

Latest update on RT 2025 BMUC

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Iridium Network

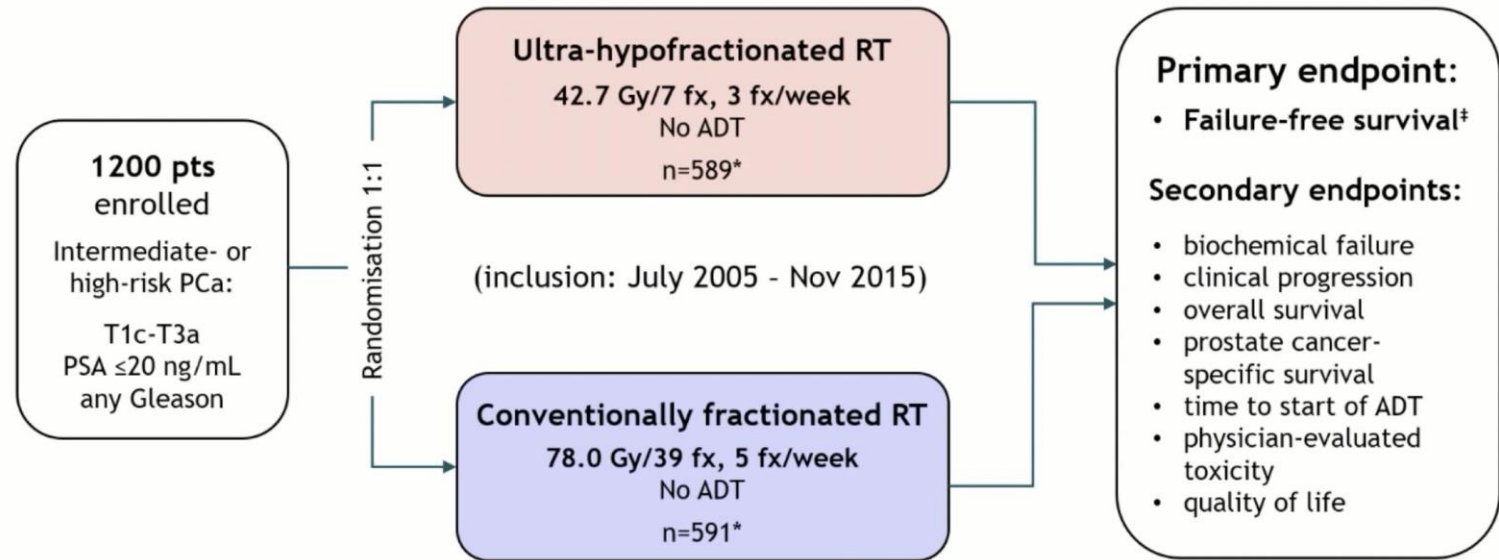


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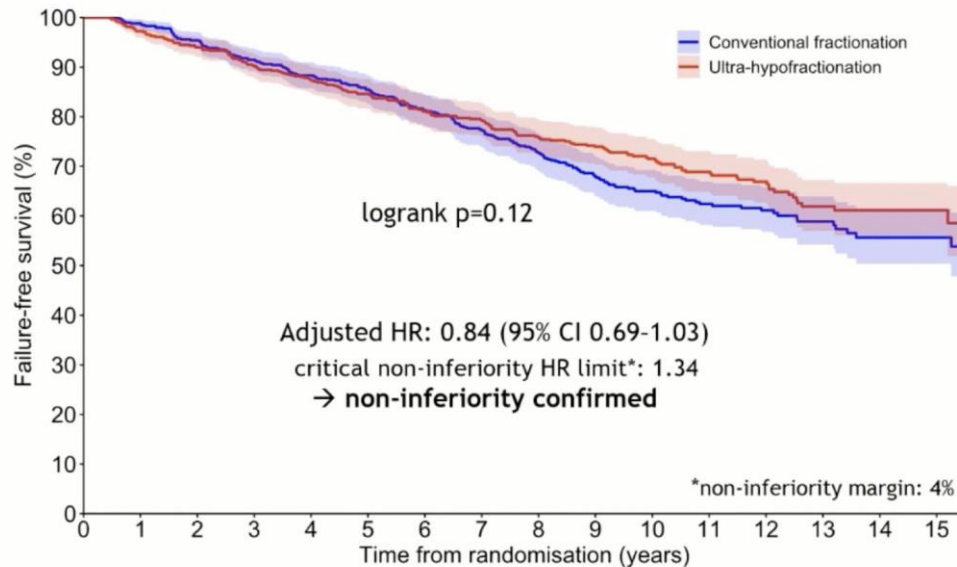
How low can we go?

Update on SBRT for primary prostate cancer

Hypo-RT-PC phase III trial:



Hypo-RT-PC phase III trial:



Number at risk

■	591	580	558	532	501	474	439	404	350	309	230	171	125	88	57	39
■	589	569	543	511	489	464	432	410	377	348	266	195	140	87	60	35

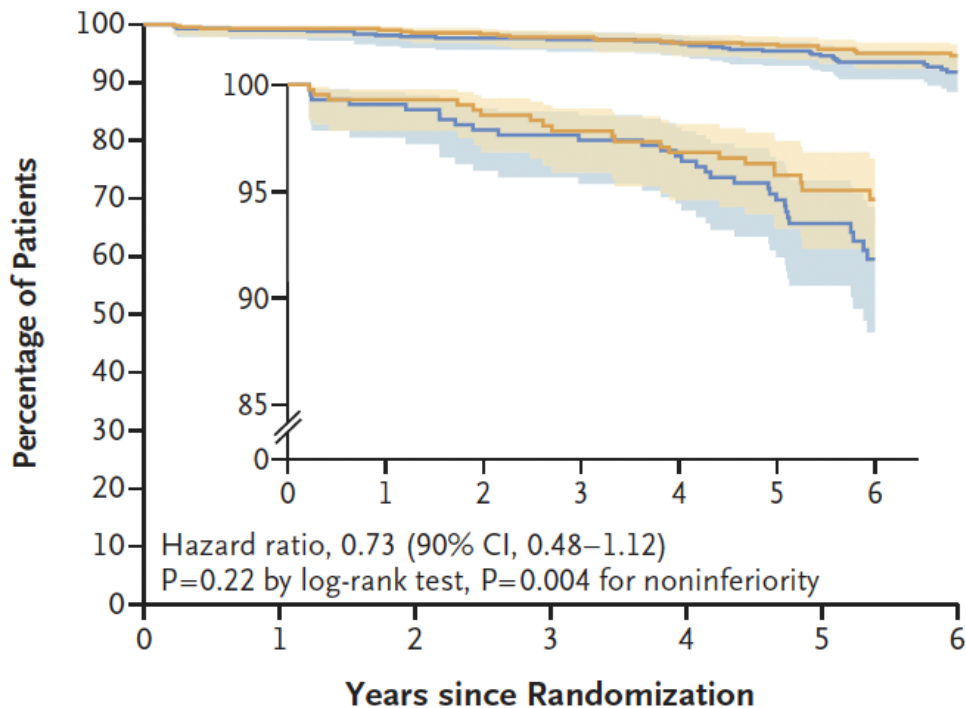
Key outcomes after 10 years:

- Failure-free survival (no return of cancer or need for additional treatment): 72% in the short-course group vs 65% in the standard group
- Overall survival: 81% for short-course vs 79% for standard
- Prostate cancer-specific mortality: 4% in both groups
- Side effects: Urinary and bowel symptoms were similar in both groups, and most were mild to moderate.

