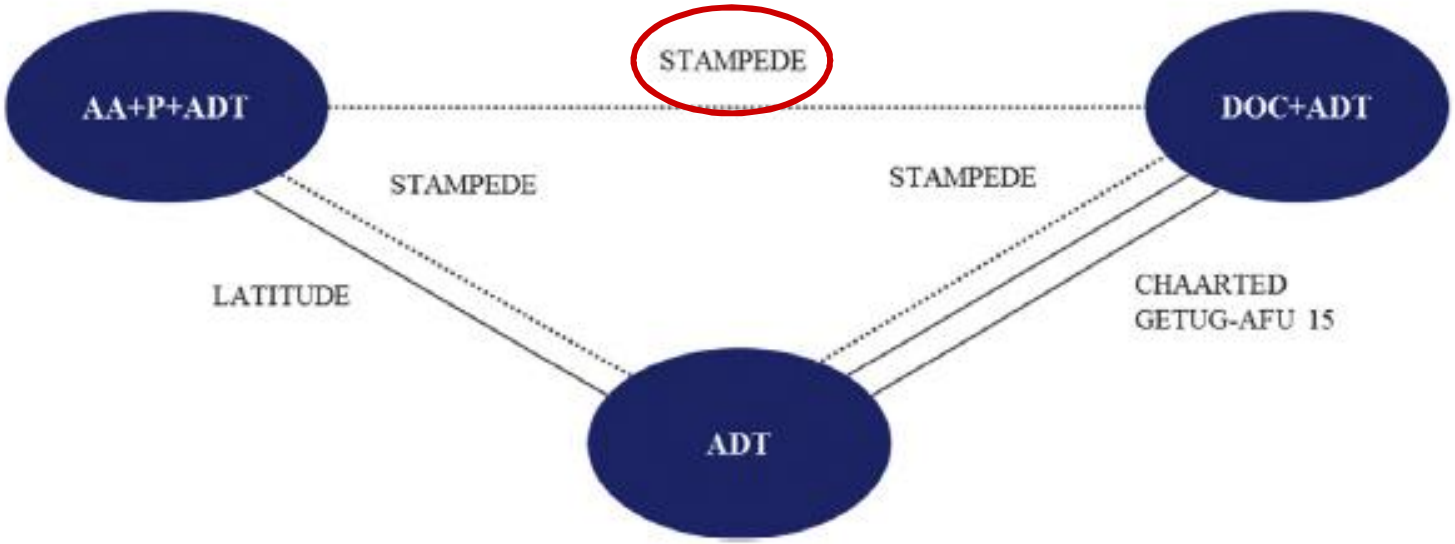
ORIGINAL ARTICLE

Abiraterone for Prostate Cancer Not Previously Treated with Hormone Therapy

N.D. James, J.S. de Bono, M.R. Spears, N.W. Clarke, M.D. Mason, D.P. Dearnaley, A.W.S. Ritchie, C.L. Amos, C. Gilson, R.J. Jones, D. Matheson, R. Millman, G. Attard, S. Chowdhury, W.R. Cross, S. Gillessen, C.C. Parker, J.M. Russell, D.R. Berthold, C. Brawley, F. Adab, S. Aung, A.J. Birtle, J. Bowen, S. Brock, P. Chakraborti, C. Ferguson, J. Gale, E. Gray, M. Hingorani, P.J. Hoskin, J.F. Lester, Z.I. Malik, F. McKinna, N. McPhail, J. Money-Kyrle, J. O'Sullivan, O. Parikh, A. Protheroe, A. Robinson, N.N. Srihari, C. Thomas, J. Wagstaff, J. Wylie, A. Zarkar, M.K.B. Parmar, and M.R. Sydes, for the STAMPEDE Investigators*

STAMPEDE


Combination therapy by Kaplan–Meier estimates
ADT alone by Kaplan–Meier estimates
Combination therapy by flexible parametric model
ADT alone by flexible parametric model
A Overall Survival in All Patients
Probability of Overall Survival
Months since Randomization
No. of Patients (no. of deaths)
Combination therapy 960 (26) 917 (63) 840 (67) 541 (25) 161
ADT alone 957 (37) 909 (88) 806 (92) 491 (36) 123
B Failure-free Survival in All Patients
Probability of Failure-free Survival
Months since Randomization
No. of Patients (no. of treatment-failure events)
Combination therapy 960 (104) 837 (75) 737 (52) 477 (14) 141
ADT alone 957 (319) 625 (140) 476 (56) 284 (18) 62
C Overall Survival in Patients with Metastatic Disease
Probability of Overall Survival
Months since Randomization
No. of Patients (no. of deaths)
Combination therapy 500 (22) 469 (50) 415 (57) 256 (18) 81
ADT alone 502 (35) 460 (80) 371 (73) 215 (23) 60
D Failure-free Survival in Patients with Metastatic Disease
Probability of Failure-free Survival
Months since Randomization
No. of Patients (no. of treatment-failure events)
Combination therapy 500 (92) 399 (65) 326 (40) 202 (11) 63
ADT alone 502 (258) 236 (93) 139 (33) 83 (9) 23


AA+P+ADT
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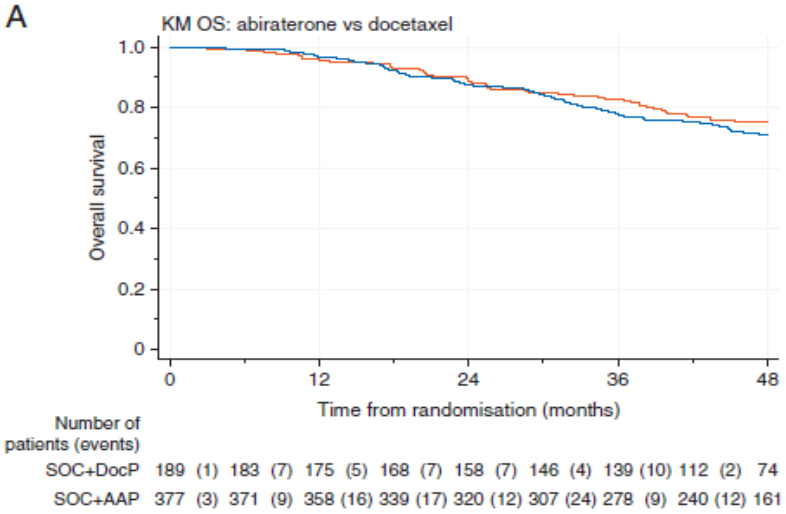
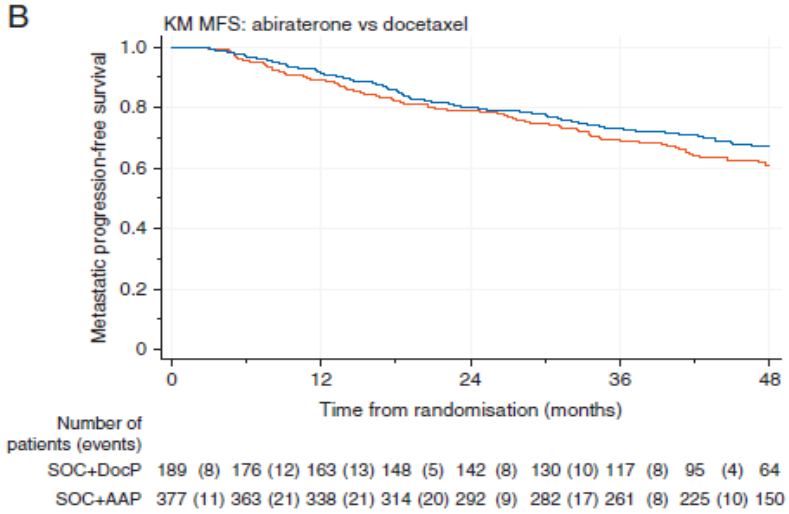
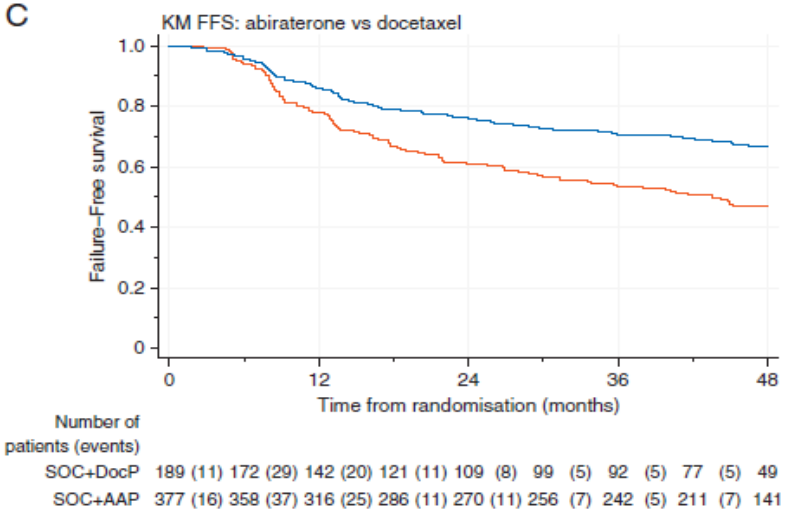
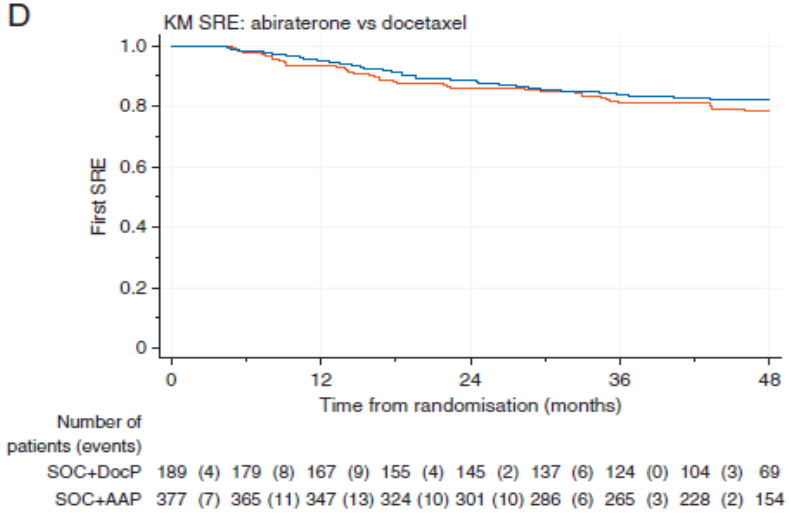
LATITUDE
CHAARTED
GETUG-AFU 15
ADT

Docetaxel vs Abiraterone







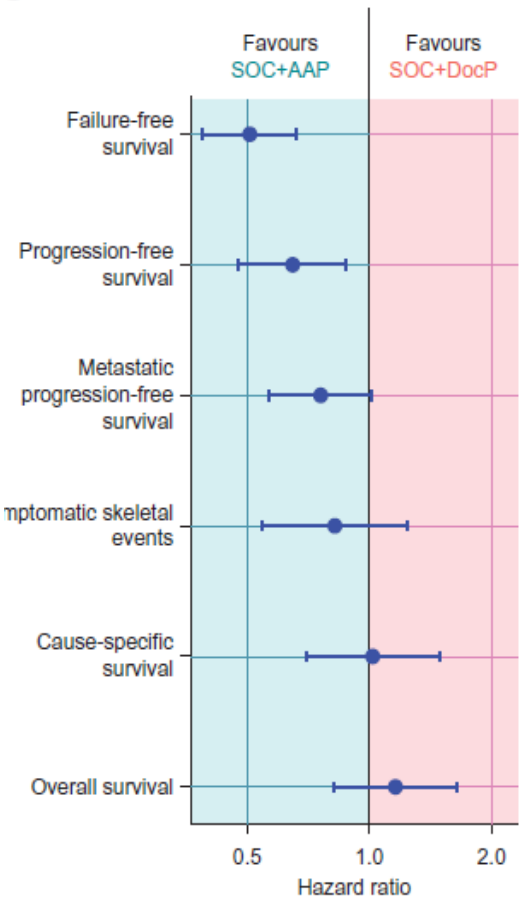


Docetaxel vs Abiraterone

Table 2. Hazard ratio for SOC + AAP relative to SOC + DocP from adjusted Cox models

