



II SIMPÓSIO INTERNACIONAL

GU - REVIEW 2018 - LACOG

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

Radioterapia adjuvante x resgate

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Conceitos

Radioterapia adjuvante

PSA indetectável após cirurgia

Radioterapia de resgate

PSA ≥ 0.2 ng/ml após cirurgia

Fatos

- **Pacientes com pT3 ou margem (+)**
 - 50-75% recorrência da doença após prostatecmia (PR)
- **Radioterapia após PR tem papel importante**
 - Maior controle de PSA, metástases e sobrevida global

Quem e Quando?

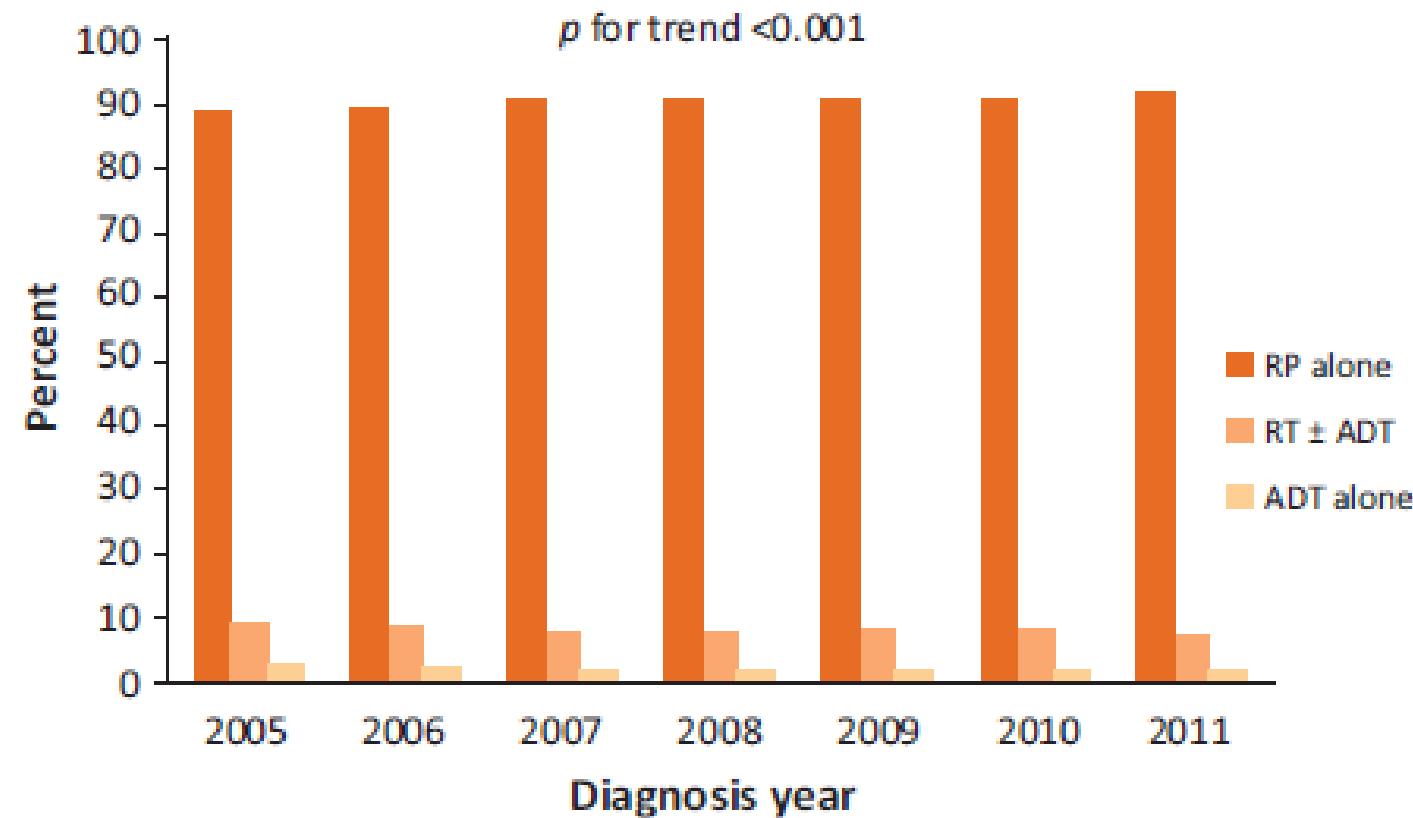
RT “adjuvante” para pT3 ou R1

Estudo	Nº pcts	F/U med	PFS HR	DM HR	OS HR
SWOG	431	12.6 anos	0.43	0.71;p=.02	0.72;p=.02
EORTC	1005	10.6 anos	0.49	p=0.94	p=0.20
ARO	315	9.3 anos	0.51	p=0.56	p=0.59

