

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

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Disclosure for Dr. Pollack

- Employment
 - University of Miami Miller School of Medicine: Chair and Professor of Radiation Oncology, Deputy Director Sylvester Comprehensive Cancer Center: Employee
- Compensation
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Background

- Biochemical failure after salvage prostate bed radiation therapy (**PBRT**) is typically 30-40% at 5-10 years.
- Neoadjuvant and concurrent short term androgen deprivation therapy (**STAD**) is an effective addition to primary radiation therapy and in 2005 had not yet been tested with salvage PBRT.
- Pelvic lymph node radiation therapy (**PLNRT**) has shown promise, but has never been conclusively proven to be effective in a Phase III randomized trial.
- Trial hypothesis: For prostate cancer patients with a rising PSA after prostatectomy, there will be an incremental gain in freedom from progression with the addition of:
 - STAD to PBRT
 - PLNRT + STAD to PBRT

NRG Oncology/RTOG 0534/SPPORT Trial Design

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

Primary endpoint:
FFP at 5 years

Failure defined as first occurrence of:

- PSA \geq Nadir+2 ng/mL
- Clinical progression (local, regional or distant)
- Death due to any cause

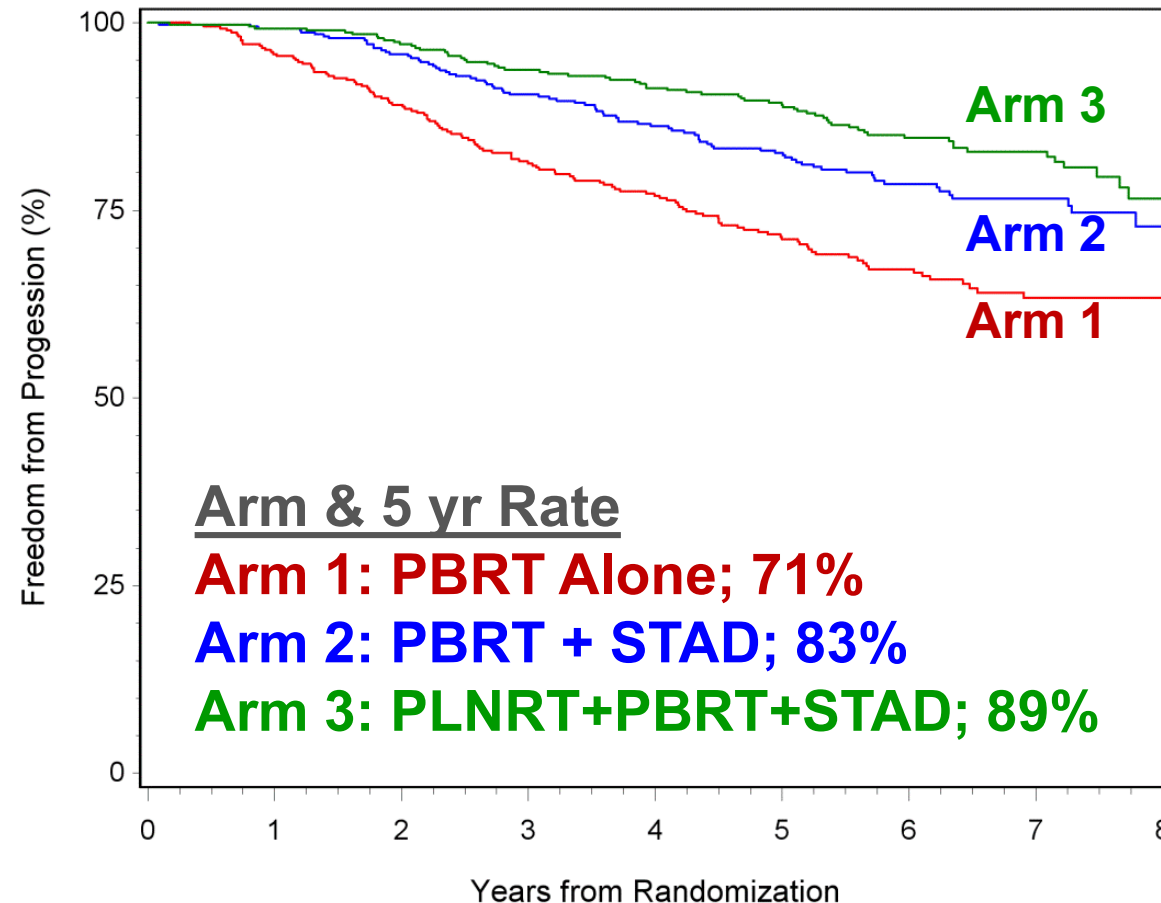
Patient characteristics

	PBRT Alone (n=574)		PBRT+STAD (n=585)		PLNRT+PBRT+STAD (n=577)		Total	
Patient/Tumor Characteristic	n	%	n	%	n	%	n	%
Zubrod Performance Status								
0	533	92.9	546	93.3	543	94.1	1622	93.4
1	41	7.1	39	6.7	34	5.9	114	6.6
Seminal Vesicle Involvement								
No	492	85.7	498	85.1	489	84.7	1479	85.2
Yes	82	14.3	87	14.9	88	15.3	257	14.8
Prostatectomy Stage								
pT2	304	53.0	326	55.7	312	54.1	942	54.3
pT3 NOS	19	3.3	17	2.9	22	3.8	58	3.3
pT3a ECE	173	30.1	160	27.4	156	27.0	489	28.2
pT3b SVI	78	13.6	82	14.0	87	15.1	247	14.2
Prostatectomy Margins								
Positive	292	50.9	292	49.9	286	49.6	870	50.1
Negative	273	47.6	286	48.9	288	49.9	847	48.8
Unknown	9	1.6	7	1.2	3	0.5	19	1.1

Median Age=64y; Caucasian 83%; Non-Hispanic 91%

FFP: Interim analysis population (1,191 patients)

**Minimum
potential FU 5 yr;
Median FU 6.4 yr**



No. at Risk									
PBRT Alone	399	363	324	286	259	223	150	84	34
PBRT+NC-STAD	398	381	360	329	299	265	170	91	37
PLNRT+PBRT+NC-STAD	394	385	371	352	334	311	208	125	51

