

GU Radiotherapy highlights from ESTRO 2025

dr. Benedikt Engels
AZORG, Aalst, Belgium



BMUC 2025
17 May 2025
Holiday Inn Brussels Airport



**12th Belgian Multidisciplinary
Meeting on Urological Cancers**

Conflicts of interest

- I have no potential conflict of interest to report



Overview



ESTRO
2025

2-6 May 2025

Vienna, Austria

- PSMA-PET/CT stage migration in PC: Thunder trial
- Prostate SBRT: Hypo-RT-PC phase 3 trial
- Focal boosting in prostate RT: FLAME phase 3 trial
- Pelvic nodal oligorecurrent PC: PEACE V-STORM randomized phase 2 trial
- Nivolumab + RCT in bladder cancer: HGUCG randomized phase 2 trial



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



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



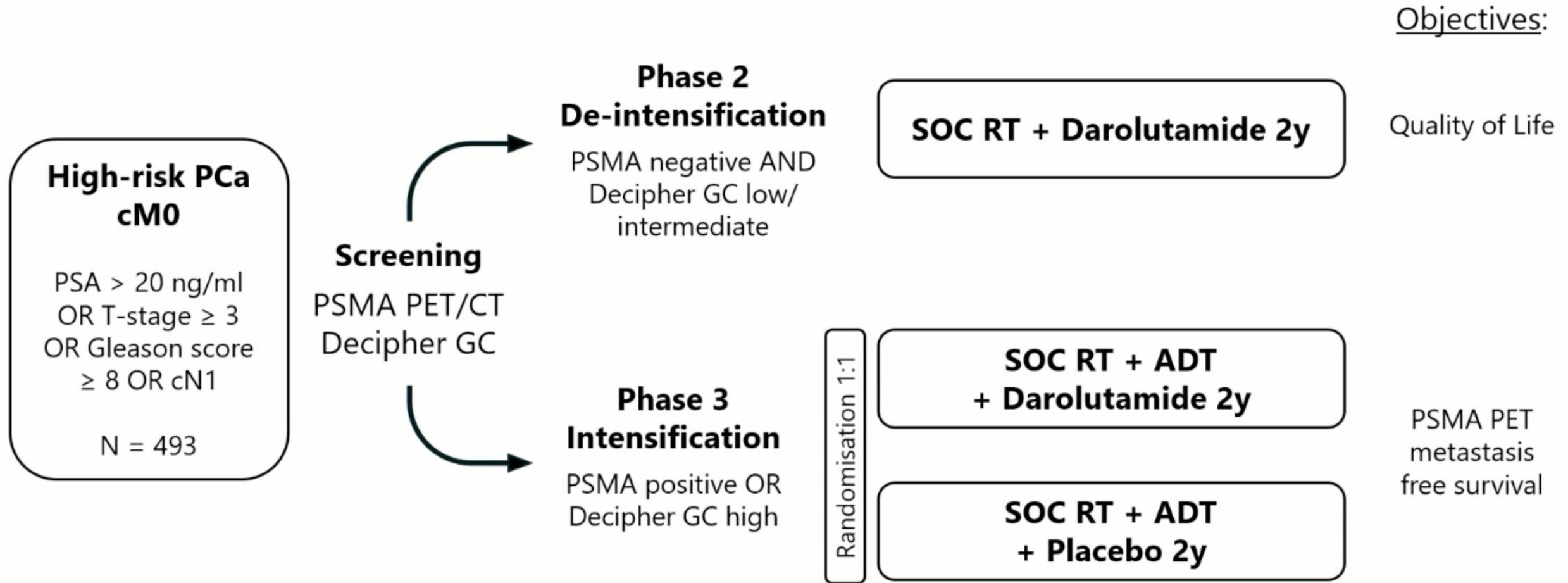
PSMA PET/CT Stage Migration and Genomic Classifier Scores in High-Risk Prostate Cancer

First-Year Results from the Thunder trial (NCT06282588)

The Thunder trial is supported by Bayer and Veracyte



Multicenter Thunder phase 2/3 study



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

Introduction

Study aim

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

Patient characteristics

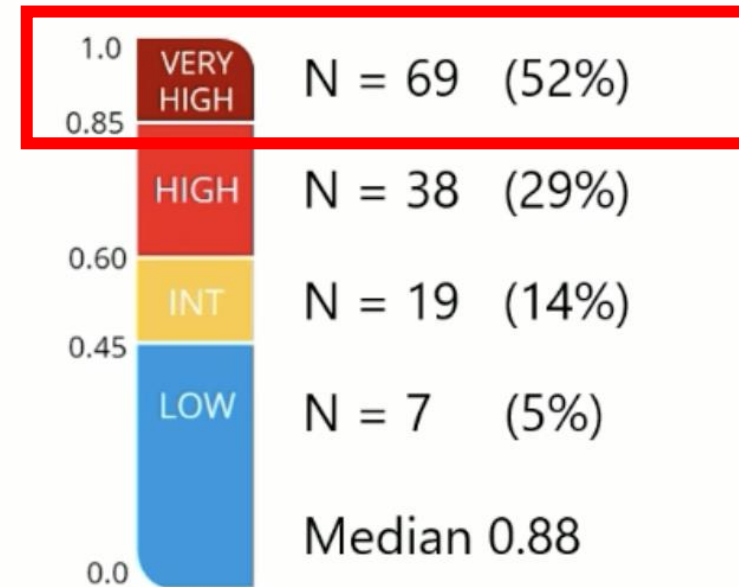
Very high-risk population

PSMA PET/CT:

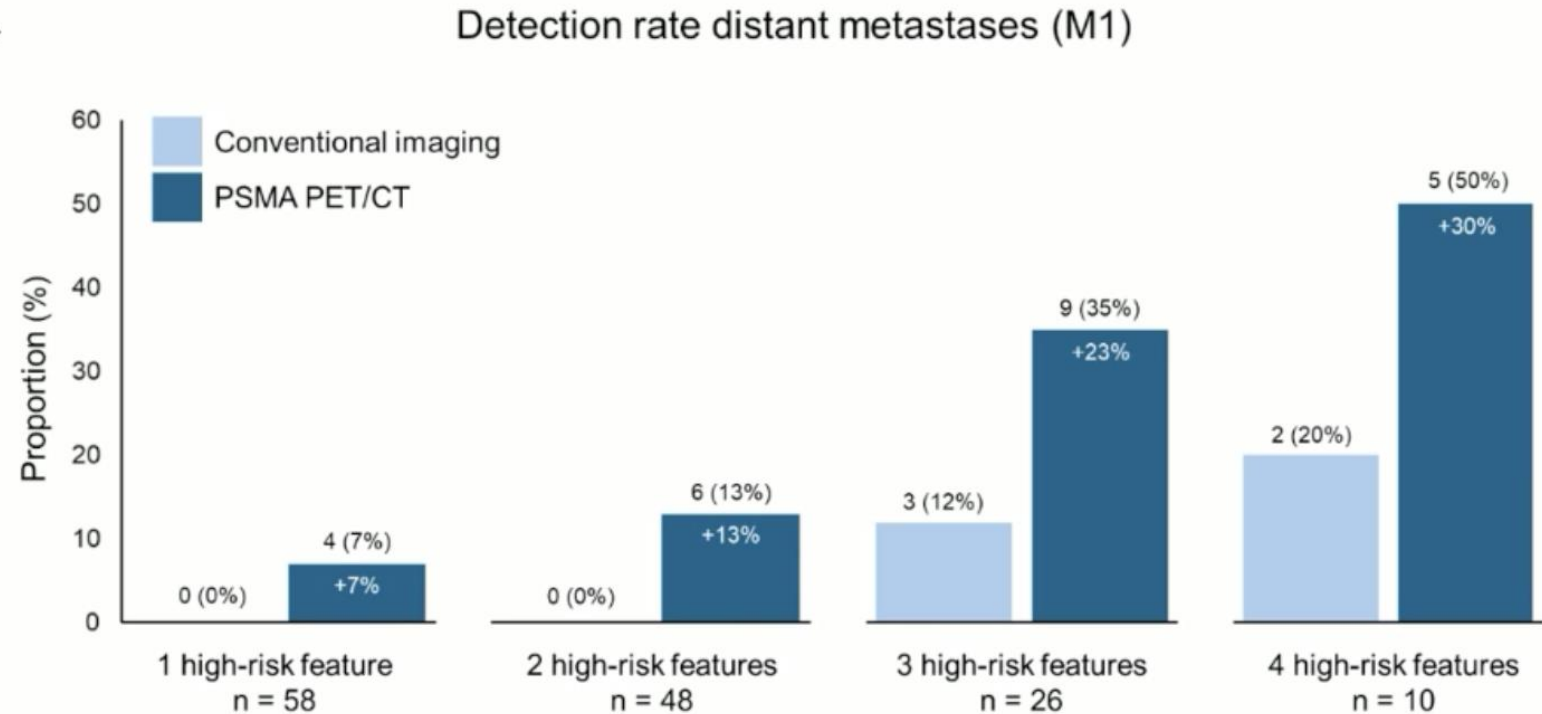
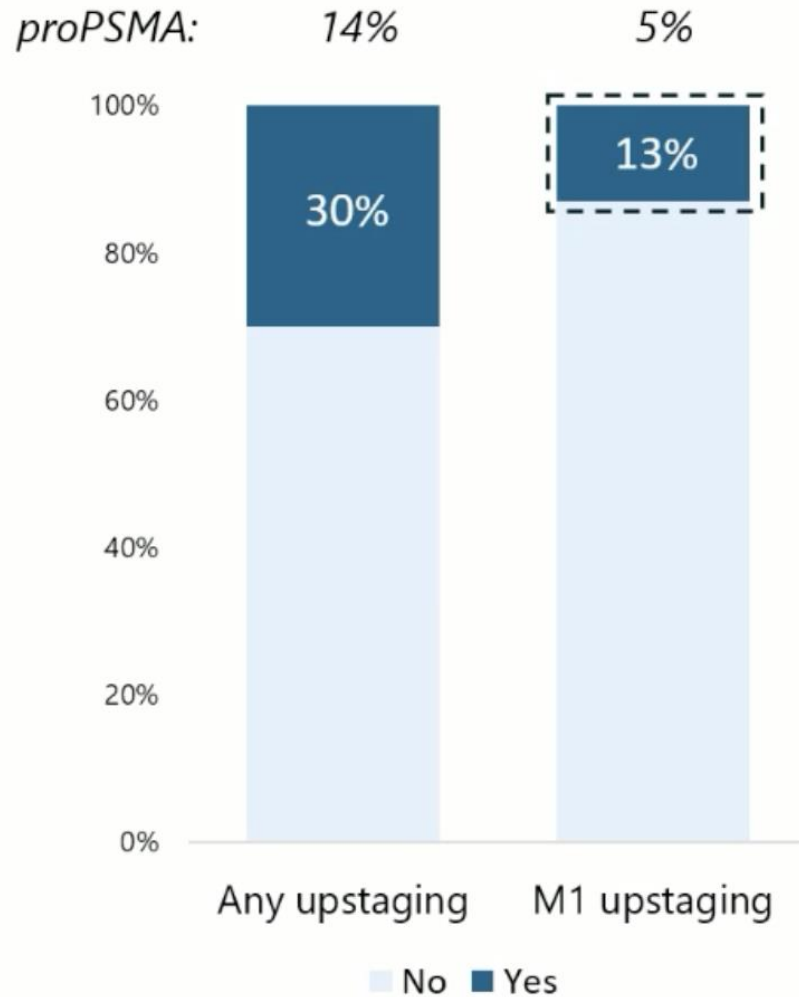
- Metastatic N = 24 (17%)
- Nodal only N = 38 (27%)
- Localised N = 80 (56%)