Tendência de indicação de RT adjuvante USA

2005-2011

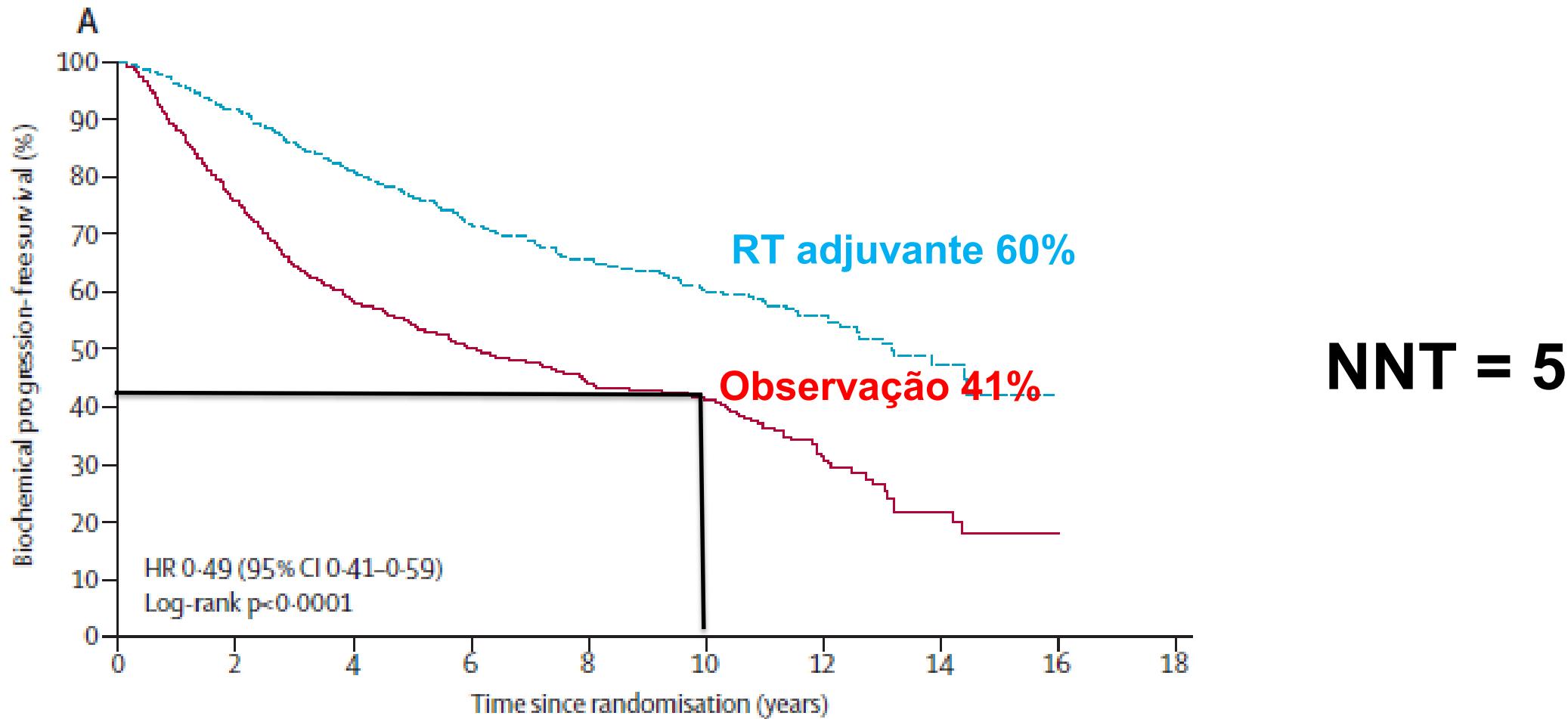
9.1% para 7.3%



Principais razões contra RT adjuvante

- Nem todos os pacientes irão falhar
- Efeitos colaterais relacionados a RT
- RT de resgate precoce pode ser equivalente

Nem todos irão falhar



Efeitos colaterais da RT após PR

Toxicidade	Observação	RT adjuvante
Retal	0%	3.3%
Estenose	9.5%	17.8%
Incontinência	2.8%	6.5%

