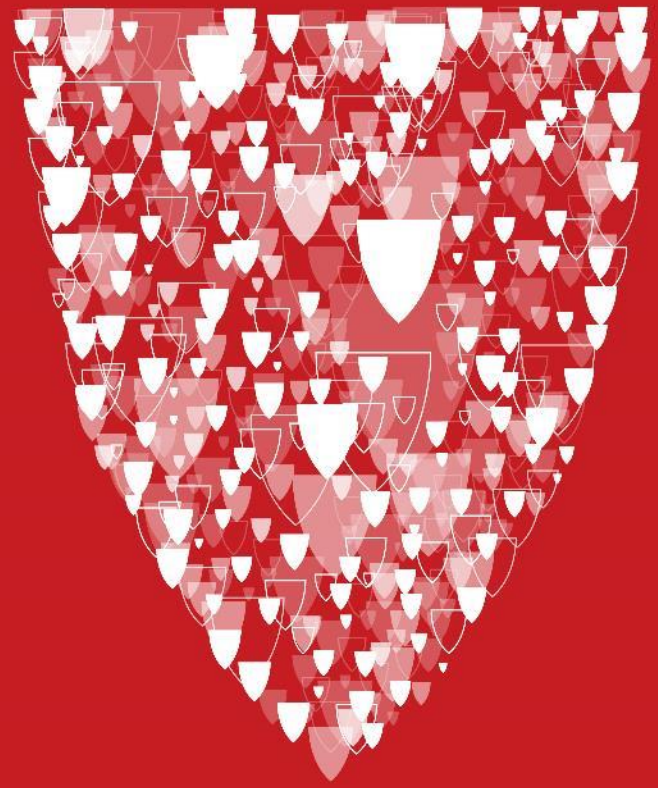
INTEGRATION OF TRADITIONAL AND NEW HORMONAL THERAPIES WITH PROSTATE SBRT:

DETERMINING THE OPTIMAL TIMING AND PATIENT SELECTION



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Disclosures

Personal fees from Astellas, AstraZeneca, Bayer, Boston Scientific, GSK, Janssen, Novartis, Pfizer

NIH Funding:

- R01: G-MAJOR Randomized Trial
- U01: STAMPEDE2 North America Randomized Trial: METANOVA

Study PI or Study Chair:

-ASCLEPIUS; niraparib, abiraterone (Janssen); no personal financial support

-OPTYX; relugolix (Myovant/Sumitomo); no personal financial support

-NRG GU006; apalutamide (Janssen), PAM50; no personal financial support

-NRG GU009; apalutamide (Janssen), Decipher; no personal financial support

-NRG GU010; darolutamide (Bayer), Decipher; no personal financial support

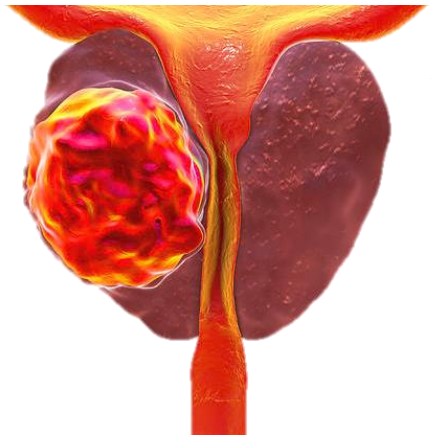
-STARLiT; 177Lu-PSMA-617

Leadership:

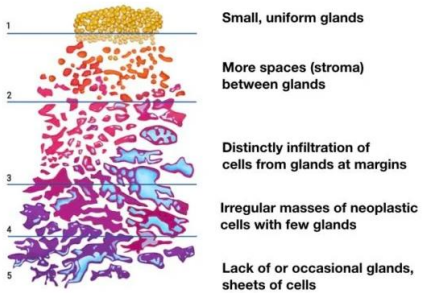
-Chair, NCCN Prostate Cancer Guidelines

-Standing Member, FDA Oncology Drug Advisory Committee

Prostate Cancer Risk Stratification

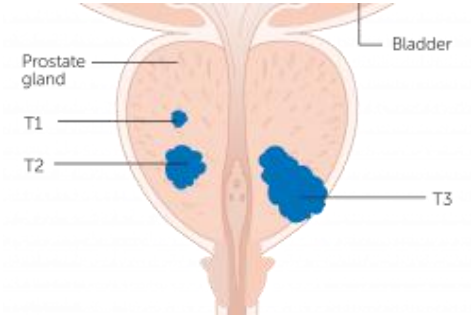


Gleason Grading



PSA blood test

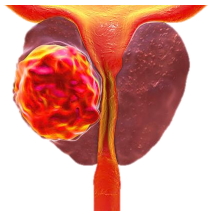
Extension of tumor



NCCN National Comprehensive Cancer Network®

Risk Groups

Prostate Cancer Risk Stratification



NCCN National Comprehensive Cancer Network®

Risk Groups

- ~~Very Low Risk~~
- Low Risk
- Favorable Intermediate Risk
- Unfavorable Intermediate Risk
- High Risk
- Very High Risk
- Node Positive
- Metastatic

Increasing risk of recurrence after local therapy

i.e.

Increasing aggressiveness

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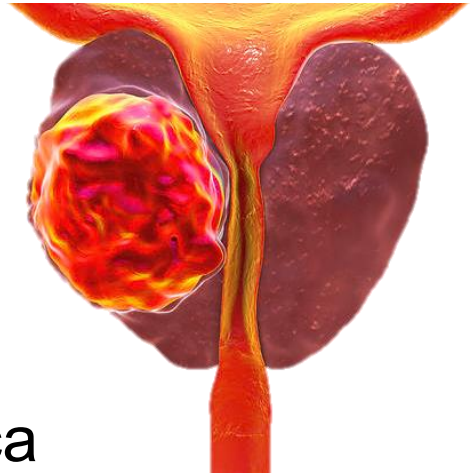
Potential Solutions

ADT

- Targets biologic driver of PCa
- Inhibits DNA repair
- Reduces intratumoral hypoxia
- Inhibits proliferation of micrometastatic disease
- Enhances immunogenicity of Pca

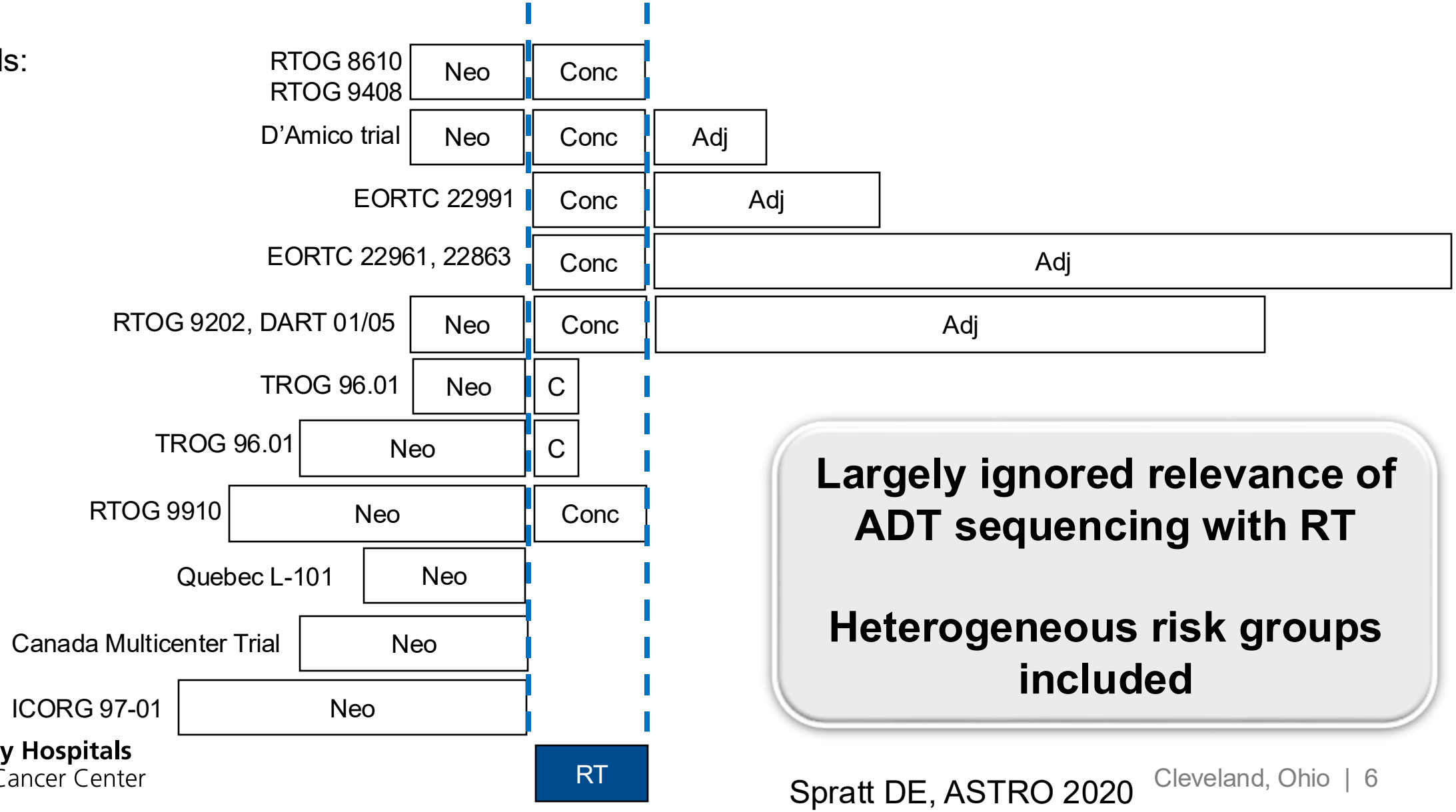


RT Dose Escalation

- Increase log cell kill

30 Years of RT + ADT trials

Select trials:



Largely ignored relevance of ADT sequencing with RT

Heterogeneous risk groups included

Spratt DE, ASTRO 2020

Meta-Analysis of Randomized trials in Cancer of the Prostate

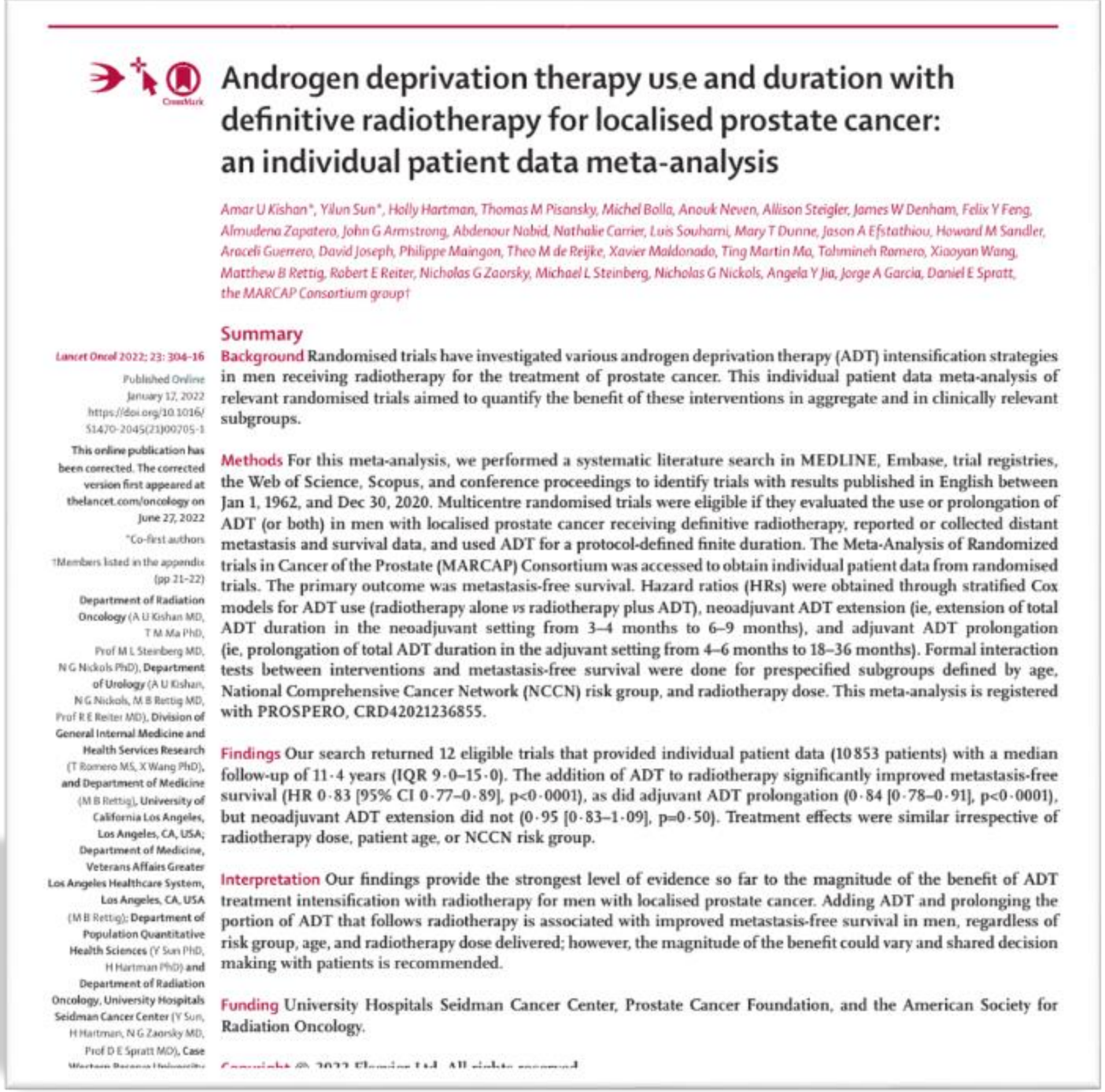
MARCAP

Independent Data Repository and Statistical Analysis Team

University Hospitals Seidman Cancer Center

UCLA Health

Co-PIs: Drs. Amar Kishan and Dan Spratt



Androgen deprivation therapy use and duration with definitive radiotherapy for localised prostate cancer: an individual patient data meta-analysis

Amar U Kishan, Yilun Sun*, Holly Hartman, Thomas M Pisansky, Michel Bolla, Anouk Neven, Allison Steigler, James W Denham, Felix Y Feng, Almudena Zapatero, John G Armstrong, Abdenour Nabid, Nathalie Carrier, Luis Souhami, Mary T Dunne, Jason A Efstathiou, Howard M Sandler, Araceli Guerrero, David Joseph, Philippe Maingon, Theo M de Reijke, Xavier Maldonado, Ting Martin Ma, Tahmineh Romero, Xiaoyan Wang, Matthew B Rettig, Robert E Reiter, Nicholas G Zaorsky, Michael L Steinberg, Nicholas G Nickols, Angela Y Jia, Jorge A Garcia, Daniel E Spratt, the MARCAP Consortium group†*

Lancet Oncol 2022; 23: 304–16

Published Online January 17, 2022 https://doi.org/10.1016/S1470-2045(21)00705-1

This online publication has been corrected. The corrected version first appeared at thelancet.com/oncology on June 27, 2022

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Summary

Background Randomised trials have investigated various androgen deprivation therapy (ADT) intensification strategies in men receiving radiotherapy for the treatment of prostate cancer. This individual patient data meta-analysis of relevant randomised trials aimed to quantify the benefit of these interventions in aggregate and in clinically relevant subgroups.

Methods For this meta-analysis, we performed a systematic literature search in MEDLINE, Embase, trial registries, the Web of Science, Scopus, and conference proceedings to identify trials with results published in English between Jan 1, 1962, and Dec 30, 2020. Multicentre randomised trials were eligible if they evaluated the use or prolongation of ADT (or both) in men with localised prostate cancer receiving definitive radiotherapy, reported or collected distant metastasis and survival data, and used ADT for a protocol-defined finite duration. The Meta-Analysis of Randomized trials in Cancer of the Prostate (MARCAP) Consortium was accessed to obtain individual patient data from randomised trials. The primary outcome was metastasis-free survival. Hazard ratios (HRs) were obtained through stratified Cox models for ADT use (radiotherapy alone *vs* radiotherapy plus ADT), neoadjuvant ADT extension (ie, extension of total ADT duration in the neoadjuvant setting from 3–4 months to 6–9 months), and adjuvant ADT prolongation (ie, prolongation of total ADT duration in the adjuvant setting from 4–6 months to 18–36 months). Formal interaction tests between interventions and metastasis-free survival were done for prespecified subgroups defined by age, National Comprehensive Cancer Network (NCCN) risk group, and radiotherapy dose. This meta-analysis is registered with PROSPERO, CRD42021236855.