Decipher Genomic Classifier:



Upstaging with PSMA PET/CT



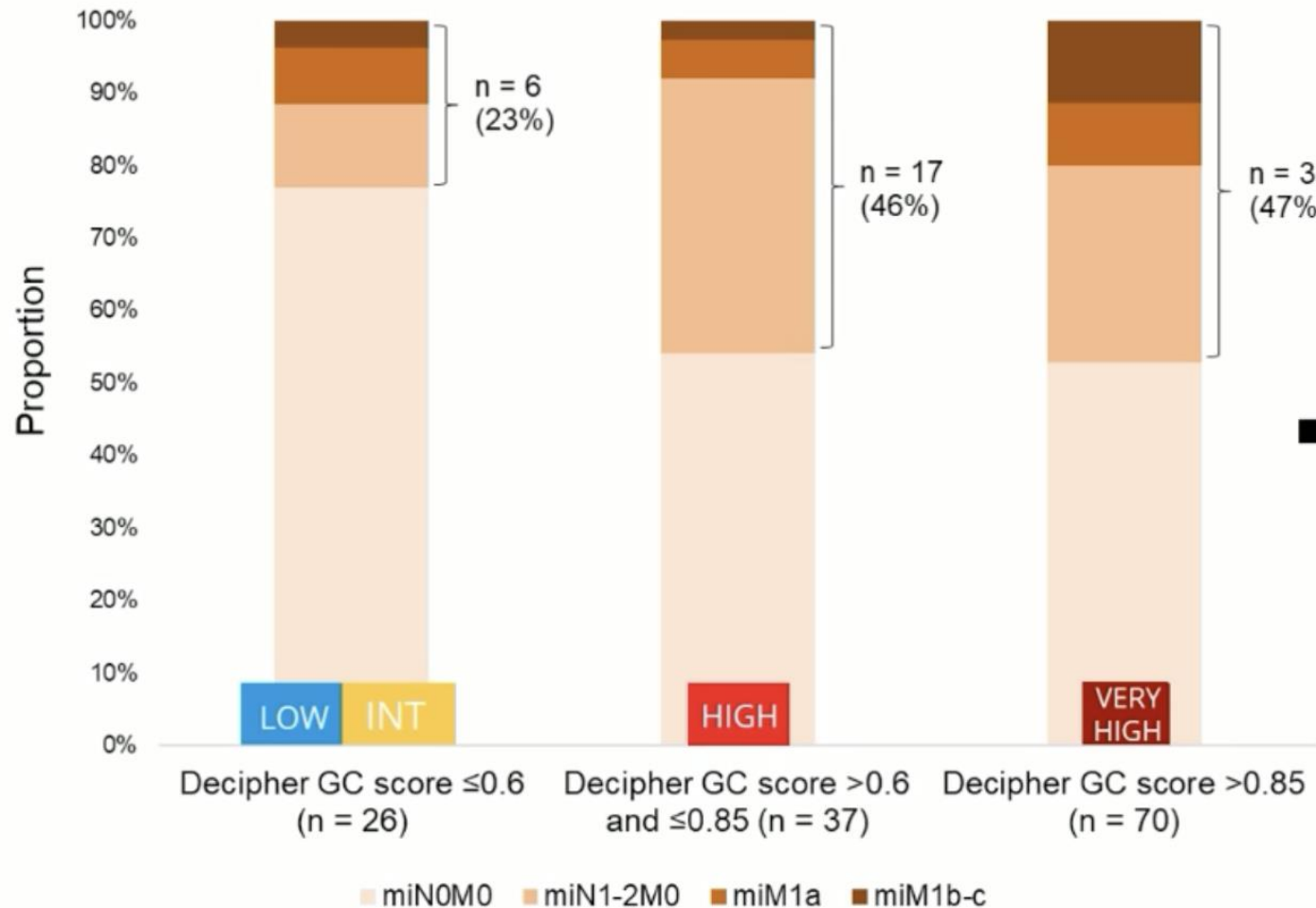
PSA > 20 ng/ml, T-stage $\geq$ 3, Gleason score $\geq$ 8, cN1

Results

Decipher GC scores



Extraprostatic disease on PSMA PET/CT



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



False or true negative?

Results

In 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

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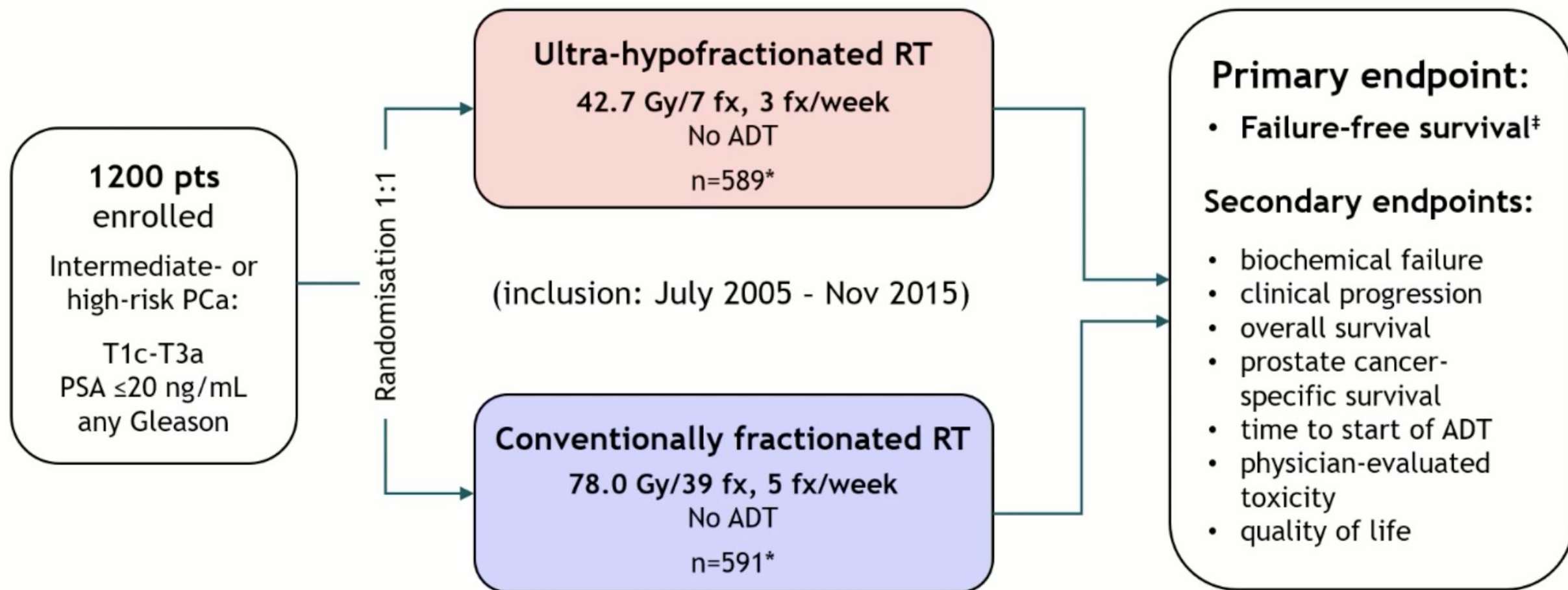


Per Nilsson¹, Adalsteinn Gunnlaugsson¹, Lars Beckman², Anders Widmark³, Per Fransson³, Morten Hoyer⁴, Magnus Lagerlund⁵, Jon Kindblom⁶, Bengt Johansson⁷, Kirsten Björnlinger⁸, Claes Ginman⁹, Martha Olsson¹⁰, Måns Agrup¹¹, Elisabeth Kjellén¹, Björn Zackrisson³, Harald Anderson¹, Björn Tavelin³, Lars Franzén³, Camilla Thellenberg Karlsson³

Ultra-hypofractionated radiotherapy for localised prostate cancer: 10-year outcomes of the HYPO-RT-PC phase 3 trial

¹Skåne University Hospital, Lund University, Lund, Sweden. ²Sundsvall Hospital, Sundsvall, Sweden. ³Umeå University, Umeå, Sweden. ⁴Aarhus University Hospital, Denmark. ⁵Kalmar Hospital, Kalmar, Sweden. ⁶Sahlgrenska Academy, Goteborg, Sweden. ⁷Örebro University Hospital, Örebro, Sweden. ⁸Ryhov Hospital, Jönköping, Sweden. ⁹Central Hospital, Karlstad, Sweden. ¹⁰Central Hospital, Växjö, Sweden. ¹¹Linköping University Hospital, Linköping, Sweden.

HYPO-RT-PC trial overview

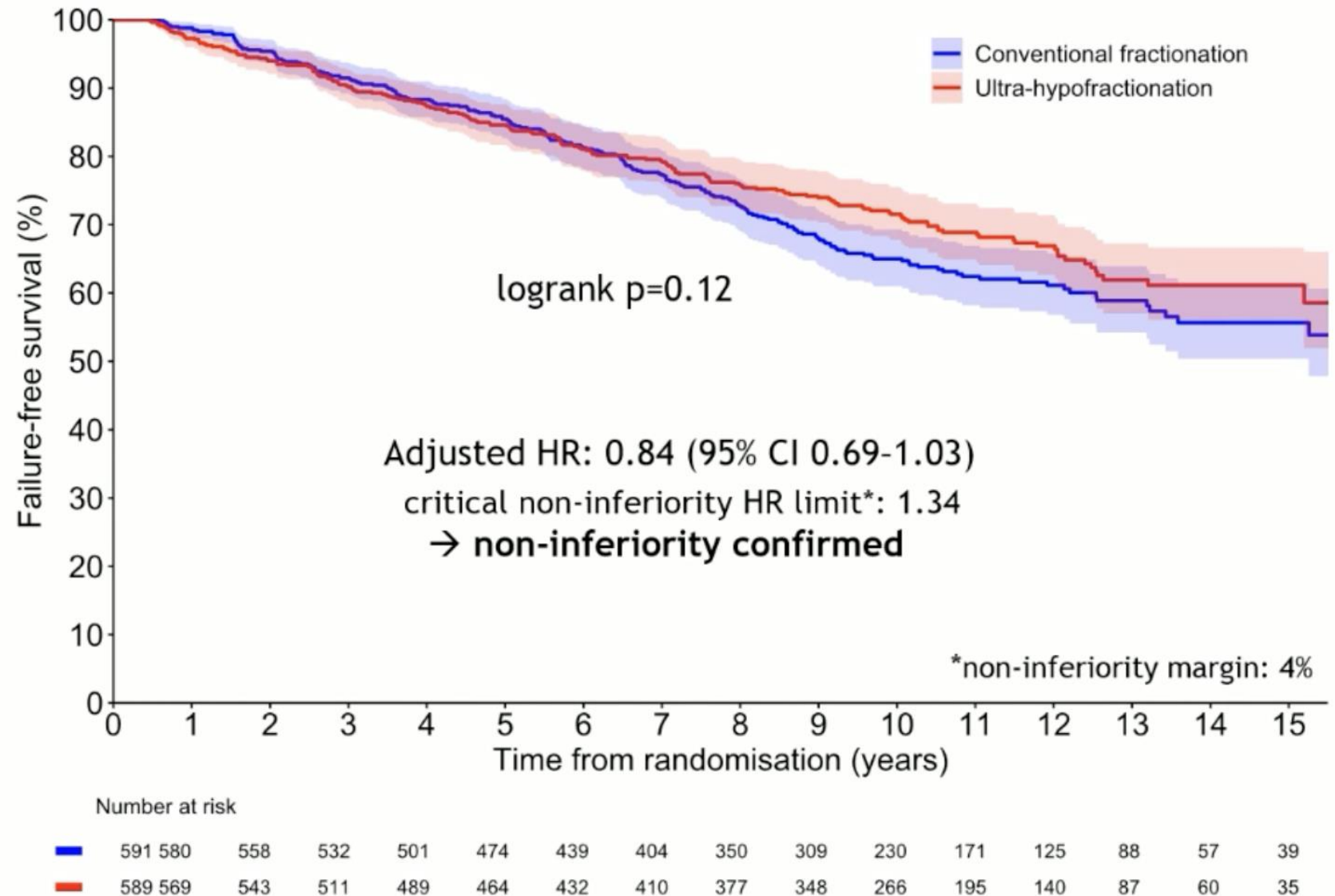


*11 and 9 pts withdrew consent or were ineligible for evaluation in the ultra-hypofractionated and conventionally fractionated RT groups, respectively.

