SBRT in Oligometastatic Prostate Cancer: A Targeted Approach to the Primary and Mets

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The ROYAL MARSDEN NHS Foundation Trust

Potential conflicts of interest

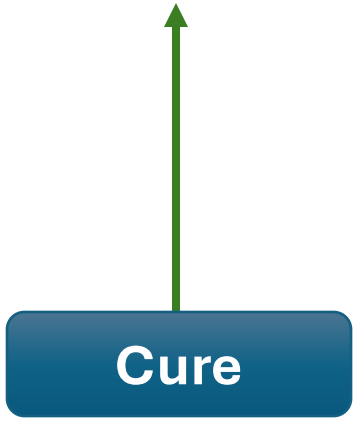
- Research funding from Elekta, Varian, Accuray, Artera
- Honoraria/Travel grants from Elekta, Accuray, Janssen, Bayer, Astellas
- Chair of the MR linac consortium

Outline

- Prostate radiotherapy in metastatic prostate cancer
  - What is the evidence?
  - How do we do it?
- Radiotherapy to oligomets
  - Evidence in metachronous oligometastases
  - Evidence in oligoprogression/oligopersistence
  - How do we do it?

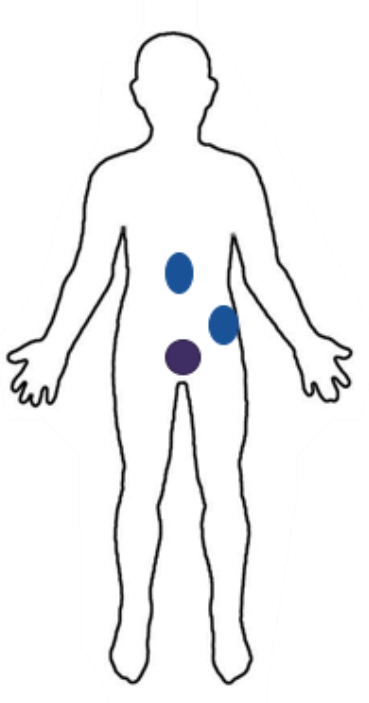
The concept of oligometastases - can we shift the therapeutic paradigm?

- Intermediary state of metastatic disease
- ≤ 3-5 metastatic sites

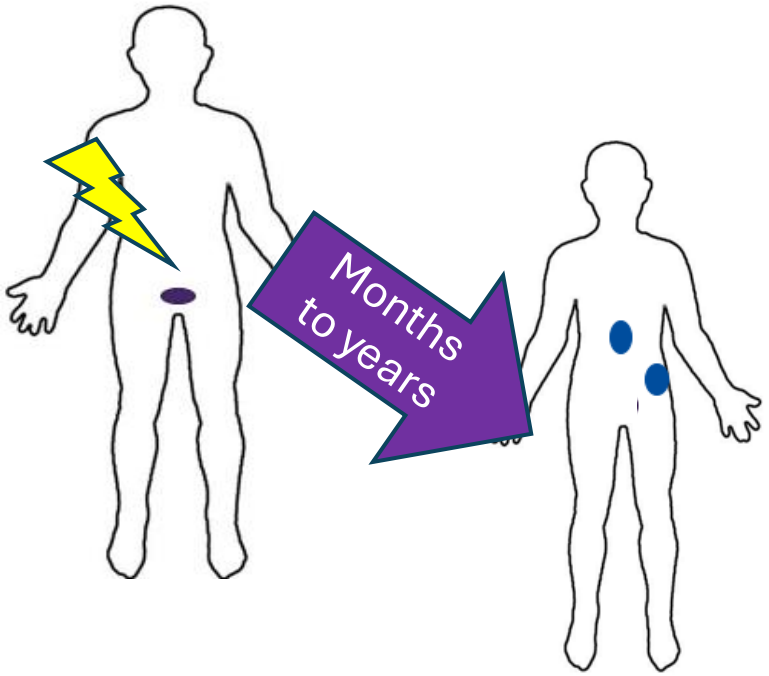


Three main scenarios

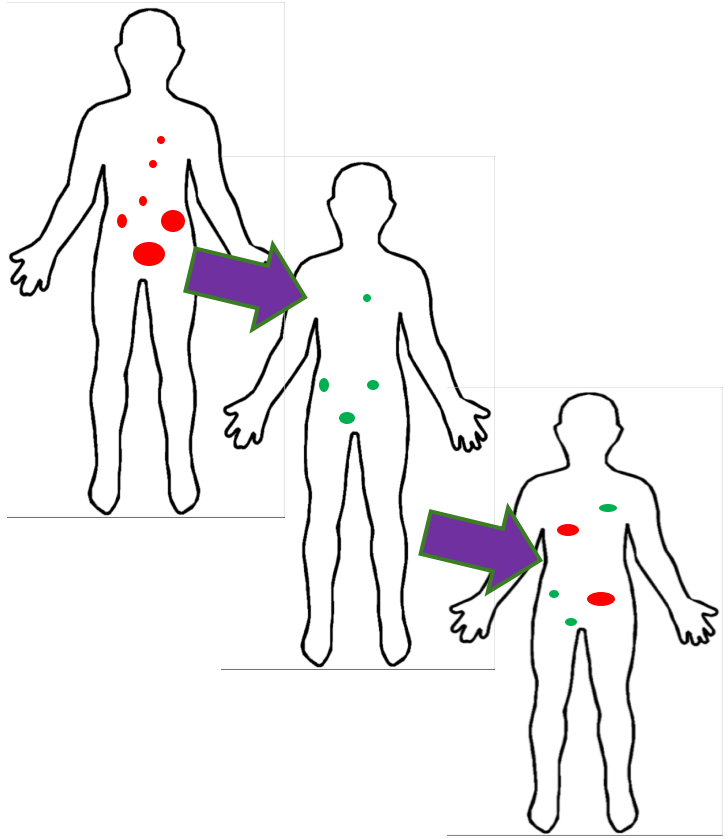
Synchronous oligometastases



Metachronous oligometastases



Oligoprogression



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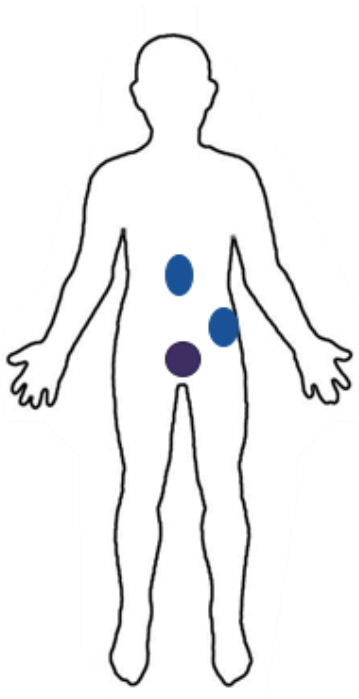

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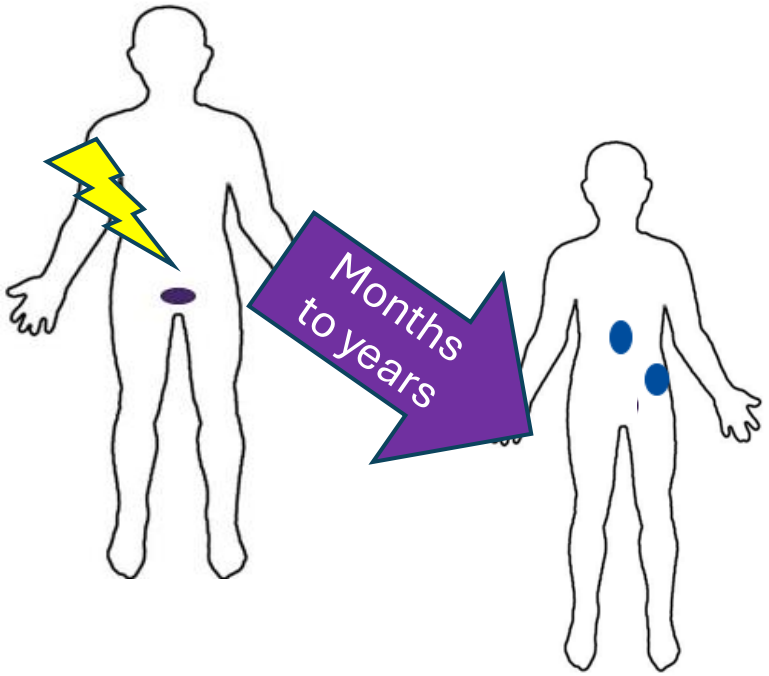

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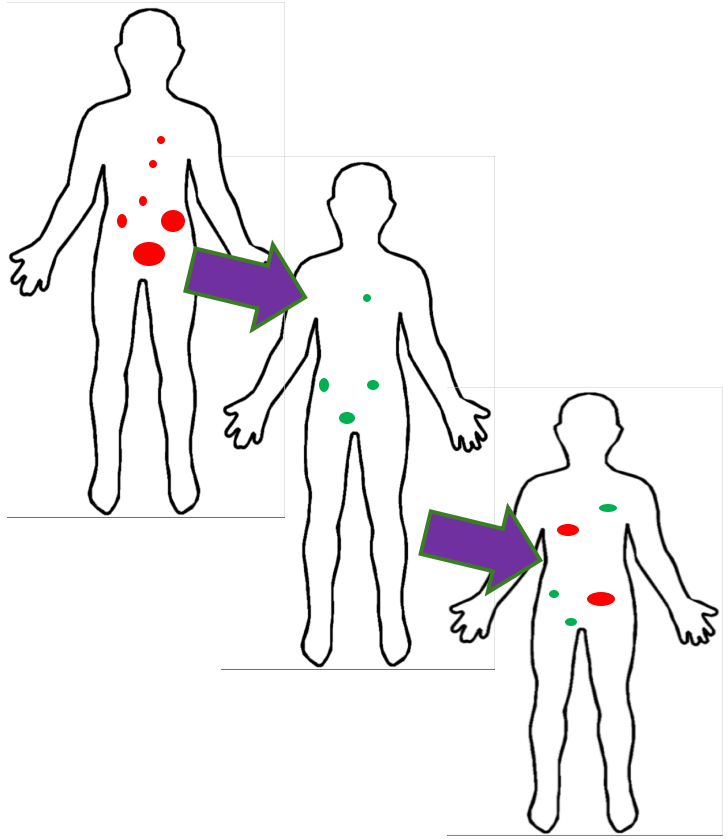
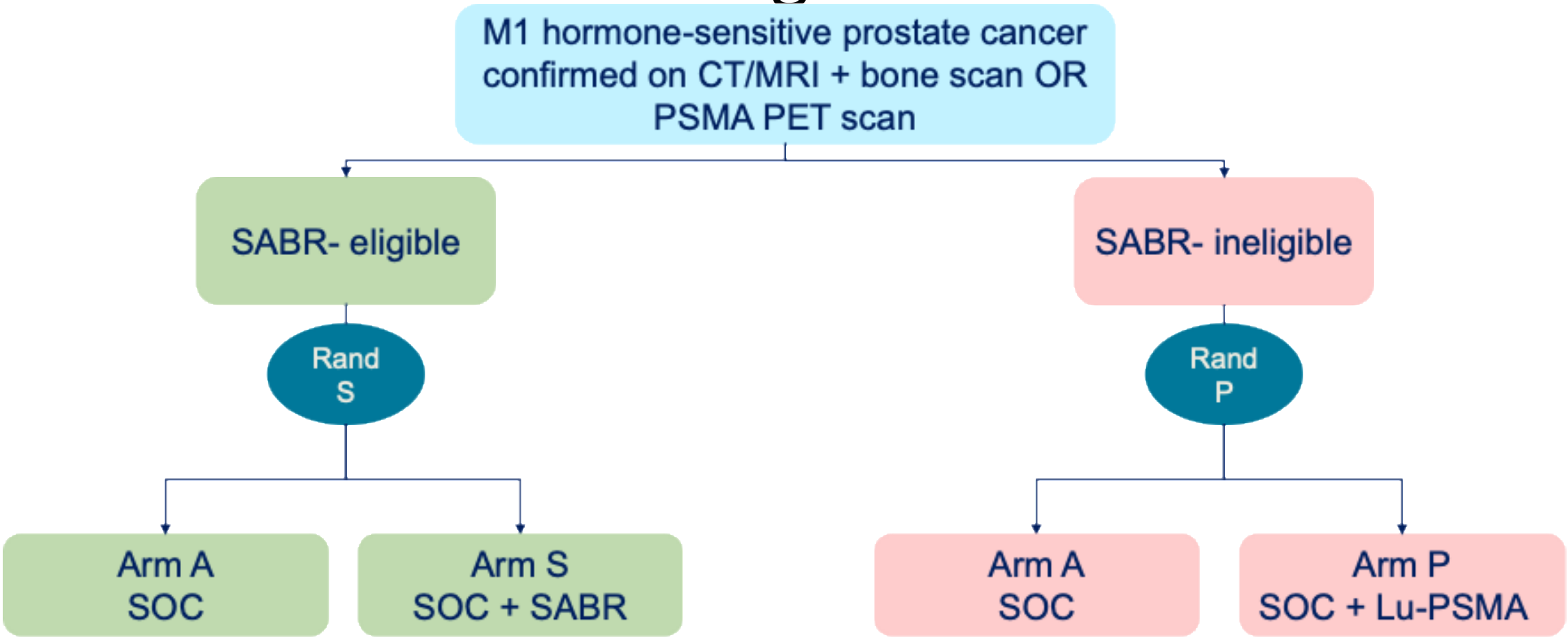


