IX REUNIÓN NACIONAL: CÁNCER DE PRÓSTATA, CÁNCER RENAL Y CÁNCER DE VEJIGA

GUADALAJARA 2017

PAPEL DE LA QUIMIOTERAPIA BASADA EN TAXANOS EN EL CÁNCER DE PRÓSTATA NO METASTÁSICO Y DE ALTO RIESGO

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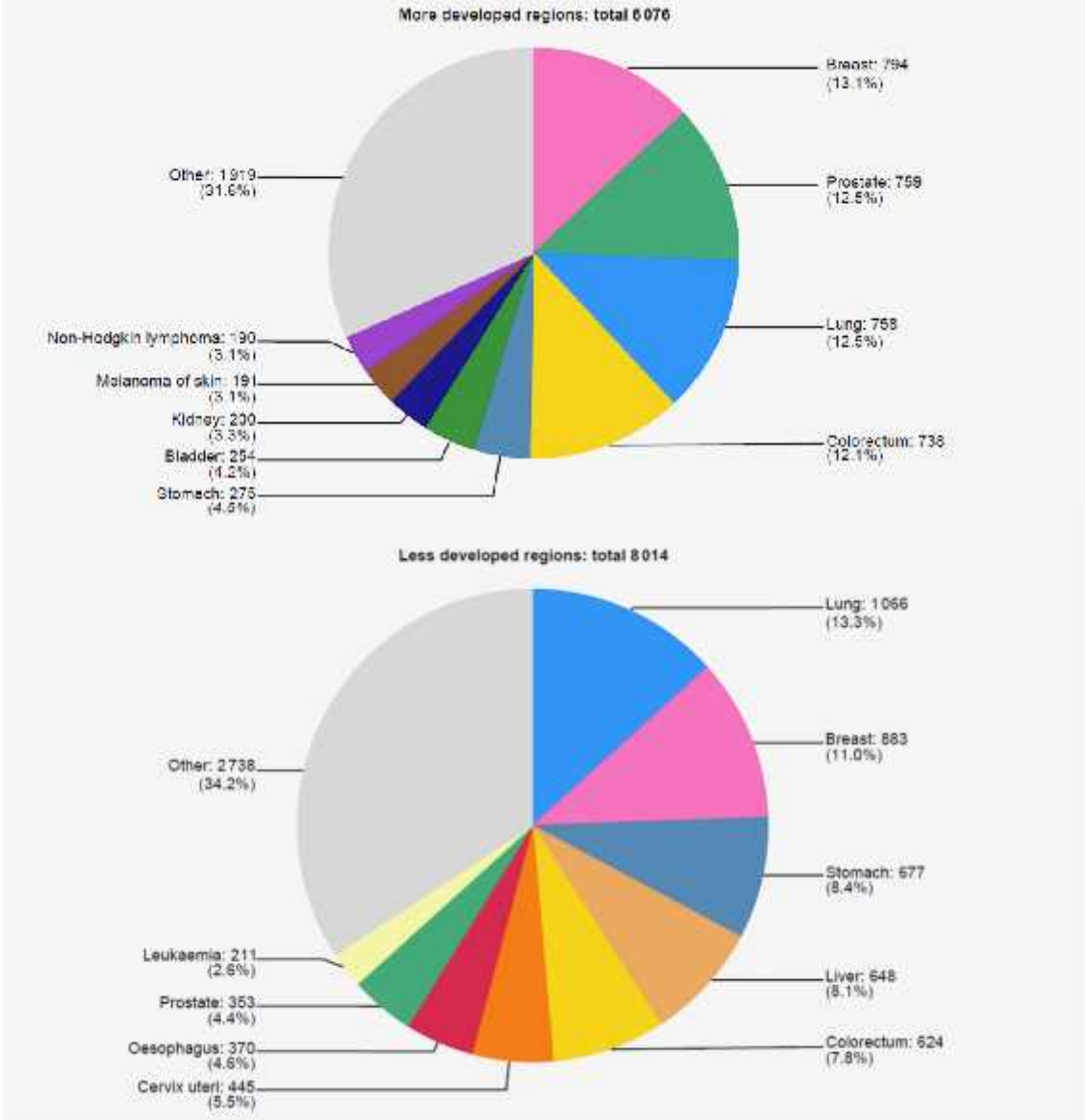
Guadalajara, 16 de junio de 2017

DISCLOSURES

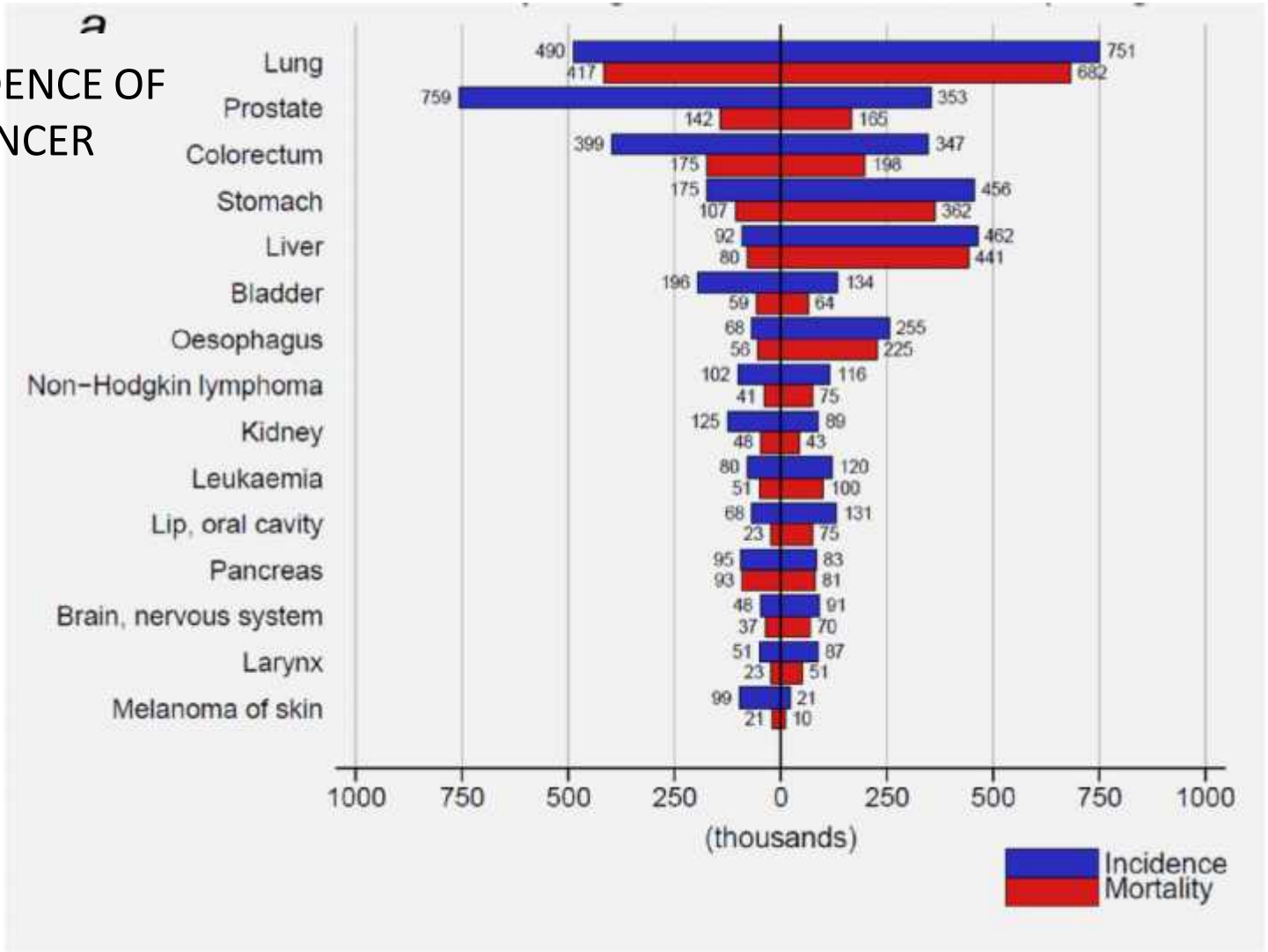
- *Advisory boards*: Sanofi, Janssen, Astellas, Bayer, Roche, Ipsen.
- *Honoraria (speaker)*: Astellas, Sanofi.
- *Travel expenses*: Sanofi, Janssen, Astellas, Bayer.
- *Clinical trials*: Sanofi, Astellas, Bayer, Ipsen, Bavarian-Nordic, Roche.

WORLD INCIDENCE OF PROSTATE CANCER



Ferlay J, et al. Int J Cancer 2015;136:E359-E386

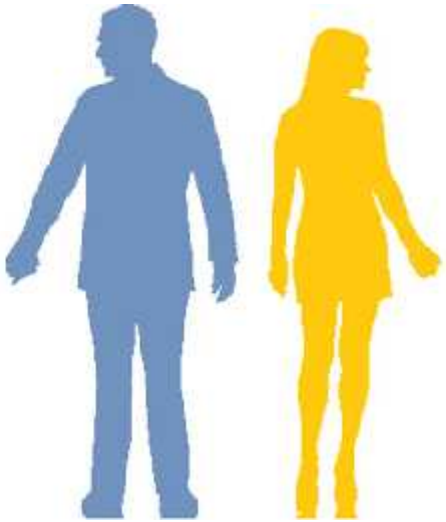
WORLD INCIDENCE OF PROSTATE CANCER



Ferlay J, et al. Int J Cancer 2015;136:E359-E386

INCIDENCE OF CANCER IN SPAIN, REDECAN 2015

	CASES	%
Prostate	33370	22
Colon & Rectum	24764	17
Lung	22430	15
Urinary Bladder	17439	12
Stomach	5150	3
Lip, Oral Cavity & Pharynx	4980	3
Liver	4252	3
Non Hodgkin's Lymphomas	4190	3
Leukaemias	3782	3
Kidney	3590	2
ALL (Except skin non melanoma)	148827	100



	CASES	%
Breast	27747	28
Colon & Rectum	16677	17
Corpus Uteri	6160	6
Lung	5917	6
Urinary Bladder	3654	4
Non Hodgkin's Lymphomas	3480	4
Pancreas	3401	3
Stomach	3306	3
Ovary	3228	3
Leukaemias	2736	3
ALL (Except skin non melanoma)	98944	100

Galceran J, et al. Clin Transl Oncol 2017;19(7):799-825

COMMON DEFINITIONS OF HIGH-RISK

American Urological Association
- Preoperative PSA >20 ng/ ml, and/ or preoperative Gleason score of 8–10, and/ or clinical stage ≥ T2c[4,5]

European Association of Urology
- Preoperative PSA >20 ng/ ml, and/ or preoperative Gleason score of 8–10, and/ or clinical stage ≥T3a[141]

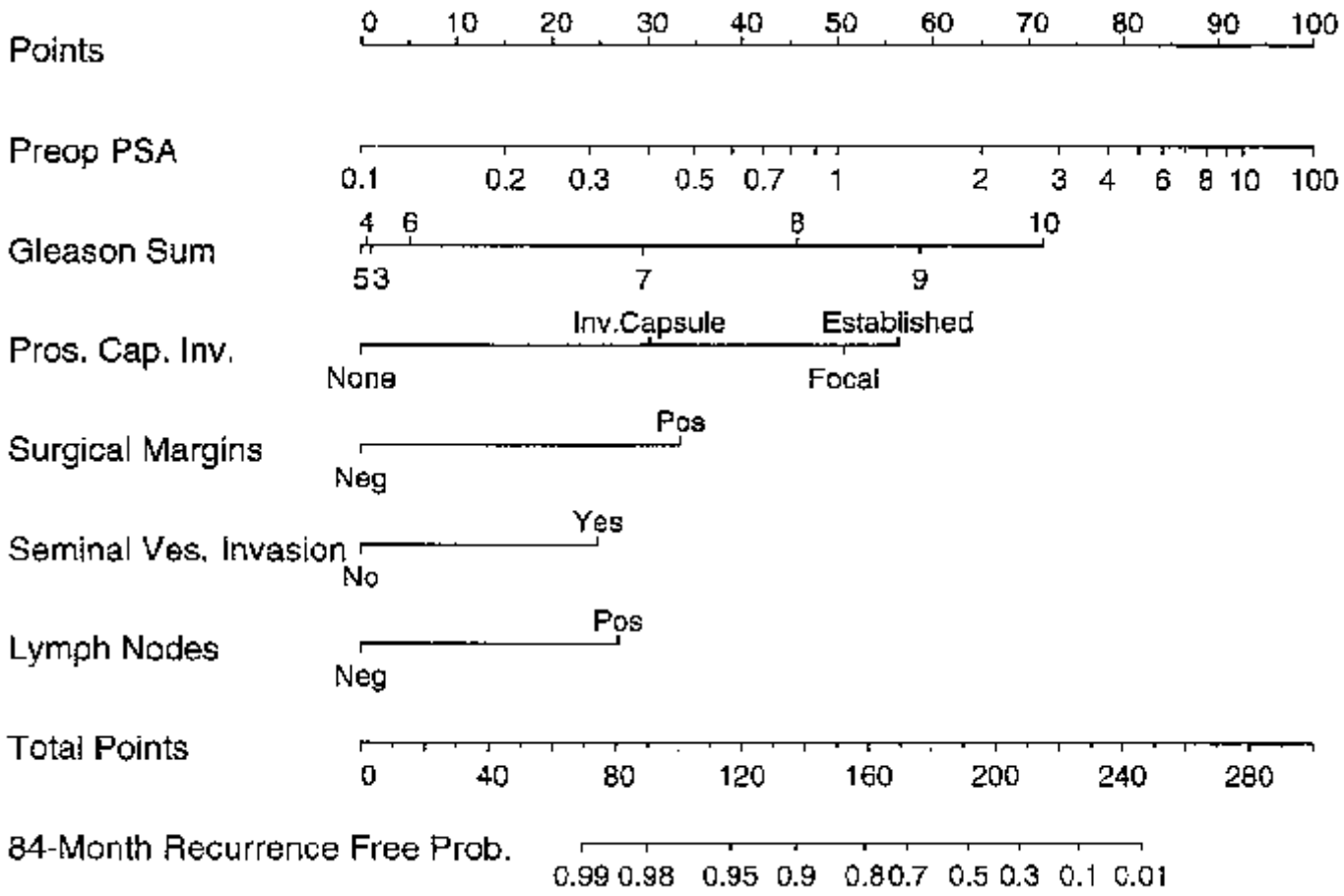
Radiation Therapy Oncology Group
- High risk: T1–2 and Gleason 8–10, or T3 or N1 with Gleason 7
- Very high risk: T3 or N1 with Gleason 8–10[6]

National Comprehensive Cancer Network
- High risk: Preoperative PSA >20 ng/ ml, preoperative Gleason score of 8–10, or clinical stage T3a
- Very high risk: T3b–T4

Cancer of the Prostate Risk Assessment (CAPRA)
- Includes age, PSA, clinical stage, Gleason score, and percentage of positive biopsy cores[9,142]

Chang AJ, et al. Nat Rev Clin Oncol 2014;11:308-23

Postoperative Nomogram for Prostate Cancer Recurrence



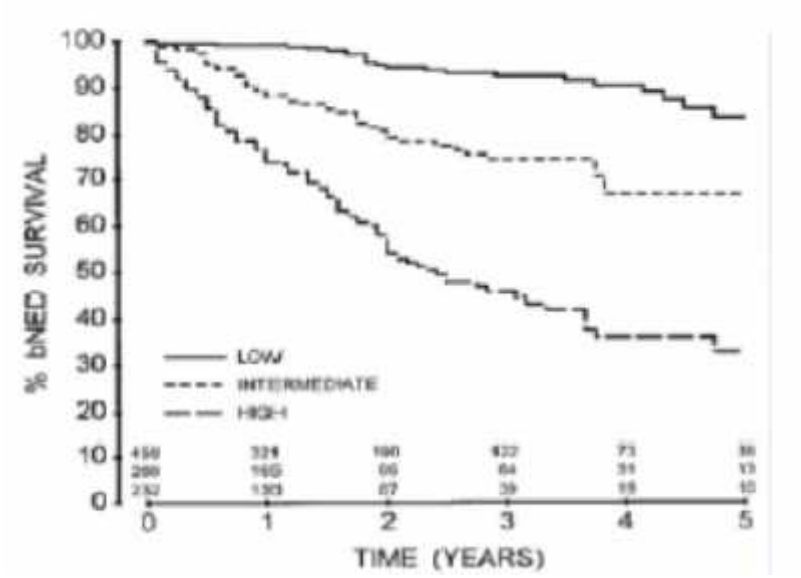
Kattan MW, et al. J Clin Oncol 1999;17:1499-1507