Findings Our search returned 12 eligible trials that provided individual patient data (10 853 patients) with a median follow-up of 11·4 years (IQR 9·0–15·0). The addition of ADT to radiotherapy significantly improved metastasis-free survival (HR 0·83 [95% CI 0·77–0·89], p<0·0001), as did adjuvant ADT prolongation (0·84 [0·78–0·91], p<0·0001), but neoadjuvant ADT extension did not (0·95 [0·83–1·09], p=0·50). Treatment effects were similar irrespective of radiotherapy dose, patient age, or NCCN risk group.

Interpretation Our findings provide the strongest level of evidence so far to the magnitude of the benefit of ADT treatment intensification with radiotherapy for men with localised prostate cancer. Adding ADT and prolonging the portion of ADT that follows radiotherapy is associated with improved metastasis-free survival in men, regardless of risk group, age, and radiotherapy dose delivered; however, the magnitude of the benefit could vary and shared decision making with patients is recommended.

Funding University Hospitals Seidman Cancer Center, Prostate Cancer Foundation, and the American Society for Radiation Oncology.

Purpose of this 1st report from the MARCAP consortium…

Quantify the impact of 3 treatment intensification strategies with RT:

1. Use of ADT
2. Neoadjuvant ADT prolongation
3. Adjuvant ADT prolongation

Seminal MARCAP Analysis

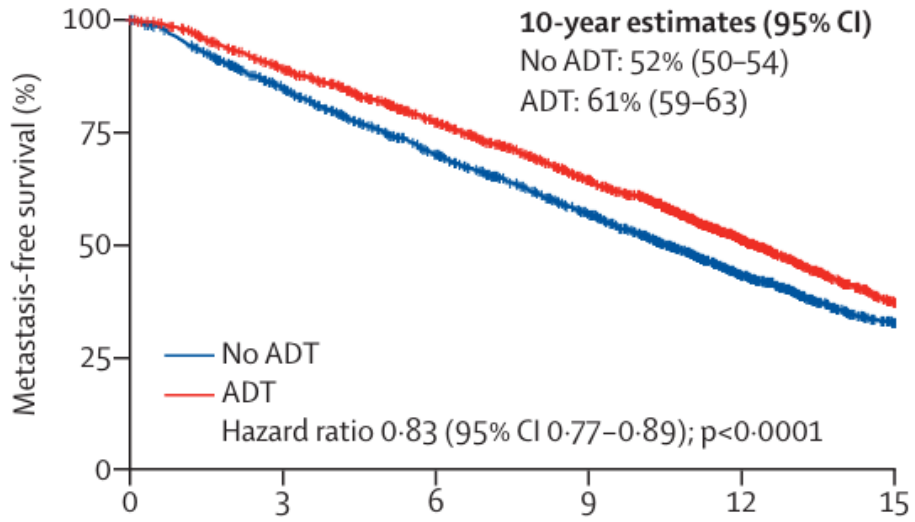
	ADT Use		Neoadjuvant ADT Prolongation		Adjuvant ADT Prolongation	
	Control RT alone	**Experimental** RT+ADT	**Control** 3-4 months ADT	**Experimental** 6-9 months ADT	**Control** 4-6 months ADT	**Experimental** 18-36 months ADT
N=	2557	2579	1103	1110	1900	1874
Follow-up (median, IQR), yrs	12.9 (9.0-17.0)		10.3 (8.8-11.2)		10.9 (7.0-14.8)	
NCCN						
Low	500 (19.9)	469 (18.6)	4 (0.4)	5 (0.5)	58 (3.1)	54 (2.9)
Intermediate	1,197 (47.6)	1,230 (48.7)	685 (62.1)	671 (60.5)	482 (25.4)	487 (26.0)
High	819 (32.6)	828 (32.8)	414 (37.5)	434 (39.1)	1,356 (71.5)	1,332 (71.1)

>5,000 patients
>12 year median f/u

>2,200 patients
>10 year median f/u

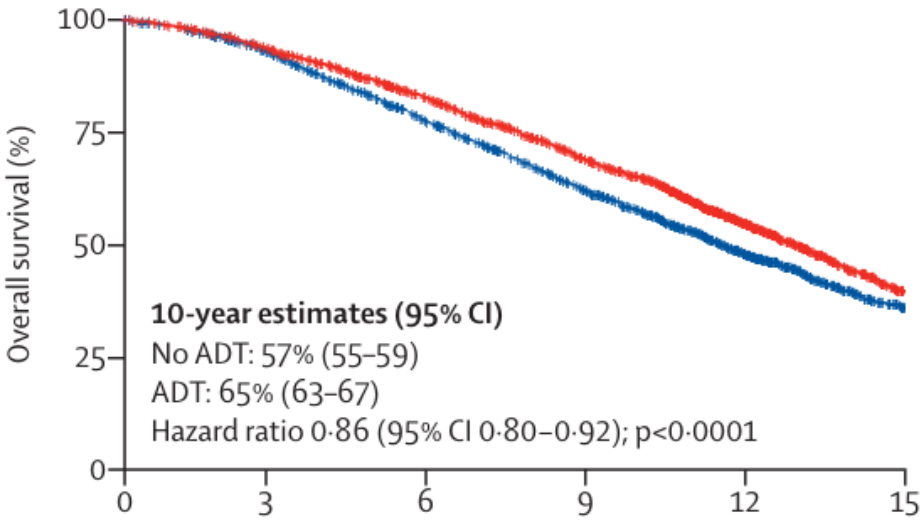
>3,600 patients
>10 year median f/u

Addition of ADT significantly improves MFS and OS



Number at risk (number censored)						
No ADT (1600 events)	2576 (2)	2128 (63)	1695 (133)	1289 (224)	722 (514)	335 (761)
ADT (1399 events)	2555 (4)	2226 (56)	1828 (166)	1415 (282)	754 (689)	332 (951)

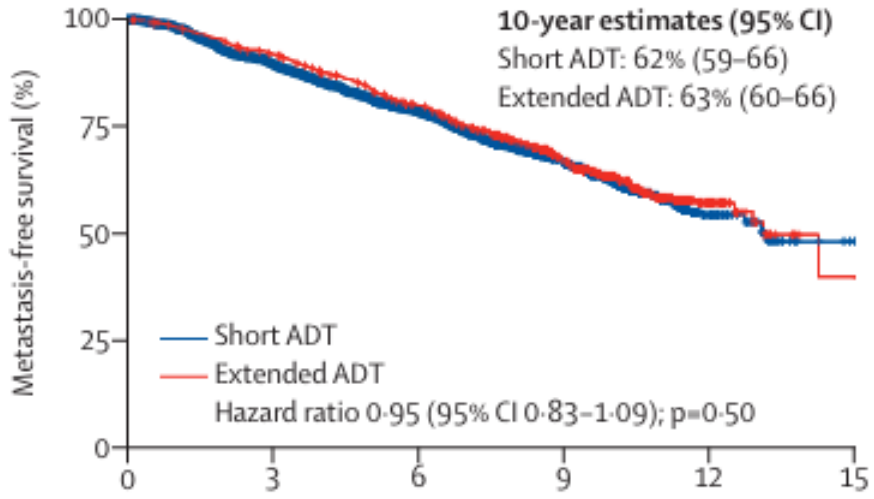
NNT of **11**



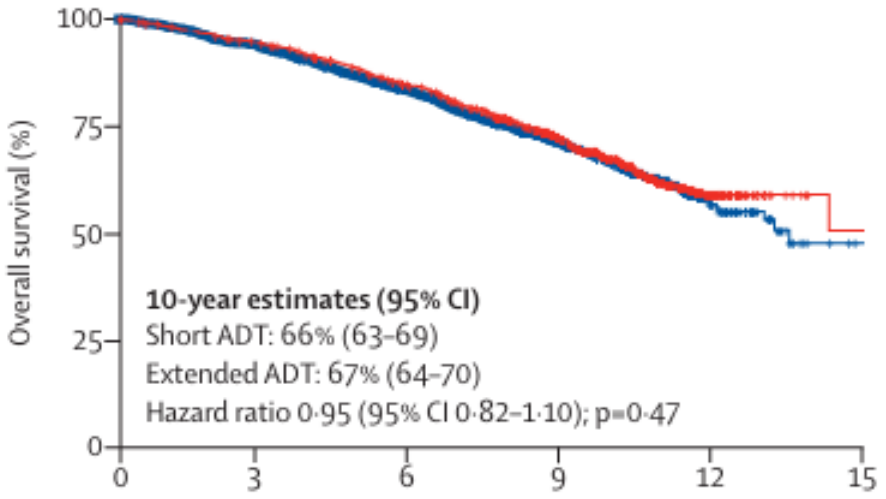
Number at risk (number censored)						
No ADT (1489 events)	2579 (2)	2304 (64)	1848 (147)	1392 (245)	782 (576)	353 (862)
ADT (1316 events)	2557 (4)	2314 (58)	1937 (172)	1509 (292)	796 (739)	344 (1024)

NNT of **12.5**

Neoadjuvant ADT prolongation did not improve outcomes



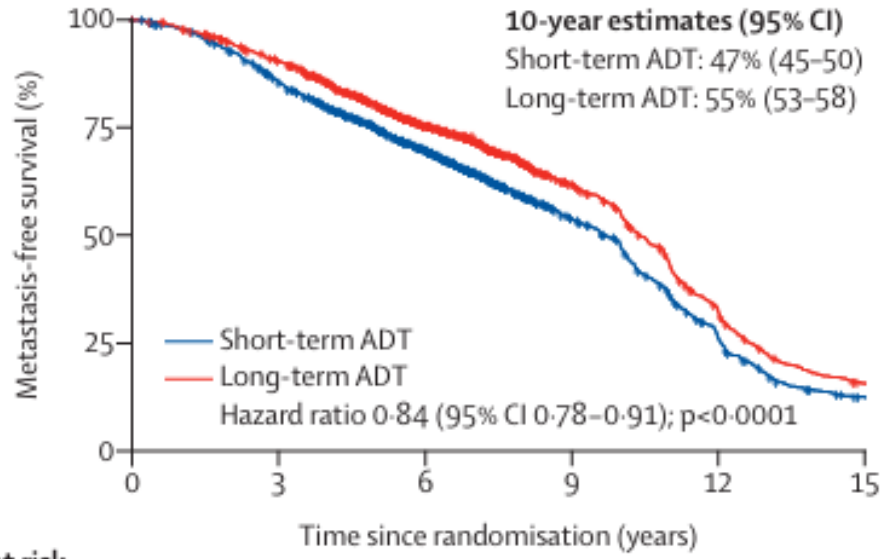
Number at risk (number censored)						
Short ADT (415 events)	1109 (0)	980 (10)	826 (47)	561 (197)	62 (637)	7 (689)
Extended ADT (400 events)	1103 (1)	999 (14)	841 (43)	524 (238)	60 (648)	4 (700)



Number at risk (number censored)						
Short ADT (379 events)	1109 (0)	1022 (10)	874 (47)	597 (204)	68 (670)	8 (725)
Extended ADT (361 events)	1103 (1)	1023 (14)	890 (43)	565 (243)	70 (673)	6 (736)

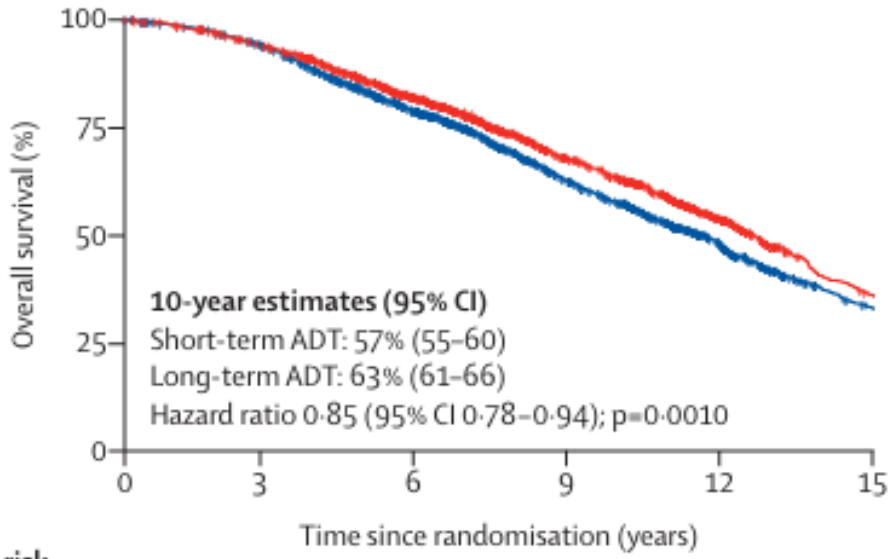
There is no oncologic benefit of neoadjuvant ADT prolongation

Adjuvant ADT prolongation significantly improves MFS and OS



Number at risk (number censored)						
Short-term ADT (1294 events)	1874 (3)	1575 (30)	1105 (225)	627 (485)	294 (508)	128 (522)
Long-term ADT (1224 events)	1900 (1)	1687 (31)	1190 (267)	711 (565)	361 (588)	169 (595)

NNT of 12.5



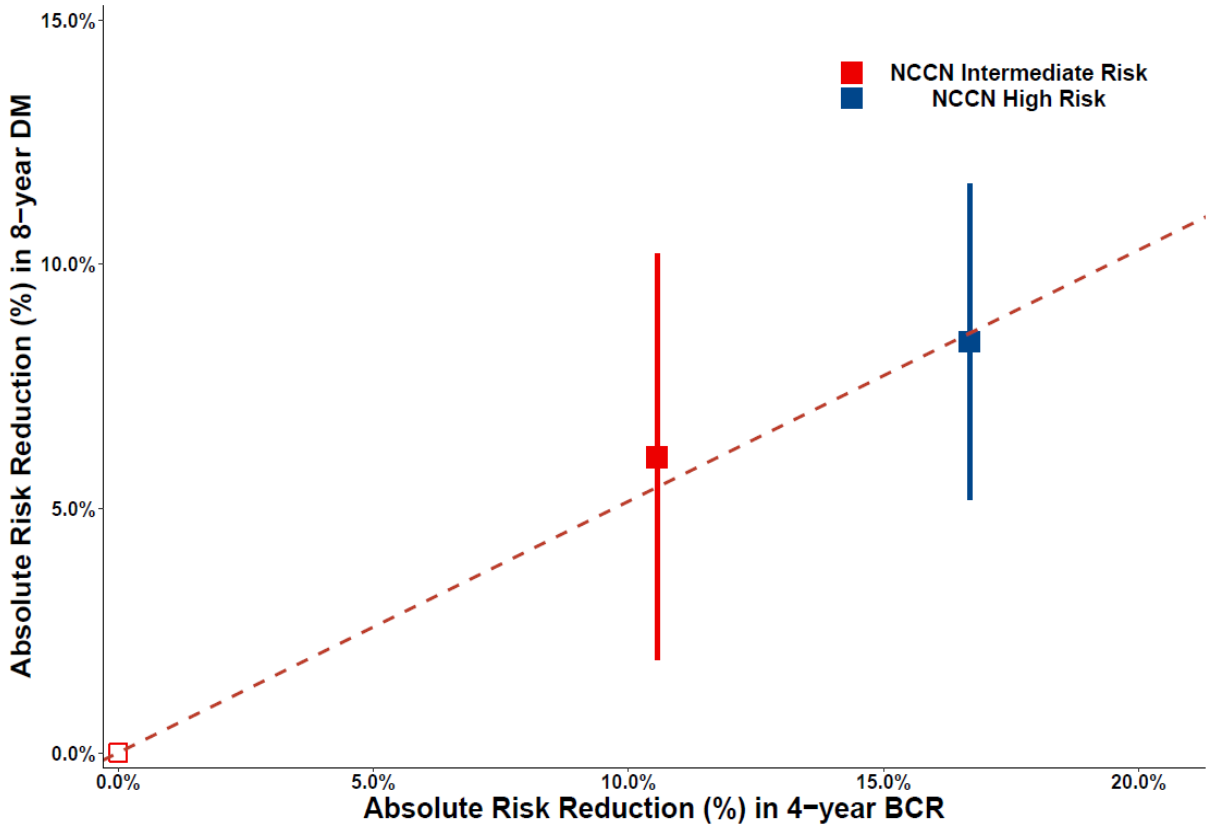
Number at risk (number censored)						
Short-term ADT (903 events)	1874 (3)	1703 (40)	1231 (256)	722 (550)	338 (791)	146 (908)
Long-term ADT (839 events)	1900 (1)	1733 (41)	1279 (288)	773 (610)	382 (867)	179 (975)