Outcome measure	Patient group	Events/Pts SOC + DocP	Events/Pts SOC + AAP	Hazard ratio[a] (95% CI)	*P*-value	Interaction by metastases *P*-value
Failure-free survival[b]						
	All	97/189	122/377	0.51 (0.39–0.67)	<0.001	
	M0	18/74	13/150	0.34 (0.16–0.69)	0.003	
	M1	79/115	109/227	0.56 (0.42–0.75)	<0.001	0.169
Progression-free survival[b]						
	All	72/189	103/377	0.65 (0.48–0.88)	0.005	
	M0	10/74	9/150	0.42 (0.17–1.05)	0.064	
	M1	62/115	94/227	0.69 (0.50–0.95)	0.023	0.323
Metastatic progression-free survival[c]						
	All	71/189	118/377	0.77 (0.57–1.03)	0.079	
	M0	10/74	18/150	0.91 (0.42–2.01)	0.824	
	M1	61/115	100/227	0.76 (0.55–1.04)	0.085	0.744
Freedom from symptomatic skeletal events						
	All	36/189	63/377	0.83 (0.55–1.25)	0.375	
	M0	2/74	5/150	1.28 (0.24–6.67)	0.771	
	M1	34/115	58/227	0.82 (0.53–1.25)	0.351	0.648
Overall survival						
	All	44/189	105/377	1.16 (0.82–1.65)	0.404	
	M0	6/74	16/150	1.51 (0.58–3.93)	0.395	
	M1	38/115	89/227	1.13 (0.77–1.66)	0.528	0.691

Outcome measure	Patient group	Events/Pts SOC+Doc	Events/Pts SOC+AAP	Sub-hazard ratio[d] (95% CI)	*P*-value	Interaction by metastases *P*-value
Death from prostate cancer[e]						
	All	40/189	86/377	1.02 (0.70–1.49)	0.916	
	M0	4/74	6/150	0.82 (0.24–2.81)	0.751	
	M1	36/115	80/227	1.05 (0.71–1.56)	0.807	0.620
Death from other causes[f]						
	All	4/189	19/377	2.33 (0.77–6.99)	0.131	
	M0	2/74	10/150	3.00 (0.66–13.66)	0.155	
	M1	2/115	9/227	1.91 (0.43–8.41)	0.393	0.771



M1

- Tratamiento estandar: DA +/- QT o Abiraterone
- ¿Beneficio tratamiento sobre tumor primario?
- Estudios no randomizados, cohortes restrospectivas y análisis post-hoc de estudios prospectivos
- Estudis randomitzats publicados y en marxa

Introducción

Å ↑control local → ↑supervivencia global (OS)

(carcinoma renal, càncer colon)

Å ↓ carga tumoral (cirugia citoreductora y/o RDT)

↓

↑ OS y ↑ resposta a tratamiento sistémico

(cancer de mama, colon y ovario)

Introducción

Å Tumor primario, metástasis regionales y a distancia conectados per una red (células huesped y vias moleculares)

Å Manipulación tumor primario:

- No efecto
- Efecto beneficioso
- Efecto perjudicial

Introducción

Å **<u>Efecto beneficioso</u>:**

- Efecto Abscopal

- Eliminar carga tumoral

- Eliminar factores promotores del tumor i citoquinas inmunosupresoras

↑ Respuesta a tratamientos sistémicos

Introducción

Å **<u>Efecto beneficioso</u>:**

- Reducción cèlulas circulantes
- Eliminar fuente intraprostática de andrógenos (“santuario” para progresar a CPRC)
- Eliminar clonas resistentes a la castración (pueden estar presentes antes del inicio ADT)

↓

Evitar selección clonal con niveles bajos de Tst

Retrasar inicio fase CPRC → ↑ control enfermedad

Introducción

- **<u>Efecto perjudicial</u>:**
  - Eliminar tumor primario puede afectar el comportamiento de la enfermedad metastática por interacción de factores de crecimiento (Efecto Fisher)
  - Eliminar tumor primario puede alterar equilibrio y acelerar proceso metastásico y angiogénico (eliminación factores antimetastásicos y antiangiogénicos)(Efecto Folkman)
  - Cirugia sobre el primario puede introduir células neoplásicas en la circulación

Introducció

Å Evidencia nivel 1 en enfermedad localmente avanzada (+ enfermedad micrometastásica)

- ↓ progresión local → ↓ incidencia enfermedad a distancia → ↑ OS
- Posibilidad de eliminar enfermedad oculta sistémica con ADT

Introducció

- Nuevas técnicas de imagen:

  M0 → M1 (micrometástasis, oligometástasis)
- Cambio perfil pacientes: estadío intermedio entre enfermedad localizada y claramente diseminada
- ¿Como aplicamos evidencia previa con M1 actuales?
- Pacientes N1: ¿diseminados?
- Beneficio en supervivencia con tratamiento local (RDT o PR)

  en estudios retrospectivos (N1 y M1)

Radioterapia en N1

ARTICLE

Androgen Deprivation With or Without Radiation Therapy for Clinically Node-Positive Prostate Cancer

Chun Chieh Lin*, Phillip J. Gray*, Ahmedin Jemal, Jason A. Efstathiou

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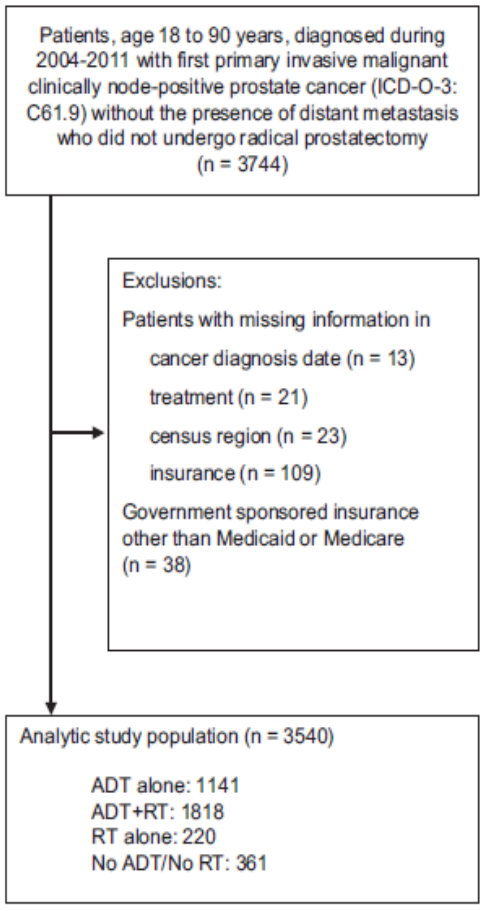
RDT en N1



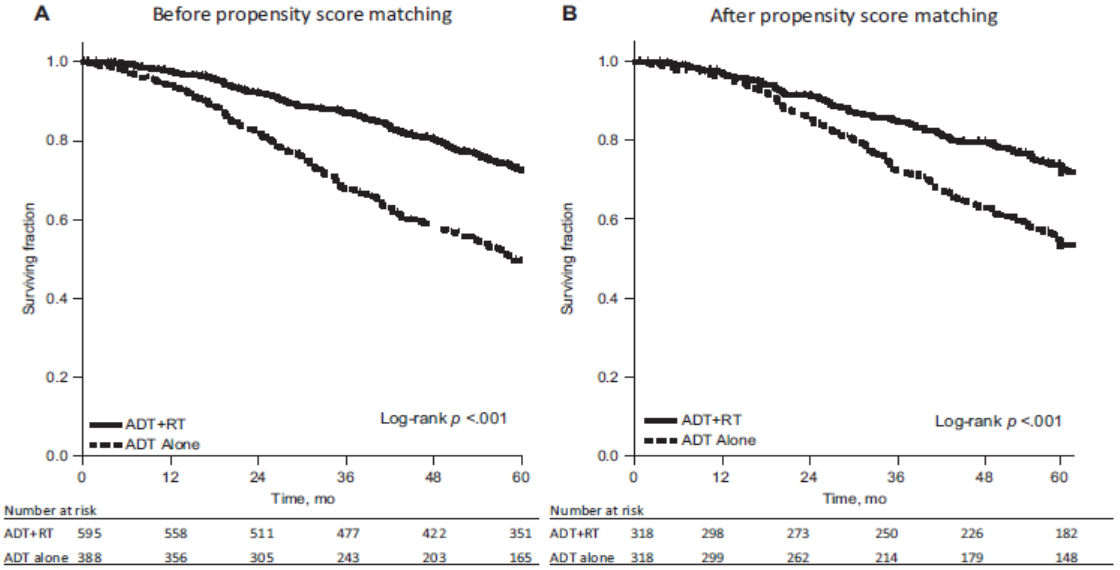


Table 4. Multivariable Cox proportional hazards analyses of five-year overall mortality, stratifying by age at diagnosis, clinical T stage, Gleason Score, and PSA level*

Stratified subset	ADT alone, No. (%) dead within 5 y	ADT plus RT, No. (%) dead within 5 y	Adjusted HR (95% CI) †	P‡
Age < 65 y	50 (37.9)	24 (16.4)	0.25 (0.14 to 0.45)	<.001
Age ≥ 65 y	89 (47.9)	59 (34.3)	0.64 (0.44 to 0.95)	.03
T1-T2	74 (38.5)	37 (19.6)	0.40 (0.26 to 0.62)	<.001
T3-T4	65 (51.6)	46 (35.7)	0.62 (0.38 to 1.01)	.05
GLS ≤7	33 (33.3)	16 (17.2)	0.49 (0.23 to 1.01)	.05
GLS ≥8	94 (48.0)	63 (30.6)	0.55 (0.38 to 0.79)	.001
PSA < 20 ng/mL	56 (38.6)	35 (24.3)	0.60 (0.35 to 1.04)	.07
PSA ≥ 20 ng/mL	74 (48.1)	45 (29.0)	0.44 (0.28 to 0.68)	<.001

Prostatectomia radical en N1

Platinum Priority – Prostate Cancer
Editorial by Urs E. Studer, Laurence Collette and Richard Sylvester on pp. 762–763 of this issue

Survival Benefit of Radical Prostatectomy in Lymph Node–Positive Patients with Prostate Cancer

Jutta Engel[a,1,*], *Patrick J. Bastian*[b,1], *Helmut Baur*[c], *Volker Beer*[d], *Christian Chaussy*[e], *Juergen E. Gschwend*[f], *Ralph Oberneder*[g], *Karl H. Rothenberger*[h], *Christian G. Stief*[b], *Dieter Hölzel*[a]

[a] *Munich Cancer Registry of the Munich Cancer Center, Department of Medical Informatics, Biometry and Epidemiology, Ludwig-Maximilians-University, Munich, Germany*
[b] *Department of Urology, Ludwig-Maximilians-University, Munich, Germany*
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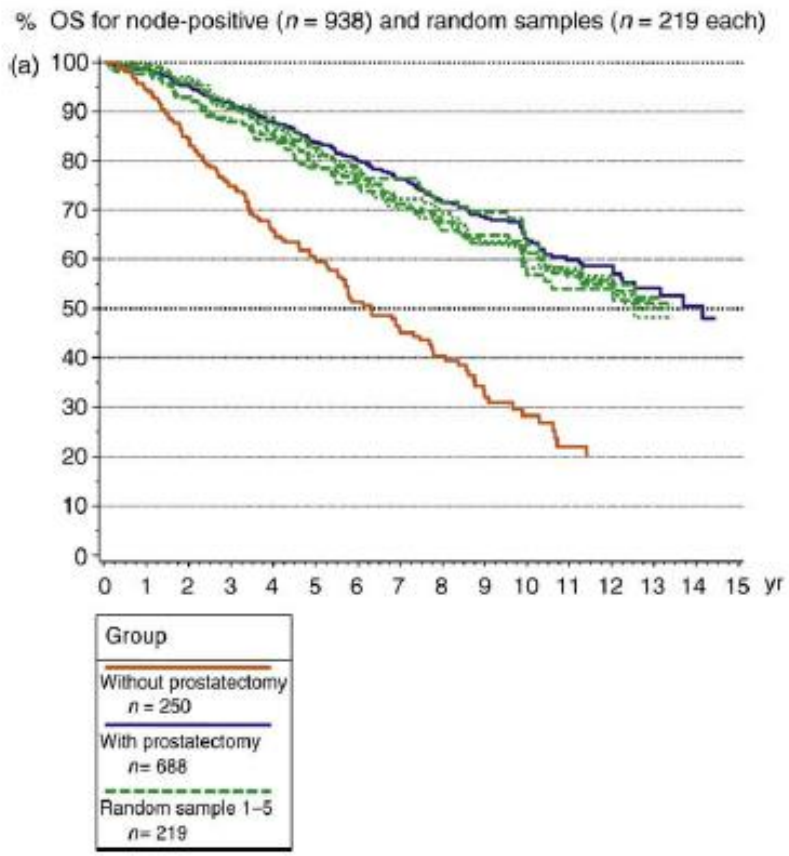
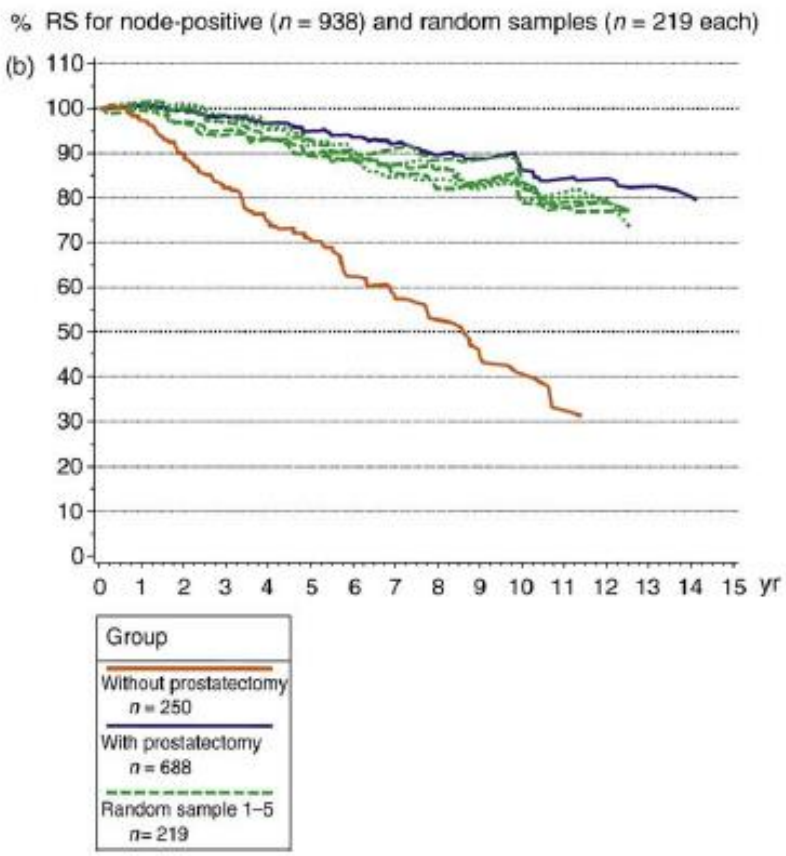
[d] *Clinic of Urology, Bogenhausen, Munich, Germany*
[e] *Clinic of Urology, Harlaching, Munich, Germany*
[f] *Department of Urology, Rechts der Isar Medical Center, Technical University, Munich, Germany*
[g] *Clinic of Urology, Planegg, Germany*
[h] *Clinic of Urology, Landshut, Germany*

