

Radiotherapy highlights

Ad Vandermeulen, MD
Cliniques Universitaires Saint-Luc



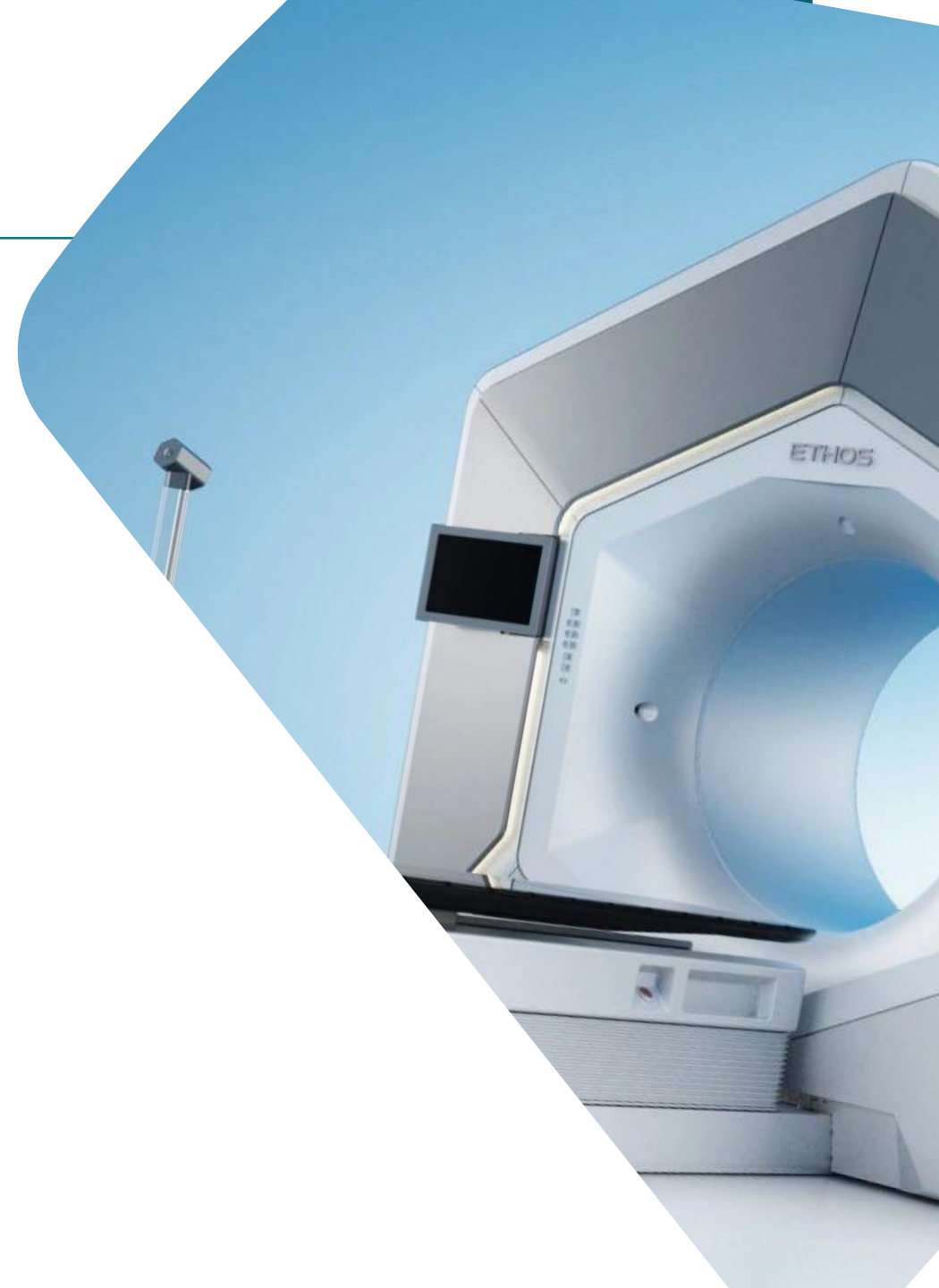
UROLOGY - RADIATION ONCOLOGY - MEDICAL ONCOLOGY

YEAR IN REVIEW
IN GU ONCOLOGY
MEETING 2025



Conflicts of interest

- I have no potential conflict of interest to report



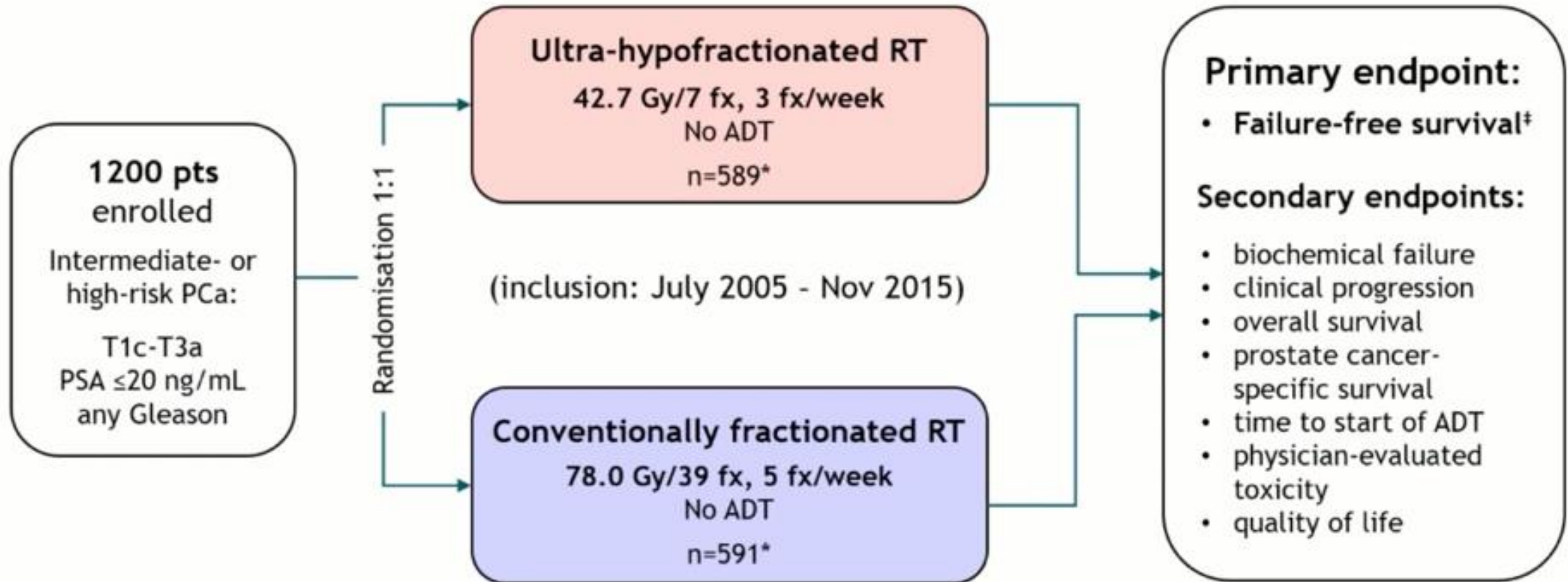
Overview



- Prostate cancer
 - Localised
 - **Hypo-RT-PC phase 3 trial:** Prostate SBRT
 - **RTOG 0924 trial**
 - **Thunder trial:** PSMA-PET/CT stage migration in PC
 - **Enzarad**
 - **PEACE V-STORM:** Pelvic nodal oligorecurrent PC
 - mHSPC
 - **STOPCAP meta-analysis**
 - mCRPC
 - **GROUQ-PCS 9**
- Bladder cancer
 - **Nivolumab plus ChemoRT** in Patients with Muscle-Invasive Bladder Cancer. Final Results of a Phase II Study by the HGUCG
 - **BART:** Bladder Adjuvant Radiotherapy Clinical Outcomes from a Phase III Multicenter RCT
- Testicular cancer
 - **SAKK 01/10:** Stage II Seminoma

HYPO-RT-PC trial overview

ESTRO



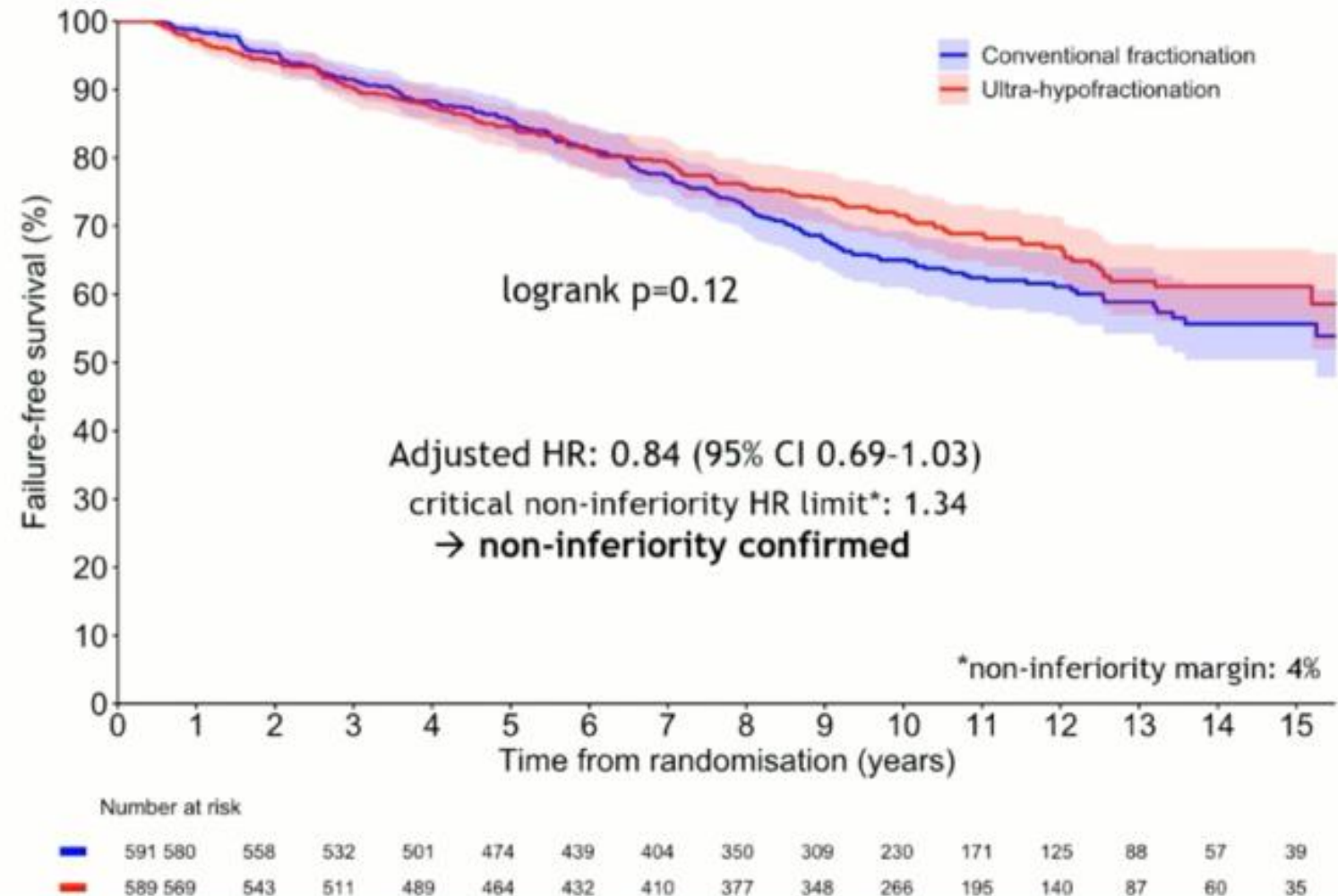
*11 and 9 pts withdrew consent or were ineligible for evaluation in the ultra-hypofractionated and conventionally fractionated RT groups, respectively.

† defined as time to biochemical failure, clinical progression, ADT initiation, or death from prostate cancer

Primary endpoint – failure-free survival

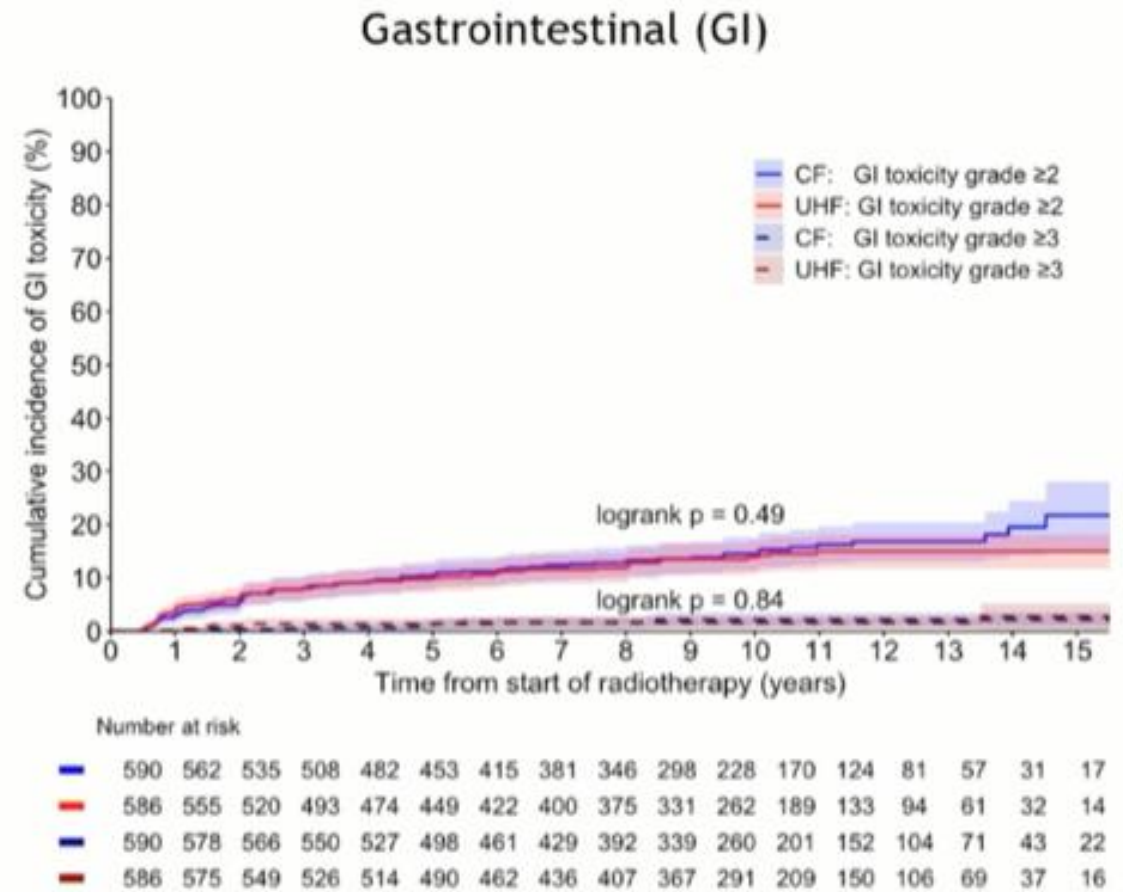
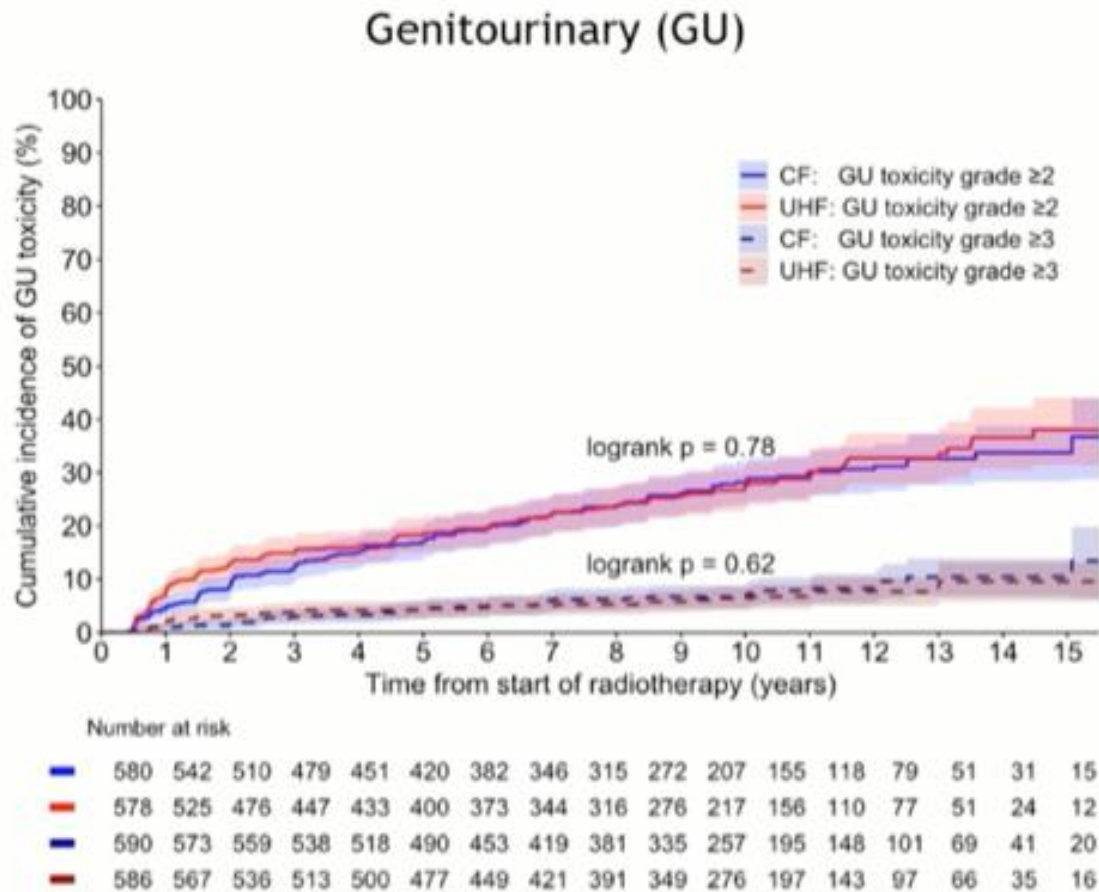
ESTRO