$$RR = 2.0$$

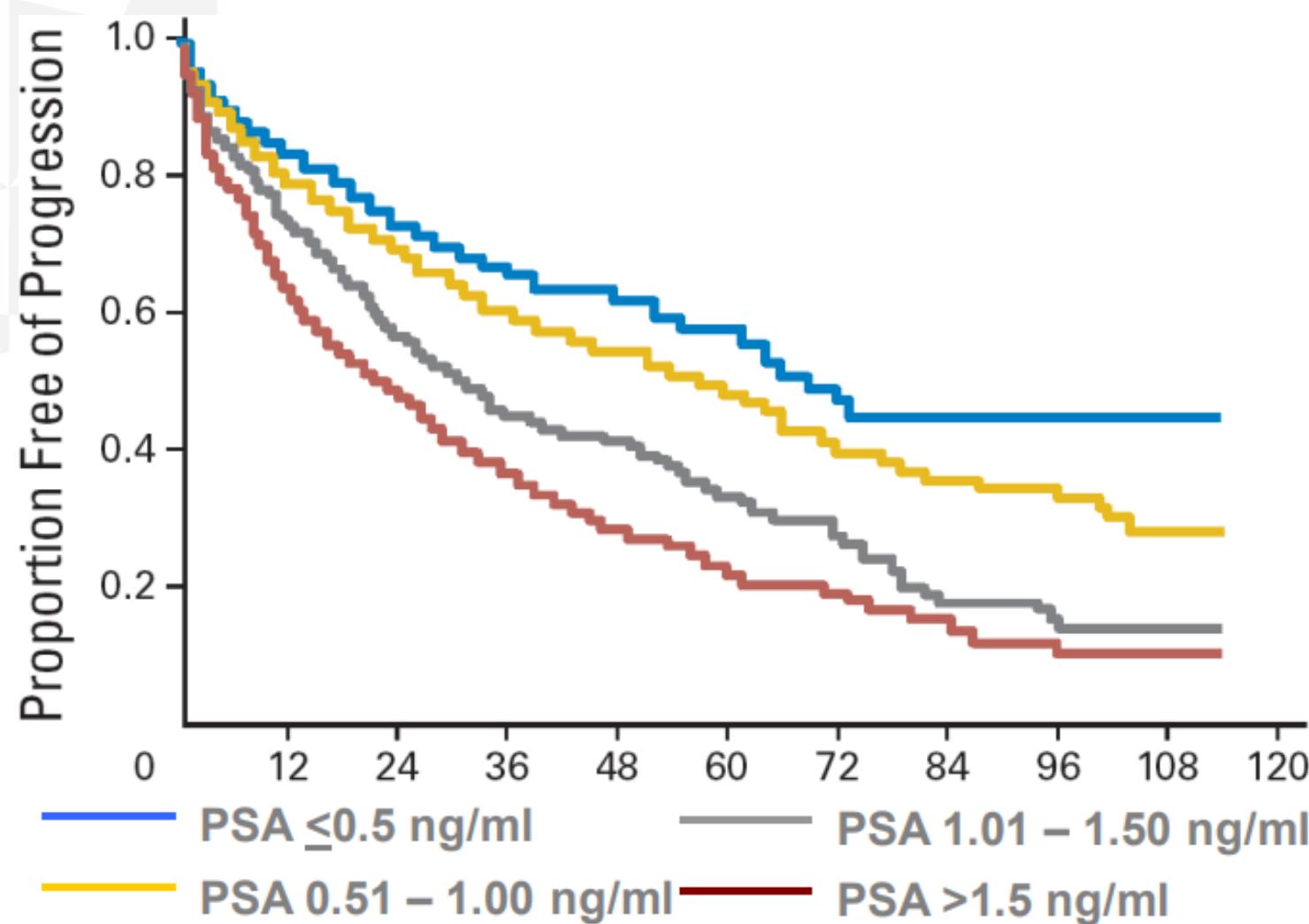
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