PR en N1


% OS for node-positive (n = 938) and random samples (n = 219 each)
(a)
100
90
80
70
60
50
40
30
20
10
0
0 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 yr
Group
Without prostatectomy
n = 250
With prostatectomy
n= 688
Random sample 1–5
n= 219


% RS for node-positive (n = 938) and random samples (n = 219 each)
(b)
110
100
90
80
70
60
50
40
30
20
10
0
0 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 yr
Group
Without prostatectomy
n = 250
With prostatectomy
n = 688
Random sample 1–5
n= 219

Prostatectomia radical en M1

PR en M1

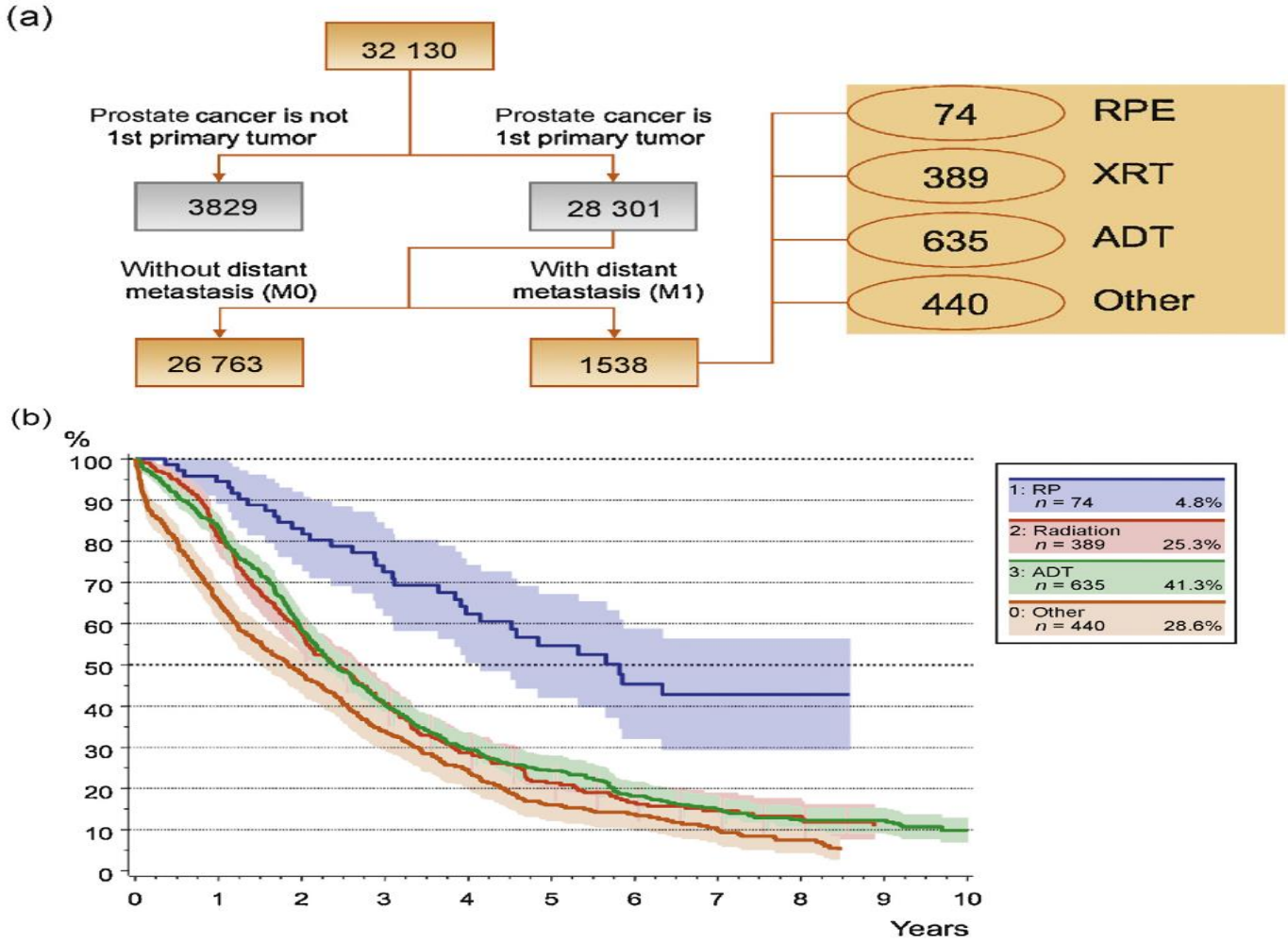
Table 1
Outcomes of radical prostatectomy in metastatic (M1) prostate cancer

SESGO SELECCIÓN:
- Mejor estado general
- Menor carga tumoral
- Más probabilidad de responder a tratamiento sistémico

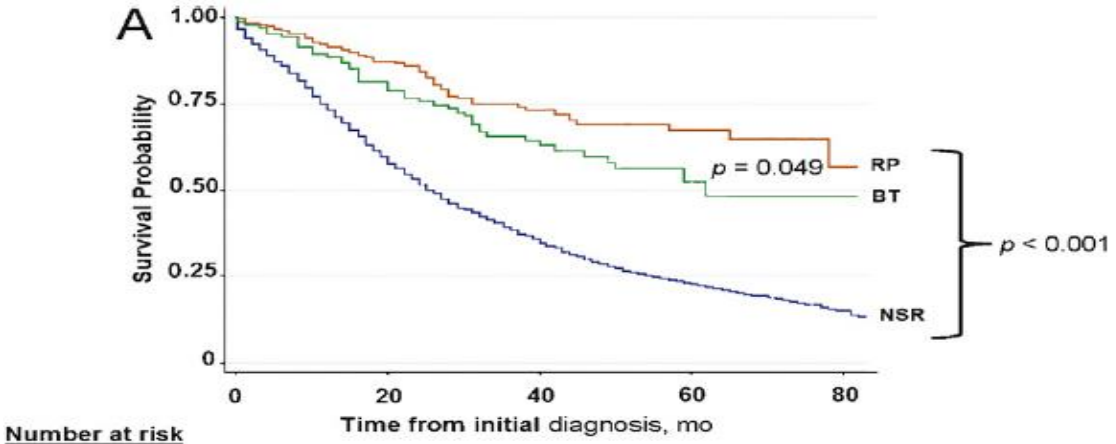
P<.001 P<.001

Abbreviations: CSS, cancer-specific survival; NA, not applicable; NLR, no local resection; NLT, no local treatment; OS, overall survival; RP, radical prostatectomy.

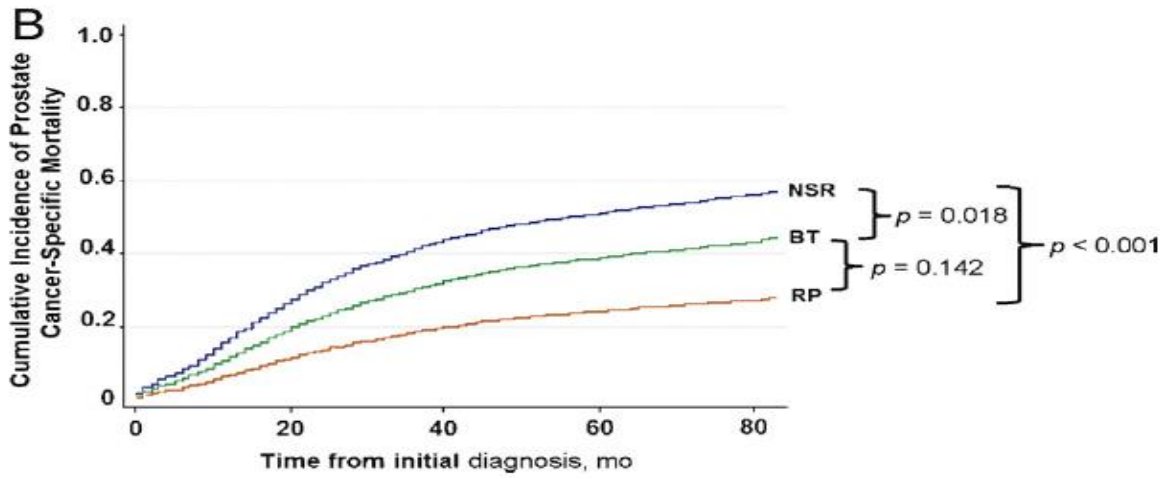
Gratzke et al



Culp et al



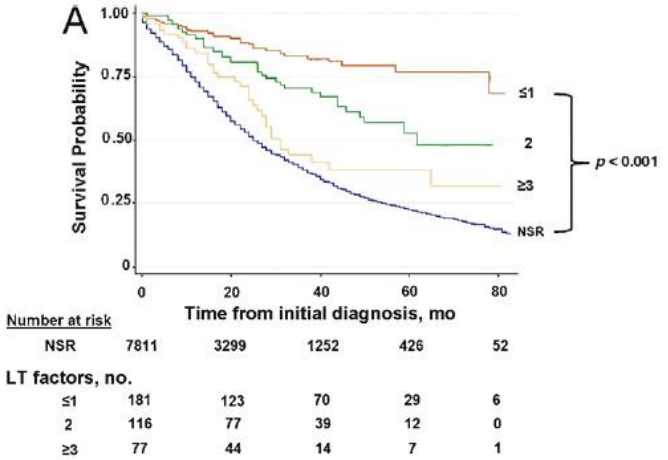
Number at risk					
NSR	7811	3299	1252	426	52
RP	245	160	76	34	5
BT	129	84	47	14	2

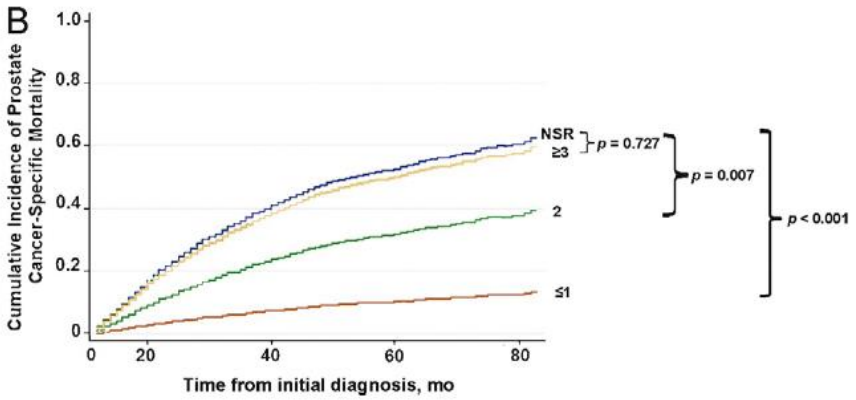


Culp et al

Characteristic	Adjusted SHR	95% confidence interval	*p* value
Age, yr^			
<70	Ref		
≥70	2.31	1.44–3.72	0.001
AJCC T stage^			
T1–T3	Ref		
T4	2.09	1.05–4.18	0.037
Grade of disease^			
Low	Ref		
High	3.79	1.30–11.07	0.015
PSA, ng/ml^			
<20	Ref		
≥20	2.24	1.37–3.66	0.001
AJCC N stage^			
N_0	Ref		
N_1	3.13	1.60–6.12	0.001
AJCC M stage^			
M1a	Ref		
M1b	3.32	1.23–9.01	0.018
M1c	3.66	1.23–10.84	0.019

SHR = subhazard ratio; Ref = reference; AJCC = American Joint Committee on Cancer; PSA = prostate-specific antigen.
* Surveillance Epidemiology and End Results, 2004–2010.
^ At the time of diagnosis.