STAMPEDE2 Trial Design

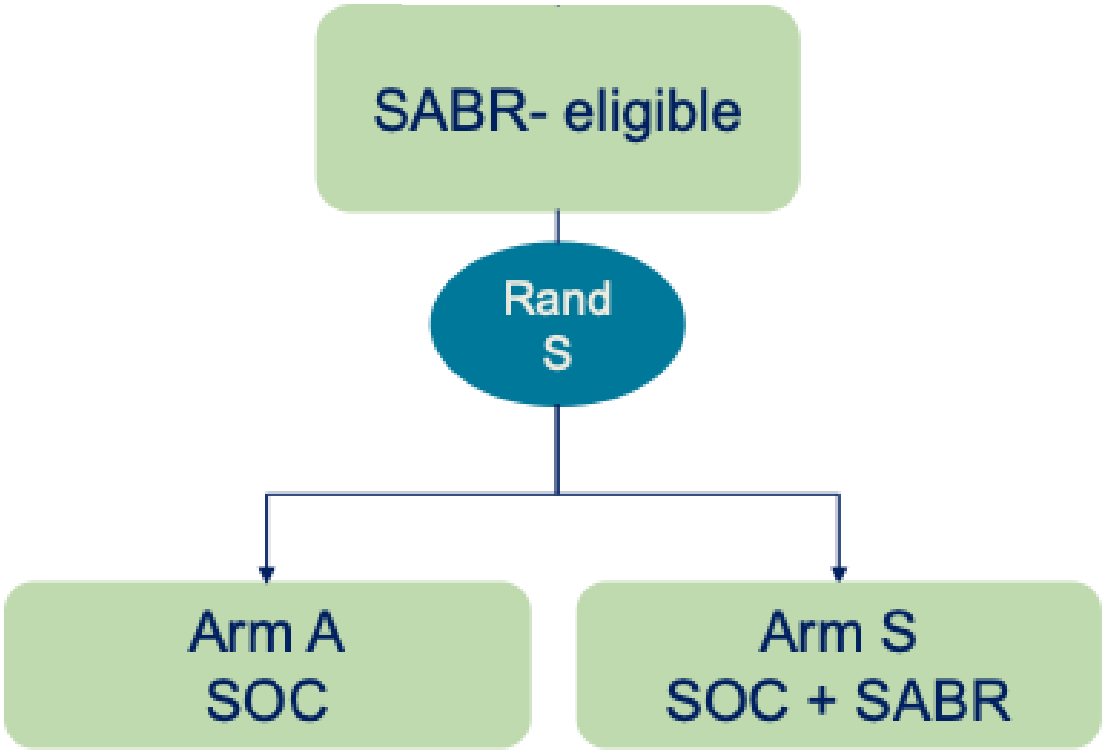


M1= metastatic hormone-sensitive prostate cancer. SABR= stereotactic ablative body radiotherapy. SOC= Standard of Care. Lu-PSMA= ^{177}Lutetium-PSMA-617.

SABR Trial (Comparison S)

SABR-Eligible Disease

- Newly diagnosed (synchronous, de novo) oligometastatic disease
- 1 to 5 bone and/or non-regional lymph nodes metastases
- All metastatic lesions considered technically suitable for SABR
- Absence of visceral metastases



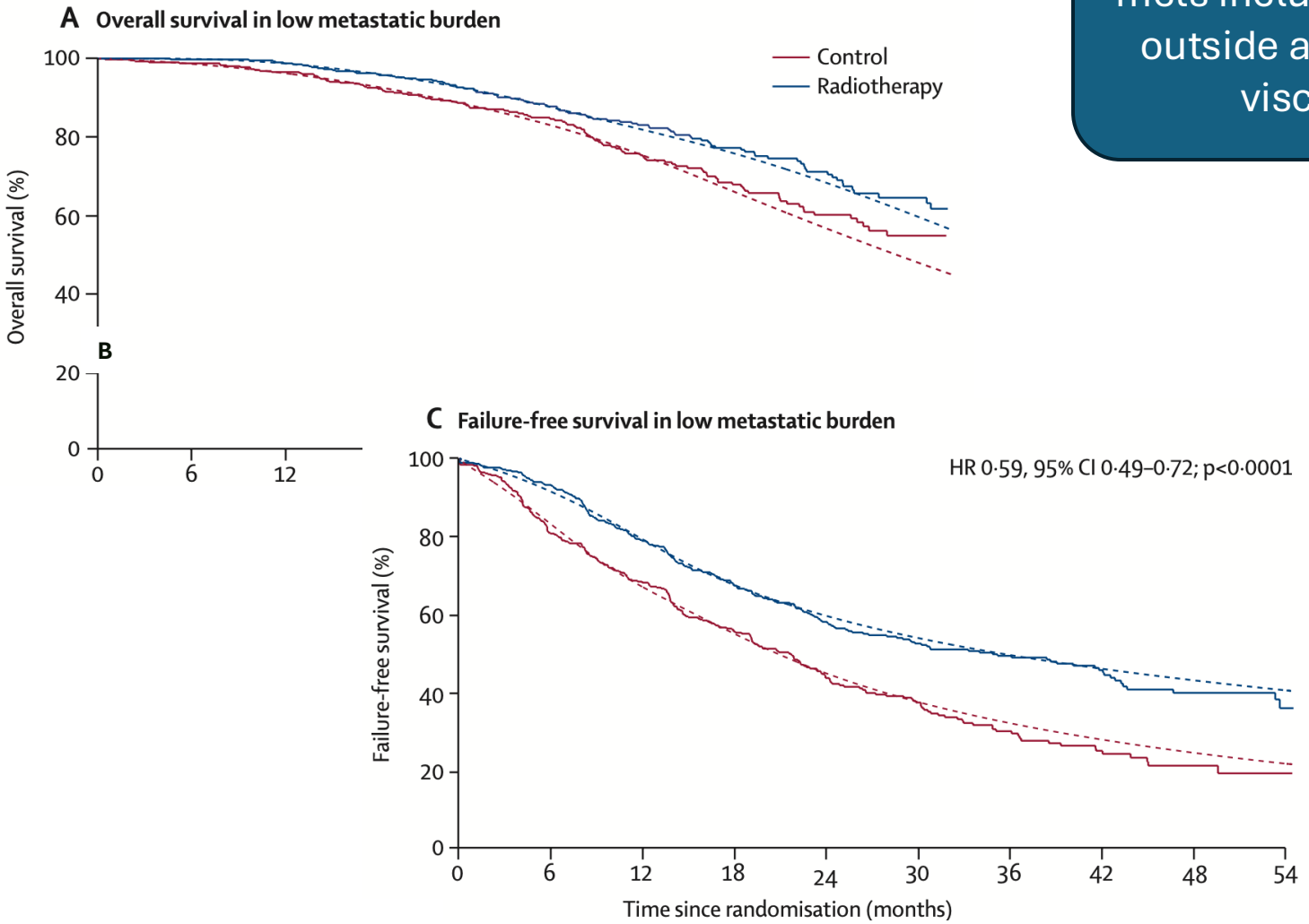
SOC= Standard of Care. SABR= Stereotactic Ablative Body Radiotherapy. CT= computerised tomography. MRI= magnetic resonance imaging. PSMA PET= prostate specific membrane antigen positron emission tomography.

Cast your mind back…to 2010

“Once cancer has spread, local treatments are useless…”

Irradiating just the prostate, in the setting of oligometastases

High burden = 4 or more mets including at least one outside axial skeleton or visceral mets



Median survival extended by 21.9 months
At 5 years, 1:8 men are alive due to radiotherapy (53% vs 65%)

Parker CC, et al, Lancet.2018. Parker et al PLoS medicine 2022

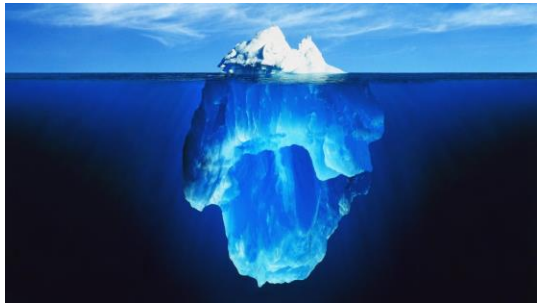
What's the downside?

Table 3. First symptomatic local event reported (patients with event reported).