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

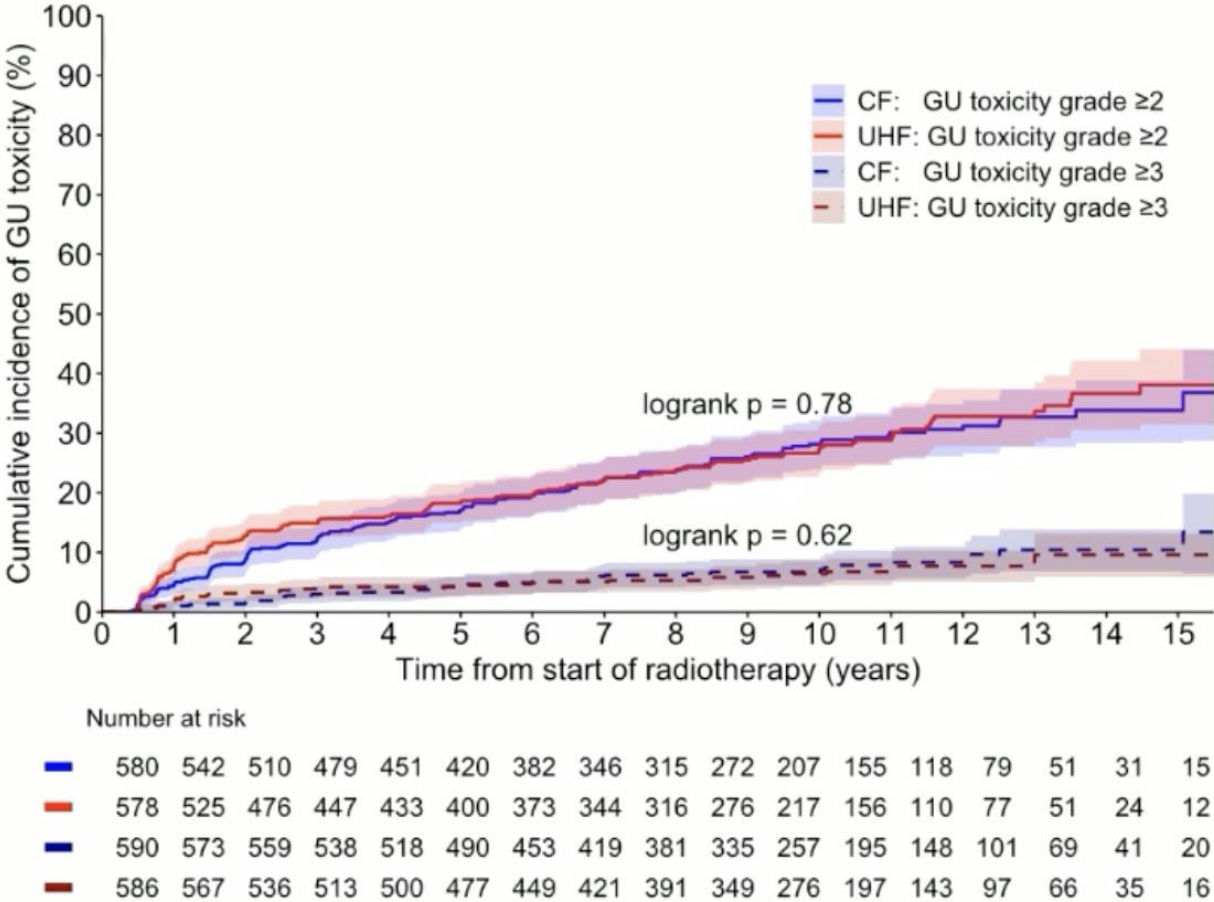
Primary endpoint – failure-free survival

- 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)

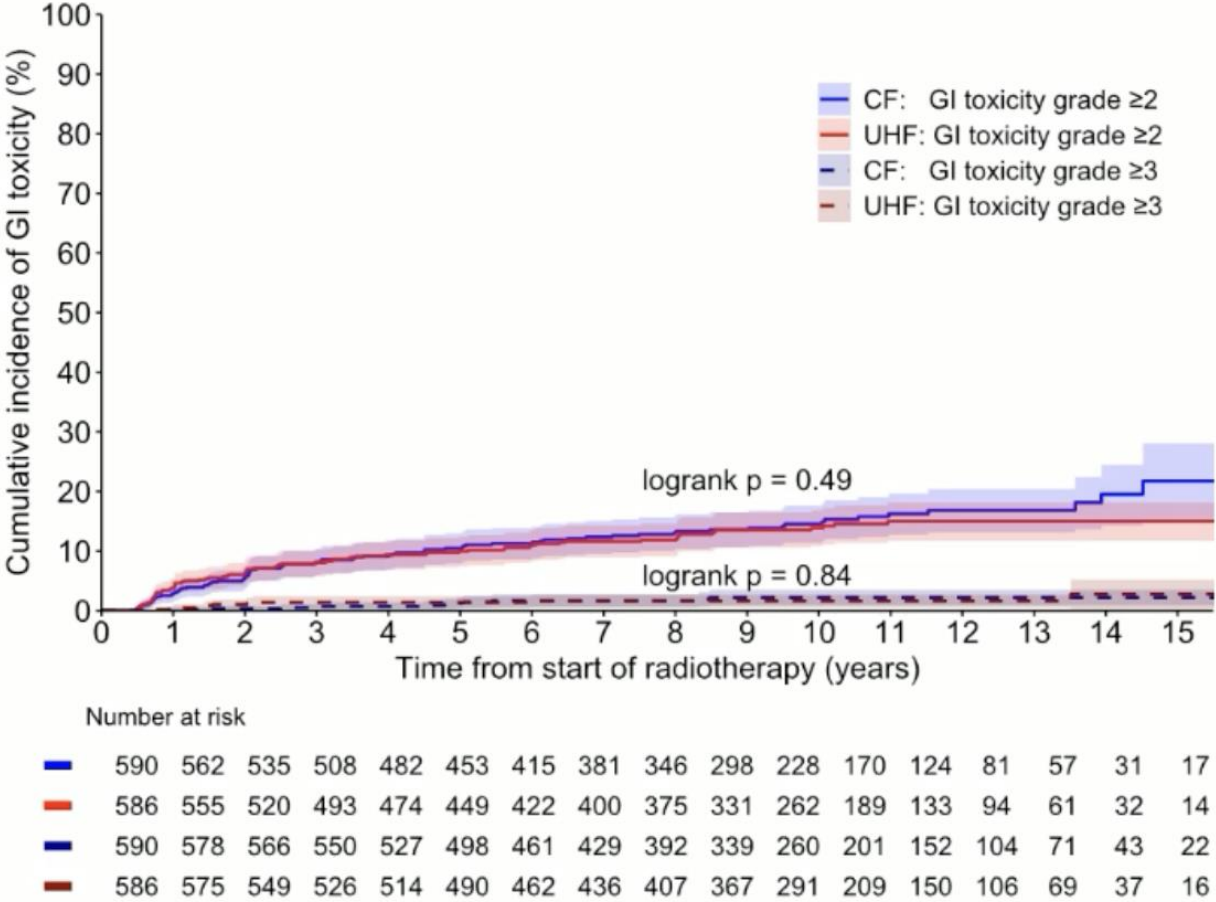


Late toxicity – cumulative incidence

Genitourinary (GU)



Gastrointestinal (GI)



Conclusion

HYPO-RT-PC

- 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-hypofractionation schedule as a safe, effective, and practical standard of care option for intermediate-risk prostate cancer

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Karolína Menne Guricová, C. Draulans, F.J. Pos, L.G.W. Kerkmeijer,
E.M. Monninkhof, R.J. Smeenk, M. Kunze-Busch, J.C.J. de Boer,
J. van der Voort van der Zyp, K. Haustermans, U.A. van der Heide



Focal boost to the intraprostatic tumor for intermediate and high risk prostate cancer: 10-year results of the FLAME-trial



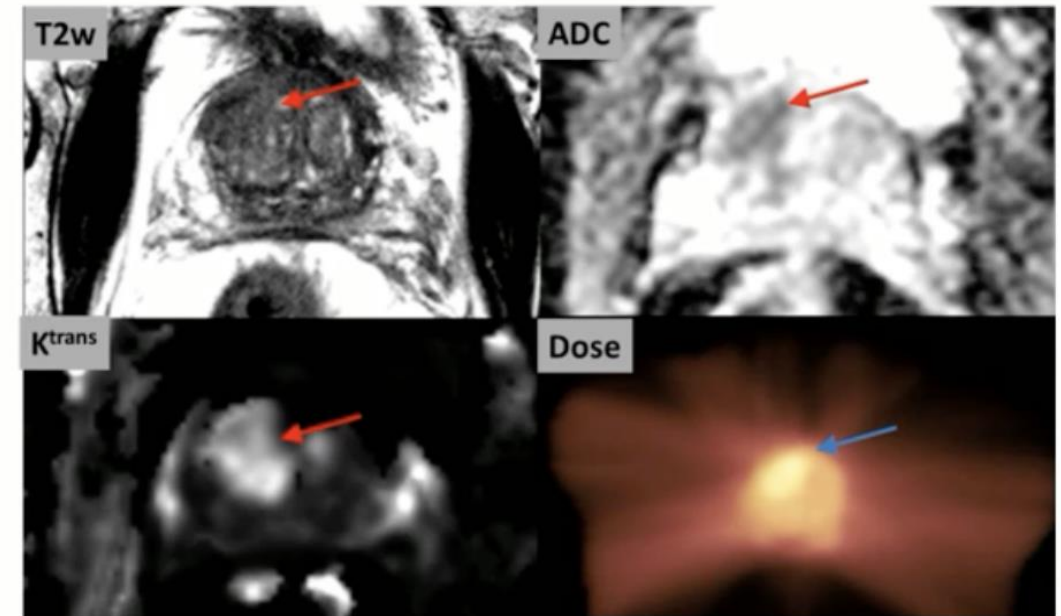
FLAME trial hypothesis



Does dose escalation at the location of intraprostatic lesion(s) improve 5-year biochemical disease-free survival (bDFS) without increasing toxicity?