5 yr Rate Comparison

Arm 3 vs Arm 1: $p < 0.0001$

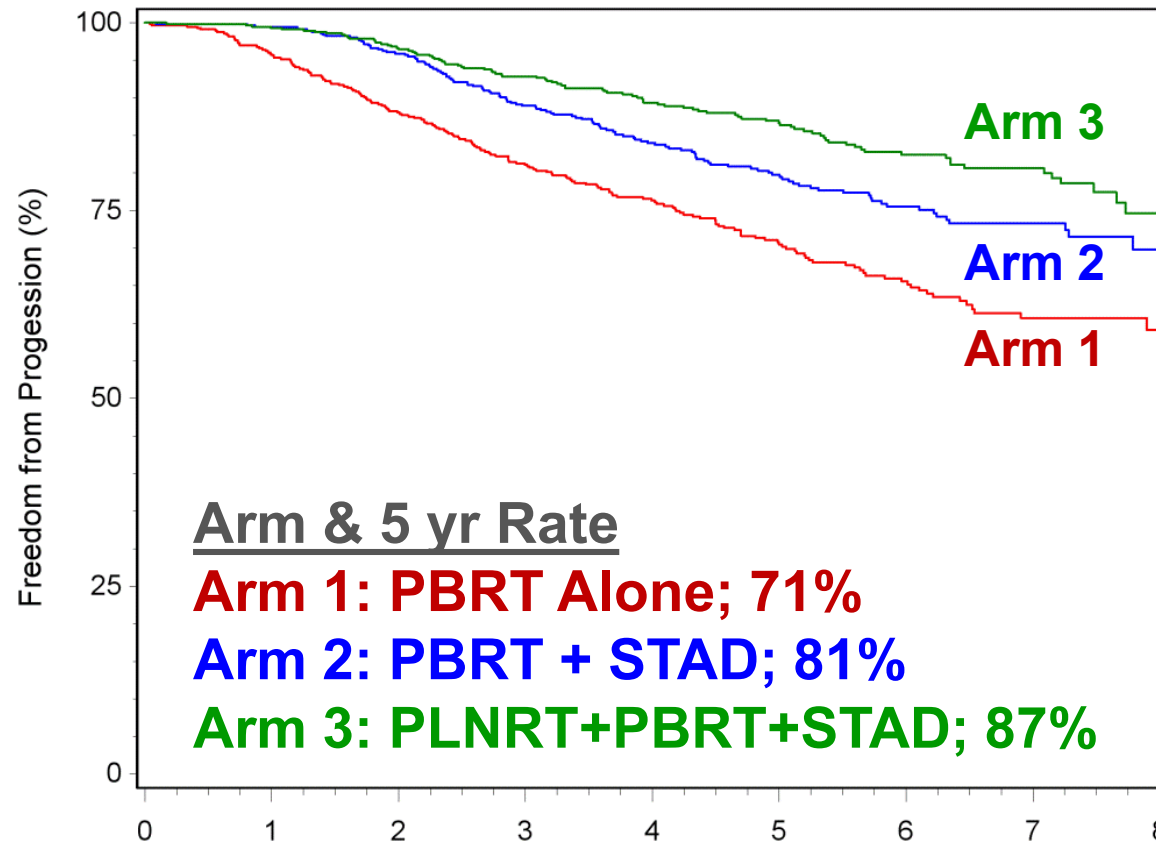
Arm 2 vs Arm 1: $p = 0.0001$

Arm 3 vs Arm 2: $p = 0.0063$

DMC Recommendation

**Report findings for all
three arms**