NNT of 16.7

Absolute Benefit of Adjuvant ADT Greater in High vs Intermediate Risk

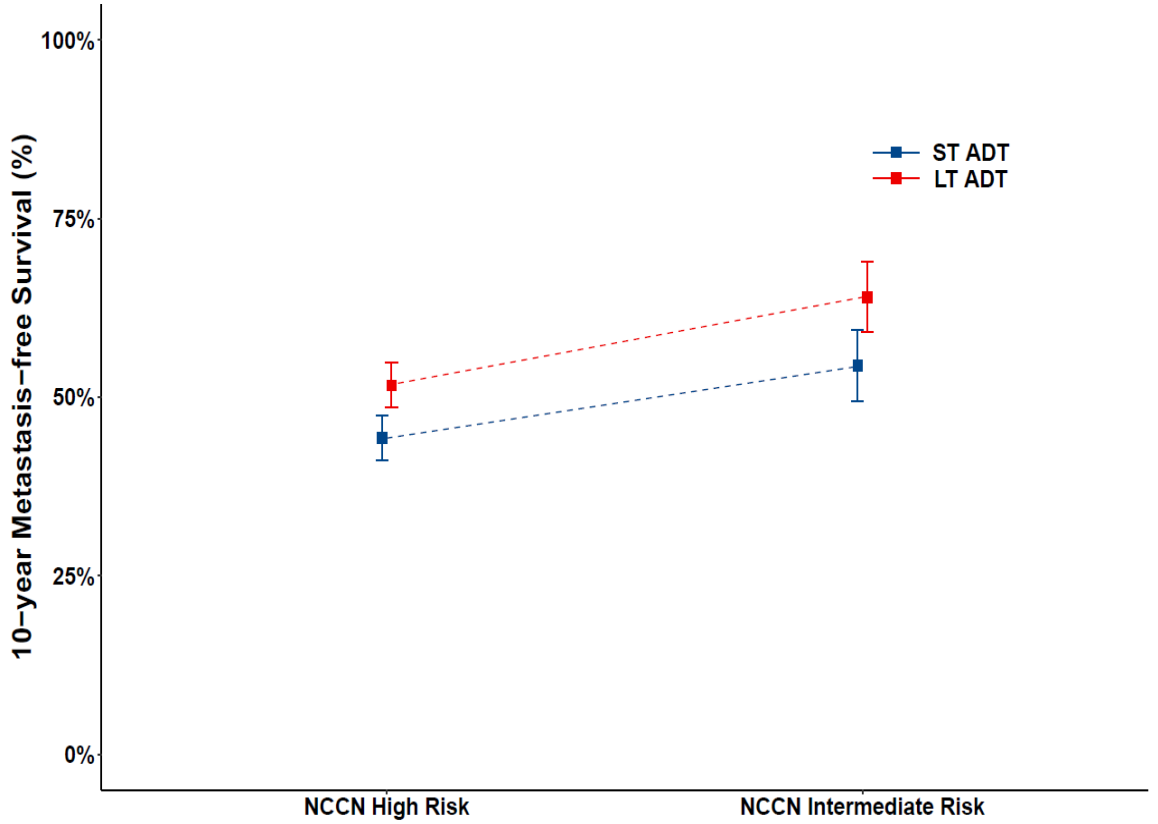
Number Needed to Treat:

- Intermediate Risk: **16.1** for 10-year DM
- High Risk: **10.4** for 10-year DM



Relative Benefit of Adjuvant ADT Similar Irrespective of NCCN Risk Group

Adjuvant ADT prolongation				
NCCN risk group	..	..	..	0·72
High	2688	0·85 (0·77–0·93)	0·0005	..
Intermediate	969	0·81 (0·69–0·94)	0·0058	..



Optimal Duration of Adjuvant ADT Variable By Prognostic Risk

DHARMA

Optimal duration of androgen deprivation therapy (ADT) with definitive radiotherapy for prostate cancer: An individual patient data (IPD) meta-analysis from the international MARCAP consortium

N. G. Zaorsky[1], Y. Sun[1], A. Nabid[2], A. Zapatero[3], M. Bolla[4], J. W. Denham[5], T. M. Pisansky[6], H. M. Sandler[7], J. A. Efstathiou[8], P. Maingon[9], A. Steigler[5], L. Souhami[10], N. Carrier[11], J. Armstrong[12], W. C. Jackson[13], A. Y. Jia[14], T. M. Ma[15], T. Romero[16], A. U. Kishan[15], and D. E. Spratt[1]

MARCAP

	Total (N=10,266)
ADT duration (mos)	
0	1853 (18 %)
3	265 (3 %)
4	2481 (24 %)
6	2087 (20 %)
8	129 (1 %)
9	729 (7 %)
18	855 (8 %)
28	884 (9 %)
36	983 (10 %)

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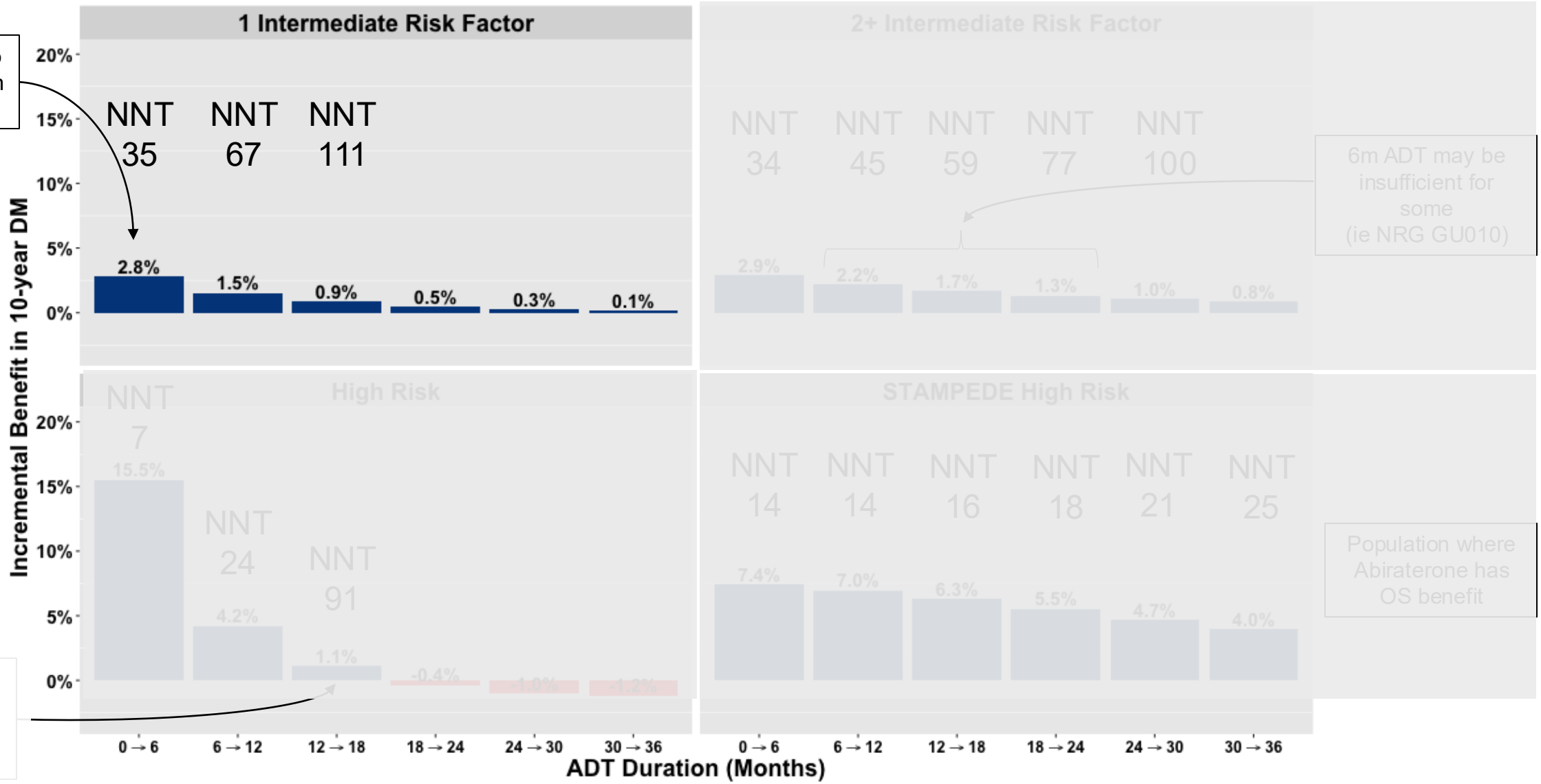
Optimal Duration of Adjuvant ADT Variable By Prognostic Risk

MARCAP

Almost identical to what was shown in NRG/RTOG 0815



6m ADT may be insufficient for some (ie NRG GU010)

Population where Abiraterone has OS benefit

Does high-risk need 18m of ADT? (NRG GU009 testing 12m)

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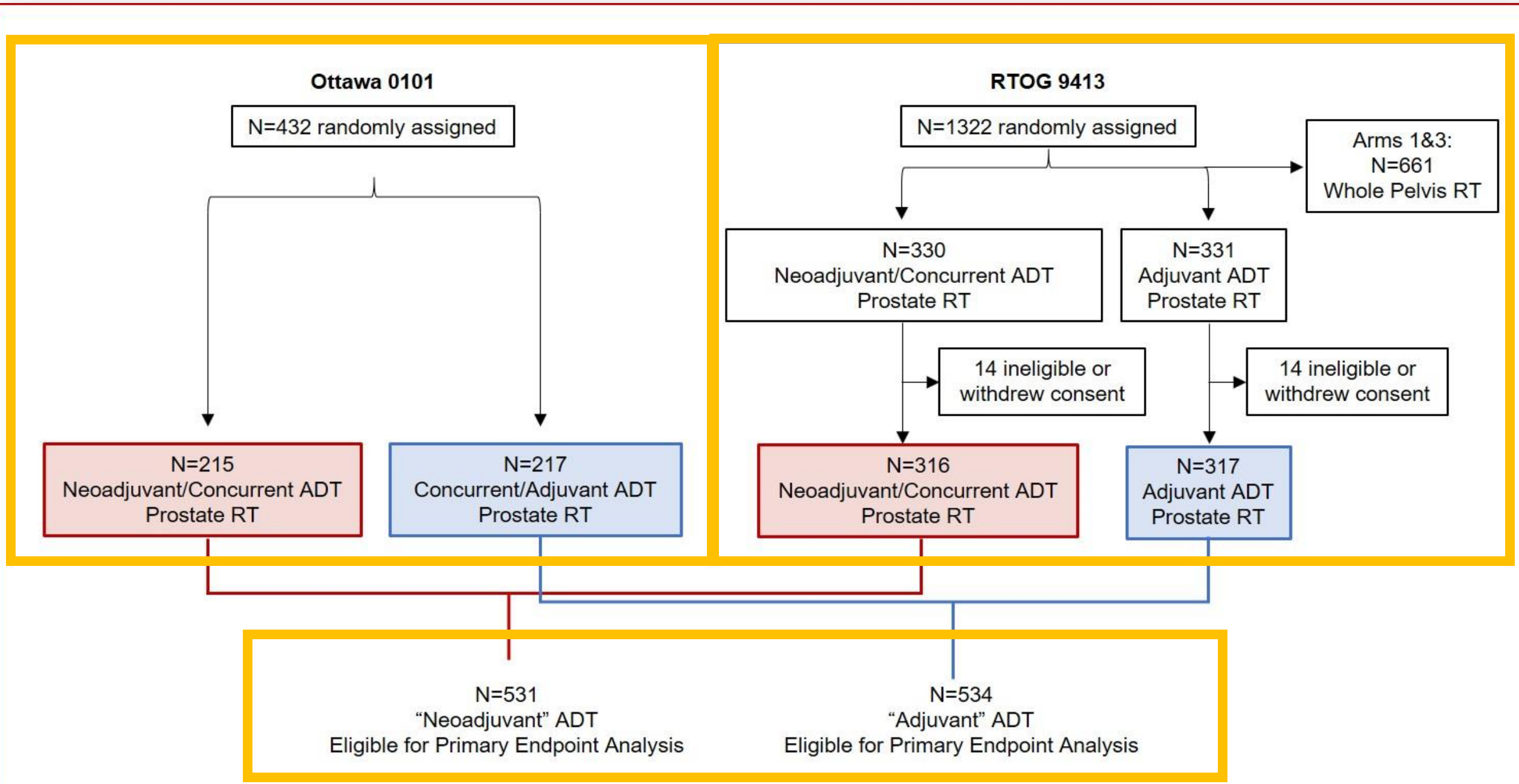
Optimal ADT Sequencing



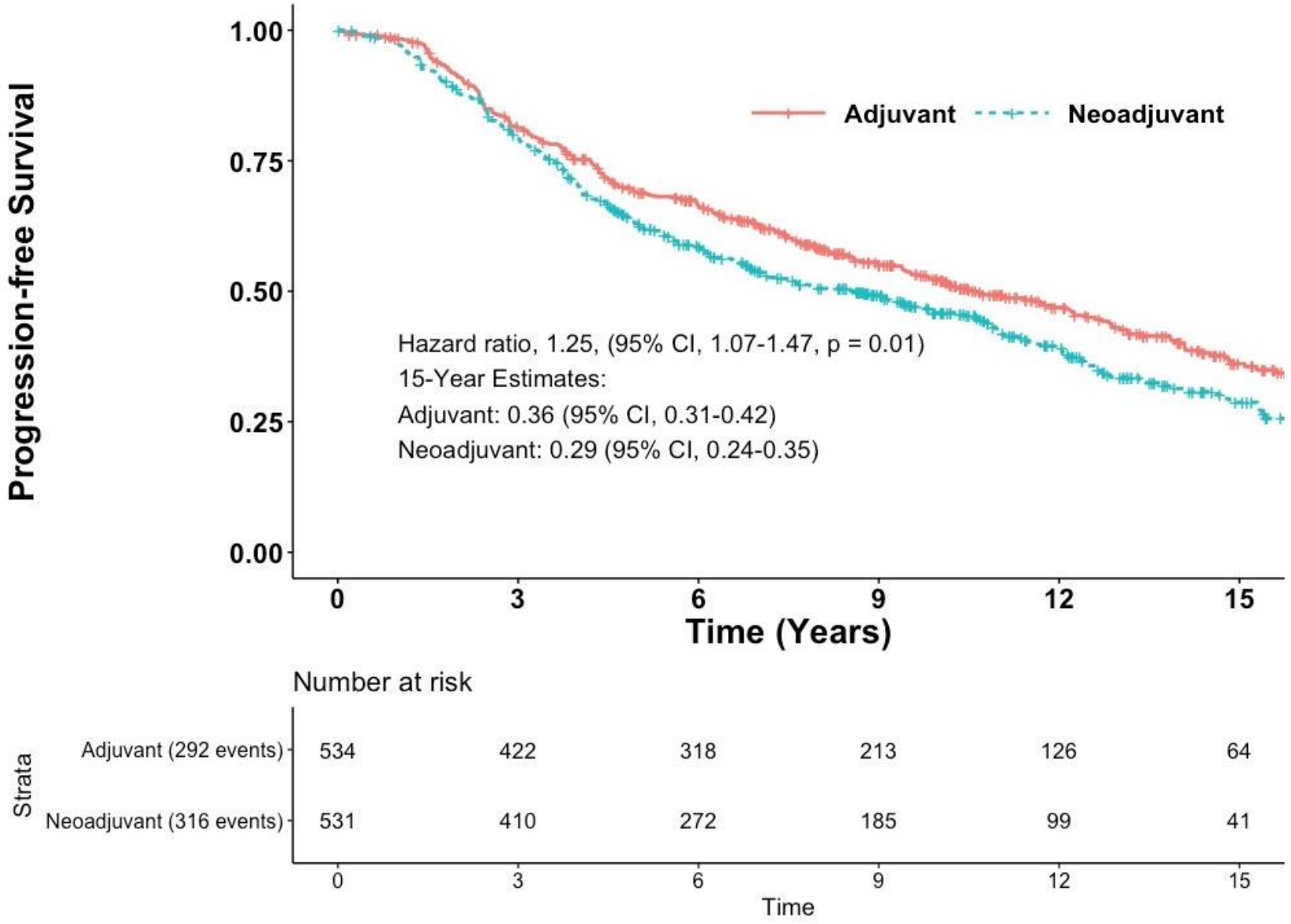
Results

	All Patients
N	1065
Age (years)	
Median (IQR)	70 (65, 74)
Gleason Score	
< 7	266 (25.0)
7	**619 (58.1)**
8 - 10	180 (16.9)
T Stage	
T1/T2a	448 (42.1)
T2b/T2c	**408 (38.3)**
T3/T4	**209 (19.6)**
PSA (ng/mL)	
Median (IQR)	14.10 (8.30, 26.50)
0-10	376 (35.3)
11-20	**310 (29.1)**
>20	**379 (35.6)**