- Median follow-up time
10.6 years (IQR 9.1-12.9)
- Number of primary events
UHF: 178
CF: 205
- Failure-free survival at 10 years
UHF: 72% (95% CI 68-76)
CF: 65% (95% CI 61-69)



Late toxicity – cumulative incidence

ESTRO



HYPO-RT-PC - summary



- The ultra-hypofractionation schedule remains non-inferior to conventional fractionation in terms of tumour control
- It may offer greater efficiency than the conventional schedule in the long term
- No differences in long-term GU or GI toxicity were observed
- The findings support the 7-fraction ultra-hypofraction schedule as a safe, effective, and practical standard of care option for intermediate-risk prostate cancer

NRG/RTOG 0924 trial - Patient Population



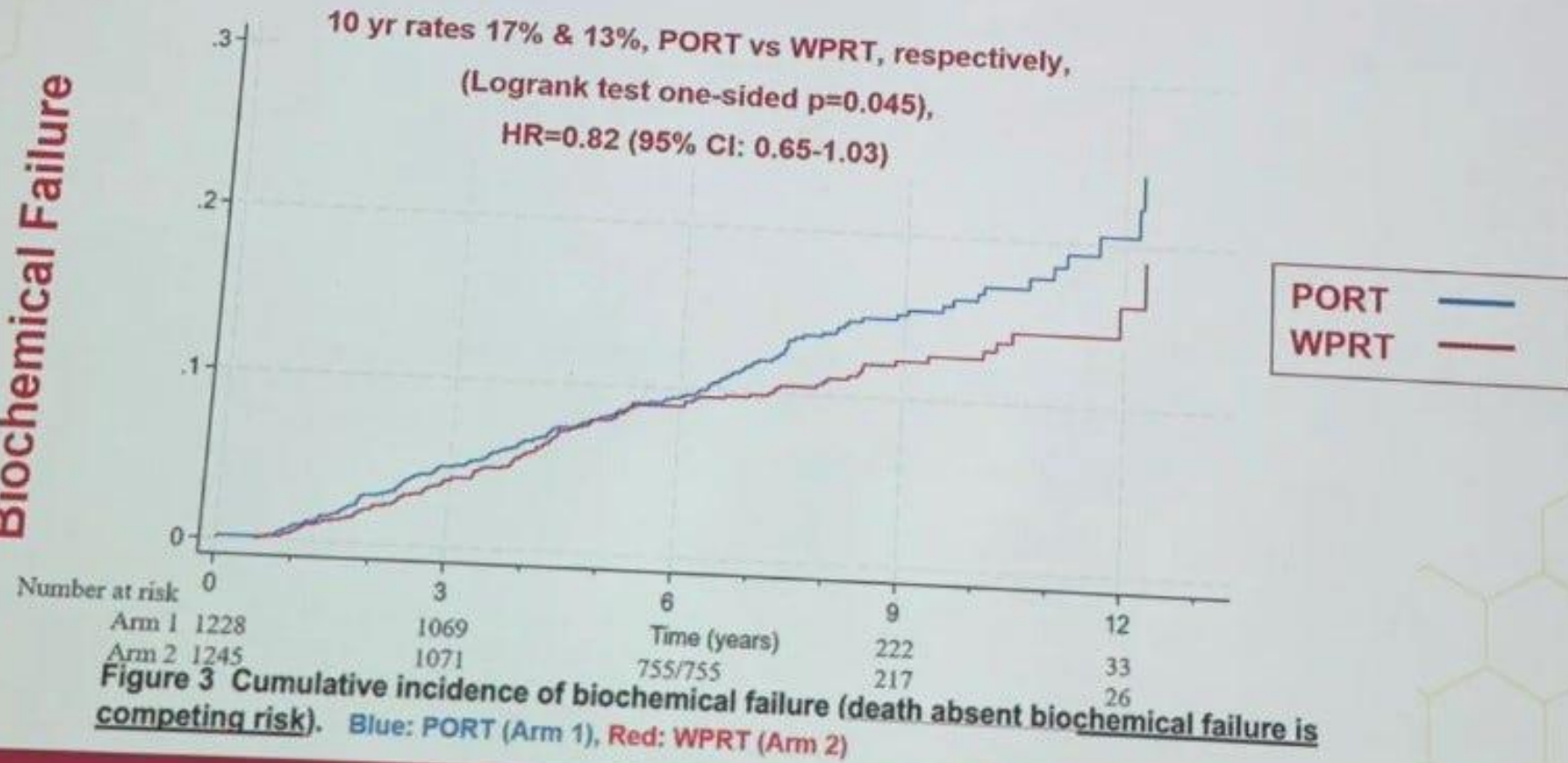
ASTRO

- Patients who are most likely to benefit from androgen deprivation therapy and whole-pelvic radiotherapy, defined as:
 - a) Having a **significant risk of lymph node involvement (e.g. >15%, based on the Roach formula);**
 - b) Being in one of the following risk groups
 - GS 7-10 + T1c-T2b (palpation) + PSA < 50 ng/ml (includes intermediate and high risk patients);
 - GS 6 + T2c-T4 (palpation) + PSA < 50 ng/ml OR Gleason score 6 + ≥ 50% biopsies + PSA < 50 ng/ml;
 - GS 6 + T1c-T2b (palpation) + PSA > 20 ng/ml
- Exclusion criteria:
 - cT3a-b (DRE)
- **Roach Nodal Risk Formula:** $(2/3 \text{ PSA} + (\text{Gleason Score} - 6) \times 10$

Biochemical Failure

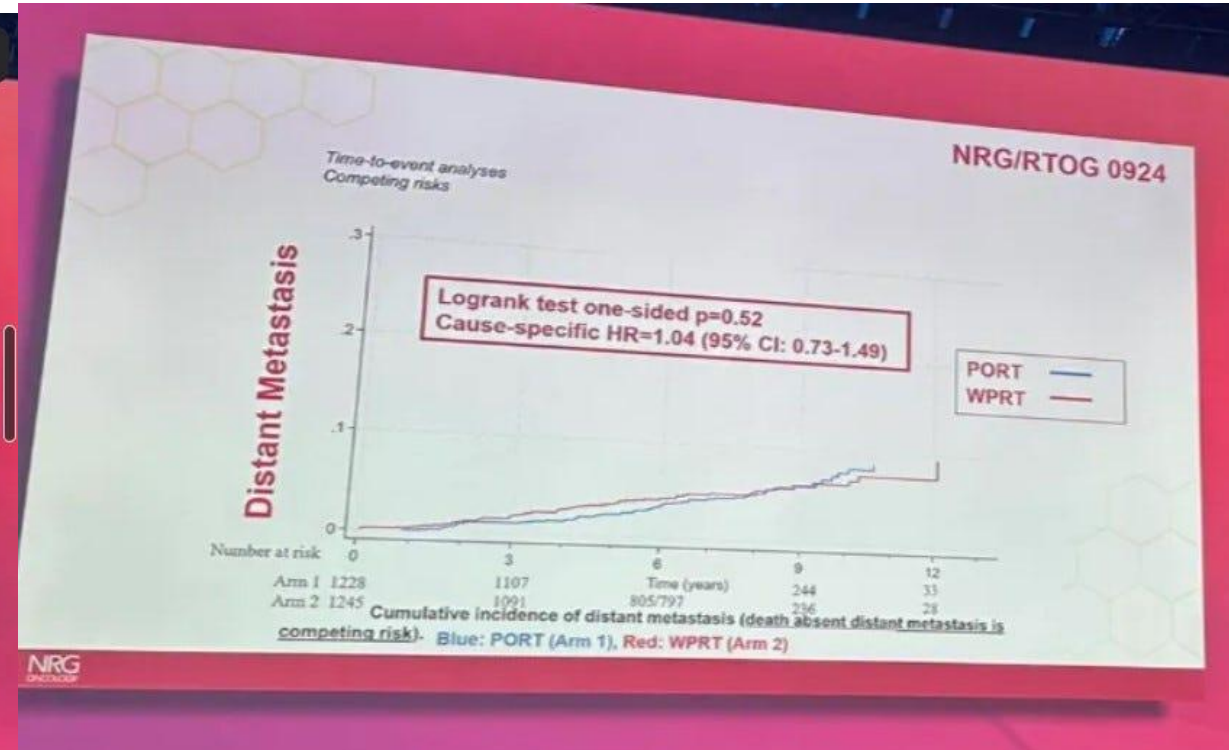
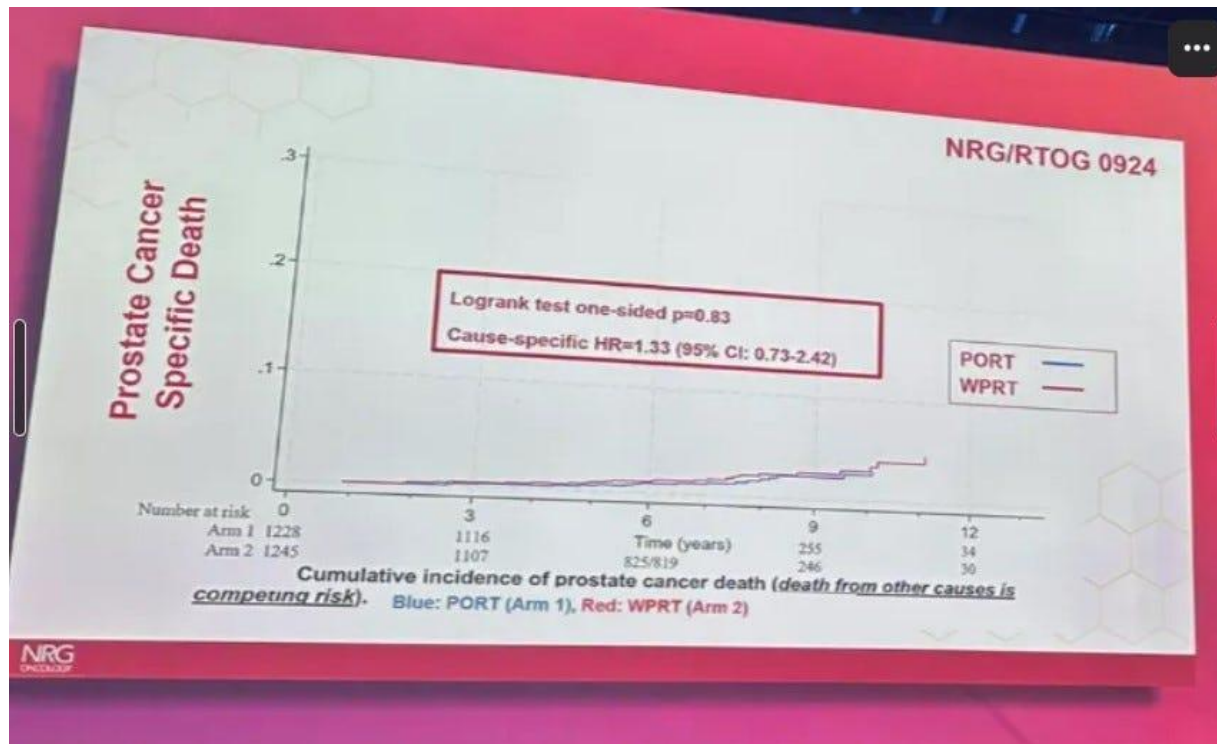
Biochemical Failure

NRG/RTOG 0924



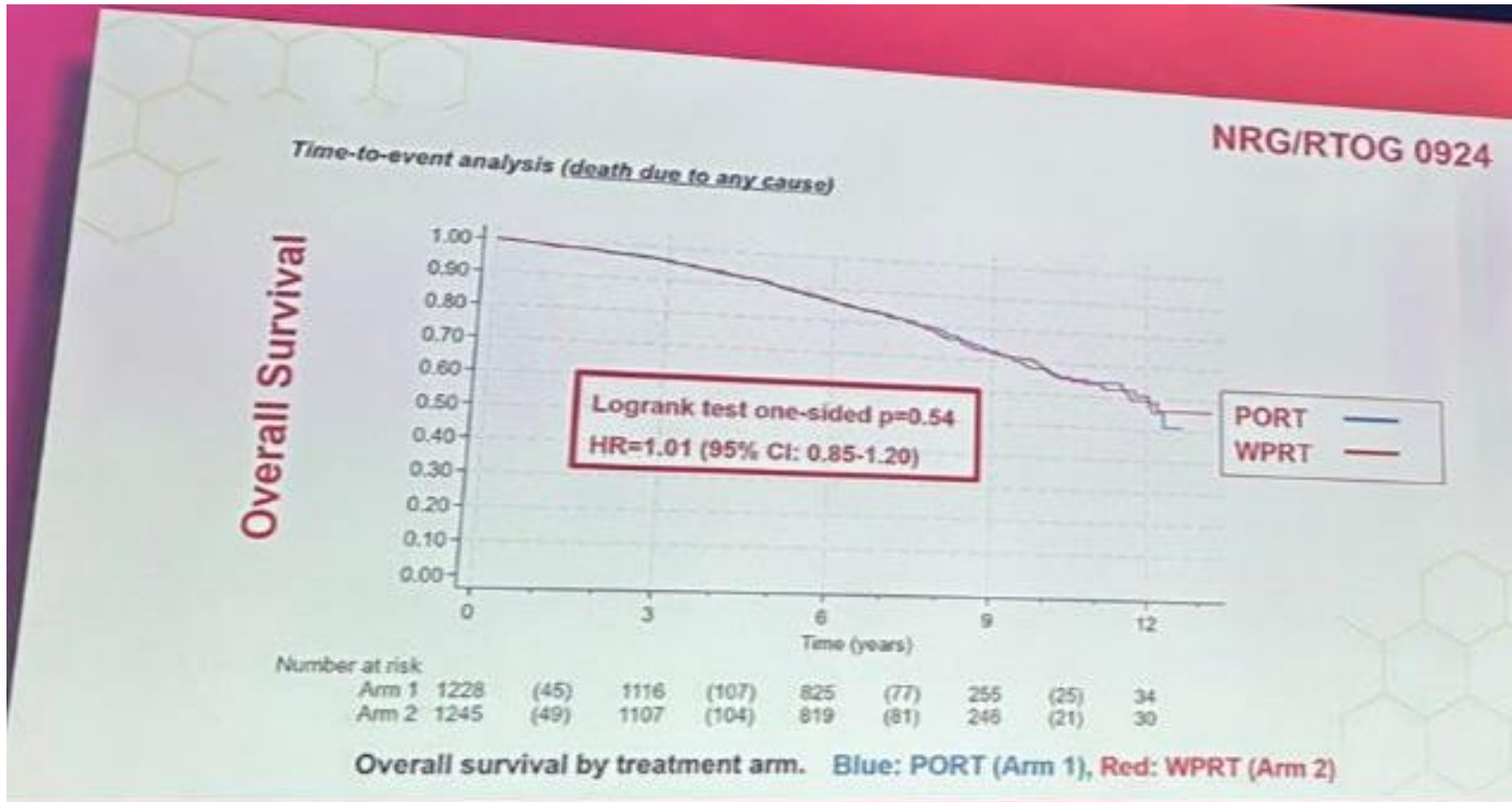
Prostate Cancer Specific Death – Distant M+

ASTRO



Overall Survival

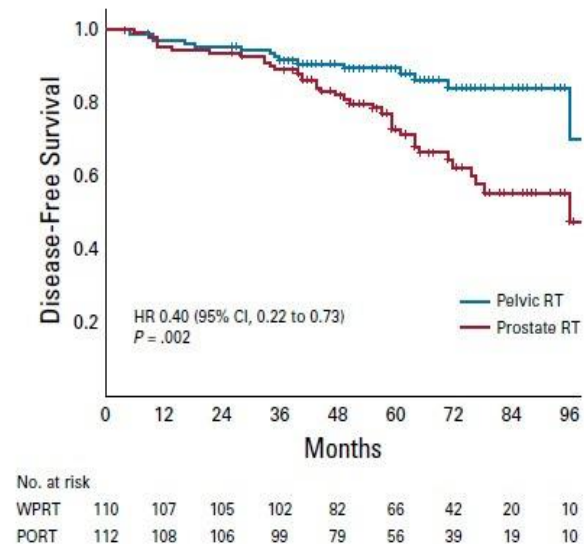
ASTRO



NRG/RTOG 0924 trial - Summary

ASTRO

- Negative trial on 2500 patients testing whole pelvic RT.
 - 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.
- But POP-RT:
 - Roach nodal risk of at least 20%.
 - WPRT showed higher 5-year DFS (89.5% v 77.2)
 - 5-year OS did not appear to differ (92.5% v 90.8).
 - Distant metastasis-free survival was also higher with WPRT (95.9% v 89.2)