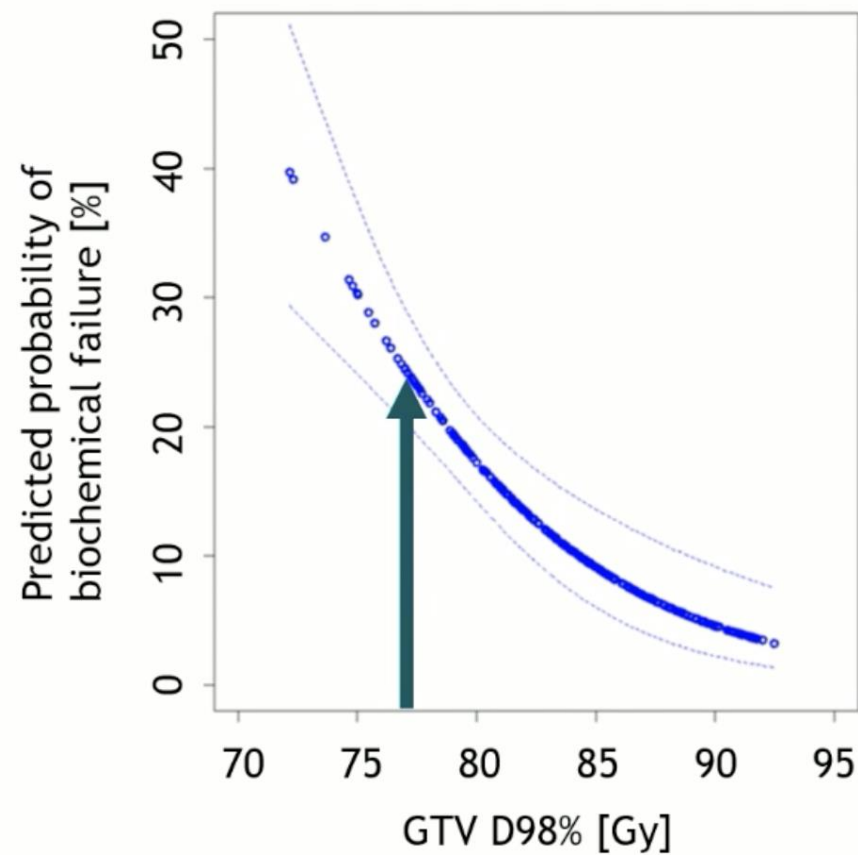
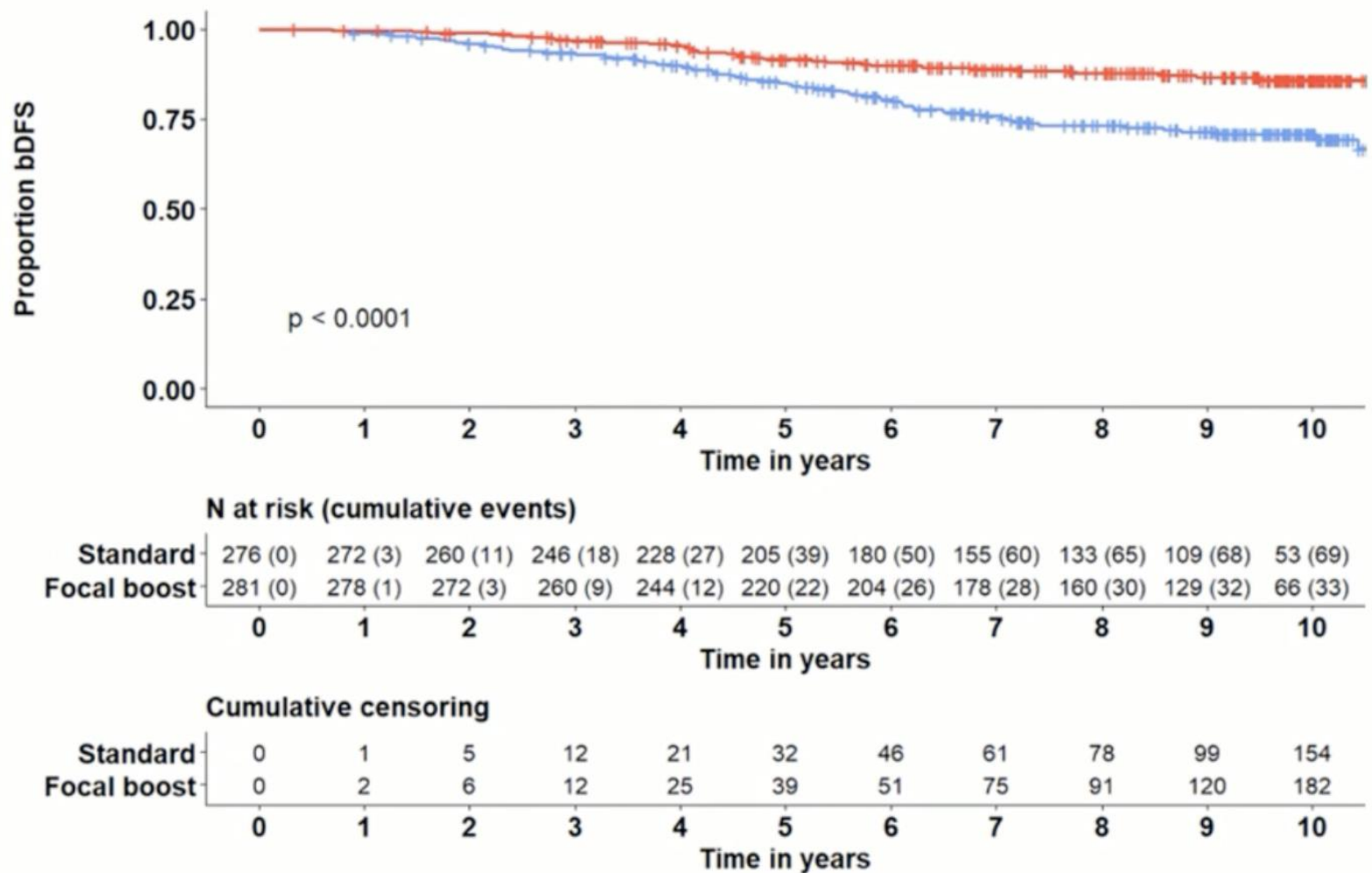
bDFS 85% vs. 92% at 5 years
+ no additional toxicity

Long term follow-up at 10 years?



Kerkmeijer et al., JCO 2021

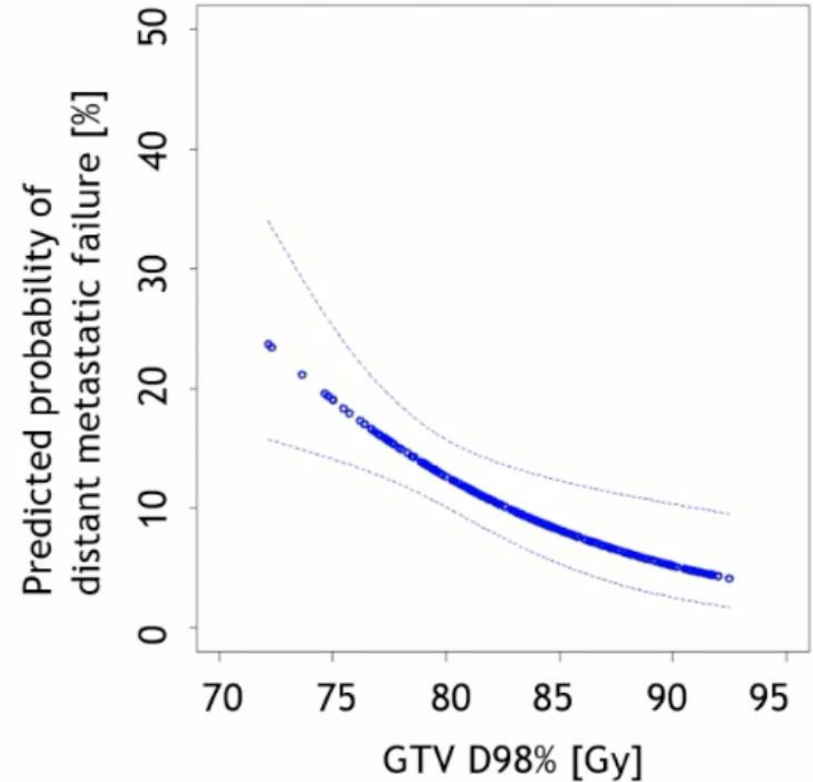
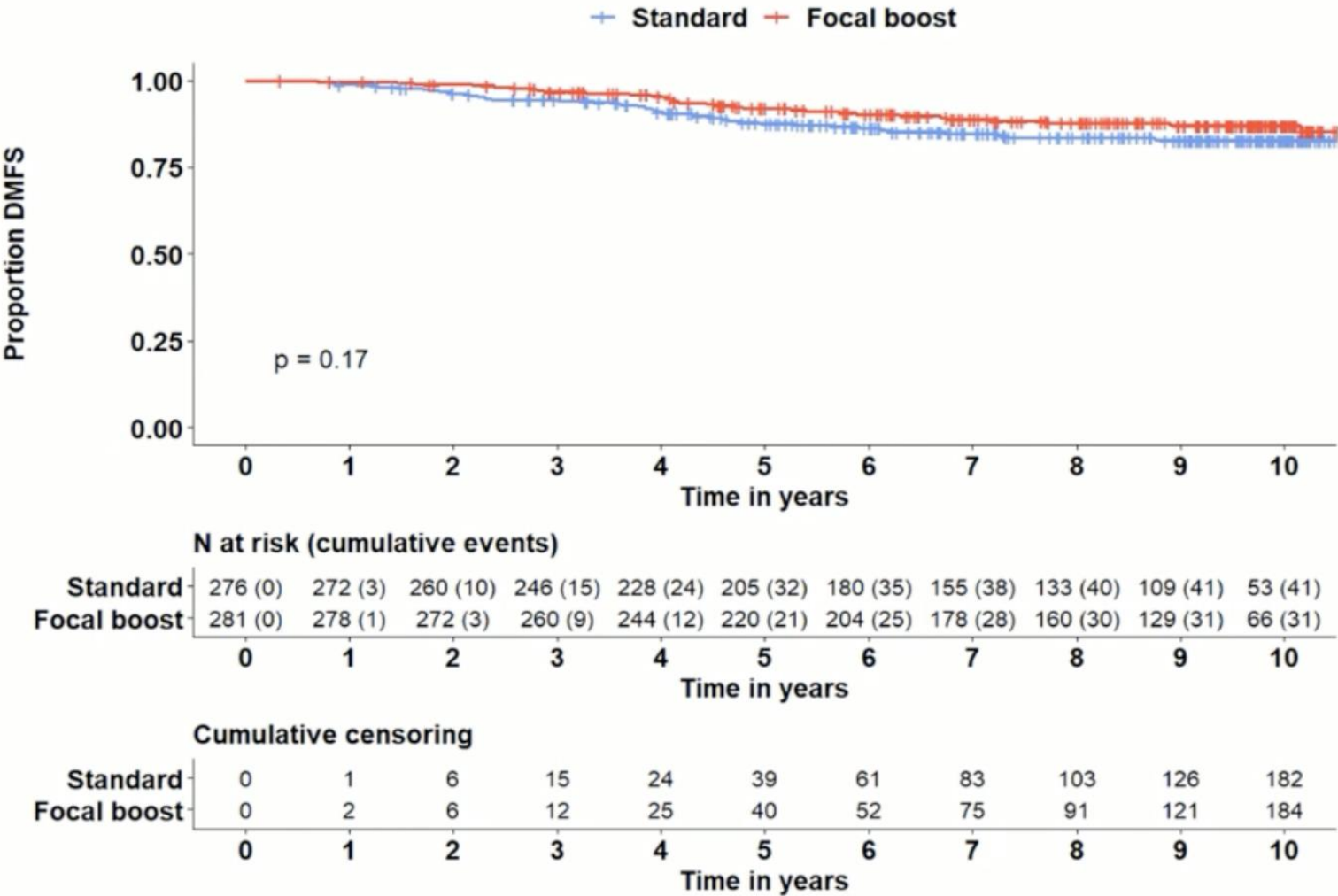
Biochemical disease-free survival



Distant metastases-free survival (DMFS)



83% vs. 87% at 10 years
HR 0.72 (0.45-1.15)



Conclusion



A **significant difference in bDFS** between trial arms (15% at 10 years) demonstrates the **benefit of focal boosting** in patients with intermediate- and high-risk prostate cancer.