FFP: All eligible patients (1,792)



5 yr Rate Comparison

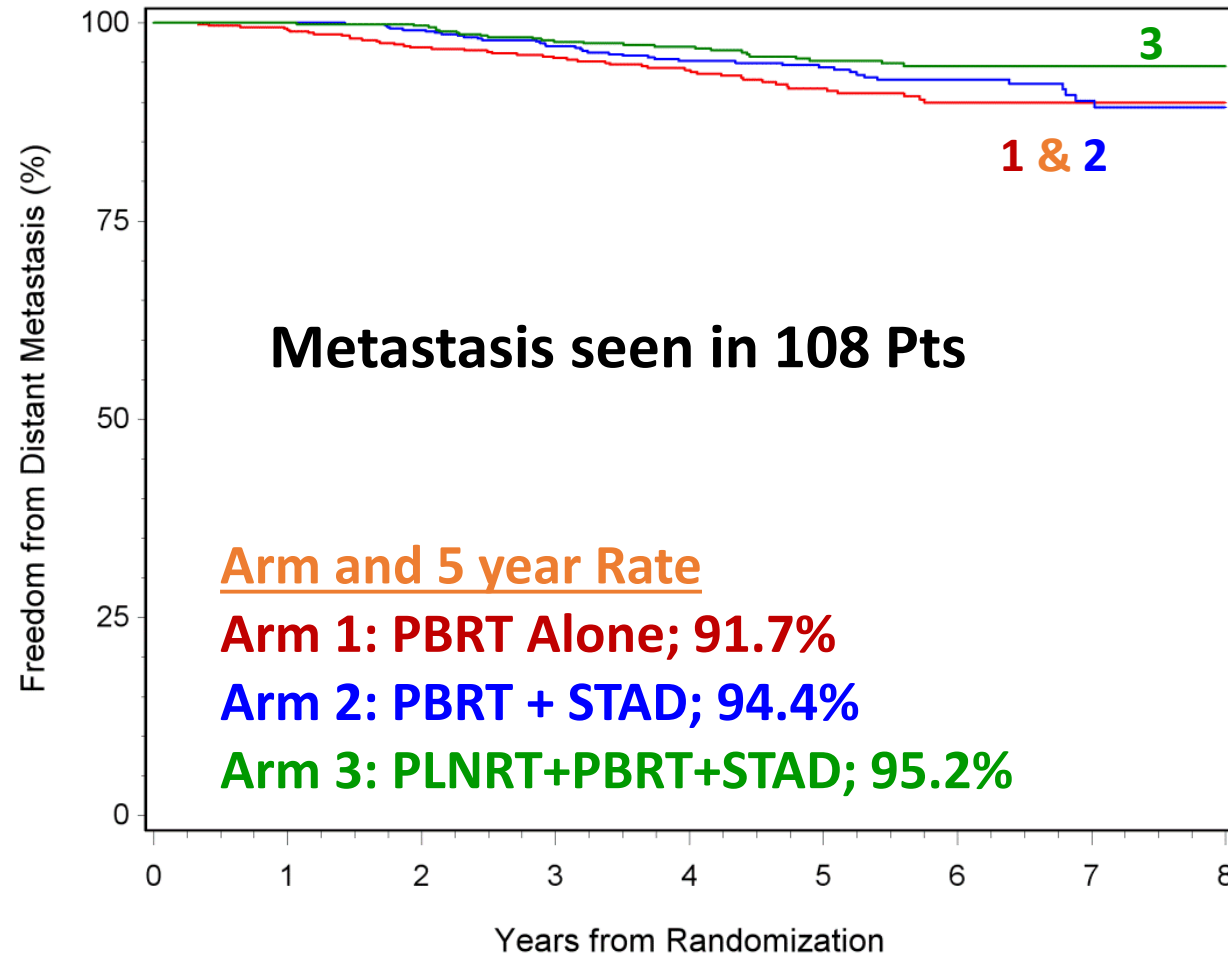
- Arm 3 vs Arm 1: $p < 0.0001$
- Arm 2 vs Arm 1: $p < 0.0001$
- Arm 3 vs Arm 2: $p = 0.0039$