"These findings confirm that the shorter course does not increase long-term side effects and provides equally durable cancer control", added Camilla Thellenberg-Karlsson, MD, PhD, at Umeå University, who presented the results at the ESTRO meeting.

PACE B: onological results

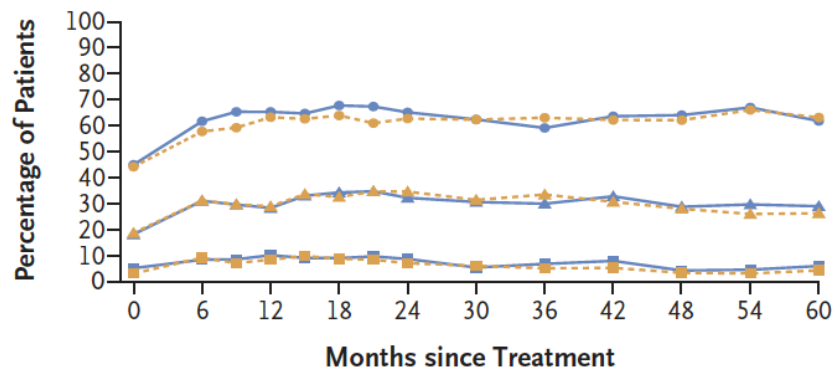
A Freedom from Biochemical or Clinical Failure



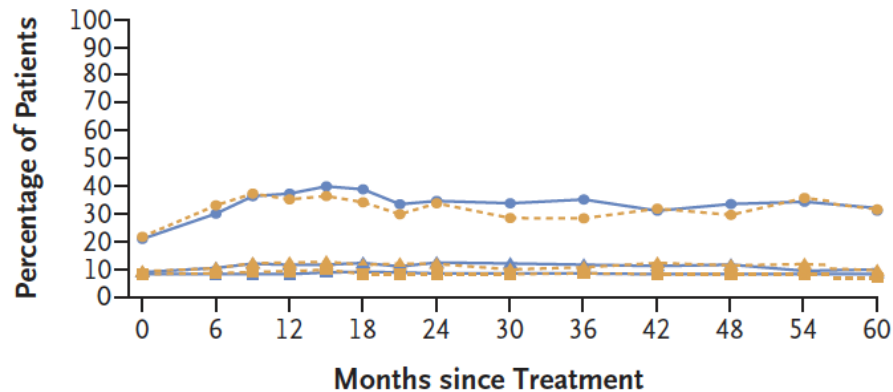
@5 years:
95% disease control

PACE B toxicity

E CTCAE-Graded Erectile Dysfunction

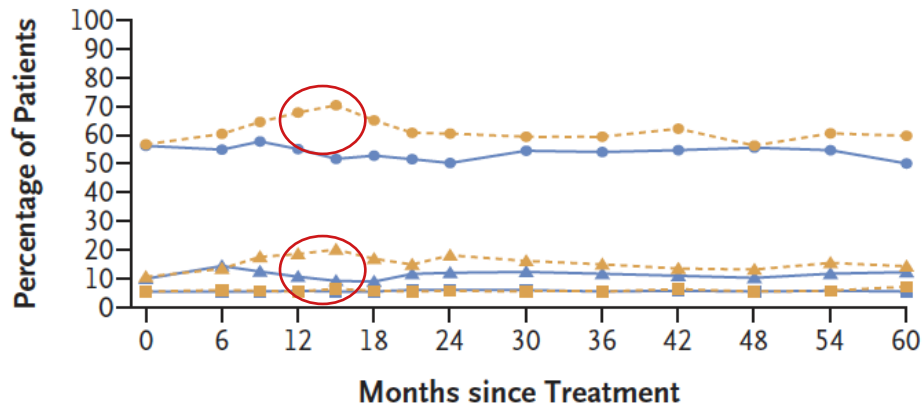


D CTCAE-Graded Gastrointestinal Toxic Effects



PACE B urinary toxicity

C CTCAE-Graded Genitourinary Toxic Effects



No. of Patients

Stereotactic body radiotherapy	413	380	393	362	383	359	372	352	355	333	355
Control radiotherapy	431	408	390	377	385	368	390	348	360	340	357

@ 5 years G2-3:

- SBRT: 7.3%
- CFRT: 4.5%

Cumulative G2-3

- SBRT: 43%
- CFRT: 30%

NRG GU 005

Arm 1: IMRT

70 Gy in 28 fractions of 2.5 Gy to the prostate
or 60 Gy in 20 fractions of 3 Gy
+/- proximal 1cm of seminal vesicles

Minimal Margins:

8 mm uniform in expansion,
5 mm posteriorly

Arm 2: SBRT

36.25 Gy in 5 fractions of 7.25 Gy to the prostate +/-
proximal 1 cm of seminal vesicles

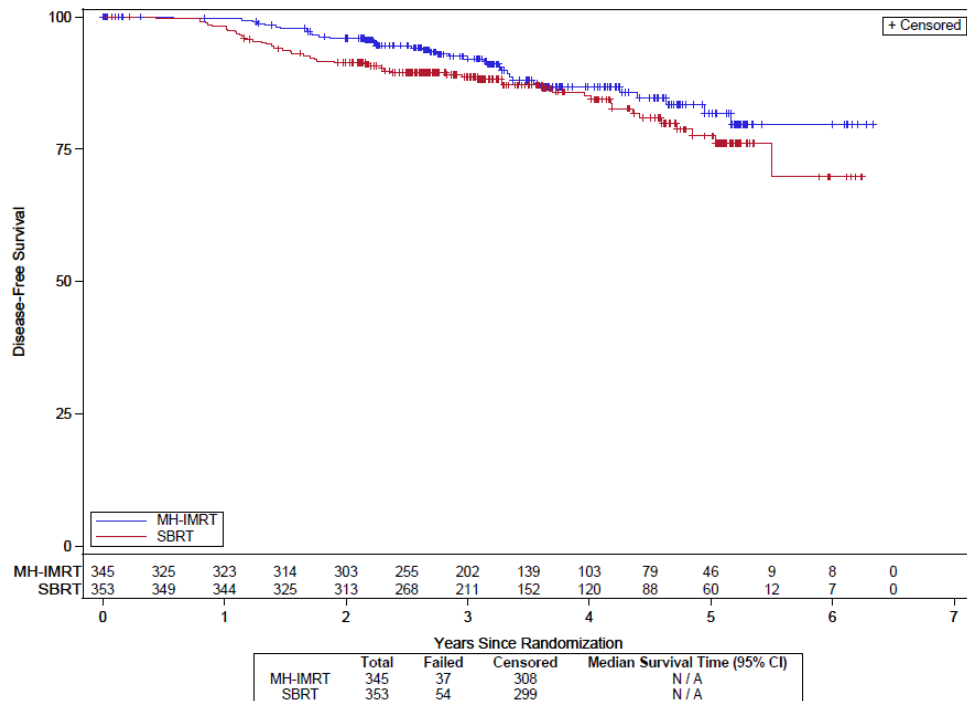
Minimal Margins:

5 mm superior inferior & laterally,
3 mm anterior & posterior

Hypothesis: SBRT is superior to moderately hypofractionated IMRT with two co-primary endpoints:

- In terms of patient-reported GI and GU toxicity
- In terms of Disease-free survival

Disease-free survival

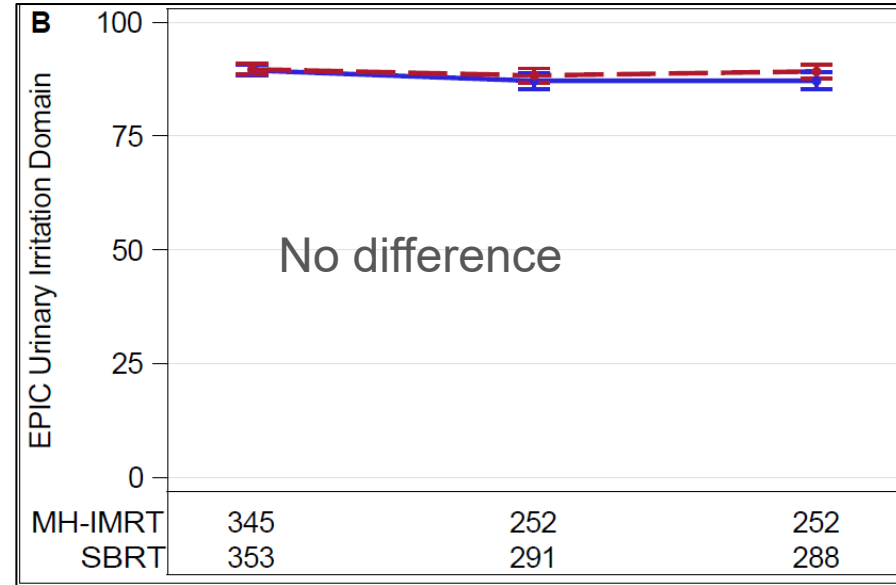
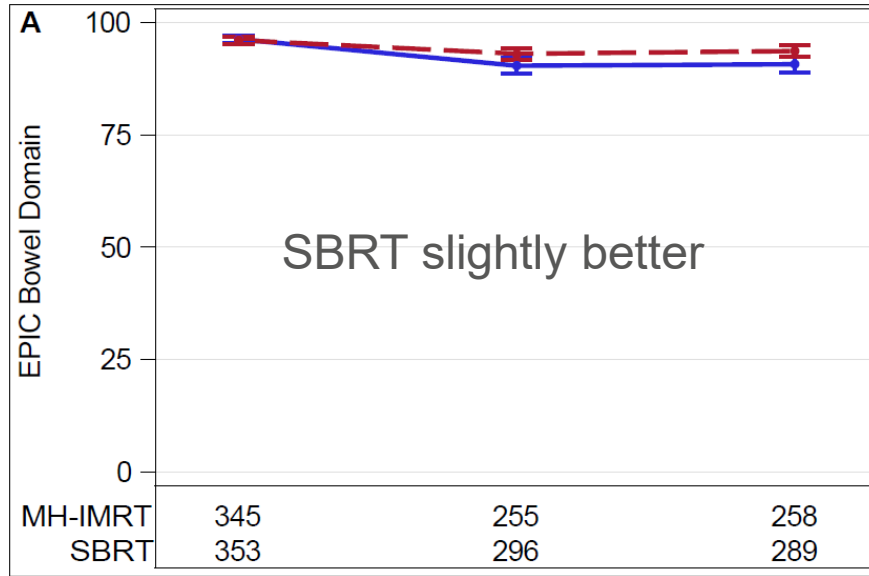


SBRT is NOT superior

Biochemical failure at 3 yrs

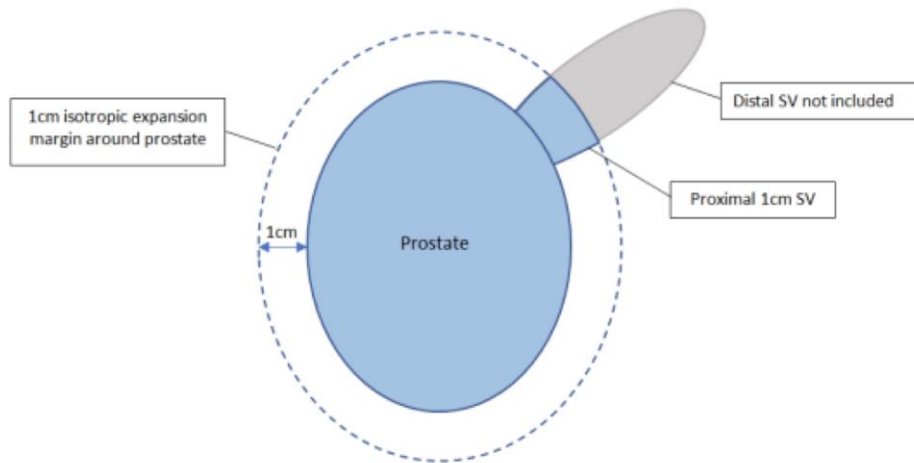
- SBRT: 8%
 - IMRT: 4%
- $p=0.037$

Toxicity



SBRT better at EPIC sexual domain and urinary incontinence

PACE B vs NRG GU005



PACE B
40Gy in 5

NRG
36.25Gy in 5

Patient selection

Which factors predict GU Tox?

- higher baseline **IPSS**
- baseline urinary **medication** use
- grade 2+ **acute** urinary toxicity