Although Kaplan-Meier analysis did not reveal a significant difference in DMFS between trial arms, the dose-effect curve suggests a **possible association between dose and distant metastatic failure**.

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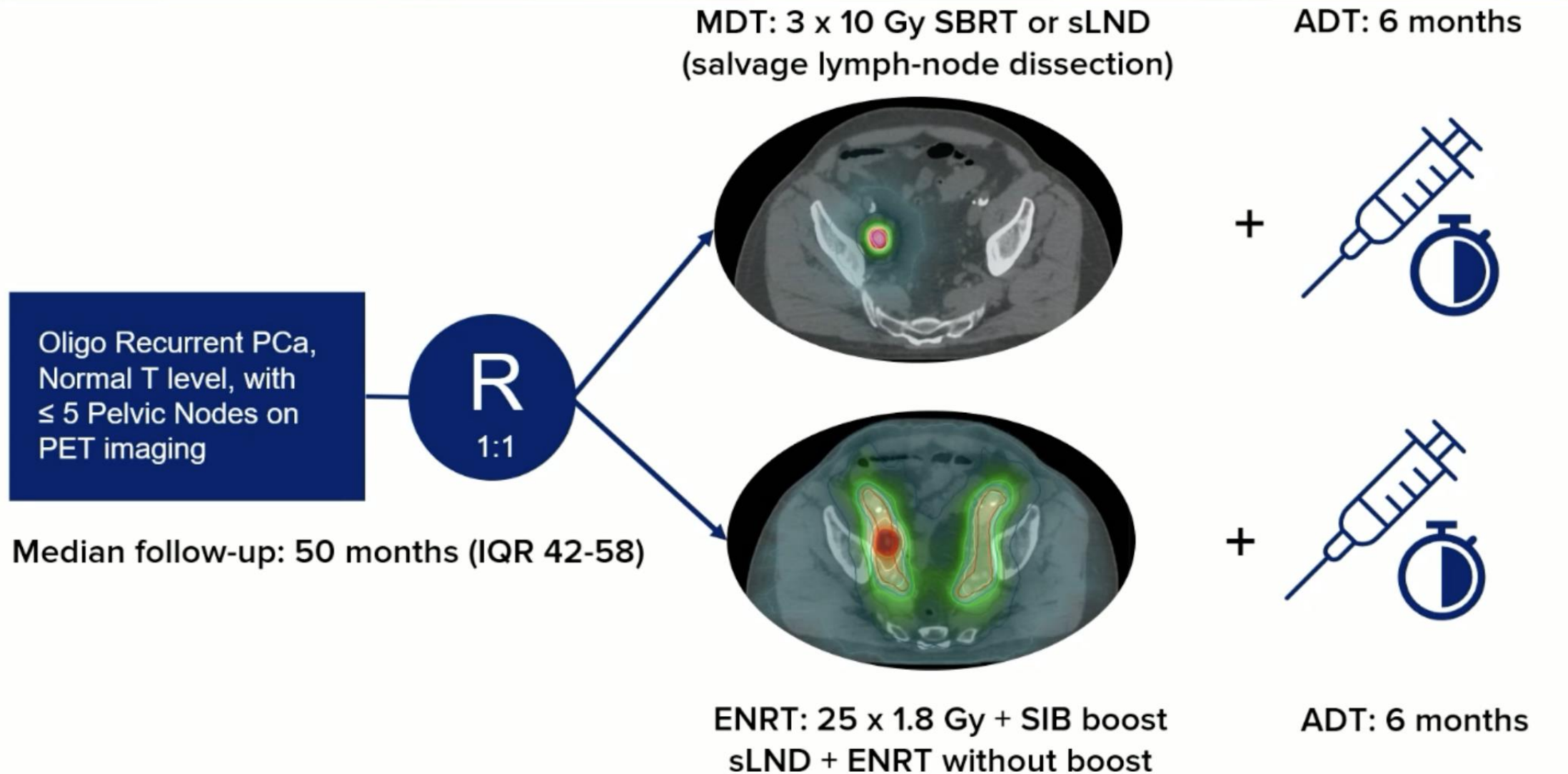
PEACE V – STORM - Salvage Treatment of OligoRecurrent nodal prostate cancer Metastases, a randomized phase II trial: report of the primary endpoint

Thomas Zilli – Oncology Institute of Southern Switzerland,
EOC, Bellinzona, Switzerland
– Geneva University Hospital, Geneva,
Switzerland (previous institution)

Piet Ost – Iridium Network, Antwerp, Belgium
– Ghent university, Ghent Belgium

and the PEACE-V - STORM investigators

PEACE-V - STORM trial



Prostate bed radiotherapy was advised in
patients with pT3, GS ≥ 8 or R1 disease

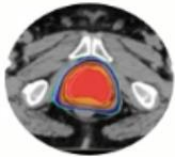
Patients

N = 97 (99 randomized)

N = 93 (97 randomized)



±



RP ± PB RT

85% (52% + 33%)

92% (63% + 29%)



High BCR risk group

91%

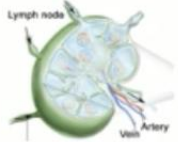
86%



PET imaging

Choline: 19%
PSMA: 81%

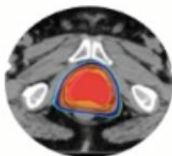
Choline: 17%
PSMA: 83%



Number of nodes

55%
27%
3-5 18%

62%
24%
3-5 14%

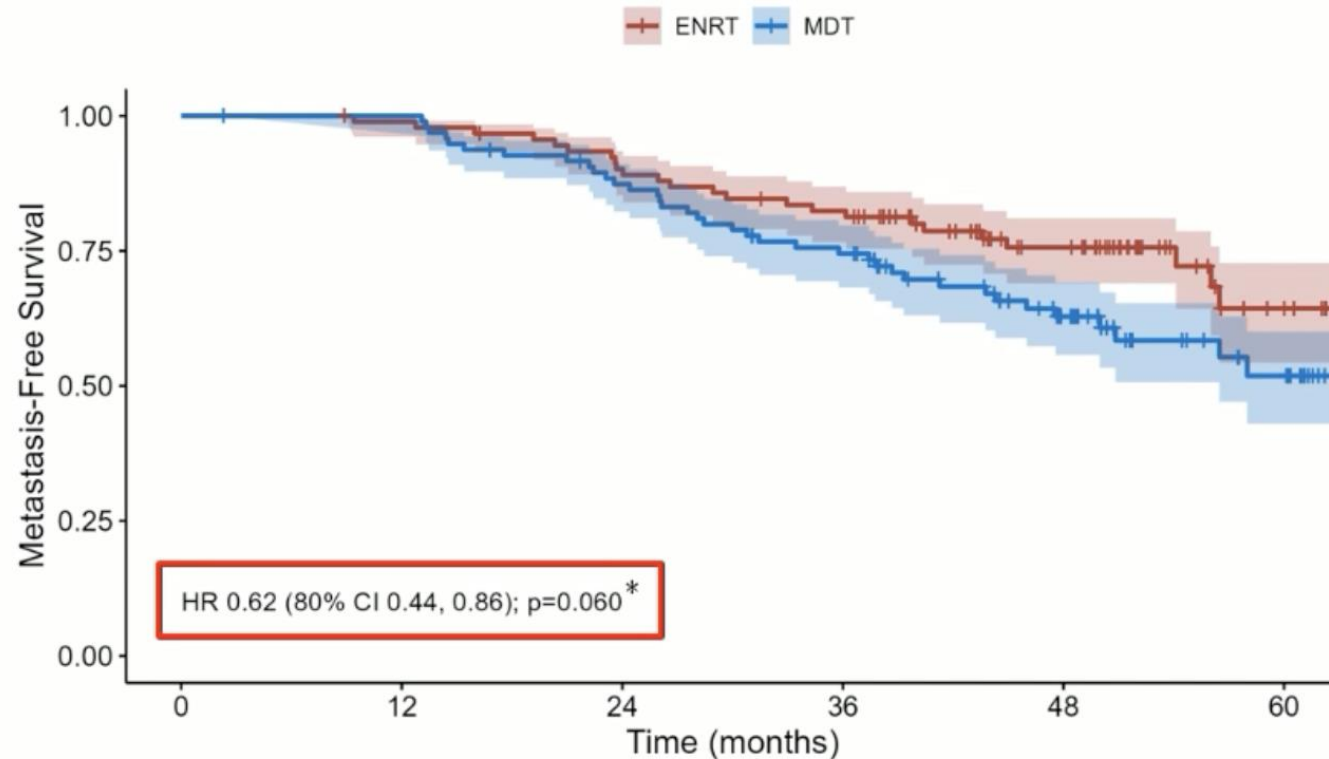


Concomitant RT
to the prostate bed

25%

42%

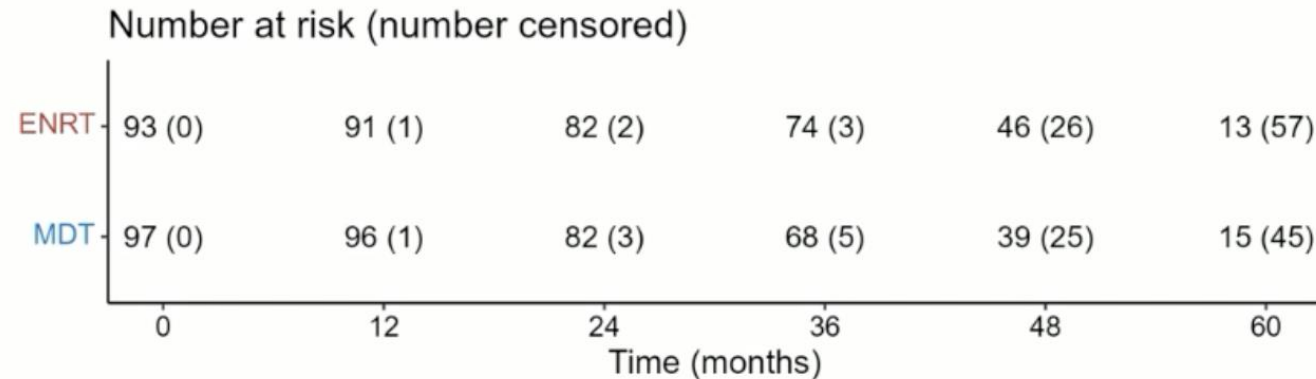
Results: metastasis-free survival (MFS) – primary endpoint