Radioterapia en M1

VOLUME 34 · NUMBER 24 · AUGUST 20, 2016

JOURNAL OF CLINICAL ONCOLOGY

ORIGINAL REPORT

Improved Survival With Prostate Radiation in Addition to Androgen Deprivation Therapy for Men With Newly Diagnosed Metastatic Prostate Cancer

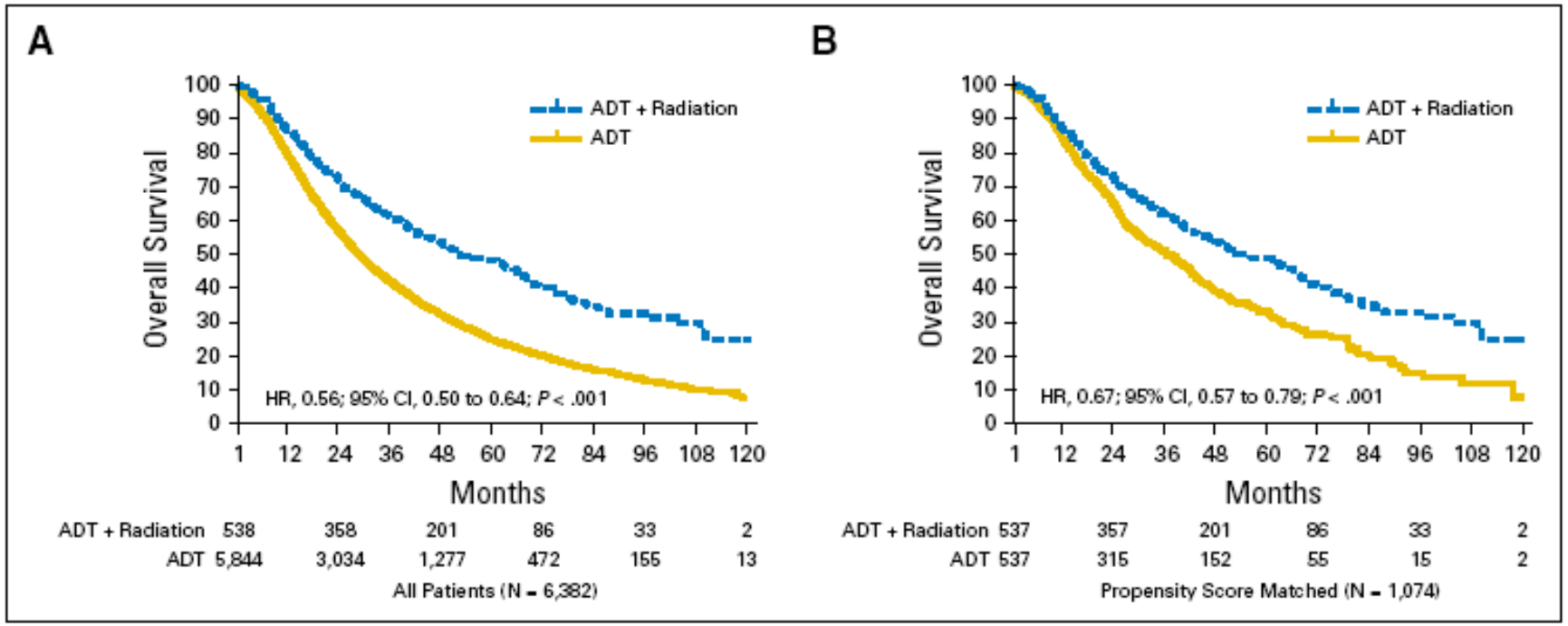
Chad G. Rusthoven, Bernard L. Jones, Thomas W. Flaig, E. David Crawford, Matthew Koshy, David J. Sher, Usama Mahmood, Ronald C. Chen, Brian F. Chapin, Brian D. Kavanagh, and Thomas J. Pugh

Rusthoven et al

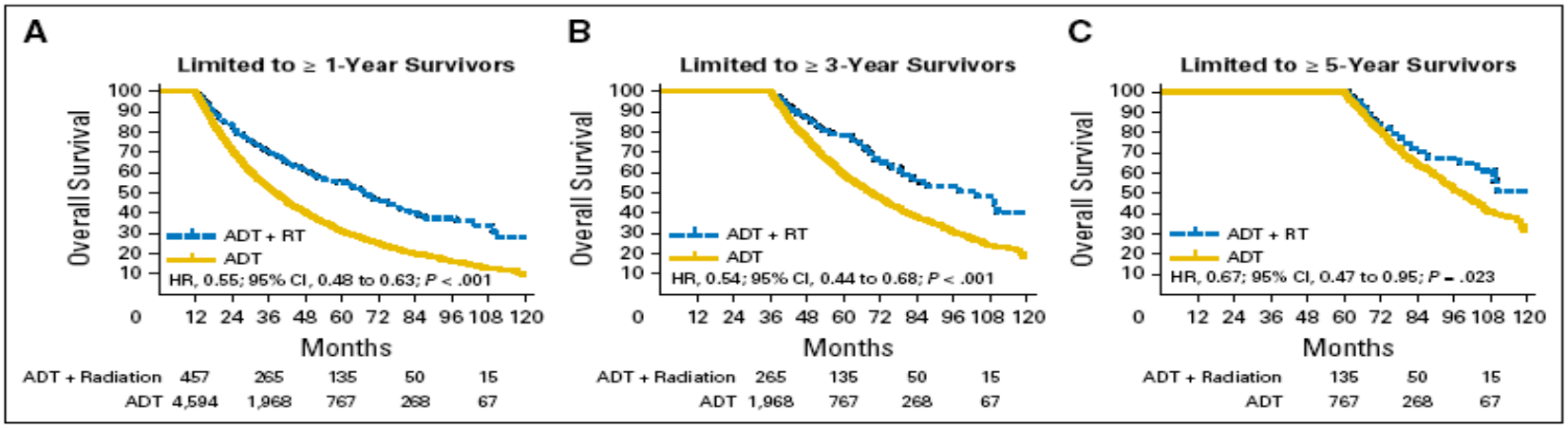
Table 1. Patient Characteristics

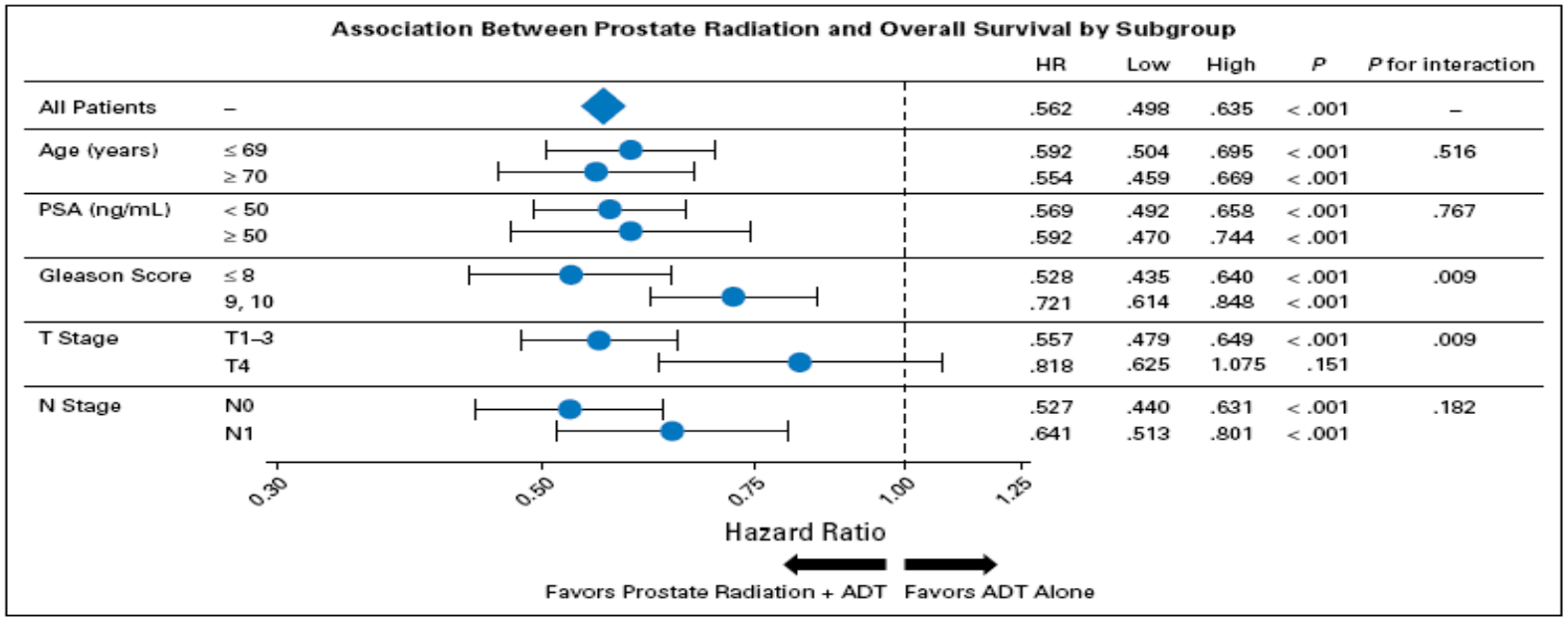
Characteristic	Total No.	ADT Alone*, No. (%)	Prostate Radiation + ADT*, No. (%)	P†
All patients	6,382	5,844 (100)	538 (100)	—
Year				
2004-2008	3,580	3,265 (56)	315 (59)	.231
2009-2012	2,802	2,579 (44)	223 (41)	
Age (years)				< .001
Median	69	69	66	
Range	40-90+	40-90+	40-90+	
Interquartile range	61-77	61-78	59-74	
Age‡ (years)				< .001
40-49	215	193 (3)	22 (4)	
50-59	1,130	1,013 (17)	117 (22)	
60-69	1,929	1,740 (30)	189 (35)	
70-79	1,877	1,712 (29)	165 (31)	
≥ 80	1,231	1,186 (20)	45 (8)	
Race				.065
White	4,808	4,382 (75)	426 (79)	
Black	1,277	1,190 (20)	87 (16)	
Other/unr	297	272 (5)	25 (5)	
Comorbidity score§				.017
0	5,214	4,750 (81)	464 (86)	
1	864	810 (14)	54 (10)	
≥2	304	284 (5)	20 (4)	
PSA (ng/mL)				< .001
< 20	2,013	1,746 (30)	267 (50)	
20-49.9	1,402	1,275 (22)	127 (24)	
50-97.9	993	926 (16)	67 (13)	
≥98	1,974	1897 (33)	77 (14)	
Gleason score				.247
6	203	189 (3)	14 (3)	
7	1,251	1,137 (20)	114 (21)	
8	1,542	1,397 (24)	145 (27)	
9	2,731	2,522 (43)	209 (39)	
10	655	599 (10)	56 (10)	
T stage				< .001
T1	1,631	1,504 (26)	127 (24)	
T2	1,811	1,653 (28)	158 (29)	
T3	965	848 (15)	117 (22)	
T4	800	718 (12)	82 (15)	
Tx	1,175	1,121 (19)	54 (10)	
N stage				< .001
N0	2,756	2,477 (42)	279 (52)	
N1	1,581	1,433 (25)	148 (28)	
Nx	2,045	1,934 (33)	111 (21)	
Facility				.028
Academic	2,500	2,313 (40)	187 (35)	
Community	3,882	3,531 (60)	351 (65)	
Insurance				<.001
Private	1,793	1,570 (27)	223 (41)	
Medicare	3,521	3,262 (56)	259 (48)	
Medicaid/other govt	538	510 (9)	28 (5)	
Uninsured	397	381 (7)	16 (3)	
Unreported	133	121 (2)	12 (2)	
Chemotherapy				.724
Not administered/unr	5,992	5,485 (94)	507 (94)	
Administered	390	359 (6)	31 (6)	
Status at last F/U				—
Alive	2,016	1,755 (30)	261 (48)	
Deceased	4,366	4,089 (70)	277 (52)	