Thunder trial: PSMA-PET/CT stage migration in PC

ESTRO



Fleur Kleiburg
PhD Nuclear Medicine
Leiden University Medical Centre,
Leiden, The Netherlands



PI: Dr. Piet Ost
Radiation Oncologist
Iridium Network, Antwerp,
Belgium



PSMA PET/CT Stage Migration and Genomic Classifier Scores in High-Risk Prostate Cancer

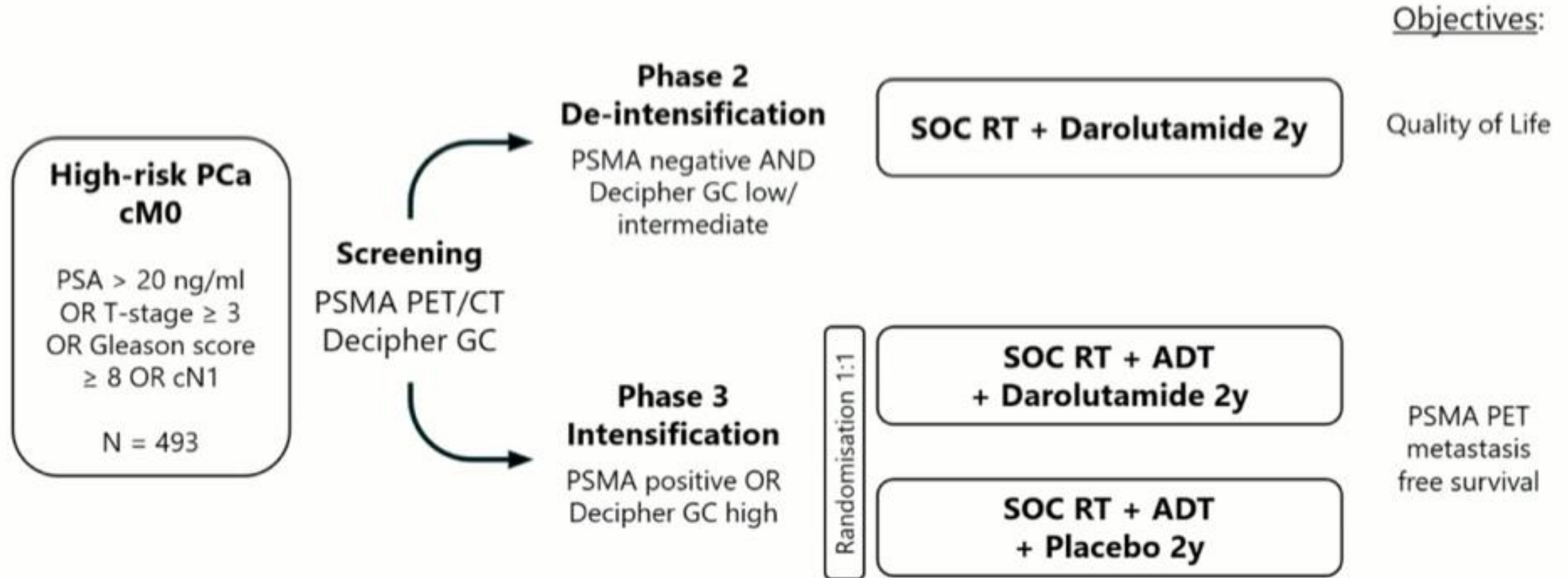
First-Year Results from the Thunder trial (NCT06282588)

The Thunder trial is supported by Bayer and Veracyte



Multicenter Thunder Phase 2/3 study

ESTRO



NCT06282588, currently recruiting, first inclusion 13-12-2023

Introduction

Baseline data of patients included in the first year of the THUNDER trial



1. Assess stage migration on PSMA PET/CT compared to conventional imaging



2. Assess the correlation between Decipher Genomic Classifier scores and PSMA PET/CT findings

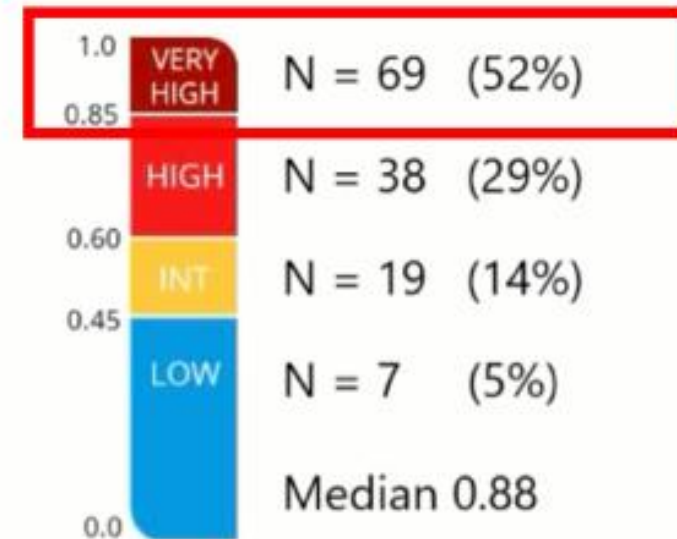
Very high-risk population



PSMA PET/CT:

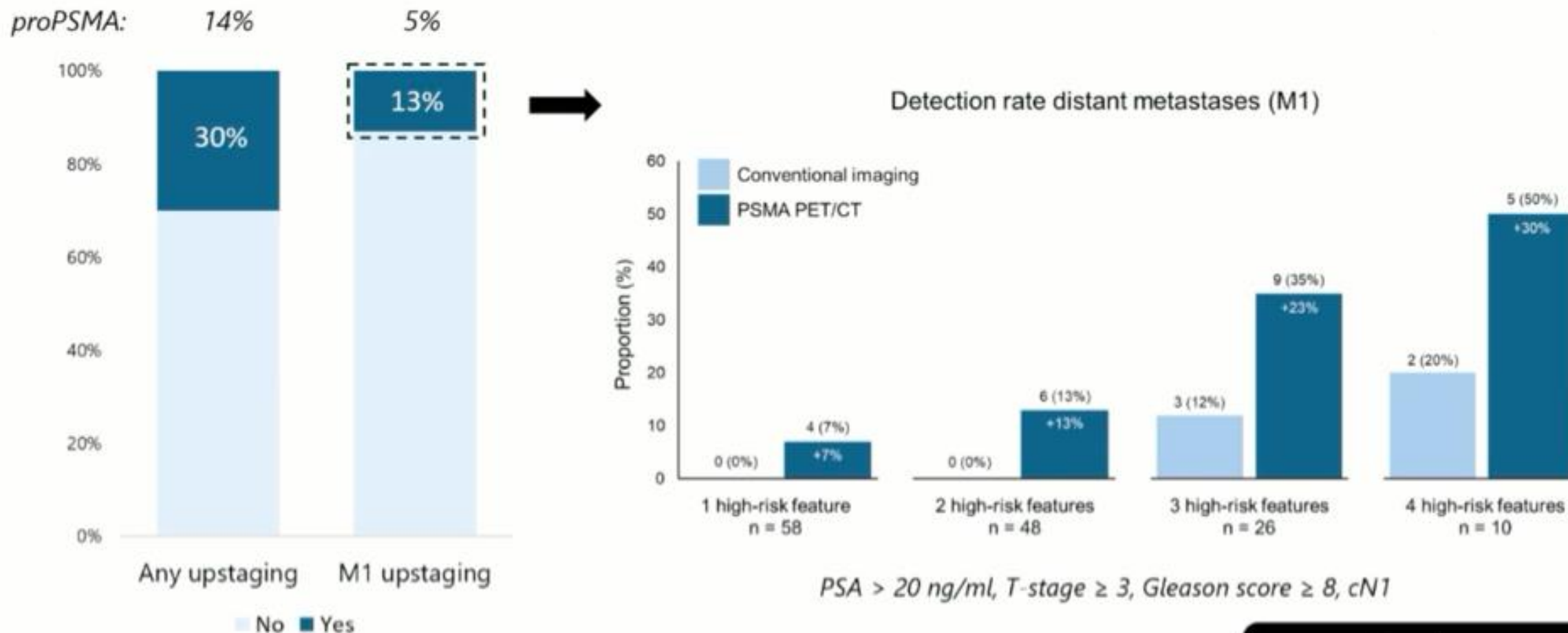
- Metastatic N = 24 (17%)
- Nodal only N = 38 (27%)
- Localised N = 80 (56%)

Decipher Genomic Classifier:



Upstaging with PSMA PET-CT

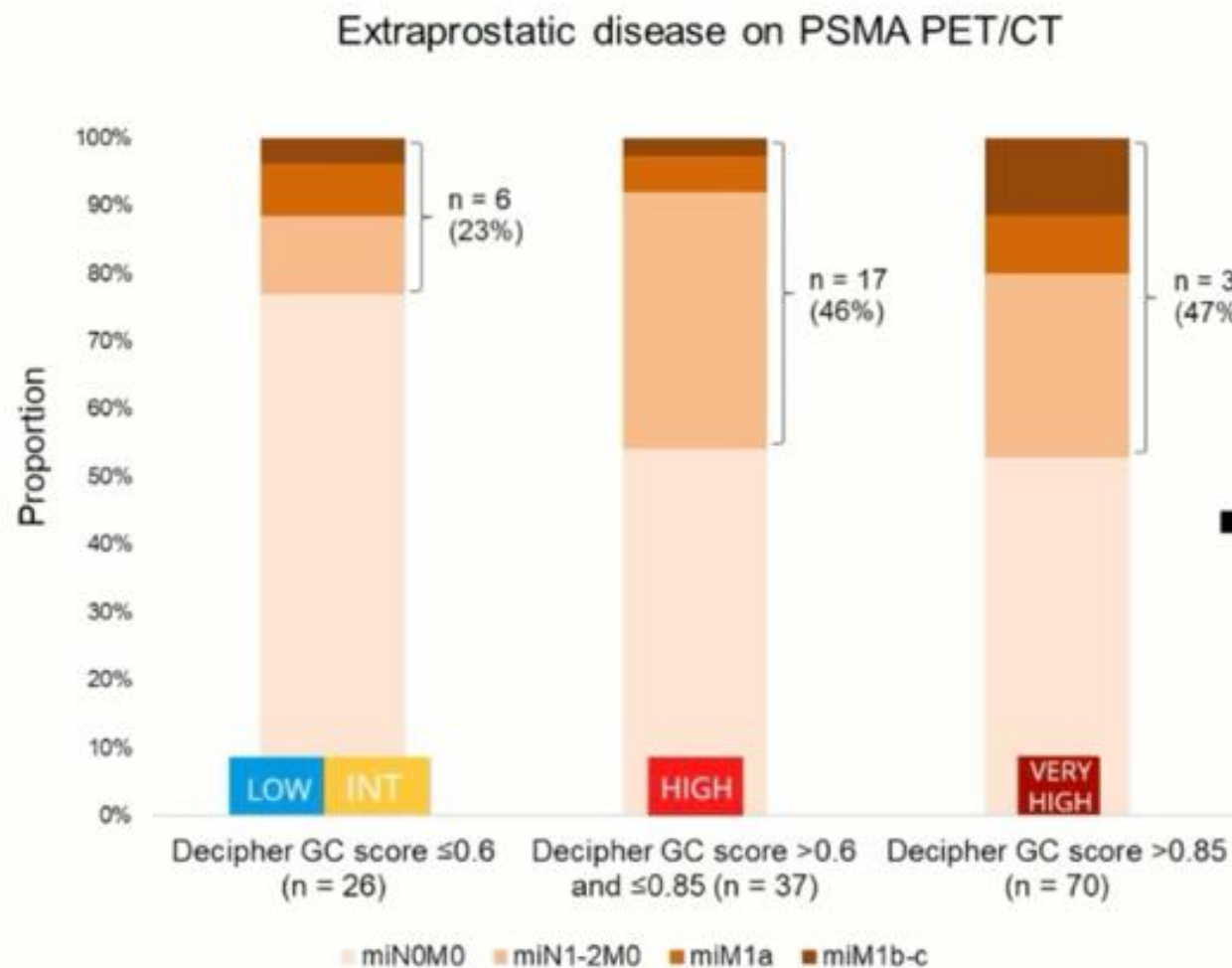
ESTRO



Results

Decipher GC scores

ESTRO



Decipher GC > 0.85
(10-year DM risk of 42%)
over half had negative PSMA PET



False or true
negative?

Results

Thunder - summary

- Very high-risk PCa cohort
- Stratification based on PSMA PET/CT and Decipher GC scores

PSMA PET/CT upstaged
one in three patients

More than double compared to proPSMA

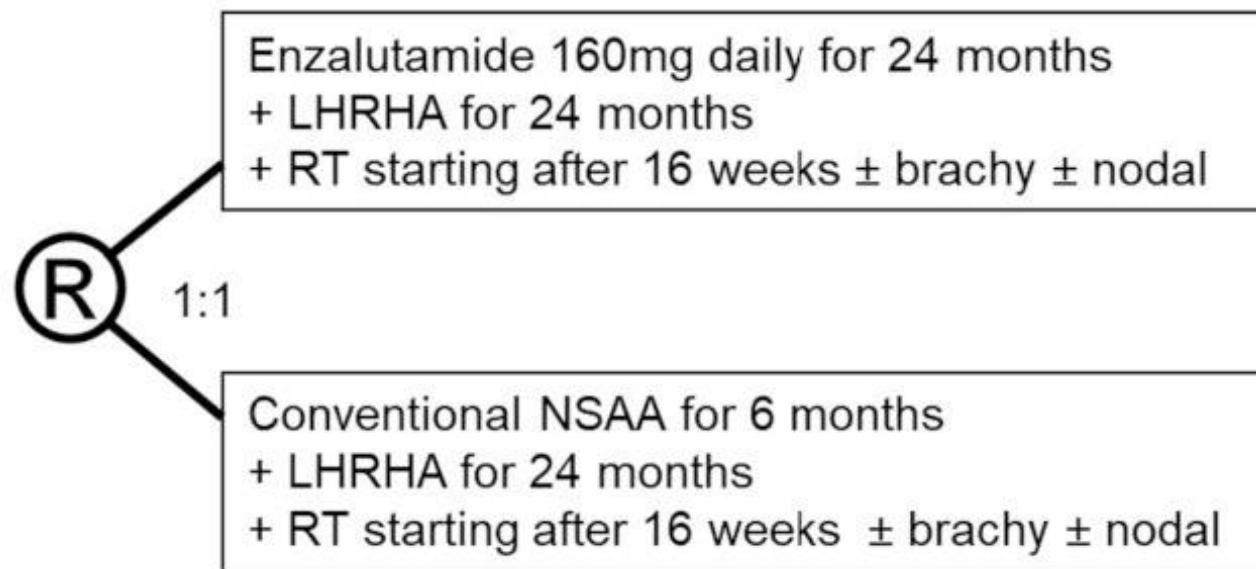
Upstaging increased with number of
risk factors and Decipher GC score

