II SIMPÓSIO INTERNACIONAL

GU - REVIEW 2018 - LACOG

23 E 24 | NOVEMBRO 2018 | HOTEL INTERCONTINENTAL | SÃO PAULO

Doença Localizada de Alto Risco: Quando não indico radioterapia

Robson Ferrigno

Considerações

- Não há estudos prospectivos e randomizados com poder estatístico que comparem prostatectomia radical com radioterapia externa no tratamento do câncer de próstata de alto risco

- A radioterapia, quando indicada, deve ser realizada com dose escalonada (~78 Gy na próstata e vesículas seminais) associada com bloqueio hormonal de longa duração (18 a 36 meses)

- A decisão do tratamento deve levar em consideração as características do paciente e a extensão local do tumor

A Randomized Trial Comparing Radical Prostatectomy Plus Endocrine Therapy versus External Beam Radiotherapy Plus Endocrine Therapy for Locally Advanced Prostate Cancer: Results at Median Follow-up of 102 Months

Koichiro Akakura[1], Hiroyoshi Suzuki[1], Tomohiko Ichikawa[1], Hiroyuki Fujimoto[2], Osamu Maeda[3], Michiyuki Usami[3], Daisaku Hirano[4], Yukie Takimoto[4], Toshiyuki Kamoto[5], Osamu Ogawa[5], Yoshiteru Sumiyoshi[6], Jun Shimazaki[1]* ,Tadao Kakizoe[2]* and the Japanese Study Group for Locally Advanced Prostate Cancer[†]

[1]Department of Urology, School of Medicine, Chiba University, Chiba, [2]Urology Division, National Cancer Center Hospital, Tokyo, [3]Department of Urology, Osaka Medical Center for Cancer and Cardiovascular Diseases, Osaka, [4]Department of Urology, Nihon University School of Medicine, Tokyo, [5]Department of Urology, Faculty of Medicine, Kyoto University, Kyoto and [6]Shikoku Cancer Center, Matsuyama, Japan

