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PRESENCIAL RETRANSMITIDO EN DIRECTO
FACE-TO-FACE AND LIVE STREAMING



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Espacio Maldonado, Madrid

Early Salvage RT Is Equivalent to Adjuvant RT in Patients With High-Risk Localized or Locally Advanced Disease

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Outline

Part 1 — The Randomized Evidence (2020–2024)

- Three pivotal RCTs: GETUG-AFU 17, RAVES, RADICALS-RT
- ARTISTIC prospective meta-analysis
- Critical synthesis: what the trials do and do not show

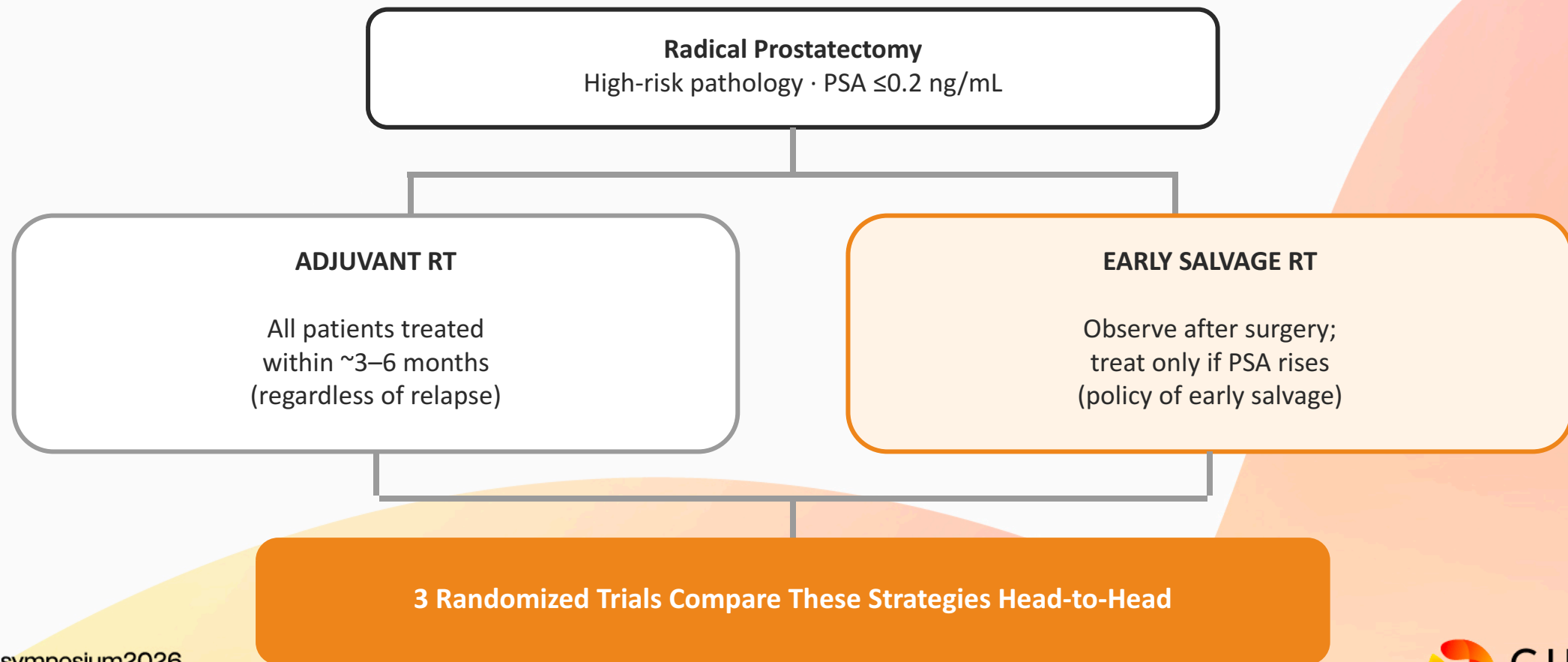
Part 2 — Open Questions for 2026

- Q1. How early is early? (PSA threshold)
- Q2. How much can we hypofractionate? (NRG-GU003, SCIMITAR, POPART)
- Q3. Is there a role for adaptive RT? (SCIMITAR, DART-PHASER)

PART 1

Adjuvant vs. Early Salvage RT: The Randomized Evidence

The Central Decision After Radical Prostatectomy



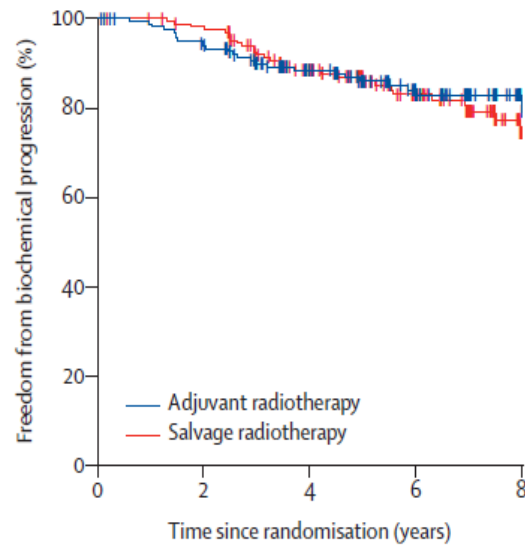
Three Trials, One Question

RAVES (Australia / NZ)

n= 333 closed early

R+, ECE, or SVI; no mandatory ADT

Kneebone et al., Lancet 2020



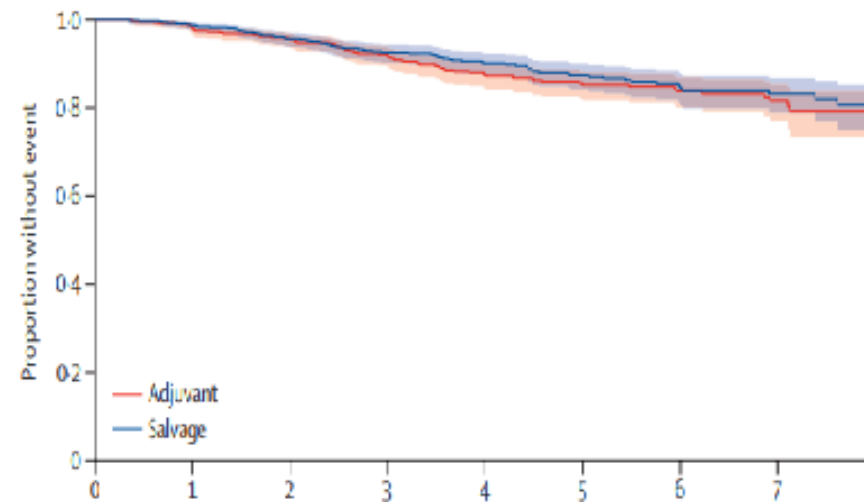
8-year bRFS 80% vs 77%

RADICALS-RT (UK/Canada/DK/Ireland)

n= 1396

≥1 risk factor: pT3/4, Gleason 7–10, R1, or PSA ≥10

Parker et al., Lancet 2020



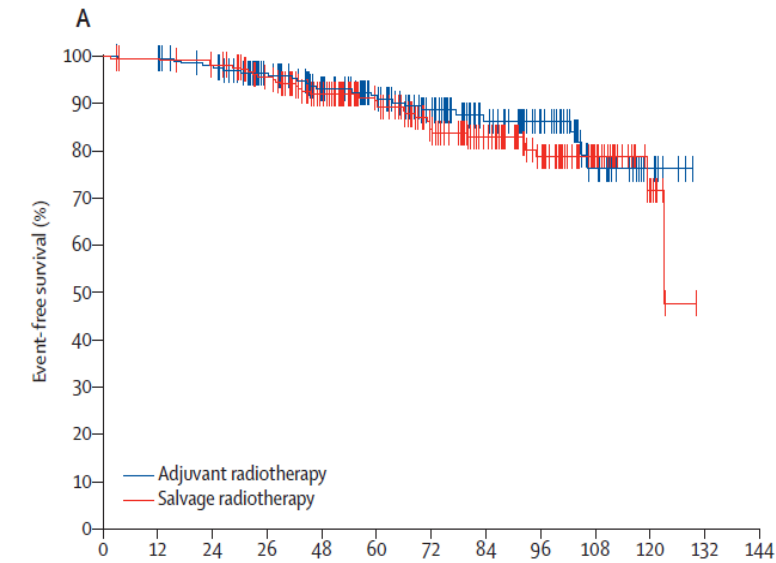
5-year bPFS 85% vs 88%

GETUG-AFU 17 (France)

n= 424 (closed early)