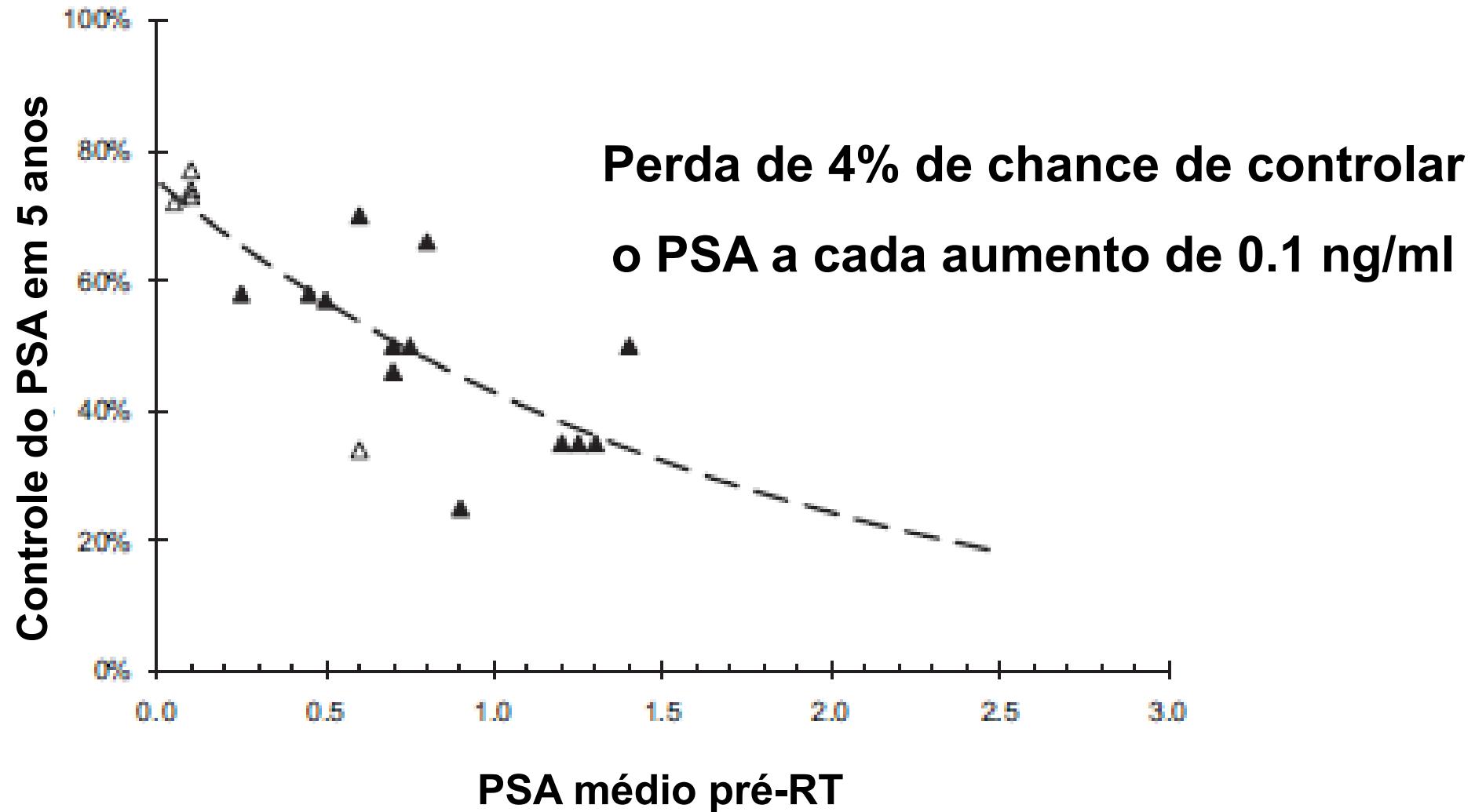
**Apesar do mesmo HR para PFS, porque os resultados são
diferentes para DM e OS?**