95 T2b-3 N0 M0

→ **8 meses HT => PR => HT**

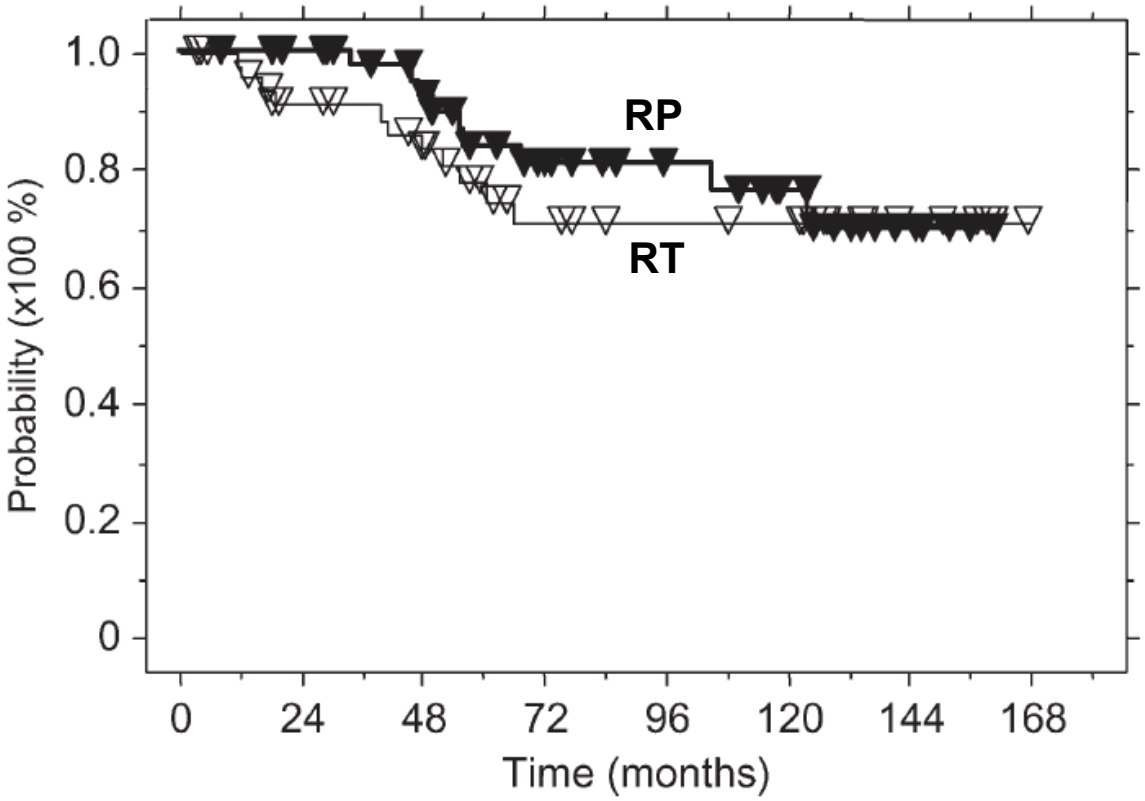
→ **8 meses HT => RT => HT**

Akakura K, et al. *Jpn J Clin Oncol* 2006

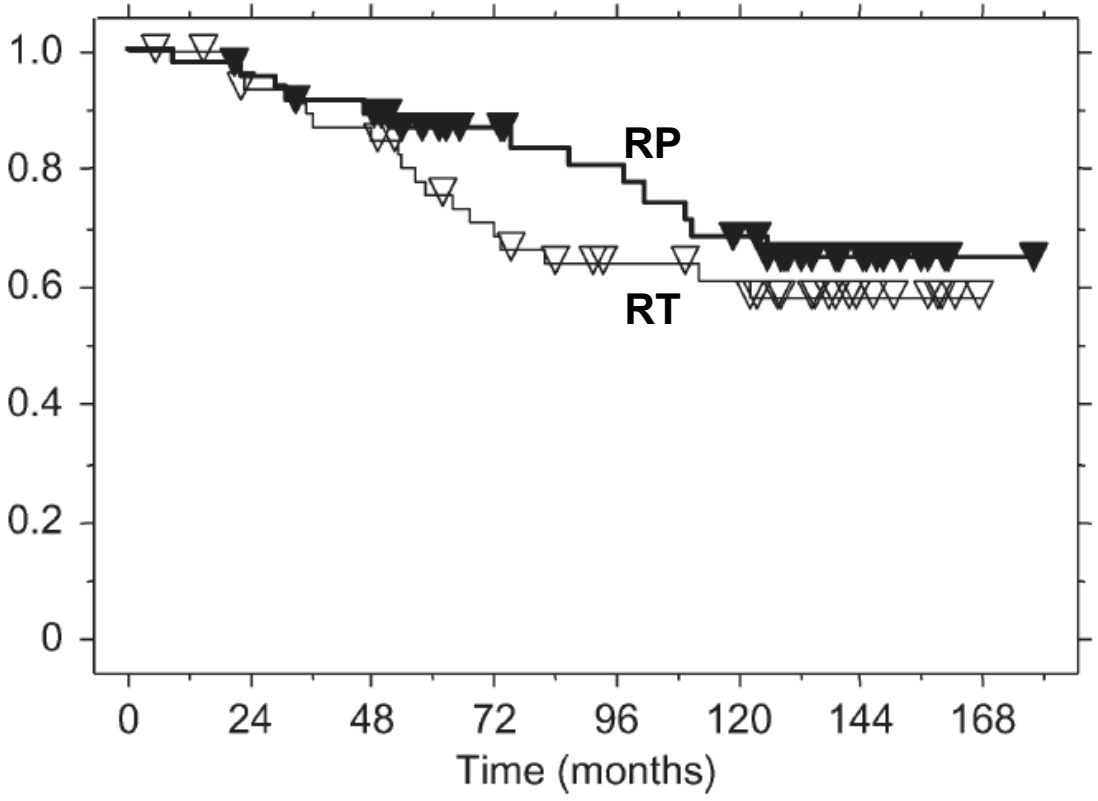
Estudo Japonês

Prostatectomia radical + HT *Vs* Radioterapia externa + HT

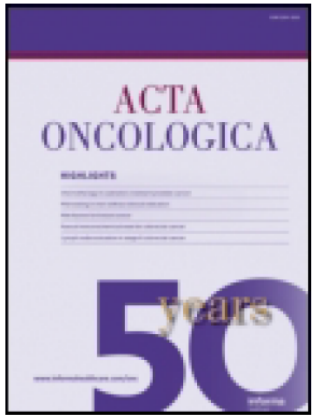
Sobrevida livre de doença



Sobrevida global



Akakura K, et al. *Jpn J Clin Oncol* 2006



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Taylor & Francis Group

Acta Oncologica

ISSN: 0284-186X (Print) 1651-226X (Online) Journal homepage: http://www.tandfonline.com/loi/ionc20

Radical prostatectomy versus high-dose irradiation in localized/locally advanced prostate cancer: A Swedish multicenter randomized trial with patient-reported outcomes

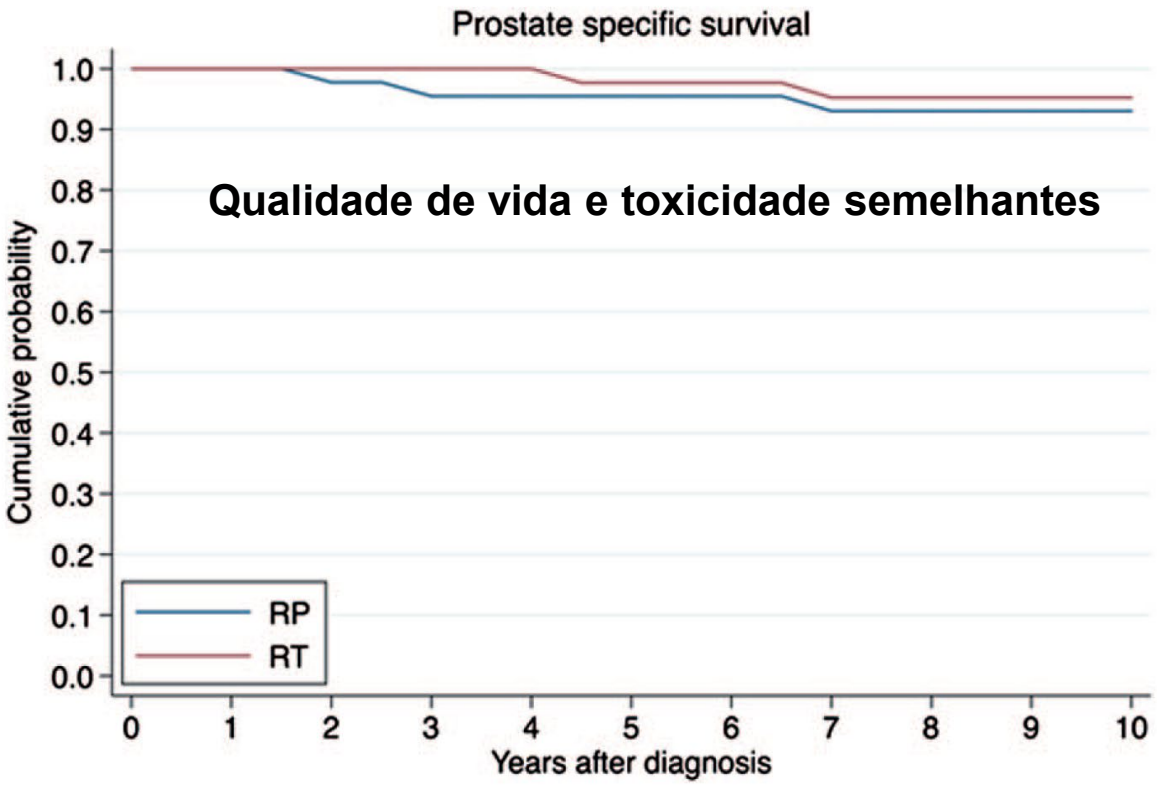
Bo Lennernäs, Khairul Majumder, Jan-Erik Damber, Per Albertsson, Erik Holmberg, Yvonne Brandberg, Ulf Isacsson, Gunilla Ljung, Ole Damm & Sten Nilsson