4-year MFS:

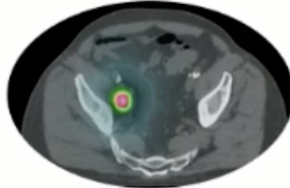
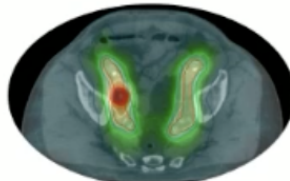
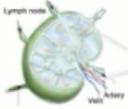
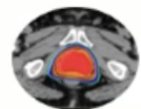
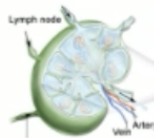
- MDT = 63% [80% CI: 0.56-0.69]
- ENRT = 76% [80% CI: 0.69-0.81]

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



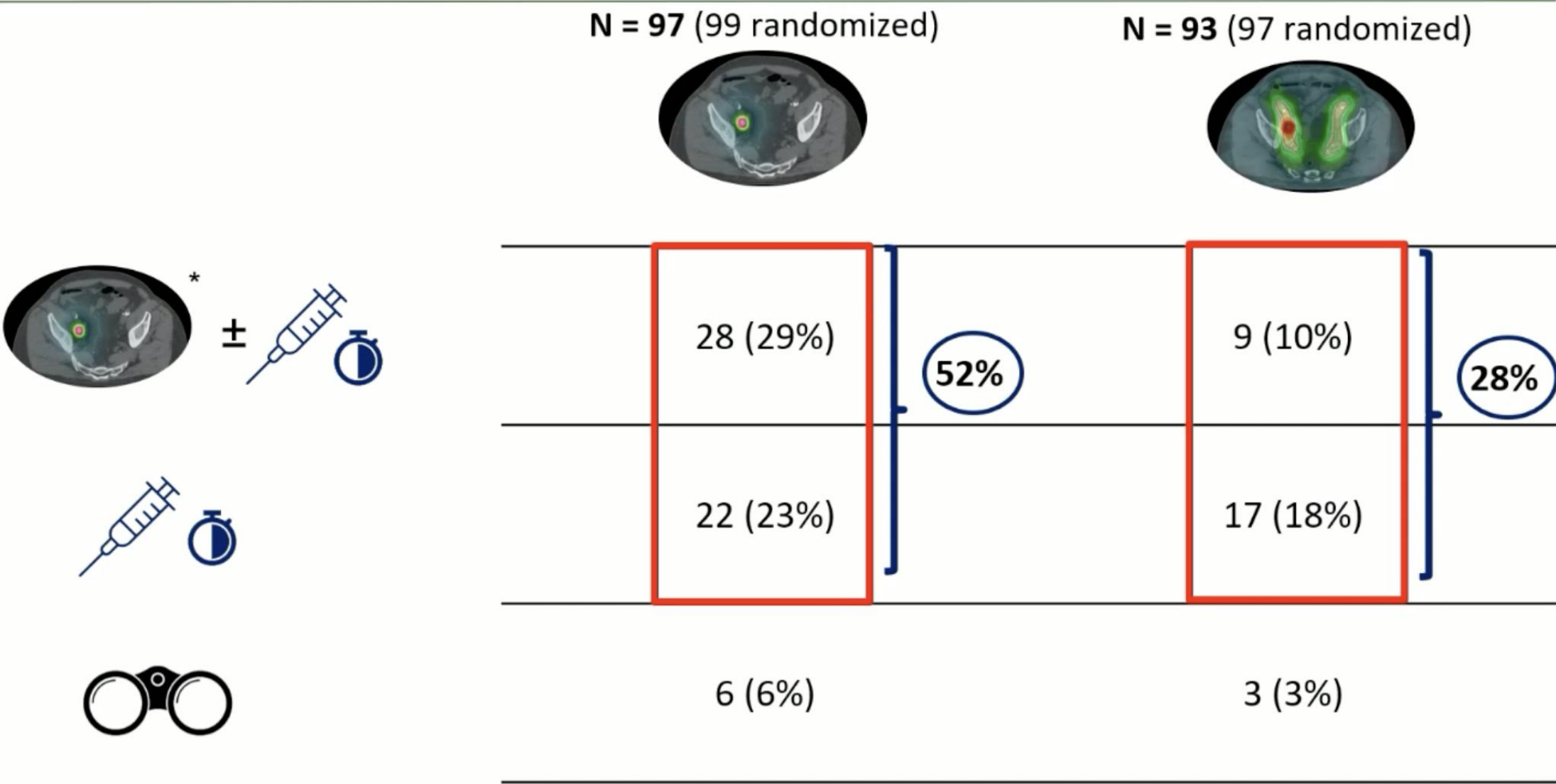
* The two-sided significance level alpha set at 0.20 and power maintained at 80%

Location of relapses

		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)