- RT de resgate mais cedo nos estudos EORTC/ARO vs SWOG no braço observação

Valor do PSA vs RT resgate

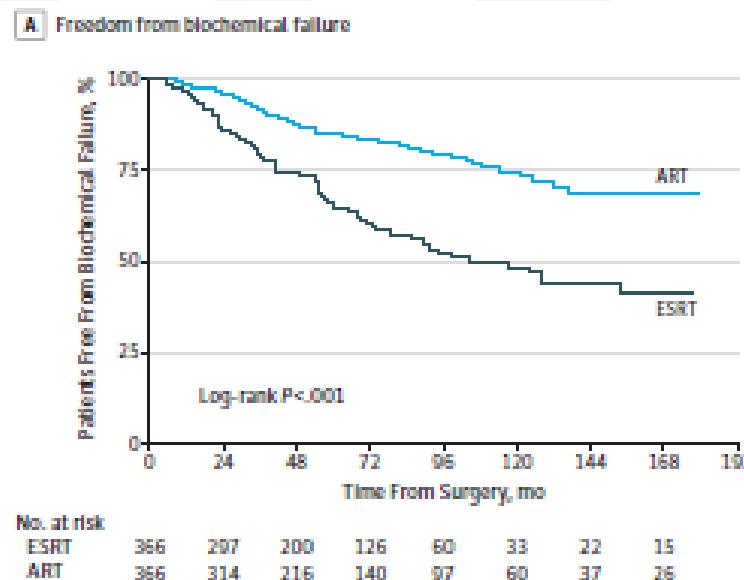


Valor do PSA vs RT resgate

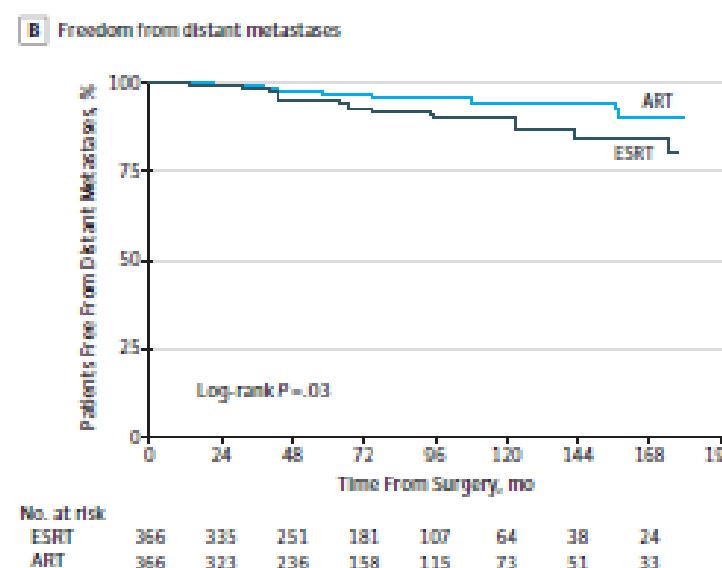


RT adjuvante vs RT resgate precoce

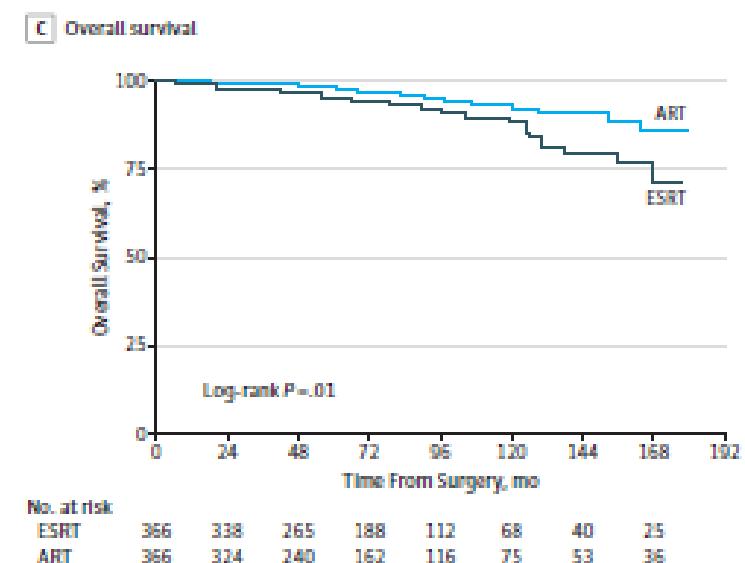
Controle PSA



Metástases



Sobrevida Global

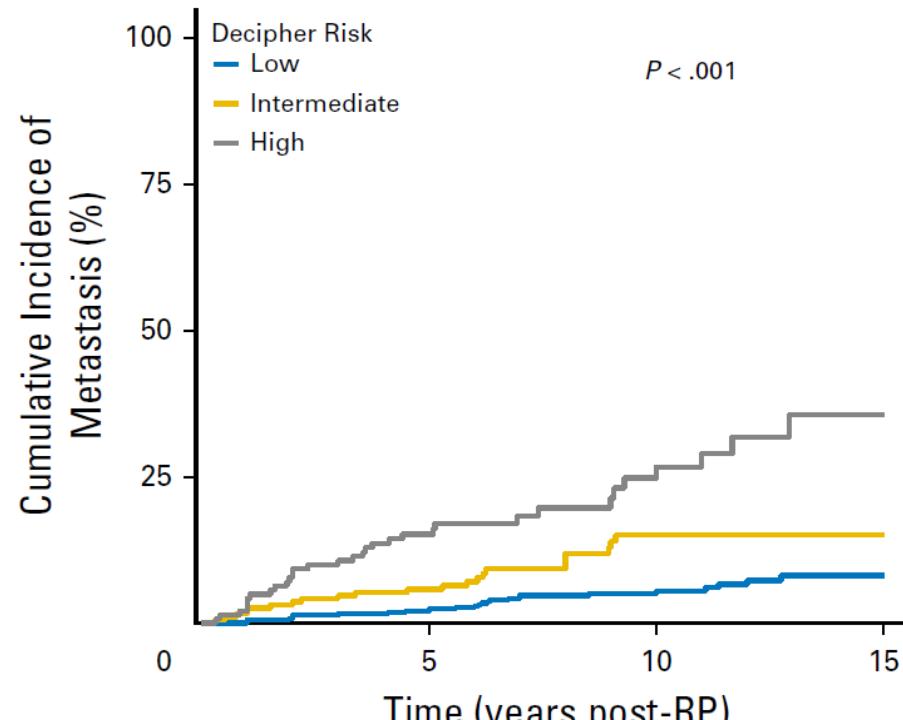


Guidelines AUA/ASTRO e NCCN

Physicians should “offer” adjuvant radiotherapy to patients with adverse pathologic findings

Testes genéticos

Metanálise *Decipher* em 975 pacientes após PR



No. at risk				
Decipher > 0.60	142	95	32	6
Decipher 0.45–0.60	193	147	58	12
Decipher < 0.45	520	427	196	36

Estudos de fase 3

RT adjuvante vs RT resgate precoce

- **RADICALS**
 - pT3a-b ou margem +; pT4; GS7-10; Pre op PSA >10 (n = 3000)
- **FNCLCC-GETUG-17/0702**
 - pT3a-b ou margem + (n = 718)
- **TROG 08.03 RAVES**
 - pT3a-b ou margem + (n = 718)

Enquanto isto.....