Type of event	SOC (*n* = 608)	SOC+RT (*n* = 601)
Urinary tract infection	57 (9%)	80 (13%)
Urinary catheter	52 (9%)	44 (7%)
Acute kidney injury	33 (5%)	34 (6%)
TURP	24 (4%)	24 (4%)
Urinary tract obstruction	15 (2%)	15 (3%)
Ureteric stent	19 (3%)	8 (1%)
Nephrostomy	5 (1%)	2 (<1%)
Colostomy	3 (<1%)	3 (1%)
Surgery for bowel obstruction	0 (0%)	2 (<1%)
PCa death	400 (66%)	389 (65%)

Parker et al, PLoS Medicine 2022

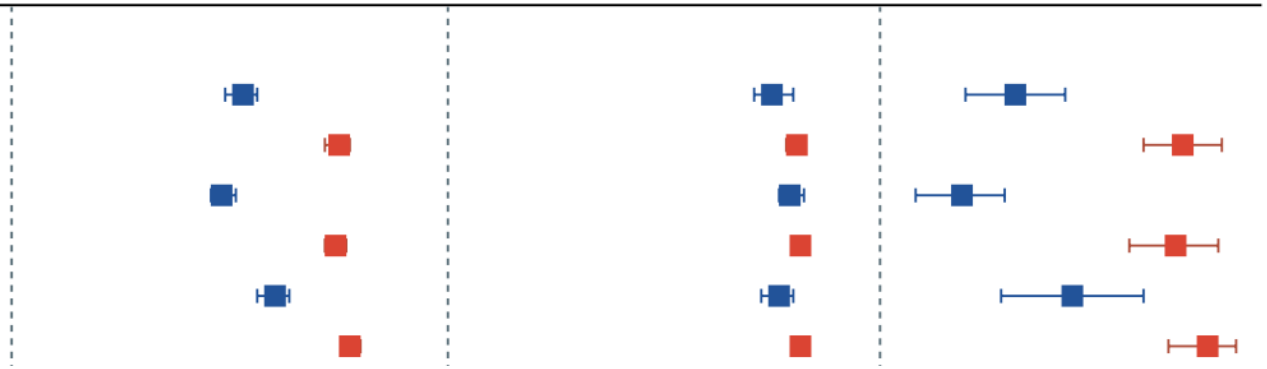
Number of metastases depends on how hard you look



proPSMA:

Sensitivity:
conventional imaging **38%** vs
85% PSMA PET

	N	Positive True/False	Negative True/False	AUC (95% CI)	Specificity (95% CI)	Sensitivity (95% CI)
Primary analysis						
Any metastatic disease	150	18/9	94/29			
	145	34/2	103/6			
Pelvic nodal	150	9/4	106/31			
	145	29/1	109/6			
Distant metasases	150	13/9	117/11			
	145	22/1	120/2			



Conventional imaging PSMA PET-CT

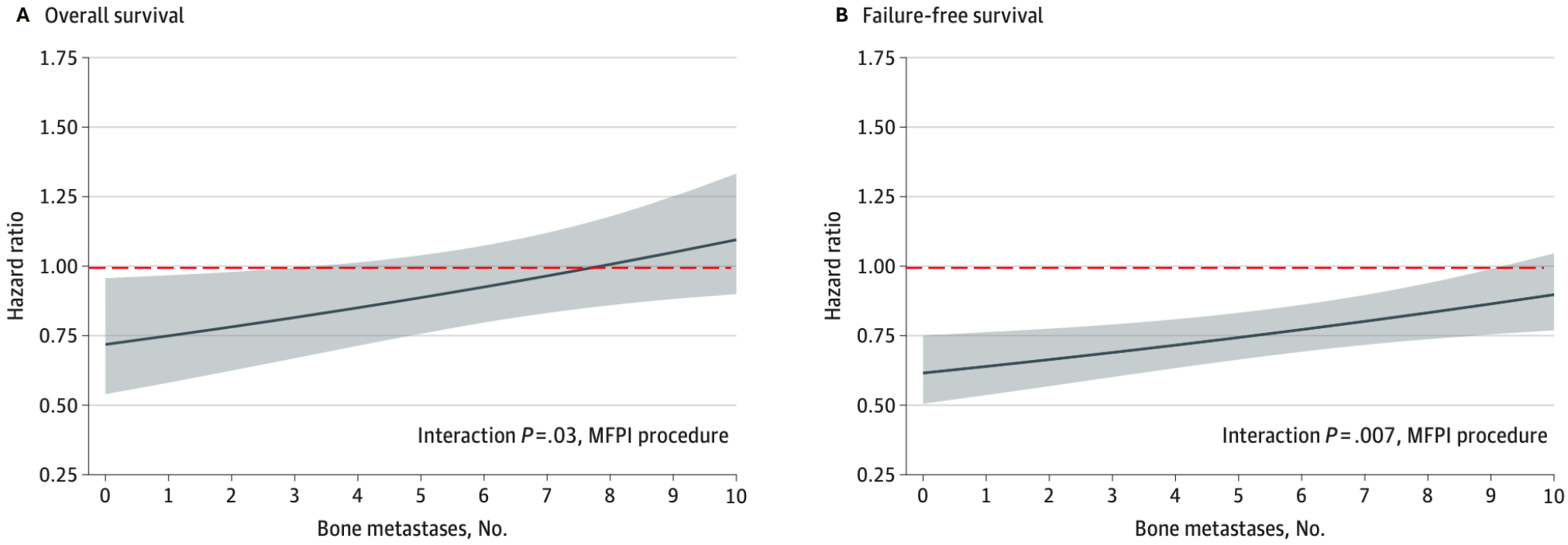
Hofman et al, Lancet 2020

EAU guidelines 2025

Recommendations	Strength rating
Any risk group staging	
Use pre-biopsy magnetic resonance imaging (MRI) for local staging information.	Weak
Low-risk localised disease	
Do not use additional imaging for staging purposes.	Strong
Intermediate-risk disease	
For patients with International Society of Urological Pathology (ISUP) grade group 3 disease perform prostate-specific antigen-positron emission tomography/computed tomography (PSMA-PET/CT) if available to increase accuracy or at least cross-sectional abdominopelvic imaging and a bone scan.	Weak
High-risk localised disease/locally advanced disease	
Perform metastatic screening using PSMA-PET/CT if available or at least cross-sectional abdominopelvic imaging and a bone-scan.	Strong

How oligo is oligo?

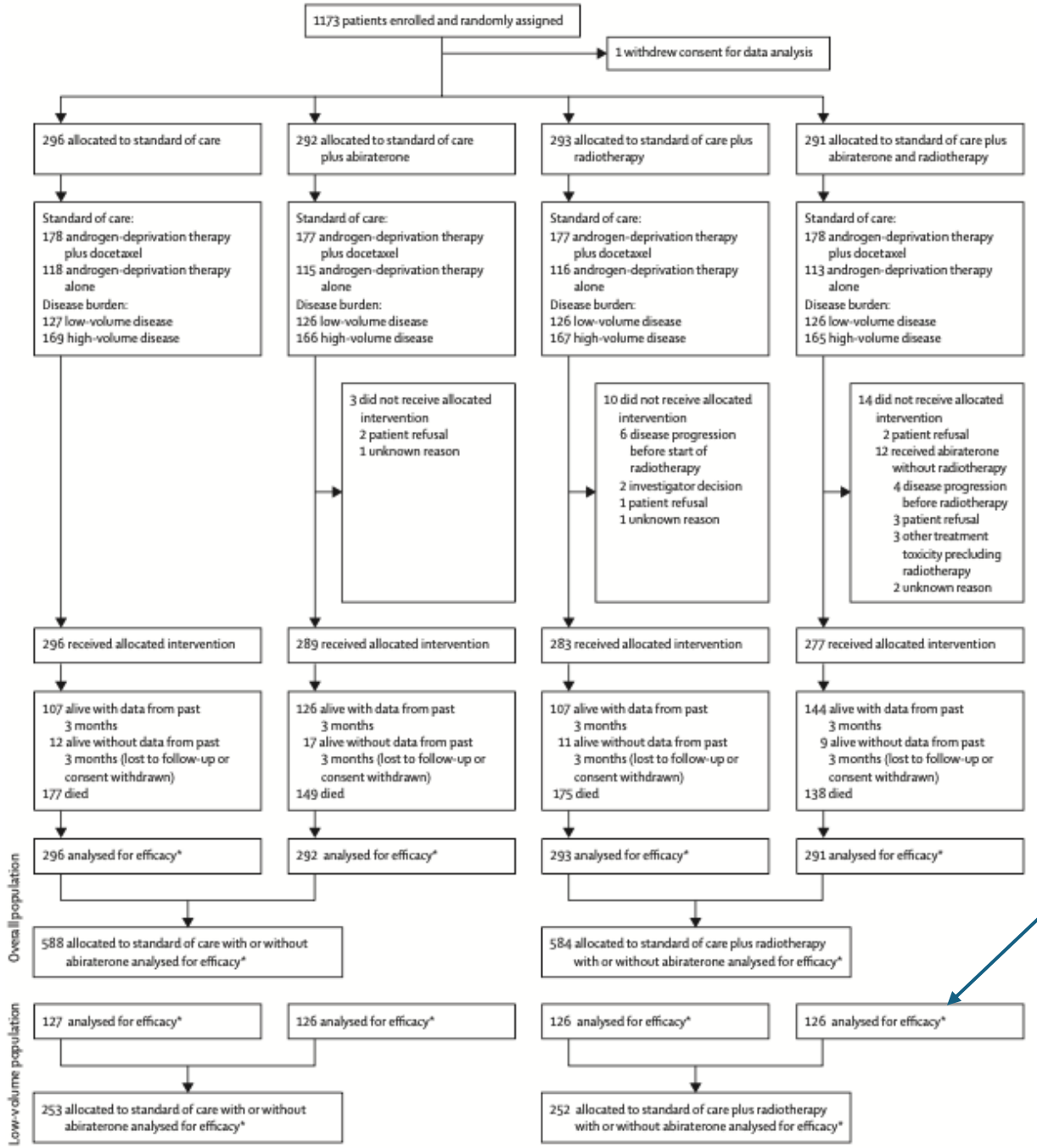
Figure 2. Treatment Effect Plots for Bone Metastasis Count



Estimated treatment effect (solid line) with pointwise 95% CI (shaded area) is shown for overall survival (A) and failure-free survival (B). The horizontal gray line at hazard ratio 1.00 denotes equivalence of treatment effects, with values below 1.00 favoring prostate radiotherapy. MFPI indicates multivariable fractional polynomial interaction.