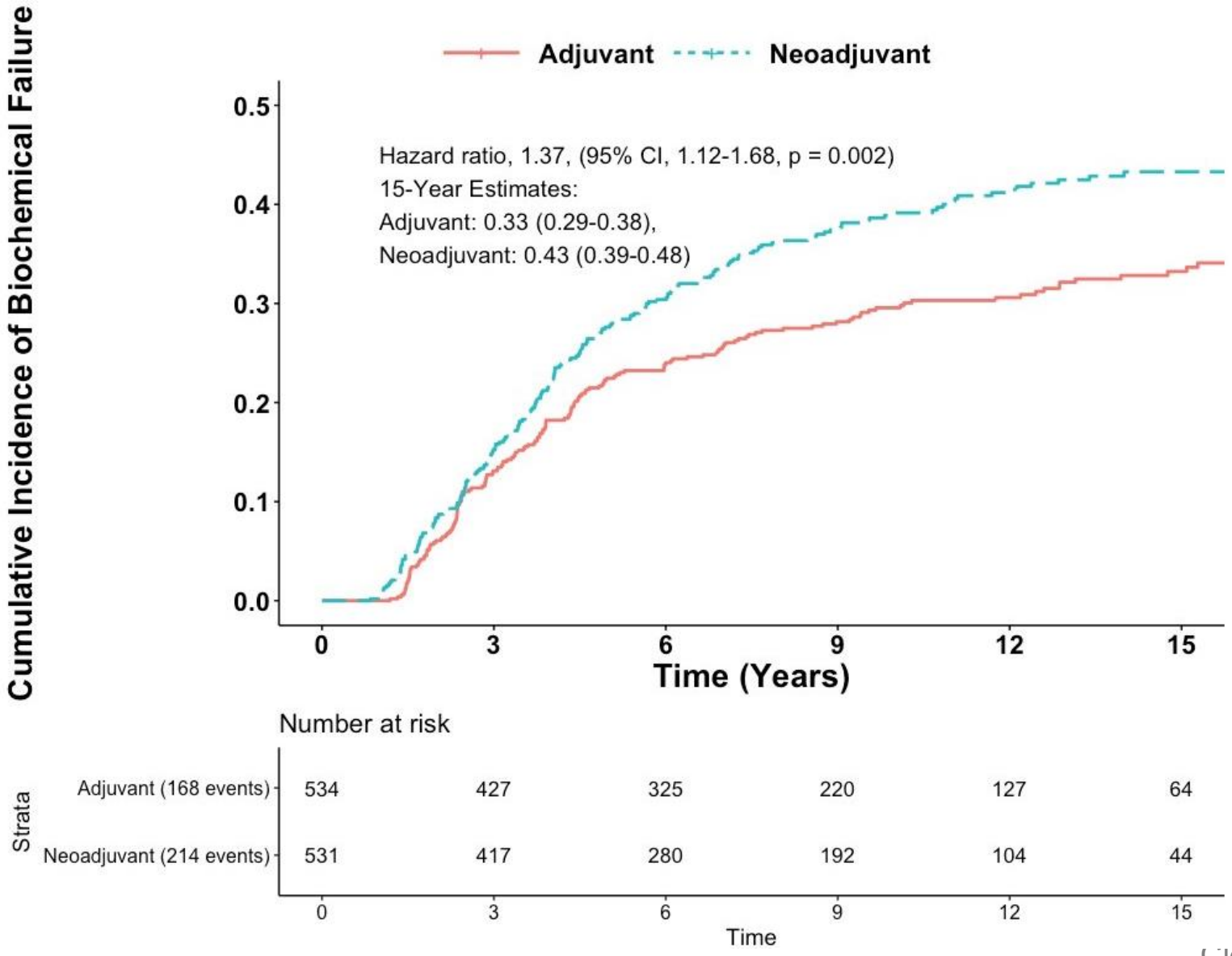
Median follow-up: 14.9 years

All baseline characteristics were well balanced between groups

Progression-free survival was superior with adjuvant ADT



Biochemical recurrence was lower with adjuvant ADT



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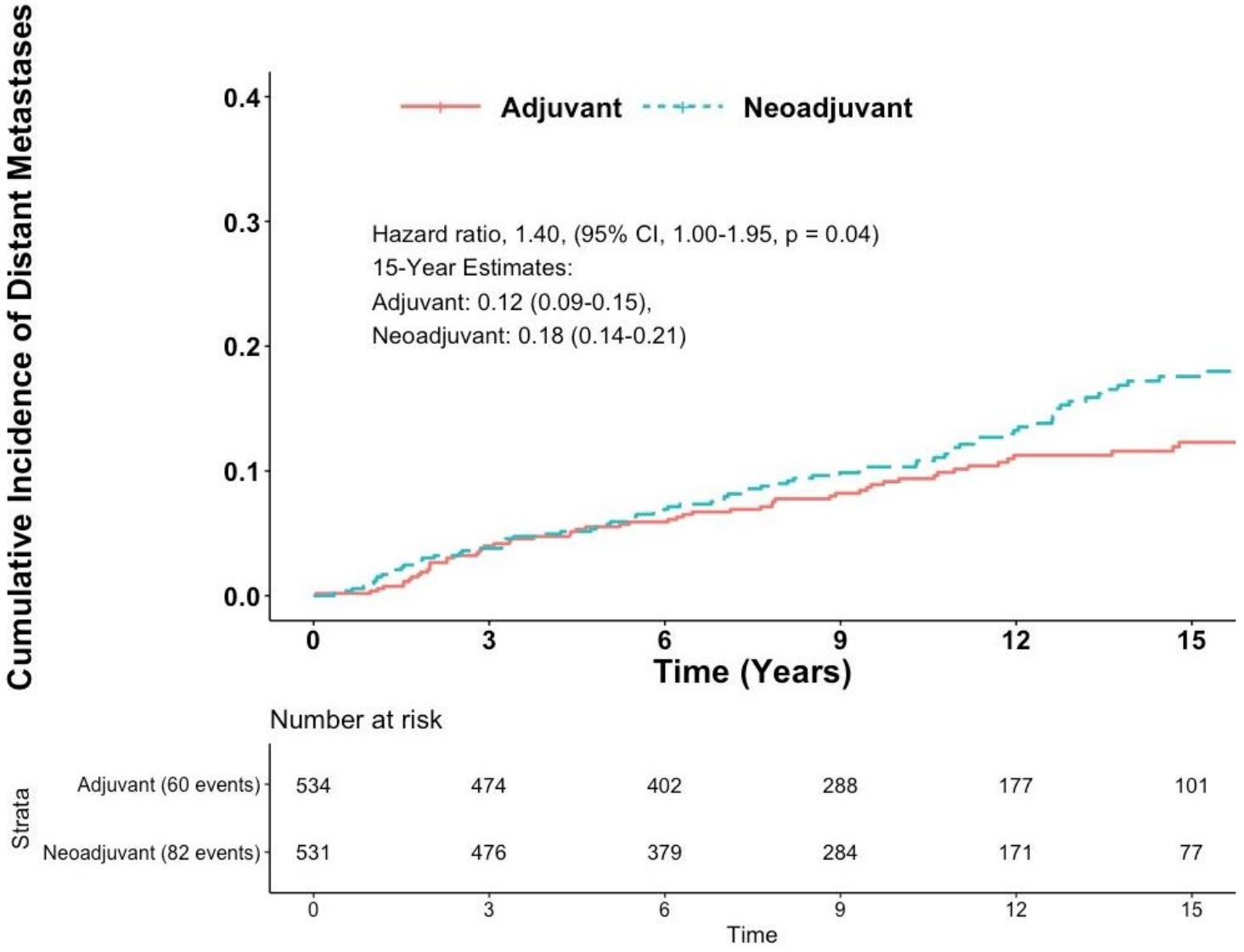
Distant metastases were lower with adjuvant ADT



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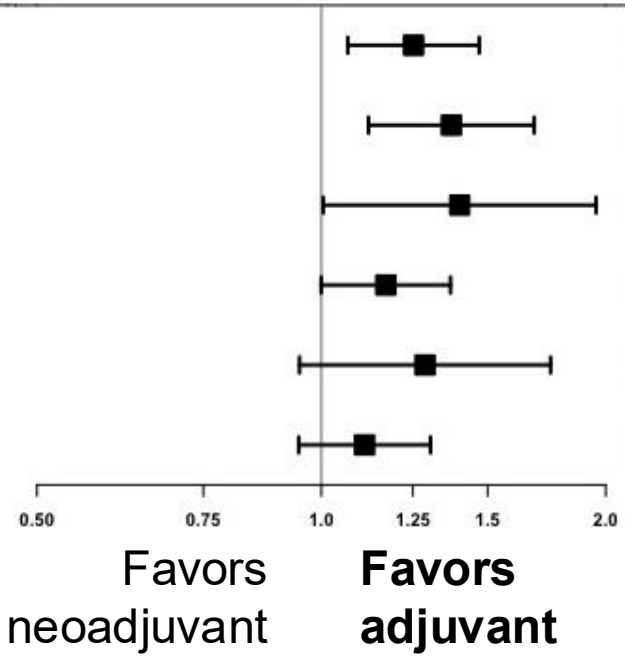
Point estimates favored adjuvant ADT for all endpoints with no increase in late toxicity

Endpoint	Neoadjuvant Incidence/N	Adjuvant Incidence/N	15-yr Absolute Benefit of Adjuvant ADT (%, CI 95%)	HR (95%)	p value
Progression-free Survival	316/531	292/534	7.4 (-0.1, 14.8)	1.25 (1.07, 1.47)	0.01
Biochemical Failure	214/531	168/534	10.1 (3.8, 16.3)	1.37 (1.12, 1.68)	0.002
Distant Metastasis	82/531	60/534	5.3 (0.5, 10.1)	1.40 (1.00, 1.95)	0.04
Metastasis-free Survival	324/531	298/534	7.2 (0.3, 14.1)	1.17 (1.00, 1.37)	0.050
Prostate Cancer-specific Mortality	91/531	73/534	5.8 (0.5, 11.0)	1.29 (0.95, 1.75)	0.10
Overall Survival	307/531	291/534	5.4 (-1.6, 12.3)	1.11 (0.95, 1.30)	0.20



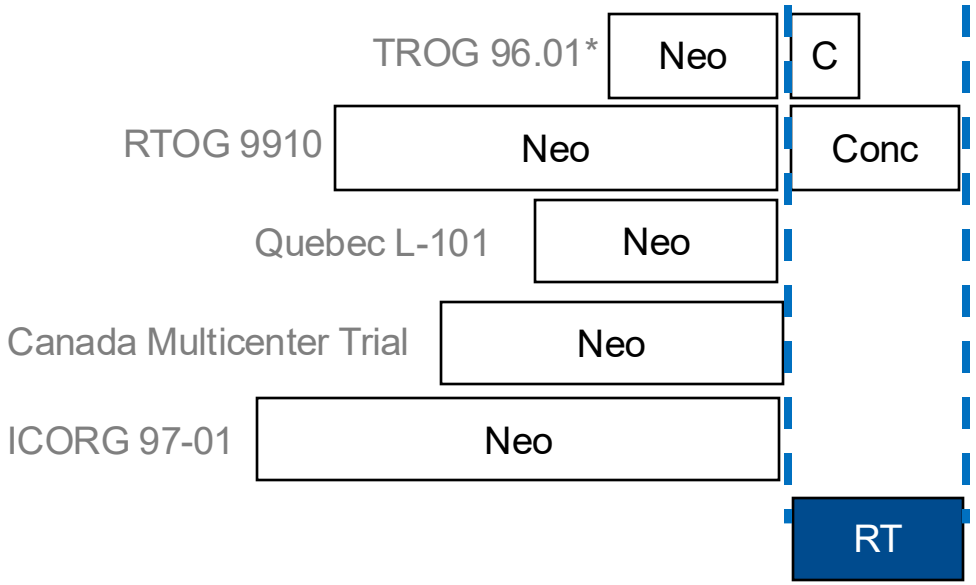
15-year cumulative incidence of late grade 3-5 toxicity:

GU 5% vs 5% (p=0.76)

GI 3% vs 2% (p=0.33)

Does this make sense? Or just another post-hoc analysis

These trials *adding* neoadjuvant ADT or *prolonging* neoadjuvant ADT:
All NEGATIVE FOR Metastasis, PCSM, and OS

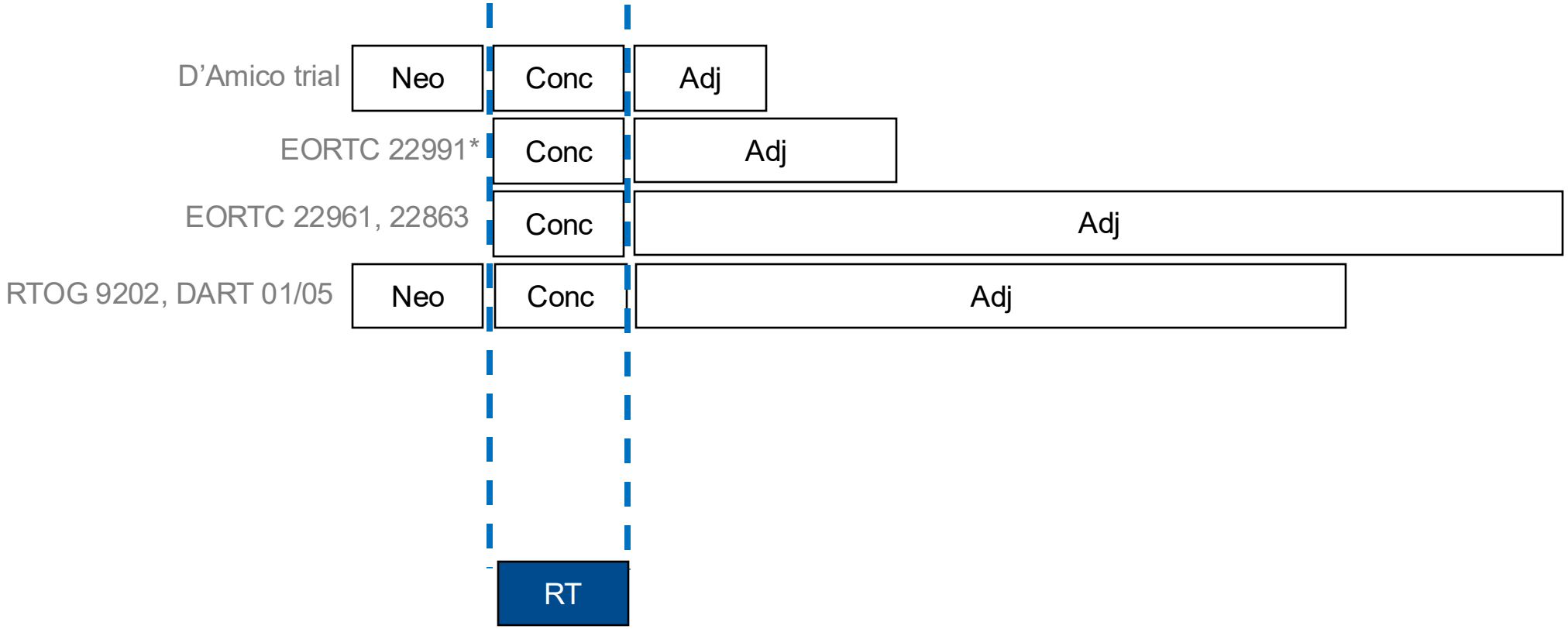


*0 vs 3m was negative for metastasis, PCSM, and OS

Does this make sense? Or just another post-hoc analysis

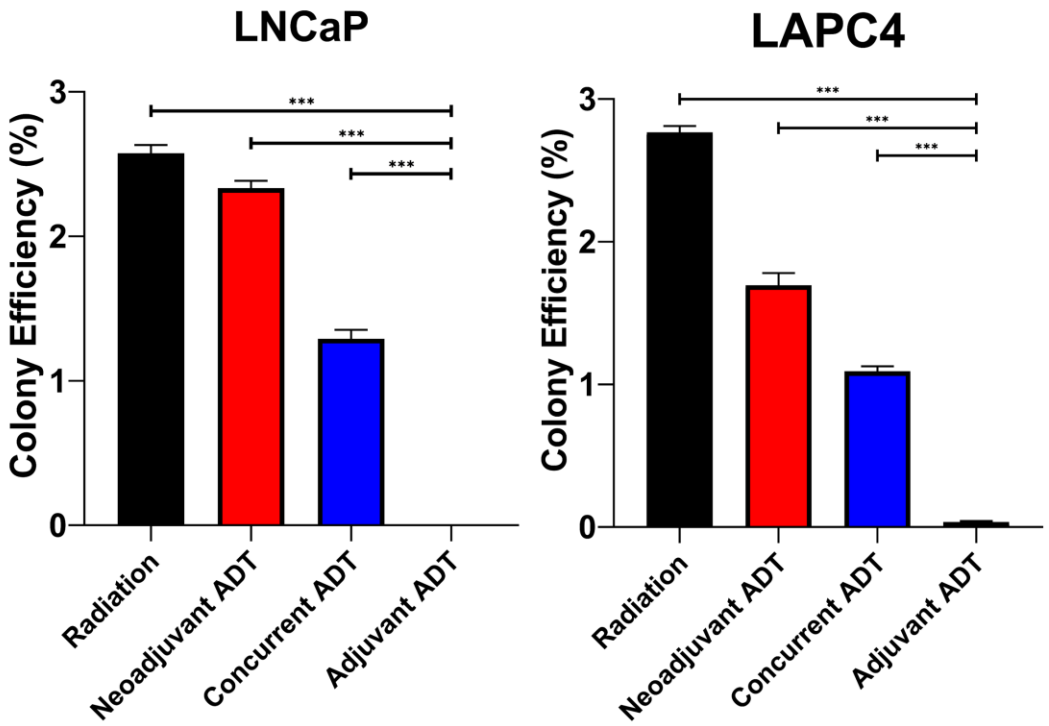
These trials using adjuvant ADT or *prolonging* adjuvant ADT:

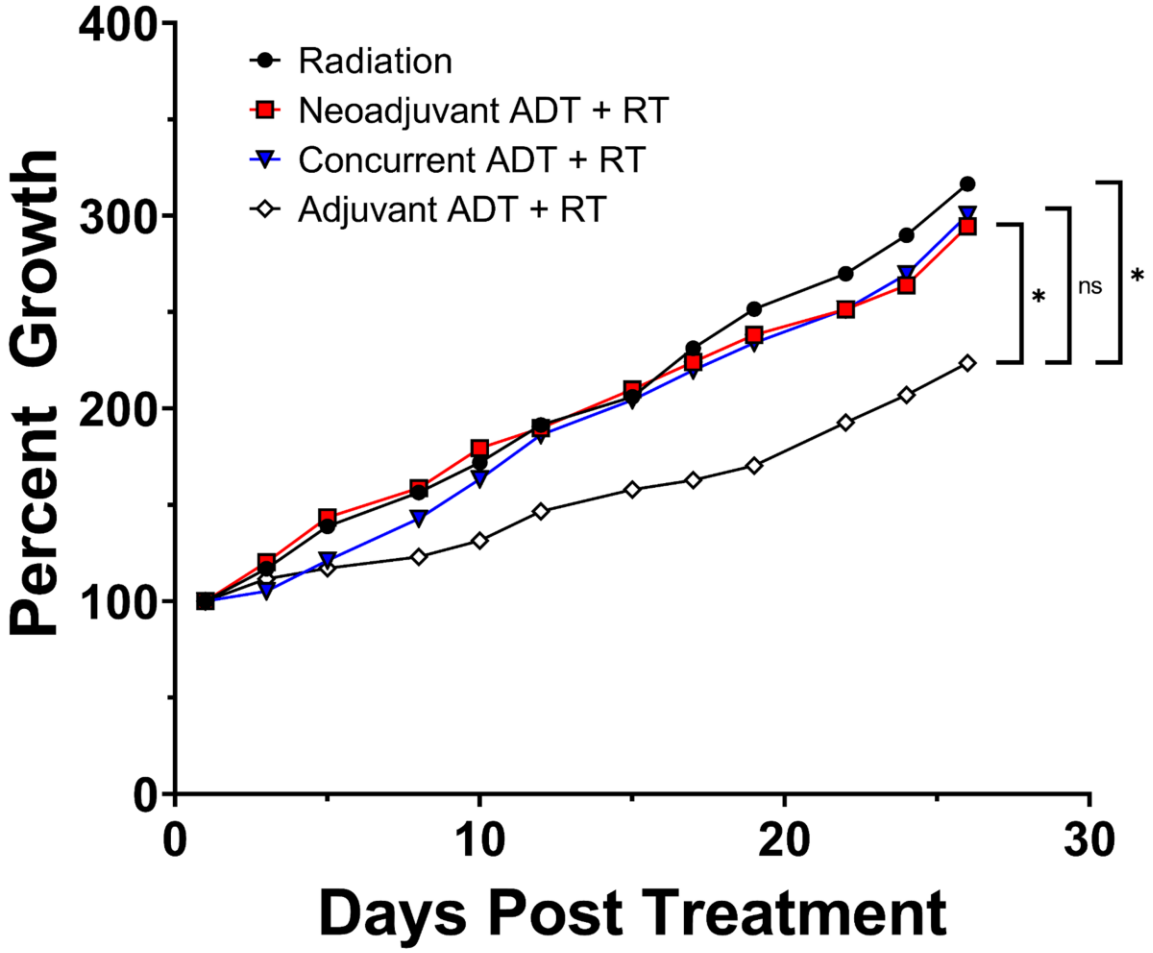
All POSITIVE for Metastasis, PCSM, or OS



*p=0.053 for metastases

Grounded in Biology





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ADT Intensity

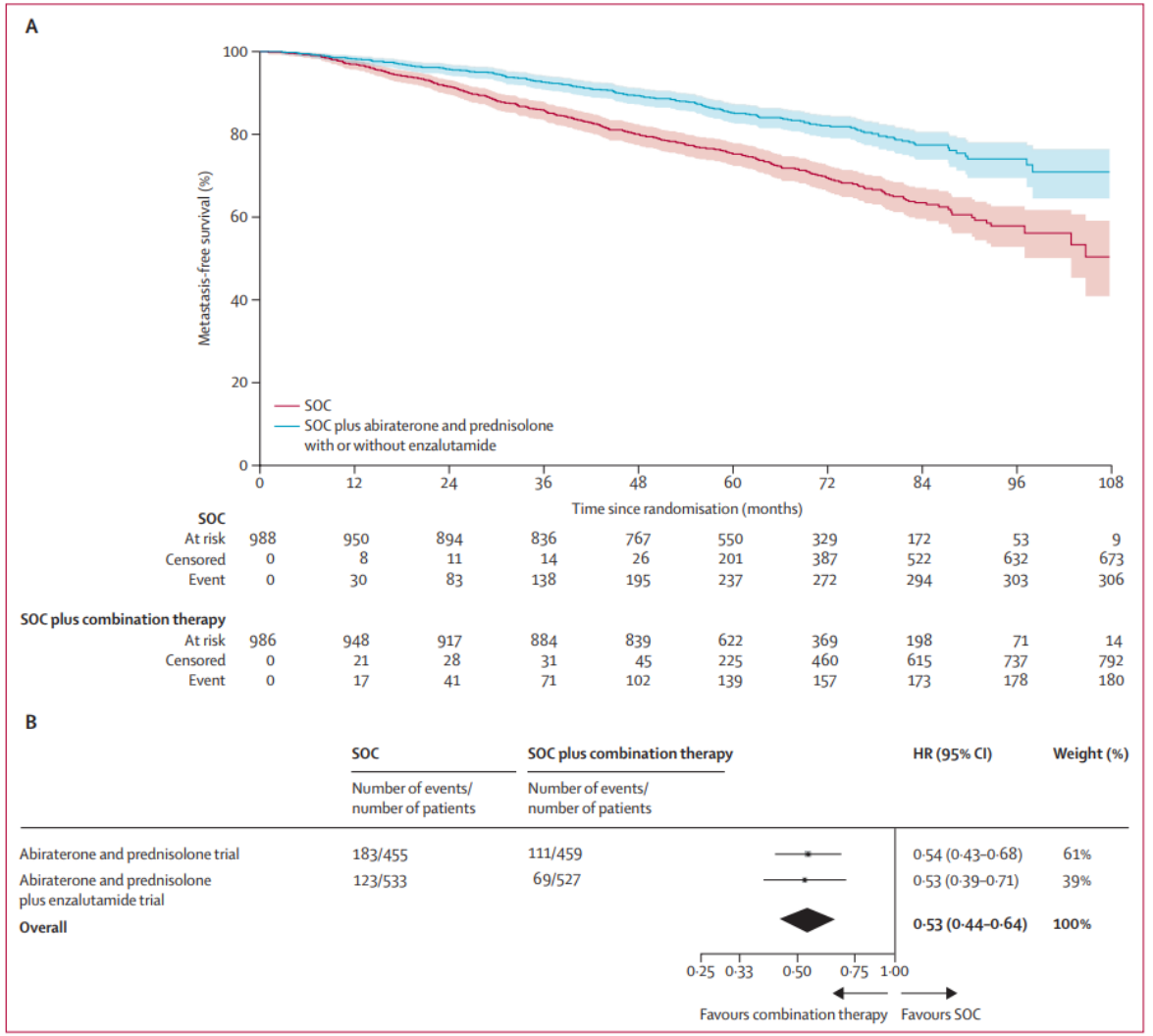
Abiraterone

Abiraterone acetate and prednisolone with or without enzalutamide for high-risk non-metastatic prostate cancer: a meta-analysis of primary results from two randomised controlled phase 3 trials of the STAMPEDE platform protocol

	Control group in the abiraterone trial (n=455)	Control group in the abiraterone and enzalutamide trial (n=533)	Combination therapy group in the abiraterone trial (n=459)	Combination therapy group in the abiraterone and enzalutamide trial (n=527)
Age at randomisation, years				
Median (IQR)	67 (62–73)	69 (64–73)	68 (63–73)	68 (63–73)
Range	48–83	43–86	44–84	46–86
PSA at randomisation, ng/ml				
Median (IQR)	40 (16–83)	34 (15–74)	34 (15–68)	32 (13–74)
Range	1–1000	1–2773	1–2300	0–556
Nodal status of newly diagnosed patients				
N0	256 (56%)	327 (61%)	253 (55%)	325 (62%)
N1	187 (41%)	190 (36%)	181 (39%)	187 (35%)
Nodal status of relapsed patients				
N0	7 (2%)	8 (2%)	14 (3%)	7 (1%)
N1	5 (1%)	7 (1%)	10 (2%)	7 (1%)
Nx	0	1 (<1%)	1 (<1%)	1 (<1%)
WHO performance status				
0	375 (82%)	435 (82%)	370 (71%)	429 (81%)
1–2	80 (17%)	98 (18%)	89 (19%)	98 (19%)
Time from diagnosis to randomisation				
Median (IQR)	83 (63–107)	84 (65–104)	83 (62–105)	85 (68–105)
Range	5–2771	4–4807	1–5274	2–5434
Gleason sum score				
<8	105 (23%)	95 (18%)	107 (23%)	98 (19%)
8–10	348 (76%)	437 (82%)	351 (77%)	427 (81%)
Missing	2	1	1	2
T stage at randomisation				
T0–T2	39 (9%)	30 (6%)	30 (7%)	26 (5%)
T3–T4	41 (90%)	496 (93%)	423 (92%)	493 (94%)
TX	5 (1%)	7 (1%)	6 (1%)	8 (2%)
Local radiotherapy as standard of care				
No	83 (18%)	62 (12%)	87 (19%)	58 (11%)
Yes	372 (82%)	471 (88%)	372 (81%)	469 (89%)

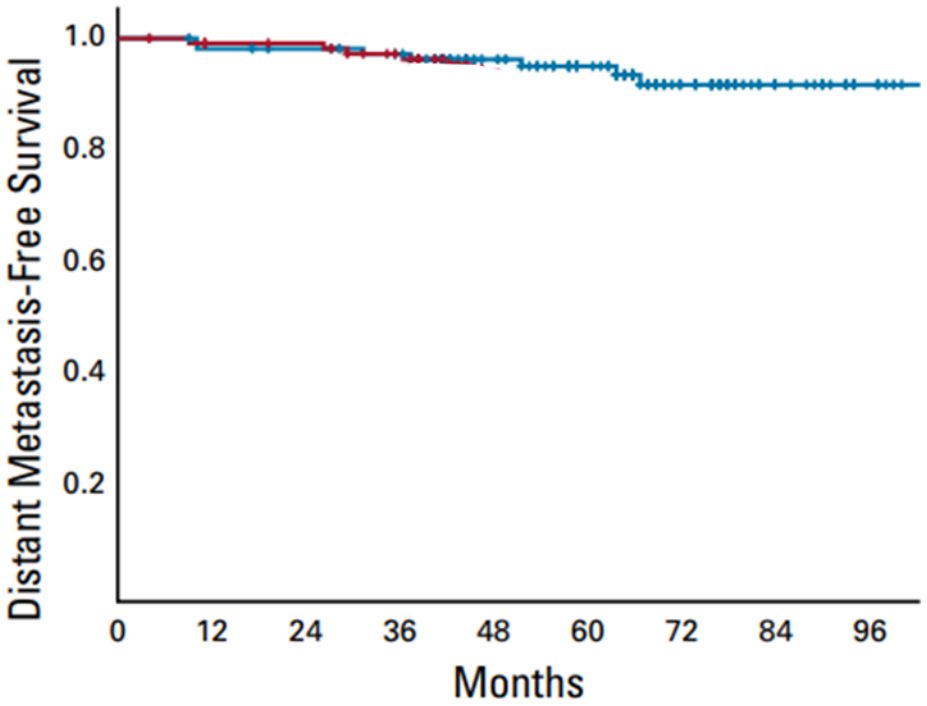
Data are n (%) or n, unless stated otherwise. PSA=prostate-specific antigen.

Table 1: Baseline characteristics

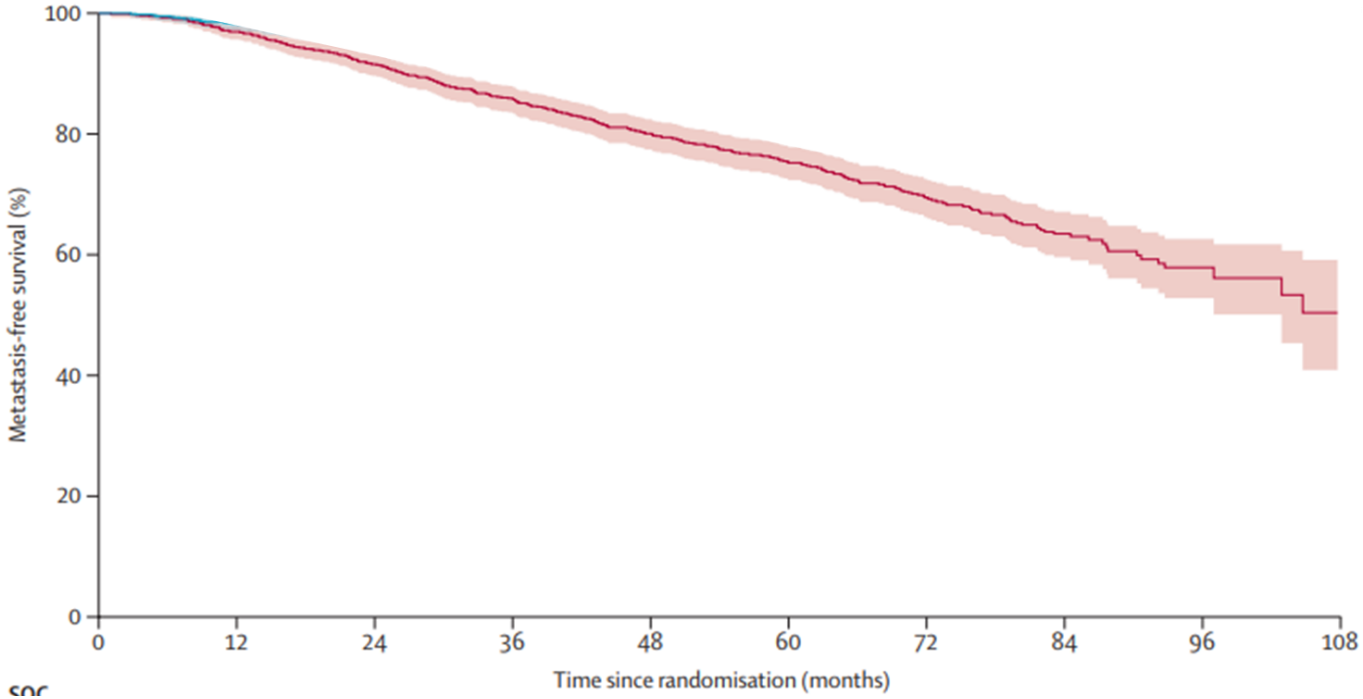


Is this our normal high risk?