Lennernäs B, et al. *Acta Oncol* 2014

Estudo Sueco

Prostatectomia radical *Vs* Radioterapia externa + braquiterapia HDR

	Randomized to prostatectomy	Randomized to irradiation
T-stadium	n = 45	n = 44
	n (%)	n (%)
T1	18 (40)	17 (39)
T2	17 (38)	16 (36)
T3	4 (9)	3 (7)
Unknown	6 (13)	8 (18)
Bone scan		
Performed	27 (60)	28 (64)
Not performed	10 (22)	8 (18)
Unknown	8 (18)	8 (18)
Age		
Median	64 years	66 years



Qualidade de vida e toxicidade semelhantes

Lennernäs B, et al. *Acta Oncol* 2014

VOLUME 28 · NUMBER 9 · MARCH 20 2010

JOURNAL OF CLINICAL ONCOLOGY

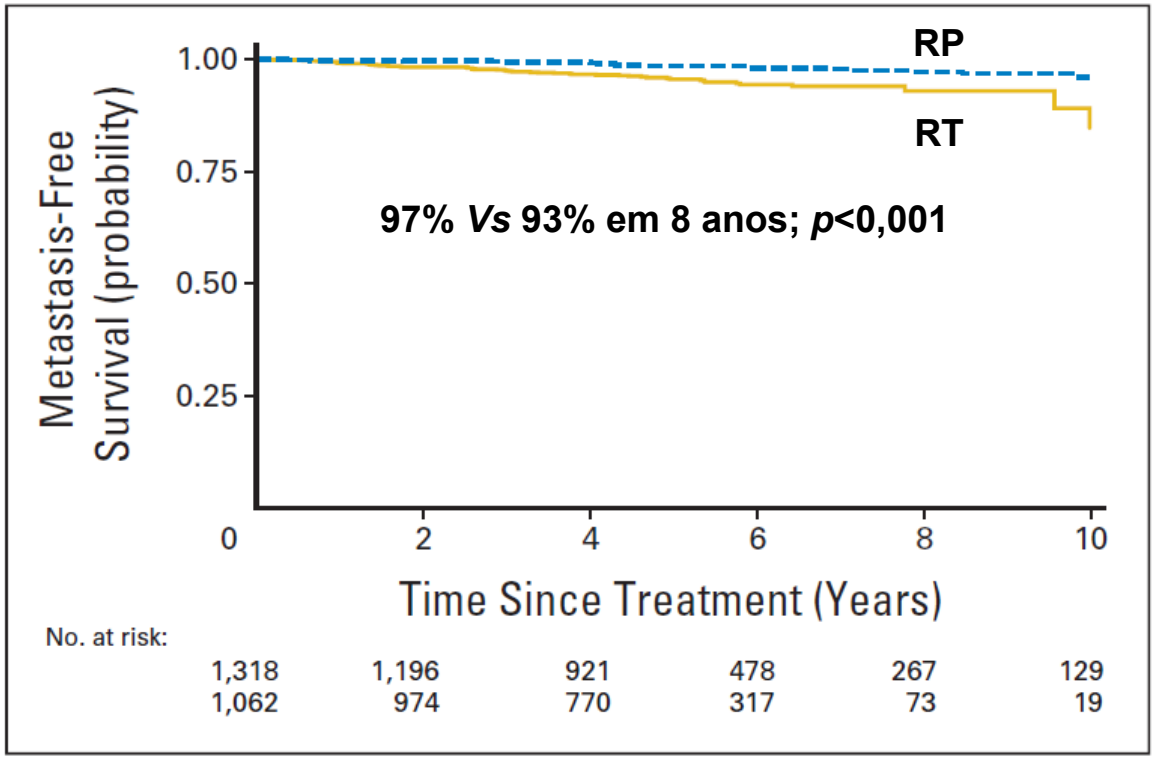
ORIGINAL REPORT

Metastasis After Radical Prostatectomy or External Beam Radiotherapy for Patients With Clinically Localized Prostate Cancer: A Comparison of Clinical Cohorts Adjusted for Case Mix

Michael J. Zelefsky, James A. Eastham, Angel M. Cronin, Zvi Fuks, Zhigang Zhang, Yoshiya Yamada, Andrew Vickers, and Peter T. Scardino

Characteristic	Surgery (n = 1,318) No.	Surgery (n = 1,318) %	Radiation (n = 1,062) No.	Radiation (n = 1,062) %
Median age at surgery, years	60		69	
Interquartile range	55-65		64-73	
Median total PSA, ng/mL	6.2		7.6	
Interquartile range	4.5-8.7		5.1-12	
Median preoperative 5-year Kattan nomogram progression-free probability	84		80	
Interquartile range	73-90		63-88	
Clinical stage				
T1c	574	44	527	50
T2a	379	29	267	25
T2b	191	14	114	11
T2c	122	9	58	5
T3a	51	4	55	5
T3b	1	0.1	41	4
Biopsy Gleason score*				
≤ 6	866	66	516	49
7	394	30	406	38
≥ 8	58	4	140	13
Year of treatment				
1993-1995	348	26	38	4
1996-1997	243	18	135	13
1998-2000	323	25	582	55
2001-2002	404	31	307	29
Positive surgical margins	155	12	NA	
Extracapsular extension	336	26	NA	
Seminal vesicle invasion	87	7	NA	
Lymph node involvement	52	4	NA	