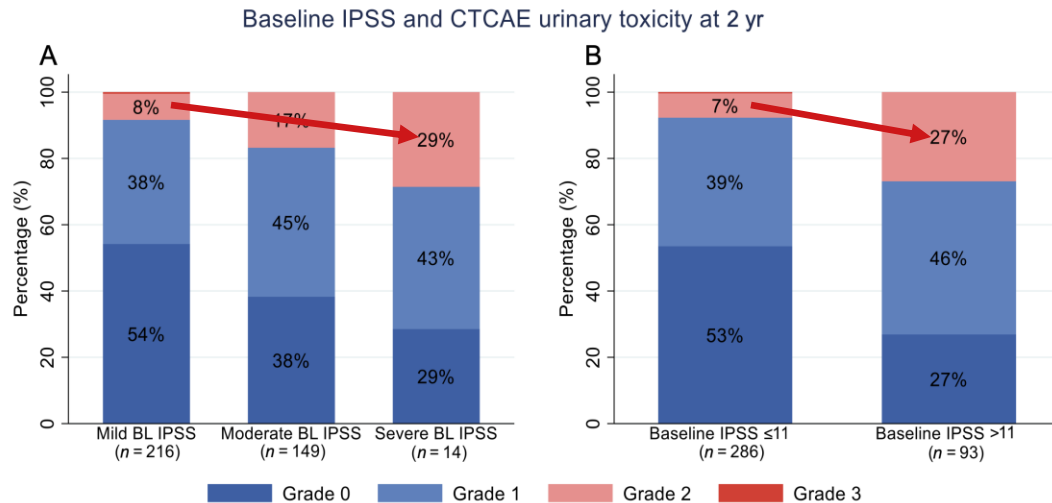
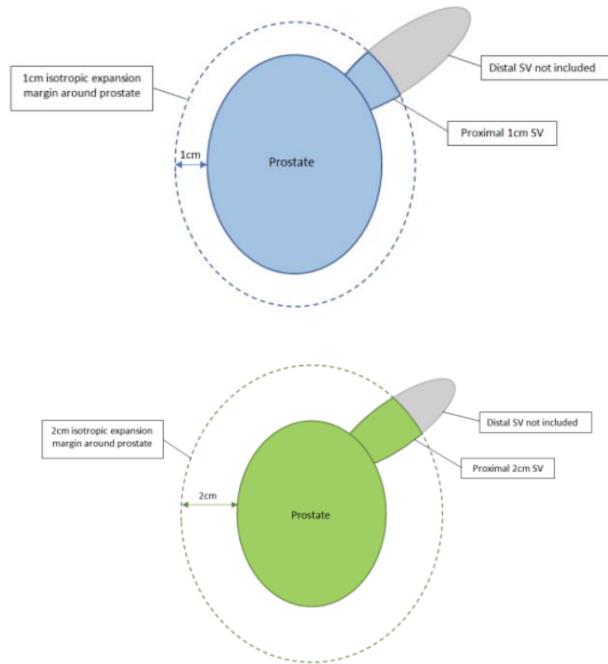


Fig. 1 – Stacked bar chart: CTCAE urinary toxicity at 2 yr following SBRT in patients with (A) mild, moderate, and severe baseline IPSS grades and (B) baseline IPSS (with imputation) ≤11 and >11. No/mild symptoms: total IPSS score 0–7; moderate symptoms: total IPSS score 8–19; and severe symptoms: total IPSS score 20–35. One patient experienced a grade 3 event at 2 yr with a mild baseline IPSS and IPSS ≤11. Two-year CTCAE toxicity data were missing in 35/414 patients (8%). BL = baseline; CTCAE = Common Terminology Criteria for Adverse Events; IPSS = International Prostate Symptom Score; SBRT = stereotactic body radiotherapy.



Should we treat high risk with SBRT?

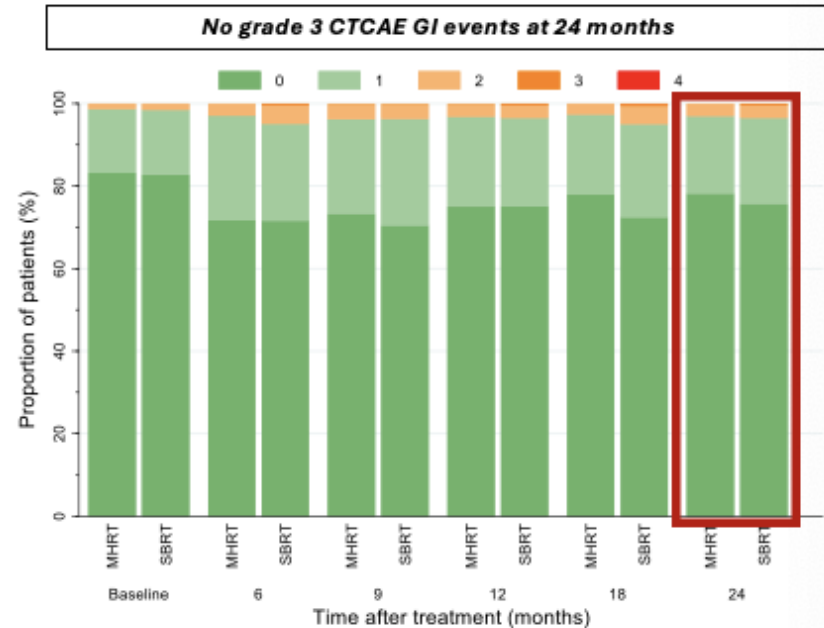
PACE C: 2 year GI toxicity



Worst CTCAE gastrointestinal toxicity

Grade 2+ CTCAE GI at 24 months:

3% SBRT vs **3% MHRT** ($p=0.67$)



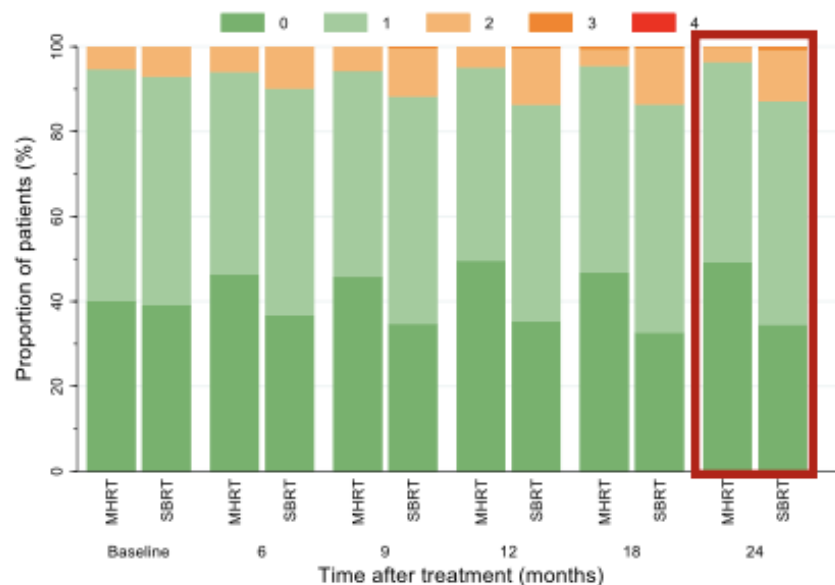
PACE C: 2 year GU toxicity

Worst CTCAE genitourinary toxicity

Grade 2+ CTCAE GU at 24 months:

13% SBRT vs **4% MHRT** ($p < 0.001$)

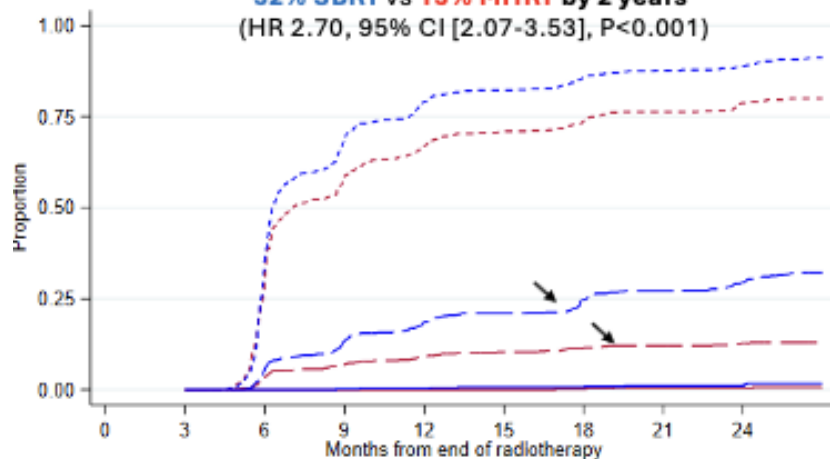
Grade 3 CTCAE GU events at 24 months: 1% SBRT and 0% MHRT