Rusthoven et al

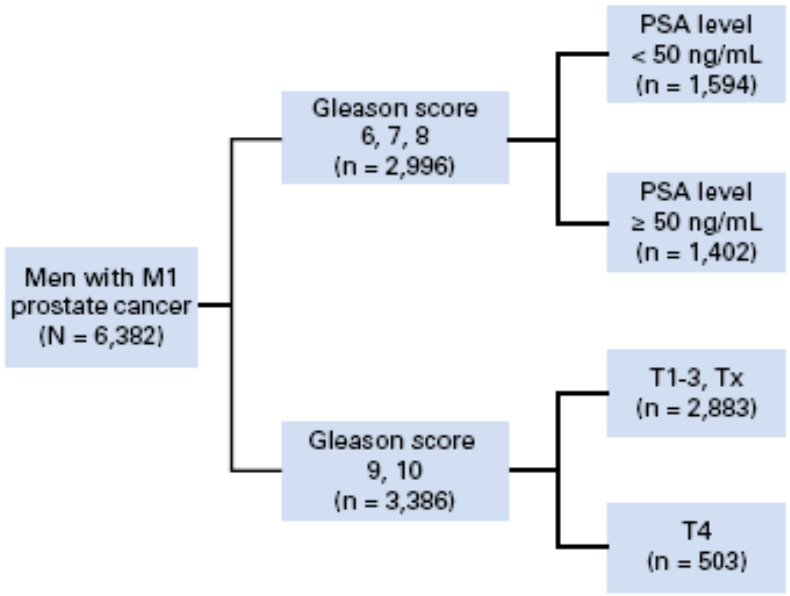


Rusthoven et al



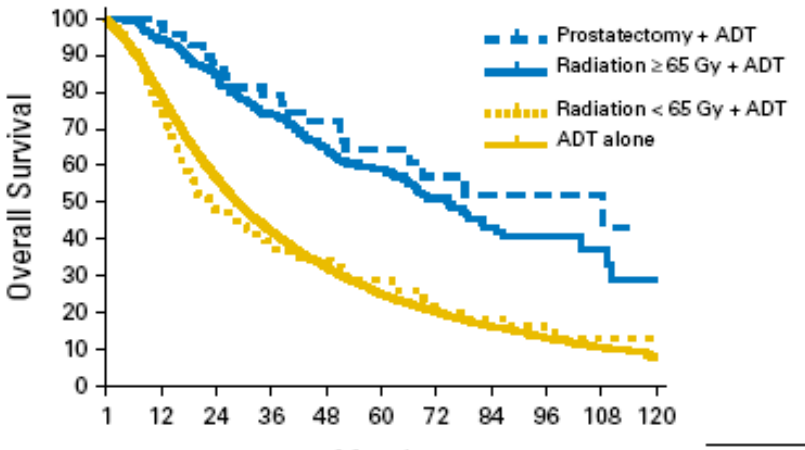


Rusthoven et al



Risk Tier	5-Year OS Entire Tier, %	5-Year OS ADT Alone, %	5-Year OS ADT Plus RT, %	Multivariate HR With RT	*P*
Low risk	39	36	65	0.49 (0.39 to 0.62)	< .001
Intermediate risk	31	29	51	0.59 (0.42 to 0.83)	< .001
High risk	21	20	41	0.64 (0.53 to 0.78)	< .001
Very high risk	11	10	15	0.91 (0.67 to 1.25)	.570

Rusthoven et al



							Multivariate		
							HR	95% CI	*P*
ADT alone	5,844	3,034	1,277	472	155	13	Ref	–	–
Radiation < 65 Gy + ADT	163	73	41	15	7	1	1.02	0.84 to 1.23	.874
Radiation ≥ 65 Gy + ADT	324	254	146	61	21	1	0.45	0.38 to 0.54	< .001
Prostatectomy + ADT	69	56	30	13	7	0	0.38	0.25 to 0.58	< .001

			Multivariate Survival Analysis			Univariate Survival Analysis		
Treatment	No. of Patients (no. of events)	5-year OS, %	HR*	95% CI	*P*	HR	95% CI	*P*
ADT alone	5,844 (4,089)	25	Reference			Reference		
Prostate radiation < 65 Gy + ADT	163 (114)	29	1.015	0.842 to 1.225	.874	1.045	0.867 to 1.259	.644
Prostate radiation ≥65 Gy + ADT	324 (135)	59	0.454	0.382 to 0.540	< .001	0.397	0.335 to 0.472	< .001
Prostatectomy + ADT	69 (23)	64	0.383	0.254 to 0.579	< .001	0.310	0.206 to 0.472	< .001

Tractament local (PR o RDT) en M1

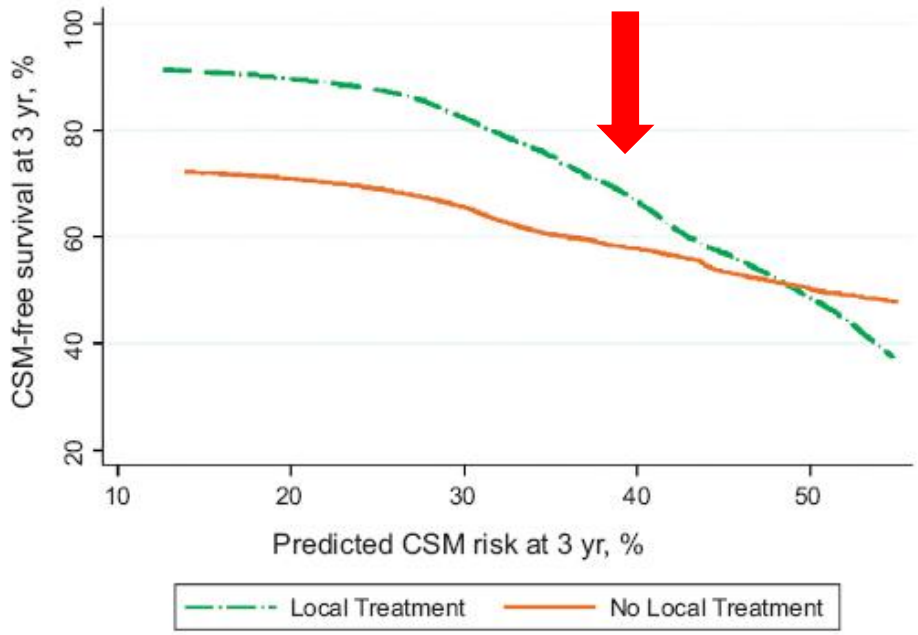
Brief Correspondence

Identifying Optimal Candidates for Local Treatment of the Primary Tumor Among Patients Diagnosed with Metastatic Prostate Cancer: A SEER-based Study

Nicola Fossati [a,b], *Quoc-Dien Trinh* [c], *Jesse Sammon* [d], *Akshay Sood* [d], *Alessandro Larcher* [b,e], *Maxine Sun* [e], *Pierre Karakiewicz* [e], *Giorgio Guazzoni* [b], *Francesco Montorsi* [b], *Alberto Briganti* [b], *Mani Menon* [d], *Firas Abdollah* [d,*]

Variables	Local treatment (n = 628, 8%)	Nonlocal treatment (n = 7569, 92%)	p value
Age, yr, median (IQR)	65 (59–73)	71 (63–79)	<0.0001
Race, n (%)			0.7
White	466 (74)	5602 (74)	
Black	119 (19)	1445 (19)	
Other	41 (6.7)	423 (6)	
Unknown	2 (0.3)	99 (1)	
Marital status, n (%)			<0.0001
Married	431 (68)	4334 (57)	
Not married	171 (28)	2641 (35)	
Unknown	26 (4)	594 (8)	
PSA, ng/ml, median (IQR)	16 (7–54)	61 (20–98.0)	<0.0001
Gleason score, n (%)			<0.0001
≤6	70 (12)	380 (5)	
7	153 (24)	1562 (21)	
≥8	405 (64)	5627 (74)	
T stage, n (%)			<0.0001
T1	151 (24)	2306 (30)	
T2	220 (35)	3219 (43)	
T3a	66 (10)	580 (7)	
T3b	60 (10)	346 (5)	
T4	131 (21)	1118 (15)	
N stage, n (%)			0.7
N0	360 (57)	4318 (57)	
N1	143 (23)	1647 (22)	
Nx	125 (20)	1604 (21)	
M Stage			0.003
M1a	51 (8)	435 (5)	
M1b	432 (69)	5651 (75)	
M1c	145 (23)	1483 (20)	
Year of diagnosis, n (%)			0.9
2004	65 (10)	903 (12)	
2005	83 (13)	918 (12)	
2006	85 (13)	965 (13)	
2007	73 (12)	945 (13)	
2008	79 (13)	926 (12)	
2009	75 (12)	928 (12)	
2010	80 (13)	1000 (13)	
2011	88 (14)	984 (13)	

IQR = interquartile range; PSA = prostate-specific antigen.

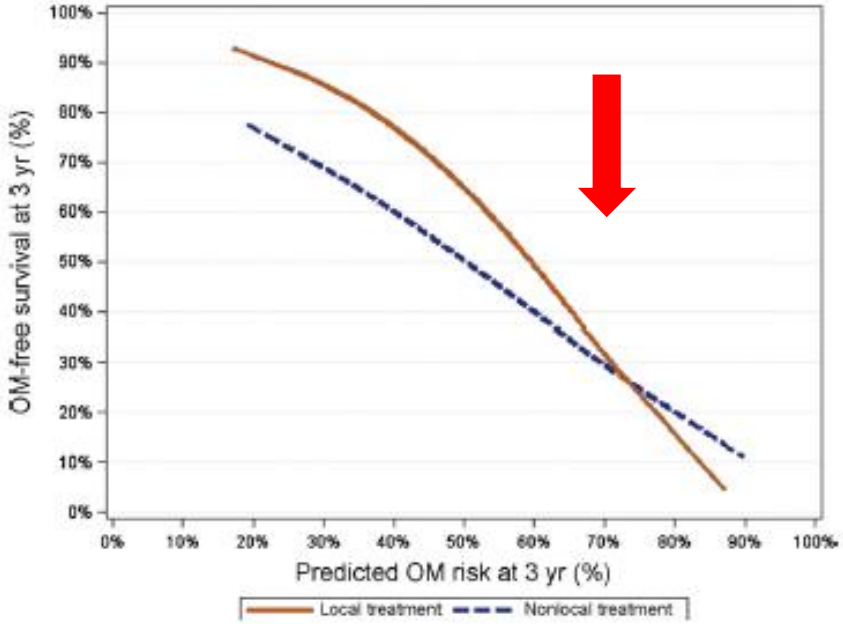


Platinum Priority – Prostate Cancer

Editorial by XXX on pp. x–y of this issue

The Impact of Local Treatment on Overall Survival in Patients with Metastatic Prostate Cancer on Diagnosis: A National Cancer Data Base Analysis

Björn Löppenberg [a,b,†], Deepansh Dalela [a,†], Patrick Karabon [a,c], Akshay Sood [a], Jesse D. Sammon [a], Christian P. Meyer [d], Maxine Sun [d], Joachim Noldus [b], James O. Peabody [a], Quoc-Dien Trinh [d], Mani Menon [a], Firas Abdollah [a,]*



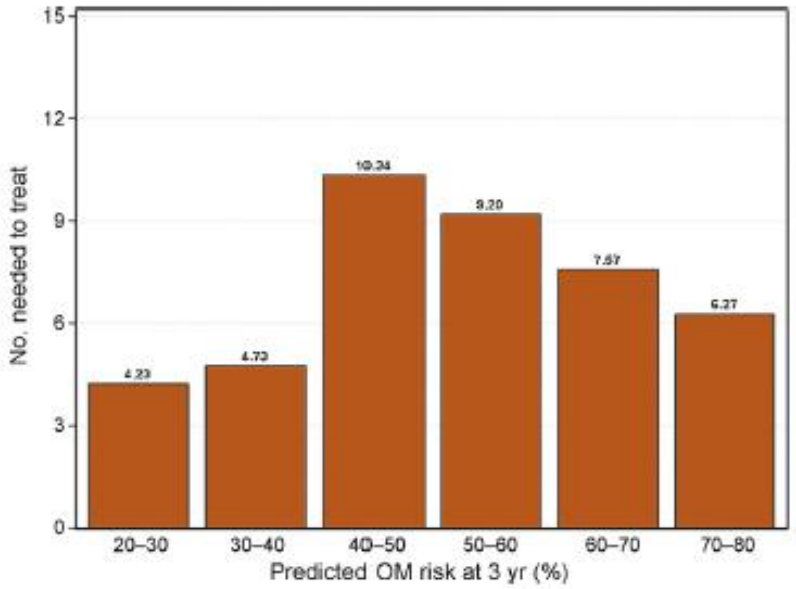


Fig. 2 – Overall mortality (OM)-free survival rate plotted against predicted probability of OM at 3 yr after diagnosis. Dashed line indicates local treatment of the primary tumor. Solid line indicates no local treatment of the primary tumor.