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



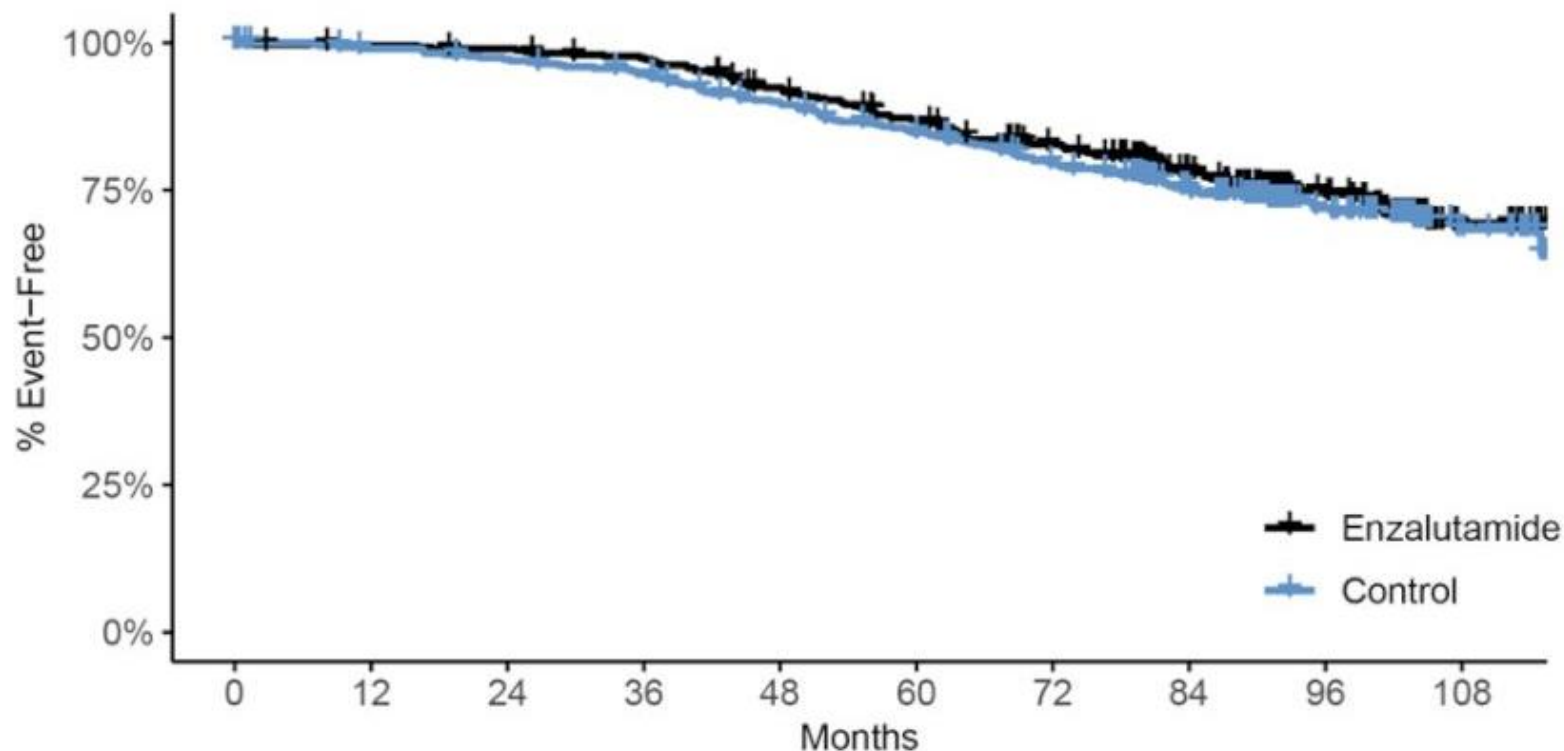
Endpoints

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

800 participants

ENZARAD: Primary endpoint: MFS by conventional imaging

ESMO



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

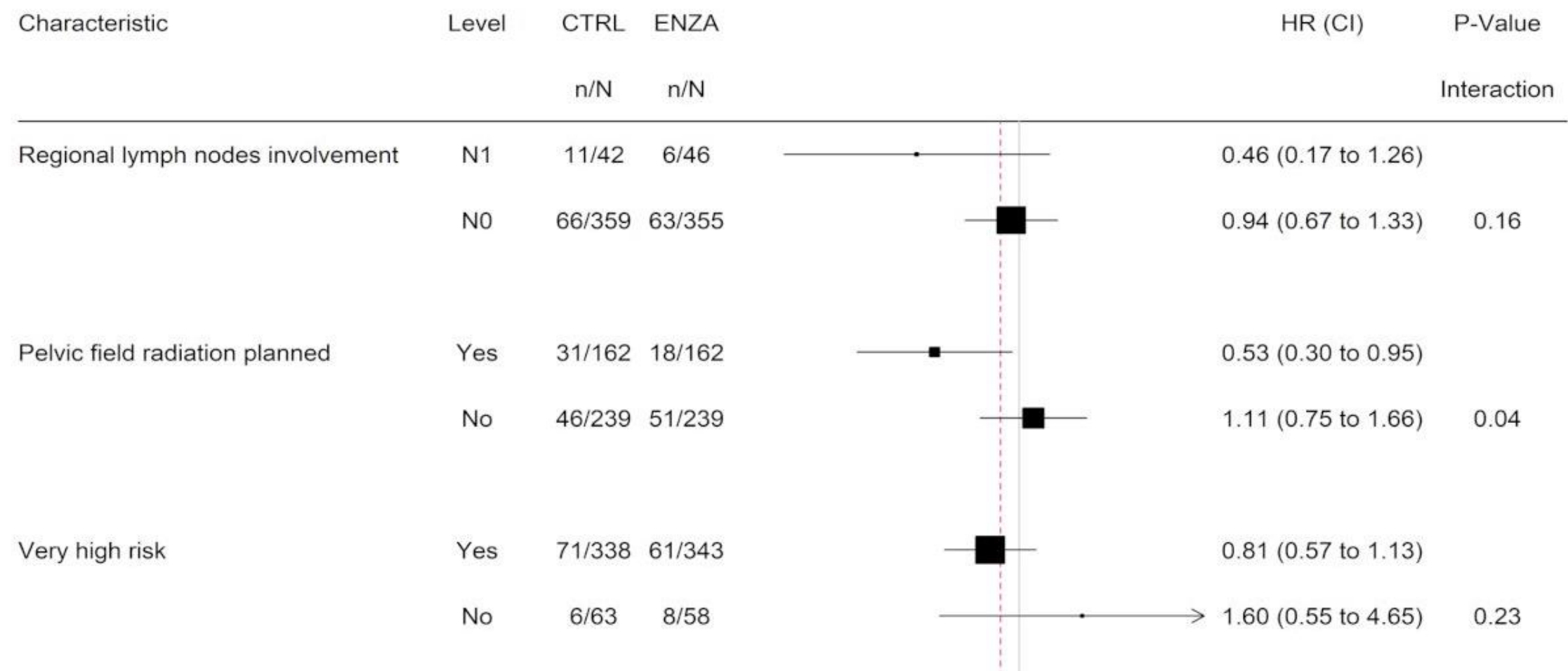
HR = 0.88 (95% CI 0.67, 1.15)
2p = 0.34 (log-rank test)

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)

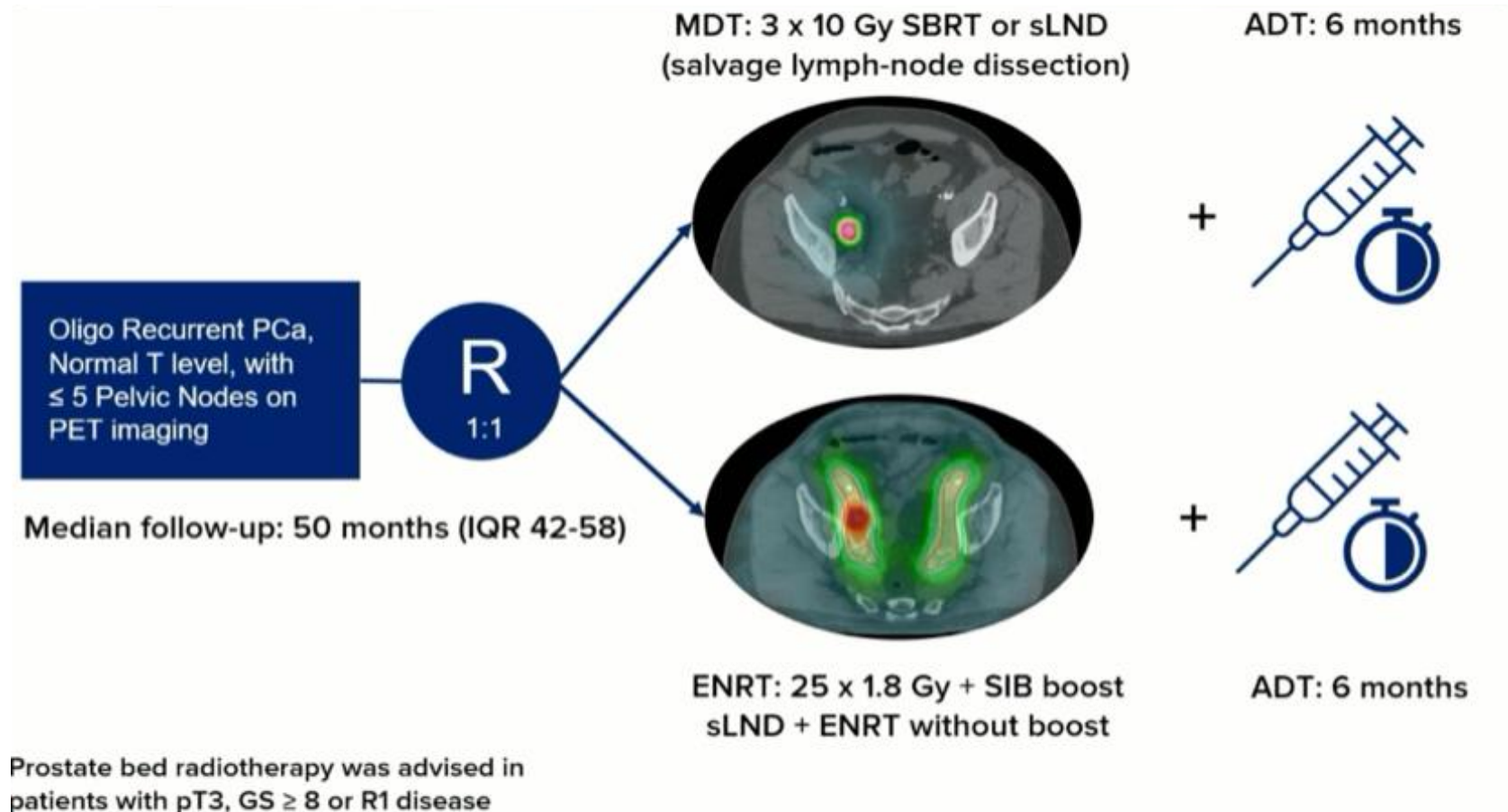
Effects of enzalutamide on OS in prespecified subgroups



PEACE V – STORM – Salvage Treatment of OligoRecurrent nodal prostate cancer Metastases

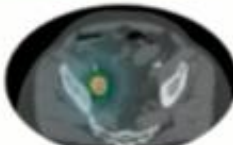
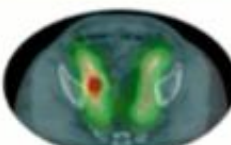
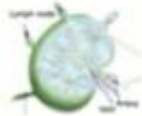
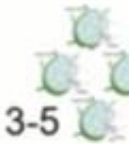
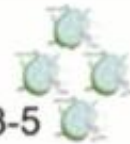
ESTRO

- Randomized phase II trial



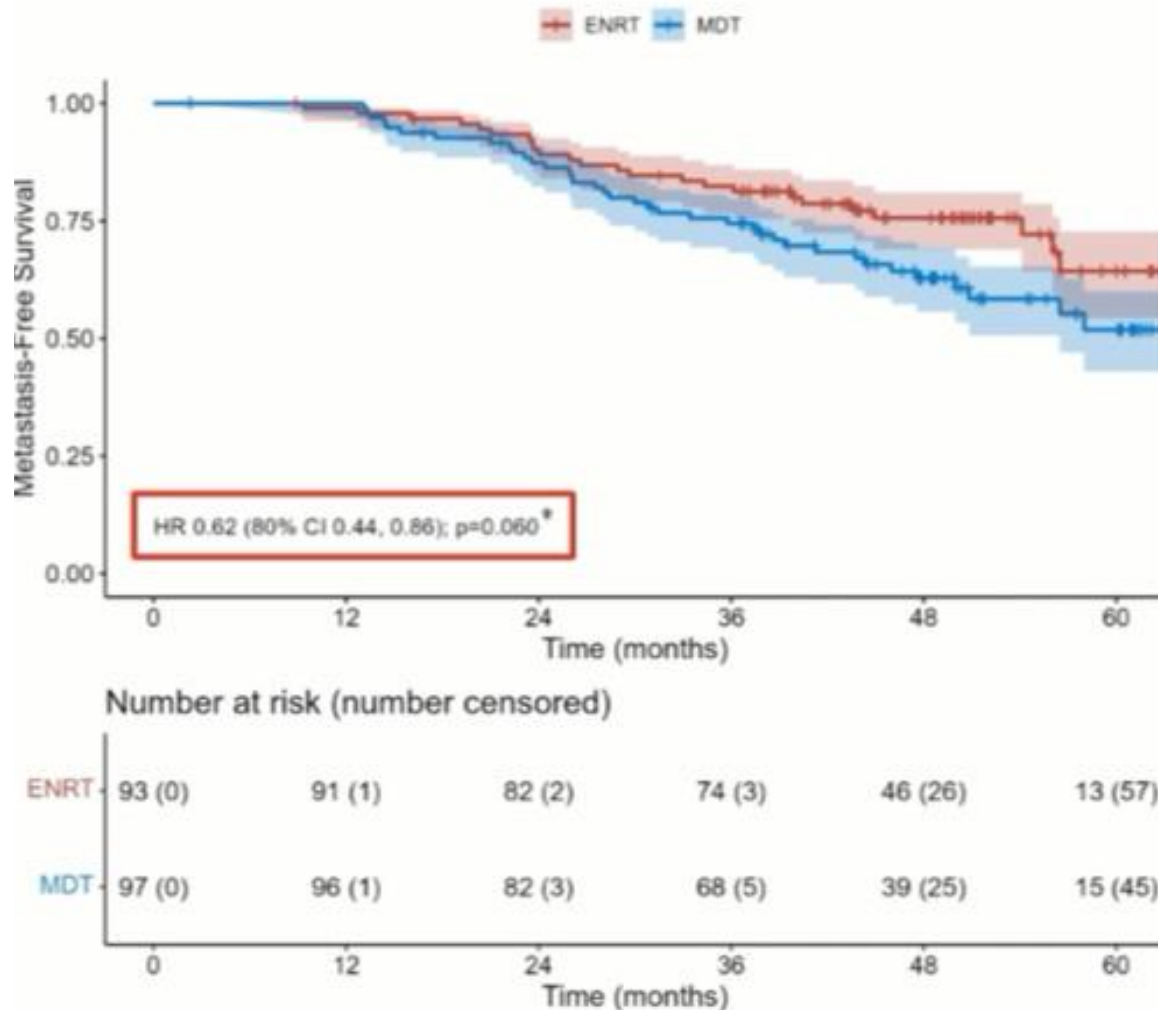
Population

ESTRO

Patients		N = 97 (99 randomized)	N = 93 (97 randomized)
		  N=6	  N=6
 ±  RP ± PB RT		85% (52% + 33%)	92% (63% + 29%)
 European Association of Urology High BCR risk group		91%	86%
 PET imaging		Choline: 19% PSMA: 81%	Choline: 17% PSMA: 83%
 Number of nodes		 55% 27% 3-5 18%	 62% 24% 3-5 14%
 Concomitant RT to the prostate bed		25%	42%

Primary endpoint: metastasis-free survival (MFS)

ESTRO



4-year MFS:

- MDT = 63% [80% CI: 0.56-0.69]
- ENRT = 76% [80% CI: 0.69-0.81]

12.8% [80% CI: 3.8-21.8] MFS
difference between MDT and ENRT

* The two-sided significance level alpha set at 0.20
and power maintained at 80%

Location of relapses

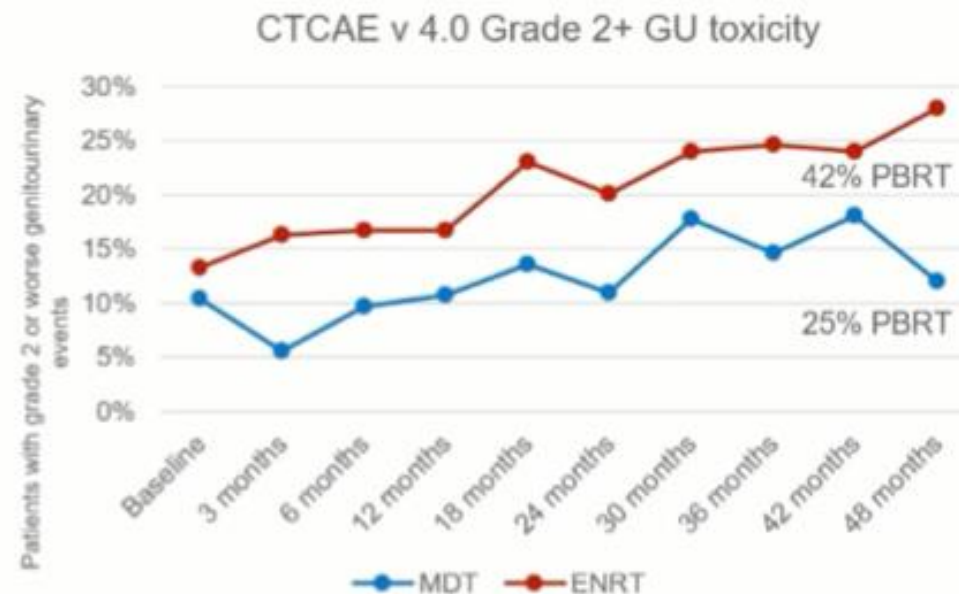
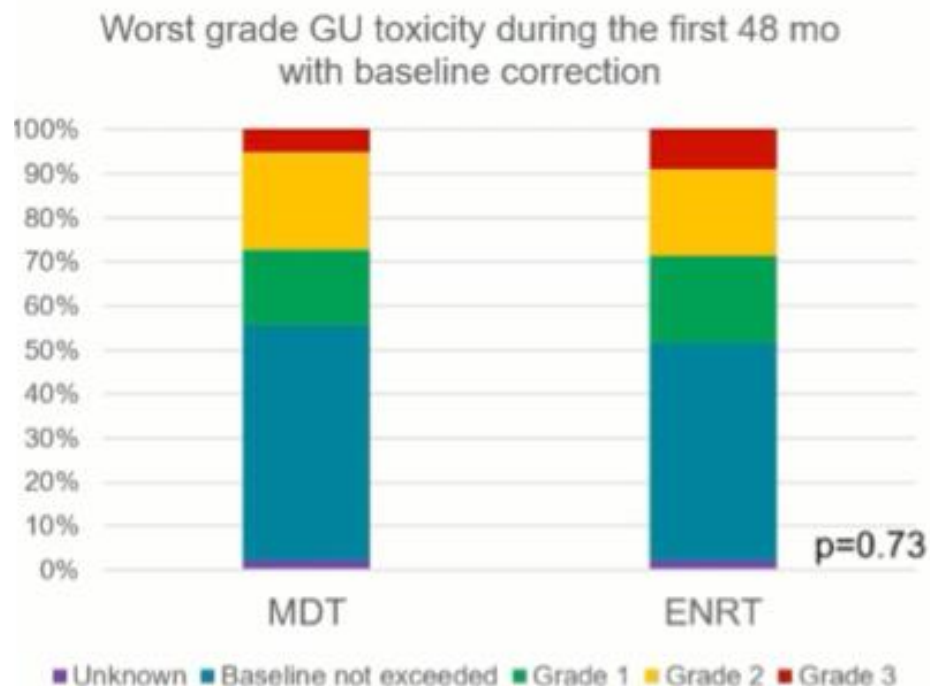
ESTRO