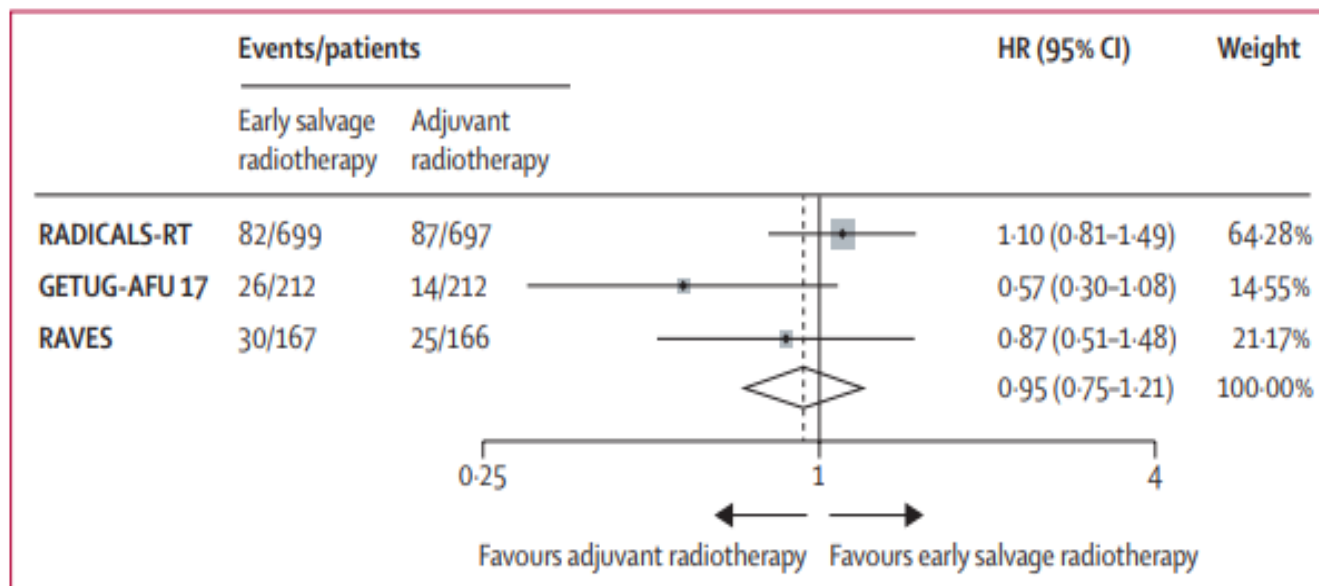
pT3/T4a or R1; all pts received 6-mo ADT

Sargos et al., Lancet Oncol 2020



5-year event-free survival 90% vs 92%

ARTISTIC - Meta-Analysis



Method

- Prospectively-planned pooled analysis
- 2153 patients; harmonised event-free survival definition across all 3 trials

Result

- Pooled HR 0.95 (95% CI 0.75–1.21; $p=0.70$)
- 5-yr EFS: 89% (adjuvant) vs 88% (salvage) — a 1-point difference
- Low heterogeneity across trials ($I^2=42\%$, $p=0.18$)

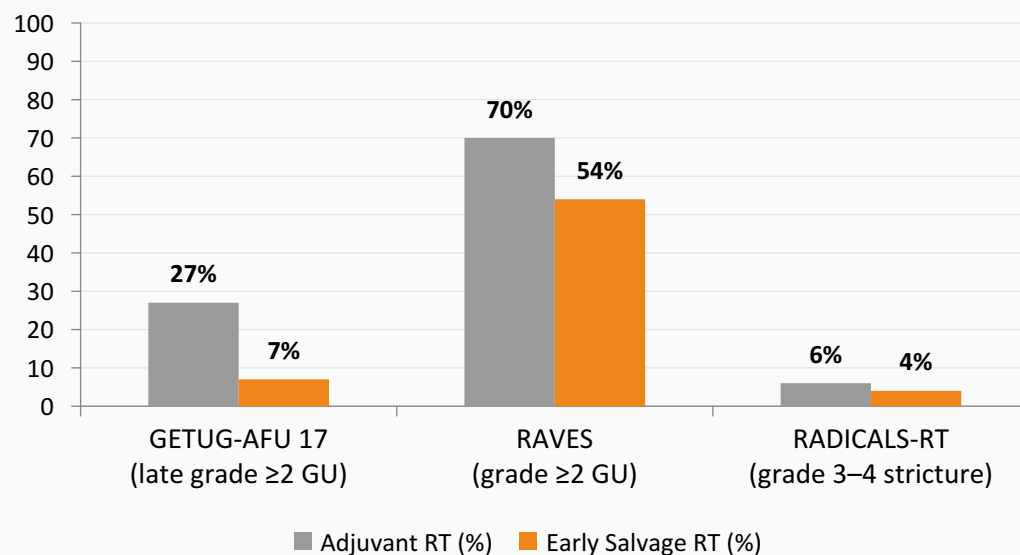
Source

- Vale et al., Lancet 2020

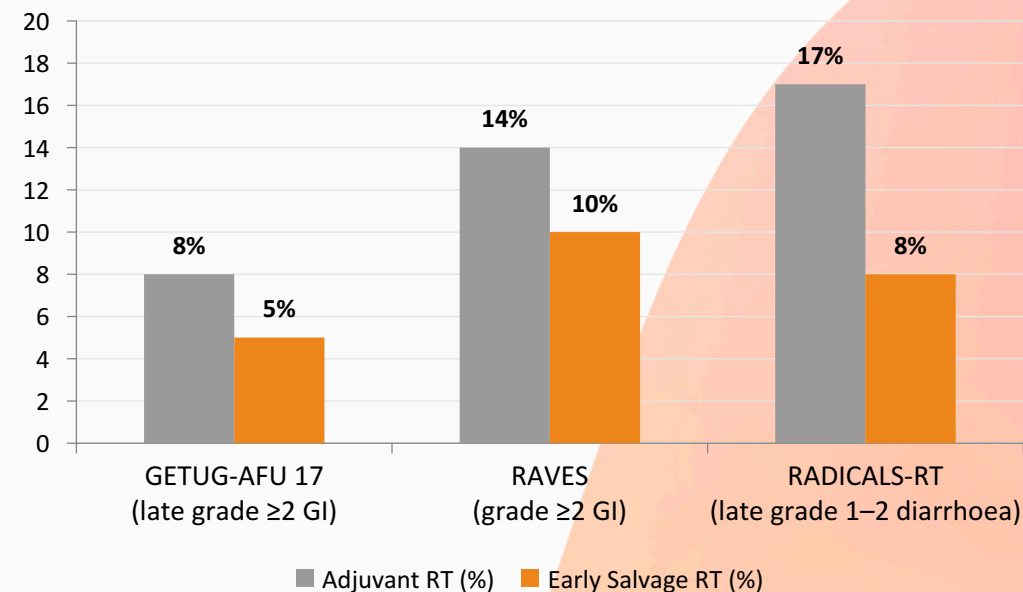
CRITICAL APPRAISAL — A methodologically strong, prospectively-designed pooled analysis — but it inherits each trial's limitations (early stopping, heterogeneous salvage triggers/ADT use) and median follow-up is still only 5–6.5 years; long-term overall-survival data are not yet mature.