Table 1. Available Tissue-Based Tests for Prostate Cancer Prognosis

Test	Platform	Populations studied	Outcome Reported (Test independently predicts)	References	Molecular Diagnostic Services Program (MolDX) Recommendations
Decipher	Whole-transcriptome 1.4M RNA expression (44,000 genes) oligonucleotide microarray optimized for FFPE tissue	Post radical prostatectomy (RP), adverse pathology/high-risk features	Metastasis Prostate cancer-specific mortality	142,507-518	Cover post-RP for 1) pT2 with positive margins; 2) any pT3 disease; 3) rising PSA (above nadir)
		Post RP, biochemical recurrence	Metastasis Biochemical failure		
		Post RP, adjuvant or salvage radiotherapy	Metastasis		
Ki-67	IHC	Biopsy, intermediate- to high-risk treated with EBRT	Metastasis	519-522	Not recommended
		Biopsy, conservatively managed (active surveillance)	Prostate cancer-specific mortality		
Onco*type* DX Prostate	Quantitative RT-PCR for 12 prostate cancer-related genes and 5 housekeeping controls	Biopsy, low- to intermediate-risk treated with RP	Non-organ-confined pT3 or Gleason grade 4 disease on RP	63,523	Cover post-biopsy for NCCN very-low- and low-risk prostate cancer in patients with at least 10 years life expectancy who have not received treatment for prostate cancer and are candidates for active surveillance or definitive therapy
Prolaris	Quantitative RT-PCR for 31 cell cycle-related genes and 15 housekeeping controls	Transurethral resection of the prostate (TURP), conservatively managed (active surveillance)	Prostate cancer-specific mortality	59-62,524,525	Cover post-biopsy for NCCN very-low- and low-risk prostate cancer in patients with at least 10 years life expectancy who have not received treatment for prostate cancer and are candidates for active surveillance or definitive therapy
		Biopsy, conservatively managed (active surveillance)	Prostate cancer-specific mortality		
		Biopsy, localized prostate cancer	Biochemical recurrence Metastasis		
		Biopsy, intermediate-risk treated with EBRT	Biochemical failure		
		RP, node-negative localized prostate cancer	Biochemical recurrence		
ProMark	Multiplex immunofluorescent staining of 8 proteins	Biopsy, Gleason grade 3+3 or 3+4	Non-organ-confined pT3 or Gleason pattern 4 disease on RP	526	Cover post-biopsy for NCCN very-low- and low-risk prostate cancer in patients with at least 10 years life expectancy who have not received treatment for prostate cancer and are candidates for active surveillance or definitive therapy.
PTEN	Fluorescent in situ hybridization or IHC	Transurethral resection of the prostate (TURP), conservatively managed (active surveillance)	Prostate cancer-specific mortality	527-531	Not recommended
		Biopsy, Gleason grade 3+3	Upgrading to Gleason pattern 4 on RP		
		RP, high-risk localized disease	Biochemical recurrence		

DEFINICIÓN DE ALTO RIESGO

Riesgo	Institución	PSA (ng/ml)		Gleason		Estadio
Bajo	D'Amico	≤10	y	≤6	y	cT1c-2a
	NCCN	≤10		≤6		cT1c-2a
Intermedio	D'Amico	10.1-20	o	7	o	cT2b
	NCCN	10.1-20		7		cT2b-c
Alto	**D'Amico**	**≥20**	**o**	**≥8**	**o**	**≥cT2c**
	NCCN	**≥20**	**o**	**≥8**	**o**	**≥cT3**



Aproximadamente, el 15% de los pacientes con cáncer de próstata son diagnosticados en situación de alto riesgo de progresión/recidiva.

D'Amico AV, et al. J Clin Oncol 1999;17:168-72
NCCN 2017 Guidelines

LOCALIZED PROSTATE CANCER IS SOMETIMES A SYSTEMIC DISEASE

- High risk of failure of local therapy alone:
  - Clinical stage T3, T4
  - PSA $\geq$ 20 ng/mL
  - Gleason 8-10 (groups 4-5)
  - High volume Gleason 7
  - PSA velocity > 2 ng/mL/year

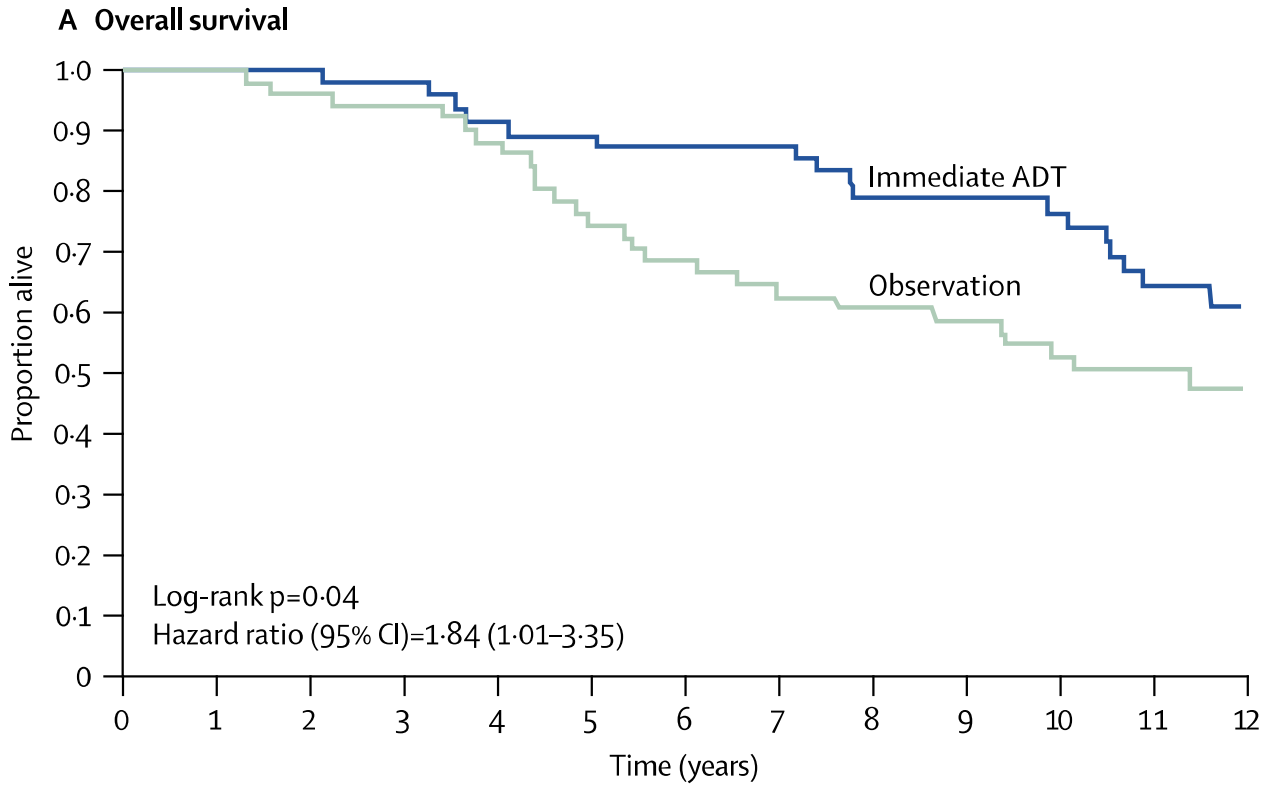
EL CÁNCER DE MAMA COMO PARADIGMA

- El cáncer de mama es el paradigma del tratamiento sistémico en pacientes con tumor localizado en riesgo de recidiva.
- Beneficio del tratamiento neoadyuvante y adyuvante, tanto del tratamiento hormonal como de la quimioterapia.

LA HORMONOTERAPIA MEJORA LA SUPERVIVENCIA CON UN NIVEL DE EVIDENCIA I

Study	Duration of ADT	n	Absolute Risk Reduction	NNT
EORTC 22863	3 years adjuvant	415	**16% OS**	5.5
RTOG 8531	Lifelong adjuvant	977	**10% OS**	10
RTOG 8610	4 mo N/C	456	**9% OS**	11
DFCI	6 mo N/C/A	206	**10% OS**	10
TROG	6 mo N/C	802	**13% OS**	7.5
RTOG 9408	4 mo N/C	1979	**5% OS**	20

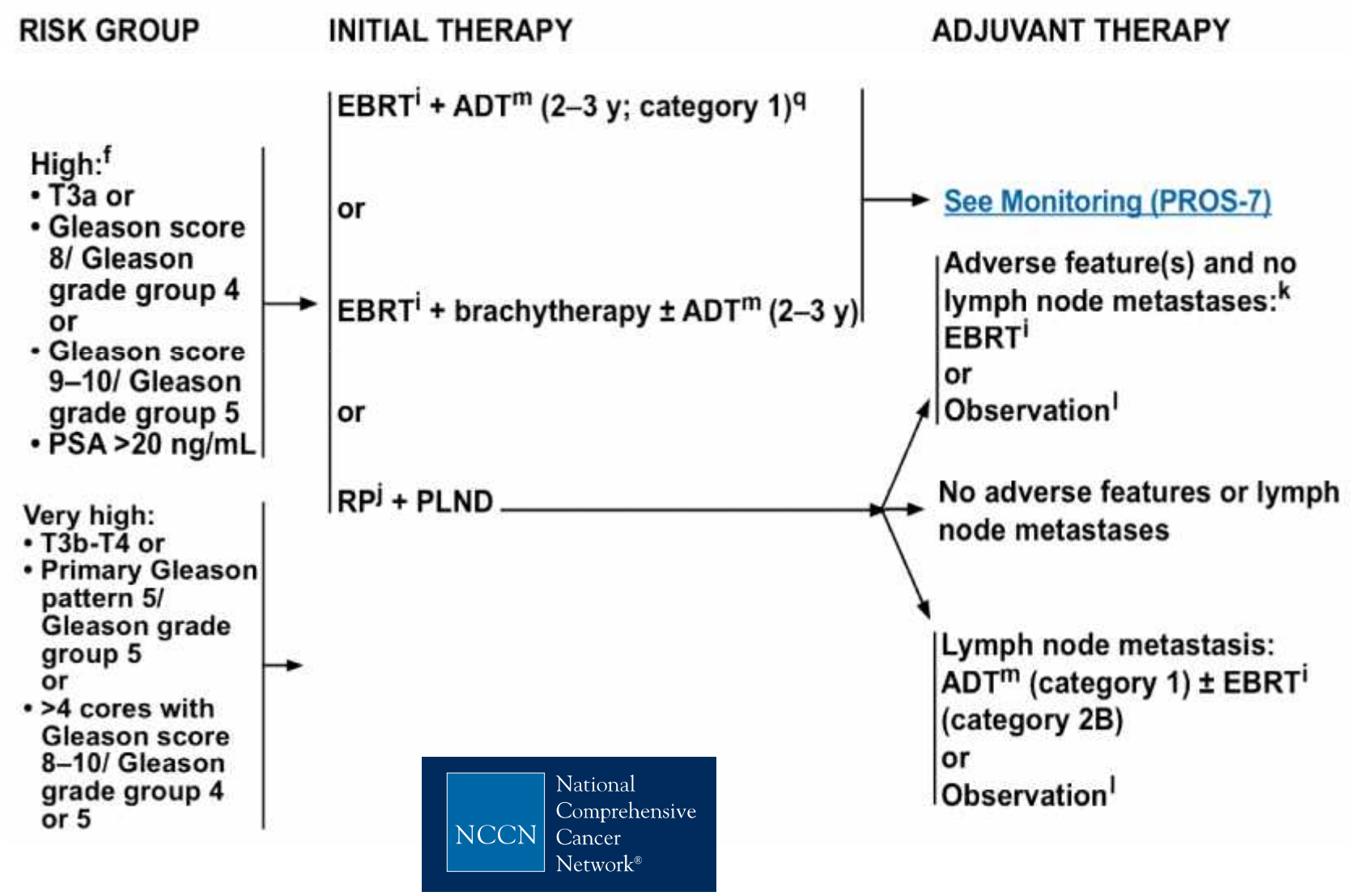
HORMONOTERAPIA ADYUVANTE TRAS CIRUGÍA CON GANGLIOS POSITIVOS



Number at risk

Immediate ADT	47	47	47	46	43	42	41	41	36	35	33	25	14
Observation	51	51	49	48	45	38	35	32	31	30	25	17	10

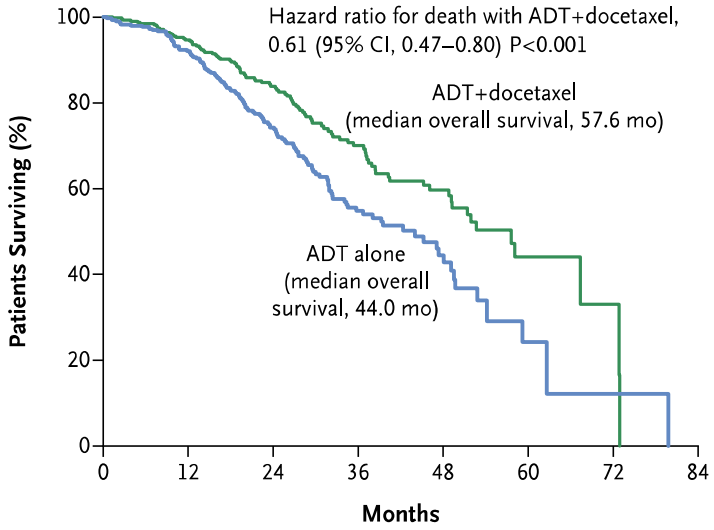
Messing EM, et al. Lancet Oncol 2006:7:472–79


RISK GROUP
INITIAL THERAPY
ADJUVANT THERAPY
High:[f]
• T3a or
• Gleason score 8/ Gleason grade group 4 or
• Gleason score 9–10/ Gleason grade group 5
• PSA >20 ng/mL
Very high:
• T3b-T4 or
• Primary Gleason pattern 5/ Gleason grade group 5 or
• >4 cores with Gleason score 8–10/ Gleason grade group 4 or 5
EBRT[i] + ADT[m] (2–3 y; category 1)[q]
or
EBRT[i] + brachytherapy ± ADT[m] (2–3 y)
or
RP[j] + PLND
See Monitoring (PROS-7)
Adverse feature(s) and no lymph node metastases:[k]
EBRT[i]
or
Observation[l]
No adverse features or lymph node metastases
Lymph node metastasis:
ADT[m] (category 1) ± EBRT[i] (category 2B)
or
Observation[l]
NCCN
National Comprehensive Cancer Network®

QUIMIOTERAPIA

DOCETAXEL ES ESTÁNDAR EN PRIMERA LÍNEA DE QUIMIOTERAPIA EN CPHS

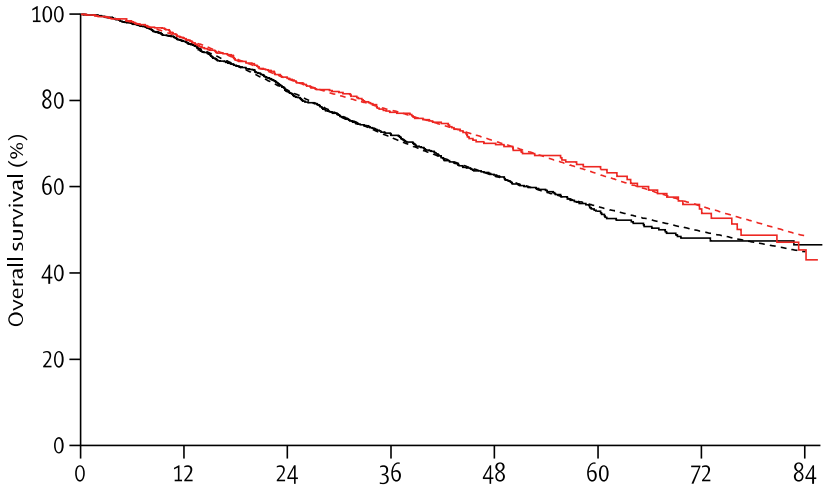
CHAARTED



No. at Risk								
ADT+docetaxel	397	333	189	89	46	5	2	0
ADT alone	393	318	168	71	27	3	1	0

Sweeney CJ, et al. N Engl J Med 2015;373:737-46

STAMPEDE

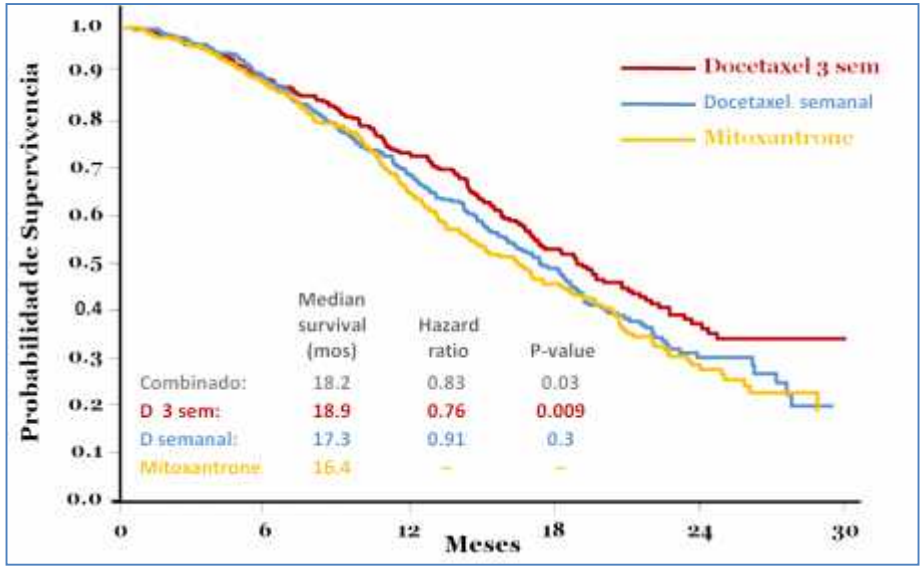


1184	(73)	1093	(134)	876	(92)	538	(60)	322	(35)	166	(17)	87	(2)	43
592	(33)	545	(52)	447	(35)	290	(22)	181	(12)	93	(13)	51	(6)	20