Zelefsky M, et al. *J Clin Oncol* 2010



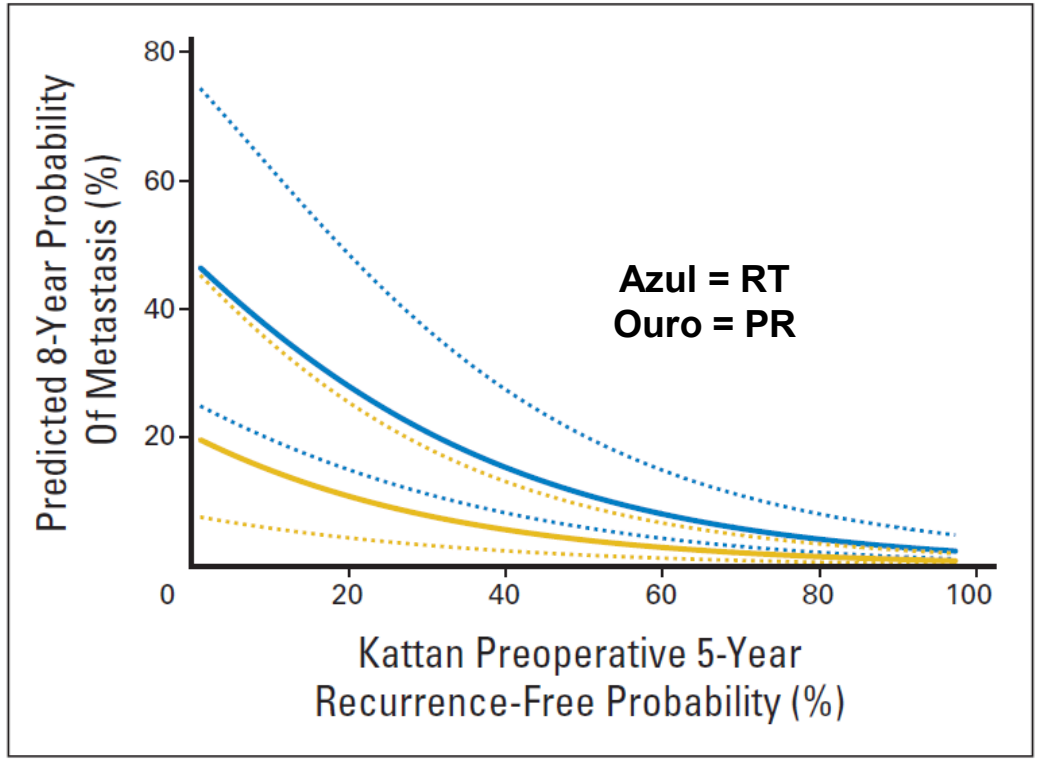


Table 3. Unadjusted Actuarial Probabilities of Prostate Cancer Death According to Treatment Group by NCCN Risk Group

			Kaplan-Meier Probability of Prostate Cancer Death							
			5 Year				8 Year			
			Radiotherapy		Surgery		Radiotherapy		Surgery	
NCCN Risk	No. of Patients	No. of Events	%	95% CI	%	95% CI	%	95% CI	%	95% CI
Low	952	1	0.0		0.0		0.0		0.0	
Intermediate	1,019	10	0.0		0.2	0.0 to 1.7	4.5	1.8 to 10.8	1.9	0.5 to 6.3
High	409	19	3.7	1.8 to 7.4	1.0	0.1 to 7.0	9.5	4.9 to 17.9	3.8	1.2 to 11.5

Abbreviation: NCCN, National Comprehensive Cancer Network.

Zelefsky M, et al. *J Clin Oncol* 2010

Associação com bloqueio hormonal

Principais estudos fase III com RT +/- HT

Estudo	N	Braços	Duração	SLD	SG
RTOG 92-02	1554	RT+HT	**28 meses**	**89%**	**54%**
	T2c- T4	RT+HT	4 meses	84%	52%
EORTC 22863	415	RT+HT	36 meses	**89,7%**	**58%**
	T1-T4	RT		69,6%	40%
EORTC 22961	970	RT+HT	**36 meses**	96,8%	**85%**
	T1c-T2b/N0-N2	RT+HT	6 meses	95,3%	81%
Canadense	630	RT+HT	36 meses	-	63,6%
	T3/T4 / PSA > 20	RT+HT	**18 meses**		63,2%

Bloqueio hormonal + RT escalonada

MRC RT01

833 pacientes

BR (19%)

RI (37%)

AR (44%)