Late AEs

Genitourinary Toxicity by Trial and Treatment Arm



Gastrointestinal Toxicity by Trial and Treatment Arm



CRITICAL APPRAISAL — *RADICALS-RT reported incontinence and stricture rather than a single GU-toxicity composite, so it is not directly comparable on this axis — shown here for trial-name reference only. Despite differing endpoints and ADT policies across trials, every trial found more toxicity with adjuvant RT.

GI toxicity is a smaller but consistent signal, and less often statistically significant than GU toxicity: GETUG-AFU 17's late GI difference (8% vs 5%) was NOT significant ($p=0.24$), unlike its acute GI difference (11% vs 4%, $p=0.010$). RAVES and RADICALS-RT differences were directionally consistent but of modest magnitude. RADICALS-RT's late grade 3+ diarrhoea/proctitis events were rare in both arms.

Part 1 — Critical Synthesis

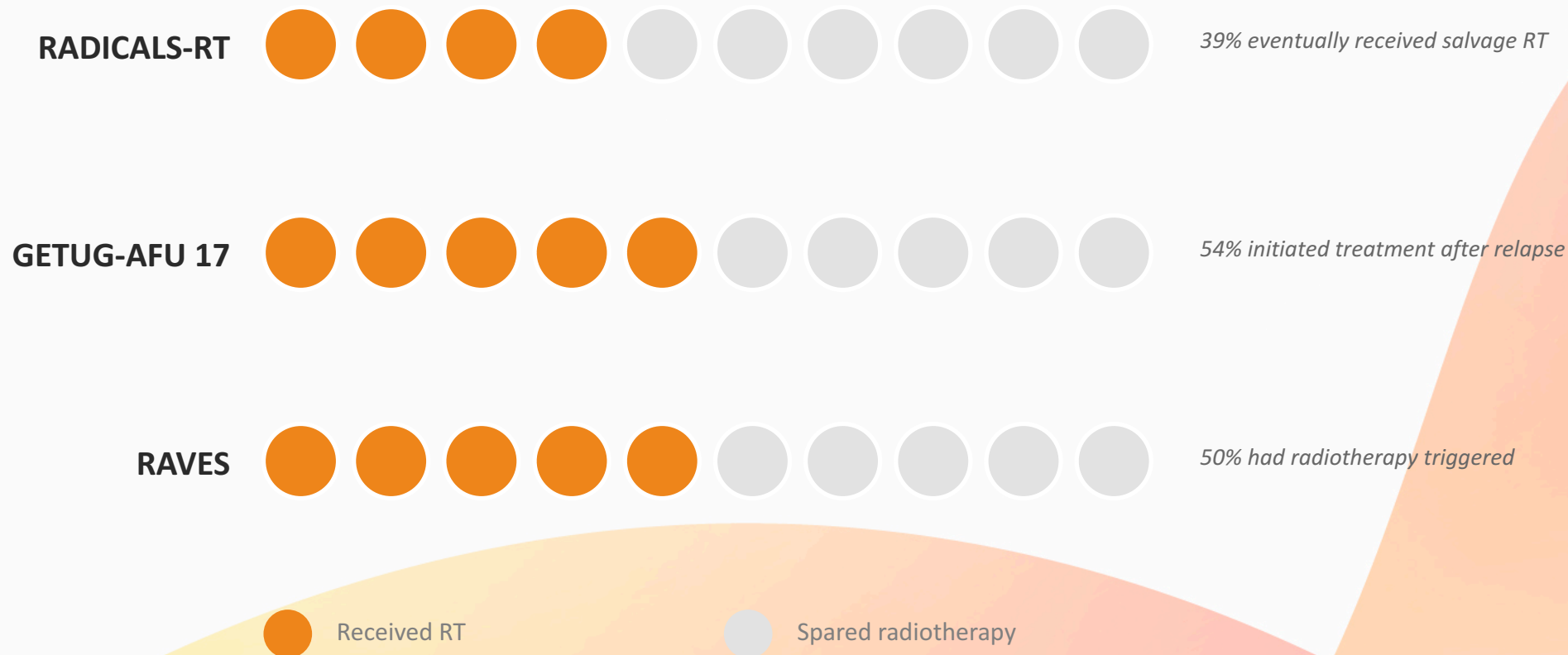
What the evidence supports

- No clear oncologic benefit of adjuvant RT, but more side effects

What it does NOT establish

- All three trials closed early for low event rates — each is individually underpowered; only the pooled analysis has adequate power
- Median follow-up (5–8 years) may be too short for prostate cancer survival
- RADICALS-RT's HR of 0.68 (CI 0.43–1.07) for metastasis ($p=0.095$) leaves real uncertainty for the highest-risk patients
- "Early salvage" definitions differed ($\text{PSA} \geq 0.1$ vs ≥ 0.2 vs biochemical relapse) — these are not interchangeable strategies

How Many Men Avoided Radiotherapy Altogether?



Each row = 10 men allocated to the observation/early-salvage policy in that trial. Sources: Parker et al. Ann Oncol 2024; Sargos et al. Lancet Oncol 2020; Kneebone et al. Lancet Oncol 2020.

Early salvage RT is the new standard of care

at least for most patients — but important uncertainties remain

Who Wasn't Studied: Node-Positive Disease

None of the three pivotal trials enrolled node-positive (pN1) patients

Trial	Node-positive (N1) patients
GETUG-AFU 17	Excluded (required pN0/pNx)
RAVES	Excluded
RADICALS-RT	Excluded

This is precisely the population where treatment intensification is most biologically plausible — and where we still have no randomized evidence comparing adjuvant vs. salvage strategies.

Adjuvant Versus Early Salvage Radiation Therapy After Radical Prostatectomy for pN1 Prostate Cancer and the Risk of Death

Tilki et al. JCO 2022

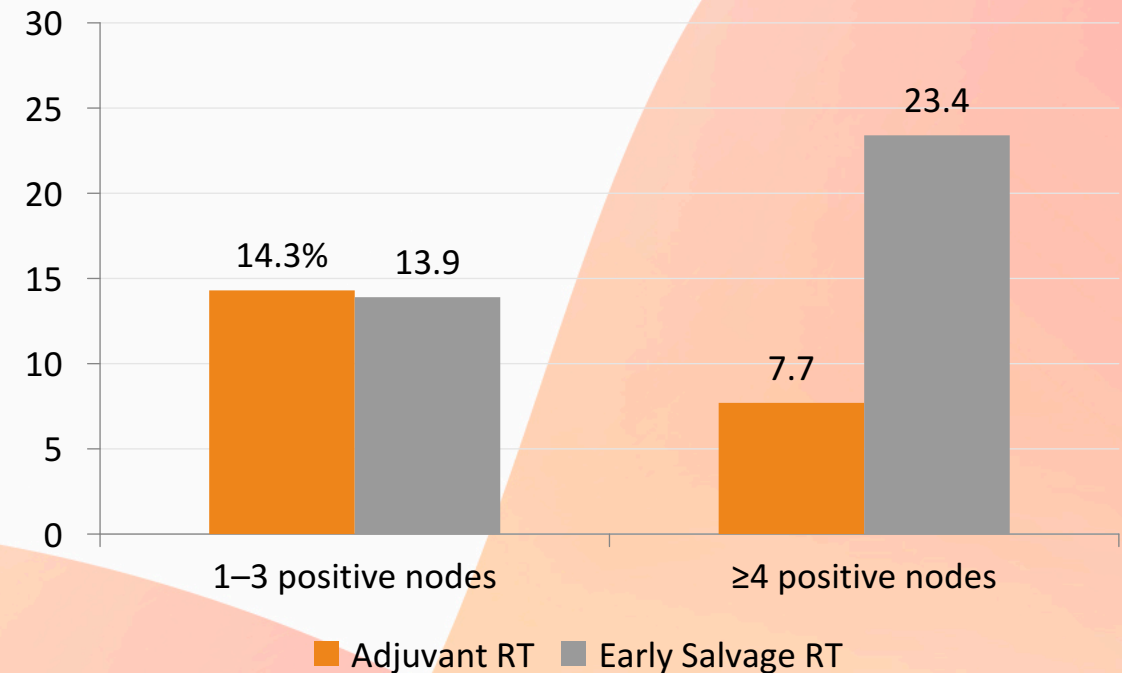
Design

- Single-center retrospective study of 1,614 pN1 patients

Result

- adj RT vs early sRT: 8% reduction in all-cause mortality risk per additional positive node ($p=.03$)
- 7-yr adjusted all-cause mortality significantly lower with adjuvant RT in men with ≥ 4 positive nodes (7.7% vs 23.4%)
- No difference for 1–3 positive nodes