James NJ, et al. Lancet 2016;387:1163–77

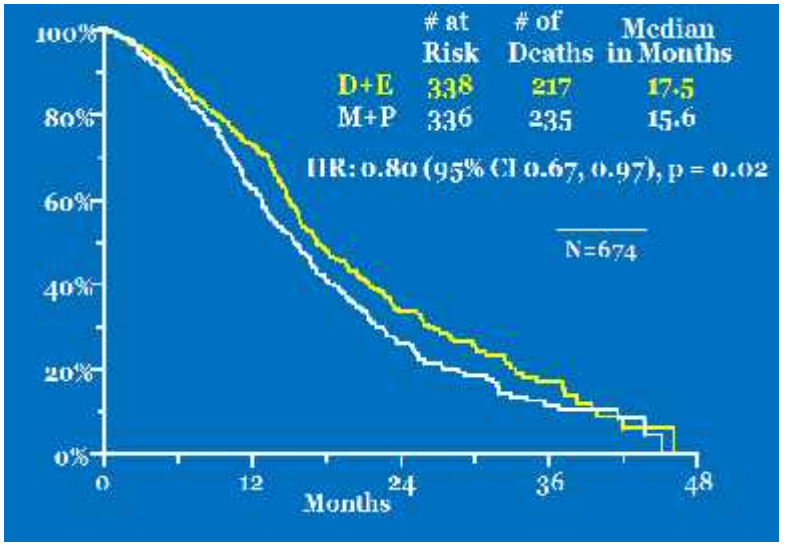
DOCETAXEL ES ESTÁNDAR EN PRIMERA LÍNEA DE QUIMIOTERAPIA EN CPRCm

Docetaxel plus Prednisone or Mitoxantrone plus Prednisone for Advanced Prostate Cancer



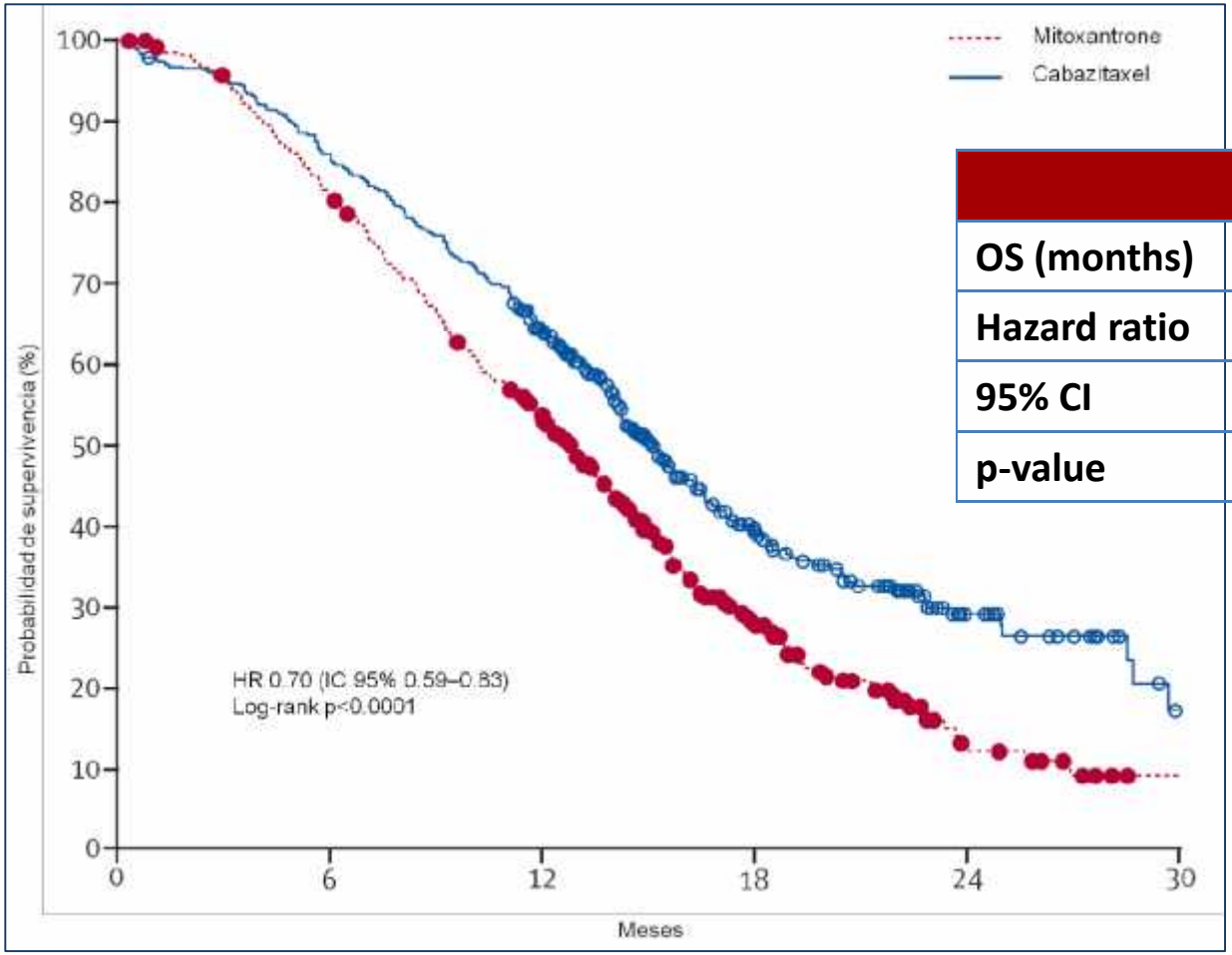
Tannock IF, et al. N Engl J Med 2004;351(15):1502-12

Docetaxel and Estramustine Compared with Mitoxantrone and Prednisone for Advanced Refractory Prostate Cancer



Petrylak D, et al. N Engl J Med 2004;351(15):1513-20

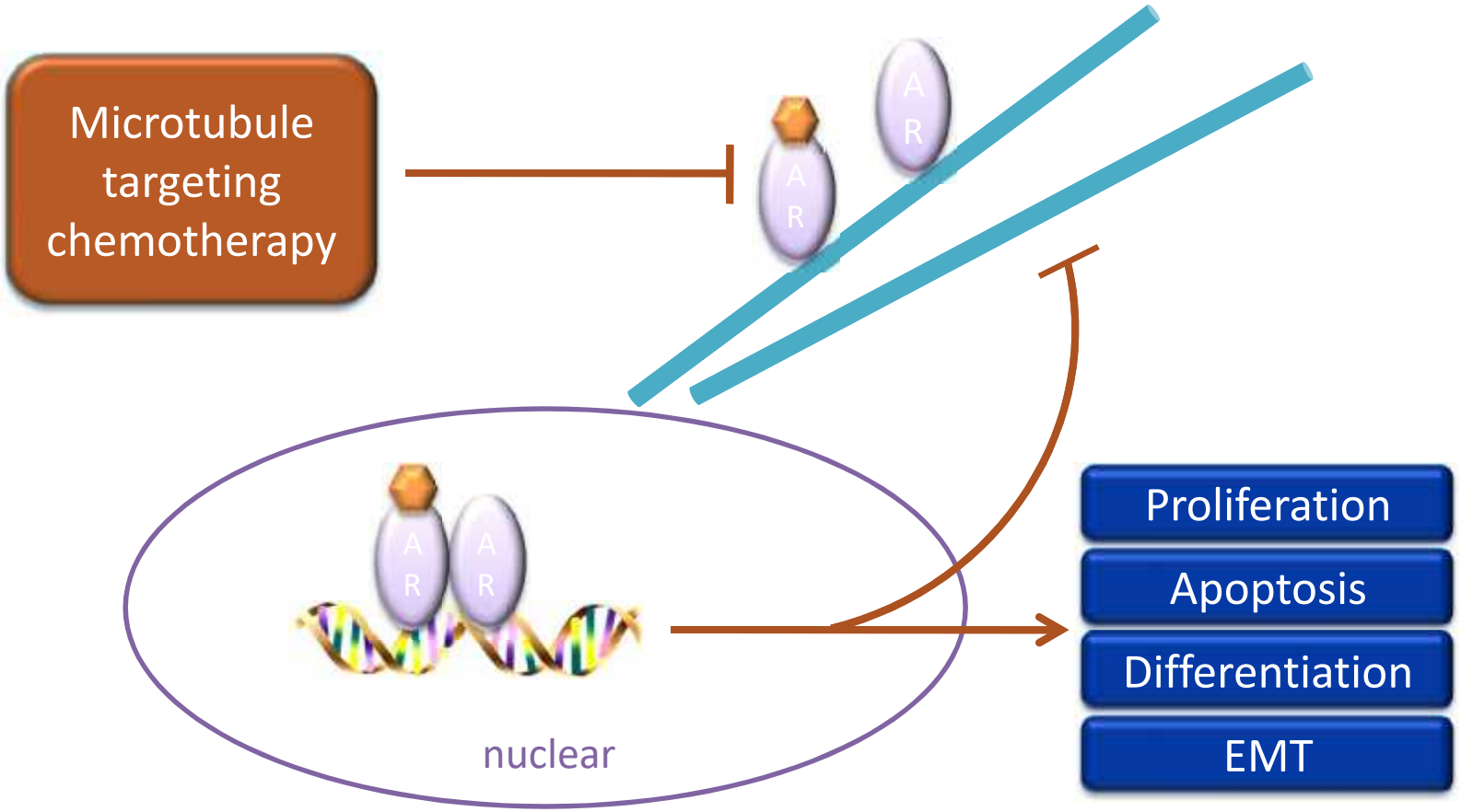
TROPIC: MEJORÍA DE SG CON CABAZITAXEL



	MP	CBZP
OS (months)	12.7	15.1
Hazard ratio	0.70	
95% CI	0.59-0.83	
p-value	<0.0001	

de Bono JS, et al. Lancet 2010;376:1147-54

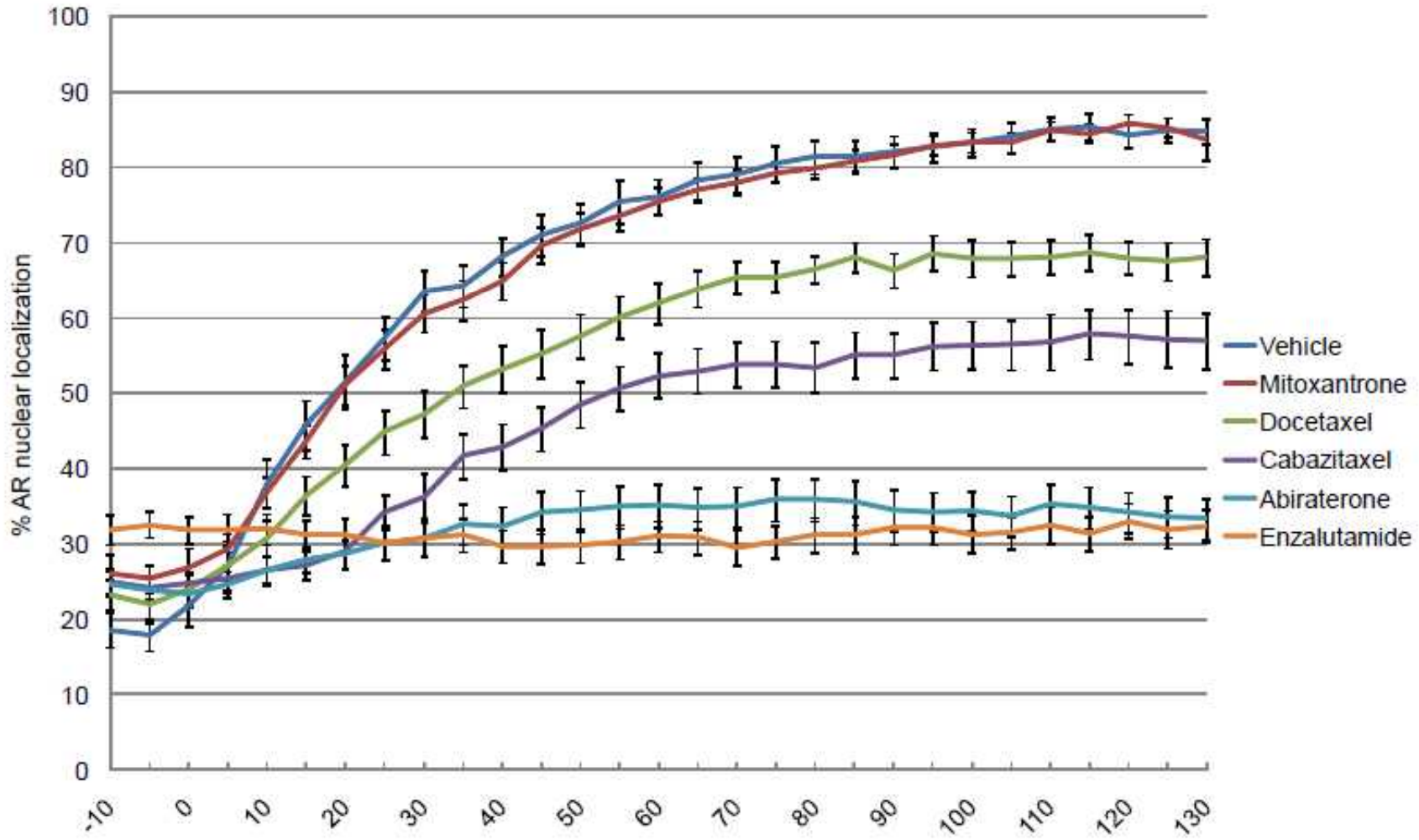
TAXANES BLOCK AR NUCLEAR TRANSLOCATION



Microtubules facilitate AR nuclear translocation and enhance downstream AR transcriptional activity - Taxanes block this pathway

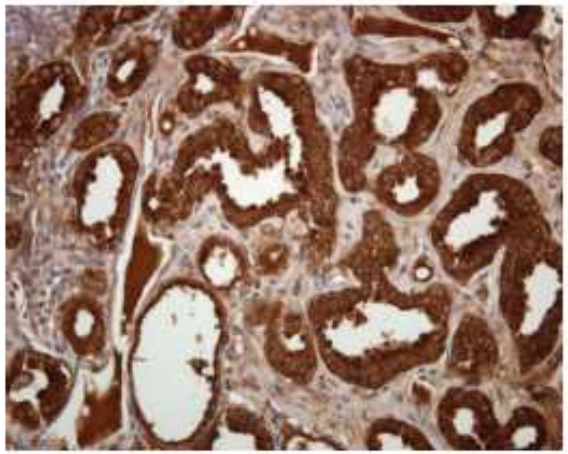
Zhu ML, et al. Cancer Res 2010;70:7992-8002

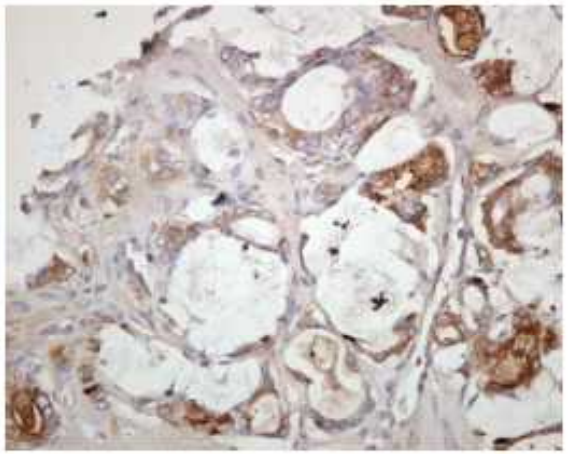
TAXANES BLOCK AR NUCLEAR TRANSLOCATION



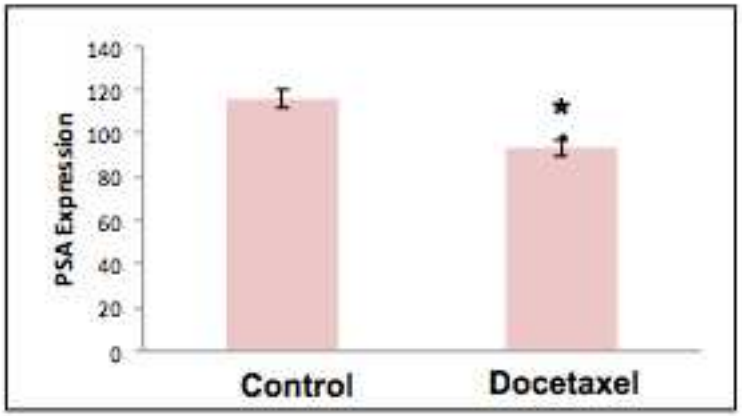
van Soest RJ, et al. Eur J Cancer 2013;49(18):3821-30