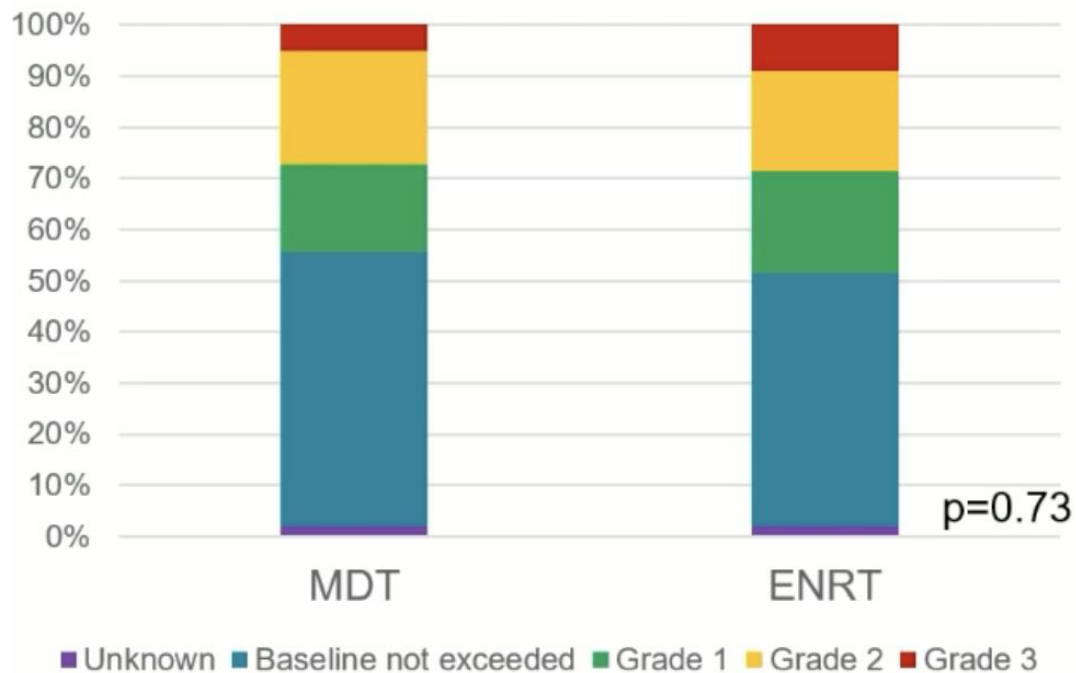
Results: subsequent management therapy



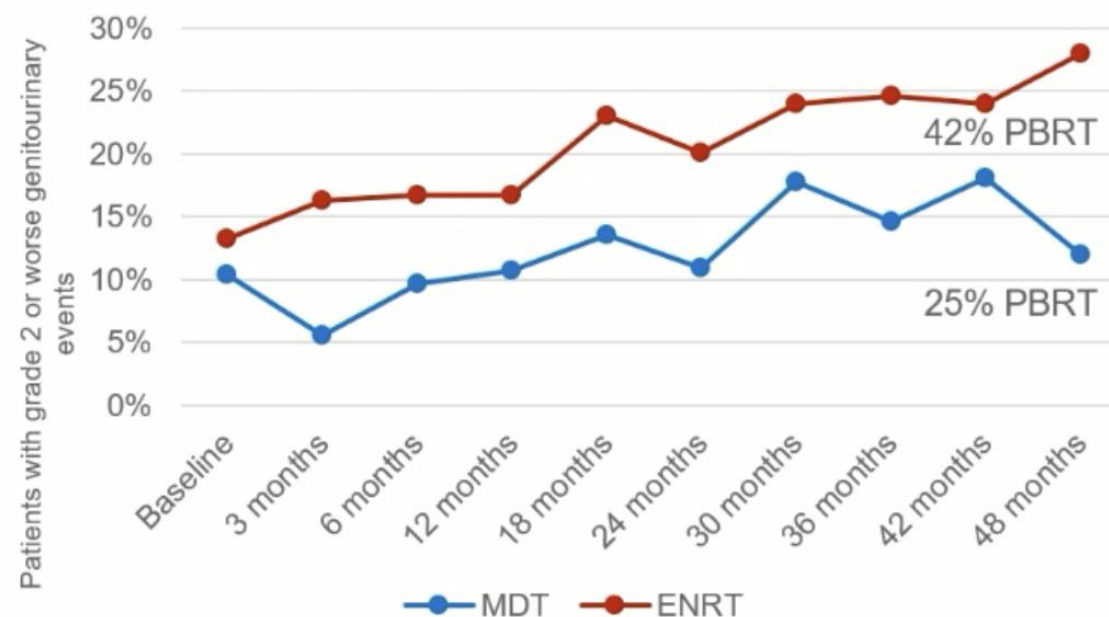
* N = 21 SBRT + ADT; N = 16 SBRT only

Genitourinary toxicity

Worst grade GU toxicity during the first 48 mo with baseline correction



CTCAE v 4.0 Grade 2+ GU toxicity

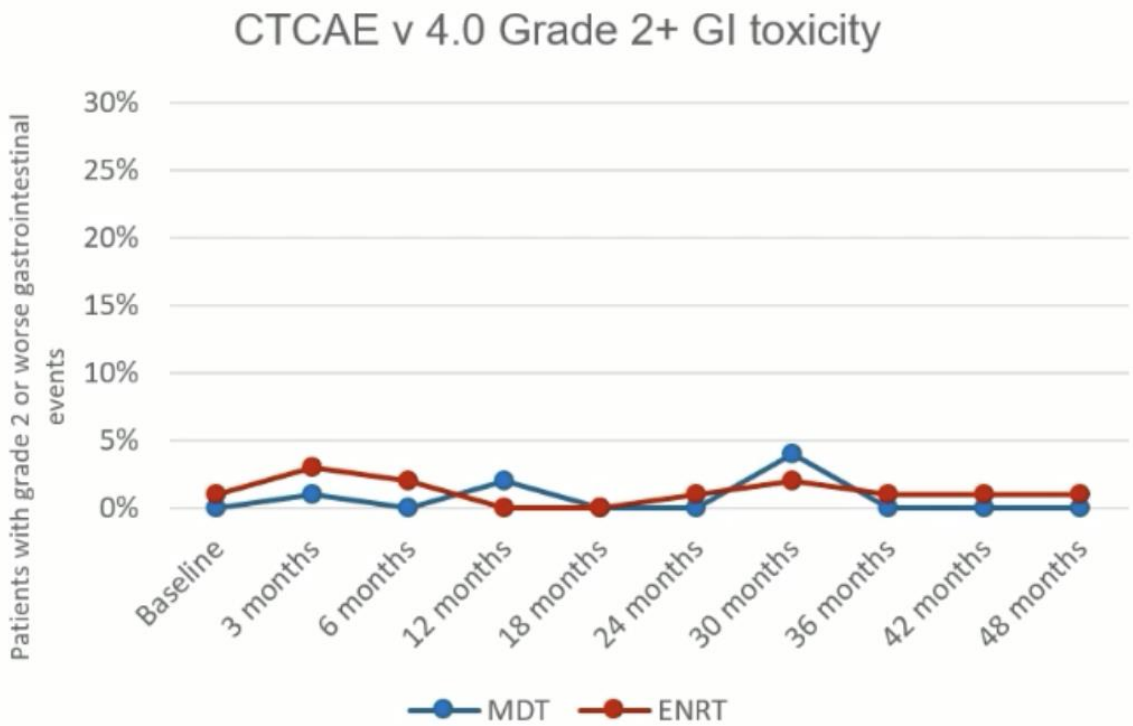
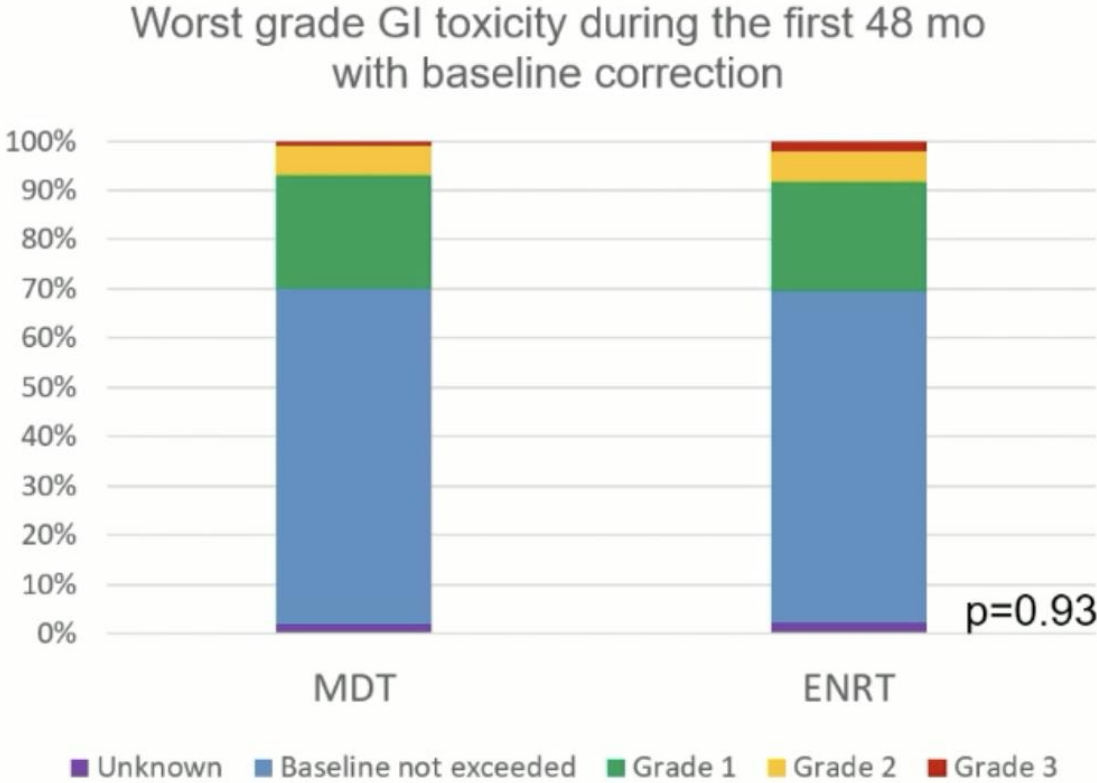


Worst 48-month grade 2+ GU toxicities: MDT vs ENRT (28.1% vs 31.5%)

GU 2+ toxicity was numerically worse with ENRT than with MDT (but not 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)

Gastrointestinal toxicity



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)

Conclusions

- 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** increases the risk of GU and GI toxicity but prevents further local relapses
- **ENRT is the most effective treatment option for reducing the probability of new pelvic recurrences and distant metastases**, positioning itself as a **potential standard** for oligorecurrent nodal disease

Salvage metastasis-directed therapy versus elective nodal radiotherapy for oligorecurrent nodal prostate cancer metastases (PEACE V-STORM): a phase 2, open-label, randomised controlled trial

Piet Ost, Shankar Siva, Sigmund Brabrand, Piet Dirix, Nick Liefhooghe, François-Xavier Otte, Alfonso Gomez-Iturriaga, Wouter Everaerts, Mohamed Shelan, Antonio Conde-Moreno, Fernando López Campos, Alexandros Papachristofilou, Matthias Guckenberger, Marta Scorsetti, Almudena Zapatero, Ana-Elena Villafranca Iturre, Clara Eito, Felipe Couñago, Paolo Muto, Wim Duthoy, Nicolas Mach, Valérie Fonteyne, Daniel Moon, Kristian Thon, Carole Mercier, Vérane Achard, Karin Stellamans, Els Goetghebeur, Dries Reynders, Thomas Zilli

Lancet Oncol 2025; published online first May 5. S1470-2045(25)00197-4

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Nivolumab plus chemoradiotherapy in patients with muscle-invasive bladder: final results of a phase II, randomized study by the HGUCG (NCT03993249).

A. Kougioumtzopoulou¹, K. Koutsoukos², R. Zakopoulou³, K. Tzannis⁴, A. Kyriazoglou⁵, A. Damatopoulou⁶, M. Liontos⁷, M. Pispirigkou⁸, K. Ntoumas⁹, K. Stravodimos¹⁰, D. Mitropoulos¹⁰, A. Dellis¹¹, A. Papatsoris¹², M. Chrisofos¹³, D. Kardamakis¹⁴, A. Zygogianni¹⁵, Z. Liakouli⁶, G. Pissakas⁶, A. Bamias¹⁶, V. Kouloulas¹⁷

¹Dept. of Clinical Radiation Oncology, Attikon University Hospital, Haidari, Greece, ²2nd Oncology Clinic, Metropolitan Hospital, Athens, Greece, ³Oncology unit, Attikon University Hospital, Haidari, Greece, ⁴National and Kapodistrian University of Athens, Attikon University Hospital, 2nd Propaedeutic Department of Internal Medicine, Athens, Greece, ⁵Oncology Unit, Attikon University Hospital, Haidari, Greece, ⁶Radiotherapy Department, General Hospital of Athens Alexandra, Athens, Greece, Athens, Greece, ⁷Oncology Unit, Department of Clinical Therapeutics, Alexandra Hospital, Athens, Greece, ⁸Oncology Department, University Hospital Patras, Patras, Greece, ⁹Department of Urology, General Hospital of Athens G.N.A. G. Gennimatas, Athens, Greece, ¹⁰1st Department of Urology, National & Kapodistrian University of Athens, Laiko Hospital, Athens, Greece, ¹¹Department of Surgery, School of Medicine, Aretaieion Hospital, National and Kapodistrian University of Athens, Athens, Greece, Athens, Greece, ¹²2nd Department of Urology, School of Medicine, Sismanoglio Hospital, National and Kapodistrian University of Athens, Athens, Greece, ¹³3rd Department of Urology, Attikon University Hospital, School of Medicine, National and Kapodistrian University of Athens, Athens, Greece, ¹⁴Department of Radiation Oncology, University Hospital Patras, Patras, Greece, ¹⁵Radiation Oncology Unit, 1st Department of Radiology, Medical School, Aretaieion Hospital, National and Kapodistrian University of Athens, Athens, Greece, ¹⁶2nd Propaedeutic Department of Internal Medicine, National & Kapodistrian University of Athens, University Hospital Attikon, Athens, Greece, ¹⁷2nd Dpt Radiology, Radiotherapy Unit, National and Kapodistrian University of Athens, Attikon University Hospital, School of Medicine, Athens, Greece

Study Design (NCT03993249)

Nivolumab Plus Chemoradiotherapy in Patients With nmMIBC Not Undergoing Cystectomy

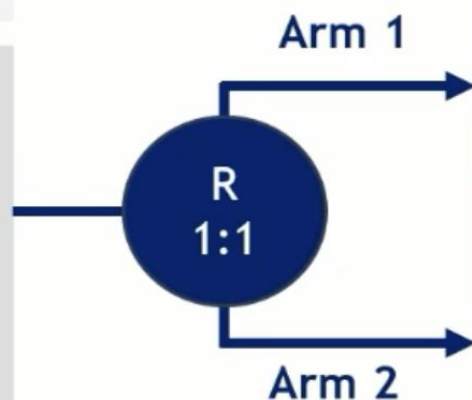
Patients with nmMIBC, not candidates for radical cystectomy

Key Eligibility:

- Treatment naïve MIBC
- cT2-T4aN0M0
- Urothelial, squamous, glandular histology
- GFR $\geq$ 40ml/min
- PS $\leq$ 1

Previously undergone a vigorous TURBT.