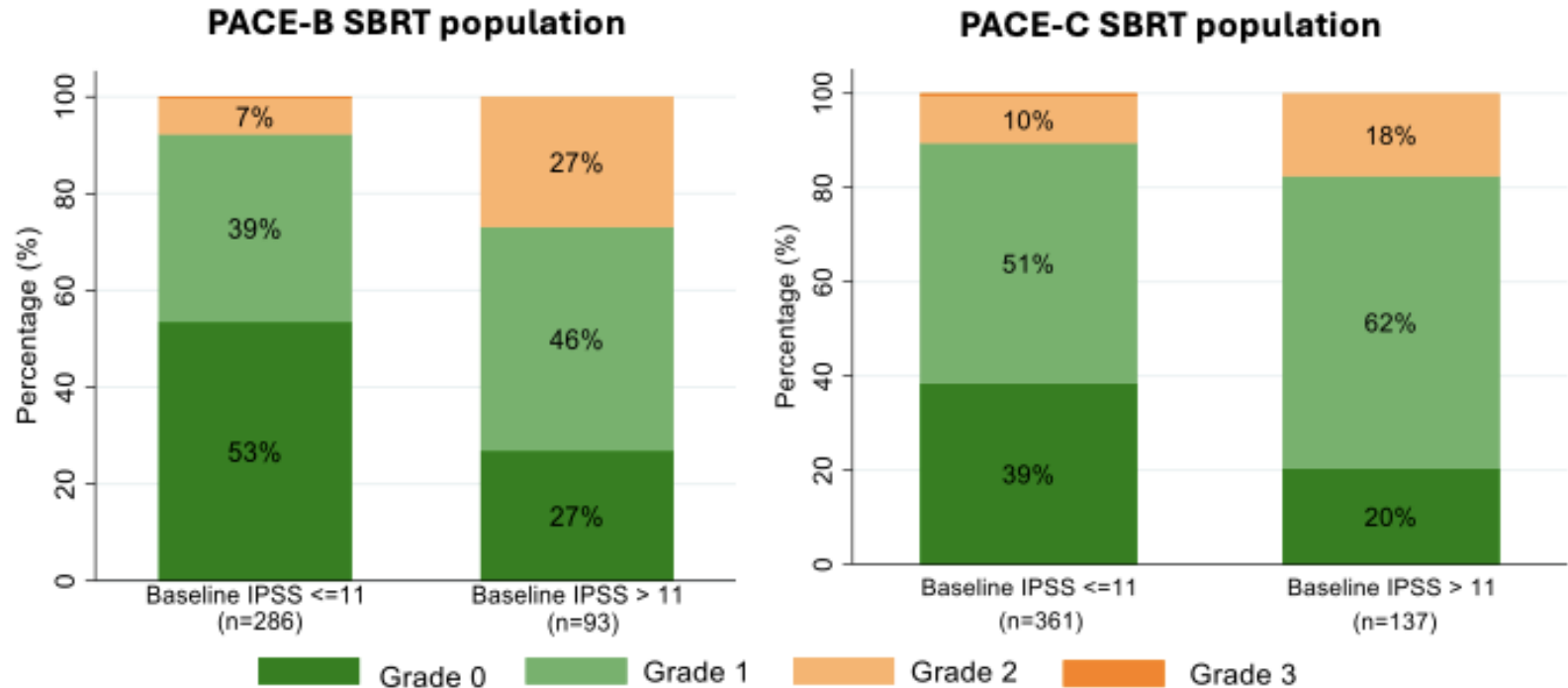
Cumulative CTCAE grade 2+ GU toxicity

32% SBRT vs **13% MHRT** by 2 years

(HR 2.70, 95% CI [2.07-3.53], $P < 0.001$)



Baseline IPSS and CTCAE: PACE B vs PACE C

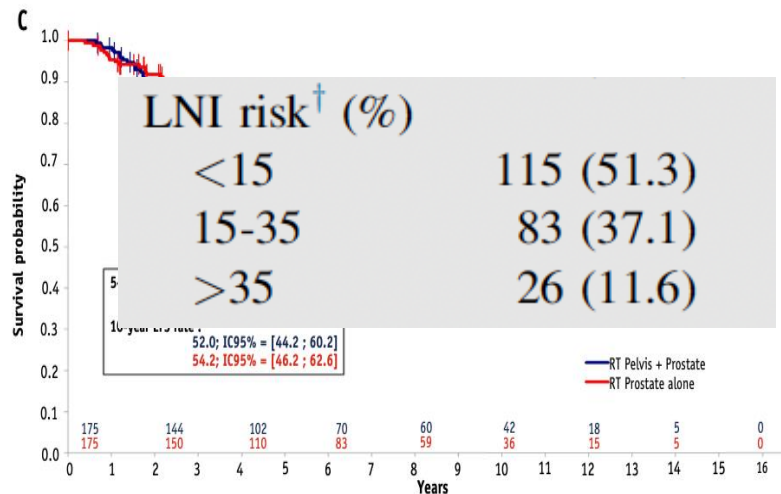


Should we treat the nodes?

Update on elective nodal RT for primary prostate cancer

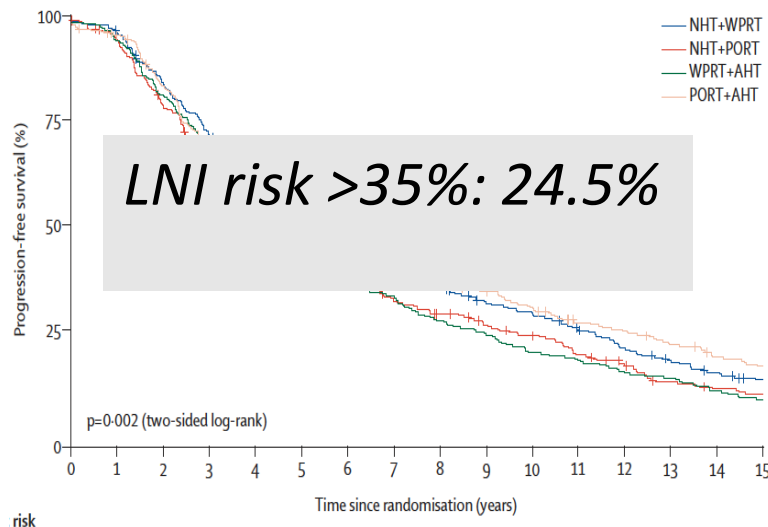
Historical trials: unclear benefit of treating nodes