DOCETAXEL INHIBITS PSA EXPRESSION IN PCa





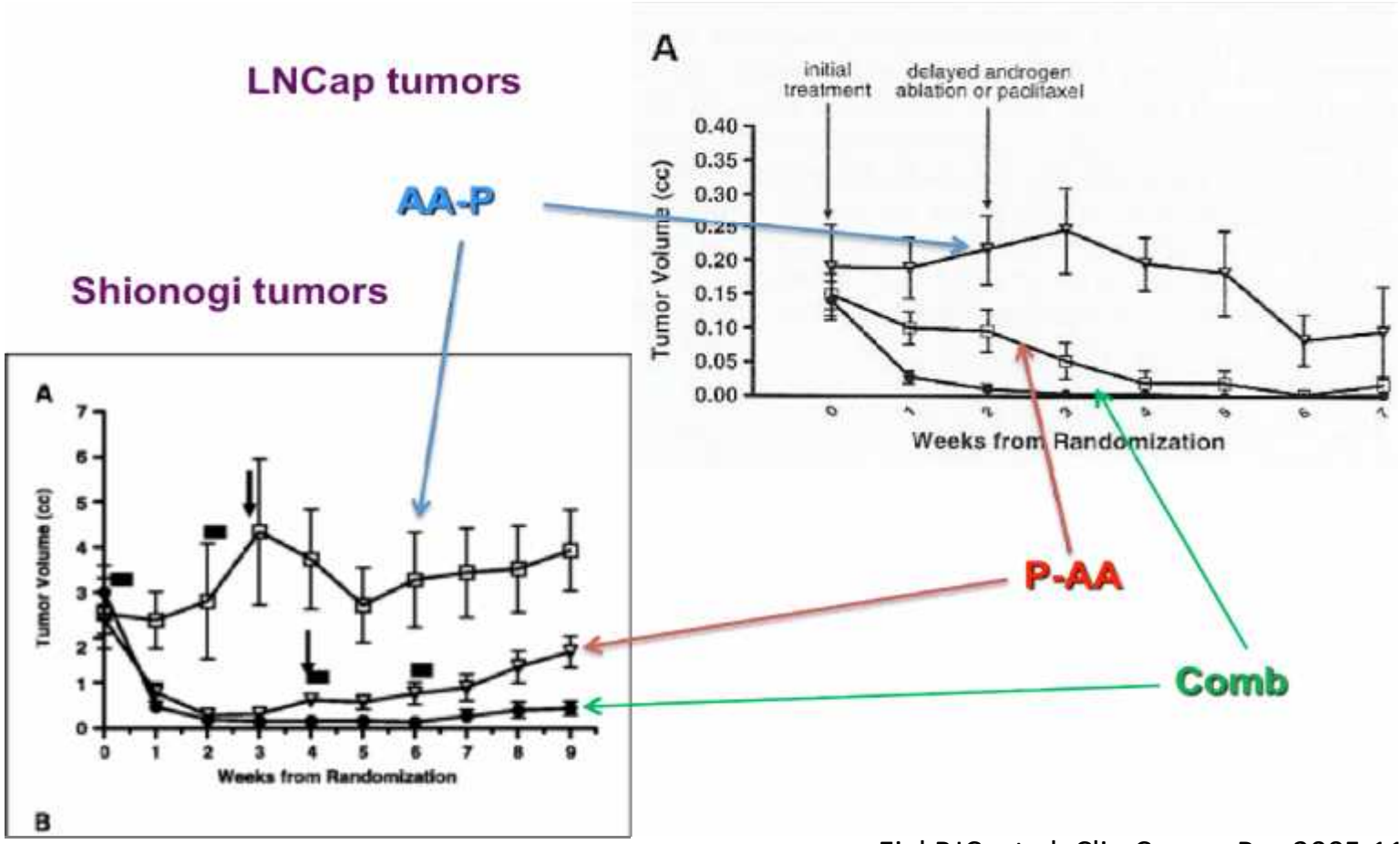
Control **Docetaxel treatment**



Significant reduction in PSA expression in prostate tumors of patients treated with docetaxel

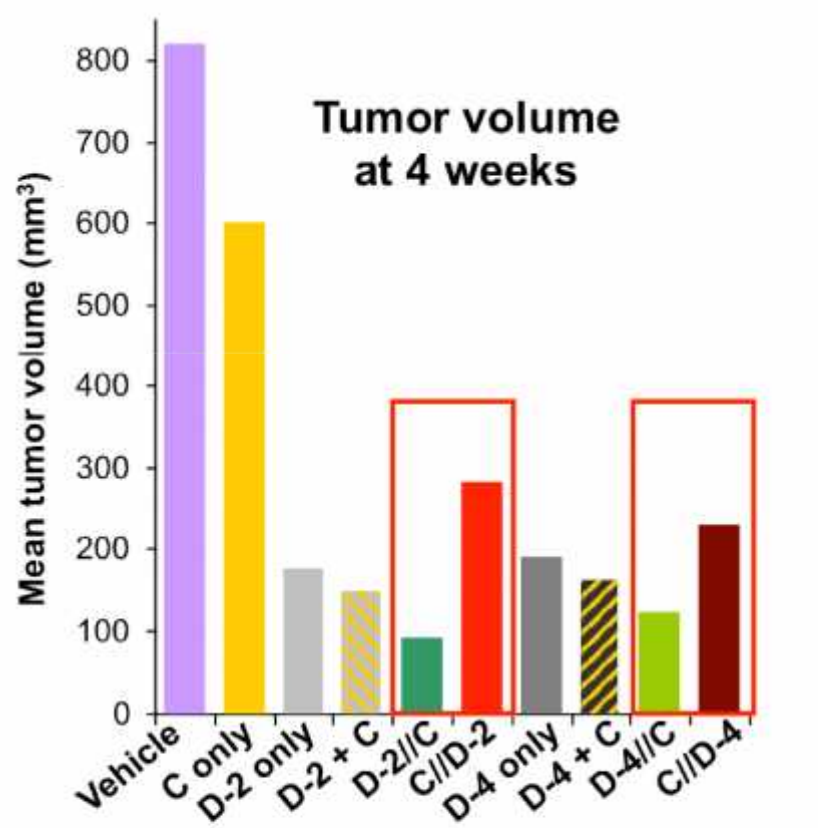
Zhu ML, et al. Cancer Res 2010;70:7992-8002

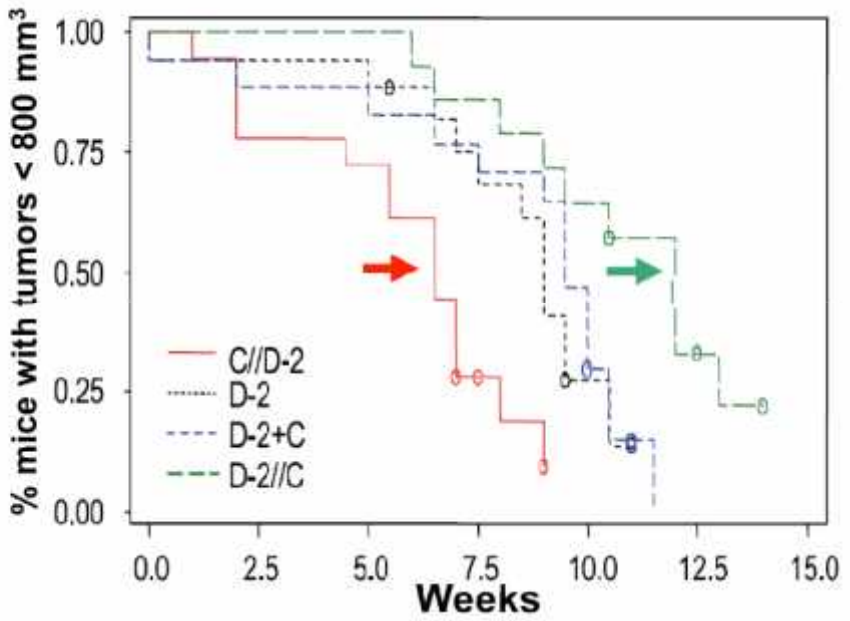
TIMING IS EVERYTHING: PRECLINICAL EVIDENCE SUPPORTING SIMULTANEOUS RATHER THAN SEQUENTIAL CHEMOHORMONAL THERAPY FOR PROSTATE CANCER



Eigl BJC, et al. Clin Cancer Res 2005;11:4905-11

SMALLER TUMOR SIZE AND GROWTH DELAY FOR DOCETAXEL → CASTRATION SEQUENCE IN MICE WITH LNCaP TUMORS





C: Castration
D-2 (or D-4): Docetaxel given for 2 (or 4) weeks
C//D (-2 or -4): Castration→Docetaxel (2 or 4 wks)
D (-2 or -4)//C: Docetaxel (2 or 4 wks) → Castration
D + C: concomitant Docetaxel+Castration

Tang Y, et al. Clin Cancer Res 2006;12:169-174

PAPEL DE LA QUIMIOTERAPIA

- Neoadyuvante a tratamiento local
- Adyuvante tras tratamiento local
- Concomitante a radioterapia

PAPEL DE LA QUIMIOTERAPIA

RESUMEN DE LOS PRINCIPALES ESTUDIOS CON DOCETAXEL

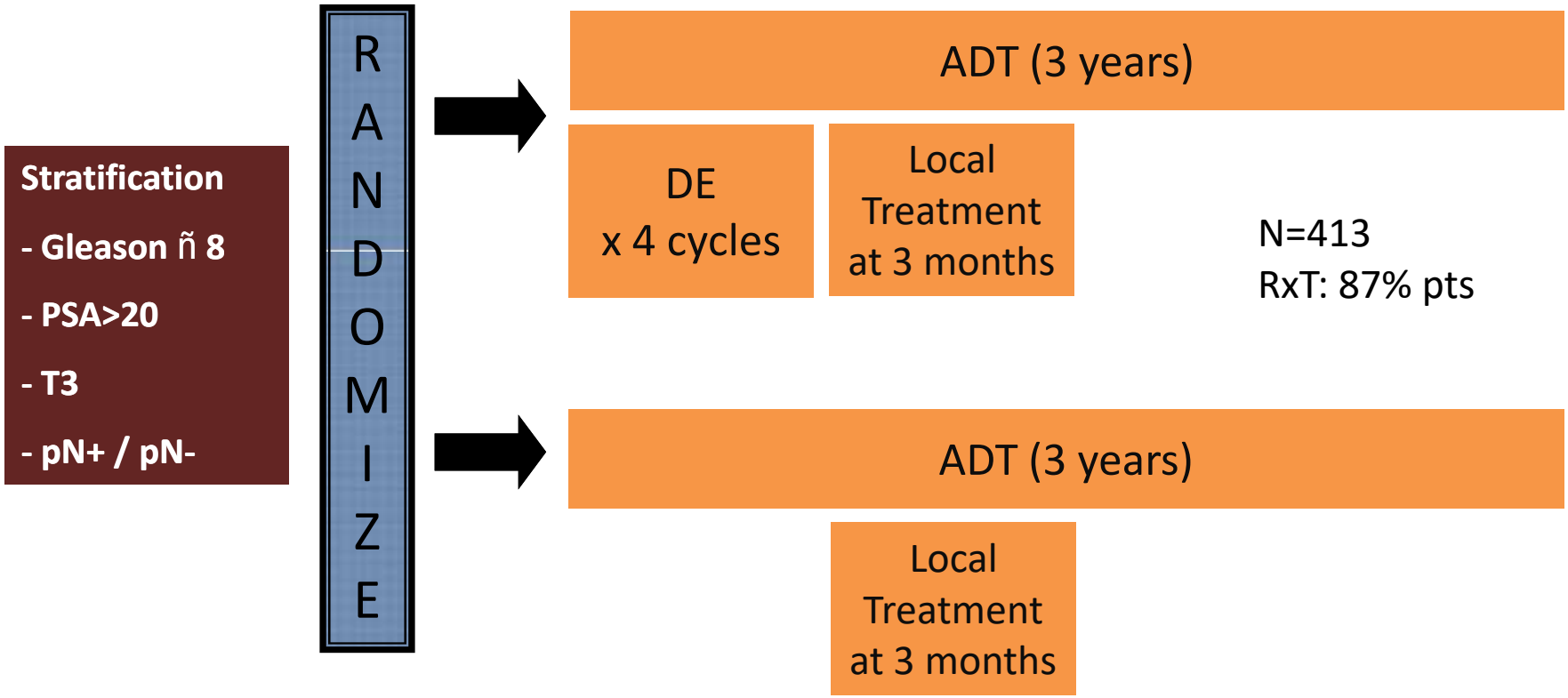
Ensayos clínicos	*Tipo de QT*	*Fecha publ.*	*Número ptes.*	*Objetivo primario*	*Gleason 8-10*	*Tiempo seguimiento resultados (años)*	*Resultados (control vs. experimental)**
TAX 3501	Docetaxel	2013	228	SLP	52%	3,25	83% *vs.* 91%
GETUG 12	Docetaxel	2014	413	SLR	42%	8	50% *vs.* 62% p = 0,017
RTOG 0521	Docetaxel	2015	612	SG	84%	4	89% *vs.* 93% p = 0,04
STAMPEDE (mayoría M1)	Docetaxel	2015	2962	SG	70%	5	55% *vs.* 63% p = 0,006
RTOG 9902	Paclitaxel, etopósido, estramustina	2009, 2015	380	SG	68%	9,2	63 vs 65% p = 0,81

VA-CSP#553

Intergroup S9921

Ferrer M & Gallardo E. Rev Cancer 2016(30):1

NEOADJUVANT TRIAL – GETUG 12



- Primary endpoint: **Relapse-free survival**
- To detect a **12%** difference with a power of 80% and an alpha risk of 0.05 (two-sided), n= 400 patients
- NCT00055731

Fizazi K, et al. Lancet Oncol 2015;16:787-94

GETUG 12

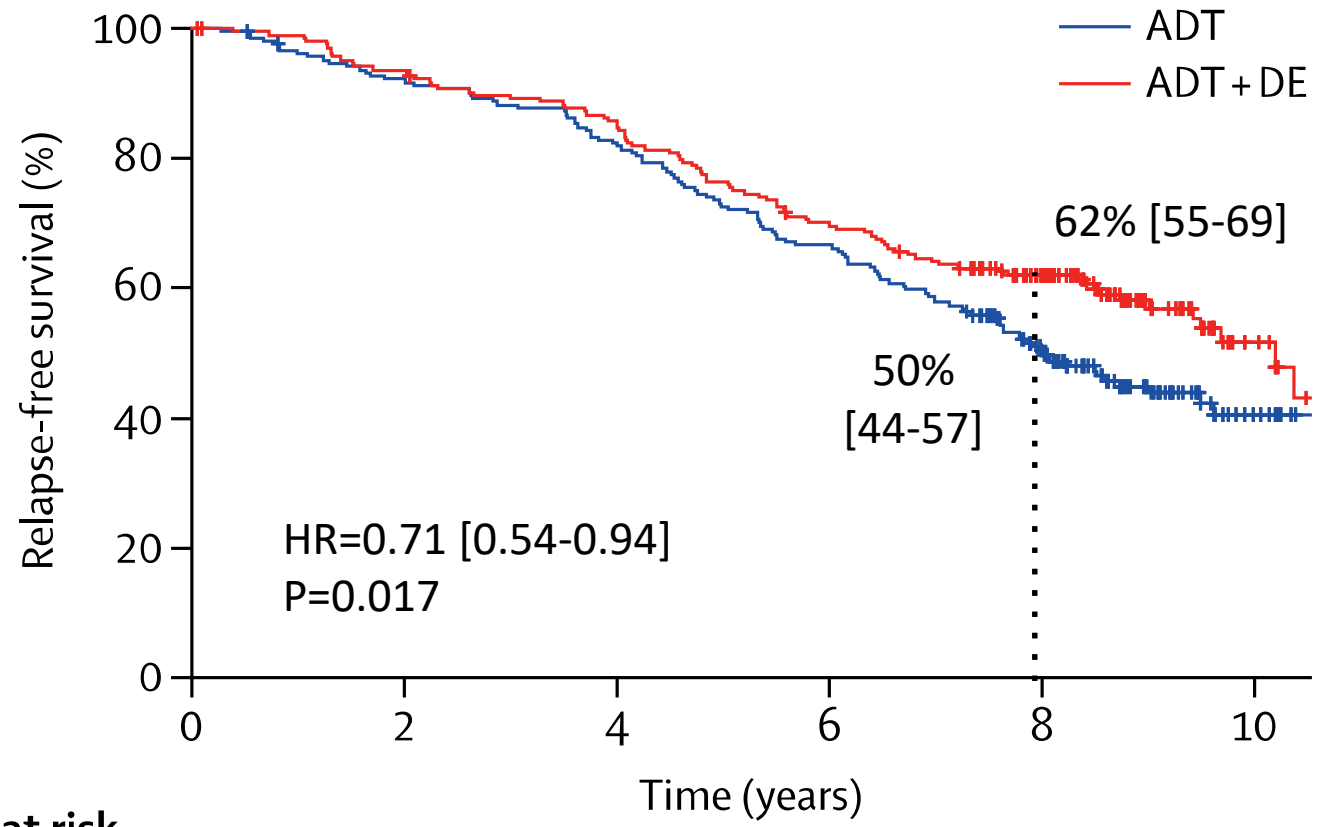
	ADT and DE group (n=207)	ADT only group (n=206)
Age (years)	62 (46–77)	64 (46–77)
Clinical stage		
T1–T2	67 (32%)	67 (33%)
T3–T4	140 (68%)	139 (67%
Median number of positive biopsy cores/total cores	6/10 (67%)	6/10 (67%)
Gleason score		
<8	120 (58%)	118 (57%)
≥8	87 (42%)	88 (43%)
Pathological nodal status		
N negative	148 (71%)	146 (71%)
N positive	59 (29%)	60 (29%)
Serum PSA concentration (ng/mL)		
≤20	84 (41%)	85 (41%)
>20	123 (59%)	121 (59%)
Serum creatinine (µmol/L)	87 (58–154)	88 (50–139)
Haemoglobin concentration (g/L)	140 (100–170)	150 (110–170)

Data are median (IQR) or n (%), unless stated otherwise. PSA=prostate-specific antigen. ADT=androgen deprivation therapy. DE=docetaxel and estramustine.