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

Raj Satkunasivam[1], Andre E. Kim[2], Mihir Desai[1], Mike M. Nguyen[1], David I. Quinn[3], Leslie Ballas[4], Juan Pablo Lewinger[2], Mariana C. Stern[2], Ann S. Hamilton[2], Monish Aron[1], and Inderbir S. Gill[1]

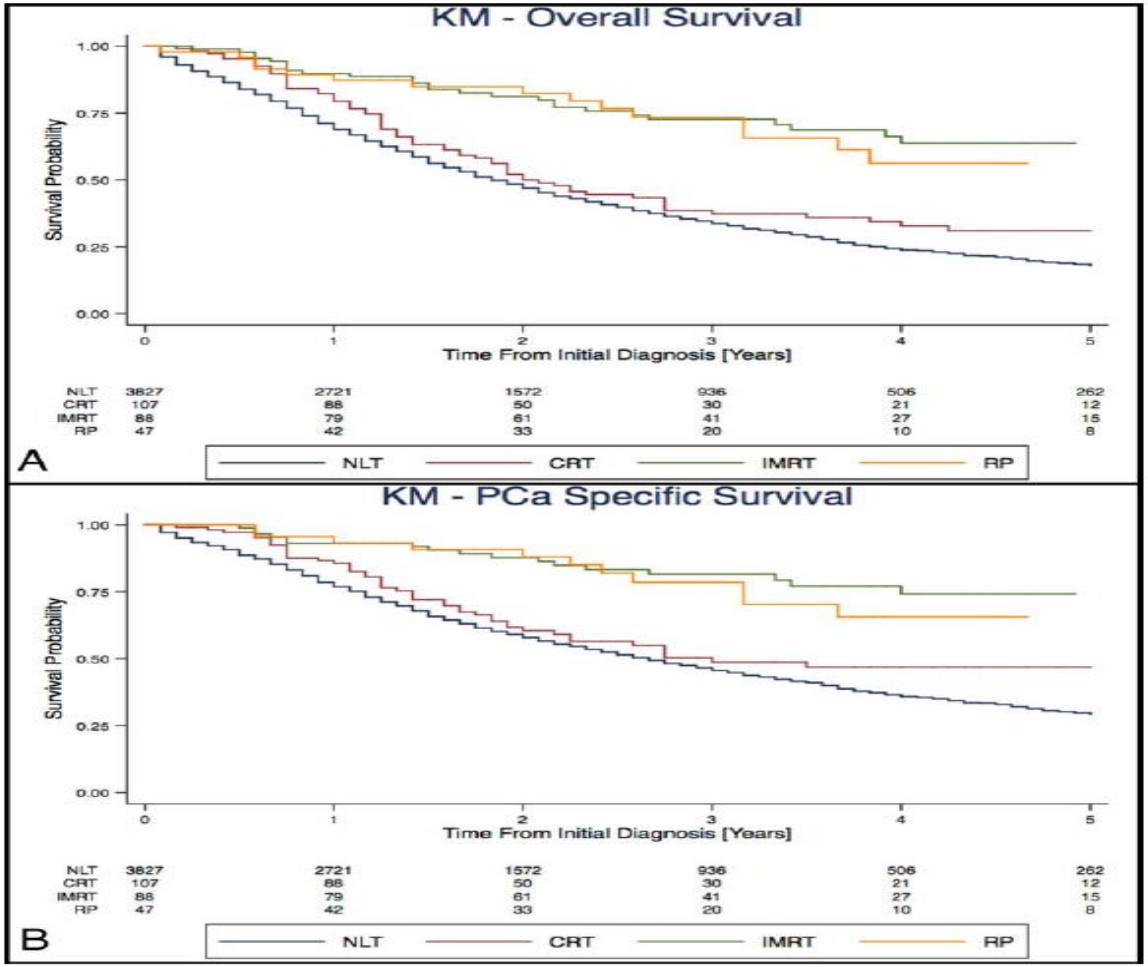
Final study po

4,069 pati

Radical Prostatectomy (RP)

Conformal Radiotherapy (CRT)

d Radiation
IRT)



Estudios randomizados

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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]*

HORRAD

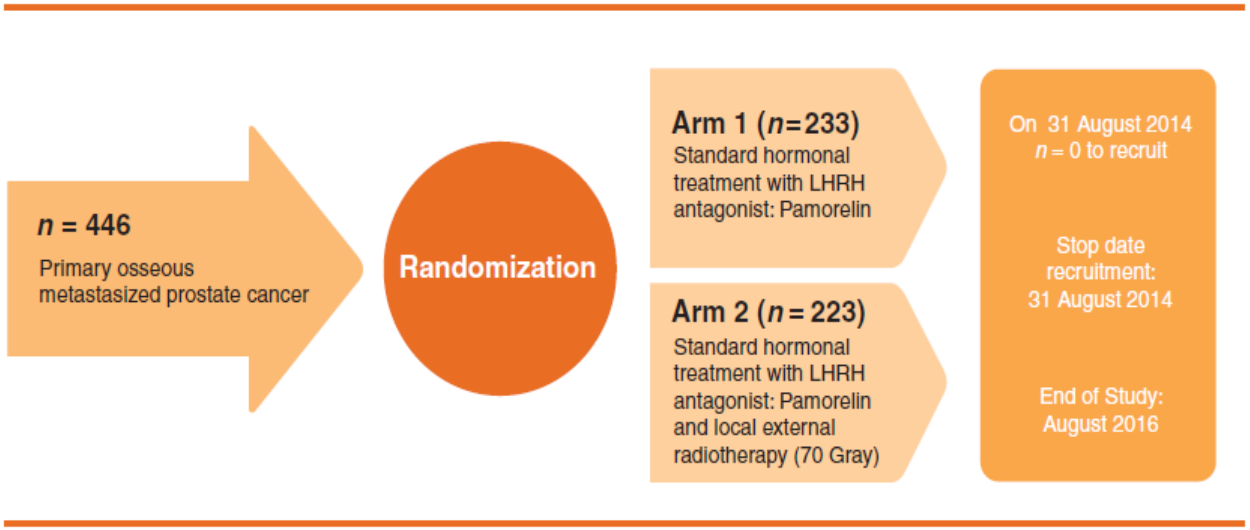
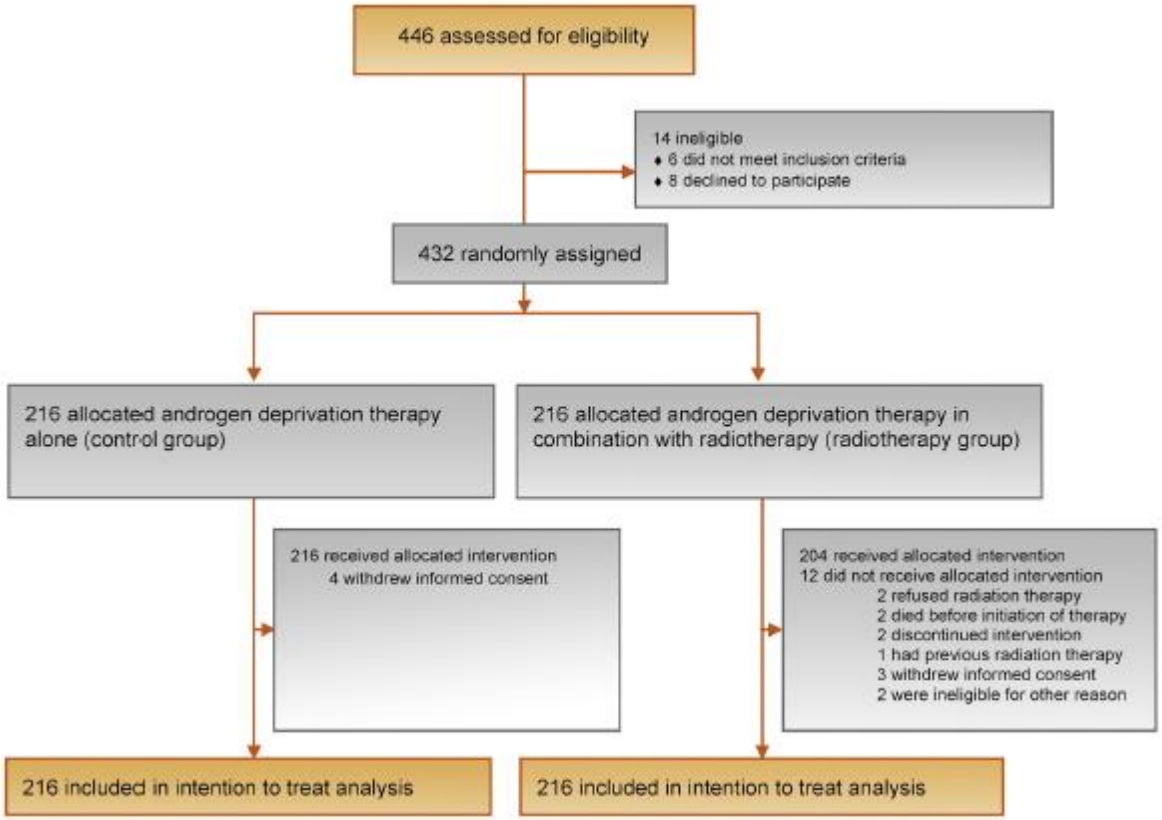


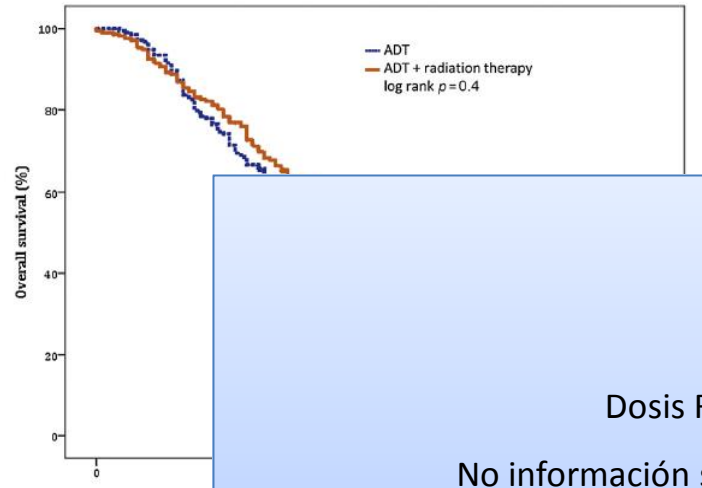
Fig. 2 – Study design for the HORRAD trial. Source: European Urological Association. HORRAD study facts and figures. http://www.uroweb.org/fileadmin/documents/2014_FactsHORRAD_Facts___Figure_update_06-Sep-2014.pdf. LHRH = luteinizing hormone–releasing hormone.