7-Year Adjusted All-Cause Mortality by Nodal Burden



“Equivalent” Is a Simplification

No trial formally met its pre-specified non-inferiority criterion

- RAVES: its 95% CI crossed the pre-set margin ($HR < 1.48$); non-inferiority was NOT met
- GETUG-AFU 17 and RADICALS-RT were framed around “no significant difference,” which is statistically not the same claim as proven equivalence
- The pooled ARTISTIC estimate ($HR\ 0.95$, 95% CI $0.75-1.21$) is still compatible with a real difference of up to ~25% in either direction

The Evidence Predates Today’s Staging Tools

When the Trials Enrolled (2007-2016)

Risk assessed by:

- Pathologic stage & margins
- Gleason score
- Conventional CT / bone scan

Today (2026)

Previous factors plus:

- PSMA-PET — detects disease at much lower PSA
- Genomic classifiers

The Longest-Term Outcomes Are Still Unknown

Trial median
follow-up

~5–8 years (RADICALS-RT longest:
7.8 yr)

Typical prostate
cancer relapse /
mortality window

Up to 15–20 years

Overall survival and prostate-cancer-specific mortality remain immature in all three trials

- RADICALS-RT (longest follow-up): only 26 deaths reported by 2018 cutoff, 8 attributed to prostate cancer
- For a man in his early 60s with a 15–20 year life expectancy, the outcome that matters most — will I die of this cancer — cannot yet be answered by any of these trials

These are real, unresolved limitations

— but they do not overturn the core conclusion

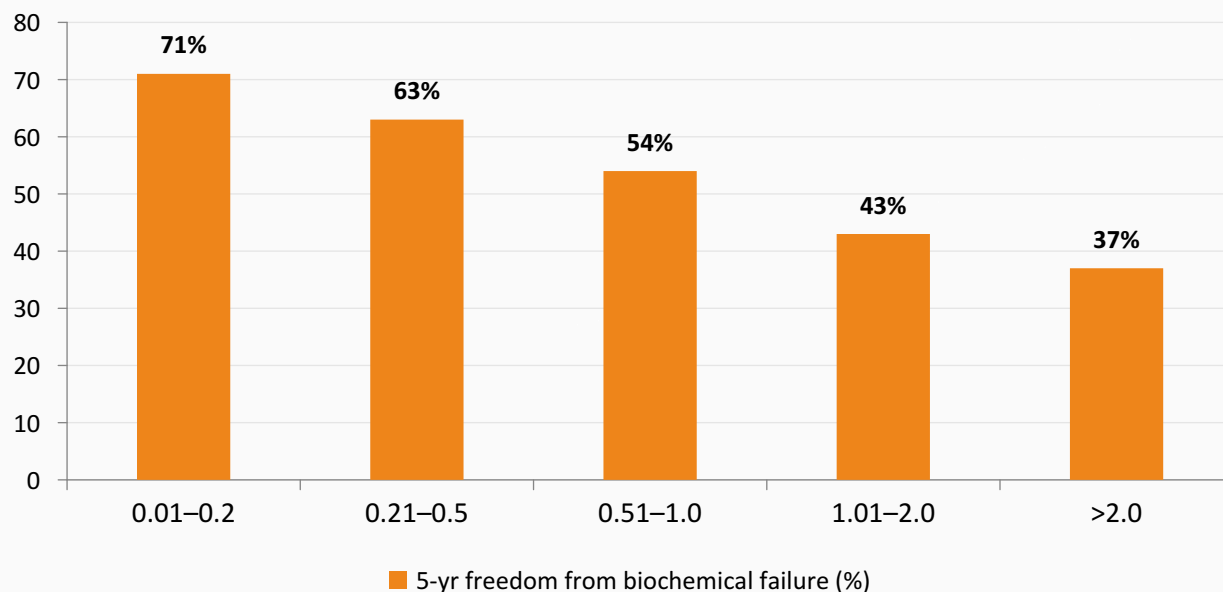
So, what's left to answer in 2026?

PART 2

Open Questions for 2026

Question 1 — How Early Is Early?

FFBF by Pre-Salvage PSA (ng/mL)



CRITICAL APPRAISAL — Retrospective, multi-institutional pooled data (not a randomized comparison of PSA thresholds) — treatment selection, ADT use, and follow-up varied considerably across centers, and this design cannot prove that *triggering* salvage earlier actually improves outcomes for an individual patient.

Pre-salvage PSA is strongly prognostic

- Multi-institutional nomogram, n=2460, 10 academic centers
- 5-yr FFBF falls from 71% to 37% as PSA rises from <0.2 to >2.0 ng/mL
- Pre-salvage PSA, Gleason score, margins, and ADT use were independent predictors

The open question

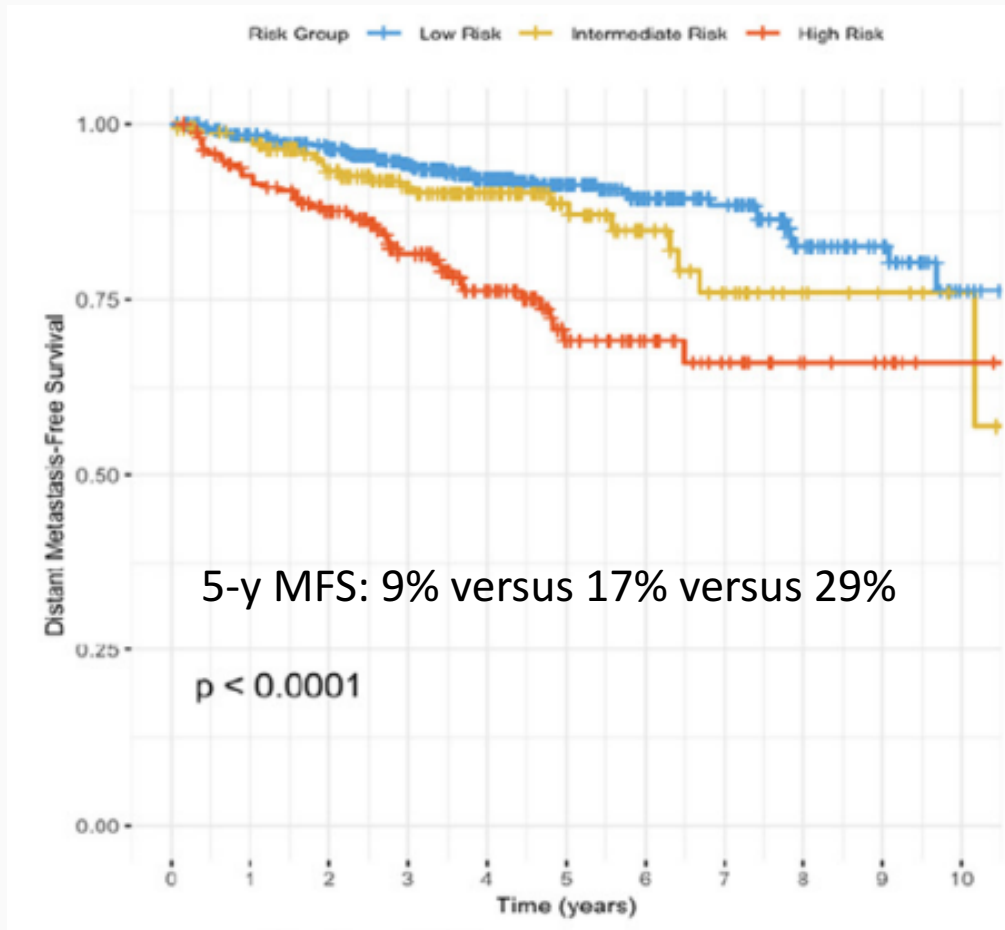
- “Ultra-early” salvage (PSA <0.2) vs waiting for a confirmed rise
- Balancing overtreatment of men who would never relapse vs missing the curable window