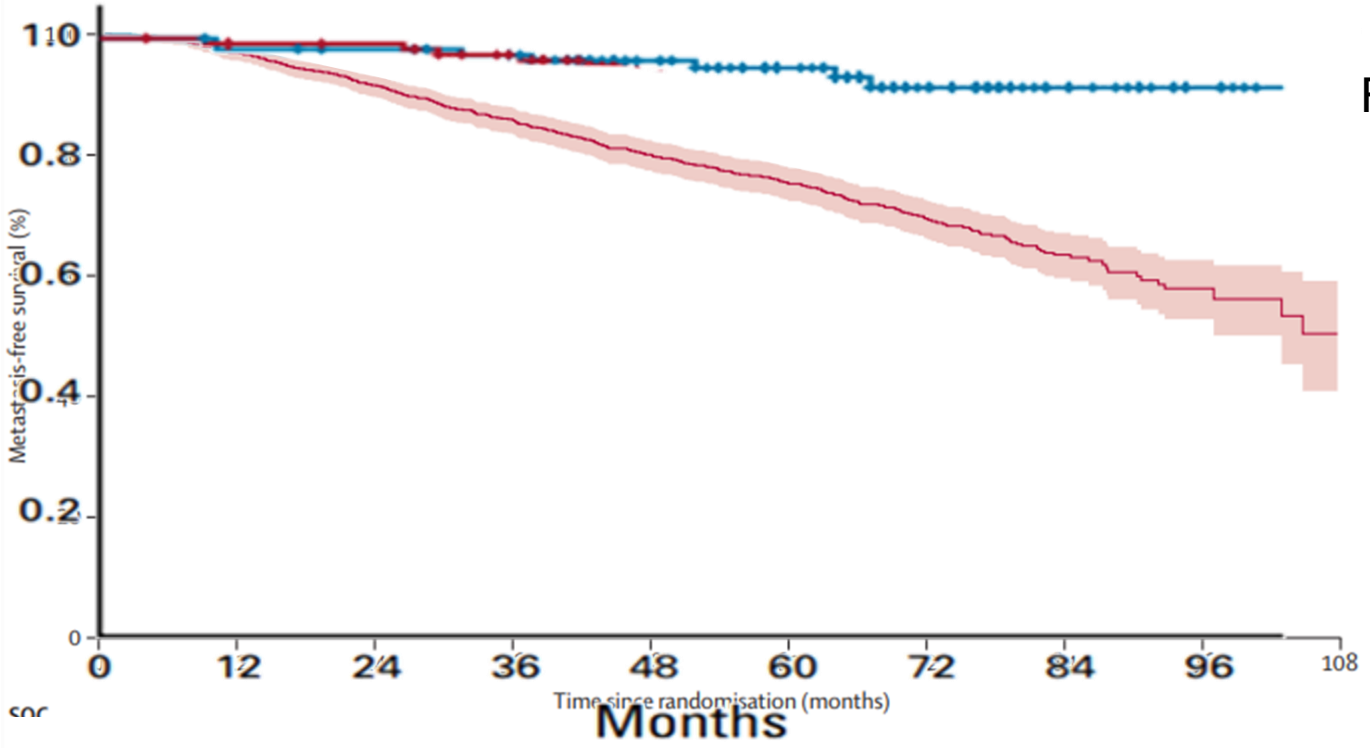
POP-RT
RT+LT-ADT



STAMPEDE
RT+LT-ADT



Is this our normal high risk?



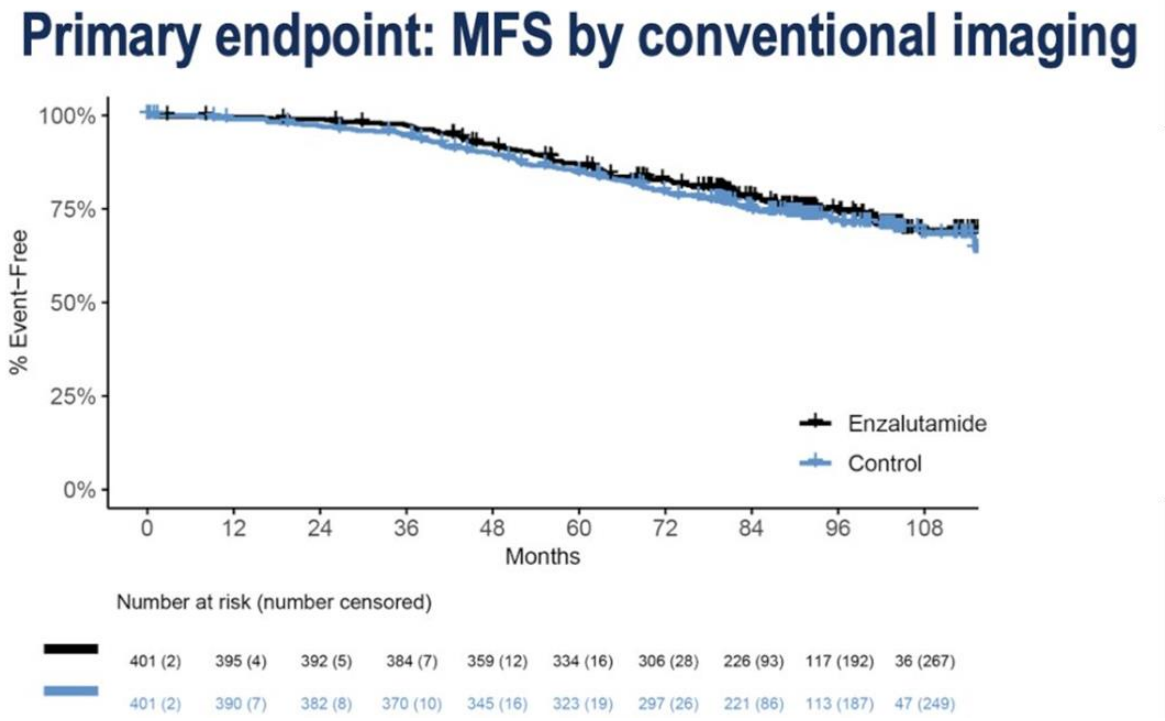
POP-RT
RT+LT-ADT

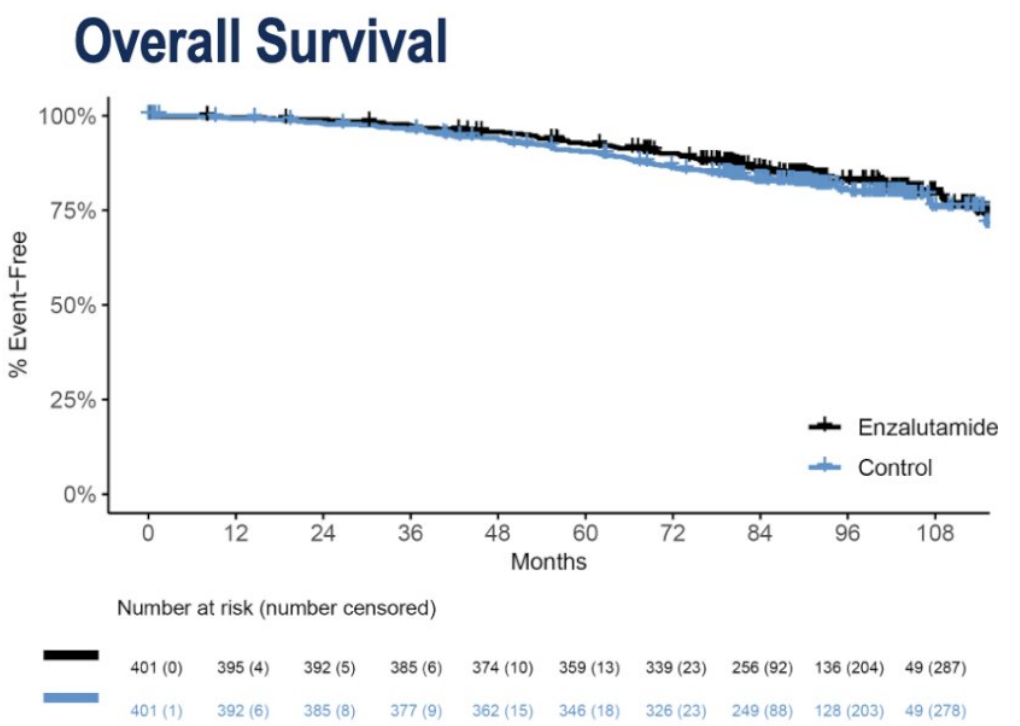
STAMPEDE
RT+LT-ADT

The truth shall set you free…

ENZARAD: High, very high risk, cN+

RT+LT-ADT +/- Enzalutamide





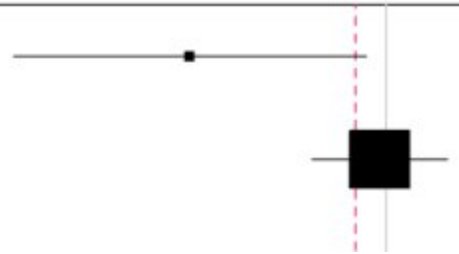
The truth shall set you free…

ENZARAD: High, very high risk, cN+

RT+LT-ADT +/- Enzalutamide

Effects of enzalutamide on MFS in prespecified subgroups

Characteristic	Level	CTRL n/N	ENZA n/N	HR (CI)	P-Value Interaction
Regional lymph nodes involvement	N1	19/42	10/46	0.43 (0.20 to 0.92)	
	N0	90/359	88/355	0.97 (0.72 to 1.30)	0.04

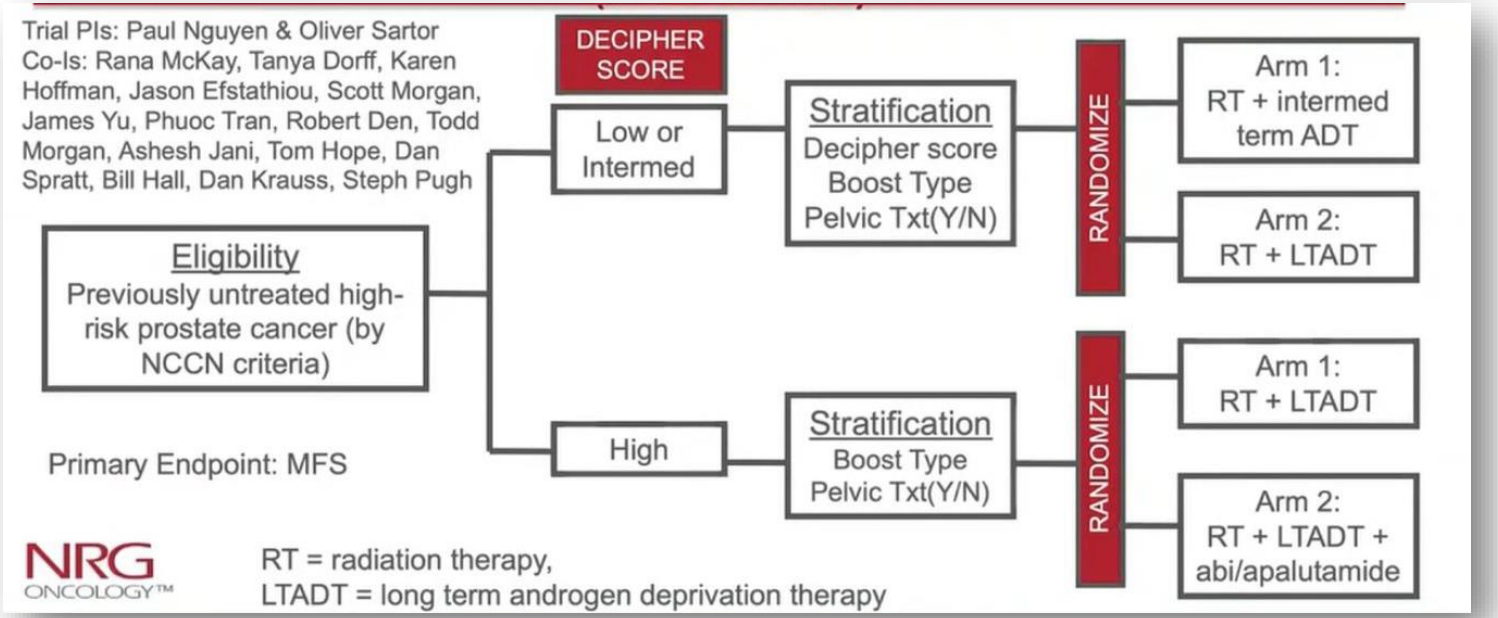


Pending results trials

ATLAS: High risk- RT+LTADT +/- Apalutamide (complete)

DASL-HiCAP: High risk/BCR- RT+ADT +/- Darolutamide (complete)

NRG GU009: High risk/Decipher very high- RT+LT-ADT +/- apalutamide



Dogma of Radiation Oncology

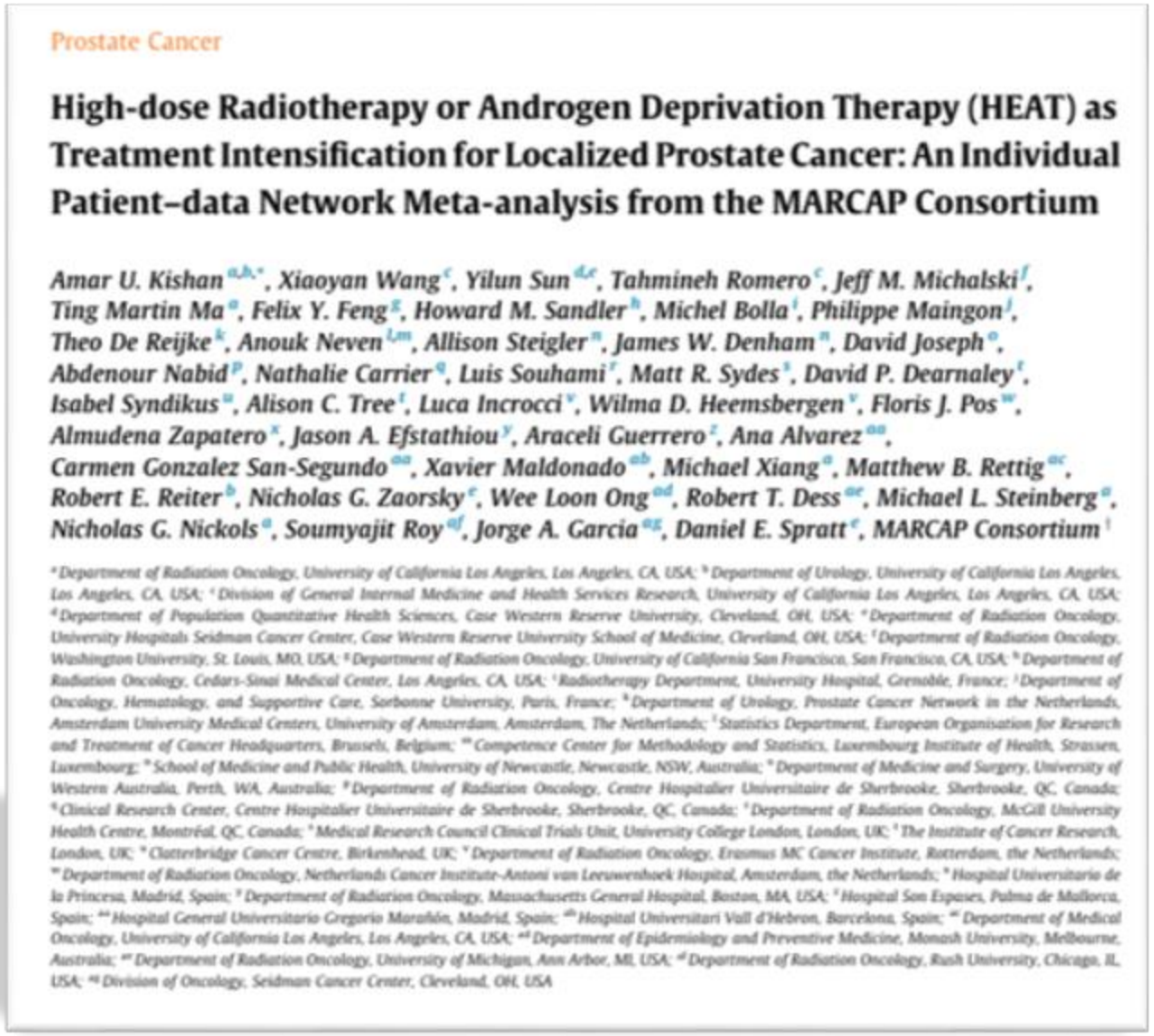
"RT dose escalation can obviate the need for ADT"

Said by many, yet to be proven

Similar Relative Benefit of ADT Use and Adjuvant Prolongation *Irrespective* of RT Dose

	Number of patients	Hazard ratio (95% CI)	p value	$p_{interaction}$
ADT use				
Radiotherapy dose	..	..	..	0·96
High (≥74 Gy)	1018	0·83 (0·68–1·01)	0·063	..
Low (<74 Gy)	4118	0·83 (0·76–0·89)	<0·0001	..