	N = 97 (99 randomized)	N = 93 (97 randomized)
 PSA only	14 (14%)	17 (18%)
 N1	28 (29%)	7 (8%)
 Prostate Bed *	10 (10%)	9 (10%)
DISTANT METASTASES		
 M1a	27 (28%)	13 (14%)
 M1b	7 (7%)	6 (6%)
 M1c	2 (2%)	1 (1%)

*PB-RT associated with a lower risk of PB recurrence: post-hoc analysis: HR 3.01, (80% CI:1.62-5.60, p=0.023)

GU toxicity

ESTRO



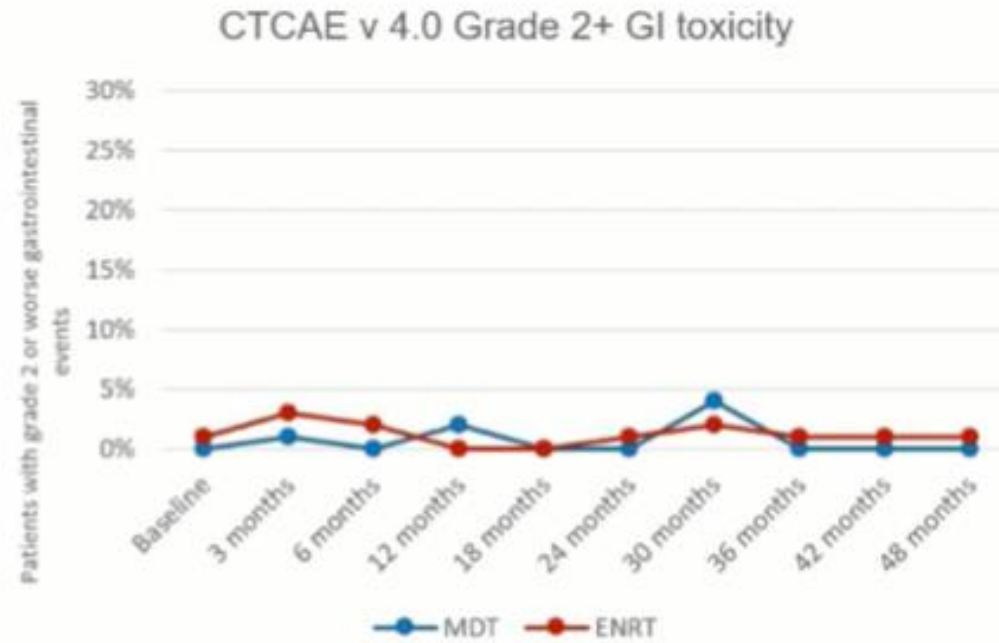
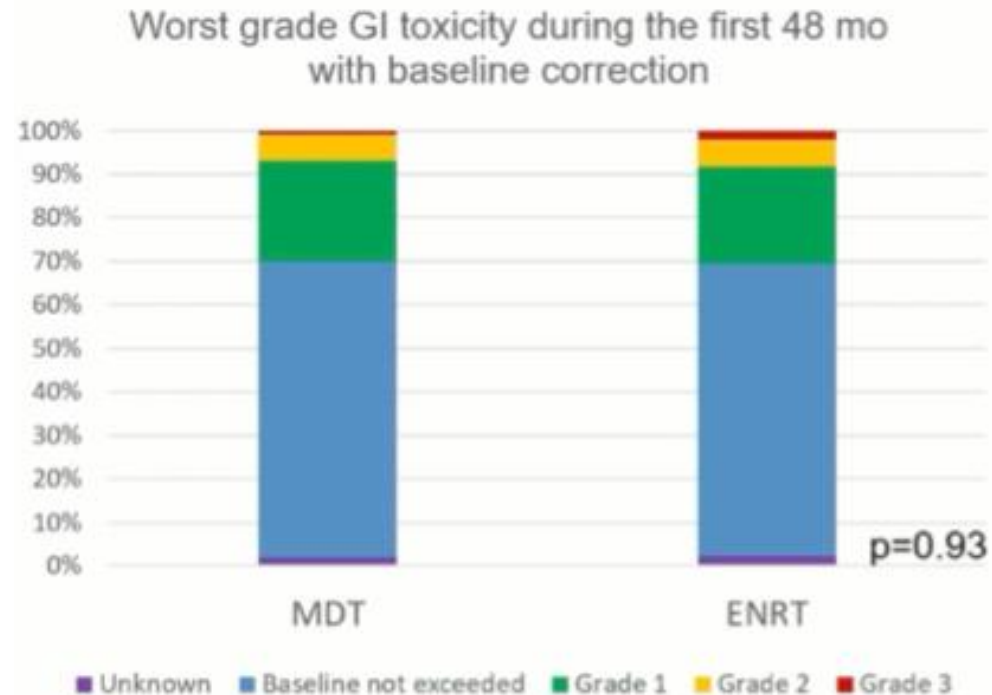
Worst 48-month grade 2+ GU toxicities: MDT vs ENRT (28.1% vs 31.5%)

GU 2+ toxicity was numerically worse with ENRT than with MDT (but no statistically different)

Increased G2+ GU toxicity with the inclusion of the PB (odds ratio 1.85 [95% CI: 0.95- 3.60%]; p=0.068)

GI toxicity

ESTRO



Worst 48-month grade 2+ GI toxicities: MDT vs ENRT (7.3% vs 8.8%)
Increased G2+ GI toxicity with the inclusion of the PB (odds ratio 4.6 [95% CI:1.5 – 15.8%]; p=0.001)

PEACE V - summary



- In oligorecurrent pelvic nodal disease, **ENRT improves MFS by 13% and IrRFS by 23%** at 4 years compared to MDT
- Toxicity and quality-of-life outcomes confirm **excellent tolerability** and show **comparable results between ENRT and MDT**
- Irradiation of the **prostate bed** increased the risk of GU and GI toxicity but prevents further local relapses
- **ENRT is the most effective treatment option for reduction** the probability of new pelvic recurrences and distant metastases, positioning itself as a **potential standard** for oligorecurrent nodal disease

STOPCAP meta-analysis: SOC $\pm$ RT to the primary

ESMO

STOPCAP individual patient data meta-analysis

SOC
systemic therapy
ADT $\pm$ Doce $\pm$ Abi



$\pm$



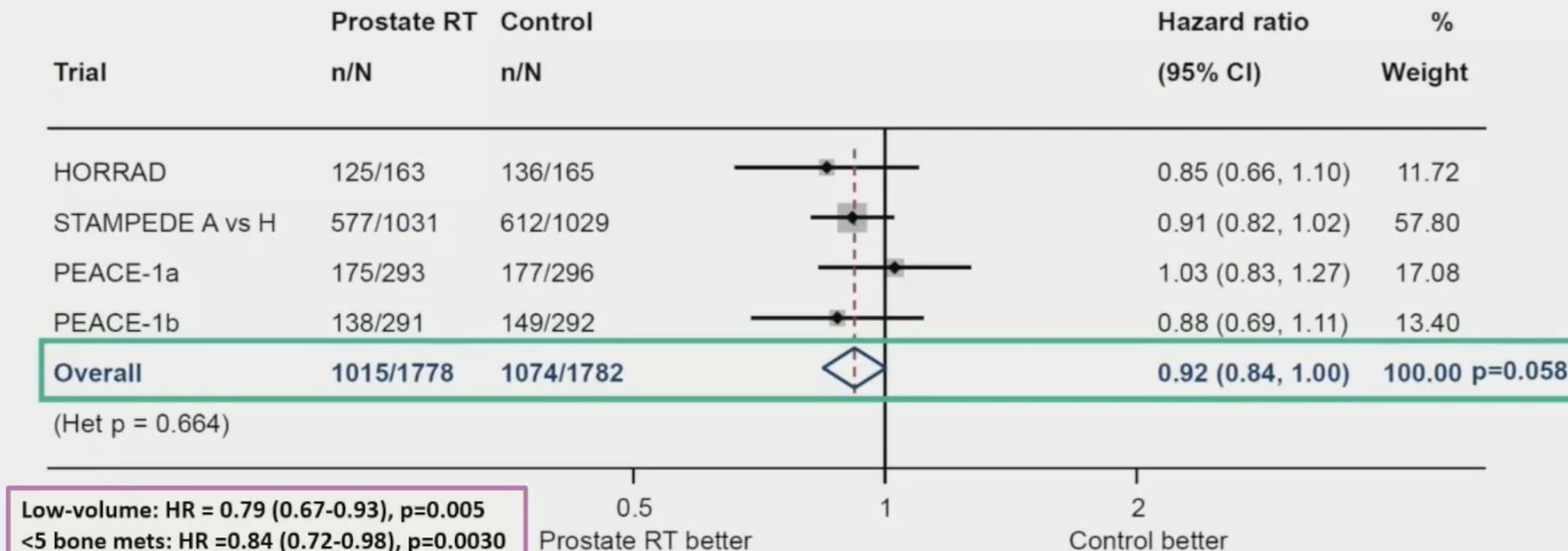
Trial	Recruitment period	Pts. included	Planned docetaxel	Follow-up	Baseline survival
HORRAD (RT)	2004 – 14	328 ADT	0%	9 years	3.2 years
STAMPEDE AvsH (RT)	2013 – 16	2061 ADT $\pm$ Doce	18%	5 years	4.2 years
PEACE-1a (RT, no abi)	2013 – 18	589 ADT $\pm$ Doce	60%	6 years	4.6 years
PEACE-1b (RT, abi)	2013 – 18	583 ADT + Abi $\pm$ Doce	61%	6 years	5.3 years

Based on HORRAD 2025 publication dataset containing 328 / 432 (76%) participants

RT to the prostate primary
(70 Gy/35 fx - 55Gy/20fx - 36Gy/6fx - 74 Gy/37fx)

Overall effect on overall survival (OS)

STOPCAP individual patient data meta-analysis

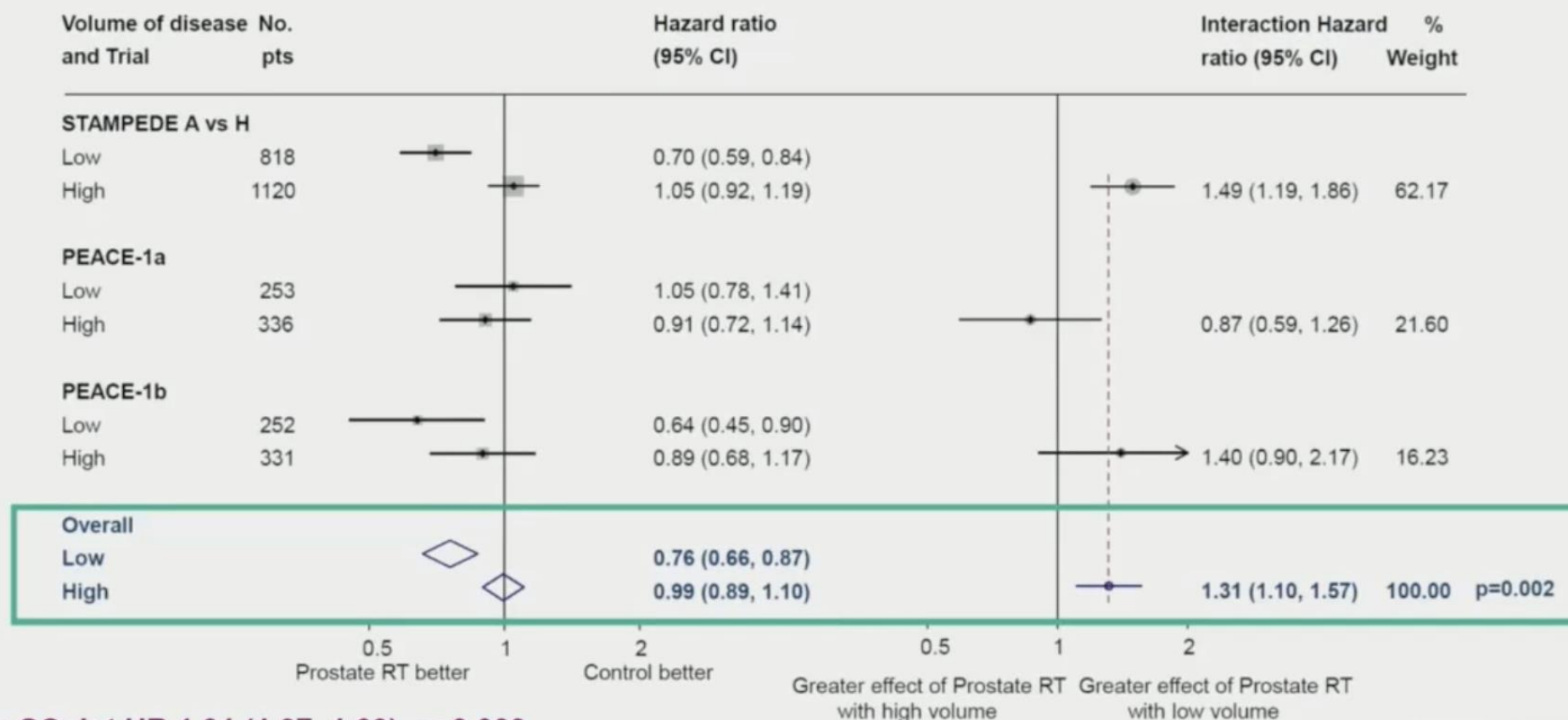


~8% absolute improvement in 5-year overall survival in patients with low-volume mHSPC and
~5% absolute improvement in patients with < 5 bone metastases~

Overall effect on PFS (low vs high volume)