Source

- Tendulkar et al., J Clin Oncol 2016

Penalized-Survival Nomogram Predicts 5-Year Metastasis-Free Survival After Salvage Radiotherapy for Postprostatectomy Patients: A Multicenter Study

Mastroleo et al., Clin Genitourin Cancer 2025



Design

- Multicenter (15 European centers), n=1720 patients receiving sRT for biochemical recurrence
- Machine-learning nomogram with 3 variables: pT3/4, ISUP grade 4–5, and time from surgery to SRT <12 months

Result

- Each factor independently predicted worse 5-yr distant metastasis-free survival (DMFS)
- ISUP 4–5: sHR 1.75 (95% CI 1.30–2.35); pT3/4: sHR 1.54 (1.11–2.13); SRT <12mo: sHR 1.49 (1.07–2.09)

Question 2 — How Much Can We Hypofractionate?

Conventional fractionation (reference)

- 66–70 Gy in 33–35 fractions — ~7 weeks of daily treatment

Moderate hypofractionation

- 52.5–62.5 Gy in 18–25 fractions (2.5–3.0 Gy/fraction) — ~4–5 weeks
- NRG-GU003, RADICALS-RT dose-analysis, Sawayanagi et al.

Ultra-hypofractionation / SBRT

- 30–34.5 Gy in 5 fractions (6–7 Gy/fraction) — ~1–2 weeks
- SCIMITAR, POPART

NRG-GU003 — Moderate hypo-sRT (Phase III)

Design

- 296 pts randomized 62.5 Gy/25fx vs 66.6 Gy/37fx
- Co-primary endpoints: change in EPIC bowel & urinary domain scores at 24 months

Result

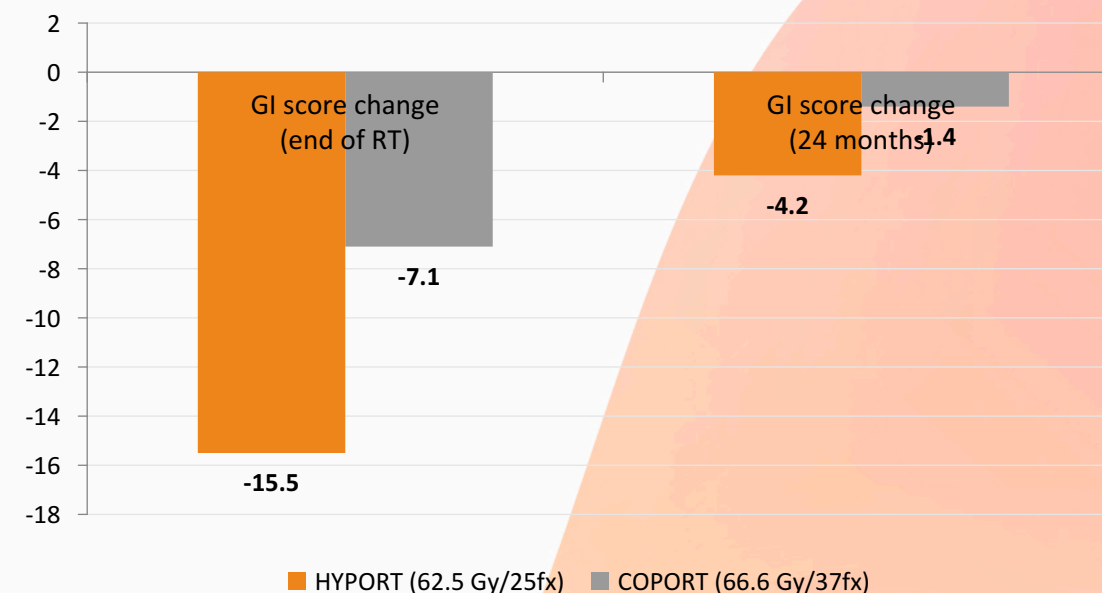
- HYPOR non-inferior to COPORT for GU & GI patient-reported toxicity at 24 months
- Acute GI worse with HYPOR at end of RT, but recovered by 6 months
- No diff in 2-y biochemical failure (12% vs 8%, $p=0.28$)

Source

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Buyyounouski et al., JAMA Oncol 2024

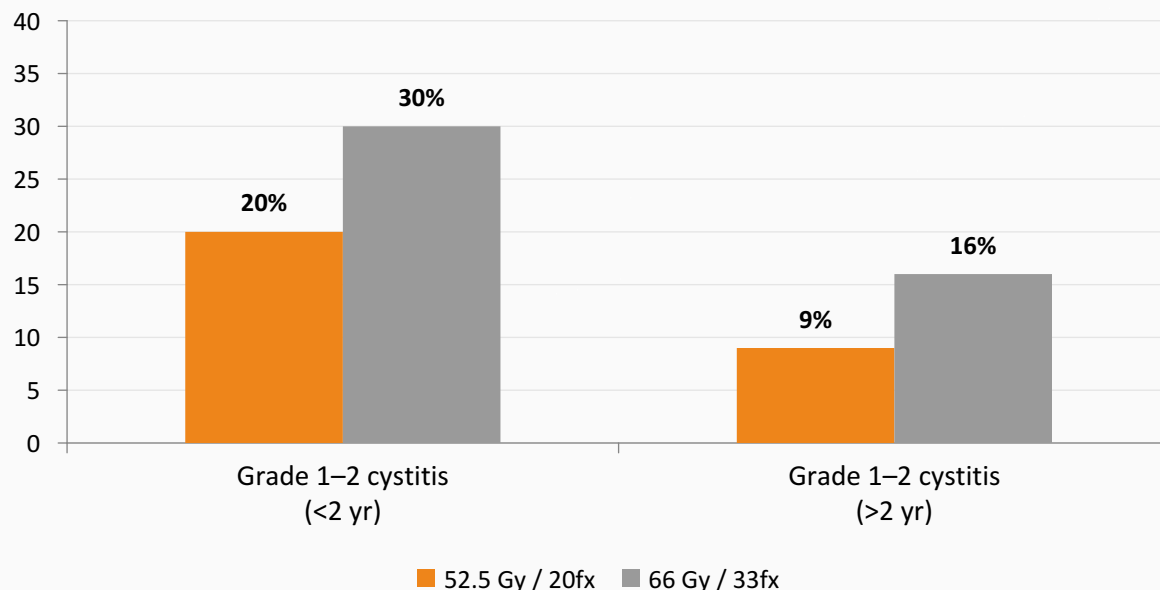
Patient-Reported GI Symptom Change From Baseline (EPIC)



CRITICAL APPRAISAL — Only 2.1 years of median follow-up— the non-inferiority conclusion on toxicity is solid, but longer-term disease control data are still awaited.

RADICALS-RT — Dose-Fractionation Analysis

Cystitis by RT Schedule (Adjuvant-RT Patients)



CRITICAL APPRAISAL — This is a non-randomized comparison nested within an RCT — center/clinician choice of fractionation is a potential confounder, so causal claims about the schedules themselves are limited. Still, it is reassuring supportive data for moderate hypofractionation.