Se PSA indetectável e pT3 ou margem positiva:

Seguimento com PSA trimestral e se duas elevações consecutivas $>0.05\text{ng/ml}$ ou um valor isolado $>0.1\text{ng/ml}$,
iniciar RT de resgate



Short Term Androgen Deprivation Therapy Without or With Pelvic Lymph Node Treatment Added to Prostate Bed Only Salvage Radiotherapy: The NRG Oncology/RTOG 0534 SPPORT Trial

A Pollack, TG Garrison, AG Balogh, D Low, DW Bruner, JS Wefel, LG Gomella, E Vigneault, JM Michalski, S Angyalfi, H Lukka, SL Faria, G Rodrigues, MC Beauchemin, SA Seaward, AM Allen, DC Monitto, W Seiferheld, and HM Sandler

RTOG 0534

NRG/RTOG 0534/SPPORT Trial Design

A Phase III Trial of Short Term Androgen Deprivation with Pelvic Lymph Node or Prostate Bed Only Radiotherapy (SPPORT) in Prostate Cancer Patients with a Rising PSA after Radical Prostatectomy

S	SV Involvement 1. No 2. Yes	R	Arm 1: PBRT Alone
T	Prostatectomy Gleason Score	A	PBRT 64.8-70.2 Gy
R	1. Gleason ≤ 7 2. Gleason 8-9	N	Arm 2: PBRT + STAD
A		D	PBRT 64.8-70.2 Gy + STAD for 4-6 months
T		O	beginning 2 months before RT
I	Pre-Radiotherapy PSA 1. PSA ≥ 0.1 and ≤ 1.0 ng/mL 2. PSA > 1.0 and < 2.0 ng/mL	M	Arm 3: PLNRT + PBRT + STAD
F		I	PLNRT to 45 Gy and PBRT to 64.8-70.2 Gy, +
Y	Pathology Stage 1. pT2 and margin negative 2. All others	Z	STAD for 4-6 months beginning 2 months before RT
		E	

SV = seminal vesicle; RT = radiotherapy; PBRT = prostate bed RT; PLNRT = pelvic lymph node RT;
STAD = neoadjuvant and concurrent short term androgen deprivation