Ali et al, JAMA Oncol 2021

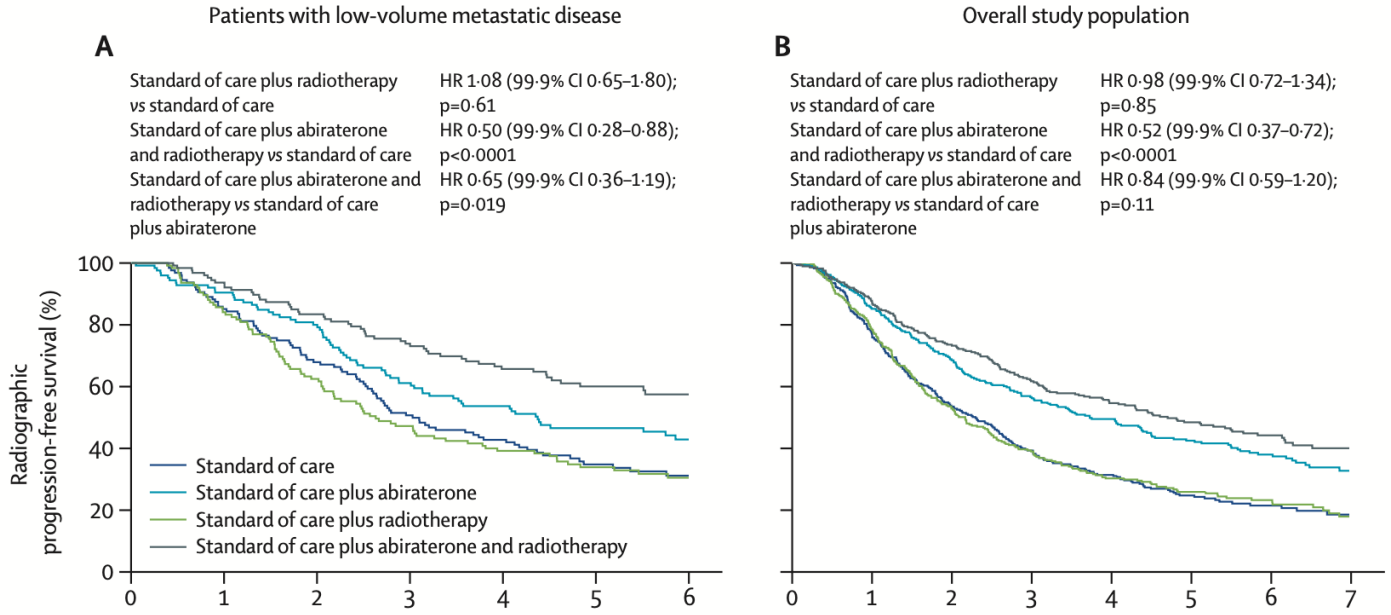
PEACE-1



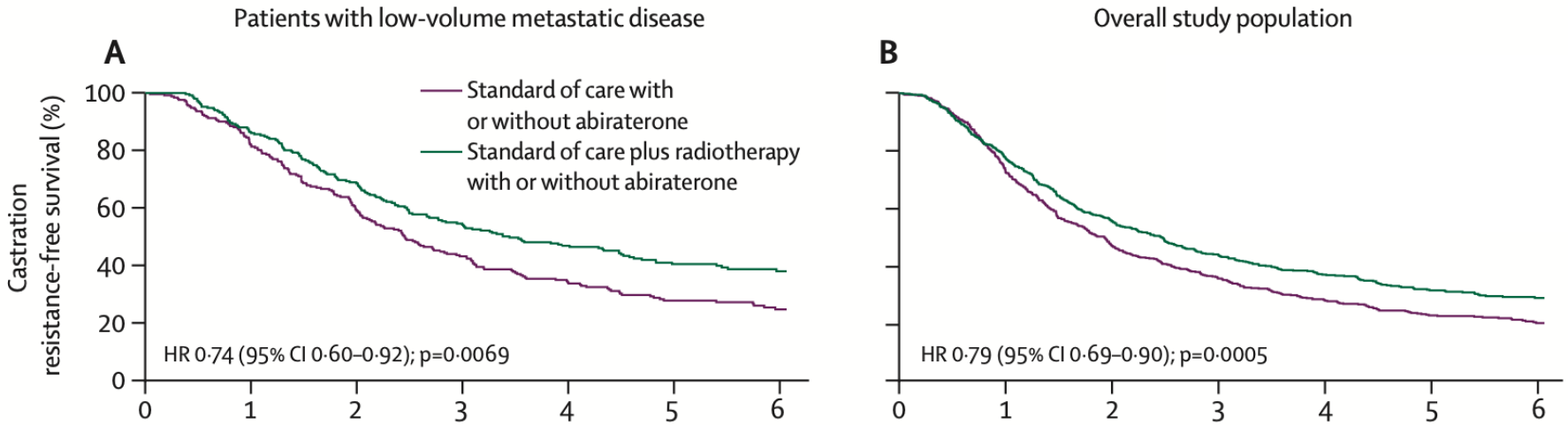
1173 patients

<150 patients per low volume group, half of which had chemo

Bossi et al, Lancet 2024



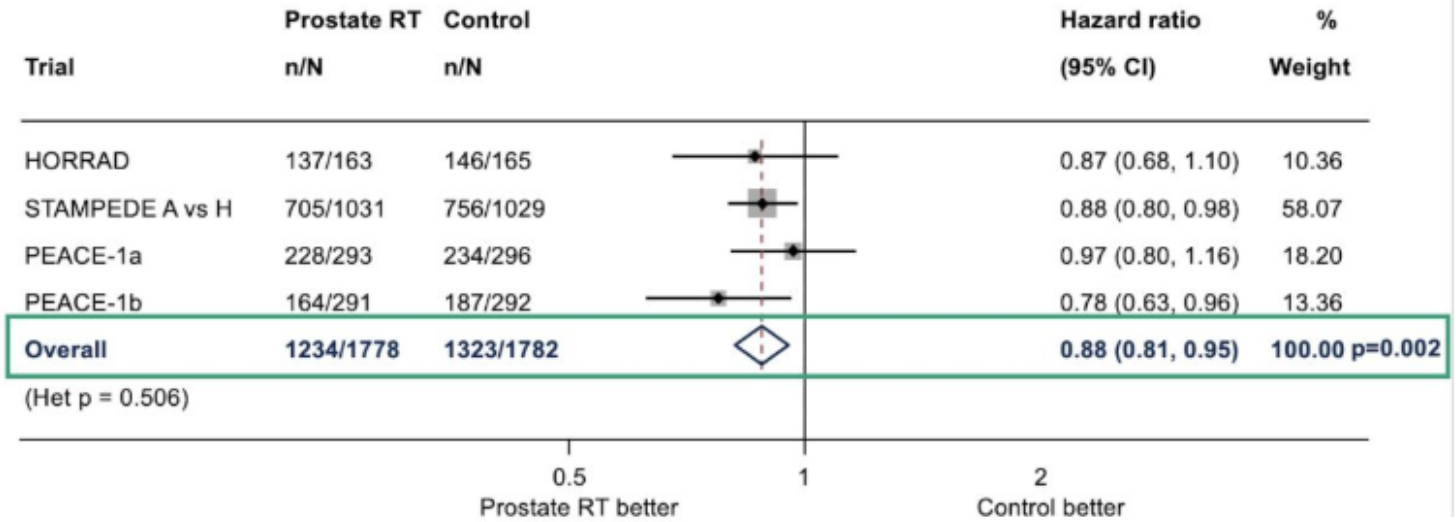
No improvement in OS, even in low burden group
Interaction between Abi and radiotherapy



Improvement in time to CRPC in all patients, reduction in GU events in all patients

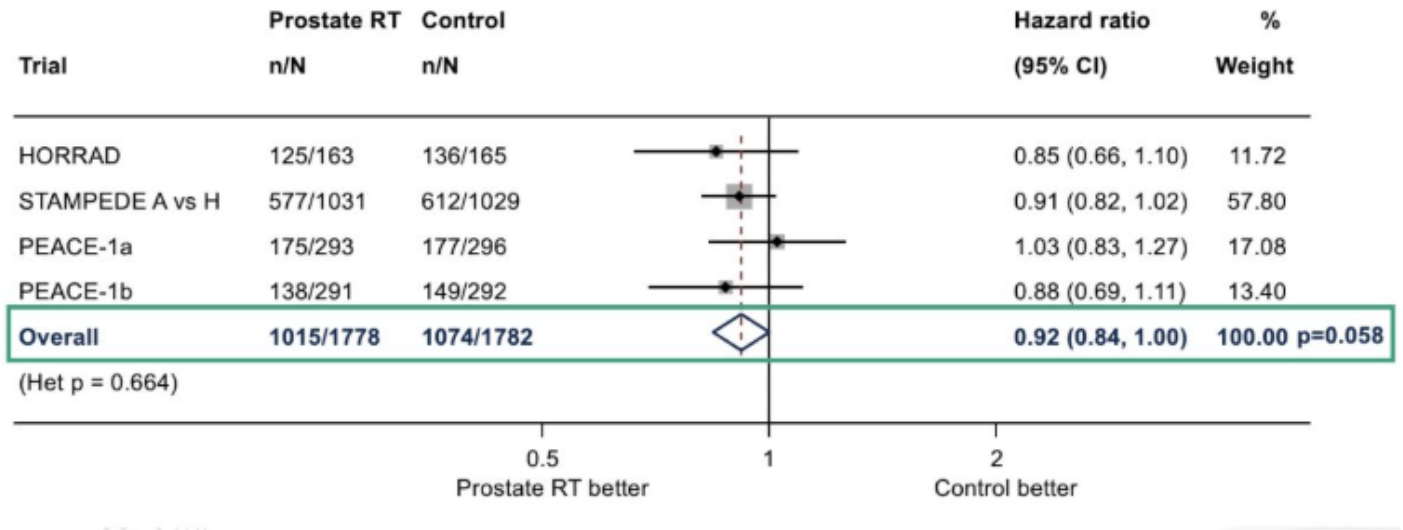
Bossi et al, Lancet 2024

Overall effects of prostate RT on PFS



STOP-CAP meta-analysis

Overall effects of prostate RT on OS



Godolphin et al, presented at ESMO 2025

So who should receive radiotherapy to the prostate for M1 HSPC?

- All men with low burden (on conventional imaging) M1 HSPC without contraindications to radiotherapy
- Pragmatically we approximate this to 3 or less mets on bone scan (more on PET)
- Men with bulky disease, at risk of local complications
- ?Consider for high burden M1HSPC to delay CRPC?

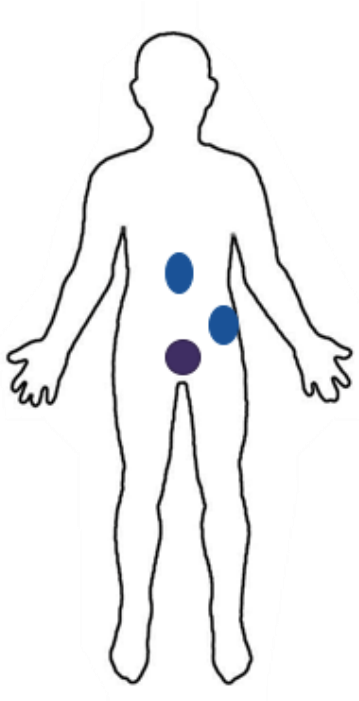
How to irradiate the prostate in the setting of low burden mHSPC

- Evidence based schedules include
  - 36 Gy in 6 fractions weekly (STAMPEDE)
  - 55 Gy in 20 fractions (STAMPEDE)
  - 74 Gy in 37 fractions (PEACE-1)
  - 70 Gy in 35 or 57.76 in 19 Gy (HORRAD)

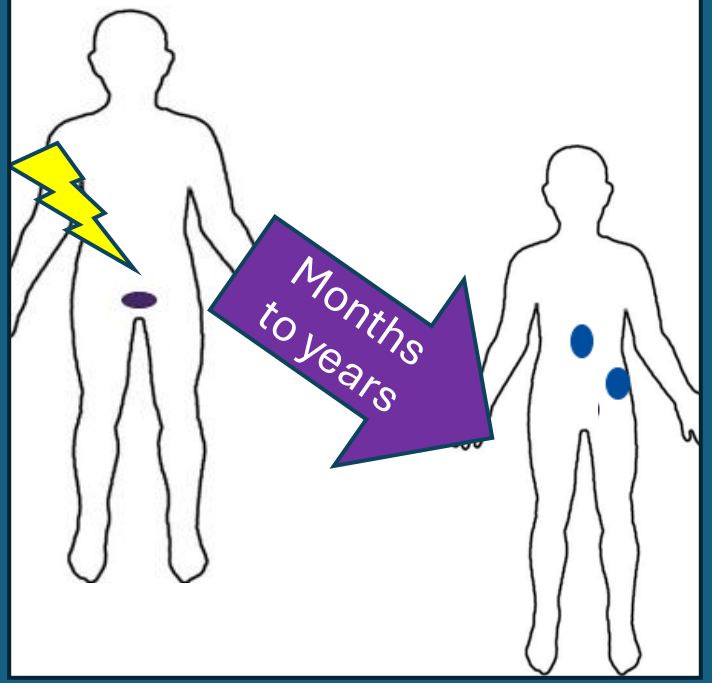
- No evidence from STAMPEDE that dose schedule alters benefit
- Our standard is 36 Gy in 6 fractions
- No trial evidence for SBRT doses, but allowed in STAMPEDE2