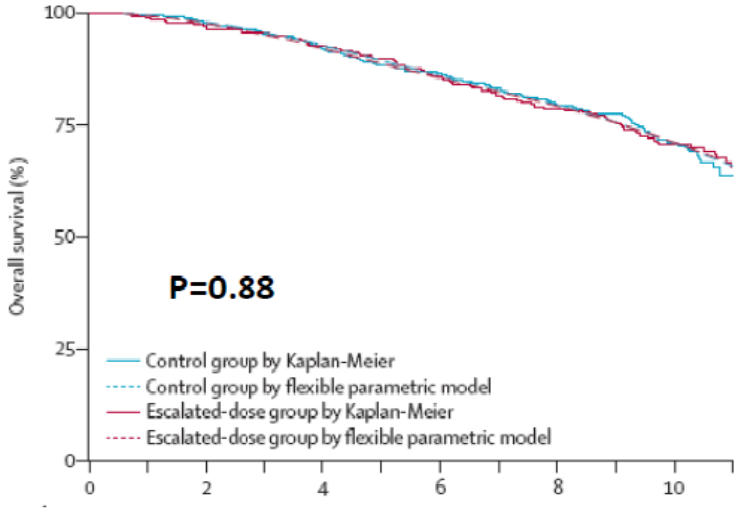
HT: 3 – 6 meses

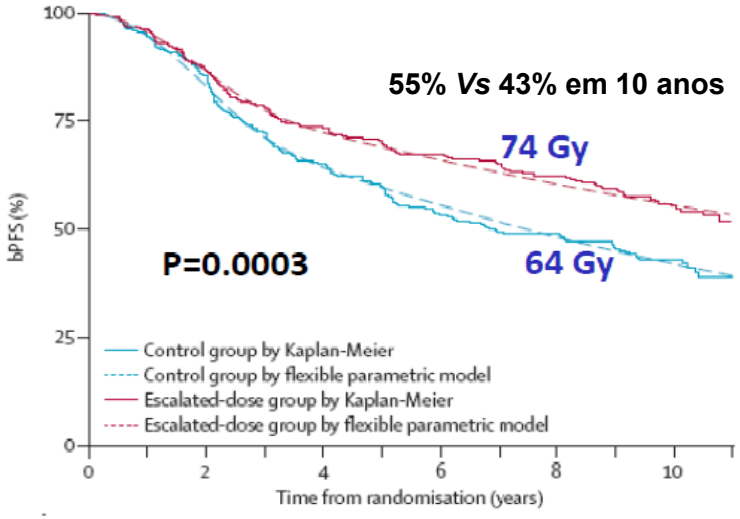
416: RT (64 Gy) + HT

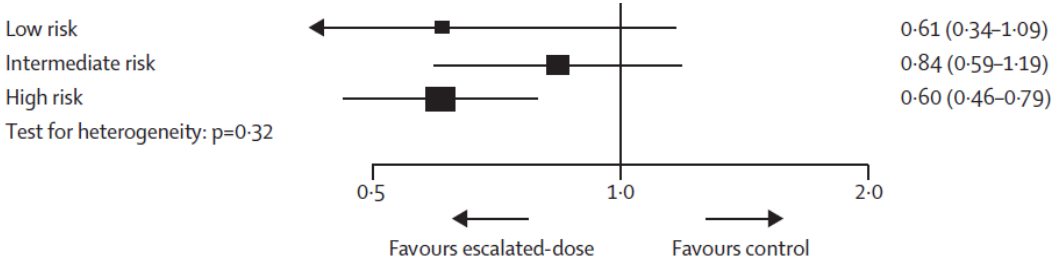
417: RT (74Gy) + HT

Dearnaley , et al. *Lancet Oncol* 2014

MRC RT01







Dearnaley , et al. *Lancet Oncol* 2014

Estudo Espanhol

355 pacientes

T1c-T3b

N0M0

Intermediário e alto

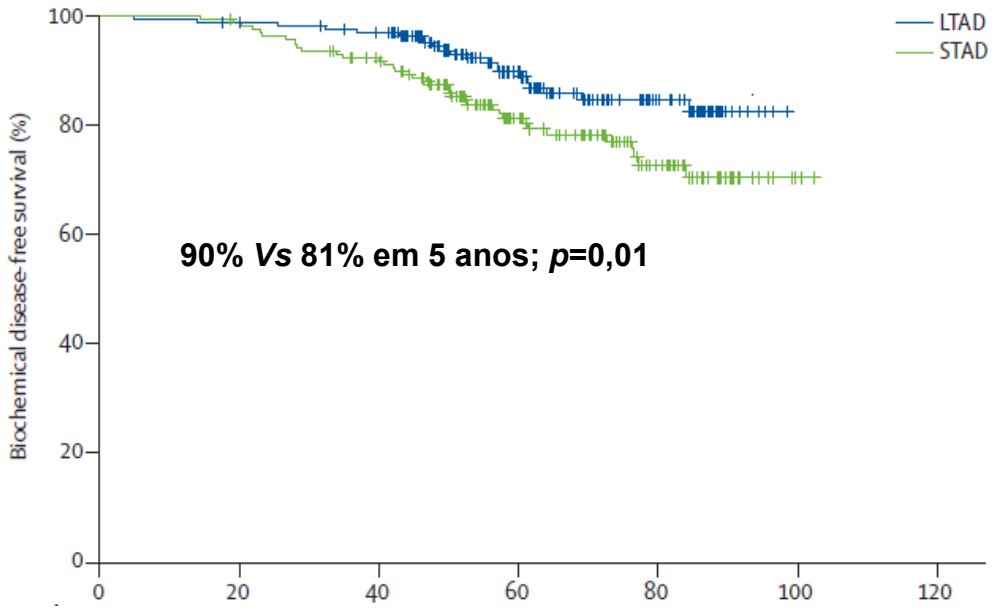
178: RT + HT (4 meses)

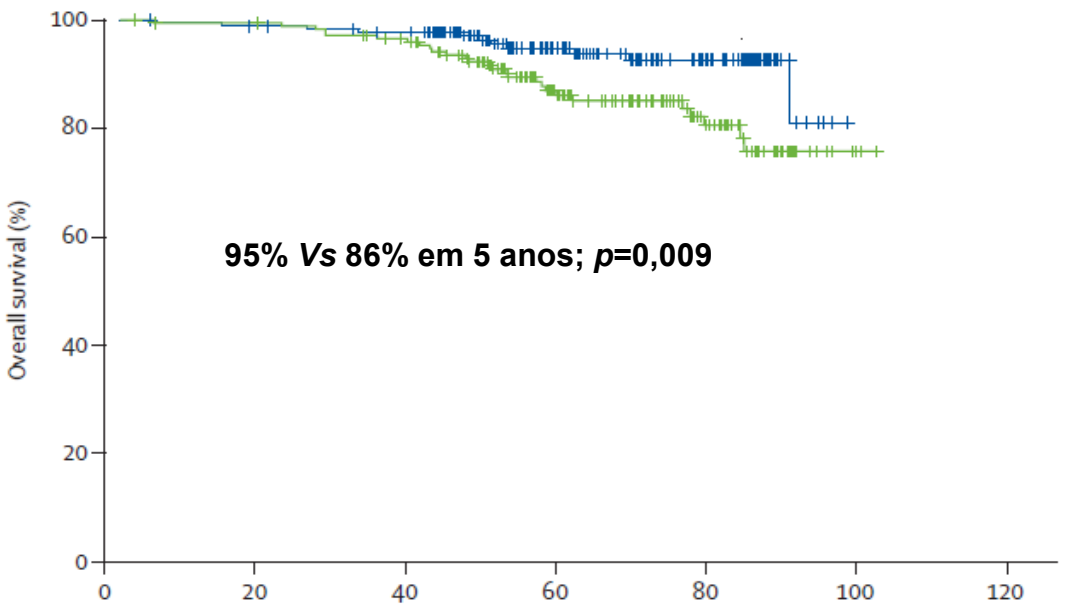
177: RT + HT (28 meses)