Design

- Non-randomized, exploratory analysis of the 634 RADICALS-RT patients who received adjuvant RT
- Dose schedule (52.5 Gy/20fx or 66 Gy/33fx) chosen by treating center, not by randomization

Result

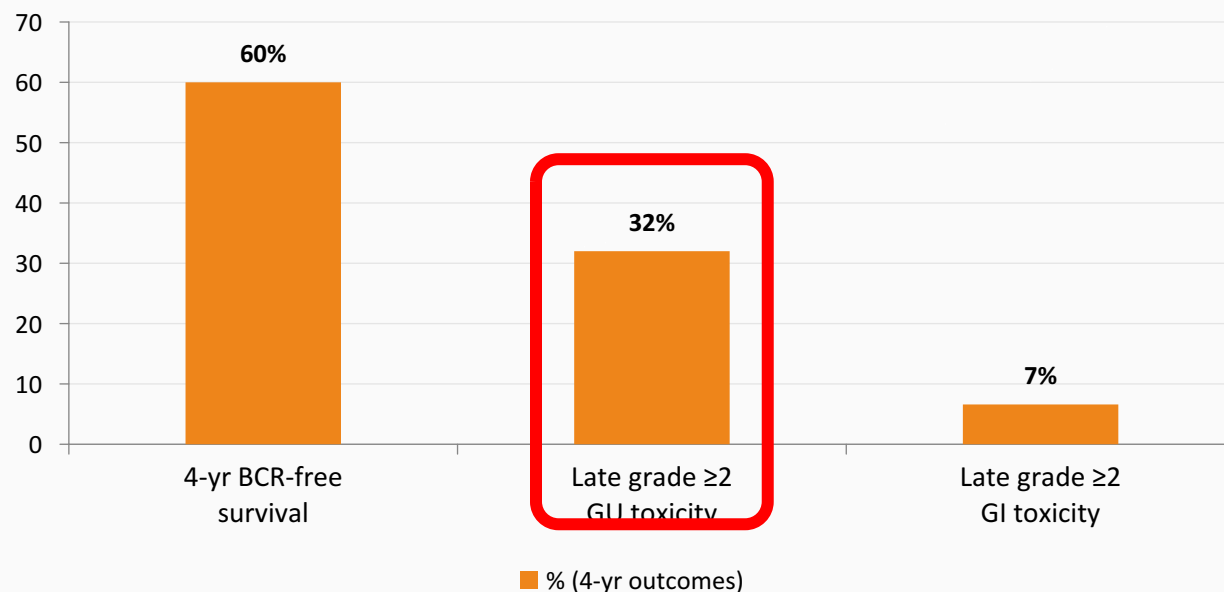
- Grade 1-2 cystitis more frequent with 66 Gy/33fx, both <2yr (30% vs 20%, $p=0.04$) and >2yr (16% vs 9%, $p=0.08$)
- No meaningful difference in patient-reported incontinence between schedules
- Grade 3-4 toxicity rare in both groups

Source

- Petersen et al., Int J Radiat Oncol Biol Phys 2023

SCIMITAR — SBRT to the Prostate bed

Phase II Outcomes at 4 Years (n=100)



Design

- Phase II, dual-center, single-arm; SBRT 30–34 Gy in 5 fractions $\pm$ nodes/ADT
- Compared to a phase III conventional-RT cohort via inverse-probability weighting (not randomized)

Result

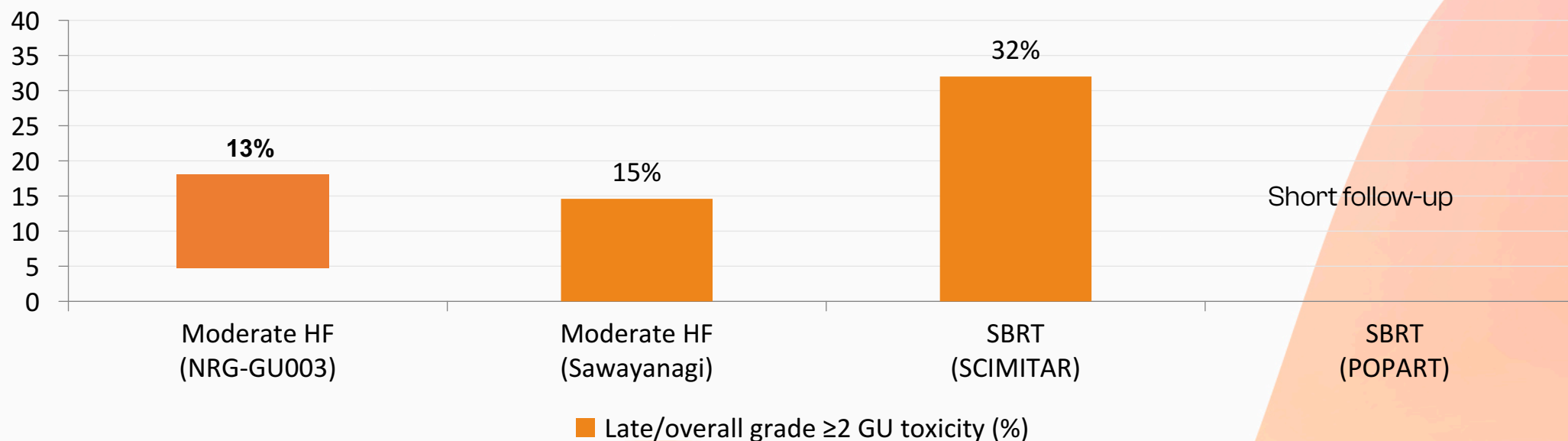
- 4-yr BCR-free survival: **60%** (95% CI 50–70)
- Without ADT: lower BCR risk vs conventional RT (sHR 0.49, $p=0.008$)
- With ADT: no significant difference — possible signal of worse control with SBRT+ADT (sHR 1.58, wide CI)
- 23% had a clinically meaningful decline in urinary incontinence at 48 months

Source

- Kishan et al., Eur Urol 2026

Question 2 — Where We Stand

Late Grade ≥ 2 GU Toxicity Across Hypofractionation Studies



CRITICAL APPRAISAL — Moderate hypofractionation (52.5–62.5 Gy/18–25fx) now rests on phase III non-inferiority evidence (NRG-GU003) and is a reasonable standard option. SBRT (5 fractions) remains investigational: outcomes vary widely across small, non-randomized, single-arm series — randomized trials are needed before routine adoption.

Question 3 — Is There a Role for Adaptive RT?

The problem

- Prostate bed anatomy varies fraction to fraction: bladder and rectum filling change target coverage and OAR dose
- This variability matters even more as we want to hypofractionate

The adaptive RT proposition

- Re-optimize (or at least re-evaluate) the plan on each day's imaging before treating
- Could this let us hypofractionate more aggressively while keeping side effects in check?

DART-PHASER: adaptive hypo-sRT

Design

- Prospective trial, moderately hypofractionated sRT (55-59 Gy/20fx) on Ethos
- Interim analysis of 840 fractions