GETUG-01



No EFS benefit

RTOG 9413



NHT+WPRT =
PORT + AHT

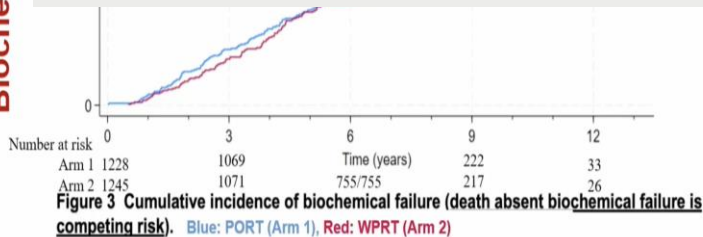
RTOG 0924

“Unfavorable Intermediate” and “Favorable High”

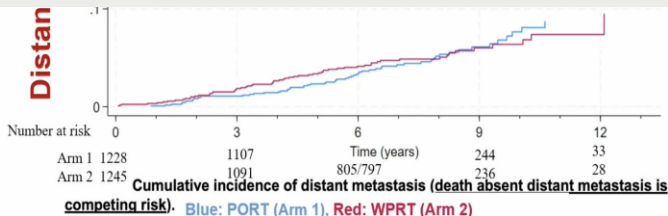
Risk Groups:

1. GS 7-10 + T1c-T2b + PSA < 50 ng/mL
2. GS 6 + T2c-T4 or $\geq 50\%$ Bx's + PSA < 50 ng/mL
3. GS 6 + T1c-T2b + PSA > 20 ng/mL

Biochemical Failure



Small benefit



No benefit

Time to let WPRT go?

- Yes, for intermediate to favorable high risk
- High to very high risk? Let's see.

Daniel Spratt: NRG Oncology RTOG 0924 Trial on Whole Pelvic RT

Daniel Spratt, Chair and Professor of Radiation Oncology at Case Western Reserve University, shared a post on [X](#):

"NRG Oncology Rtog 0924 trial on 2500 patients testing whole pelvic RT.

Negative trial

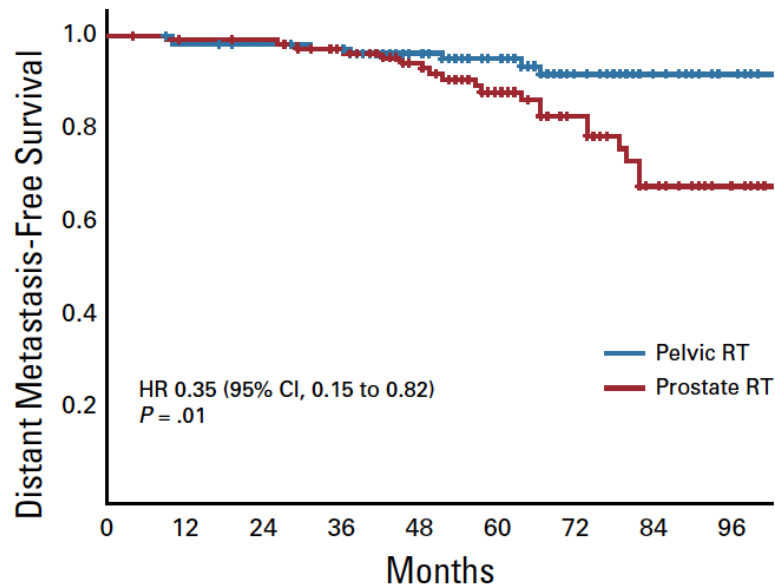
- OS no difference
- PCSM no difference
- DM no difference
- BCR was not SS different with only 4% difference at 10 years.
- toxicity increased

3 cooperative group trials now negative: **getug01**, **Rtog 9413**, **Rtog 0924**.

Goodbye WPRT"



POP-RT: the magical formula with PSMA PET?



No. at risk

WPRT	110	107	105	100	80	64	41	20	9
PORT	112	108	107	99	80	56	39	21	10

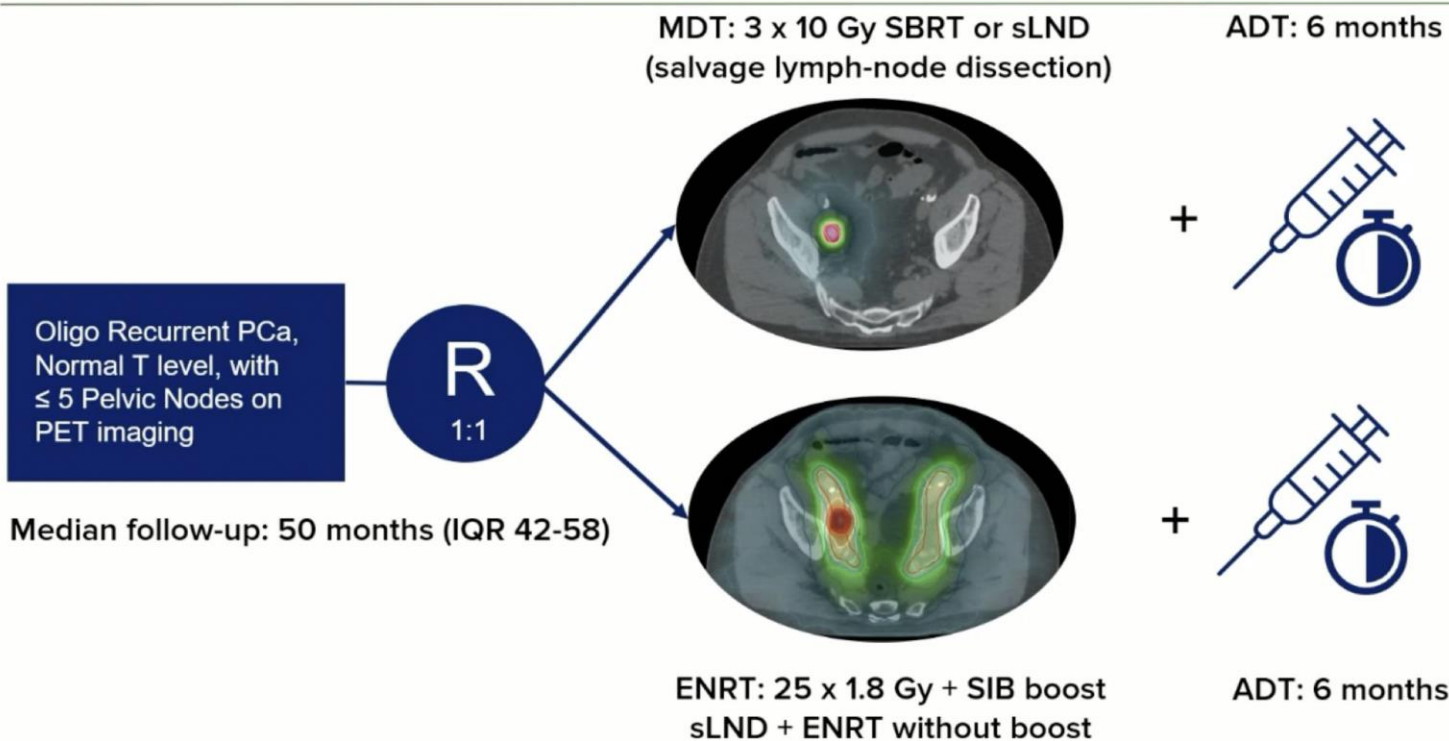
LNI risk >35%: 55%
LNI risk >50%: 29%

Prevention or salvage?