Three main scenarios

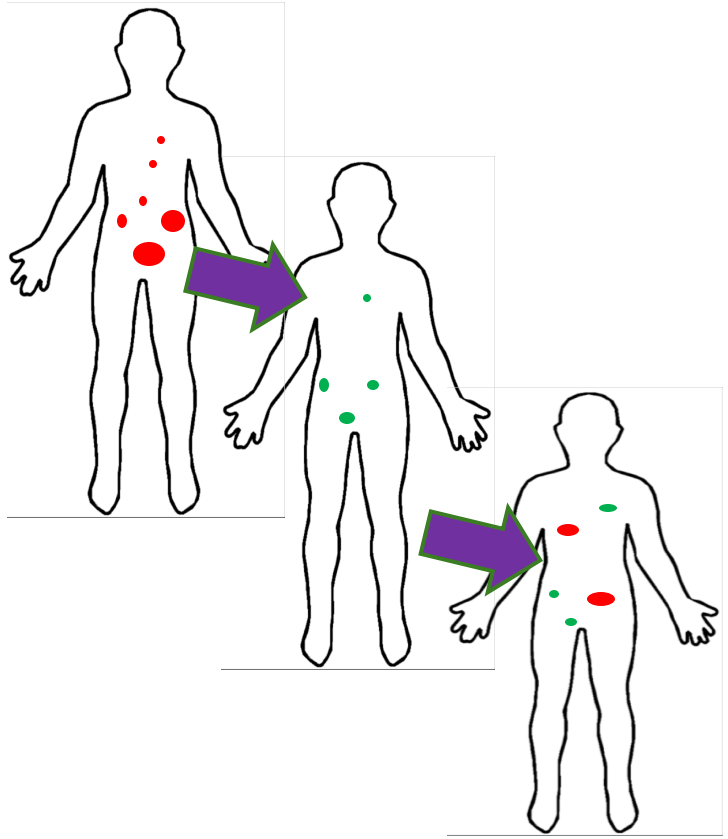
Synchronous oligometastases



Metachronous oligometastases



Oligoprogression



Early data supporting use of SBRT for metachronous oligometastases

Previous radical treatment for prostate cancer

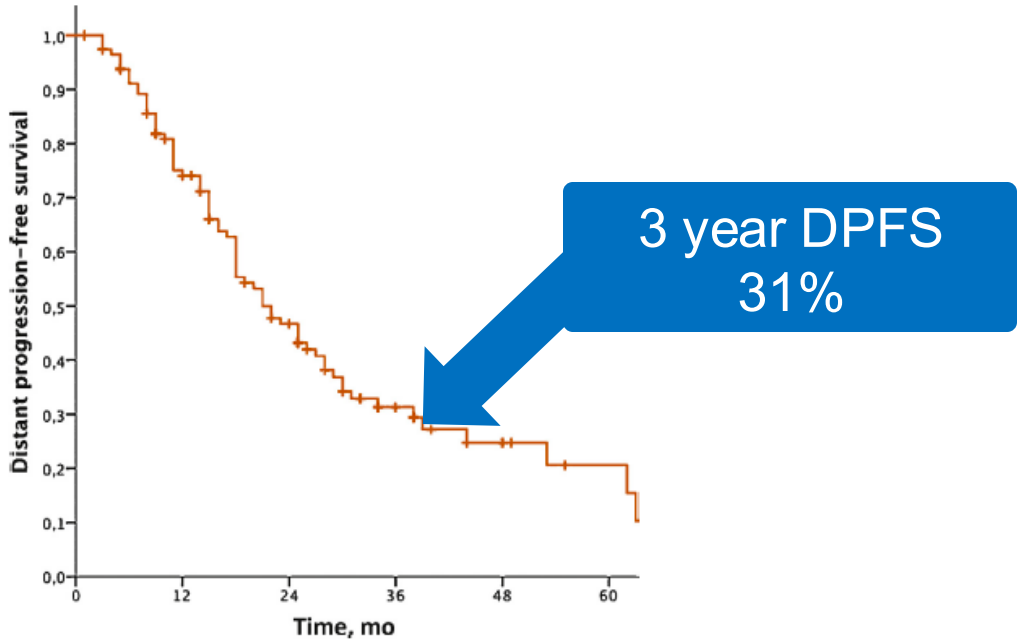
Now 3 or less metastases

3 year local control of irradiated metastases 99% if BED >100 Gy

119 patients with 163 metastases

Staged using Choline or PSMA PET

50% received ADT (usually for 2 months)



3 year DPFS 31%

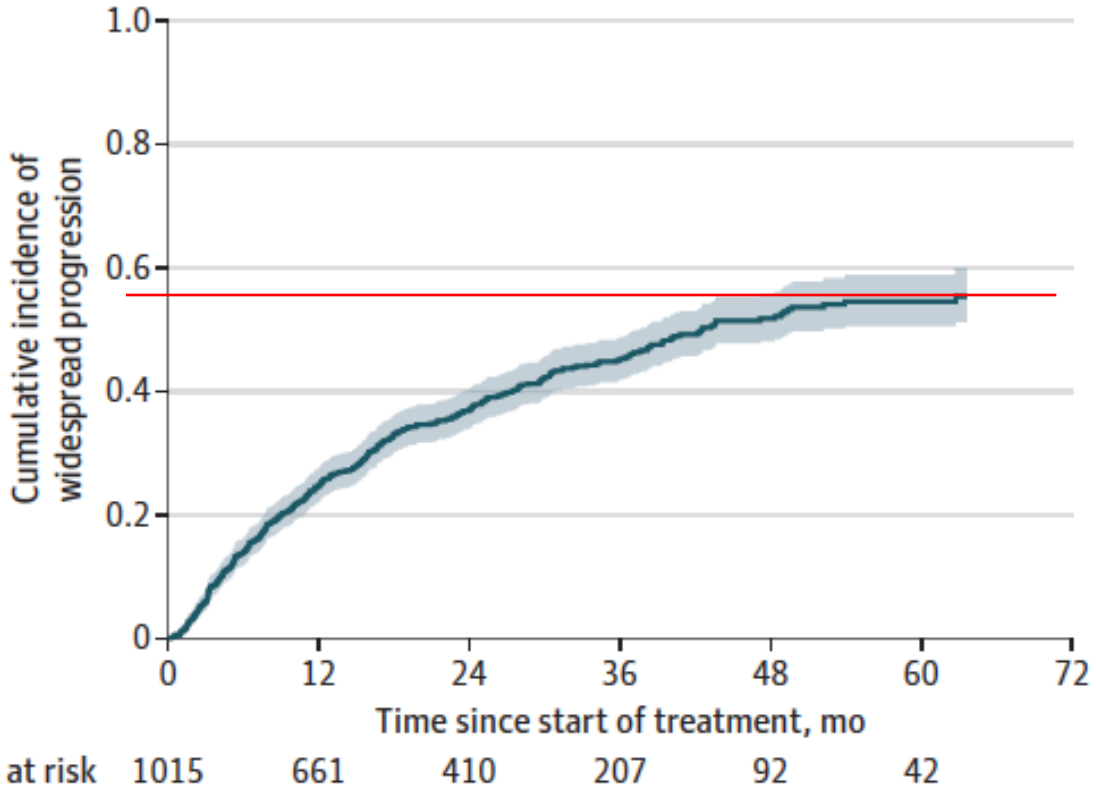
Ost *et al*, Eur Urol 2015

The reality of SBRT for oligometastases

SBRT, Stereotactic Body Radiotherapy

Some patients spend many years with subsequent oligo- metastatic episodes

C Competing risk analysis of cumulative incidence of widespread progression



1033 patients

Range of cancers

Median FU 24 months

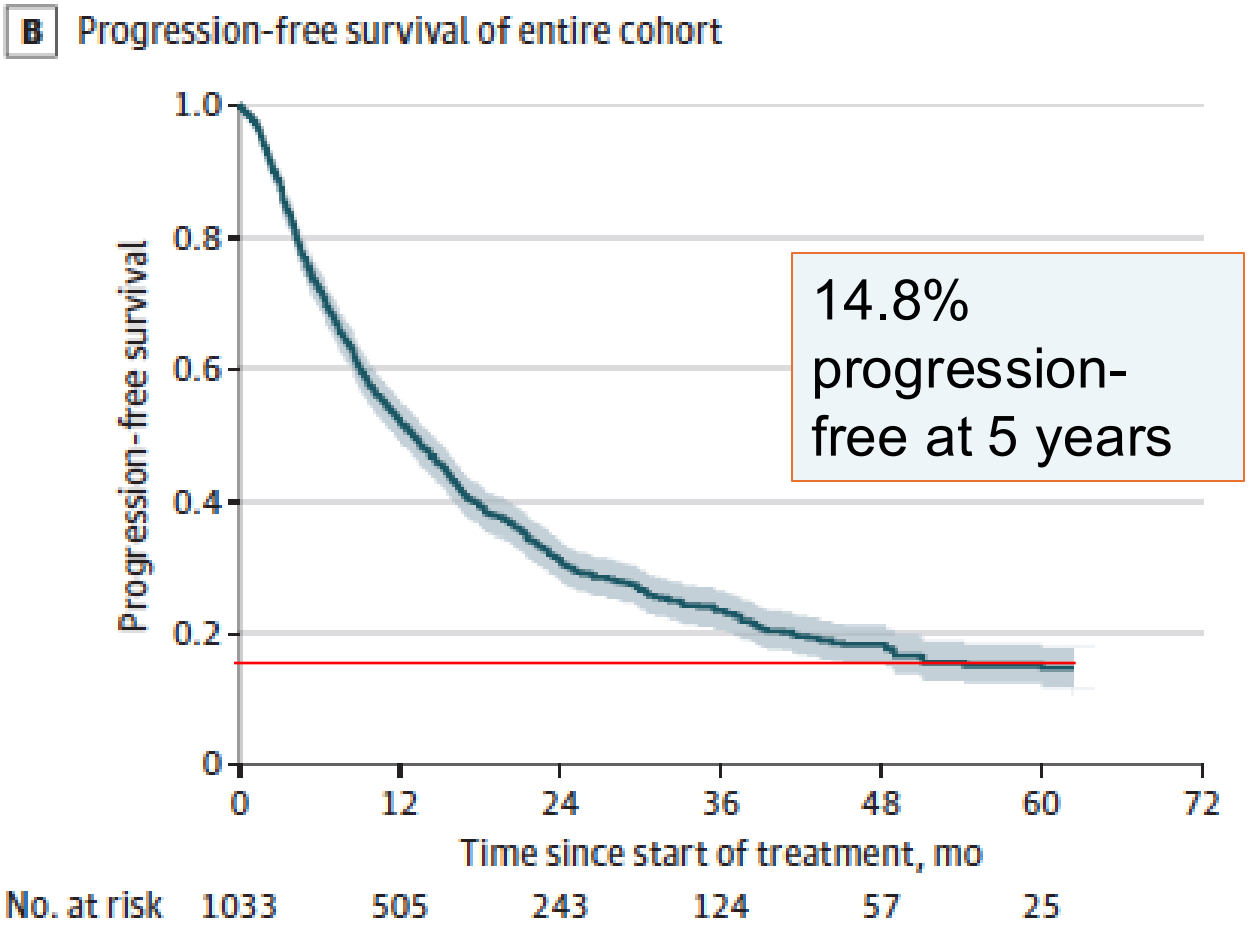
54.5% free of widespread progression at 5 years