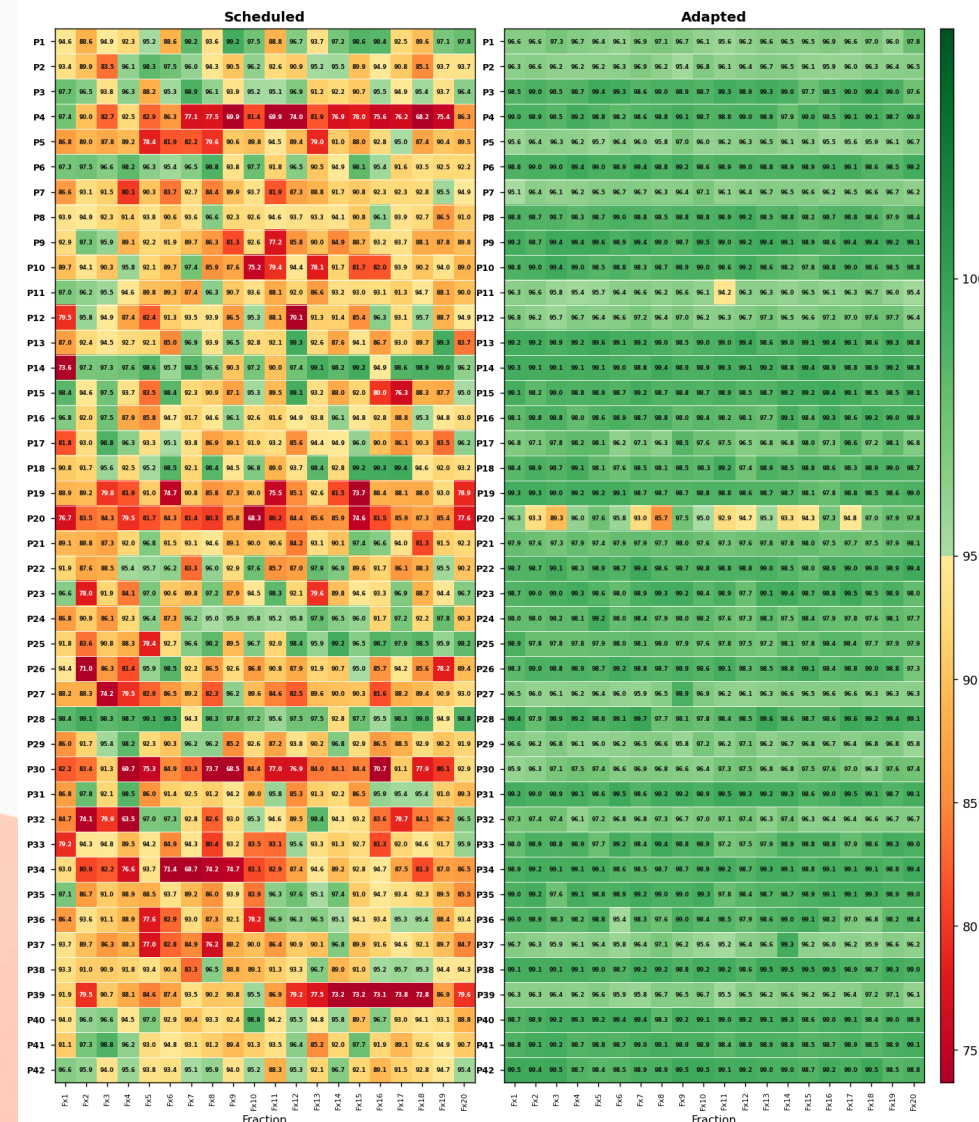
Result

- >70% treatment fraction needed adaptation (not meet offline plan criteria)
- Adapted plans significantly reduced rectal dose and improved PTV coverage (both $p < 0.0001$)
- Low acute effects: G2 GI 4.8%, G2 GU 9.5%

Source

- Nicosia et al., Clin Transl Radiat Oncol 2026

Prostate bed PTV V95%



SCIMITAR trial (Kishan et al., Eur Urol 2026)

Design

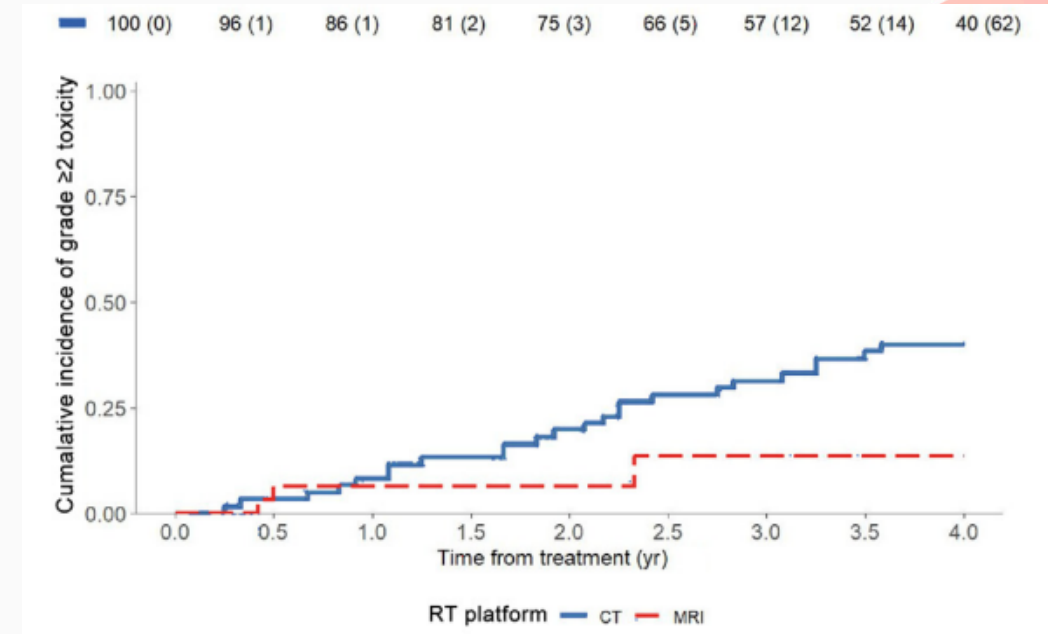
- Phase II non-randomized trial 100 patients

Result

- Treatment: prostate bed SABR (30-34 Gy/5 fx +/- bed boost +/- pelvic RT)
- CTgRT= 69
- 0.35T MRgRT= 31

End-point

- 4-y BRFS 60%



Lower $\geq$ G2 GU late AE with adaptive (14% versus 40%; HR 3.54, $p=0.023$)

No diff. for $\geq$ G2 GI late AE

Question 3 — Where We Stand

New findings

- High daily anatomical variability in postoperative setting
- Adaptive consistently improve target coverage and/or reduce OAR dose
- Early clinical side effects with adaptive hypofractionated sRT looks favorable

What's missing

- No randomized trial of adaptive vs non-adaptive RT in this setting
- No mature late-toxicity or oncologic-outcome data
- Adaptive RT is a time-consuming procedure

Take-Home Messages

Practice-changing (high-quality evidence)

- Early sRT: standard of care for most patients
- 3 RCTs + prospective meta-analysis, n=2153: equivalent oncologic control, consistently less toxicity
- The earlier sRT the better the results
- Adj RT still option for pN1

Reasonable, evidence-supported option

- Moderate hypofractionation (NRG-GU003)

Investigational — promising but unproven

- Ultra-early salvage (PSA threshold) — retrospective data only
- SBRT / ultra-hypofractionation — small, single-arm series
- Adaptive RT — strong dosimetric rationale, no randomized or long-term outcome data



Thank You!

Questions welcome

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Sawayanagi et al. 2026 — Phase II, 54 Gy/18fx

Design

- Single-arm phase II, 54 Gy in 18 fractions (VMAT) to the prostate bed
- 89% salvage, 11% adjuvant; 53% received concurrent ADT; median follow-up 37.3 months

Result

- Low acute GU effects (5.5%); acute GI effects higher (34.5%, mostly grade 2)
- 3-yr biochemical recurrence-free survival: 65.8% (95% CI 51.1–77.1)
- Quality of life largely preserved; transient bowel symptoms resolved within 3 months