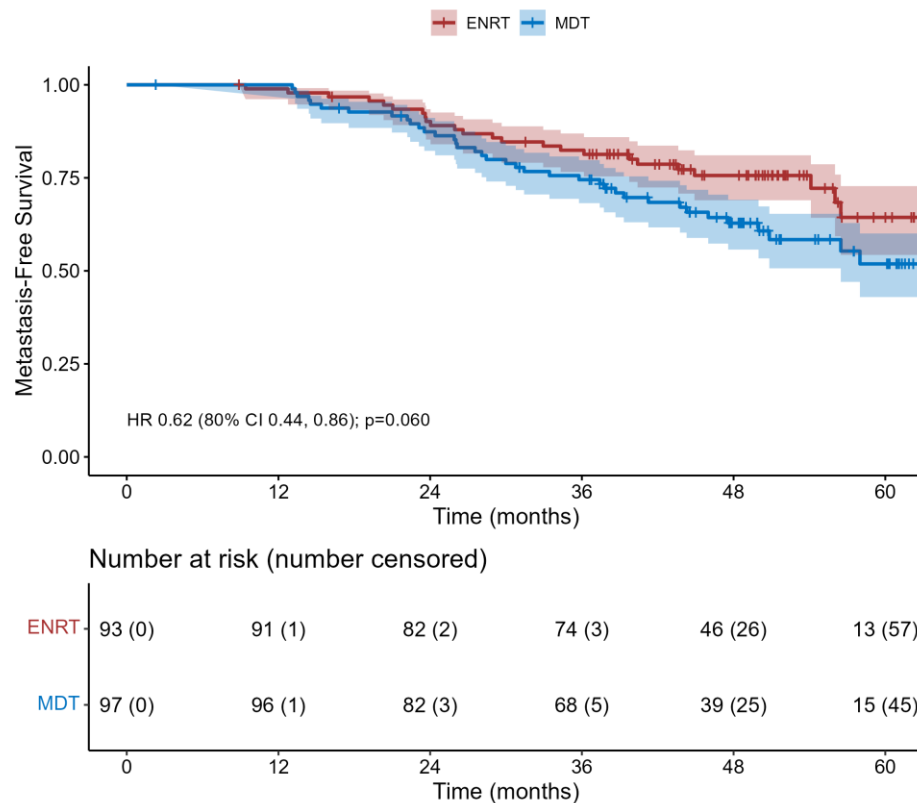
STORM

Do we need to prevent recurrences? Salvage ENRT

PEACE-V - STORM trial



Do we need to prevent recurrences? Salvage ENRT



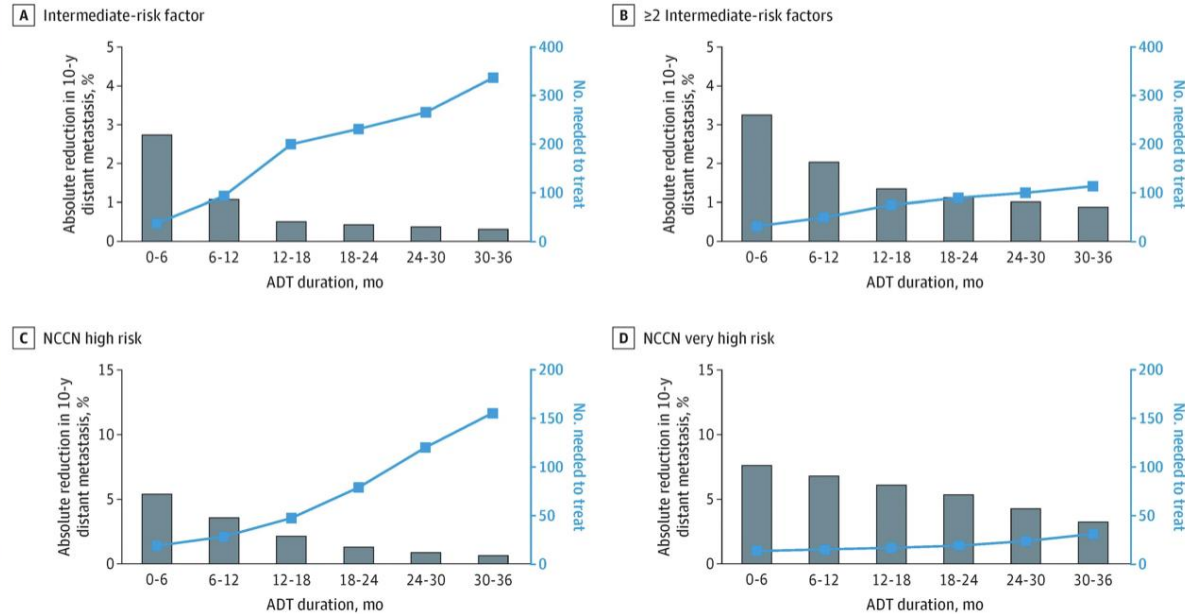
- Advantage:
 - Less overtreatment
- Disadvantage
 - More investigations
 - More anxiety
 - Might be too late?

How long should we use ADT?

Update on ADT duration.

Optimal duration of ADT in intermediate to high risk

Figure 4. Incremental Absolute Benefit in 10-Year Distant Metastasis Based on Androgen Deprivation Therapy (ADT) Duration and Prognostic Risk Group Using the Cox Generalized Additive Model



DADSPORT Trial: ADT with Postoperative RT

Duration of Androgen Suppression with Postoperative Radiotherapy for Nonmetastatic Prostate Cancer

EVIDENCE SUMMARY

Pooled Data from 5 RCTs

🎯 Study Objectives

To quantify the benefit of adding androgen deprivation therapy (HT/ADT) to postoperative radiotherapy (RT) after radical prostatectomy and assess the optimal duration of therapy.

4,411

PARTICIPANTS

96%

ELIGIBLE DATA

5

RCTS INCLUDED

8 Yrs

MEDIAN FOLLOW-UP

👤 Patient Population

- Men with nonmetastatic prostate cancer post-radical prostatectomy
- Undergoing adjuvant or salvage radiotherapy
- Median Age: 64–67 yrs | Pre-op PSA: 8.1–9.8 ng/ml
- High prevalence of pT3 stage (81%) and positive margins (60%)

📋 Study Design & Analysis

Prespecified systematic review and aggregate-data meta-analysis (PROSPERO CRD42022325769). Pairwise meta-analyses with subgroup exploration by pre-RT PSA and CAPRA-S score.