High-dose Radiotherapy or Androgen Deprivation Therapy (HEAT)



Prostate Cancer

High-dose Radiotherapy or Androgen Deprivation Therapy (HEAT) as Treatment Intensification for Localized Prostate Cancer: An Individual Patient–data Network Meta-analysis from the MARCAP Consortium

Amar U. Kishan[a,b,], Xiaoyan Wang[c], Yilun Sun[d,e], Tahmineh Romero[c], Jeff M. Michalski[f], Ting Martin Ma[a], Felix Y. Feng[g], Howard M. Sandler[h], Michel Bolla[i], Philippe Maingon[j], Theo De Reijke[k], Anouk Neven[l,m], Allison Steigler[n], James W. Denham[n], David Joseph[o], Abdenour Nabid[p], Nathalie Carrier[q], Luis Souhami[r], Matt R. Sydes[s], David P. Dearnaley[t], Isabel Syndikus[u], Alison C. Tree[t], Luca Incrocci[v], Wilma D. Heemsbergen[v], Floris J. Pos[w], Almudena Zapatero[x], Jason A. Efstathiou[y], Araceli Guerrero[z], Ana Alvarez[aa], Carmen Gonzalez San-Segundo[aa], Xavier Maldonado[ab], Michael Xiang[a], Matthew B. Rettig[ac], Robert E. Reiter[b], Nicholas G. Zaorsky[e], Wee Loon Ong[ad], Robert T. Dess[ae], Michael L. Steinberg[a], Nicholas G. Nickols[a], Soumyajit Roy[af], Jorge A. Garcia[ag], Daniel E. Spratt[e], MARCAP Consortium[†]*

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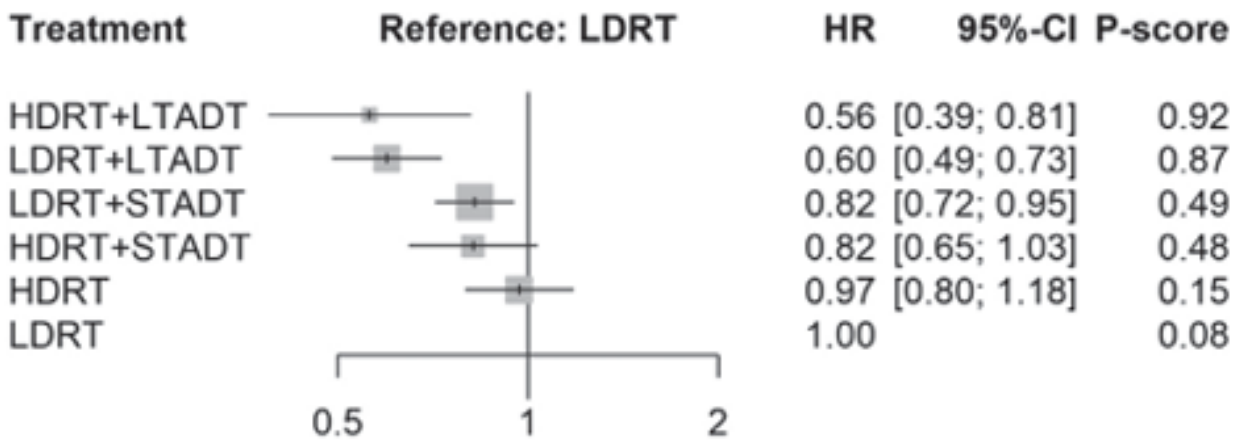
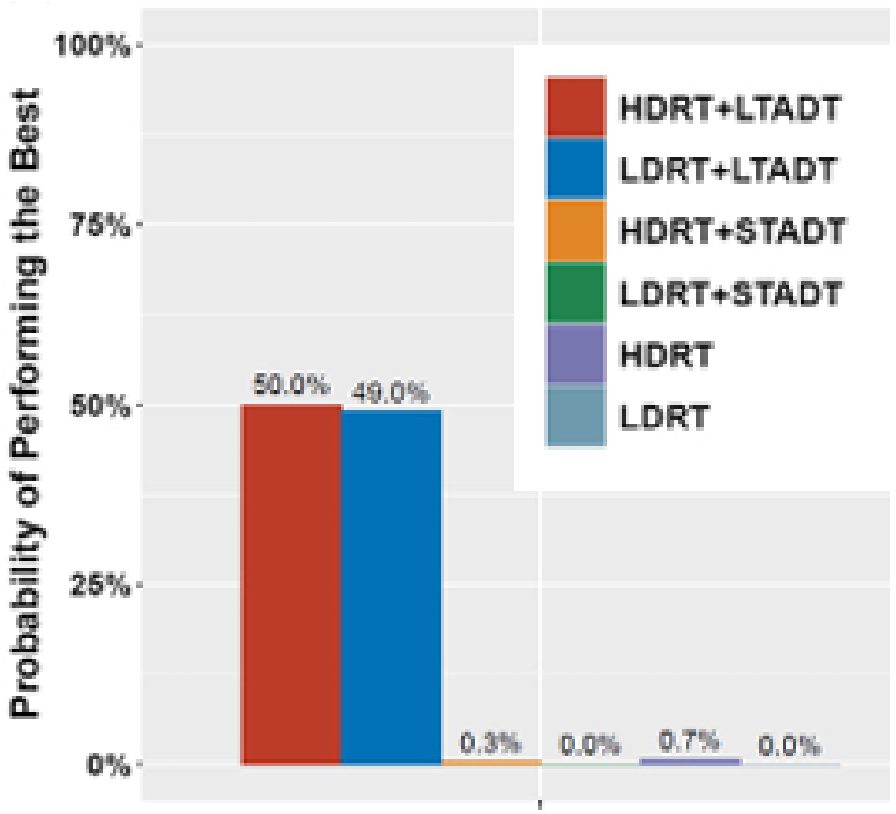
High-dose Radiotherapy or Androgen Deprivation Therapy (HEAT)

Parameter [a]	All patients (*n* = 11 862)	Low-dose RT (*n* = 2820)	Low-dose RT + STADT (*n* = 3960)	Low-dose RT + LTADT (*n* = 1695)	High-dose RT (*n* = 1535)	High-dose RT+STADT (*n* = 1383)	High-dose RT + LTADT (*n* = 469)
Follow-up (yr)	8.81(5.7–11.5)	8.6 (5.4–11.6)	9.3 (5.8–12)	7.7 (5.2–11.5)	8.8 (6.7–10.8)	9.5 (6.3–11.3)	7.5 (5.2–10.6)
Age at treatment (yr)	70 (65–74)	70 (65–74)	70 (65–73.8)	70 (65–74)	70 (65–74)	69 (64.3–73)	69.6 (64.3–73.8)
NCCN risk group, *n* (%)							
High	5373 (45)	799 (28.9)	2079 (53.3)	1425 (84.7)	191 (12.4)	552 (40.1)	327 (69.7)
Intermediate	5305 (45)	1594 (57.6)	1382 (35.4)	247 (14.7)	1246 (81.2)	694 (50.4)	142 (30.3)
Low	1056 (9)	374 (13.5)	442 (11.3)	10 (0.6)	98 (6.4)	132 (9.6)	0 (0)
Gleason score, *n* (%)							
6	4623 (39)	1170 (43.2)	1859 (48.5)	596 (38.4)	459 (30.2)	490 (36.4)	49 (10.4)
7	5033 (42)	1248 (46.1)	1335 (34.8)	573 (36.9)	996 (65.5)	630 (46.8)	251 (53.5)
8	1074 (9)	179 (6.6)	381 (9.9)	221 (14.2)	51 (3.4)	148 (11)	94 (20)
9	610 (5)	100 (3.7)	217 (5.7)	141 (9.1)	12 (0.8)	69 (5.1)	71 (15.1)
10	91 (1)	13 (0.5)	41 (1.1)	21 (1.4)	2 (0.1)	10 (0.7)	4 (0.9)
iPSA (ng/ml)	11.4 (7.2–19)	9.3 (6.1–14.2)	12.2 (7.7–21)	18 (10.2–35)	9 (5.9–13)	11.8 (7.5–18.4)	14 (8.5–22.5)
T stage, *n* (%)							
T1/T2	8101 (68)	2278 (81.5)	2462 (62.7)	520 (30.7)	1444 (95)	1120 (83)	277 (59.1)
T3/T4	3651 (31)	516 (18.5)	1463 (37.3)	1175 (69.3)	76 (5)	229 (17)	192 (40.9)

High-dose Radiotherapy or Androgen Deprivation Therapy (HEAT)

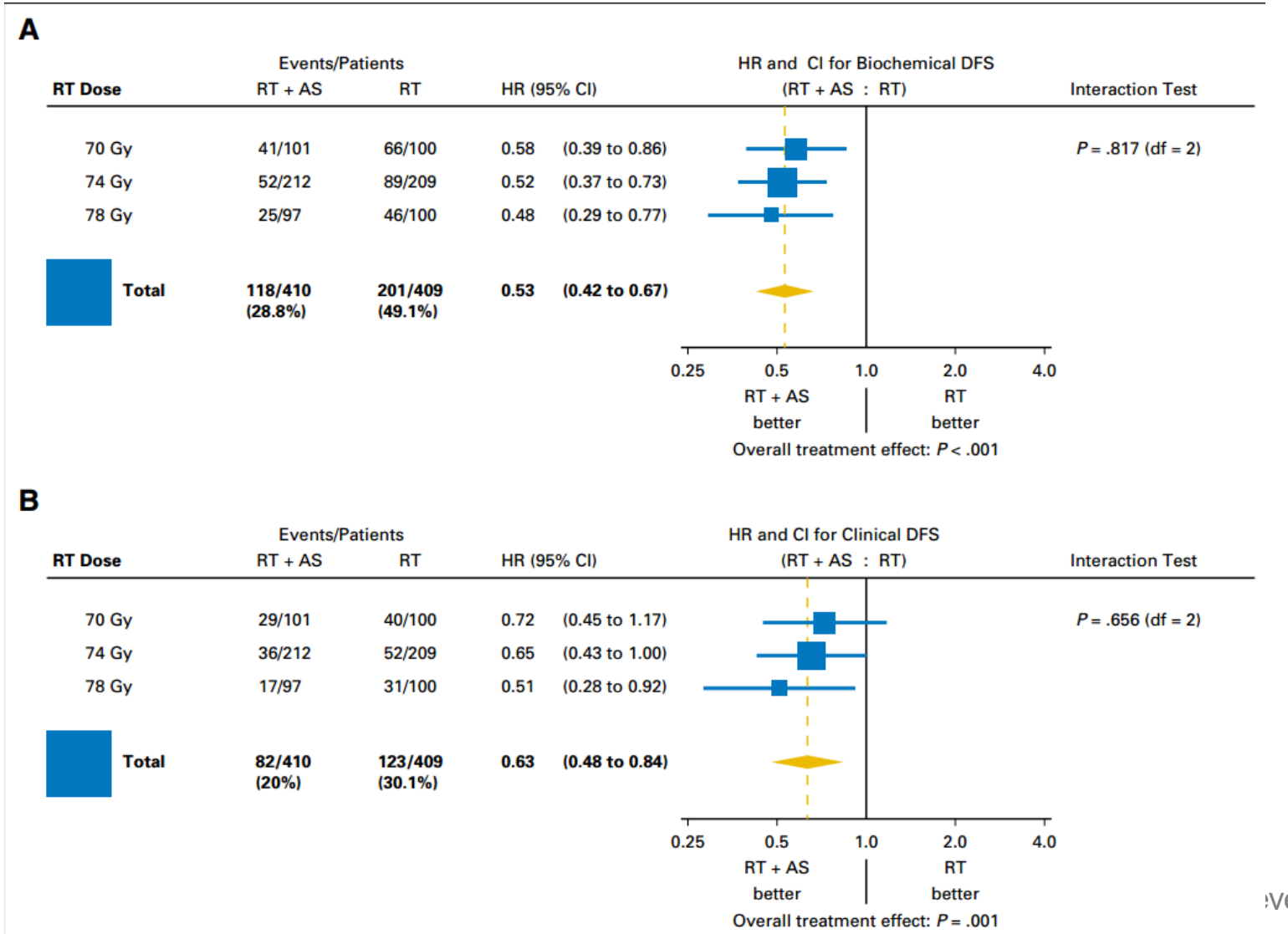
Metastasis-free survival





ADT improves outcomes irrespective of RT dose

EORTC 22991 (Bolla):



University Hospitals
Seidman Cancer Center

Addition of ADT improves outcomes more than brachy boost (ie more dose)

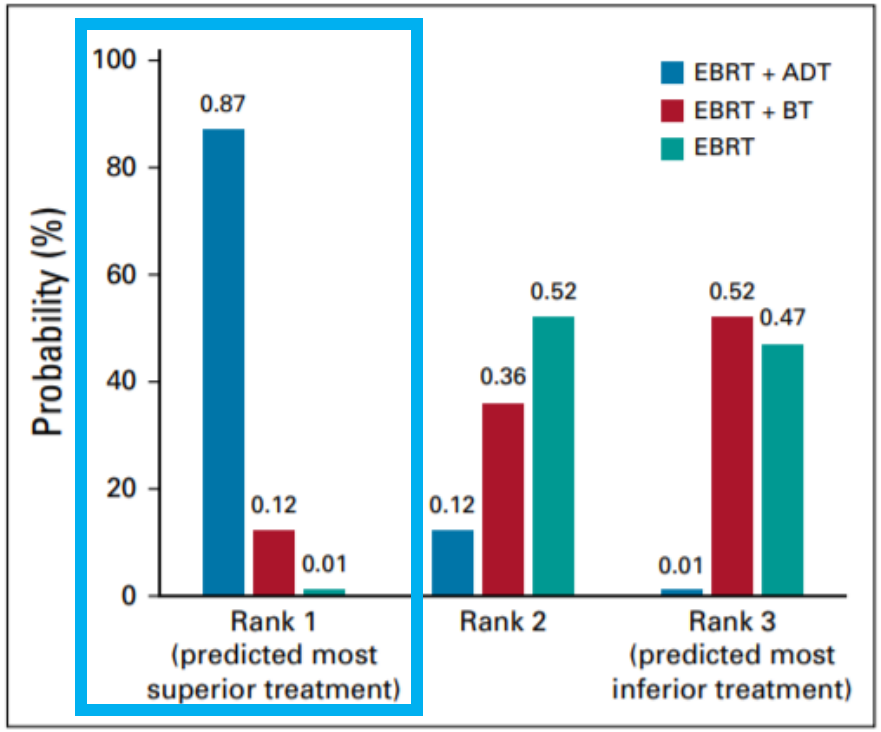
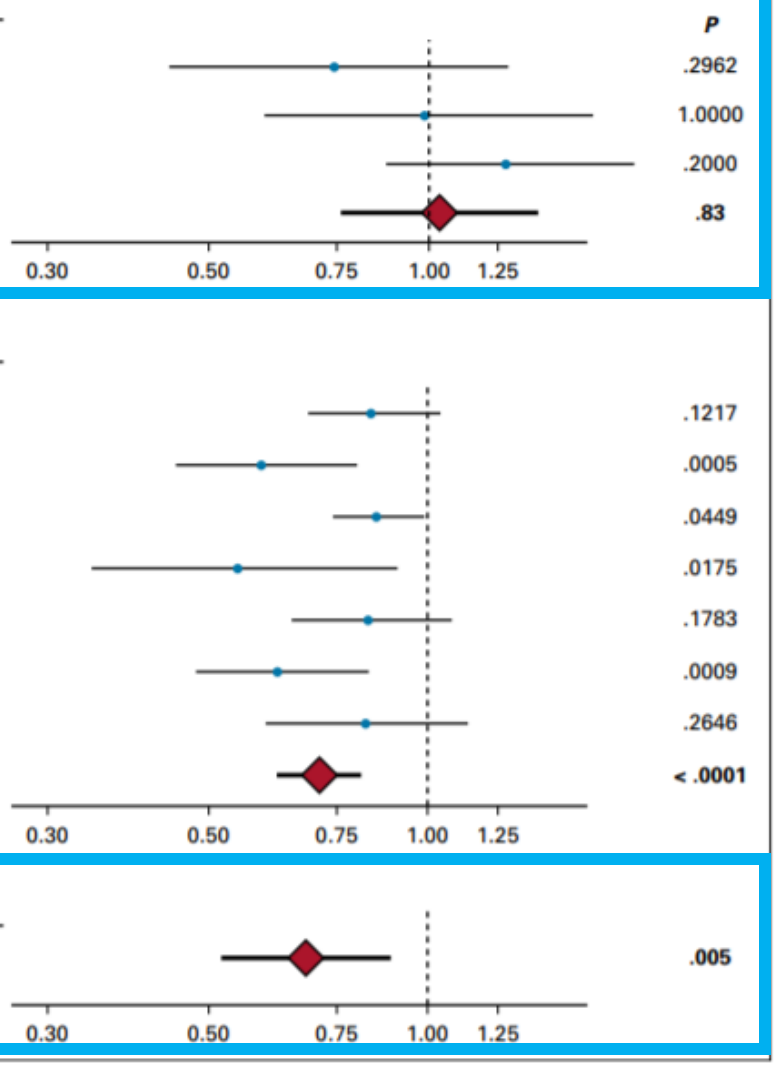


FIG 3. Predicted treatment rankings for overall survival. ADT, androgen deprivation therapy; BT, brachytherapy boost; EBRT, external beam radiotherapy.