Table 1: **Baseline characteristics**

Fizazi K, et al. Lancet Oncol 2015;16:787-94

NEOADJUVANT TRIAL – GETUG 12

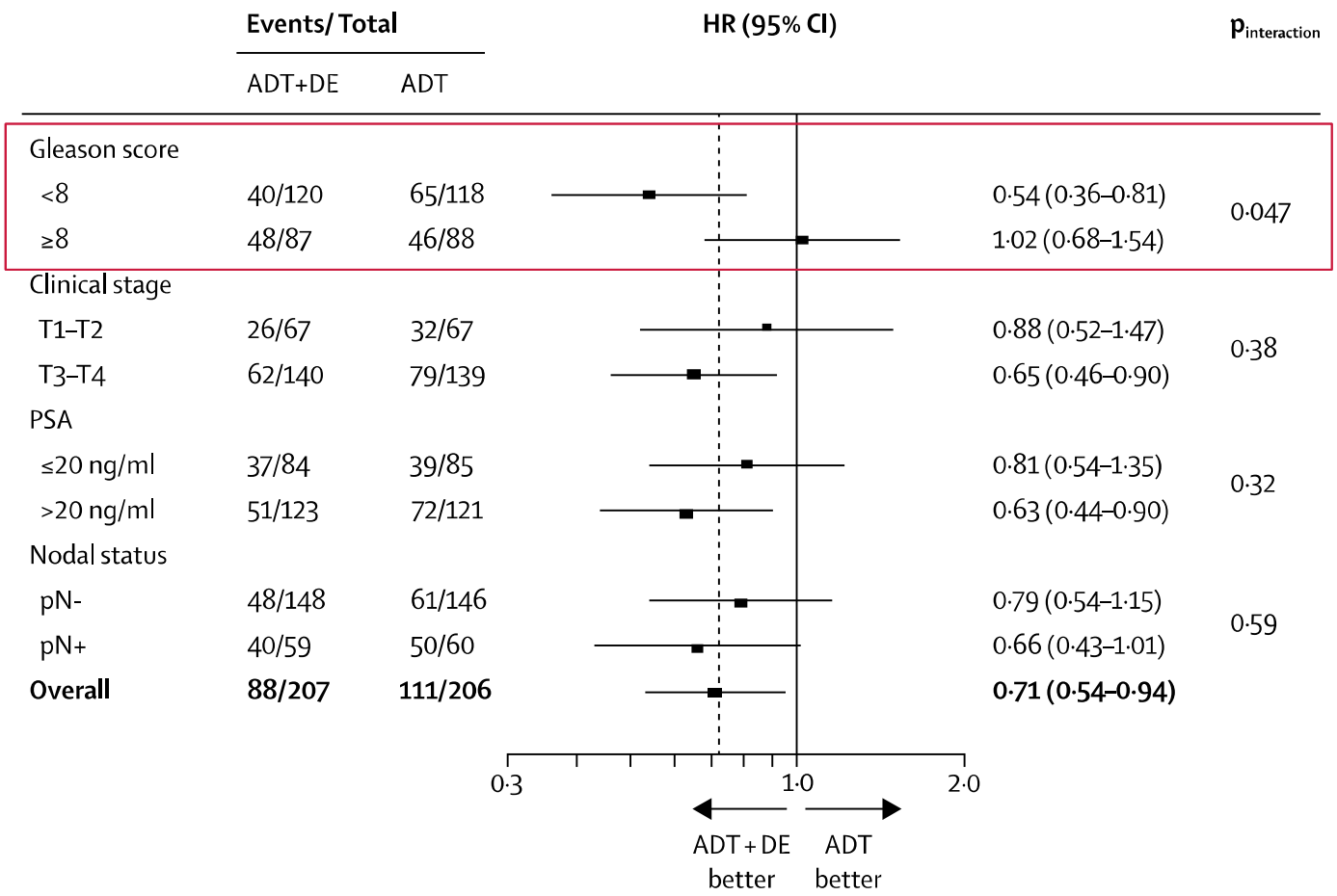


Number at risk

ADT	206	187	167	136	87	17
ADT + DE	207	191	172	141	105	16

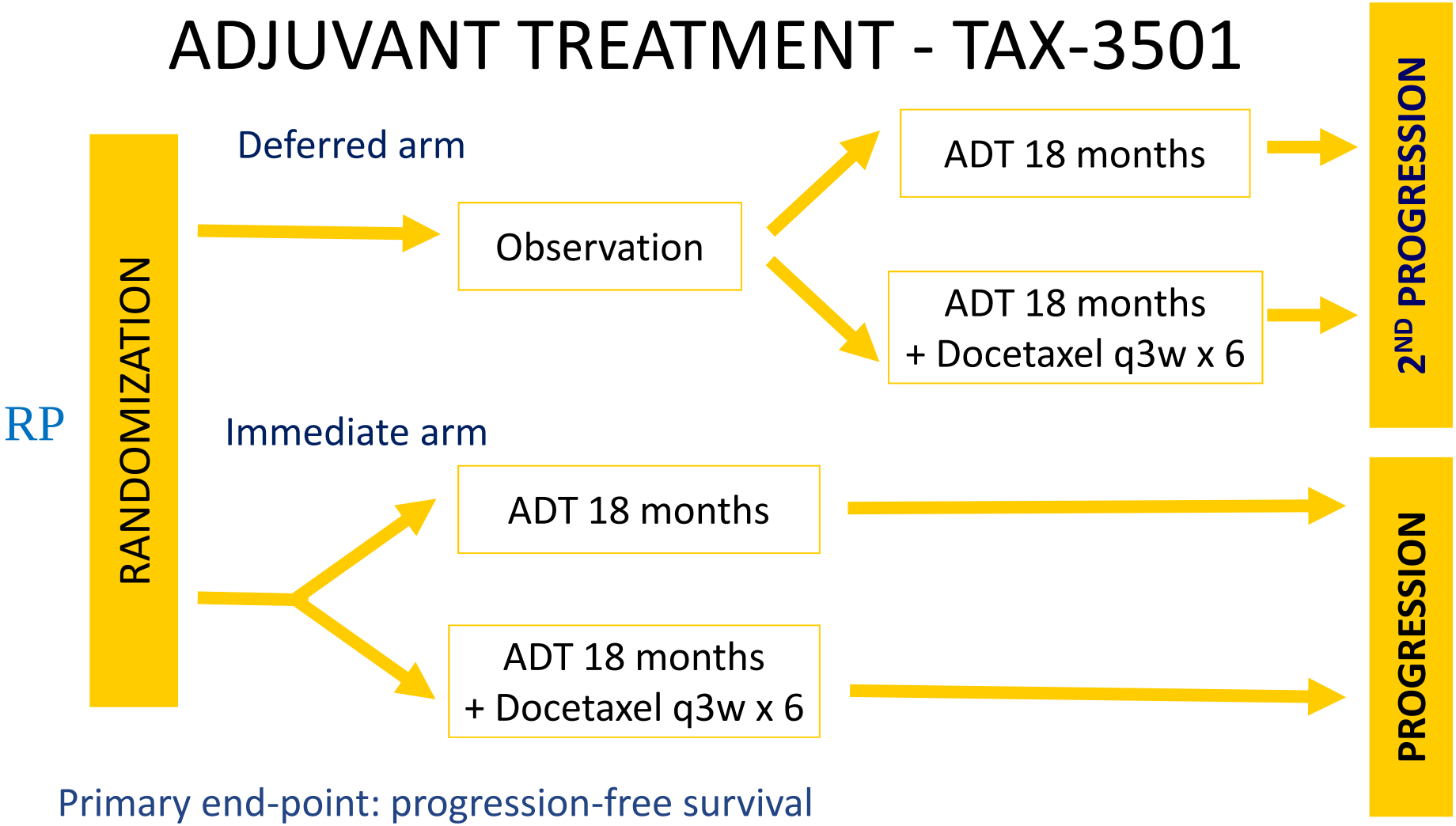
Fizazi K, et al. Lancet Oncol 2015;16:787-94

NEOADJUVANT TRIAL – GETUG 12



Fizazi K, et al. Lancet Oncol 2015;16:787-94

ADJUVANT TREATMENT - TAX-3501



Primary end-point: progression-free survival

N=**228**/1689 patients at high risk of progression (Kattan nomogram)

ClinicalTrials.gov identifier: NCT00283062

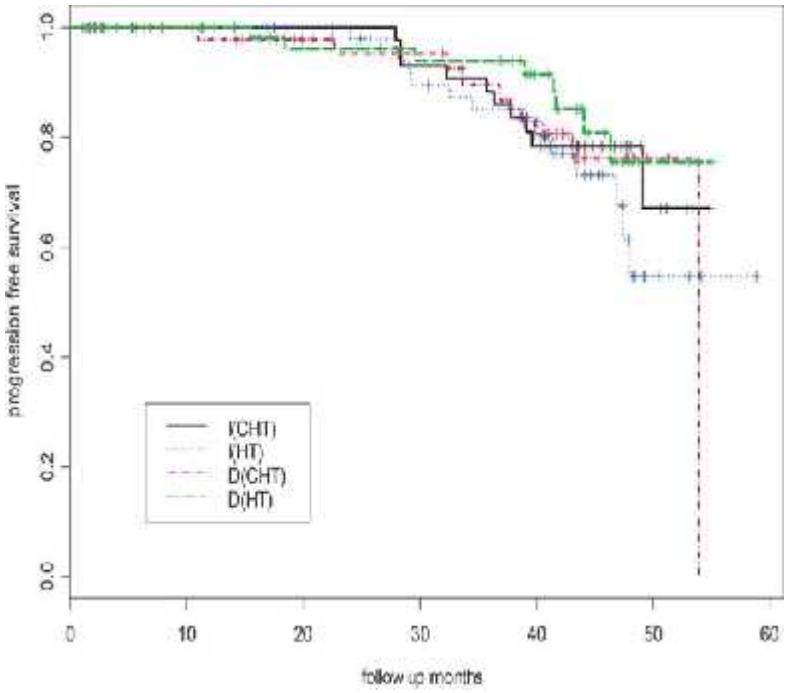
Schweizer MT, et al. Cancer 2013;119:3610-8 . Cancer 2013;119:3610-8

ADJUVANT TREATMENT - TAX-3501

TABLE 2. Disease Progression by Treatment Subgroups

Outcome	Randomized Treatment Group			
	I(CHT) N = 55	I(HT) N = 55	D(CHT) N = 56	D(HT) N = 62
Progression, no. (%)	10 (18.2)	14 (25.5)	9 (16.1)	8 (12.9)
PSA progression	10 (18.2)	12 (21.8)	9 (16.1)	8 (12.9)
Bone metastasis	0	1 (1.8)	0	0
Other	0	1 (1.8)	0	0
Death, no. (%)	0	1 (1.8)	0	1 (1.6)

Abbreviations: D(CHT), deferred hormonal therapy with chemotherapy (docetaxel); D(HT), deferred hormonal therapy without chemotherapy; I(CHT), immediate hormonal therapy with chemotherapy (docetaxel); I(HT), immediate hormonal therapy without chemotherapy; PSA, prostate-specific antigen.



Schweizer MT, et al. Cancer 2013;119:3610-8 . Cancer 2013;119:3610-8

RTOG 0521

High Risk

Stage	Gleason score	PSA
Any T stage	≥9	<150
	7-8	≥20-150
≥T2	8	<20

NRG ONCOLOGY™

Randomize

Arm 1

Androgen Suppression (24 mos) + External RT (8 wks)

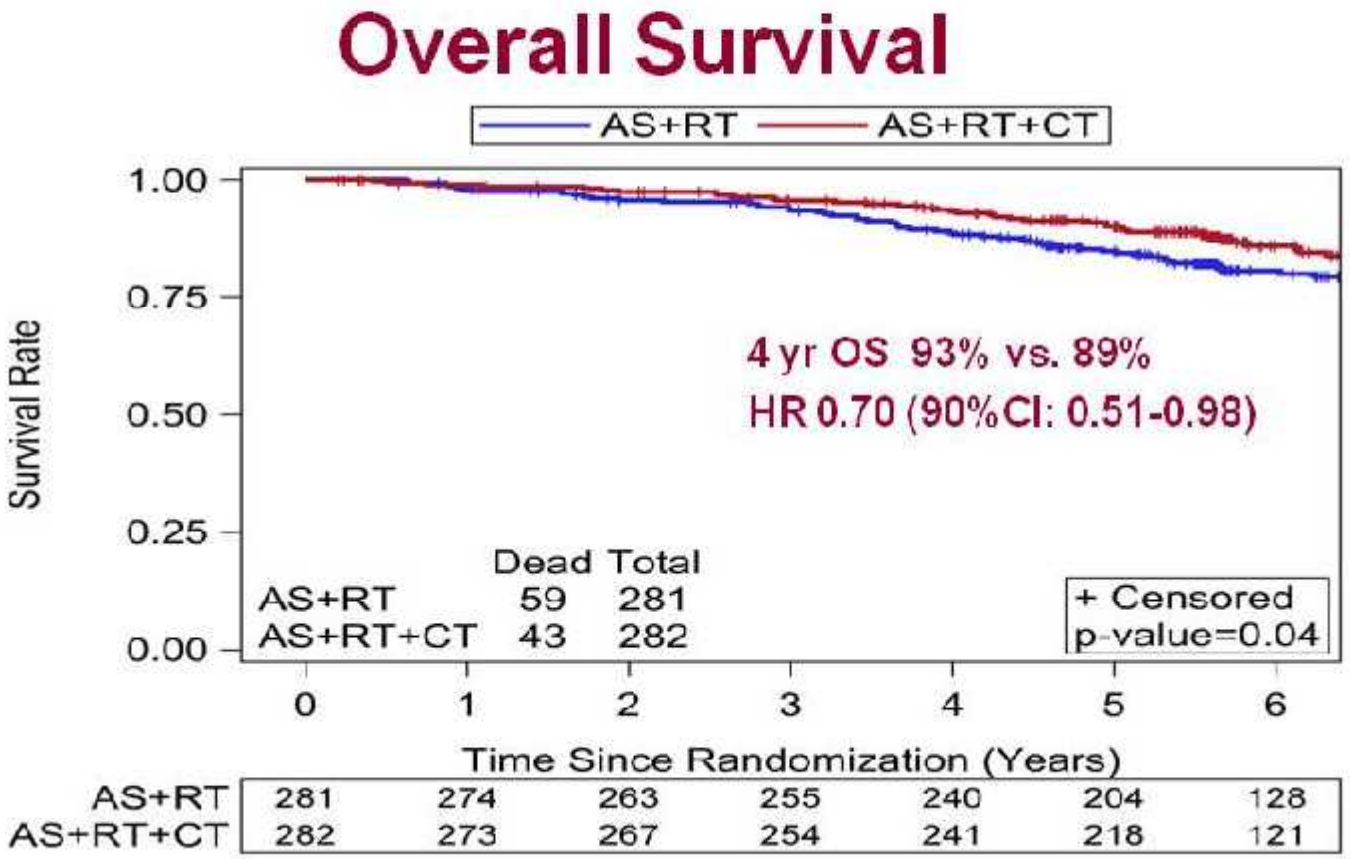
Arm 2

Androgen Suppression (24 mos) + External RT (8 wks) + Docetaxel beginning 4 wks after RT (6 cycles)

Primary endpoint: Overall survival
Design: Detect improved 4-y OS rate from 86% to 93% (HR=0.49)
Intent-to-treat, 1-sided log-rank at 0.05 significance and 90% power

Sandler HM, et al. ASCO Meeting 2015. J Clin Oncol 33, 2015 (suppl; abstr LBA5002)

ADJUVANT TRIAL – RTOG 0521



NRG ONCOLOGY™

Sandler HM, et al. ASCO Meeting 2015. J Clin Oncol 33, 2015 (suppl; abstr LBA5002)

ADJUVANT TRIAL – RTOG 0521

Cause of Death*

	AS+RT (n=59)	AS+RT+CT (n=43)
Death due to cancer under study	23	16
Death due to protocol treatment	0	2
Death due to other cause	24	16
Death due to second primary	12	5
Unknown cause of death	0	4

*Based on central review blinded to treatment arm

NRG ONCOLOGY™

Sandler HM, et al. ASCO Meeting 2015. J Clin Oncol 33, 2015 (suppl; abstr LBA5002)

Addition of docetaxel, zoledronic acid, or both to first-line long-term hormone therapy in prostate cancer (STAMPEDE): survival results from an adaptive, multiarm, multistage, platform randomised controlled trial

*Nicholas D James, Matthew R Sydes, Noel W Clarke, Malcolm D Mason, David P Dearnaley, Melissa R Spears, Alastair W S Ritchie, Christopher C Parker, J Martin Russell, Gerhardt Attard, Johann de Bono, William Cross, Rob J Jones, George Thalmann, Claire Amos, David Matheson, Robin Millman, Mymoona Alzouebi, Sharon Beesley, Alison J Birtle, Susannah Brock, Richard Cathomas, Prabir Chakraborti, Simon Chowdhury, Audrey Cook, Tony Elliott, Joanna Gale, Stephanie Gibbs, John D Graham, John Hetherington, Robert Hughes, Robert Laing, Fiona McKinna, Duncan B McLaren, Joe M O'Sullivan, Omi Parikh, Clive Peedell, Andrew Protheroe, Angus J Robinson, Narayanan Srihari, Rajaguru Srinivasan, John Staffurth, Santhanam Sundar, Shaun Tolan, David Tsang, John Wagstaff, Mahesh K B Parmar, for the STAMPEDE investigators**