🔑 Intervention Arms Compared



Control Arm

Radiotherapy (RT) Alone



Short-Course HT

RT + 4-6 months Hormone Therapy



Long-Course HT

RT + 24 months Hormone Therapy

📈 Primary Outcomes

Overall Survival (OS)

Metastasis-free Survival

PC-Specific Survival

Key Survival Outcomes & Clinical Implications

Data cut-off: April 2024 | 8-Year Absolute Benefit Analysis

Overall Survival (OS)

HR 0.86

95% CI: 0.74 – 1.00

p = 0.057 (Not Significant)

📌 Small absolute benefit (+2%)

Metastasis-free Survival

HR 0.78

95% CI: 0.69 – 0.88

p < 0.001

✓ 4% absolute improvement

PC-Specific Survival

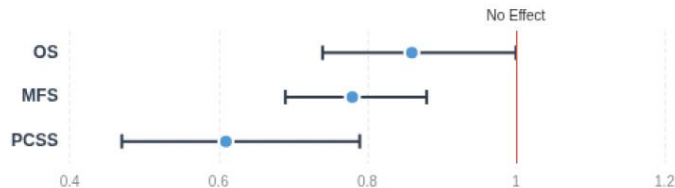
HR 0.61

95% CI: 0.47 – 0.79

p < 0.001

✓ 4% absolute improvement

Hazard Ratio Analysis (HT vs Control)



Duration Analysis: No significant difference found between Short-Course (4-6 mo) and Long-Course (24 mo) HT (Interaction p=0.6).

Clinical Takeaways



Benefit vs. Risk

Addition of HT consistently improves MFS and PCSS. However, OS benefit is small and not statistically definitive for the overall population.



Patient Selection

OS benefit signals are stronger in high-risk groups (High Pre-RT PSA, High CAPRA-S). Use risk stratification to guide HT decisions.



Optimal Duration

With no clear superiority for 24-month therapy, **Short-Course** HT is a reasonable standard to minimize long-term toxicity.



Should all high risk patients get doublet?

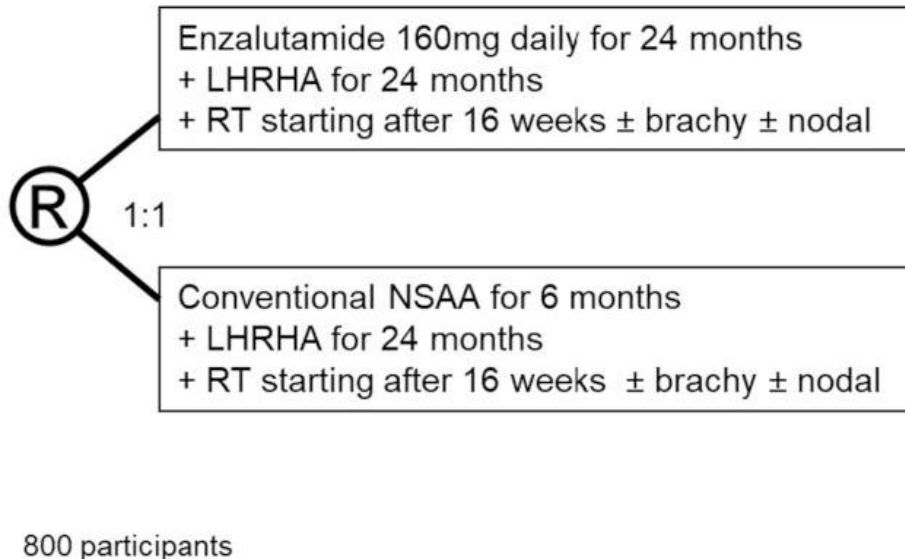
ENZARAD

Eligibility

Localised prostate cancer
High risk of recurrence
Suitable for EBRT

Stratification

Gleason score 8-10
T3-4 disease
N1 disease
PSA ≥ 20 ng/mL
Brachytherapy boost
Pelvic nodal RT
Study Site

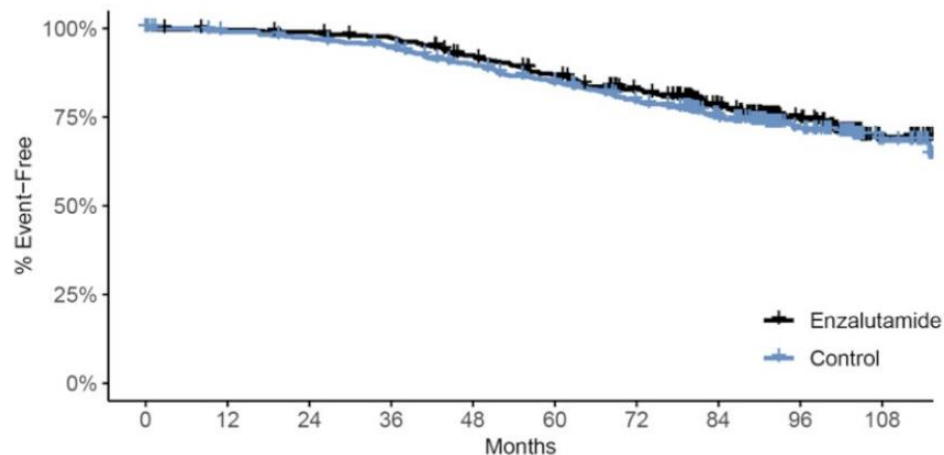


Endpoints

Metastasis-free survival (primary)
Overall survival
Cause specific survival
PSA progression free survival
Clinical progression free survival
Castration-resistance
Health related quality of life
Adverse events
Incremental cost-effectiveness

ENZARAD

Primary endpoint: MFS by conventional imaging



	events/N	MFS 8y
ENZA	98/401	74%
NSAA	109/401	72%

HR = 0.88 (95% CI 0.67, 1.15)
2p = 0.34 (log-rank test)

Median FU = 8 years

Number at risk (number censored)

401 (2)	395 (4)	392 (5)	384 (7)	359 (12)	334 (16)	306 (28)	226 (93)	117 (192)	36 (267)
401 (2)	390 (7)	382 (8)	370 (10)	345 (16)	323 (19)	297 (26)	221 (86)	113 (187)	47 (249)

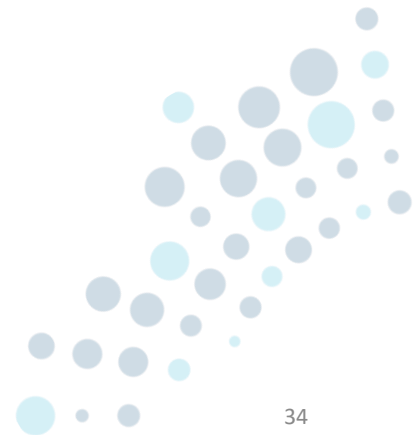
ENZARAD

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
Pelvic field radiation planned	Yes	50/162	26/162		0.47 (0.29 to 0.76)	
	No	59/239	72/239		1.25 (0.89 to 1.76)	<0.001
Very high risk	Yes	100/338	90/343		0.85 (0.64 to 1.13)	
	No	9/63	8/58		1.04 (0.40 to 2.71)	0.74

Conclusions

- SBRT is safe and has very good outcomes for low to intermediate risk PCa.
 - Watch out for dose?
 - Patient selection on baseline symptoms
- Pelvic radiotherapy: only in very selected cases
- Duration of ADT: don't overtreat
- All high risk patients need ARTA: clearly not



Future = patient selection