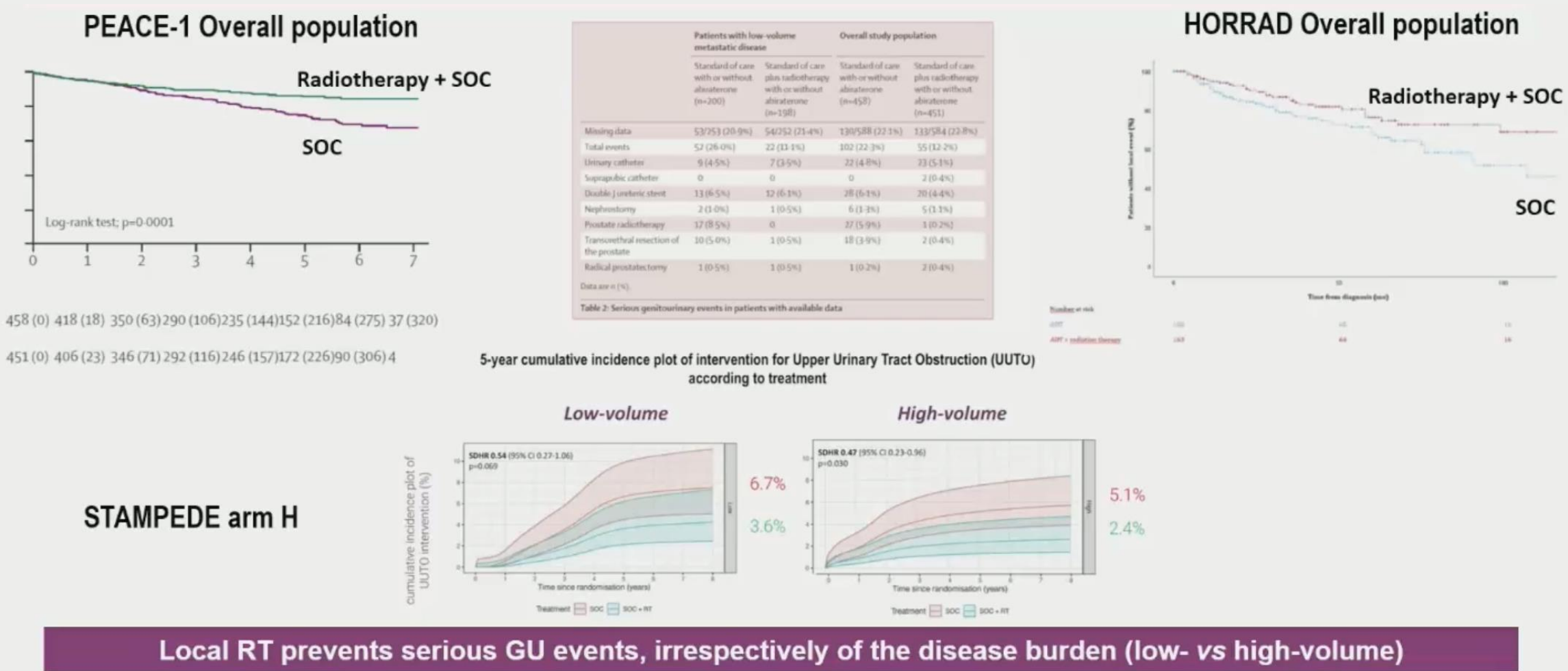
ESMO

STOPCAP individual patient data meta-analysis



Greatest benefit in PFS observed in men with low-volume disease

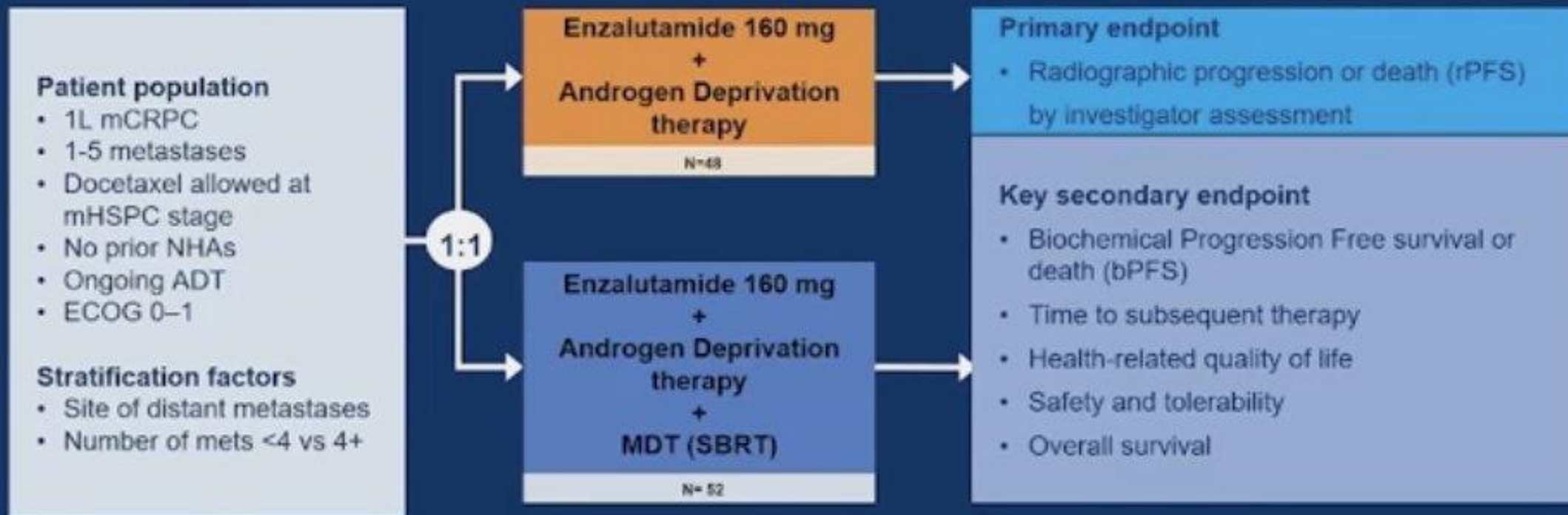
Effect on severe urinary events



MDT in Addition to Standard Systemic Therapy in Oligometastatic CRPC: A Randomized Phase II Trial (GROUQ-PCS 9)

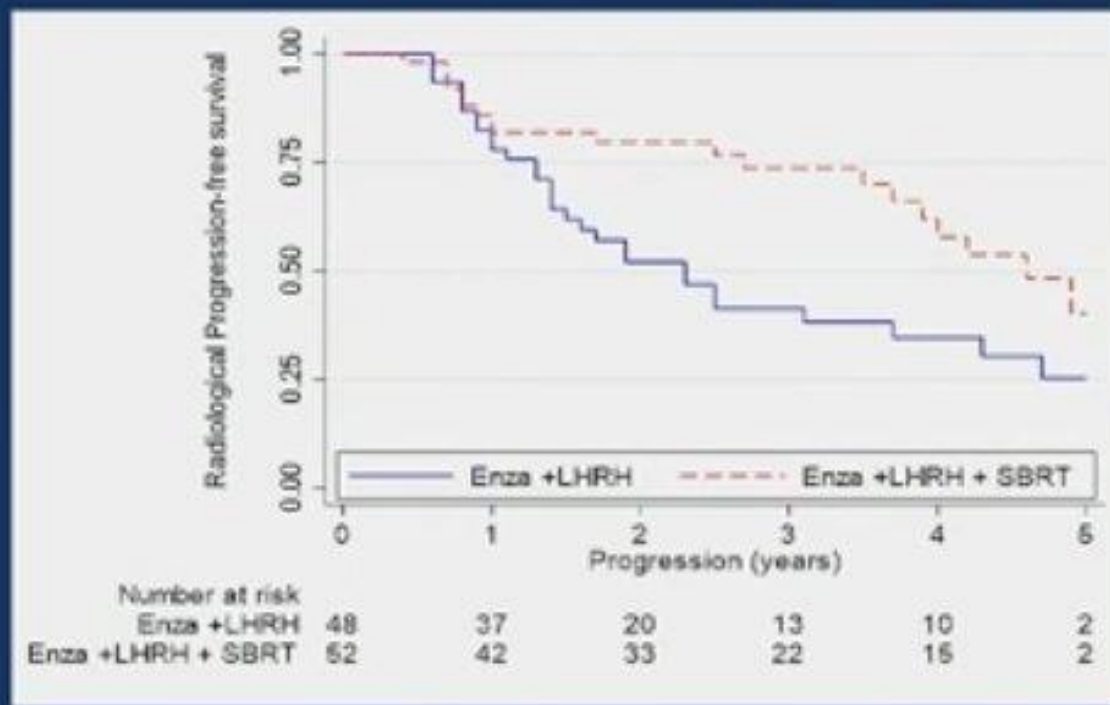
ASCO-GU

PCS-9 Study Design



PCS-9 Primary endpoint: rPFS by investigator- assessment

52% risk reduction of radiological progression or death with SBRT



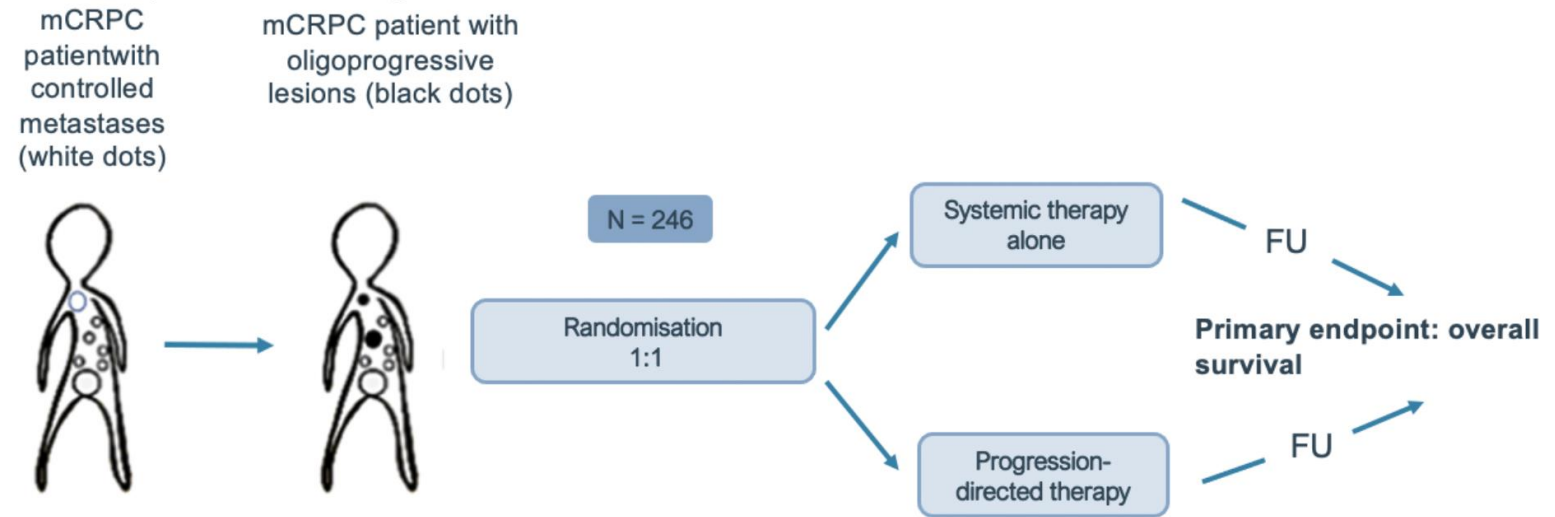
	Enza + ADT (n=48)	Enza + ADT + SBRT (n=52)
Events, n (%)	30 (62.5)	19 (36.5)
Median rPFS (years)	4.6	2.3
HR (95% CI)	0.48 (0.27–0.86); P=0.014	

Pre-specified 2-sided alpha: 0.05

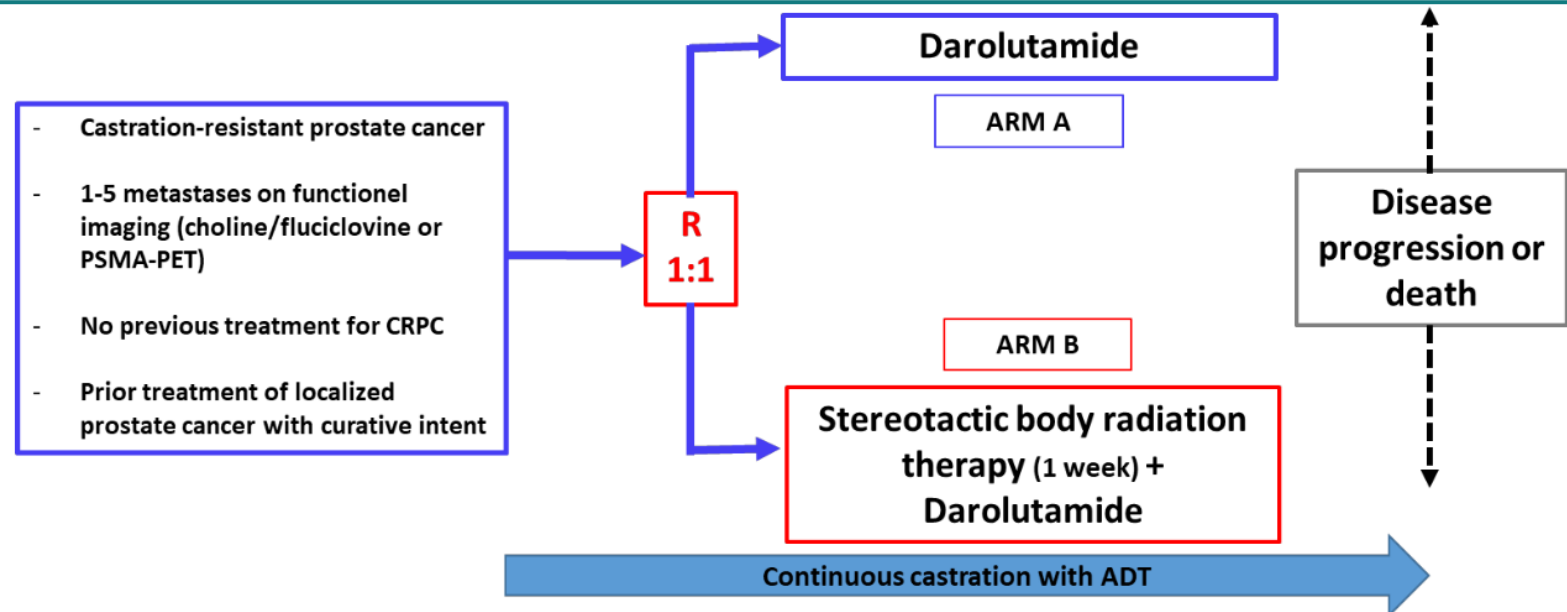
Median rPFS improvement of 2.3 YEARS
favors SBRT + Enzalutamide + ADT

Trials in mCRPC in Belgium

- Medcare 3



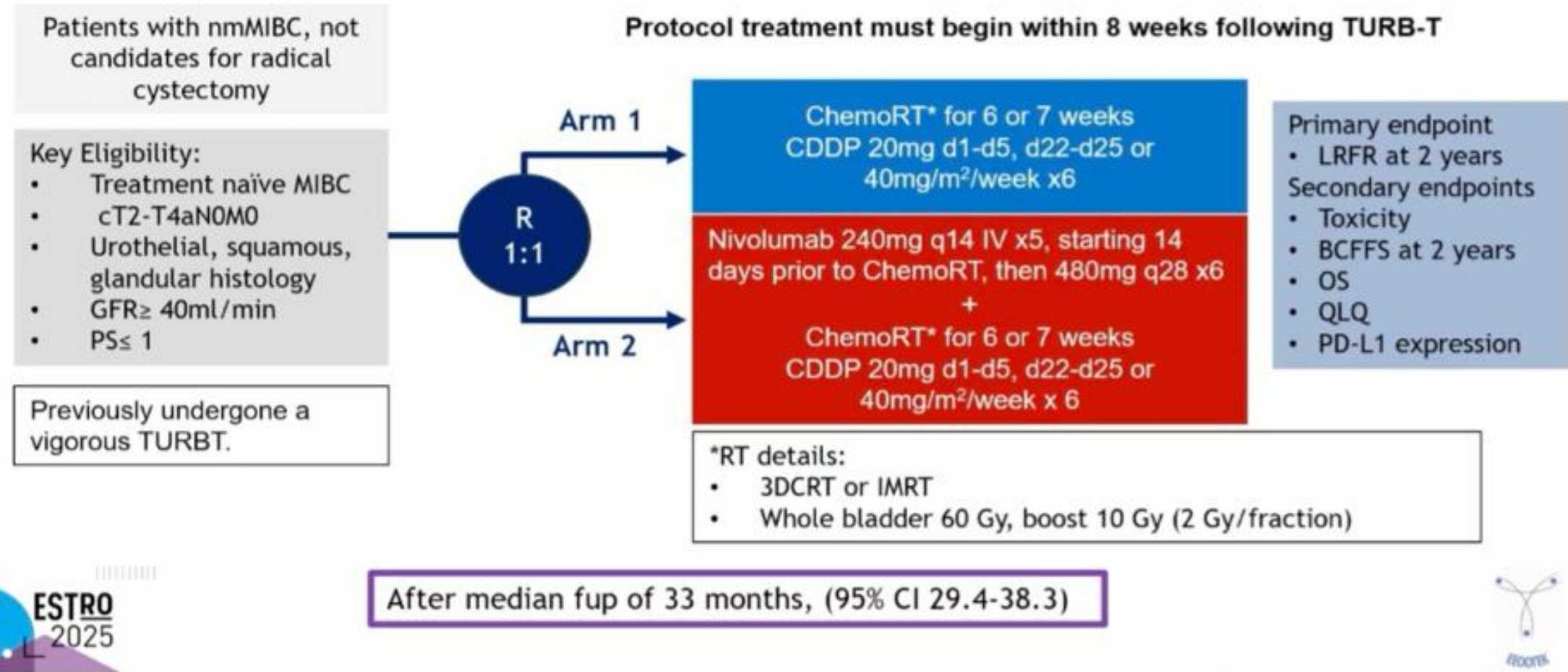
- Peace VIII



Nivolumab plus chemoradiotherapy in patients with muscle-invasive bladder cancer

ESTRO

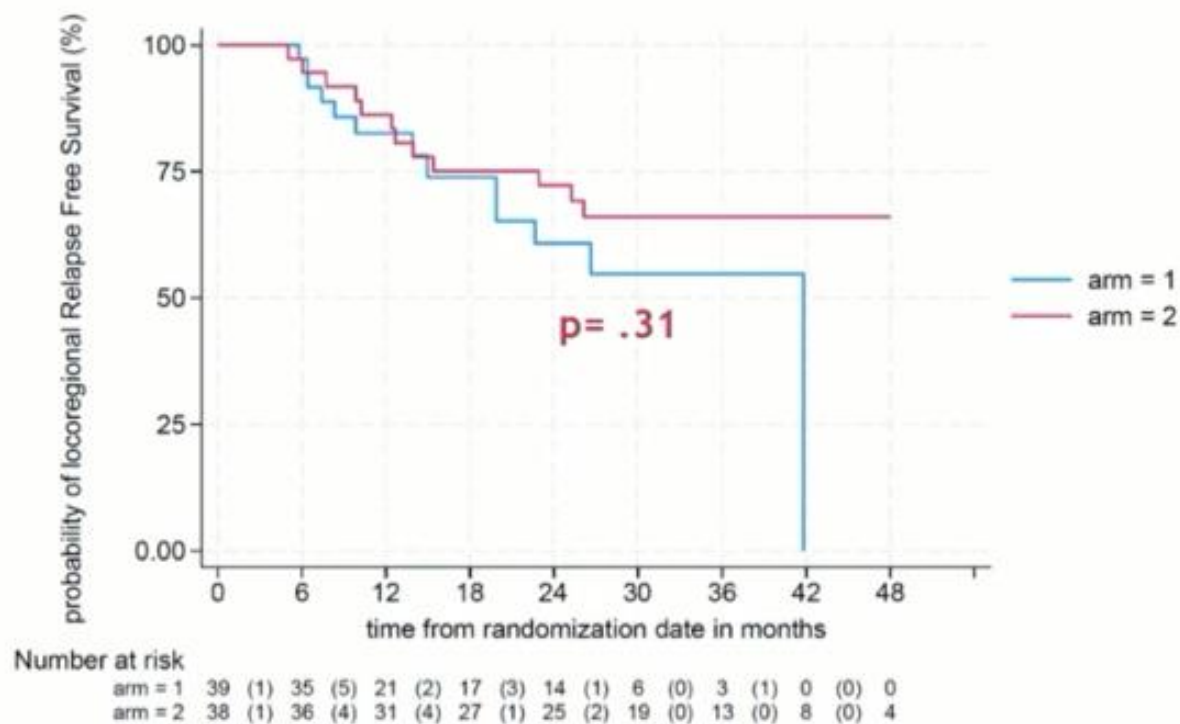
Nivolumab Plus Chemoradiotherapy in Patients With nmMIBC Not Undergoing Cystectomy