Poon et al, JAMA Network Open, 2020

The ROYAL MARSDEN NHS Foundation Trust

ICR The Institute of Cancer Research

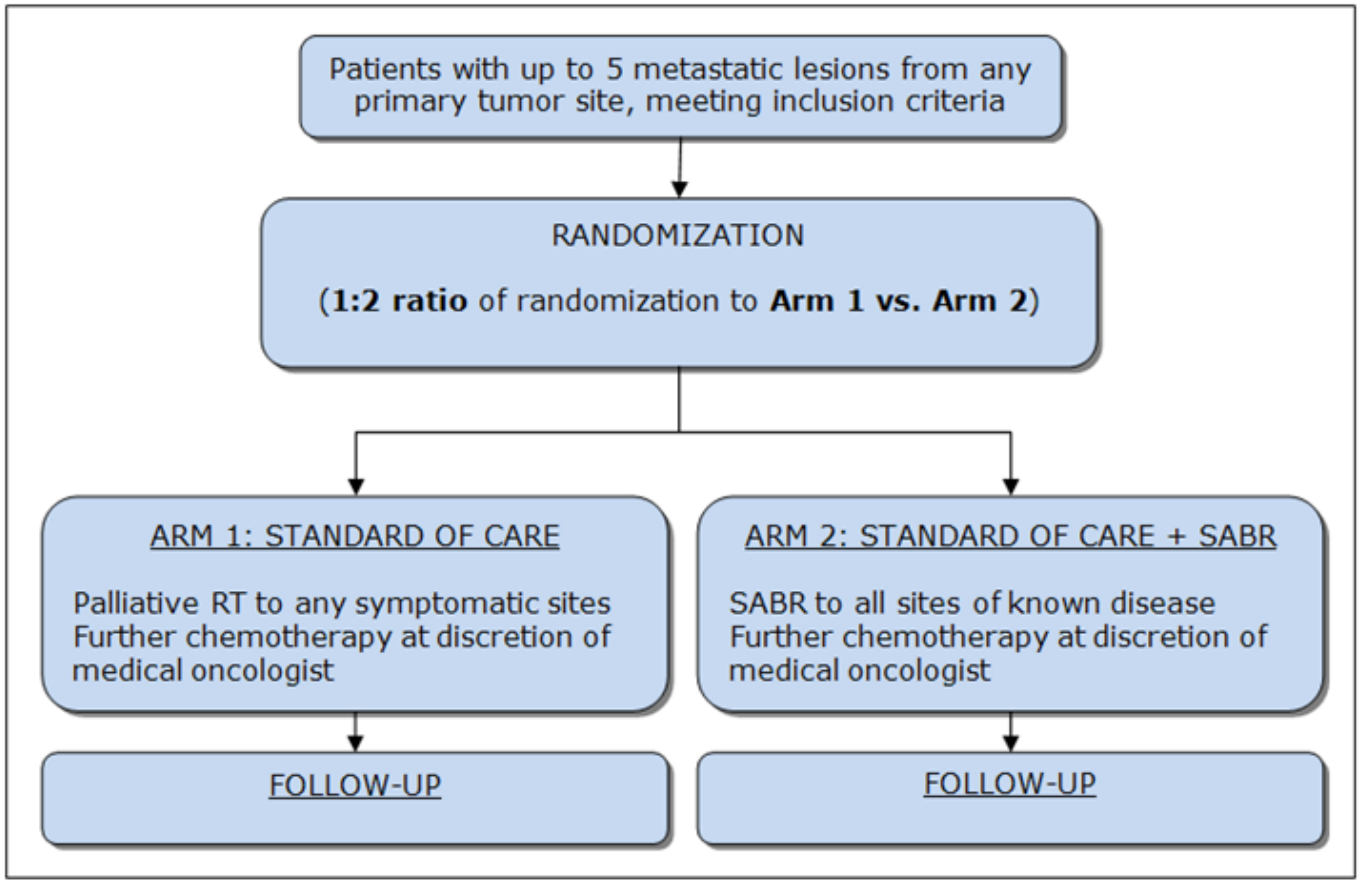
Longer follow up appearing



Very heterogeneous cohort – metachronous and synchronous, up to 5 metastases, different histologies

Poon et al, JAMA Network Open, 2020

SABR-COMET trial



5-year survival:

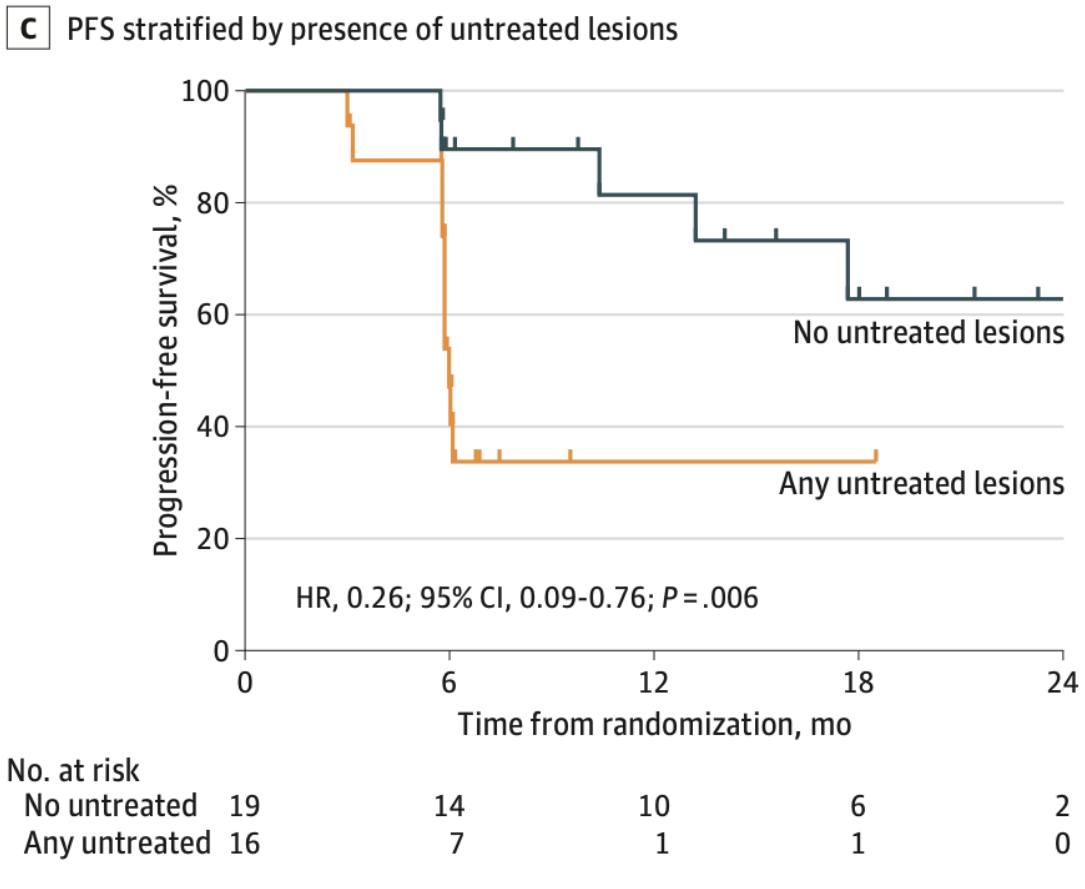
17.7% Standard care

42.3% SBRT (p=0.06)

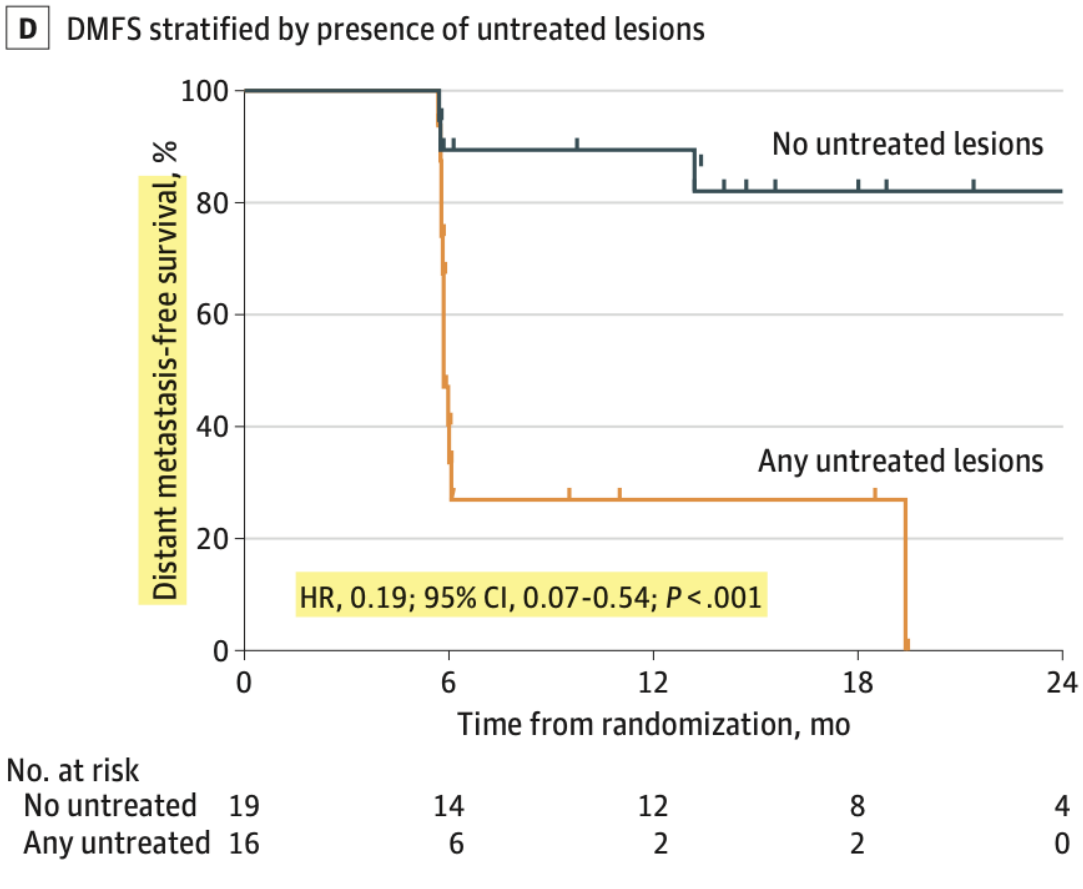
But
Phase II
Imbalance in histologies between arms