Dose de RT: 76 – 82 Gy

Zapatero, et al. *Lancet* 2015

Estudo Espanhol





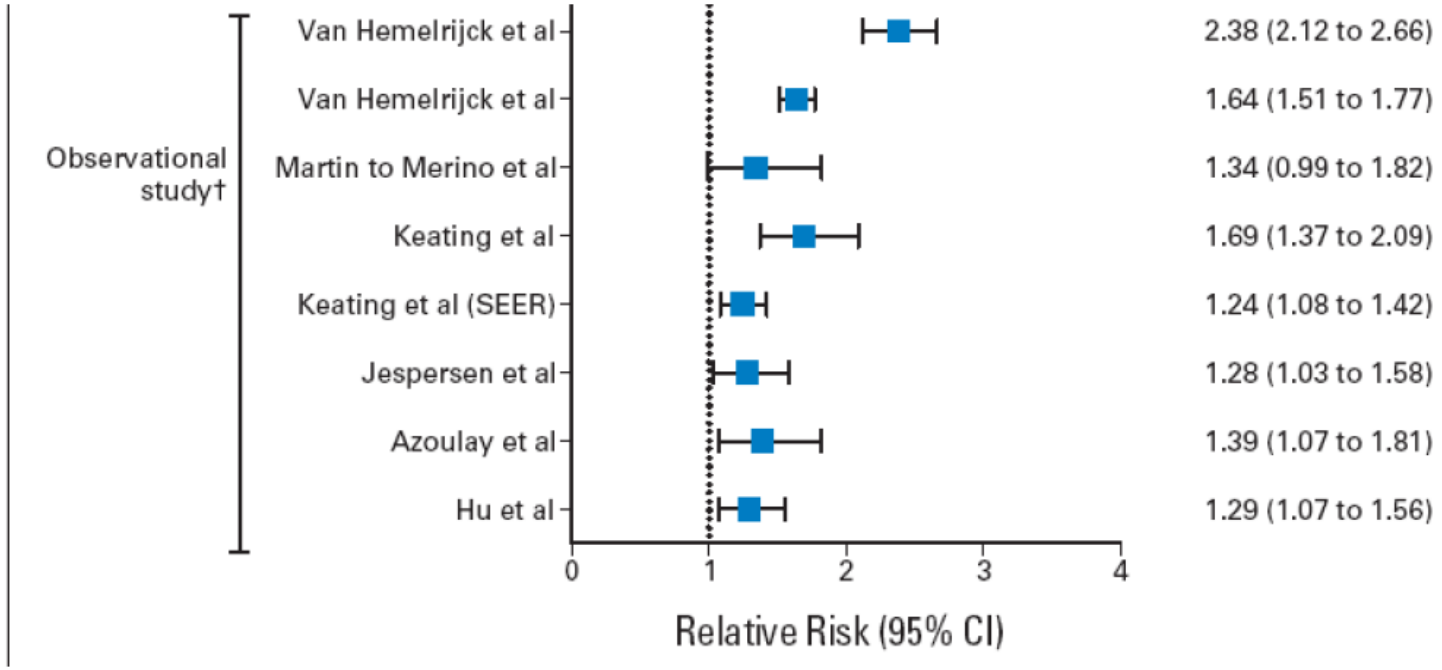
Zapatero, et al. *Lancet* 2015

VOLUME 33 · NUMBER 11 · APRIL 10 2015

JOURNAL OF CLINICAL ONCOLOGY

Risk and Timing of Cardiovascular Disease After Androgen-Deprivation Therapy in Men With Prostate Cancer

Sean O'Farrell, Hans Garmo, Lars Holmberg, Jan Adolfsson, Pär Stattin, and Mieke Van Hemelrijck



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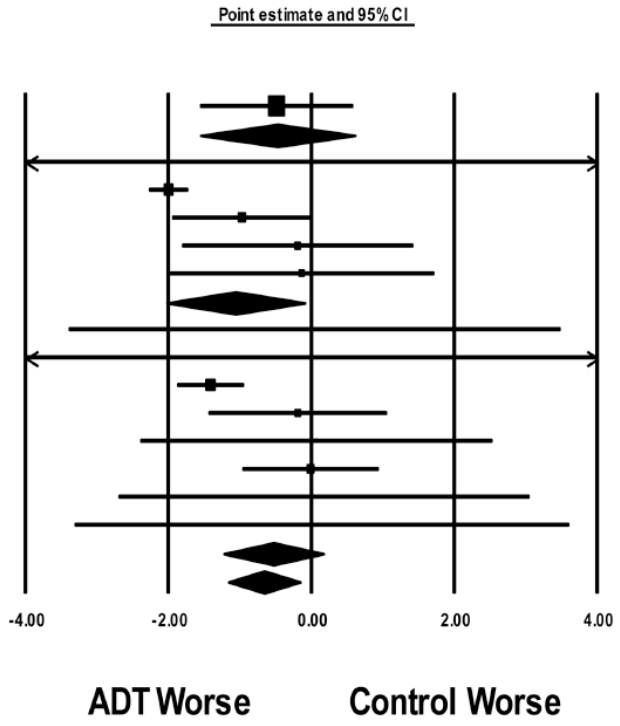
Author Manuscript
Support Care Cancer. Author manuscript; available in PMC 2015 August 01.

Published in final edited form as:
Support Care Cancer. 2014 August ; 22(8): 2271–2280. doi:10.1007/s00520-014-2285-1.