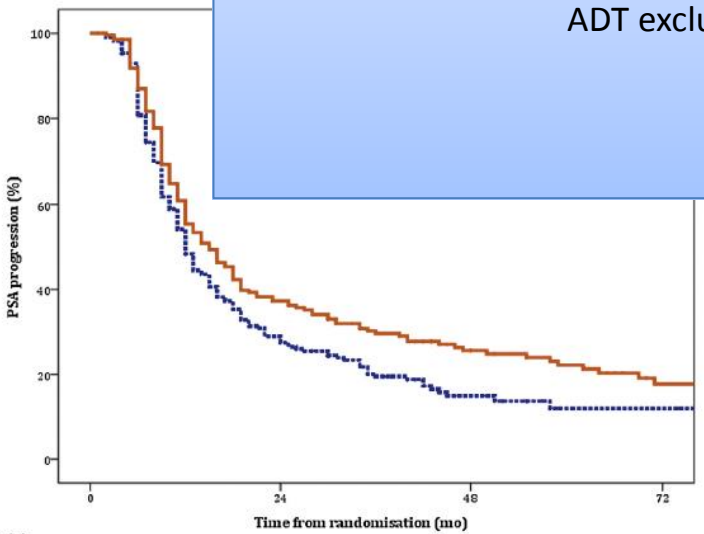
HORRAD



	ADT + radiotherapy (n = 216)[a]	ADT alone (n = 216)[a]
Age (range), yr.	67 (62–71)	67 (61–71)
PSA concentration at start of ADT, ng/ml		
Median (range).	125 (8–14 000)	149 (4–6991)
Q1	48	50
Q3	433	483
Missing data	3 (1)	5 (2)
ALP		
≤ULN	133 (61)	141 (65)
>ULN	51 (24)	54 (25)
Missing data	32 (15)	21 (10)
LDH		
≤ULN	92 (43)	95 (44)
>ULN	65 (30)	69 (32)
Missing data	59 (27)	52 (24)
Gleason sum score[b]		
6	7 (3)	7 (3)
7	66 (31)	64 (30)
8	48 (22)	65 (30)
9	85 (39)	72 (33)
10	9 (4)	7 (3)
Missing data	1 (1)	1 (1)
T stage		
1	7 (3)	5 (3)
2	33 (15)	20 (9)
3	125 (58)	128 (59)
4	51 (24)	59 (27)
Missing data	0	4 (2)
Osseous metastases		
<5 lesions	89 (41)	71 (33)
5–15	53 (25)	65 (30)
>15	74 (34)	80 (37)
WHO performance status[c]		
0	187 (87)	176 (82)
1	22 (10)	31 (14)
2	4 (2)	6 (3)
3	3 (1)	3 (1)
Pain score[d]		
0	140 (65)	139 (65)
1	39 (18)	34 (16)
2	18 (8)	18 (8)
3	3 (1)	3 (1)
4	16 (8)	22 (10)

HORRAD





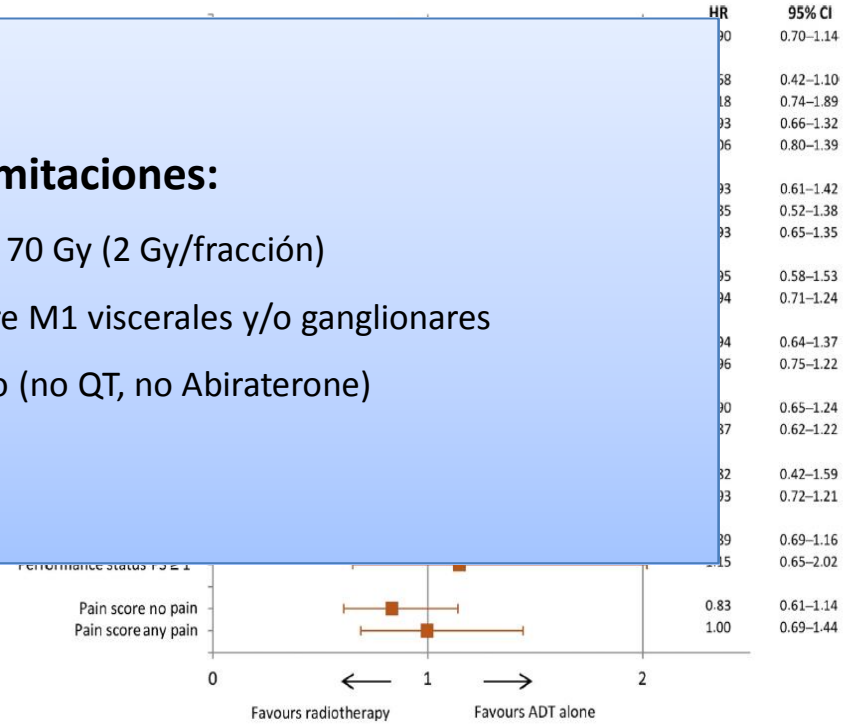
No. at risk

Limitaciones:

Dosis RDT: 70 Gy (2 Gy/fracción)

No información sobre M1 viscerales y/o ganglionares

ADT exclusivo (no QT, no Abiraterone)



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†*

STAMPEDE

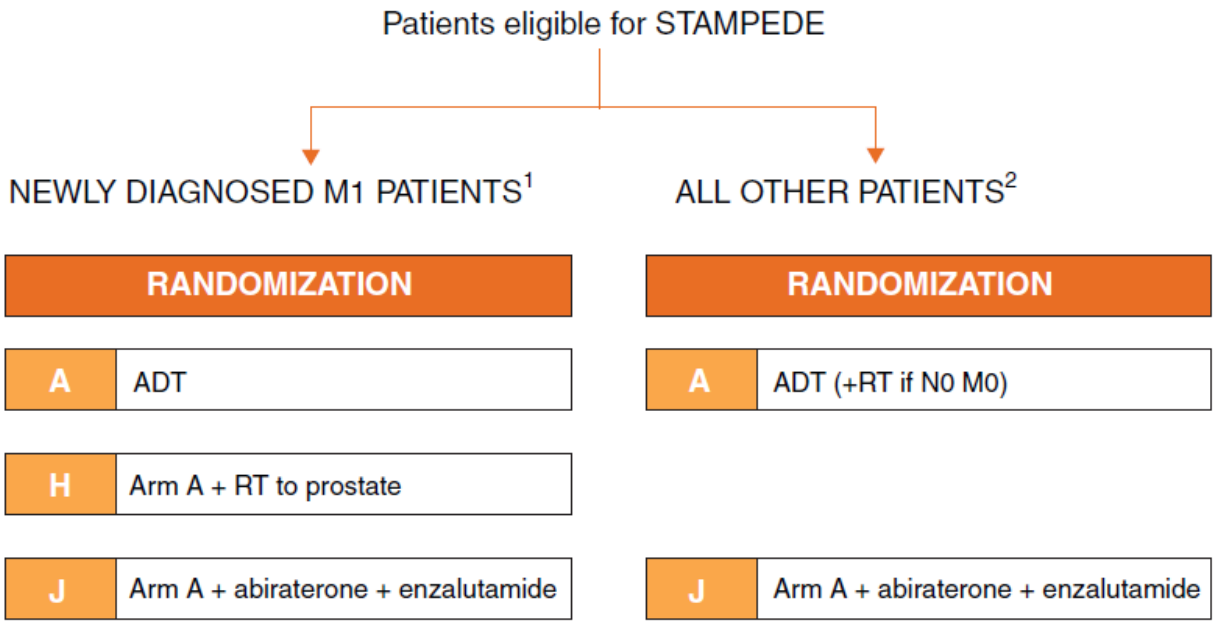
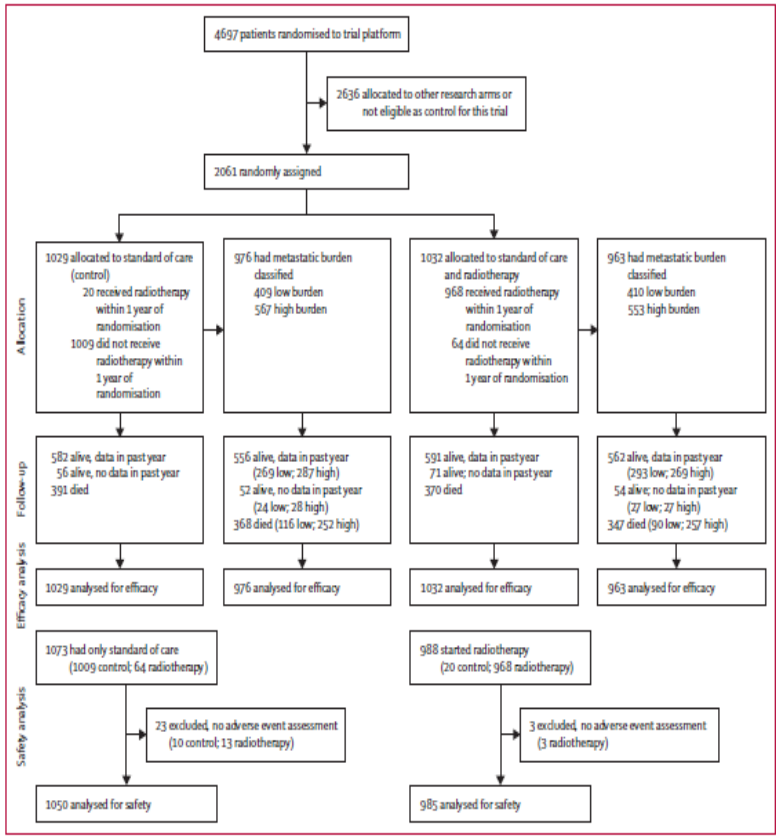


Fig. 1 – Study design for the STAMPEDE trial (protocol version 12.0 with inclusion of enzalutamide + abiraterone comparison). Source: STAMPEDE trial. Protocol version 12.0. http://www.stampedetrial.org/PDF/STAMPEDE_Protocol_v12.0_clean.pdf

[1] Except for patients with a contraindication to radiation therapy (RT).

[2] All suitable patients with newly diagnosed, locally advanced disease should also have RT to the prostate.

STAMPEDE



	Control (n=1029)	Radiotherapy (n=1032)
Age at randomisation (years)	68 (63-73)	68 (63-73)
Range	37-86	45-87
WHO performance status		
0	732 (71%)	734 (71%)
1-2	297 (29%)	298 (29%)
Pain from prostate cancer		
Absent	820 (81%)	844 (83%)
Present	198 (19%)	170 (17%)
Missing data	11	18
Previous notable health issues		
Myocardial infarction	67 (7%)	57 (6%)
Cerebrovascular disease	29 (3%)	30 (3%)
Congestive heart failure	5 (<1%)	8 (1%)
Angina	46 (4%)	51 (5%)
Hypertension	408 (40%)	440 (43%)
Missing data	5	8
T category at randomisation		
T0	0 (0%)	2 (<1%)
T1	12 (1%)	12 (1%)
T2	84 (9%)	89 (9%)
T3	585 (62%)	603 (63%)
T4	260 (28%)	246 (26%)
TX	88	80
N category at randomisation		
N0	345 (36%)	344 (36%)
N+	620 (64%)	620 (64%)
NX	64	68
Metastatic burden		
Low	409 (42%)	410 (43%)
High	567 (58%)	553 (57%)
Not classified	53	69

(Table 1 continues in next column)

	Control (n=1029)	Radiotherapy (n=1032)
(Continued from previous column)		
Sites of metastases		
Bone	919 (89%)	917 (89%)
Liver	23 (2%)	19 (2%)
Lung	42 (4%)	48 (5%)
Distant lymph nodes	294 (29%)	304 (29%)
Other	35 (3%)	33 (3%)
Gleason sum score		
≤7	173 (17%)	172 (18%)
8-10	820 (83%)	810 (82%)
Unknown	36	50
PSA before androgen deprivation therapy (ng/mL)	98 (30-316)	97 (33-313)
Range	1-20 590	1-11 156
Time from diagnosis (days)	73 (55-94)	73 (55-93)
Missing data	7	16
Time from starting hormones (days)	52 (35-70)	55 (34-70)
Range	-32 to 84	-10 to 85
Missing data	0	1
Planned docetaxel		
No	845 (82%)	849 (82%)
Yes	184 (18%)	183 (18%)
Nominated radiotherapy schedule*		
Weekly	482 (47%)	497 (48%)
Daily	547 (53%)	535 (52%)

Data are median (IQR) or n (%), unless otherwise stated. PSA=prostate-specific antigen. *The weekly schedule was 36 Gy in six fractions over 6 weeks and the daily schedule was 55 Gy in 20 fractions over 4 weeks.