Palma DA, et al, J Clin Oncol 2020

The STOMP trial



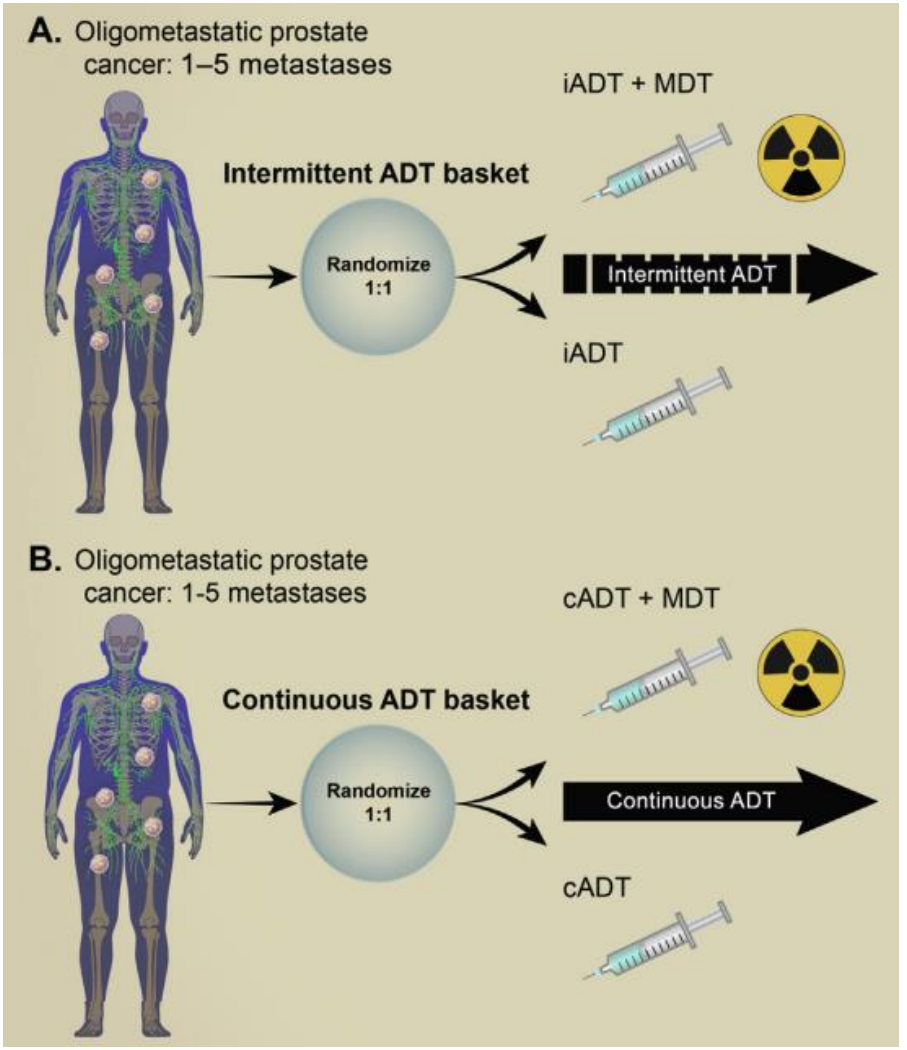
The ORIOLE trial



Phillips et al JAMA Oncol 2020

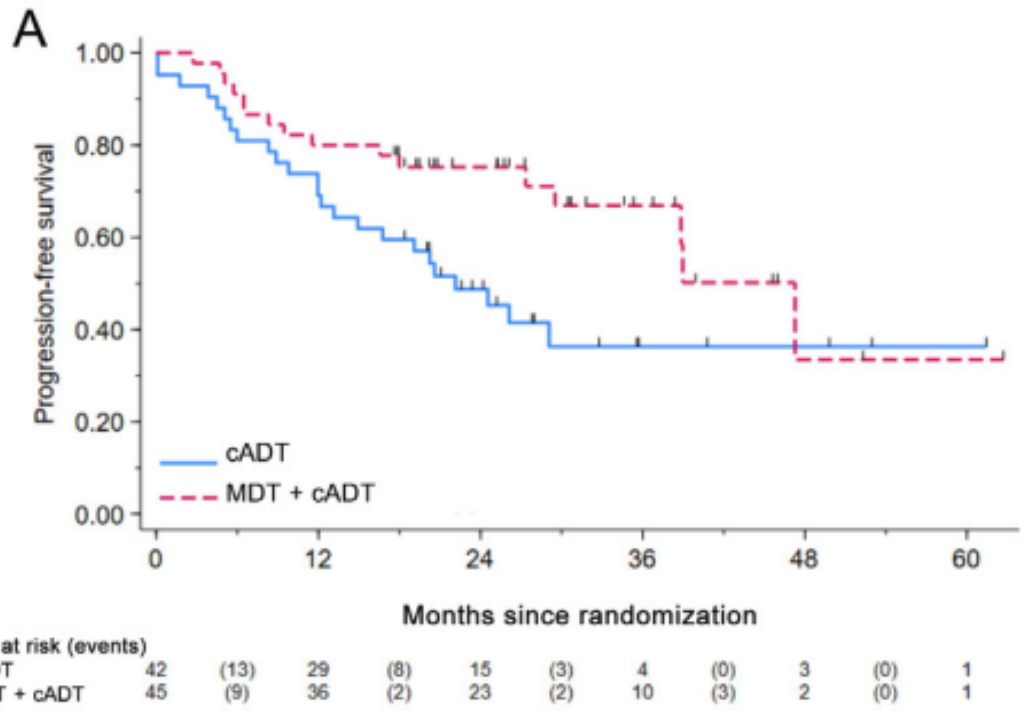
EXTEND trial

- Phase 2 randomised basket
- Two prostate cohorts – intermittent ADT or continuous ADT
- 1-5 mets amenable to MDT
- iADT cohort – mostly castration sensitive
- 59% eligible based on conventional imaging (not PET)
- 174 patients eligible for analysis



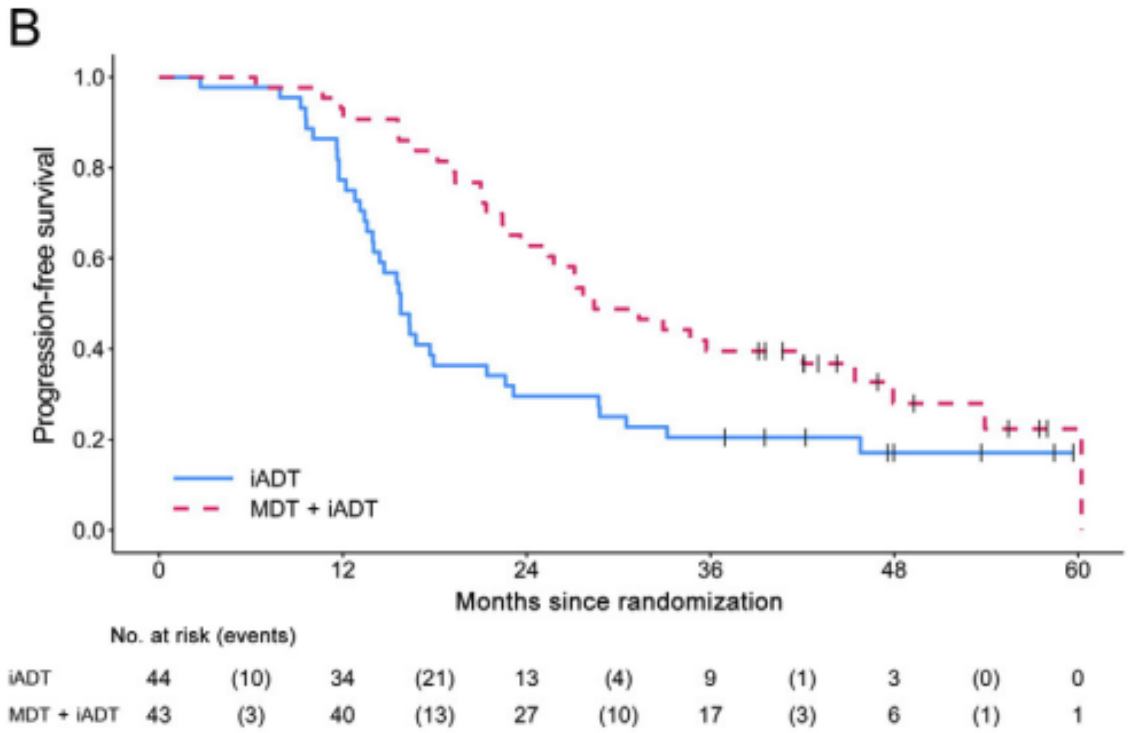
Sherry et al, Eur Urol 2026

Continuous ADT
PFS 47mo ADT+SBRT vs
22mo ADT alone
(HR 0.50, p 0.036)



No sig difference in other clinical outcomes

Intermittent ADT
PFS 28mo ADT+SBRT vs
16mo ADT alone
(HR 0.44, p <0.005)



Prolonged rPFS in MDT arm

Sherry et al, Eur Urol 2026

WOLVERINE analysis

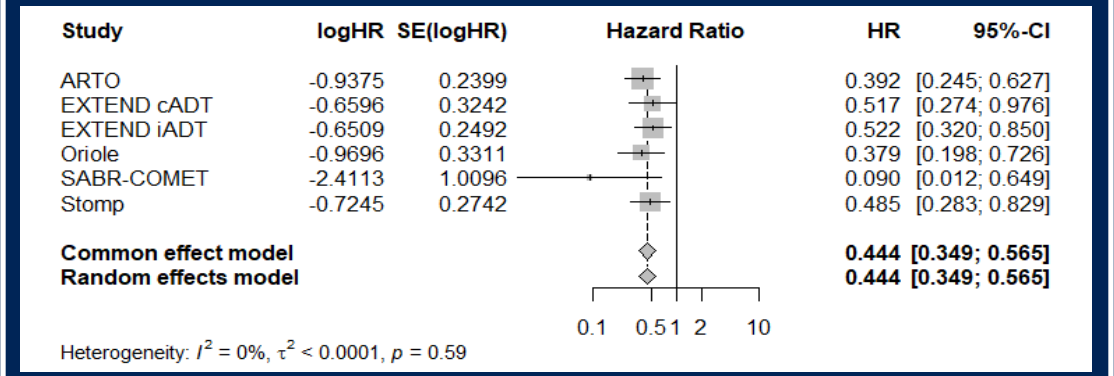
- Combination of IPD from STOMP, ORIOLE, EXTEND, ARTO (CRPC), SABR-COMET
- All randomised SOC +/-MDT
- 472 patients, prostate cancer

- 58% HSPC, 74% treated with ADT, 54% with ARPI
- MDT(SBRT) improved PFS, rPFS and castration-resistance free survival
- Not quite significant for OS

Tang et al ASCO 2025

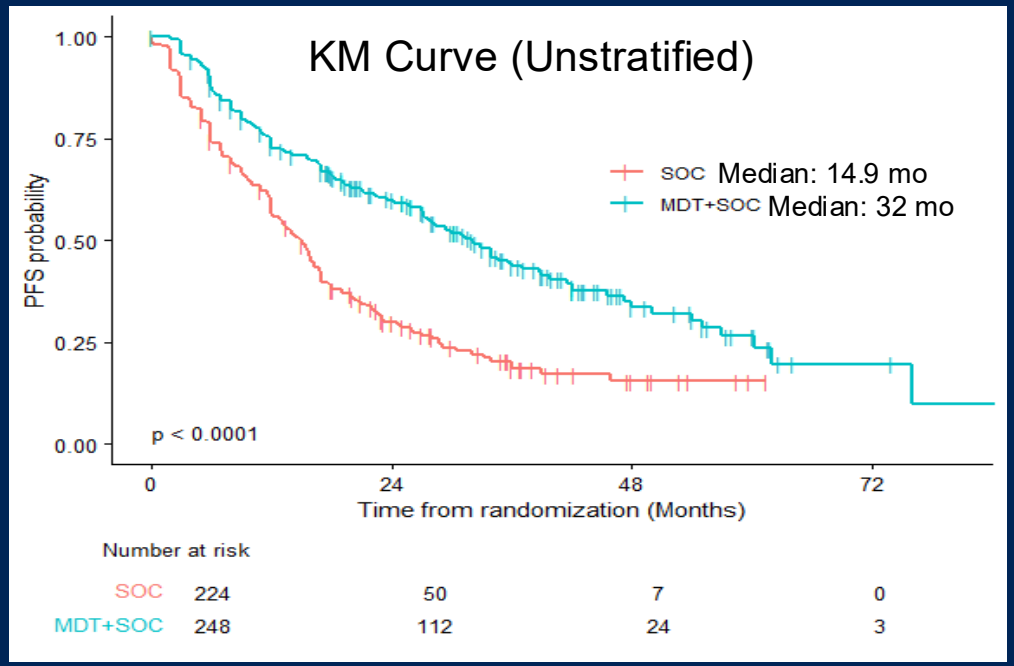
Results: Progression Free Survival (PFS)

Trial Level Analysis:
Random effects model P<0.001



Slide courtesy of Dr Chag Tang

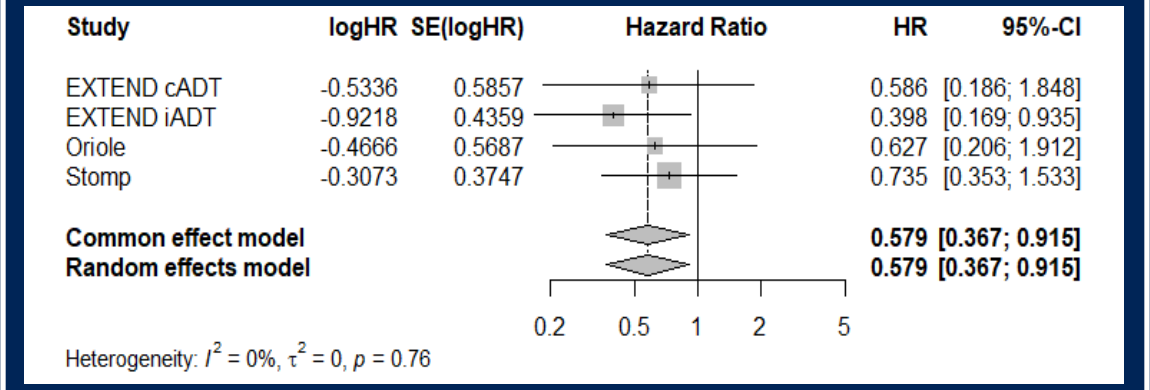
Cox Regression (Stratified by Trial):
MDT (vs SOC) HR: 0.45 (95% CI: 0.35-0.58), P <0.001