Cognitive Functioning in Men Receiving Androgen Deprivation Therapy for Prostate Cancer: A Systematic Review and Meta-Analysis



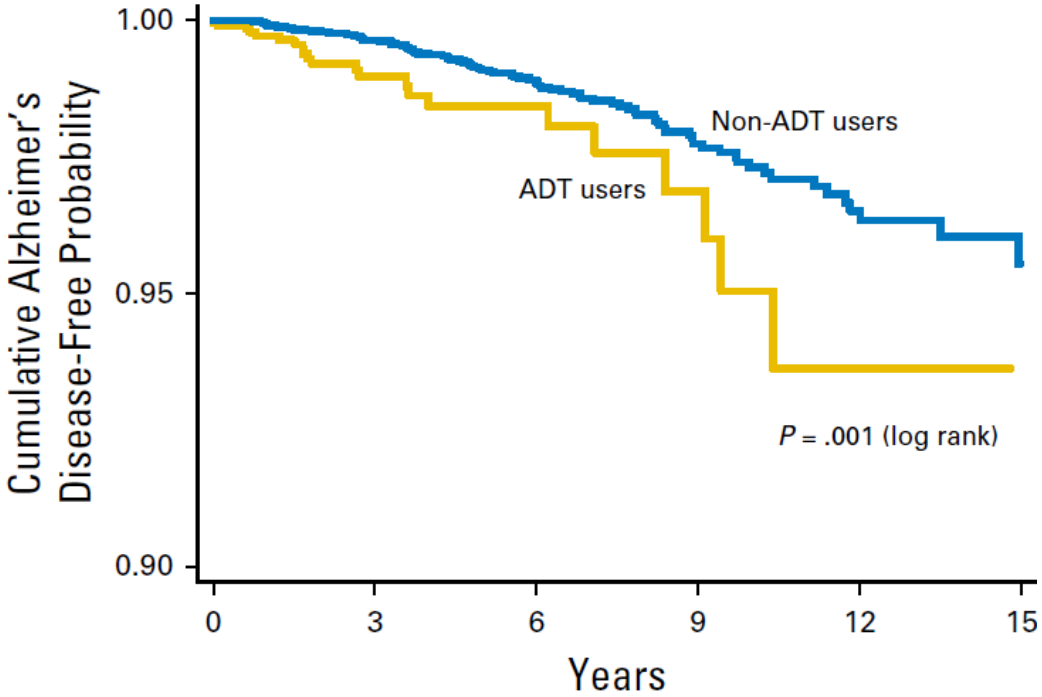
VOLUME 34 · NUMBER 6 · FEBRUARY 20, 2016

JOURNAL OF CLINICAL ONCOLOGY

ORIGINAL REPORT

Androgen Deprivation Therapy and Future Alzheimer's Disease Risk

Kevin T. Nead, Greg Gaskin, Cariad Chester, Samuel Swisher-McClure, Joel T. Dudley, Nicholas J. Leeper, and Nigam H. Shah



Duration of ADT Use (Months)	HR (95% CI)	*P*	*P* for Trend*
No ADT use	Ref	Ref	.016
ADT users			
< 12 months ADT use	1.62 (0.82 to 3.21)	.165	
≥ 12 months ADT use	2.12 (1.11 to 4.03)	.011	

Segundo tumor primário rádio induzido

ELSEVIER

Contents lists available at ScienceDirect

Radiotherapy and Oncology

journal homepage: www.thegreenjournal.com

Systematic review

Second primary cancers after radiation for prostate cancer: A systematic review of the clinical data and impact of treatment technique

- **19 estudos de registros de câncer**
- **21 estudos institucionais**
- **6 estudos com resultados de mortalidade por segundo tumor primário**

Murray L, et al. *Radiotherapy and Oncolology* 2014

Segundo tumor primário rádio induzido

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Systematic review

Second primary cancers after radiation for prostate cancer: A systematic review of the clinical data and impact of treatment technique

- **Grande heterogeneidade entre os estudos e resultados conflitantes**
- **O aumento de segundo tumor primário rádio induzido se torna evidente a partir de 10 anos (reto e bexiga)**
- **Incidência de 1/70 em pacientes com seguimento acima de 10 anos (~1,5%), sendo mais consistente quando comparados pacientes com câncer de próstata que receberam ou não radioterapia**
- **Dados insuficientes sobre técnicas mais modernas de radioterapia. Necessário seguimento mais longo**
- **Risco de segundo tumor primário rádio induzido deve ser levado em consideração para pacientes com expectativa de vida longa. Fatores como tabagismo, dieta e obesidade entram na equação**

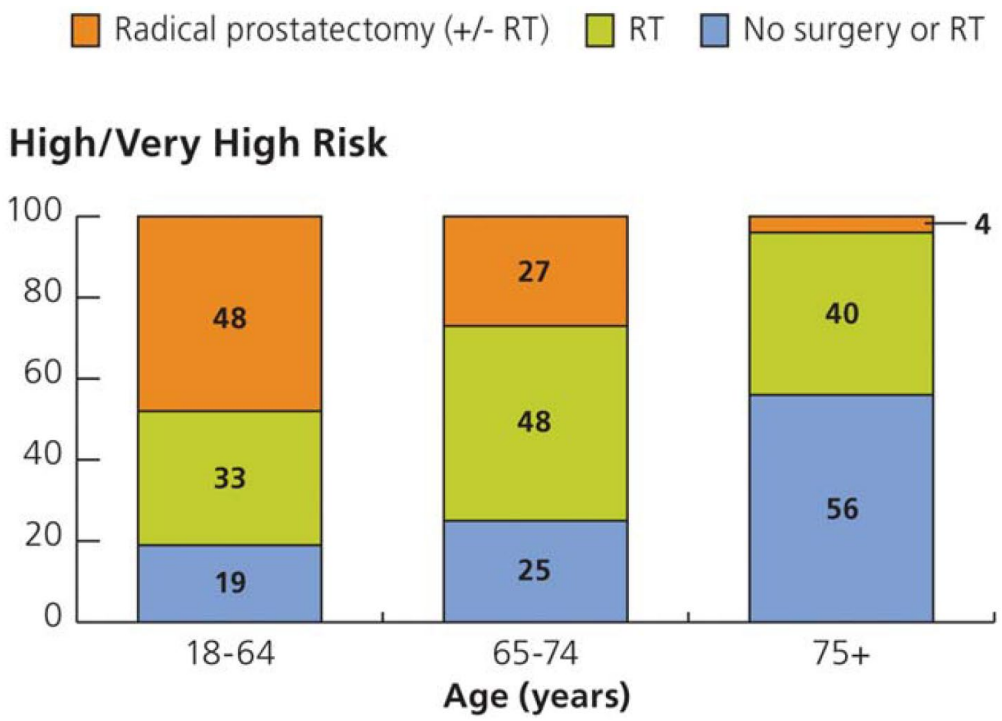
Murray L, et al. *Radiotherapy and Oncolology* 2014