Table 1: **Baseline characteristics**

STAMPEDE

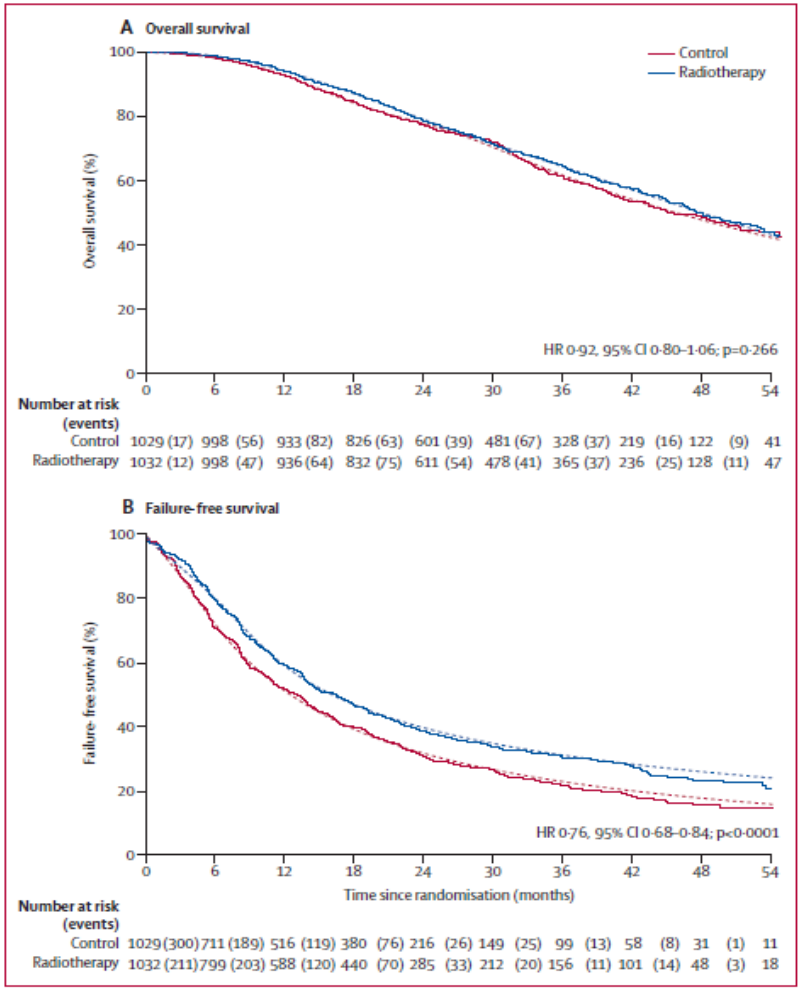
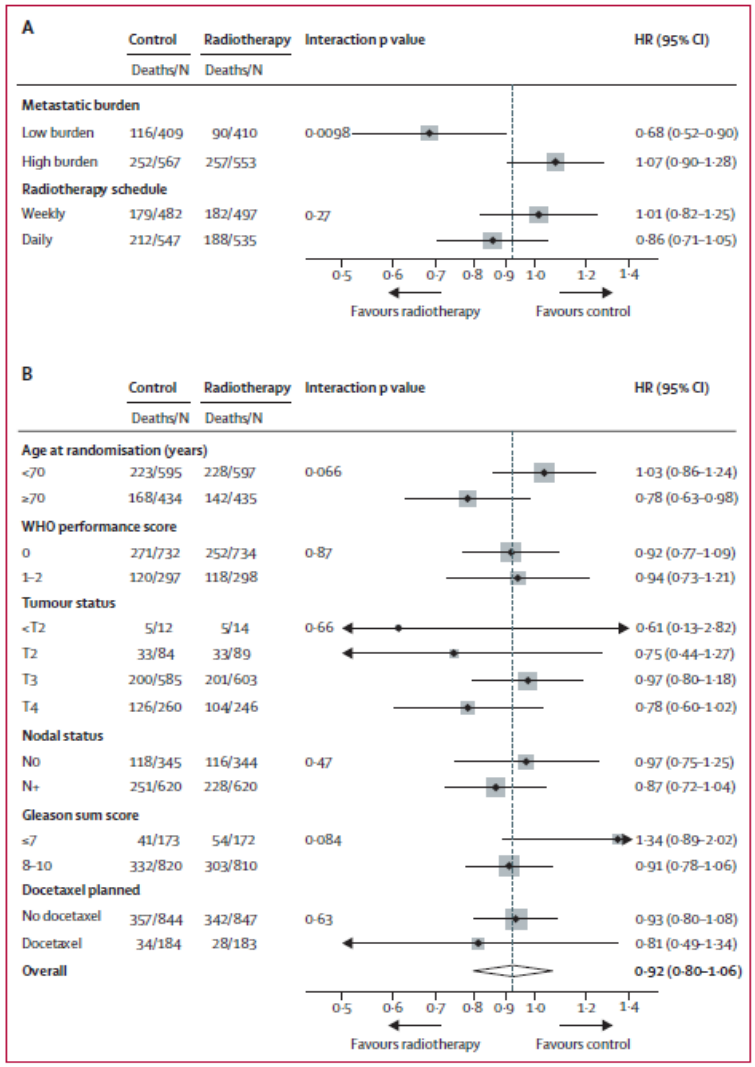
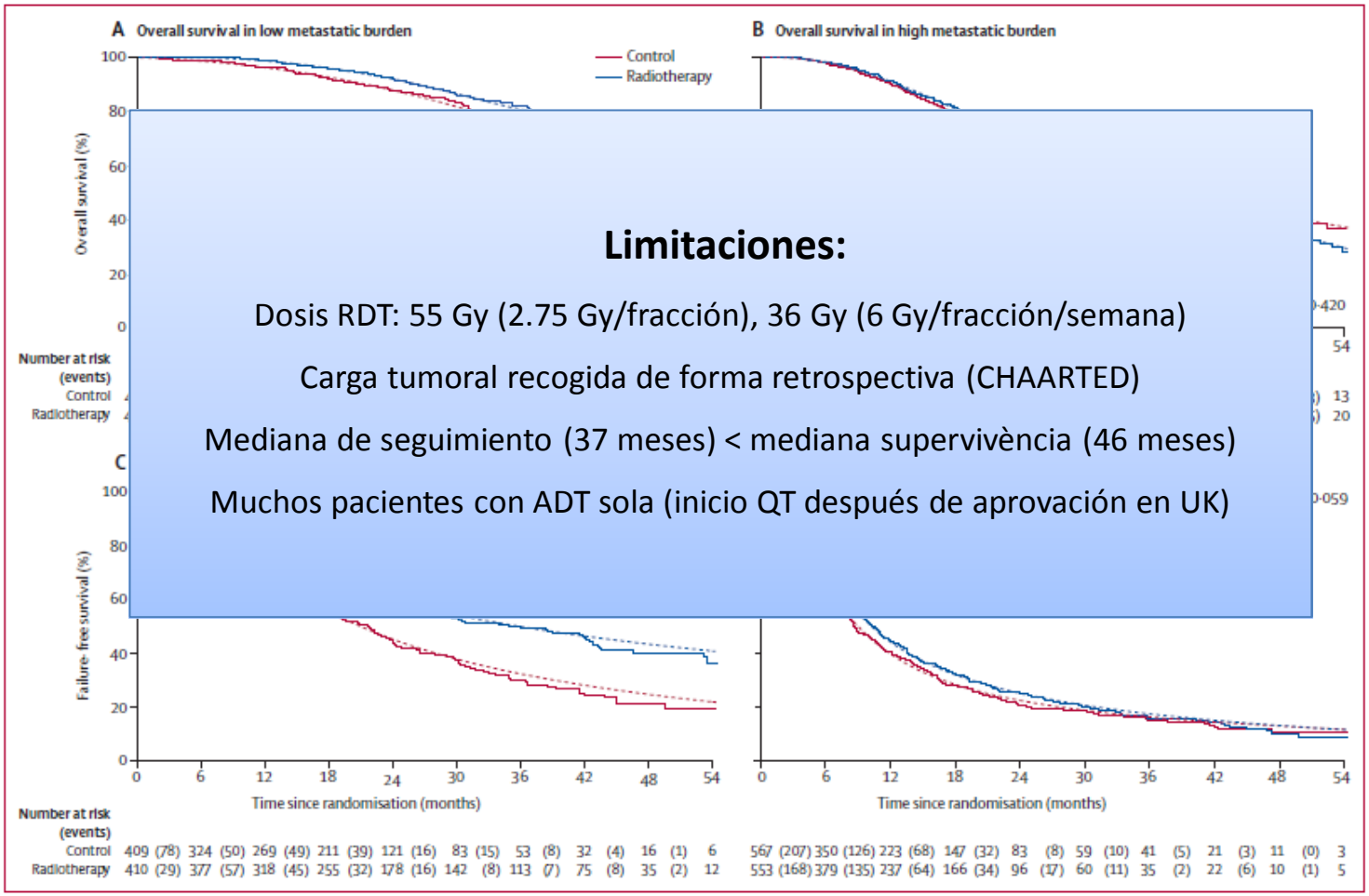


Figure 2: **Overall survival and failure-free survival, by treatment**
HR=hazard ratio. Solid lines show the Kaplan-Meier analysis and dotted lines show the flexible parametric model.



STAMPEDE



Limitaciones:

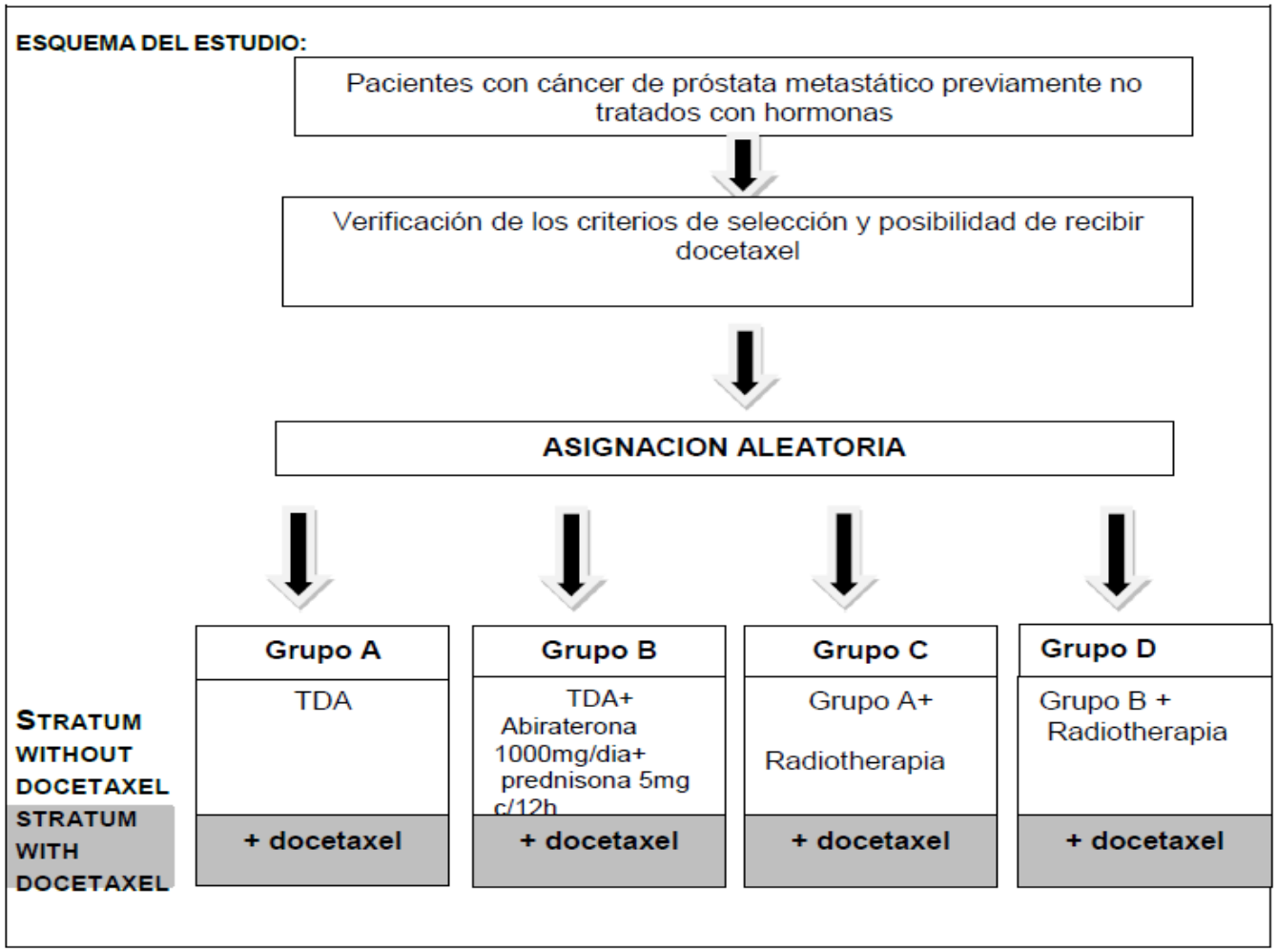
Dosis RDT: 55 Gy (2.75 Gy/fracción), 36 Gy (6 Gy/fracción/semana)

Carga tumoral recogida de forma retrospectiva (CHAARTED)

Mediana de seguimiento (37 meses) < mediana supervivència (46 meses)

Muchos pacientes con ADT sola (inicio QT después de aprovación en UK)

PEACE-1


ESQUEMA DEL ESTUDIO:
Pacientes con cáncer de próstata metastático previamente no tratados con hormonas
Verificación de los criterios de selección y posibilidad de recibir docetaxel
ASIGNACION ALEATORIA
Grupo A
Grupo B
Grupo C
Grupo D
TDA
TDA+ Abiraterona 1000mg/dia+ prednisona 5mg c/12h
Grupo A+ Radiotherapia
Grupo B + Radiotherapia
STRATUM WITHOUT DOCETAXEL
STRATUM WITH DOCETAXEL
+ docetaxel
+ docetaxel
+ docetaxel
+ docetaxel

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Departament de Salut

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