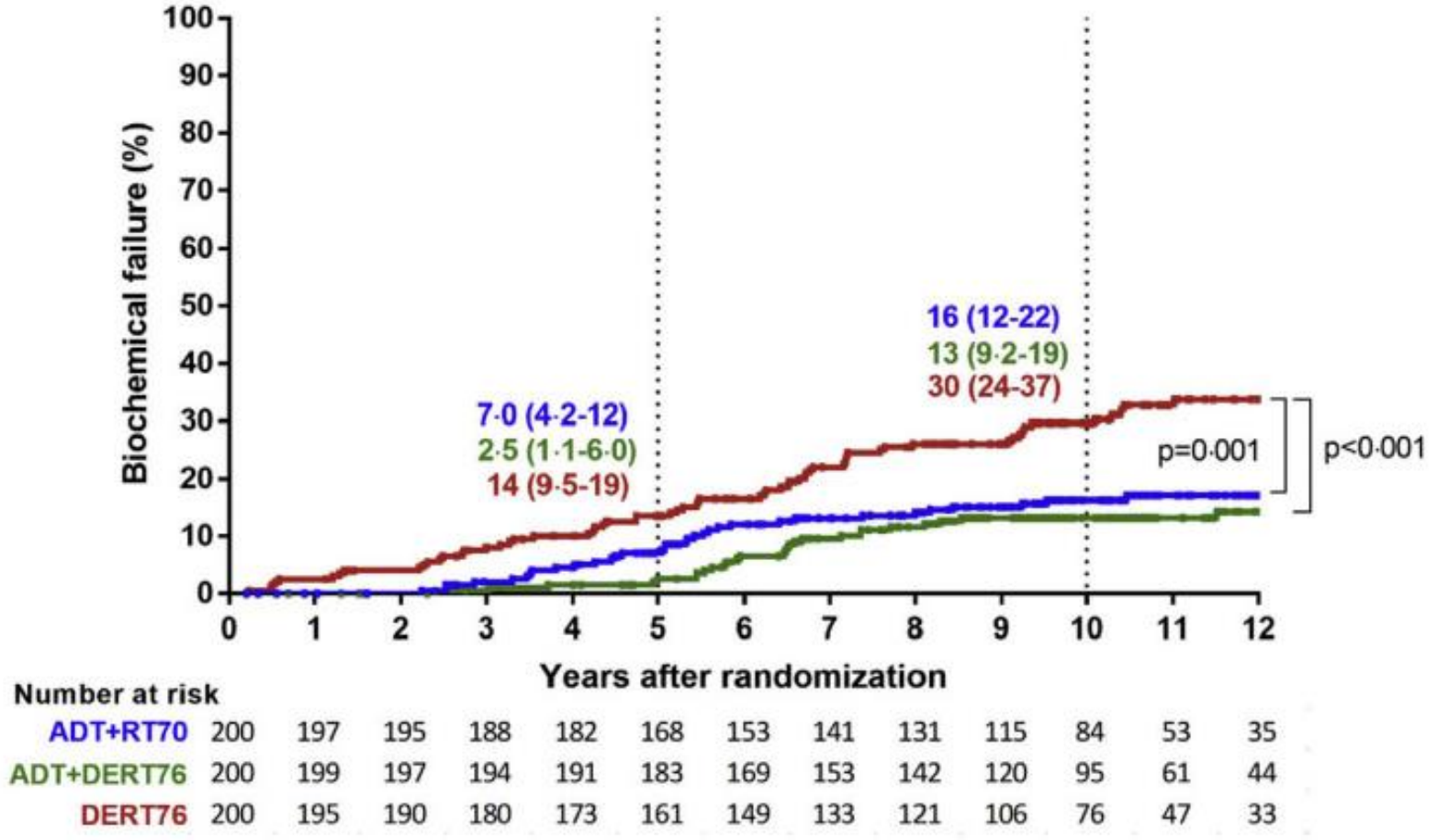
EBRT ± BT	Sample Size	Treatment	HR	Lower	Upper	P
ASCENDE-RT	398	± LDR	0.78	0.48	1.25	.2962
Sathya	104	± MDR	1.00	0.63	1.59	1.0000
Hoskin	216	± HDR	1.26	0.89	1.78	.2000
Overall			**1.03**	**0.78**	**1.36**	**.83**
EBRT ± ADT						
RTOG 8610	456	0 *v* 4 months	0.85	0.69	1.04	.1217
EORTC 22863	401	0 *v* 36 months	0.60	0.45	0.80	.0005
RTOG 9408	1979	0 *v* 4 months	0.86	0.74	0.99	.0449
DFCI 95096	206	0 *v* 6 months	0.56	0.35	0.91	.0175
TROG 9601 (1)	535	0 *v* 3 months	0.84	0.65	1.08	.1783
TROG 9601 (2)	537	0 *v* 6 months	0.63	0.48	0.83	.0009
EORTC 22991	819	0 *v* 6 months	0.83	0.60	1.14	.2646
Overall			**0.71**	**0.62**	**0.81**	**< .0001**
EBRT + ADT *v* EBRT + BT						
Overall			**0.68**	**0.52**	**0.89**	**.005**



Jackson et al, JCO 2020

ADT Benefits More than Dose Escalation

PCS III Randomized Trial



Dose Escalated Radiotherapy Alone or in Combination with Short-Term Androgen Suppression for Intermediate Risk Prostate Cancer: Outcomes from the NRG Oncology/RTOG 0815 Randomized Trial

Daniel J. Krauss, MD, Theodore Karrison, PhD, Alvaro A. Martinez, MD, FACR, Gerard Morton, MD, Di Yan, PhD, Deborah Watkins Bruner, PhD, RN, FAAN , Benjamin Movsas, MD, Mohamed Elshaikh, MD, Deborah Citrin, MD, Bruce Hershatter, M.D., FAC, Jeff M. Michalski, MD, MBA, FASTRO, Dr. Jason Alexander Efstathiou, Adam Currey, MD, Vivek S. Kavadi, MD, FASTRO , Fabio L. Cury, MD, Michael Lock, MD , Adam Raben, MD , Joseph P Rodgers , Howard Sandler, MD

Key subset analysis results

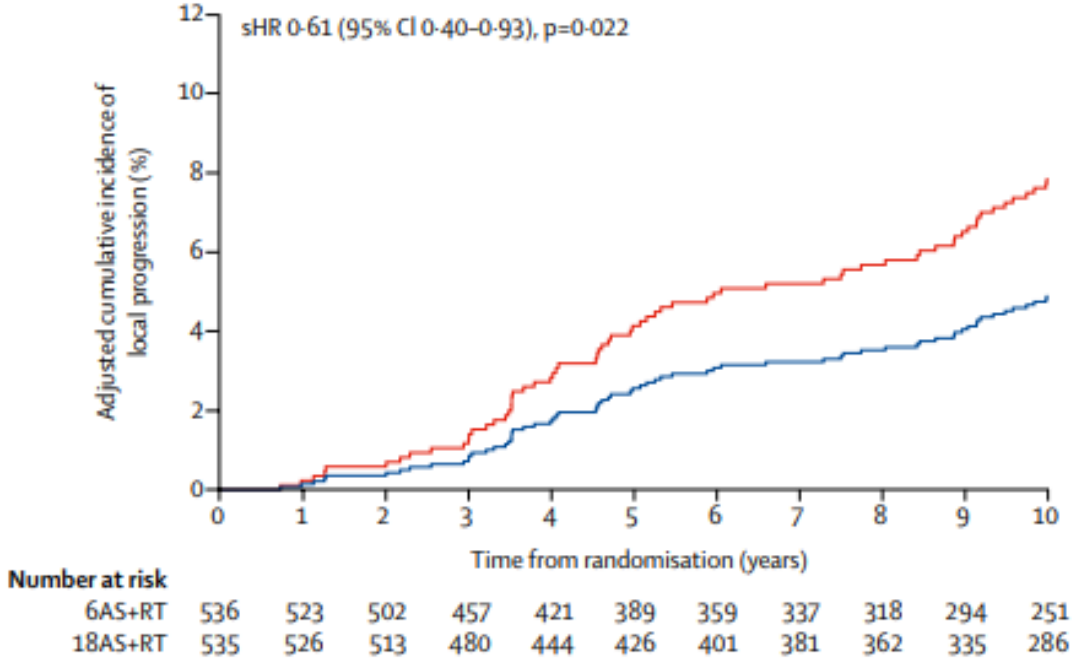
Similar relative benefit of ST-ADT with DE-EBRT as well as combo brachy

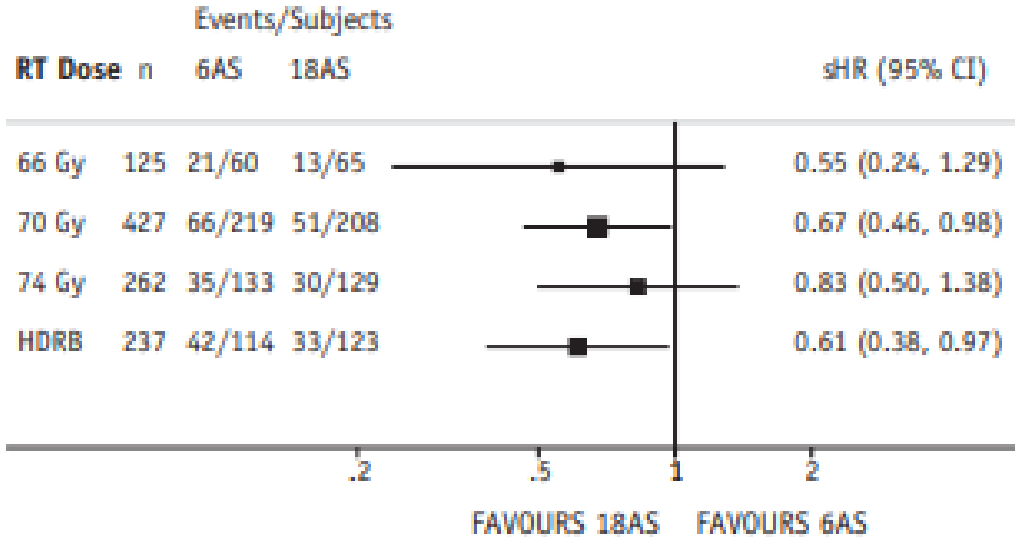
Subgroup	No.of Patients (%)	PSA Failure Free Rate(%) - 10 Years			Distant Metastasis Free Rate(%) - 10 Years	
		RT Alone	RT + STAD	P-Value*	RT Alone	RT + STAD
RT Modality						
EBRT	1321(88.5)	83.2	90.9	<0.001	96.4	99.1
EBRT + LDR/HDR	171(11.4)	84.7	90.7	0.191	95.3	98.8

LT-ADT improves outcomes irrespective of RT Dose

Short-term androgen suppression and radiotherapy versus intermediate-term androgen suppression and radiotherapy, with or without zoledronic acid, in men with locally advanced prostate cancer (TROG 03.04 RADAR): 10-year results from a randomised, phase 3, factorial trial

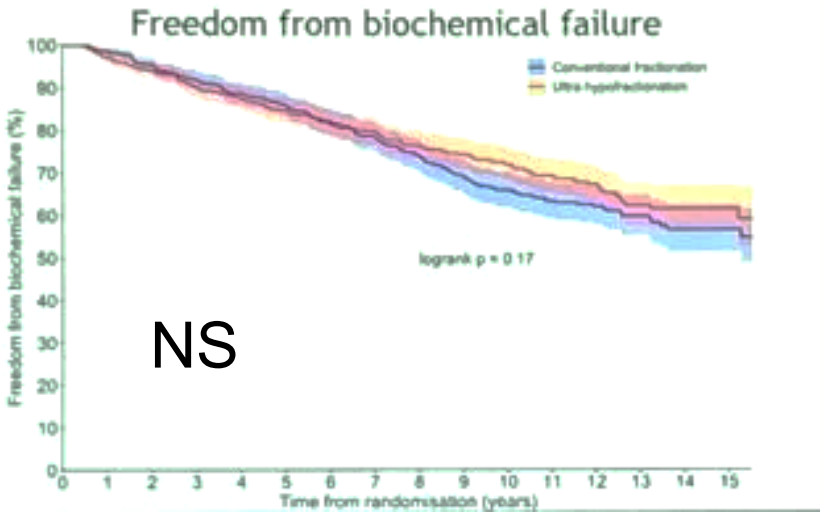
James W Denham, David Joseph, David S Lamb, Nigel A Spry, Gillian Duchesne, John Matthews, Chris Atkinson, Keen-Hun Tai, David Christie, Lizbeth Kenny, Sandra Turner, Nirdosh Kumar Gogna, Terry Diamond, Brett Delahunt, Chris Oldmeadow, John Attia, Allison Steigler





That is DE-EBRT and brachy boost…what about SBRT?

	HYPO-RT-PC	PACE-B	NRG GU005
Control	78 Gy	76 Gy	77 Gy
SBRT	77 Gy	88 Gy	74 Gy



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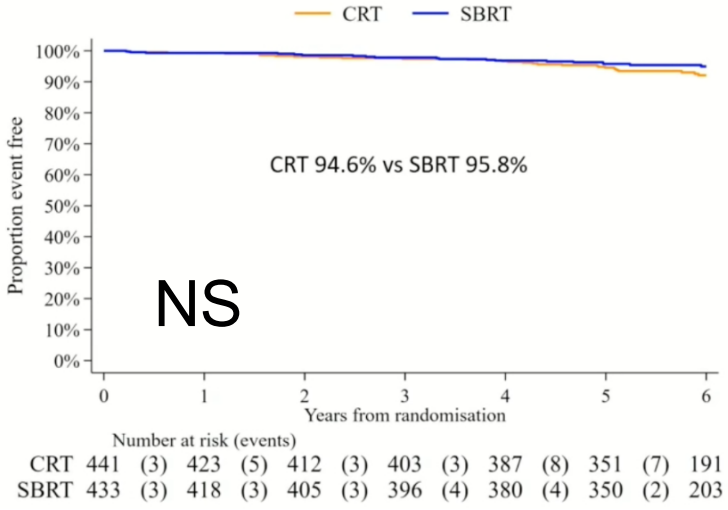

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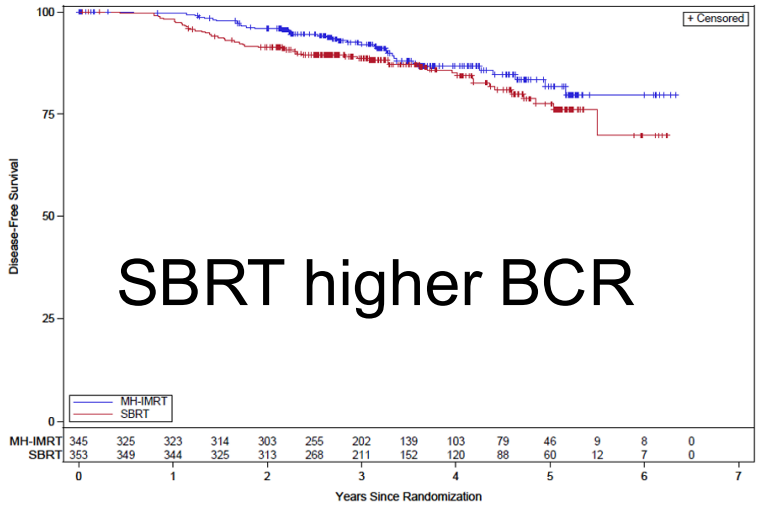

SBRT higher BCR

No clear evidence that SBRT is dramatically superior to DE-EBRT

No biologic rationale for differential ADT benefit

Will know more in the years to come…

NRG GU010 (UIR disease) and NRG GU009 (high, very high, cN+):

- Allows brachy boost
- Allows SBRT
- Allows moderate hypfrac
- Allows microboost

We will be able to better understand interplay of ADT use, ADT duration, and ARPI addition across modalities

Summary

1. ADT use and adjuvant prolongation have similar *relative* benefits irrespective of NCCN risk group
2. Optimal ‘long-term’ ADT duration closer to 12 months for high-risk and 24+ months for very high-risk
3. Neoadjuvant ADT prolongation has no clear oncologic benefit and should generally not be used
4. Addition of ARPI should rarely be used in N0M0 prostate cancer
5. Benefit of ADT use/duration not clearly impacted by RT dose or RT modality

Thank you

University Hospitals

Seidman Cancer Center

Case Western Reserve University Est. 1826

Radiation Oncology Reimagined

@DrSpratticus