Banco de dados norte americano 2009 – 2011

Cancer Treatment and Survivorship Statistics, 2014

Cancer Treatment and Survivorship Statistics, 2014

Carol E. DeSantis, MPH[1]; Chun Chieh Lin, PhD, MBA[2]; Angela B. Mariotto, PhD[3]; Rebecca L. Siegel, MPH[4];
Kevin D. Stein, PhD[5]; Joan L. Kramer, MD[6]; Rick Alteri, MD[7]; Anthony S. Robbins, MD, PhD[8]; Ahmedin Jemal, DVM, PhD[9]



Bloqueio hormonal +/- Radioterapia

NCIC / MRC / SWOG

1205 pacientes

T3 / T4

T2 / PSA >40

Gleason ≥ 8

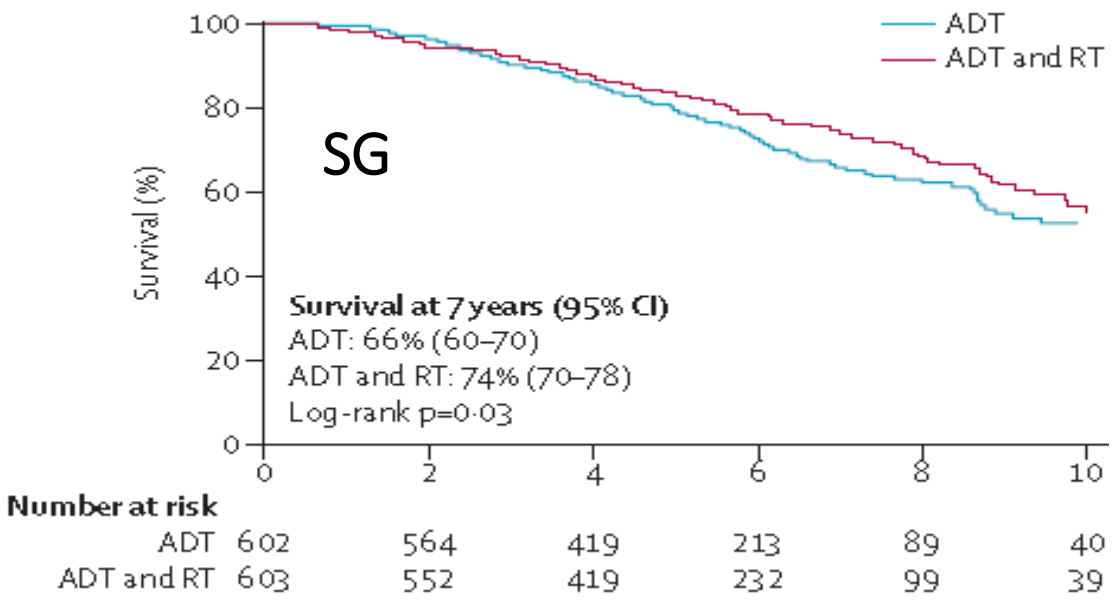
602: HT

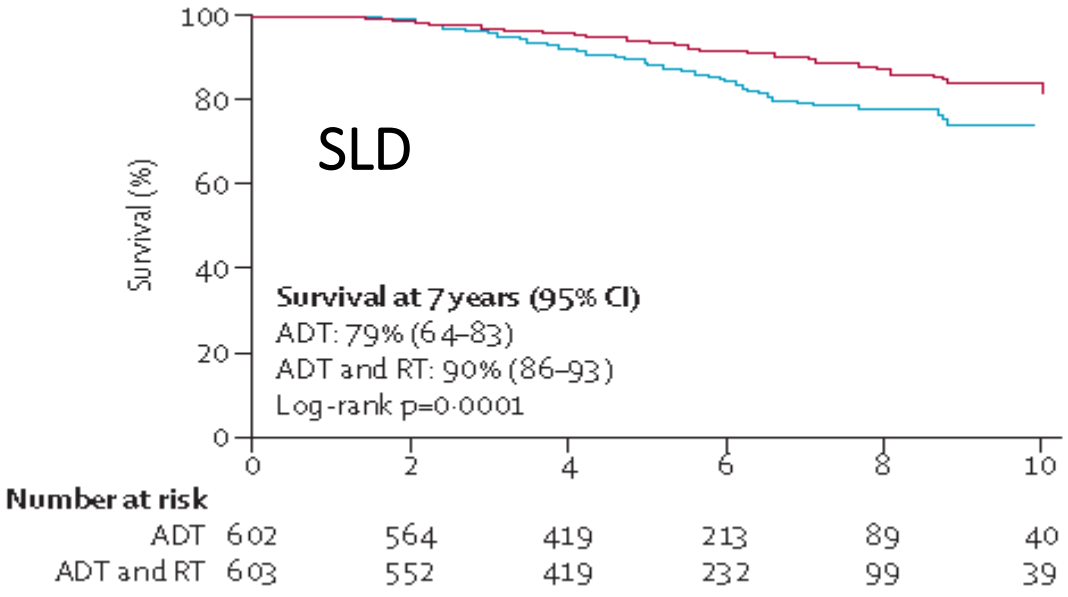
603: HT + RT (65 – 69 Gy)

HT: “lifelong"

Warde et al. *Lancet* 2011

NCIC / MRC / SWOG





Redução de risco de morte com RT (HR=0,77)

Redução de risco de doença com RT (HR=0,57)

Warde et al. *Lancet* 2011

Quando não indico radioterapia na doença localizada de alto risco?

- Pacientes jovens (< 60 anos)
- Pacientes entre 60 e 70 anos sem comorbidades e expectativa de vida acima de 10 anos
- Pacientes clinicamente operáveis
- Tumores ressecáveis
- Pacientes vulneráveis aos efeitos do bloqueio hormonal (impotência, síndrome metabólica, déficit neurocognitivo)
- Pacientes sem acesso à radioterapia conformada ou IMRT
- Considerar risco de tumor rádio induzido e dificuldade de resgate em recaída local isolada após radioterapia

OBRIGADO

BENEFICÊNCIA PORTUGUESA DE SÃO PAULO