RTOG 0534

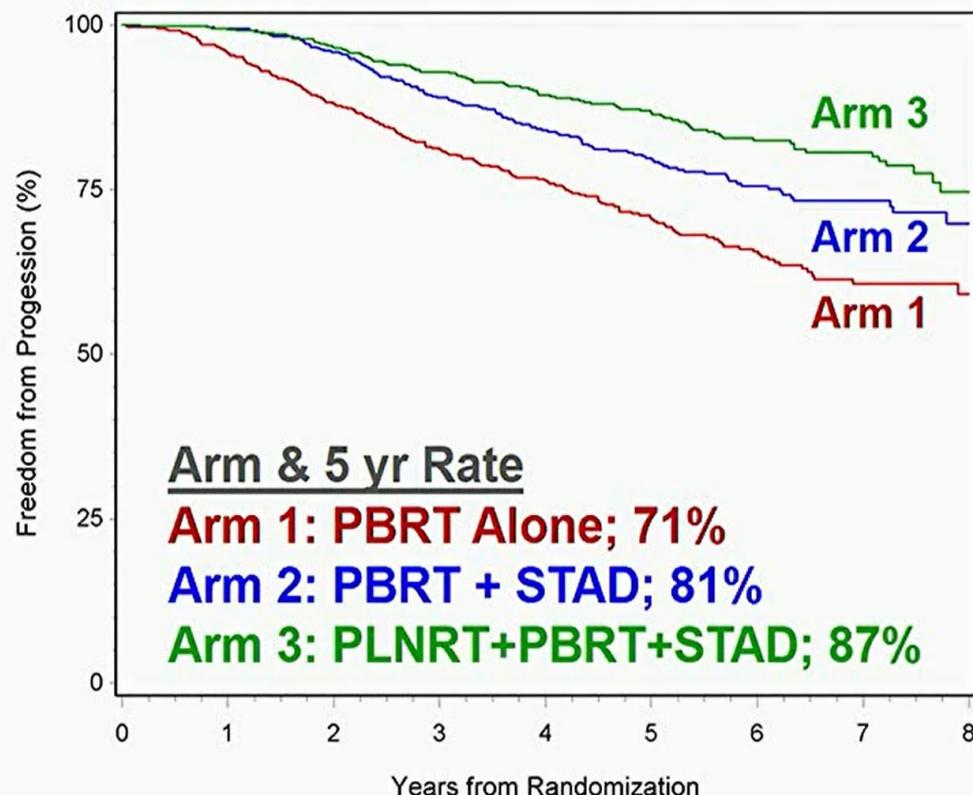
Patient Characteristics: PSA

Patient or Tumor Characteristic	PBRT Alone (n=574)		PBRT+STAD (n=585)		PLNRT+PBRT+STAD (n=577)		Total	
	n	%	n	%	n	%	n	%
Pre-RT PSA								
Mean	0.47		0.51		0.47		0.48	
Median	0.32		0.39		0.32		0.34	
Min - Max	0.1 - 1.96		0.1 - 1.93		0.1 - 1.93		0.1 - 1.96	
≥ 0.1 and ≤ 0.2ng/ml	160	27.9	127	21.7	155	26.9	442	25.5
> 0.2 and ≤ 0.5ng/ml	251	43.7	261	44.6	249	43.2	761	43.8
> 0.5 and ≤ 1.0ng/ml	104	18.1	132	22.6	114	19.8	350	20.2
> 1.0 and < 2.0ng/ml	59	10.3	65	11.1	59	10.2	183	10.5



RTOG 0534

FFP: All Eligible Patients



5 yr Rate Comparison

Arm 3 vs Arm 1: $p<0.0001$

Arm 2 vs Arm 1: $p<0.0001$

Arm 3 vs Arm 2: $p=0.0039$

HRs and 97.5% CIs

3 vs 1: 0.45 (0.34-0.61)

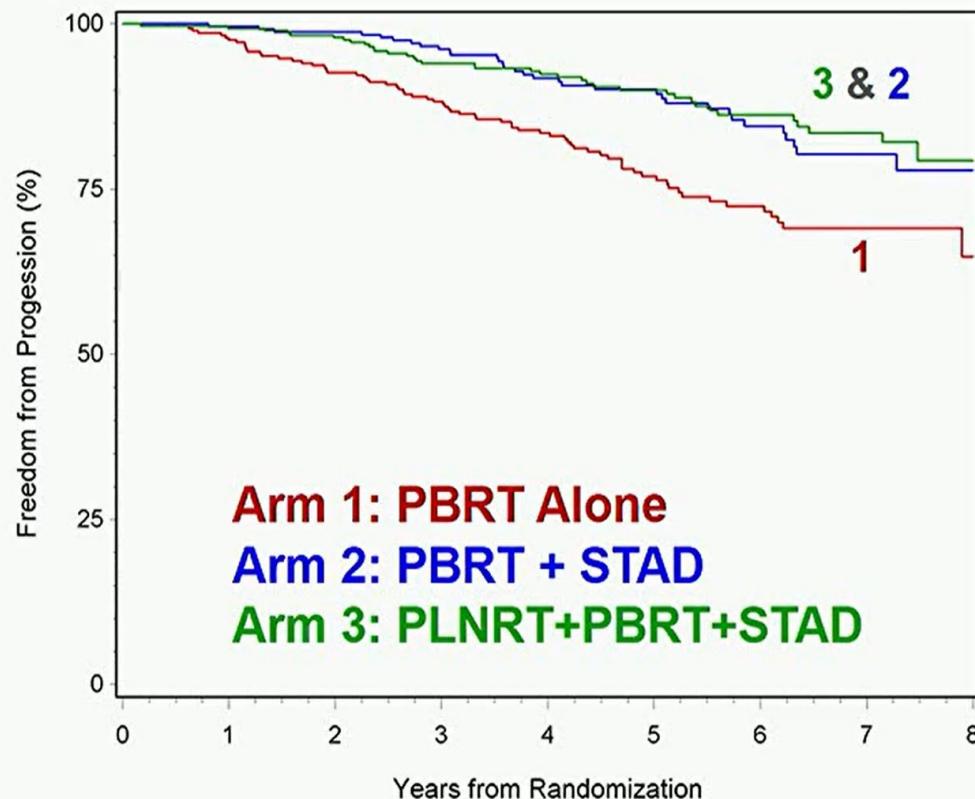
2 vs 1: 0.62 (0.47-0.82)

3 vs 2: 0.71 (0.52-0.98)

No. at Risk	Years from Randomization								
PBRT Alone	573	529	480	417	334	243	165	89	37
PBRT+NC-STAD	585	559	532	467	366	275	179	94	39
PLNRT+PBRT+NC-STAD	576	563	540	488	399	315	209	126	52