Locoregional Relapse Free Survival

ESTRO

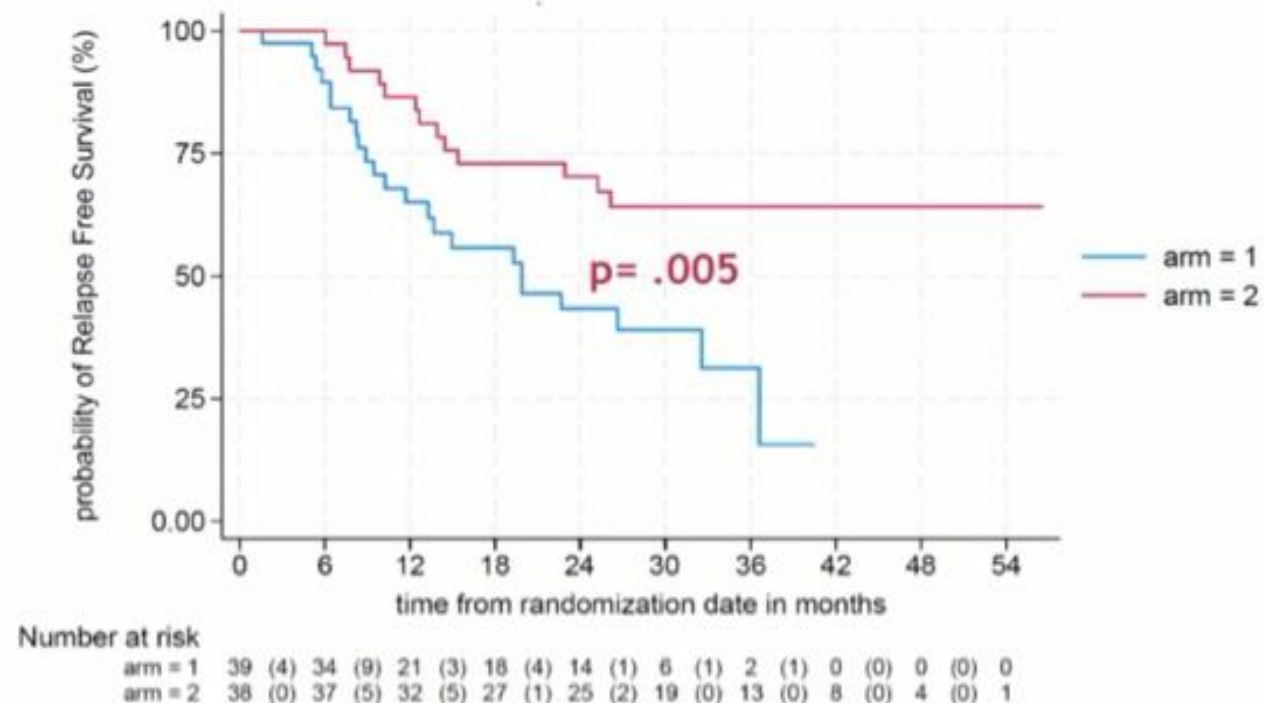
Primary endpoint: LRFR at 2 years



Median (95% CI)	2-y free (95% CI)
RT+CDDP	
41.9	60.8% (39.6-76.6)
RT+CDDP+Nivolumab	
NR	72.3% (54.7%-84.1%)

Bladder cancer failure-free survival

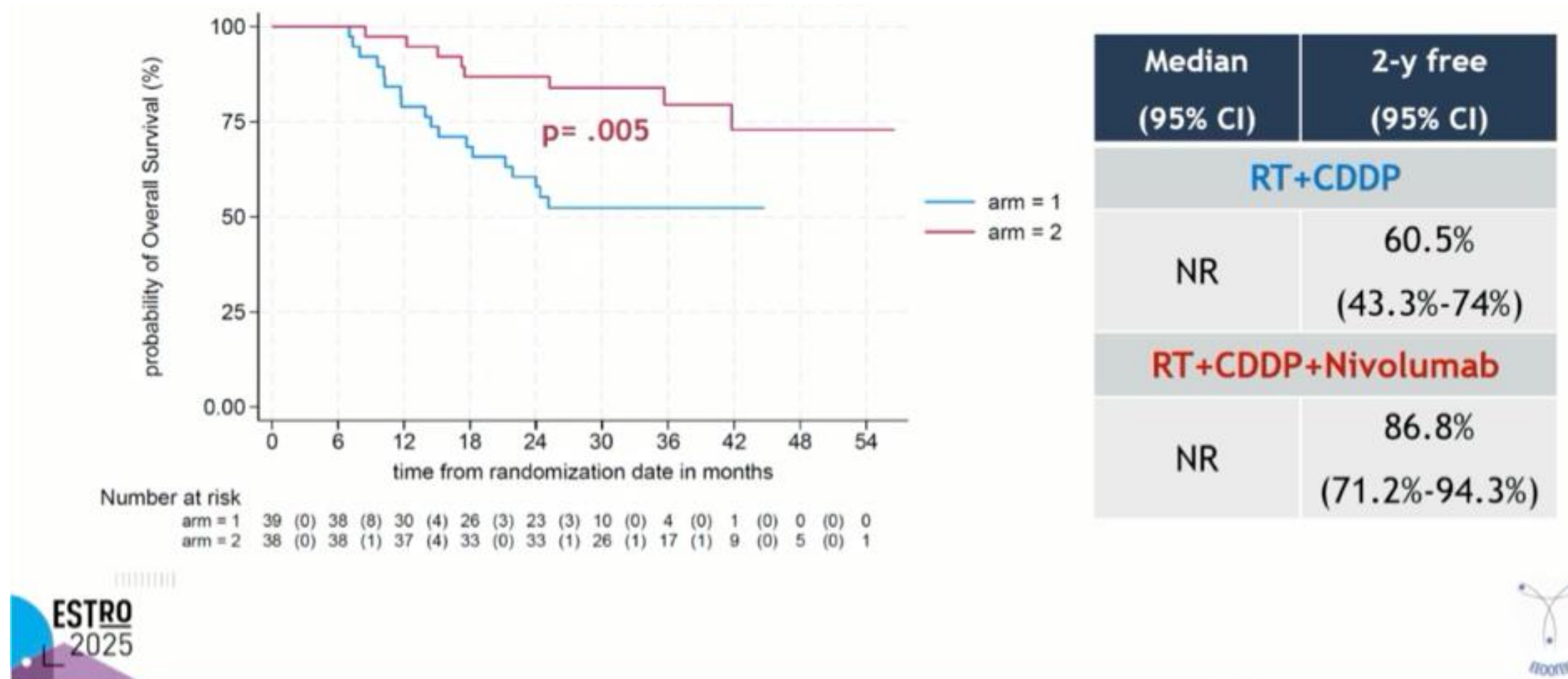
ESTRO



Median (95% CI)	2-y free (95% CI)
RT+CDDP	
19.9 (11.7-36.7)	43.4% (26.6%-59%)
RT+CDDP+Nivolumab	
NR	70.3% (52.8%-82.3%)

Overall survival

ESTRO



Patients' worst AE Grade

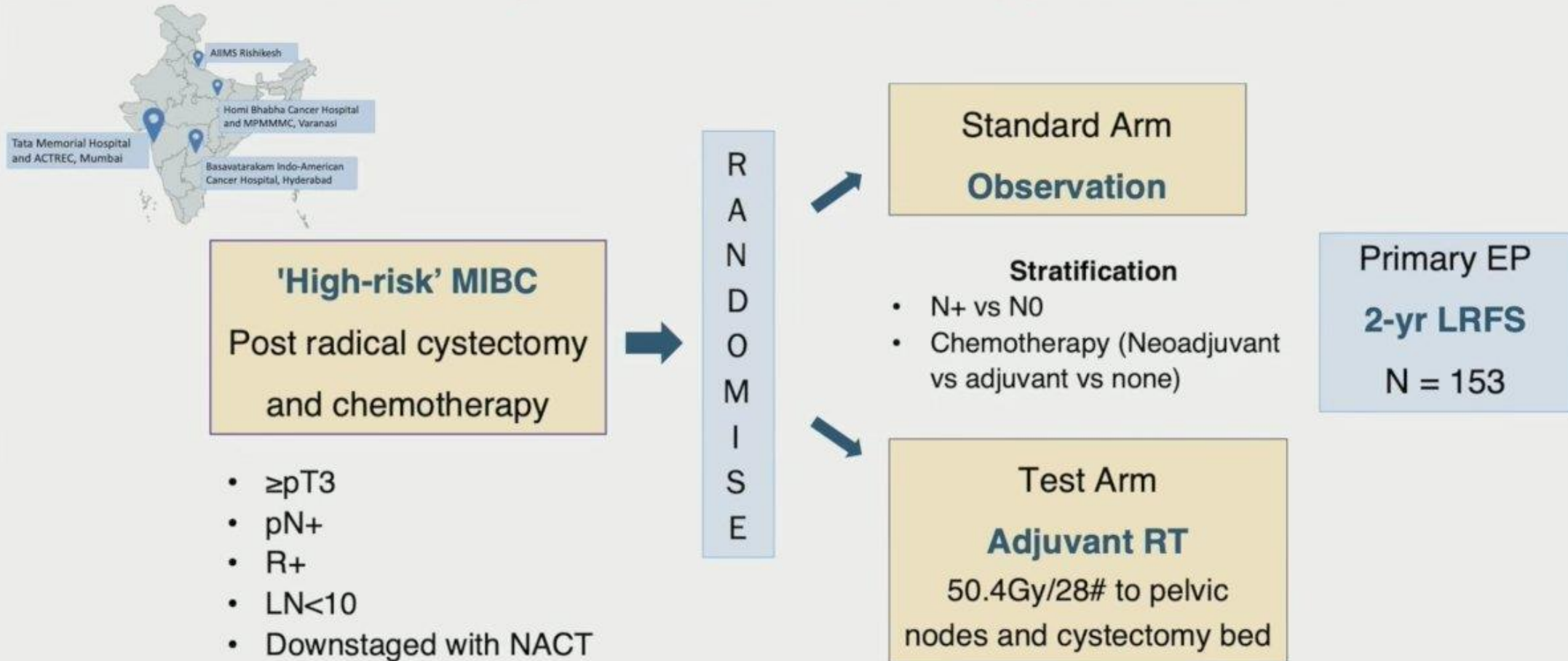
	Arm 1	Arm 2
No AE	17 (43.6)	7 (18.4)
Grade 1	7 (18)	8 (21.1)
Grade 2	5 (12.8)	9 (23.7)
Grade 3	5 (12.8)	11 (29)
Grade 4	3 (7.7)	2 (5.3)
Grade 5*	2 (5.1)	1 (2.6)

Patients without AEs were more frequent in Arm 1 than in Arm 2: 17 (43.6%) vs 7 (18.4%), $p=.017$.

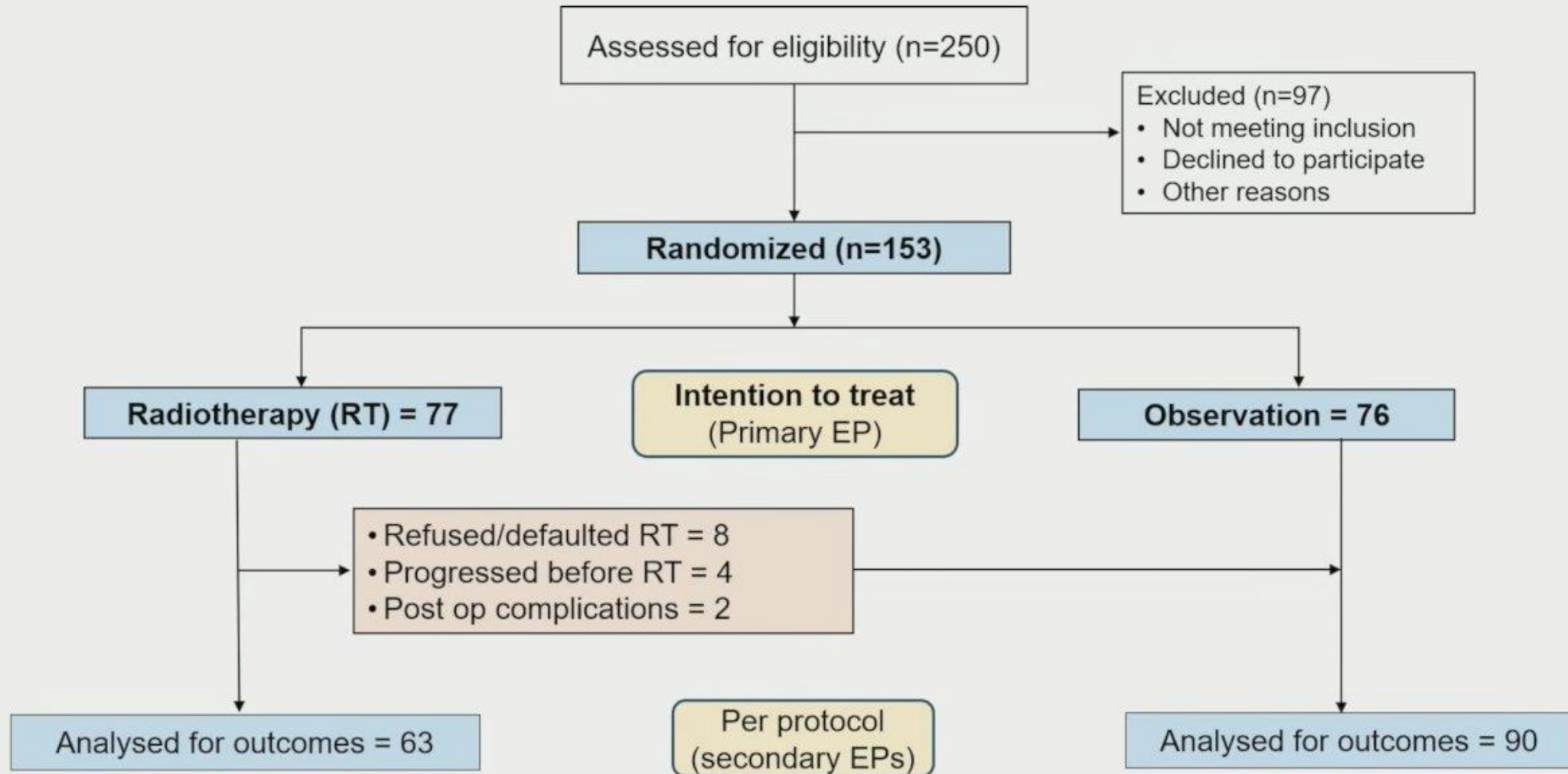
There was no difference in the frequency of Grade ≥ 3 between the two arms: 10 (25.6%) vs. 14 (36.8%), $p=.29$

*Three patients died during study treatment. No death was treatment-related: 1 due to covid infection and 2 due to disease progression.