James ND, et al. Lancet 2016;387:1163-77

ecco

Inclusion criteria

Newly-diagnosed

Any of:

- Metastatic
- Node-Positive
- ≥2 of: Stage T3/4
  PSA≥40ng/ml
  Gleason 8-10

Relapsing after previous RP or RT with ≥1 of:

- PSA ≥4ng/ml and rising with doubling time <6m
- PSA ≥20ng/ml
- Node-positive
- Metastatic

All patients

Fit for all protocol treatment

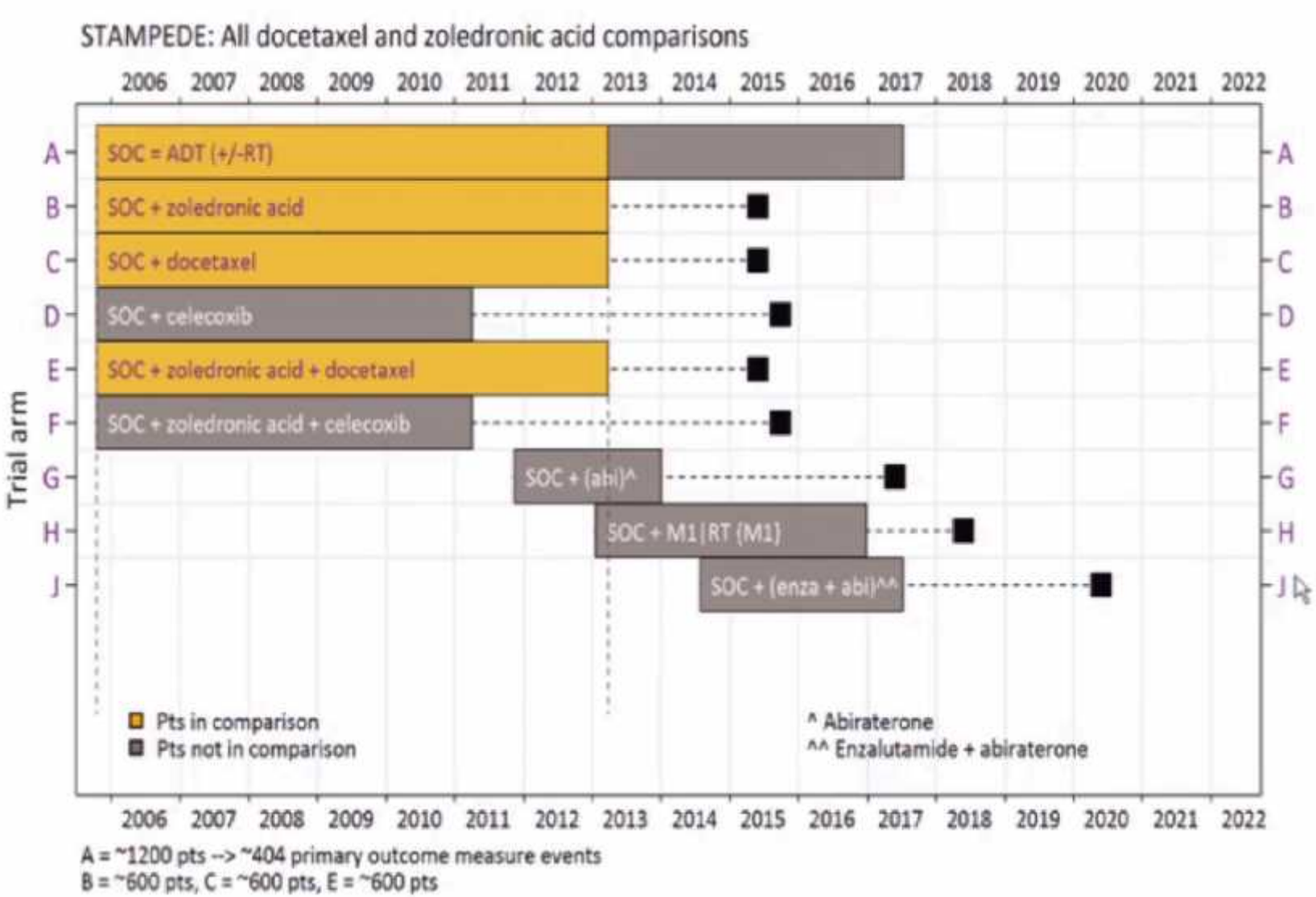
Fit for follow-up

WHO performance status 0-2

Written informed consent

Full criteria

www.stampedetrial.org



James ND, et al. Lancet 2016;387:1163-77

STAMPEDE TRIAL

1%	WHO PS 2	[s]
21%	WHO PS 1	[s]
65yr	Median age (min 40, max 84)	[s]
61%	Metastatic (85% Bony mets)	[s]
15%	N+M0	
24%	N0M0	
98%	LHRH analogues	[s]
29%	Planned for RT (72% of N0M0 pts)	[s]
6%	Previous local therapy	

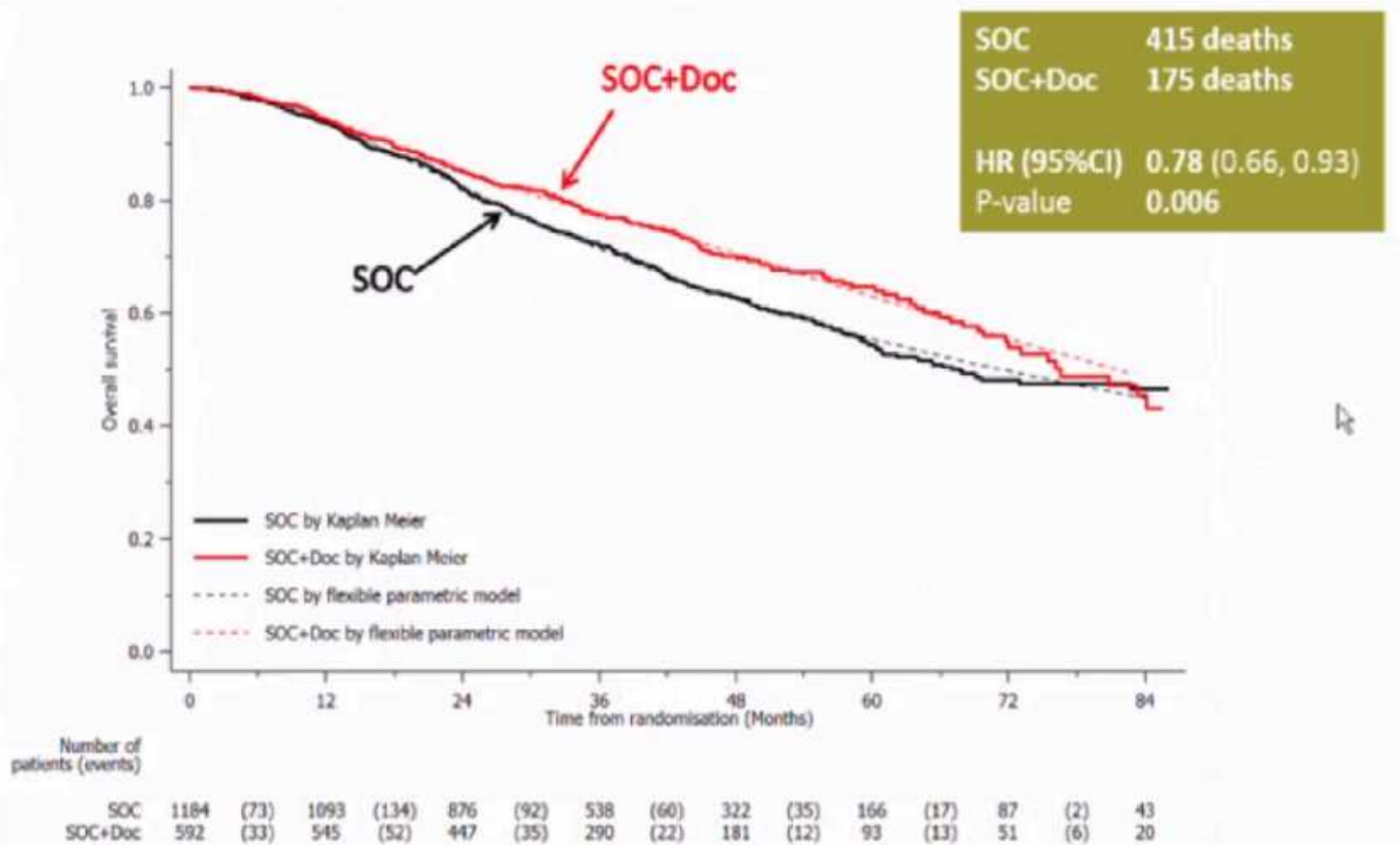
Balanced by arm
[s] Stratification factors + hospital + NSAID/aspirin

Comparison
Open: Oct-2005
Closed: Mar-2013
Accrual: 2962

Number of patients
1184 **A** Standard-of-care (SOC)
593 **B** SOC + zoledronic acid
592 **C** SOC + docetaxel
593 **E** SOC + zoledronic acid + docetaxel

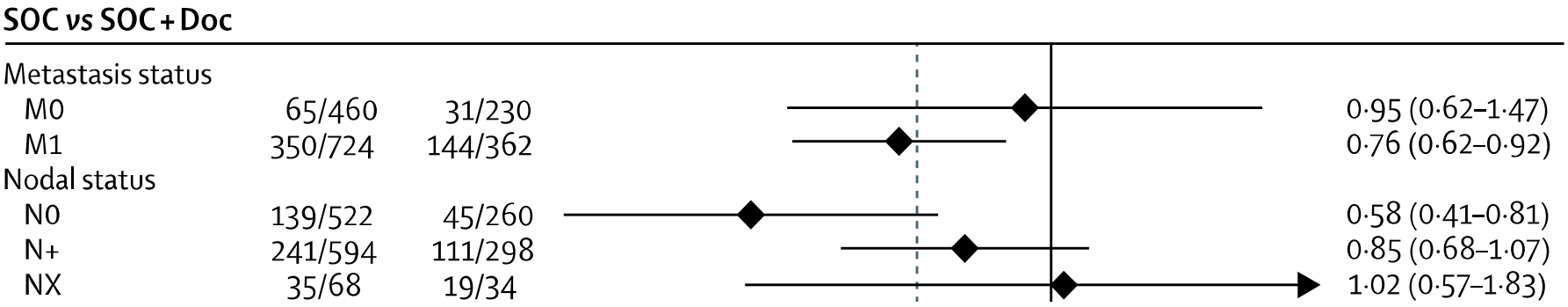
James ND, et al. Lancet 2016;387:1163-77

STAMPEDE – DOCETAXEL OVERALL SURVIVAL



James ND, et al. Lancet 2016;387:1163-77

STAMPEDE non M1 – DOCETAXEL SURVIVAL

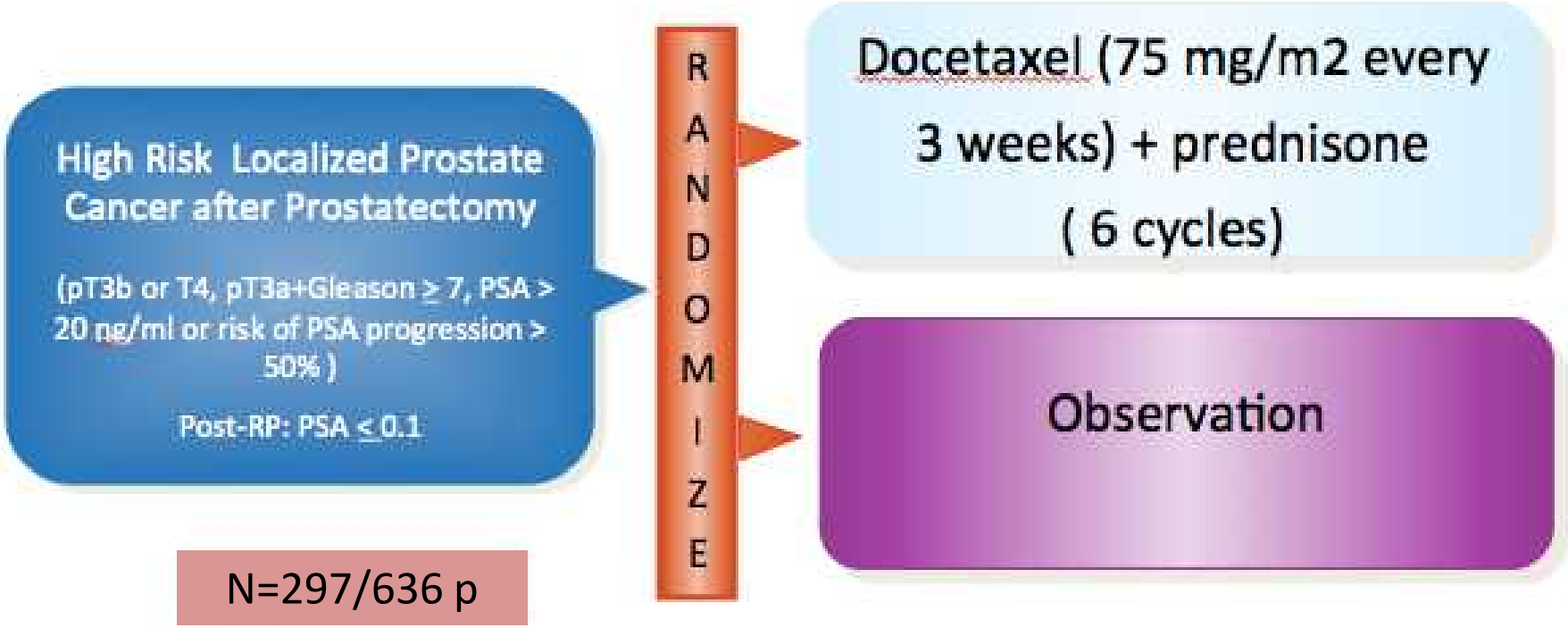


FAILURE-FREE SURVIVAL BY SUBGROUPS

	Hazard ratio	95% CI	P
Non M1	0.60	0.45-0.80	0.283×10^{-3}
M1	0.61	0.53-0.71	0.283×10^{-10}

James ND, et al. Lancet 2016;387:1163-77

ADJUVANT PHASE III VETERANS AFFAIRS CSP 553



Primary Endpoint: Progression-free survival

ClinicalTrials.gov identifier: NCT00132301

Lin D, et al. 111th AUA Meeting. Abstract PI LBA 06

Plenary I - Tuesday

Plenary

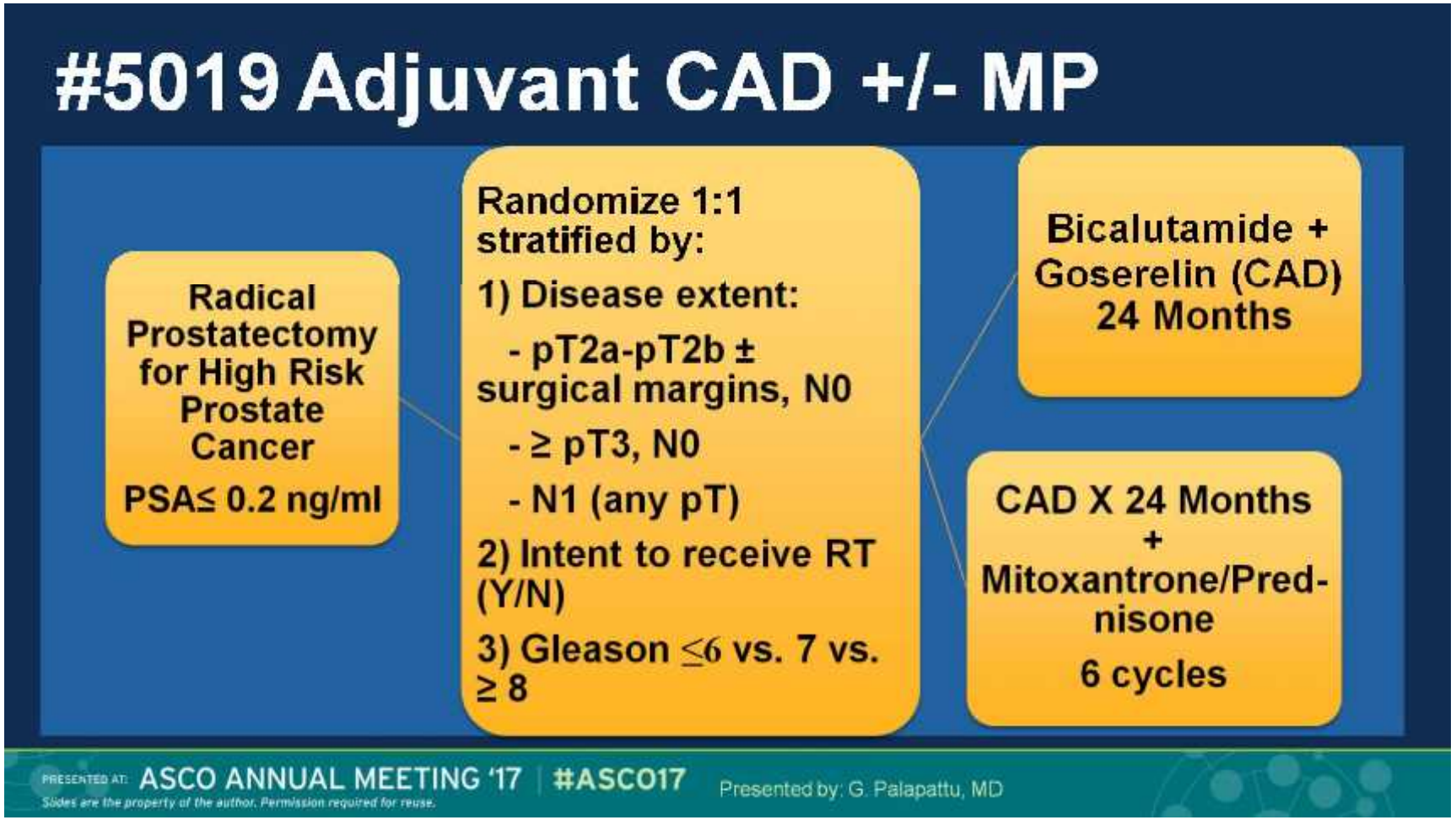
Tuesday, May 10, 2016 **7:30 AM-4:00 PM**

PI-LBA06
VA CSP#553 CHEMOTHERAPY AFTER PROSTATECTOMY (CAP) FOR HIGH RISK PROSTATE CARCINOMA: A PHASE III RANDOMIZED STUDY

RESULTS: A total of 297 patients randomized between July 2006 and October 2011 were included in the analysis (157 randomized to SOC and 140 to chemotherapy). The median follow-up was 62.4 months (range 0.2 to 104.3 months). For the primary endpoint, the two groups did not statistically differ in progression-free survival (median time to progression 55.5 months in chemotherapy group, 45.6 months in SOC group; logrank test p=0.26; adjusted hazard ratio (HR) 0.82; 95% confidence interval (CI) 0.60-1.14). Subgroup analyses showed benefit in progression-free survival for patients with tumor stage ≥T3b (HR 0.58, 95% CI 0.34-0.98, logrank test p=0.041) and for African Americans (HR 0.54, 95% CI 0.29-1.01, p=0.054). The secondary endpoint analyses are hampered by low event rates for all secondary endpoints. The most common adverse events ≥Grade 3 related or possibly related to chemotherapy included neutropenia in 40%, hyperglycemia in 18%, and fatigue in 5%, with febrile neutropenia in 1.4%.