RTOG 0534

FFP: Pre-RT PSA <0.34 (Median)



5 yr Rate Comparison

Arm 3 vs Arm 1: $p=0.0001$

Arm 2 vs Arm 1: $p=0.0002$

Arm 3 vs Arm 2: $p=0.49$

HRs and 97.5% CIs

3 vs 1: 0.51 (0.32-0.81)

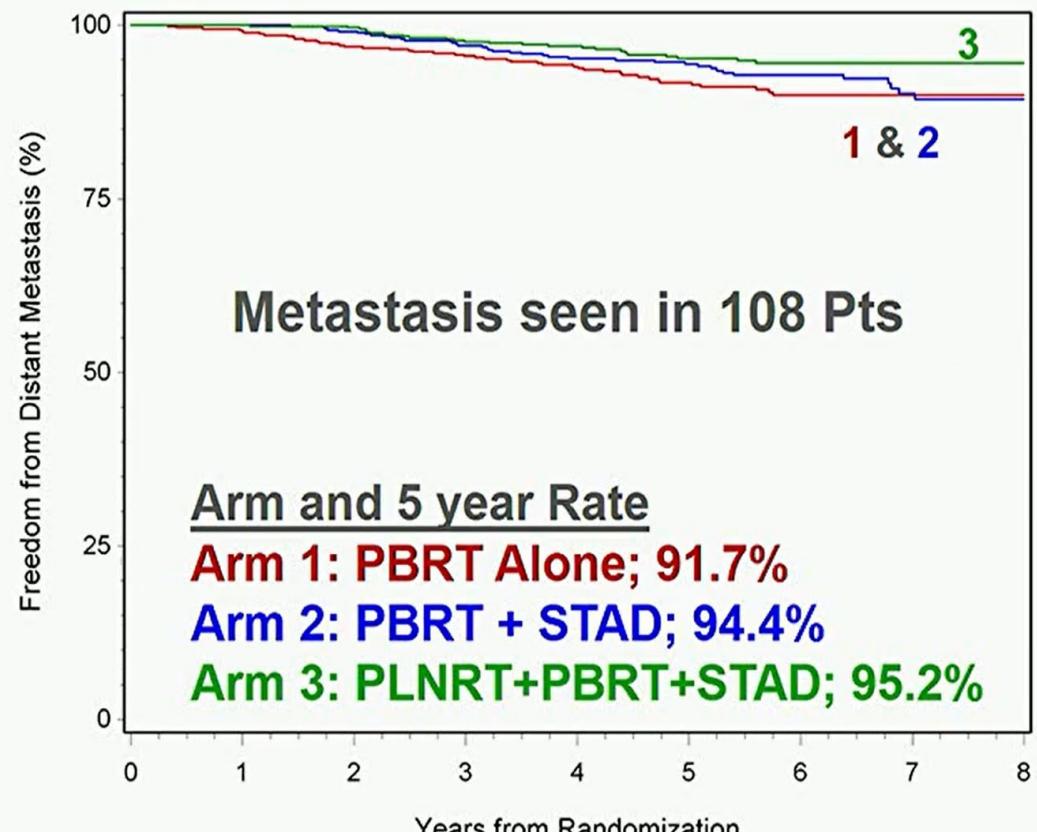
2 vs 1: 0.54 (0.33-0.87)

3 vs 2: 0.93 (0.55-1.60)

No. at Risk	Years from Randomization								
PBRT Alone	296	278	261	234	186	129	91	48	15
PBRT+NC-STAD	258	243	237	213	169	128	84	36	11
PLNRT+PBRT+NC-STAD	296	290	282	250	205	159	103	63	22

RTOG 0534

Freedom from Distant Metastasis: All Eligible Pts



5 yr Rate Comparison
Arm 3 vs Arm 1: $p=0.014$
Arm 2 vs Arm 1: $p=0.05$
Arm 3 vs Arm 2: $p=0.28$

HRs and 97.5% CIs
3 vs 1: 0.52 (0.30-0.92)
2 vs 1: 0.81 (0.49-1.33)
3 vs 2: 0.64 (0.36-1.14)

- No statistically significant differences in OS

No. at Risk	Years from Randomization								
PBRT Alone	573	546	522	482	398	302	214	123	54
PBRT+NC-STAD	585	562	547	499	405	315	213	111	48
PLNRT+PBRT+NC-STAD	576	565	551	502	417	330	220	134	56



Conclusões

- RT pós op tem importante papel em pacientes de alto risco
- RT adjuvante pode beneficiar alguns pacientes
 - Teste genético e estudos de fase 3
- RT resgate precoce é opção para pacientes com PSA indetectável
- Se falha bioquímica, considerar RT pélvica + HT
 - PET-PSMA ferramenta importante

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Obrigado.

23/11/2018



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