Bladder Adjuvant Radiotherapy (BART): Clinical Outcomes from a Phase III Multicenter RCT



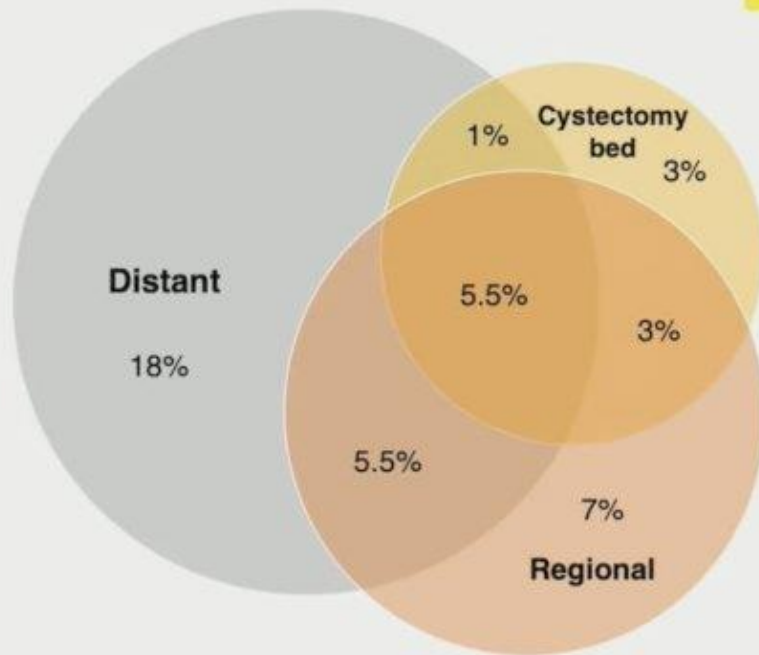
Bladder Adjuvant Radiotherapy (BART)



Bladder Adjuvant Radiotherapy (BART)

ASTRO

Observation

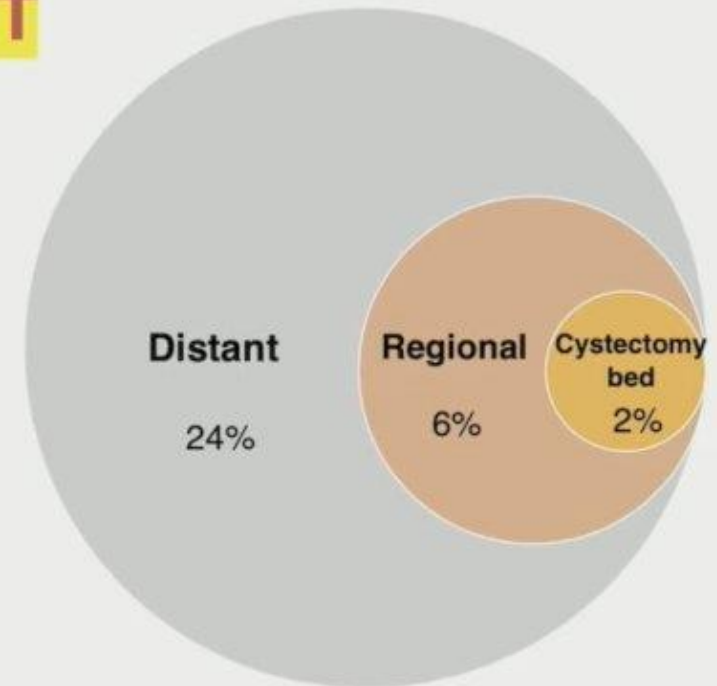


No isolated LRR with RT

LRR: 25% vs 8%

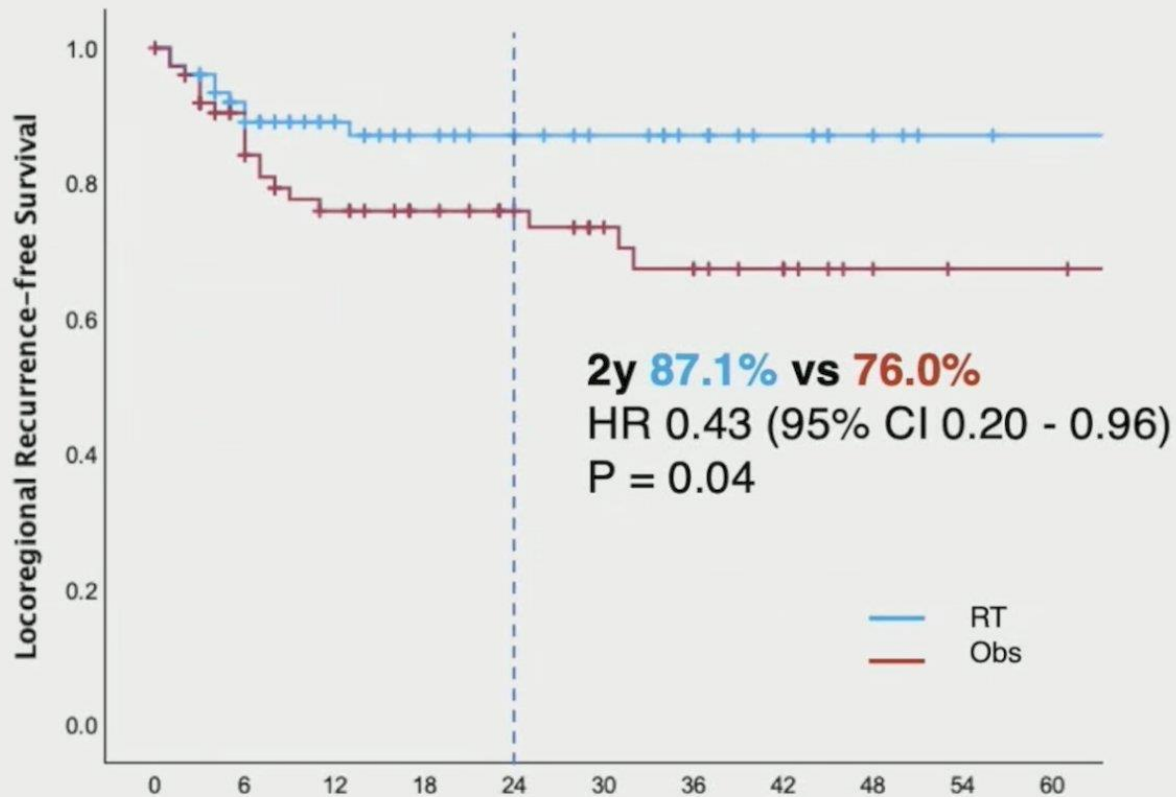
DM 30% vs 32%

RT

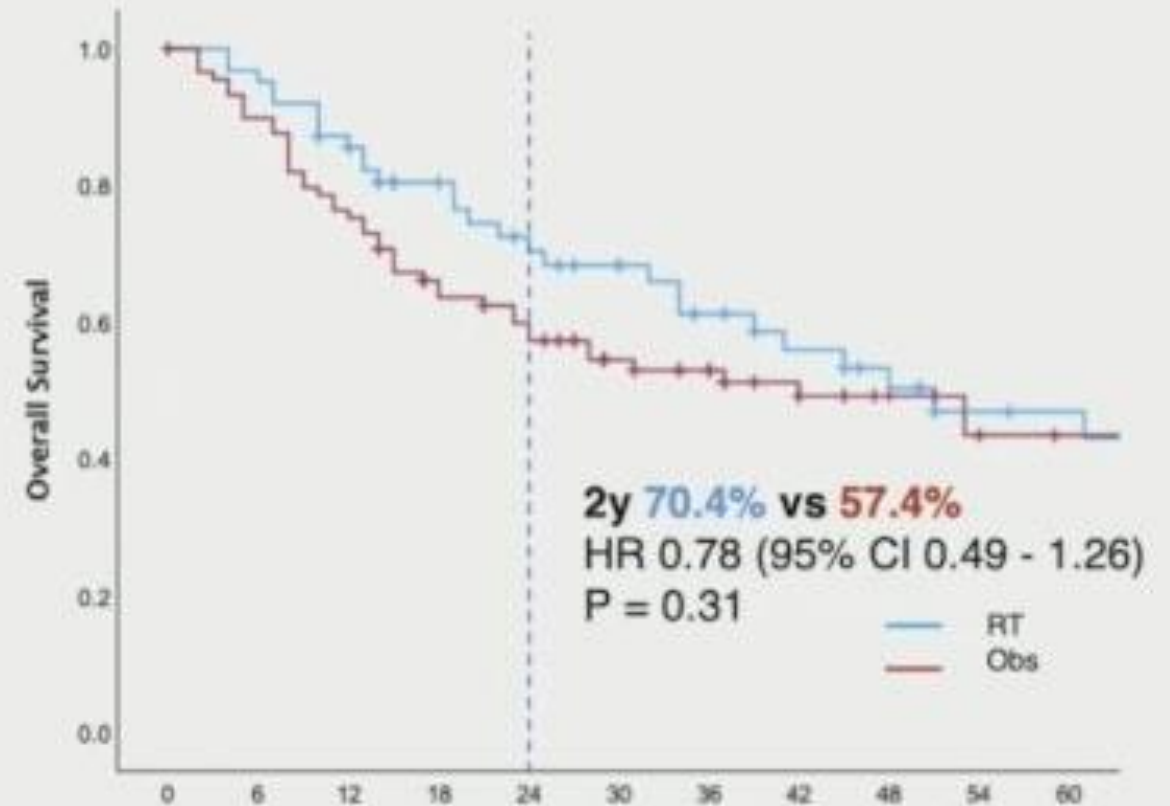


Bladder Adjuvant Radiotherapy (BART)

ASTRO



No. at risk		Follow up (Months)										
RT	77	71	49	38	35	30	25	20	16	13	12	
Obs	76	58	44	37	32	25	22	18	12	10	10	



No. at risk		Follow up (Months)										
RT	63	61	54	41	35	31	25	21	18	13	12	
Obs	90	80	68	54	47	36	32	26	20	15	13	

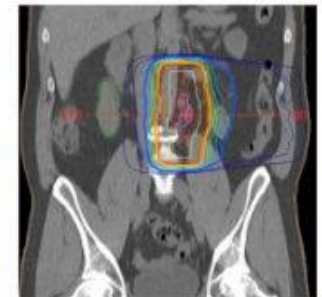
Long-Term Follow-up from the International Multicenter Phase II Trial SAKK 01/10

ESMO

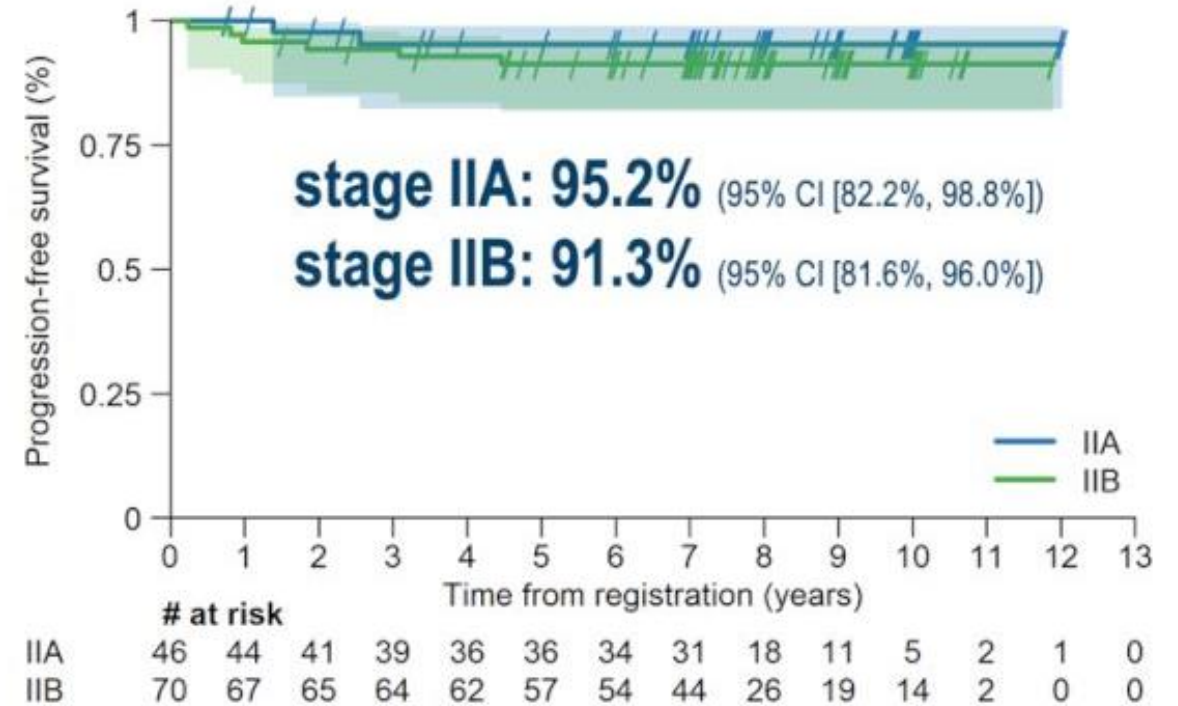
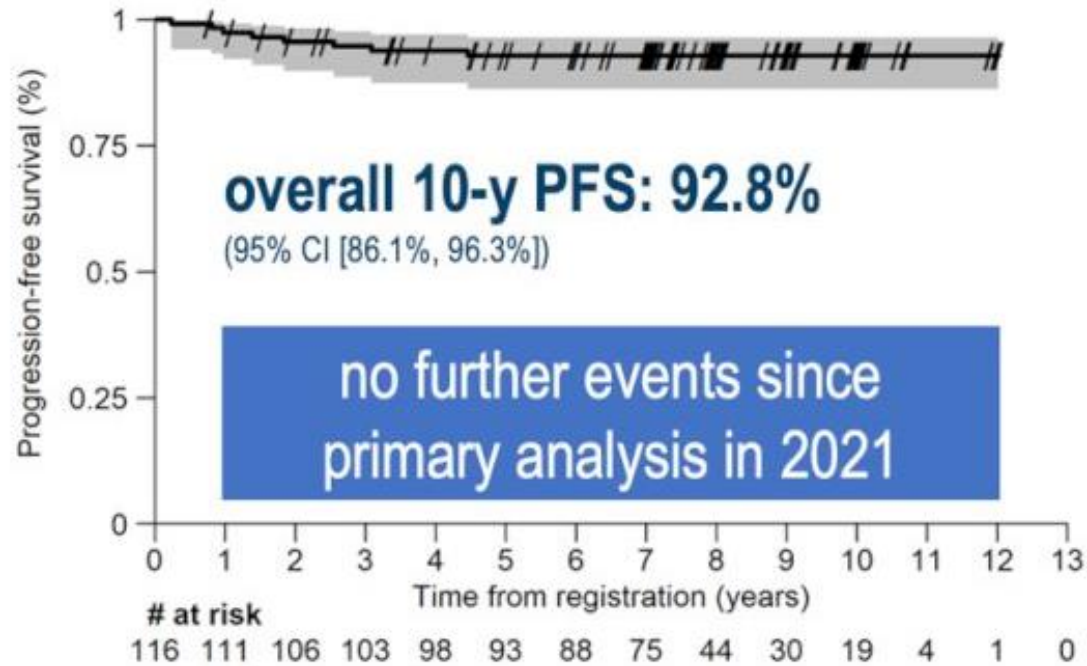
- Single-Dose Carboplatin and Involved-Node Radiotherapy for Seminoma Stage IIA/B:

Design

- 2012-2018, 20 centers in Switzerland & Germany
- single arm, phase II therapy optimization trial
- n = 116, median age: 40 (range 22 - 68)
- IIA: 46 patients, IIB: 70 patients; median lymph node size 2.5 cm (IQR 1.5-3.3cm)



SAKK 01/10: update –follow-up time: 8,1 years



SAKK 01/10 in guidelines

ESMO



National
Comprehensive
Cancer
Network®

NCCN Guidelines Version 2.2025 Testicular Cancer - Pure Seminoma

CLINICAL STAGE	PRIMARY TREATMENT ⁱ	FOLLOW-UP	RECURRENCE
Stage IIA/IIB ^{h,q}	<3 cm ^r → RT ⁱ to include para-aortic and ipsilateral iliac lymph nodes to a dose of 30 Gy (1–2 cm) or 36 Gy (2–3 cm) or First-line chemotherapy ^s : BEP ^u for 3 cycles or EP for 4 cycles or Nerve-sparing RPLND ^{t,v,w} (category 2B for 2–3 cm) or Carboplatin + RT^{x,y} (category 2B) ★	See Follow-up for Seminoma, Table 3 (TEST-A 2 of 3) → See Follow-up for Seminoma, Table 3 (TEST-A 2 of 3) → See Follow-up for Seminoma, Table 4 (TEST-A 2 of 3) or 5 (TEST-A 3 of 3) → See Follow-up for Seminoma, Table 3 (TEST-A 2 of 2)	→ → → → For recurrence, treat according to extent of disease at relapse ^o
	3–5 cm → First-line chemotherapy ^s : BEP ^u for 3 cycles or EP for 4 cycles	→ See Follow-up for Seminoma, Table 6 (TEST-A 3 of 3)	



«Late toxicities should be considered as current studies only extend out to 3 years»

SAKK 01/10: update on second primary tumors

- 4 patients with a contralateral stage I germ cell tumor
- 4 patients with other second primary tumors

Already reported – median FU: 4.5 years	Update – median FU: 8.1 years
2x contralateral GCT	2x contralateral GCT
1x renal cancer (58 y.o.)	1x urothelial cancer of the bladder <u>and</u> 1x incidental prostate cancer (52 y.o.)
1x cholangiocarcinoma (67 y.o.) 	1x basal cell carcinoma (63 y.o.)

Take home messages – prostate cancer



1. **Hypo-RT-PC phase 3 trial:** support ultra-hypofraction as a safe, effective, and practical standard of care option for intermediate-risk prostate cancer
2. **RTOG 0924 trial:** Goodbye WPRT
3. **Thunder trial:** Use PSMA-PET-CT in staging for high risk prostate cancer (PSA > 20, Gl 8-10, cT3-4, N1) → upstaging in 1/3
4. **Enzarad:** limited effect of adding enzalutamide in high risk, localized prostate cancer on MFS.
5. **PEACE V-STORM:** potential standard for oligorecurrent nodal disease
6. **STOPCAP meta-analysis:** Local radiotherapy to the prostate improved PFS and showed an OS trend in men with low metastatic burden.
7. **GROUQ-PCS 9:** MDT using SBRT should strongly be considered for CRPC patients with oligometastases

Take home messages – bladder and testicular cancer



1. **BART:** adjuvant radiotherapy improved locoregional failure-free survival, trend for improved OS
2. **TMT + nivolumab:** less distant metastases, better OS, well tolerated. Not reimbursed in this setting, but reimbursed as adjuvant therapy after cystectomy.
3. **SAKK 01/10:** de-escalation approach in patients with stage II seminoma.