Protocol treatment must begin within 8 weeks following TURB-T



ChemoRT* for 6 or 7 weeks
CDDP 20mg d1-d5, d22-d25 or
40mg/m²/week x6

Nivolumab 240mg q14 IV x5, starting 14
days prior to ChemoRT, then 480mg q28 x6

+

ChemoRT* for 6 or 7 weeks
CDDP 20mg d1-d5, d22-d25 or
40mg/m²/week x 6

Primary endpoint

- LRFR at 2 years

Secondary endpoints

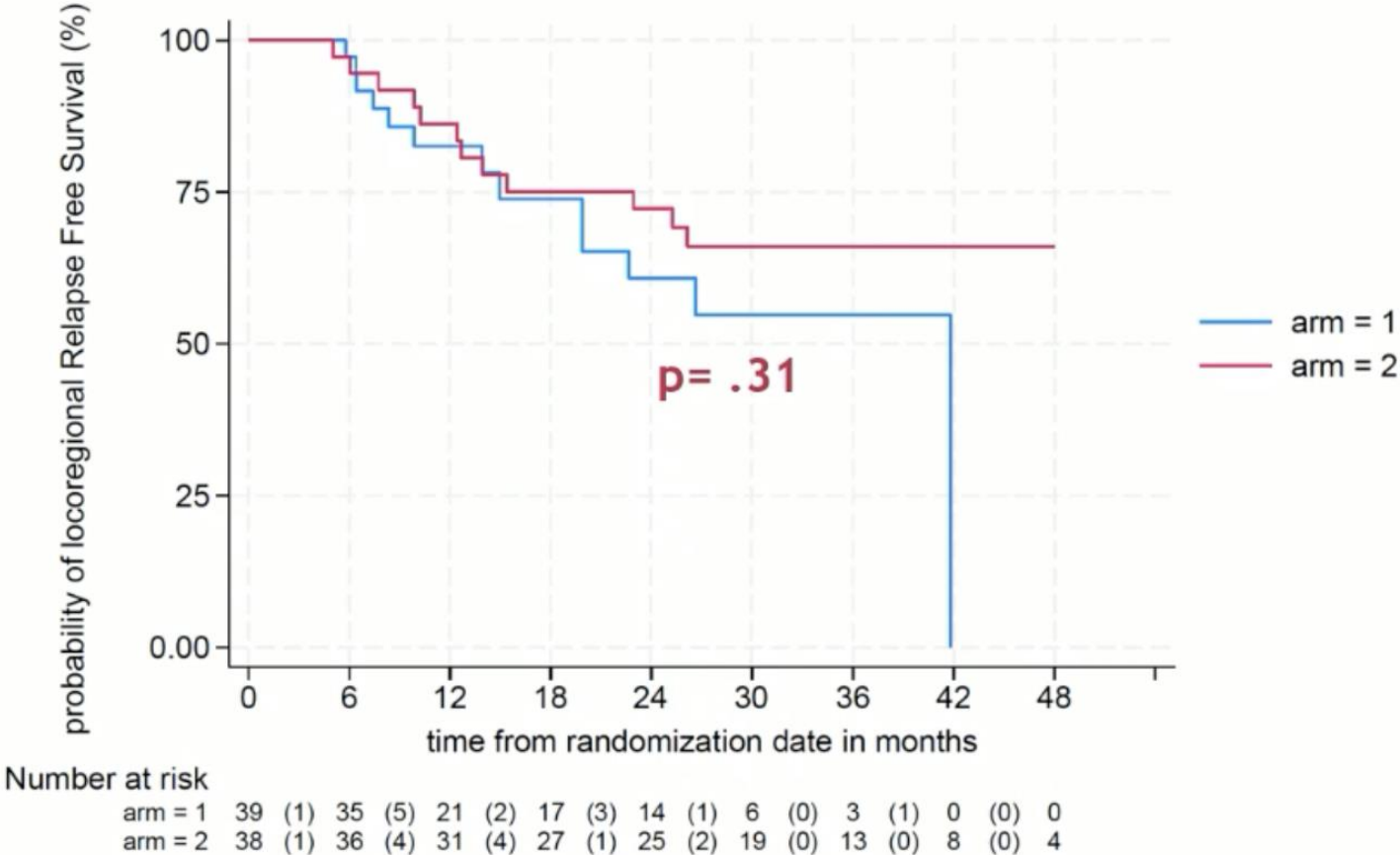
- Toxicity
- BCFFS at 2 years
- OS
- QLQ
- PD-L1 expression

*RT details:

- 3DCRT or IMRT
- Whole bladder 60 Gy, boost 10 Gy (2 Gy/fraction)

After median fup of 33 months, (95% CI 29.4-38.3)

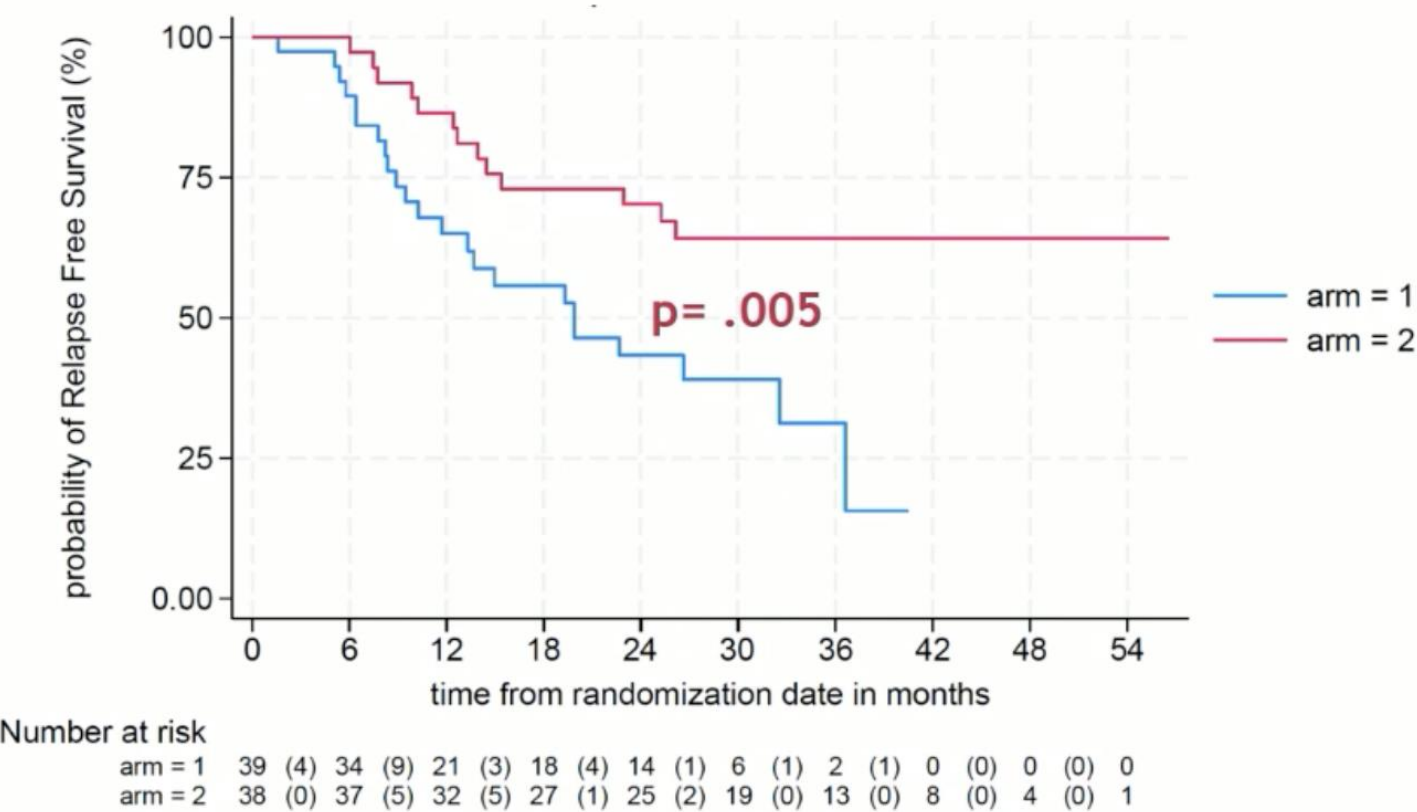
Primary endpoint: LRFR at 2 years



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%)

Efficacy

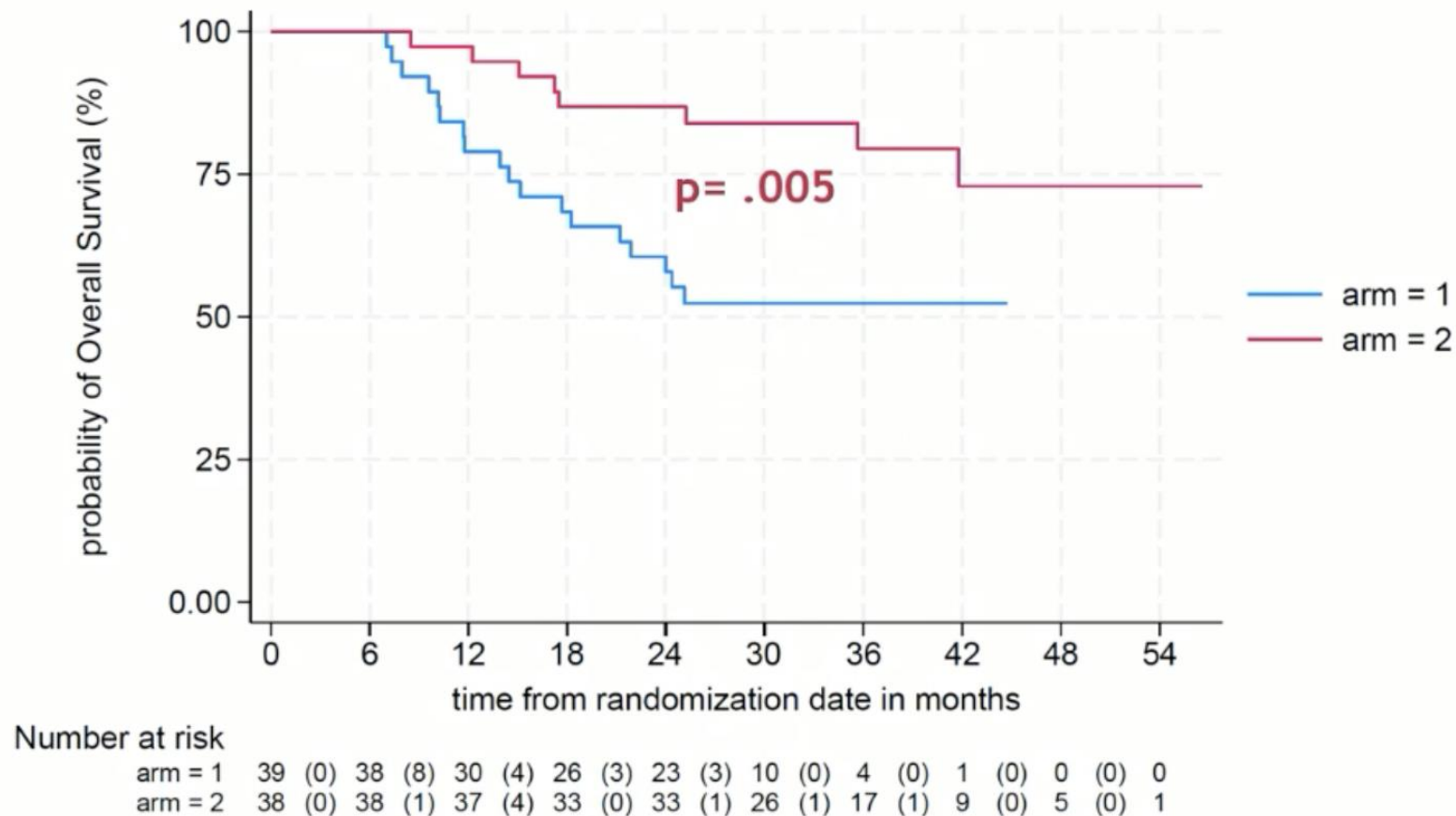
Bladder cancer failure-free survival



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%)

Efficacy

Overall survival



Median (95% CI)	2-y free (95% CI)
RT+CDDP	
NR	60.5% (43.3%-74%)
RT+CDDP+Nivolumab	
NR	86.8% (71.2%-94.3%)

Toxicity

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.

Conclusions

- The addition of nivolumab to TMT produced a significant increase in BCFFS and OS in patients with nmMIBC not undergoing radical cystectomy.
- The prolongation of BCFFS and OS resulted from a significant decrease in the occurrence of distant metastases in patients receiving nivolumab
- The combination of TMT+Nivolumab was well tolerated without any new safety signals observed
- These results warrant the conduction of a randomized phase III trial to establish nivolumab plus CRT as a new standard for patients with nmMIBC not undergoing radical cystectomy.