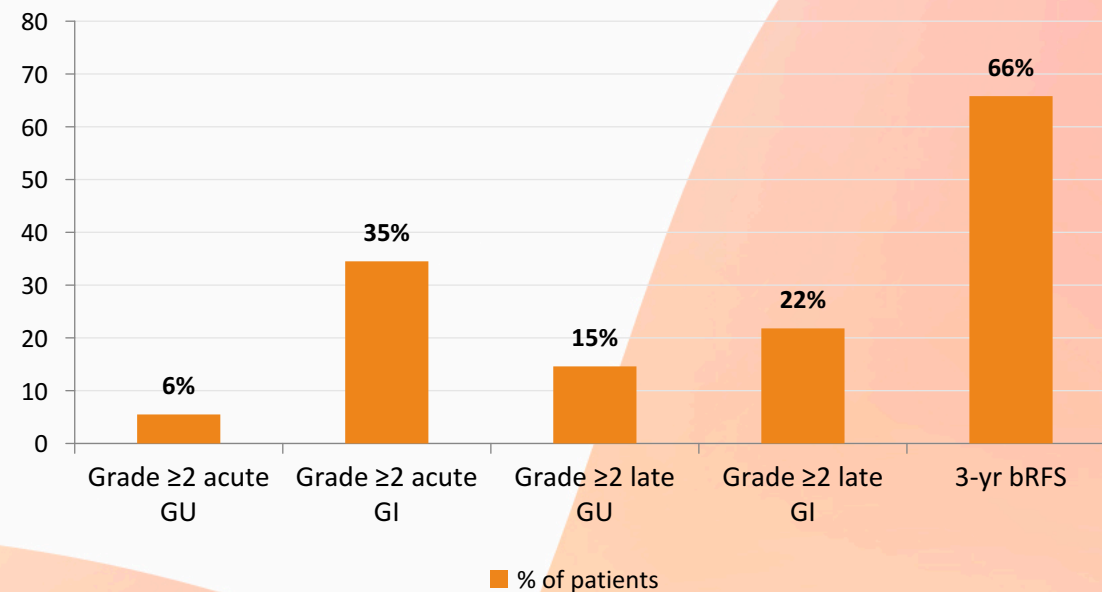
Source

- Sawayanagi et al., Radiother Oncol 2026

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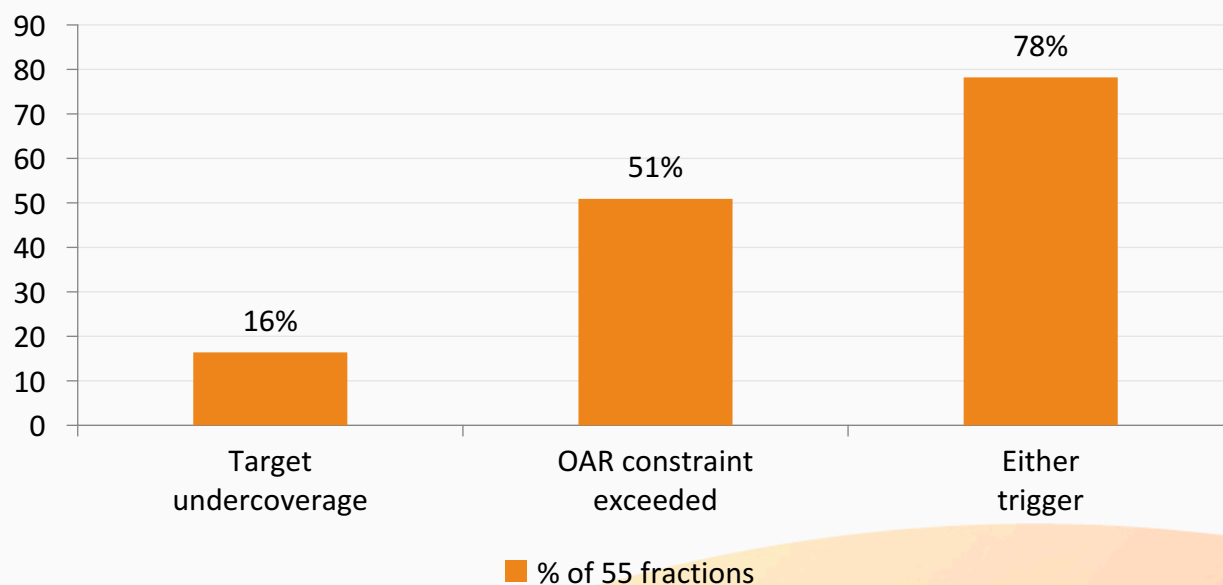
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Toxicity and Biochemical Control (n=55)



Cao et al. — SMART (MR-Linac, Post-Hoc Analysis)

Fractions in Which Adaptive RT Would Have Been Beneficial



Design

- Post-hoc analysis of 55 MRI setup scans from 11 patients in a phase II post-prostatectomy SBRT trial

Result

- Bladder volume varied by a median of -24.5% fraction to fraction
- Simulated adaptive RT (SMART) would have been dosimetrically beneficial in 78% of fractions
- Simulated adaptation met all dosimetric criteria in 100% of fractions

Source

- Cao et al., Cancers 2021

Compressing the Treatment Course

Conventional

66–70 Gy / 33–35 fx

~7 weeks

Moderate HF

52.5–62.5 Gy / 18–25 fx

~4–5 weeks

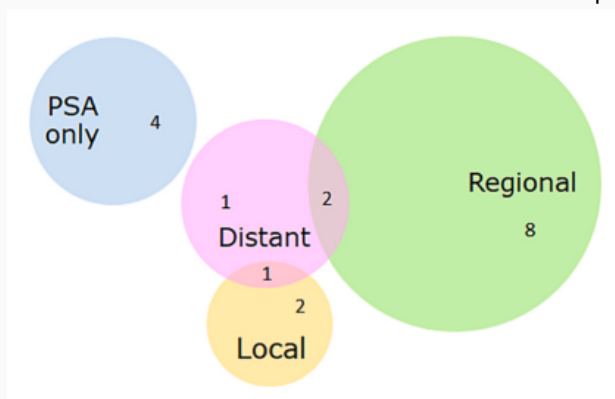
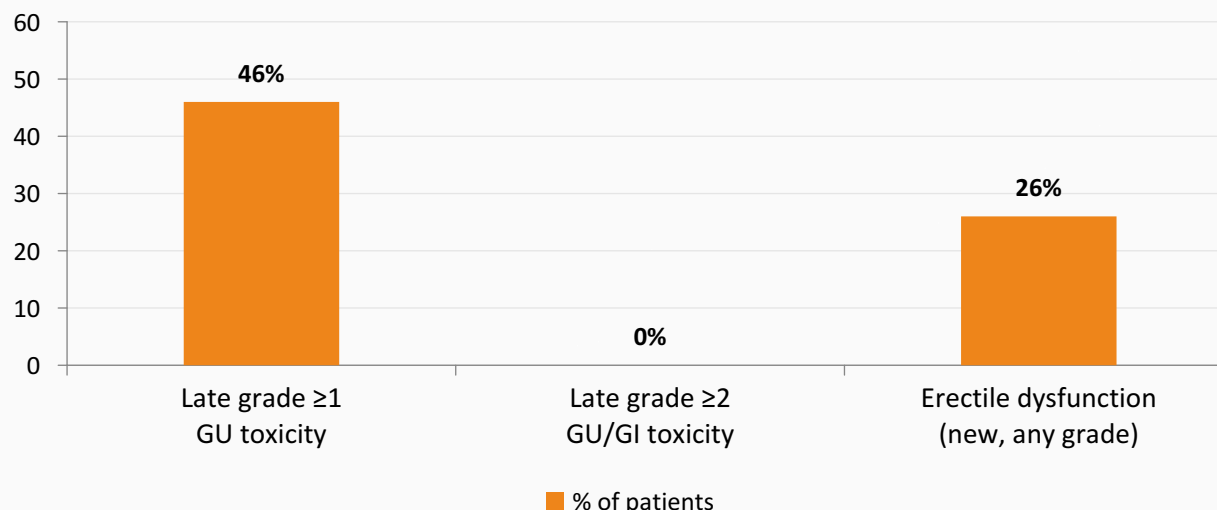
SBRT

30–34.5
Gy / 5 fx

~1 week

POPART — SBRT to the Prostate Bed

Toxicity and Patient-Reported Outcomes (n=50)



18% relapse at
median 10 months

Design

- Multicentric prospective study; SBRT 32.5 Gy in 5 fractions (EQD2 $\approx$ 74.3 Gy)
- Entry PSA 0.1–2.0 ng/mL; median follow-up 12.2 months

Result

- No late $G \geq 2$ GI or GU toxicity reported
- Late $G1$ urinary/rectal toxicity in 46% / 4%
- Median post-treatment PSA nadir: 0.04 ng/mL; 6 patients with biochemical failure at last follow-up

Source

- Ferrario et al., Clin Transl Radiat Oncol 2023

CRITICAL APPRAISAL — Very small sample (n=50) and short follow-up (~12 months) — too early to assess late toxicity or durable biochemical control; low pre-treatment PSA at entry may also select a more favorable-prognosis population.