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

Freedom from distant metastasis: All eligible patients



No. at Risk									
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

Acute Adverse Events (CTCAEv3) Without Regard For Attribution

	PBRT Alone (n=557)		PBRT+STAD (n=568)		PLNRT+PBRT+STAD (n=567)		p-value
Type	n	%	n	%	n	%	
GI							
Grade 2+	11	2.0	22	3.9	39	6.9	<0.001
Grade 3+	1	0.2	5	0.9	4	0.7	0.37
Renal/GU							
Grade 2+	54	9.7	68	12.0	69	12.3	0.35
Grade 3+	5	0.9	5	0.9	8	1.5	0.70
Blood/Bone Marrow							
Grade 2+	13	2.3	10	1.8	29	5.1	0.002
Grade 3+	3	0.5	1	0.2	15	2.6	<0.001

Late Adverse Events (CTCAEv3) Without Regard For Attribution

	PBRT Alone (n=557)		PBRT+STAD (n=571)		PLNRT+PBRT+STAD (n=570)		p-value
Type	n	%	n	%	n	%	
GI							
Grade 2+	54	9.7	50	8.8	46	8.1	0.63
Grade 3+	4	0.7	2	0.4	6	1.1	0.34
Renal/GU							
Grade 2+	188	33.8	184	32.2	197	34.6	0.70
Grade 3+	24	4.4	28	4.9	34	6.0	0.44
Blood/Bone Marrow							
Grade 2+	17	3.1	9	1.6	23	4.1	0.044
Grade 3+	2	0.4	1	0.2	6	1.1	0.12

Conclusions and treatment implications

- Strongest level I evidence supporting PLNRT
- For Arm 3 vs Arm 1, number needed to treat to prevent one progression within 5 years is 6 (95%CI 4.6-8.6)!
 - Follow-up continuing to further elucidate the magnitude of the differences between Arms 2 and 3
- Robust effect translating into a decrease in distant metastasis
- Is there a PSA cutpoint below which PLNRT is not needed?
- Role of PET in PLNRT decisions?
- Implications for the management of primarily managed prostate cancer
 - Local control needed to realize the impact of PLNRT (NRG 0924)