Lin D, et al. 111th AUA Meeting. Abstract PI LBA 06

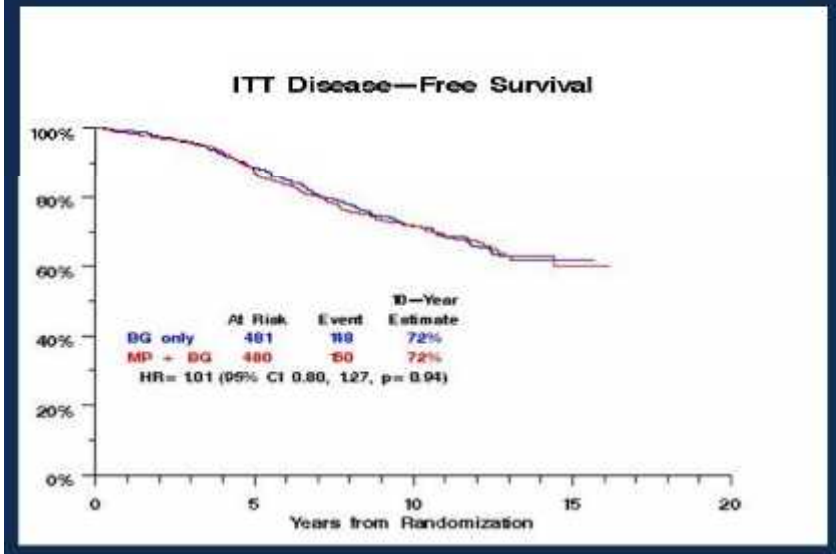
ADJUVANT PHASE III INTERGROUP S9921

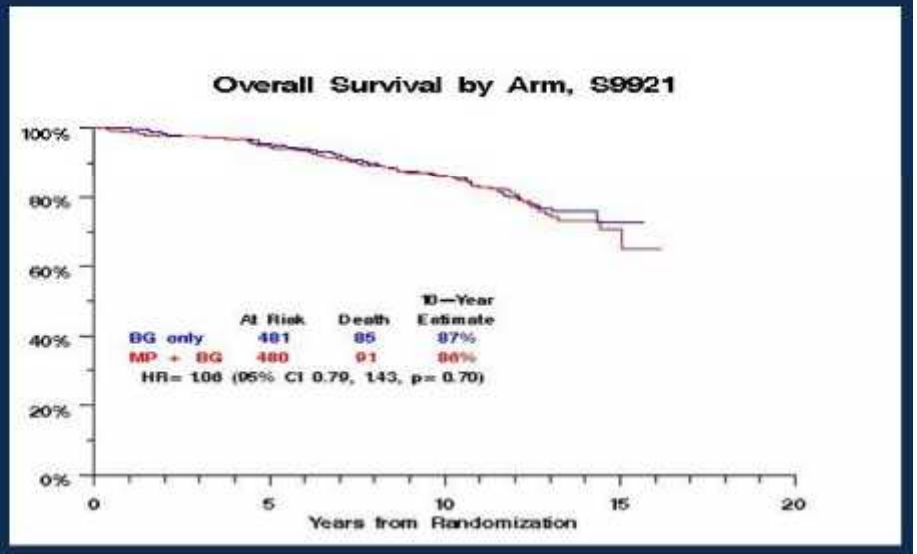


Hussain M, et al. 2017 ASCO Meeting. J Clin Oncol 35, 2017 (suppl; abstr 5019)

ADJUVANT PHASE III INTERGROUP S9921

#5019 Adjuvant CAD +/- MP





PRESENTED AT: ASCO ANNUAL MEETING '17 | #ASCO17 Presented by:

Hussain M, et al. 2017 ASCO Meeting. J Clin Oncol 35, 2017 (suppl; abstr 5019)

ADJUVANT PHASE III INTERGROUP S9921

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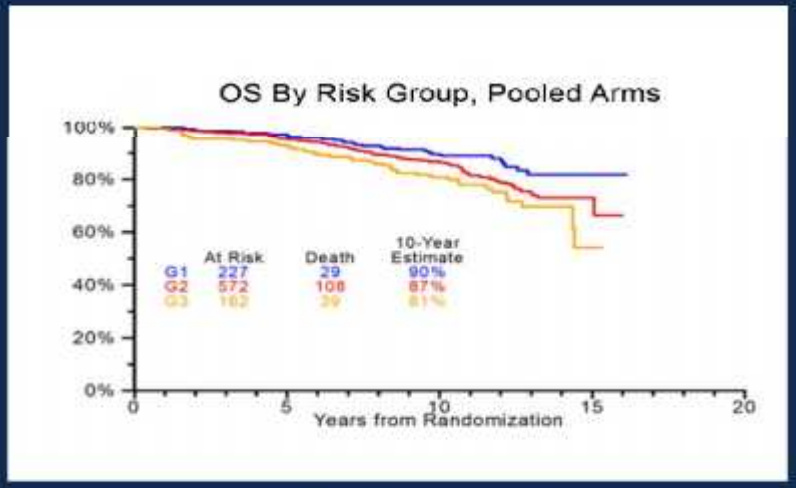
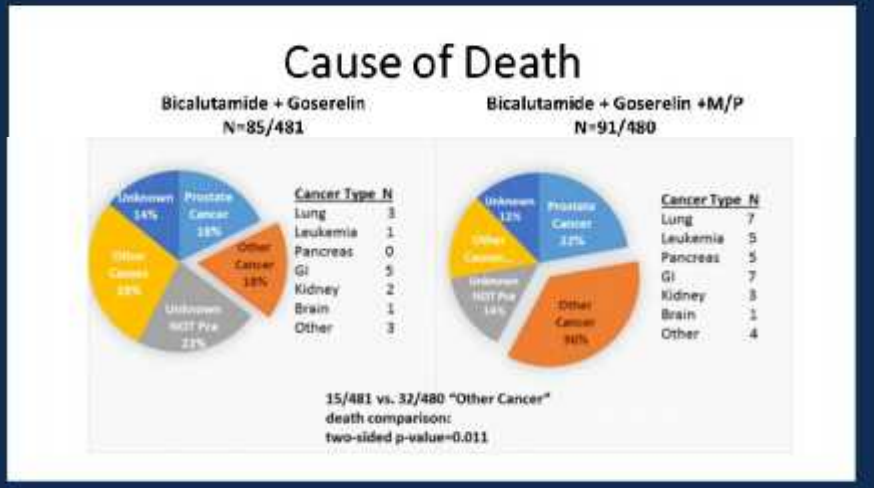




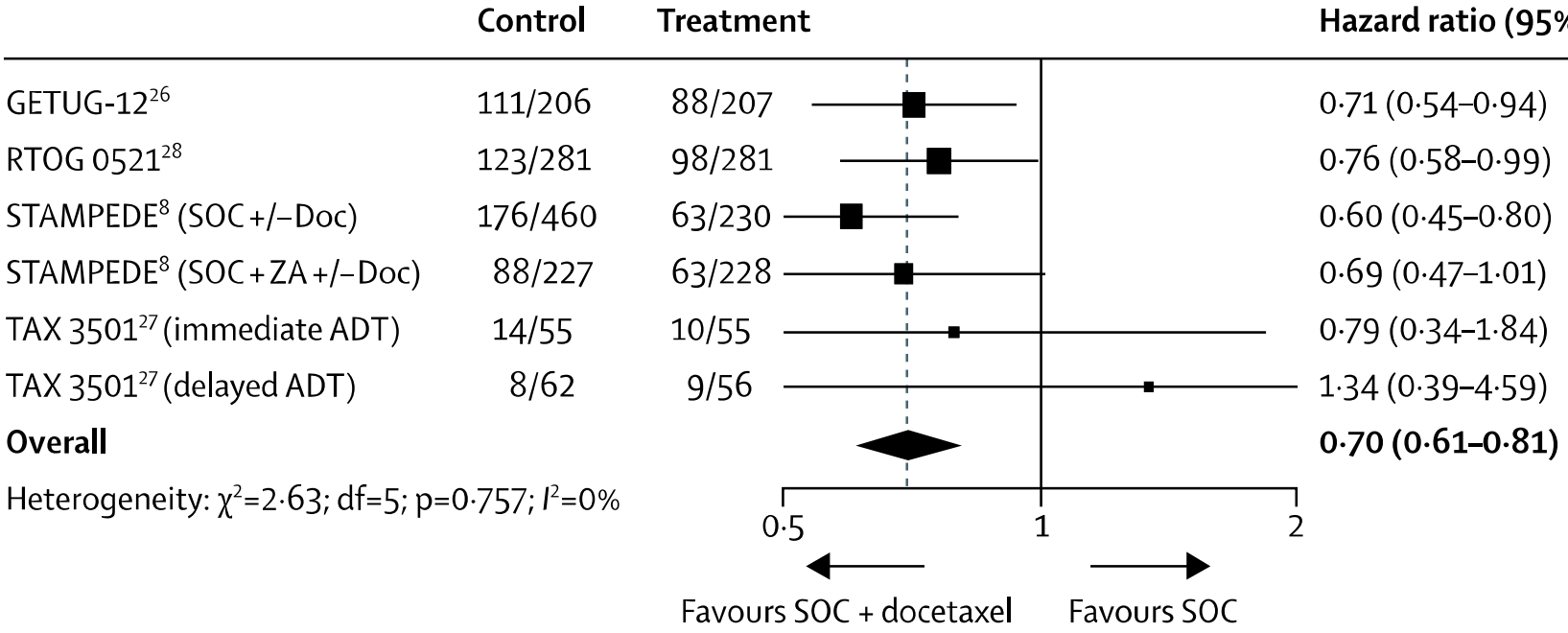
Group 1: GS 7 + positive margin or PSA > 10 or other risk factors
Group 2: GS ≥8 or T3a/b, N0
Group 3: N1

PRESENTED AT: ASCO ANNUAL MEETING '17 | #ASCO17 Presented by: G. Palapattu, MD

Hussain M, et al. 2017 ASCO Meeting. J Clin Oncol 35, 2017 (suppl; abstr 5019)

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*



Vale CL, et al. Lancet Oncol 2016;17(2):e46

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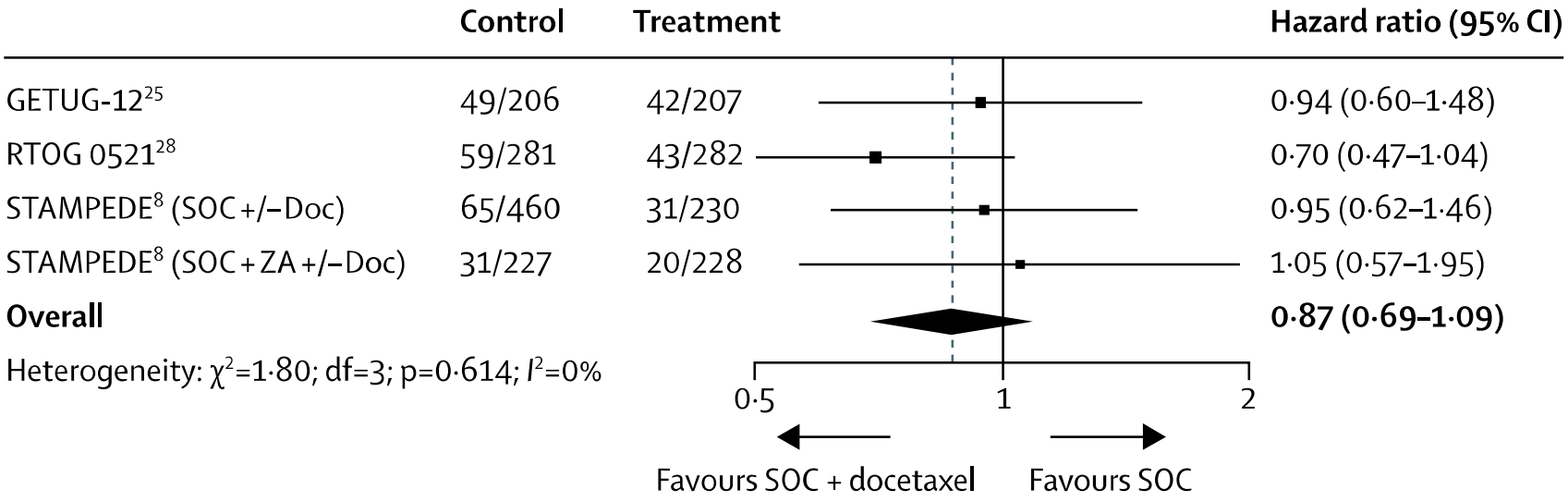


Vale CL, et al. Lancet Oncol 2016;17(2):e46

CONCOMITANT QRT-SOGUG TRIAL

Adenocarcinoma de próstata
T3N0M0 (Gleason 8,9,10)
T4N0M0
TxN1M0
PSA >20 ng/ml

N= 134

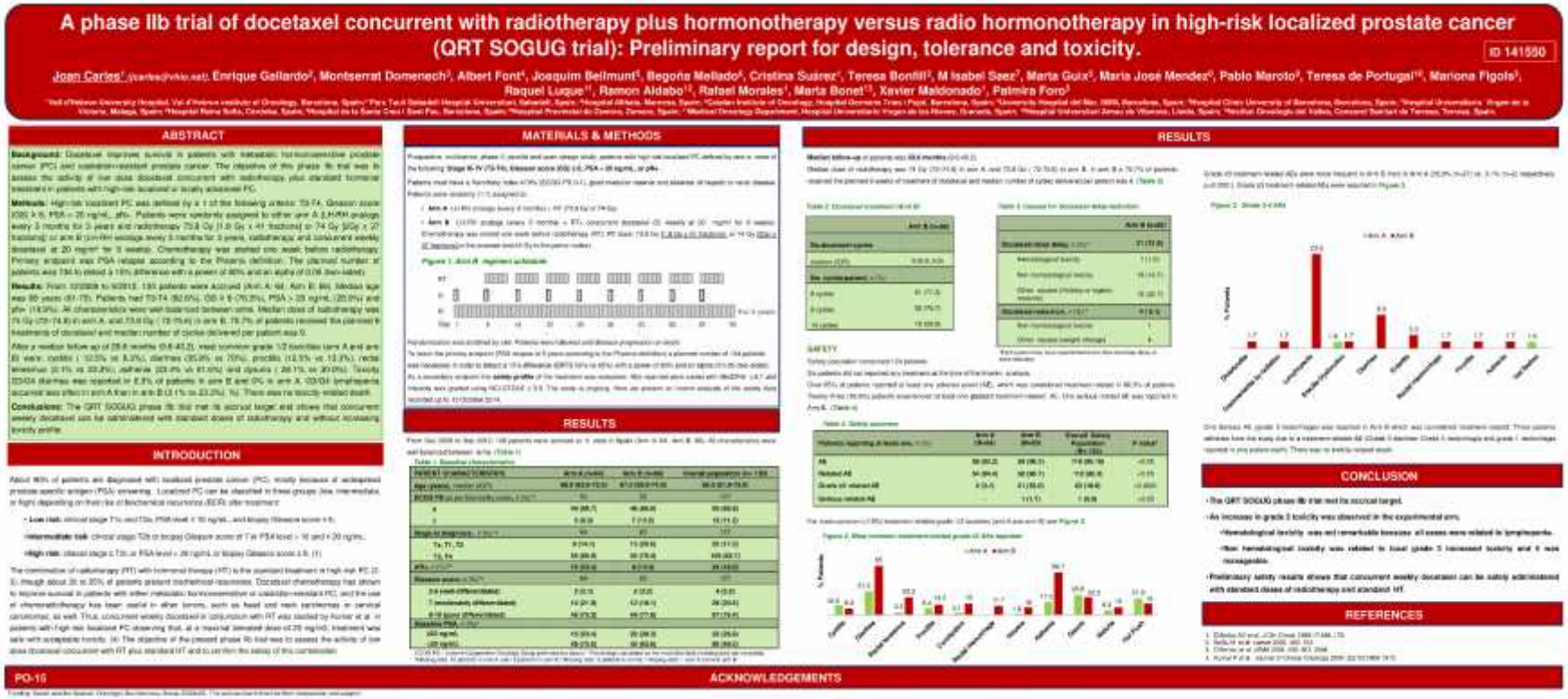
RT + HT + QT
Dosis 73.8 Gy (1.8 Gy)
Hormonas 3 años LHRH
Docetaxel 20 mg/m^2 s -1 a +8

RADIOTERAPIA + HT
Dosis 73.8 Gy (1.8 Gy)
Hormonas 3 años LHRH

IX REUNIÓN NACIONAL: CÁNCER DE PRÓSTATA, CÁNCER RENAL Y CÁNCER DE VEJIGA

GUADALAJARA 2017

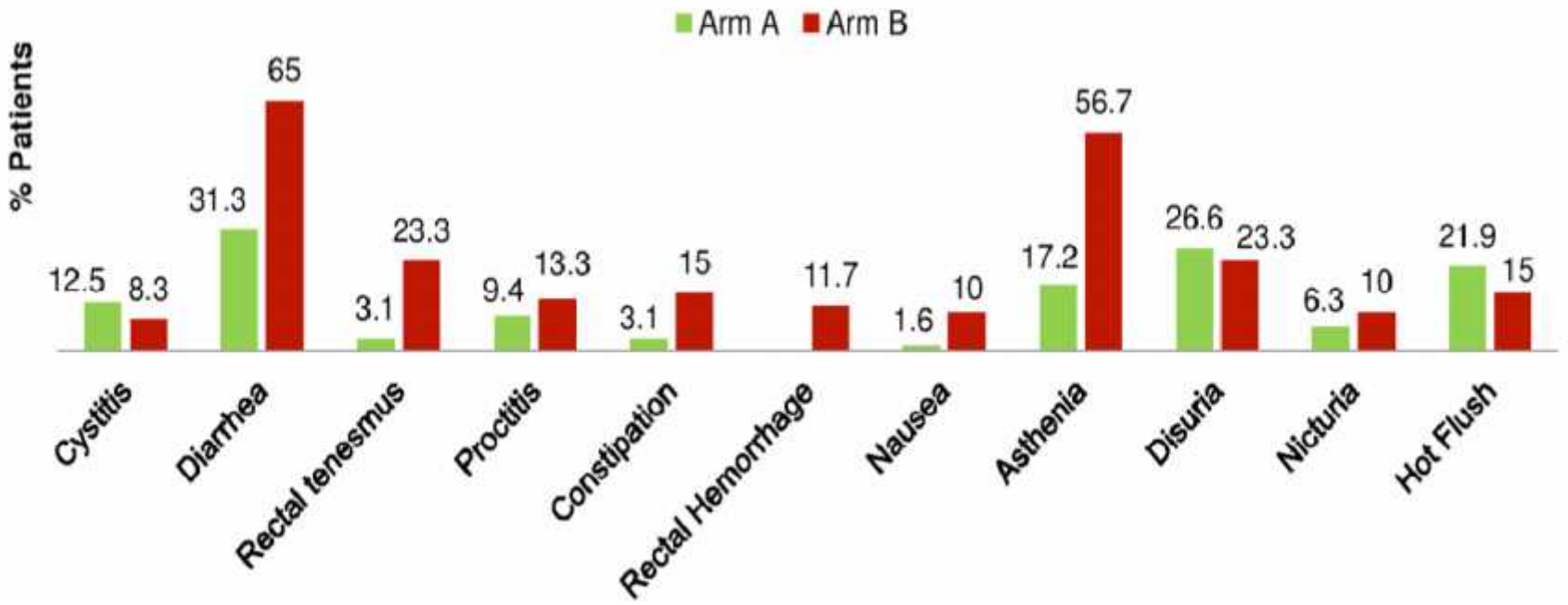
A PHASE IIB TRIAL OF DOCETAXEL CONCURRENT WITH RADIOTHERAPY PLUS HORMOTHERAPY VERSUS RADIO HORMONOTHERAPY IN HIGH-RISK LOCALIZED PROSTATE CANCER (QRT SOGUG TRIAL): PRELIMINARY REPORT FOR DESIGN, TOLERANCE, AND TOXICITY



Carles J, et al. J Clin Oncol 2015;33 (suppl 7; abstr 15)

A PHASE IIB TRIAL OF DOCETAXEL CONCURRENT WITH RADIOTHERAPY PLUS HORMOTHERAPY VERSUS RADIO HORMONOTHERAPY IN HIGH-RISK LOCALIZED PROSTATE CANCER (QRT SOGUG TRIAL): PRELIMINARY REPORT FOR DESIGN, TOLERANCE, AND TOXICITY

Figure 2. Most common treatment-related grade ≤2 AEs reported



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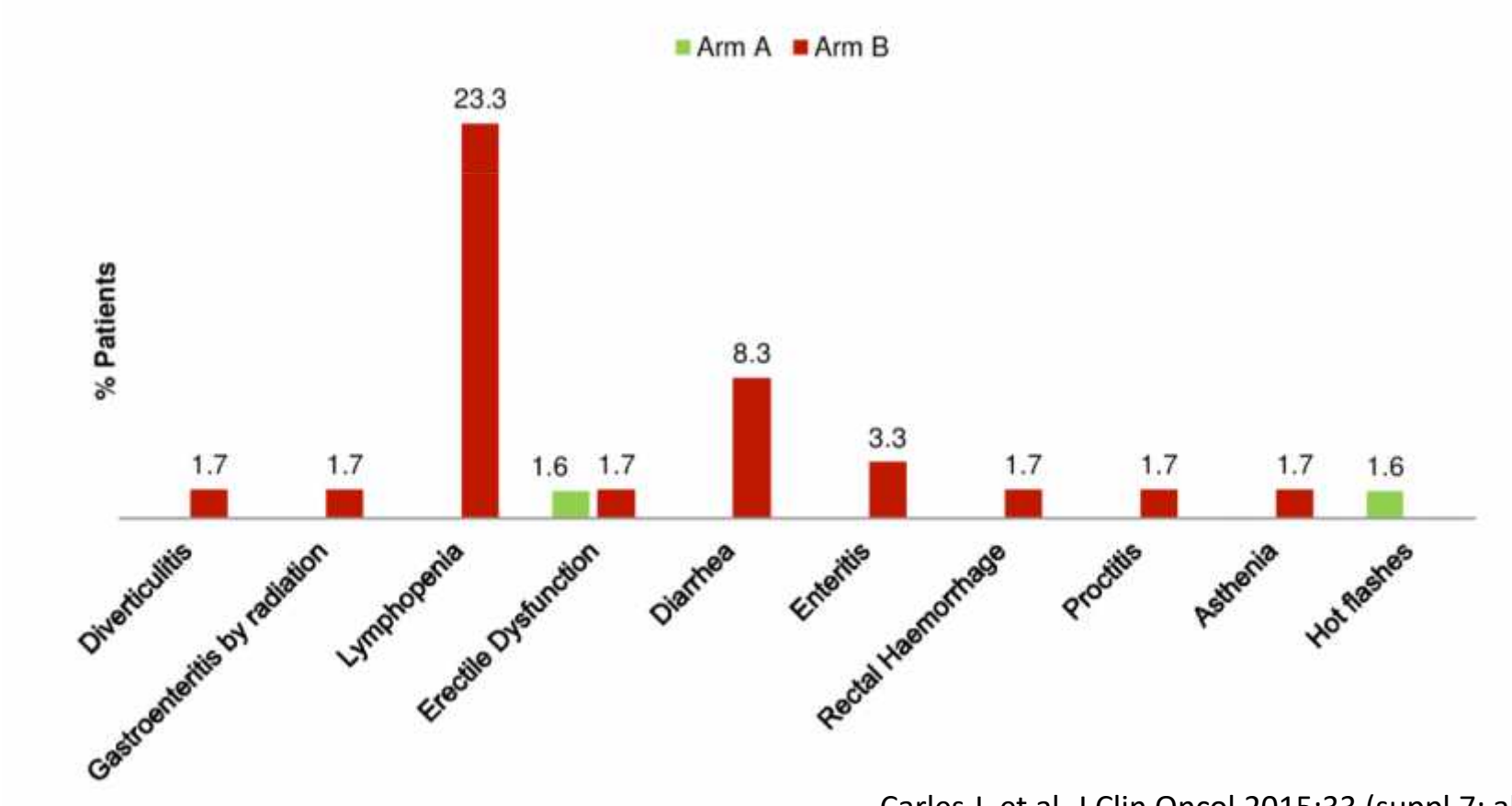
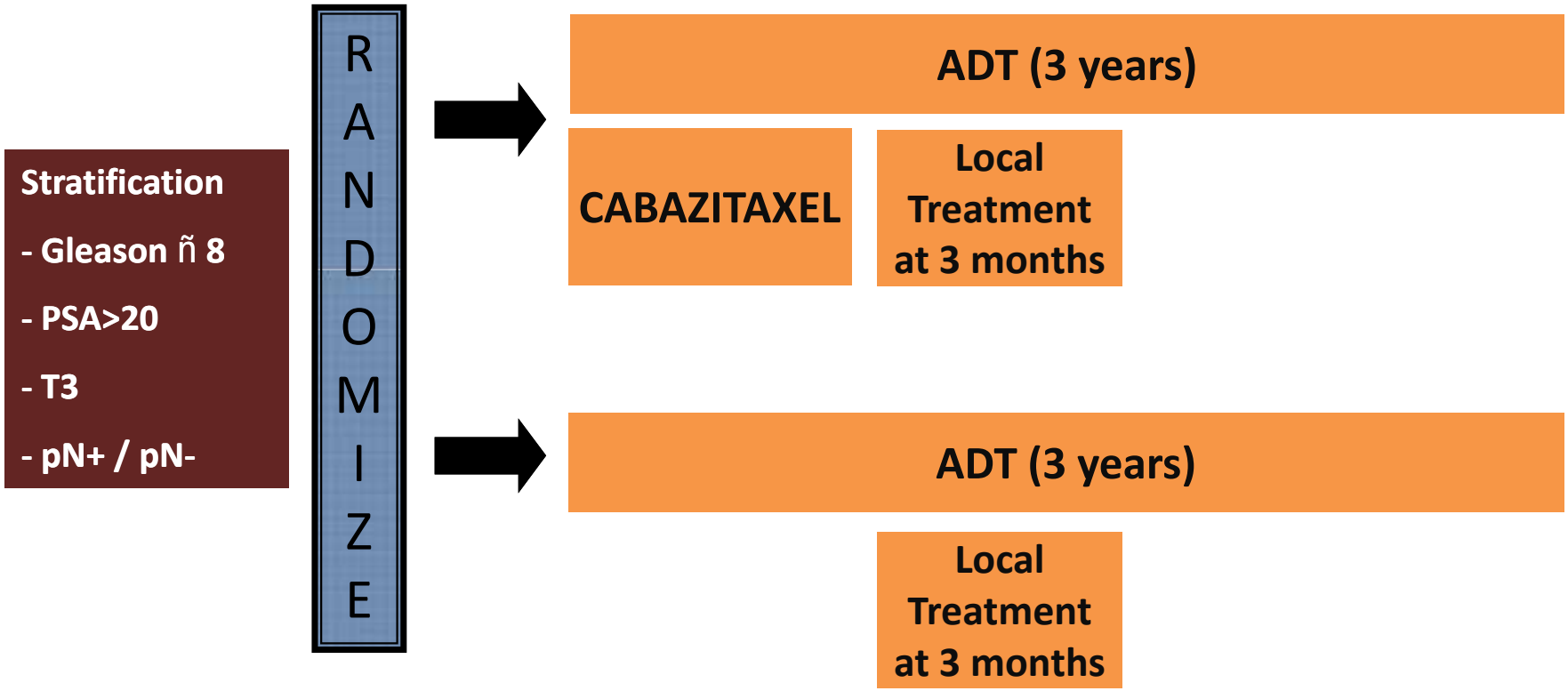


Carles J, et al. J Clin Oncol 2015;33 (suppl 7; abstr 15)

PEACE 2 TRIAL



Primary endpoint: Clinical PFS
N (estimated): 1048 patients

*ClinicalTrials.gov identifier: NCT01952223

TABLE 4. Barriers to Completing Postoperative Adjuvant Prostate Cancer Trials

- Long follow-up time needed for completion
- Lack of validated early endpoints
- Confounding relationship between testosterone and PSA in trials using PSA-based endpoints
- Lack of consensus regarding what constitutes high-risk disease
- New standards that may compete for enrollment
- Required long-term monetary support

Schweizer MT, et al. Cancer 2013;119:3610-8 . Cancer 2013;119:3610-8

OPTIMIZACIÓN DE ESTRATEGIAS

- Redefinición del "*alto riesgo*".
- Definición de objetivos clínicamente relevantes.
- Conocimiento de mecanismos de resistencia.
- Identificación de marcadores.
- Incorporación de nuevas estrategias terapéuticas.
- Incorporación de nuevas herramientas diagnósticas.

- 58 años, ECOG 0, no antecedentes.
- Asintomático. Tacto rectal no patológico.
- PSA 6.5 ng/mL.
- Biopsia prostática:
- 1.- Próstata, lóbulo derecho. Biopsia tru-cut:
  - ADENOCARCINOMA POBREMENTE DIFERENCIADO, GLEASON COMBINADO 4+4= (8/10), CON PRESENCIA DE CÉLULAS EN ANILLO DE SELLO, CON INFILTRACIÓN PERINEURAL, CON AFECTACIÓN DE UN 100% Y 75% DE DOS DE CUATRO CILINDROS.

  2.- Próstata, lóbulo izquierdo. Biopsia tru-cut:
  - SIN EVIDENCIA DE INFILTRACIÓN TUMORAL.

- RM prostática/abdominal: T2-T3a(minor) N0.
- Whole-body MRI: Sin evidencia de metástasis óseas.

- Prostatectomía radical + Linfadenectomía por vía laparoscópica (6/11/2015)

Patología:

- ADENOCARCINOMA ACINAR PROSTÁTICO POBREMENTE DIFERENCIADO, GLEASON COMBINADO 4 + 5: 9/10 CON PRESENCIA DE CÉLULAS EN ANILLO DE SELLO, QUE AFECTA A AMBOS LÓBULOS Y QUE PRESENTA MARCADA EXTENSIÓN EXTRAPROSTÁTICA A NIVEL DEL CUADRANTE POSTERIOR DERECHO.
- LA TUMORACIÓN SE ENCUENTRA EXTENSAMENTE CON CONTINUIDAD CON MARGEN POSTERIOR DE CUADRANTE POSTERIOR DERECHO.
- MARCADA INVASIÓN NEOPLÁSICA PERINEURAL.
- INFILTRACIÓN NEOPLÁSICA FOCAL DE VESÍCULA SEMINAL DERECHA.
- GANGLIOS LINFÁTICOS ILIOBTURADORES DERECHOS (18), SIN EVIDENCIA DE METÁSTASIS.
- GANGLIOS LINFÁTICOS ILIOBTURADORES IZQUIERDOS (12), SIN EVIDENCIA DE METÁSTASIS.
- GANGLIOS LINFÁTICOS PRESACROS (4), SIN EVIDENCIA DE METÁSTASIS.
- pT3b N0.

SUMARIO DOCETAXEL + ADT

- GETUG 12 neoadyuvante a PR: Positivo para RFS.
- RTOG 0521 adyuvante a RT: Beneficio de OS?
- STAMPEDE, junto a RT: Beneficio en RFS. OS, *too early*.
- VA CSP#553 adyuvante a PR: Beneficio en PFS en subgrupos de mayor riesgo?
- Metaanálisis: Beneficio en FFS.

How important is DFS (or RFS or FFS) as an endpoint?

1. Improvement in DFS is expected when one active treatment (docetaxel) is added to others (RT +ADT)
2. Improved DFS does not lead inevitably to improved OS – men who did not receive docetaxel might live longer after first disease progression.
3. For men with localized M0 disease, if there is no effect on overall survival....

..... then chemo delayed is toxicity delayed and is the preferred strategy.

Presented By Ian Tannock at 2015 ASCO Annual Meeting

RECOMMENDATION #2

Men with localized M0 prostate cancer who are to receive local treatment with radiotherapy should NOT be offered docetaxel in addition to ADT

This opinion might change with longer follow-up of the GETUG-12, STAMPEDE and RTOG 0521 trials

Presented By Ian Tannock at 2015 ASCO Annual Meeting

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