Freedom from Castration Resistance

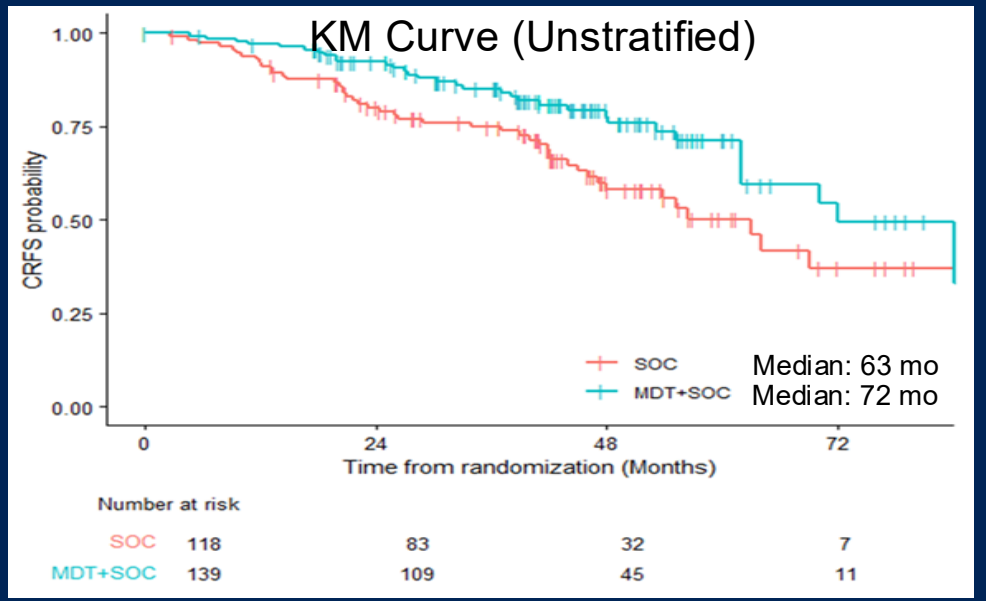
Conducted in Castration Sensitive Subset Only (n= 257)

Trial Level Analysis:
Random effects model P=0.019



Slide courtesy of Dr Chag Tang

Cox Regression (Stratified by Trial):
MDT (vs SOC) HR: 0.58 (95% CI: 0.37-0.91), P =0.02



What is the right endpoint for SBRT trials in oligometastases?

- Would we love to see a massive OS benefit? Sure!
- But is this the ONLY thing that matters to patients? No

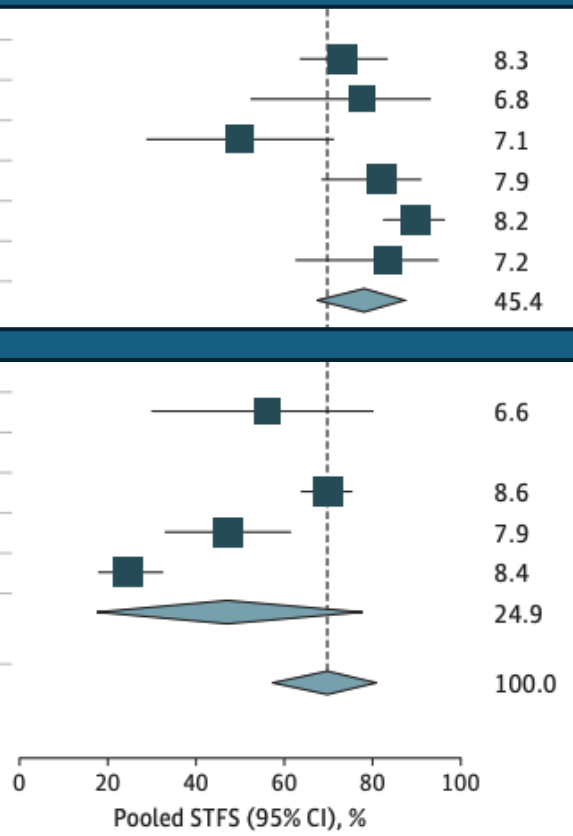
- Almost toxicity-free treatment (at least for prostate oligomets)?

- Often “the other option” is next line of systemic therapy/to start lifelong systemic therapy

Figure 2. Pooled Systemic Therapy–Free Survival (STFS) at 1 or 2 Years After Stereotactic Body Radiotherapy for Oligometastatic Disease as Reported in 13 Studies

Study or subgroup by histology	No. of events	Total No.	Pooled STFS (95% CI), %	Weight, %
Gynecological cancer				
Donovan et al,[47] 2024	118	178	66.3 (58.8-73.2)	
Renal cell cancer				
Hannan et al,[18] 2022	21	23	91.3 (72.0-98.9)	
Tang et al,[15] 2021	25	30	83.3 (65.0-93.5)	
Total		53	87.0 (76.2-95.2)	
Prostate cancer				
Werensteijn-Honingh et al,[19] 2021	66	90	73.3 (63.5-83.4)	8.3
Moyer et al,[24] 2019	14	18	77.8 (52.3-93.2)	6.8
Siva et al,[17] 2023	11	22	50.0 (28.7-71.3)	7.1
Decaestecker et al,[14] 2014	41	50	82.0 (68.4-91.1)	7.9
Mazzola et al,[21] 2021	79	88	89.8 (82.4-96.4)	8.2
Berkovic et al,[13] 2013	20	24	83.3 (62.5-95.0)	7.2
Total		292	78.1 (67.4-87.3)	45.4
Sarcoma				
Loi et al,[30] 2018	9	16	56.2 (29.9-80.2)	6.6
Various				
Sogono et al,[48] 2021	176	252	69.8 (63.8-75.4)	8.6
Shahi et al,[33] 2020	24	51	47.1 (32.9-61.5)	7.9
Willmann et al,[45] 2023	35	142	24.6 (17.8-32.6)	8.4
Total		445	47.1 (17.5-77.8)	24.9
Heterogeneity: $\tau^2 = 0.0775$; $\chi^2_2 = 80.2$; $I^2 = 97.5\%$; $P < .001$				
Total		984	69.7 (57.4-80.9)	100.0
Heterogeneity: $\tau^2 = 0.0468$; $\chi^2_{12} = 171.03$; $I^2 = 93.0\%$; $P < .001$				
Test for subgroup differences: $\chi^2_4 = 14.36$; ($P = .006$)				

78.1% free of systemic therapy 1-2 years after SBRT



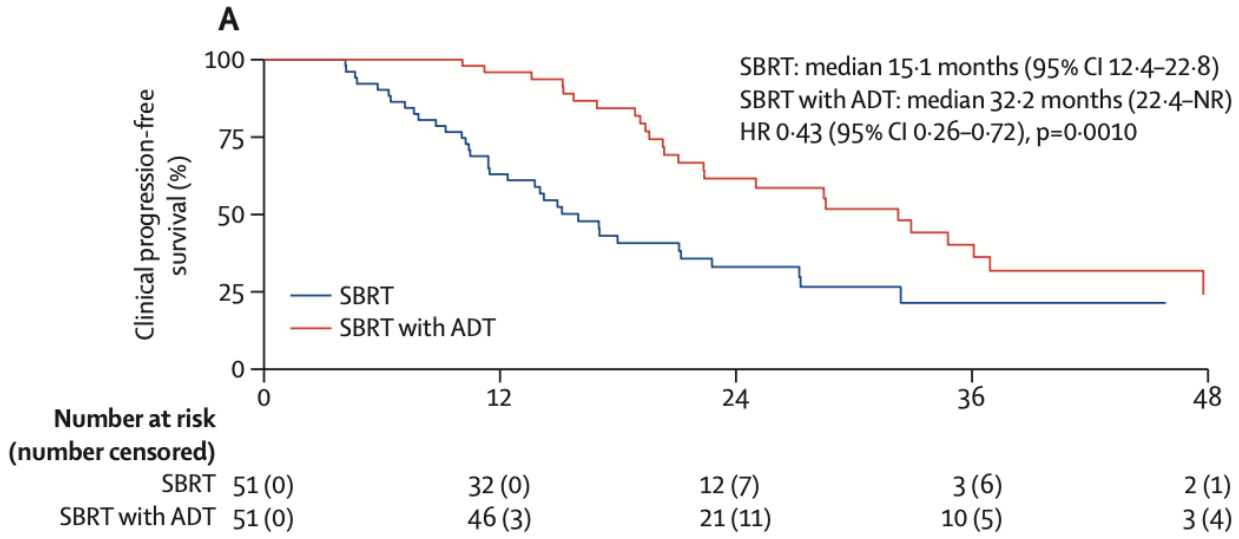
Should we prescribe ADT with SBRT or is the whole point to delay ADT?

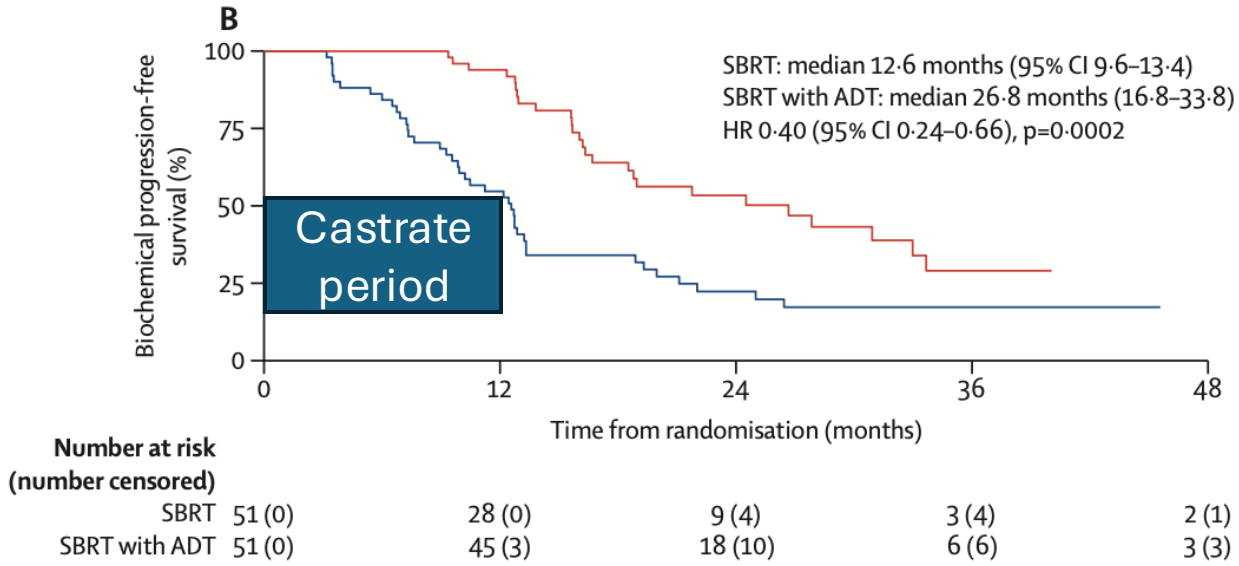
- 105 men ran
- Metachronou
- ADT given as
- Minimal toxicity seen

ADT with SBRT versus SBRT alone for hormone-sensitive oligorecurrent prostate cancer (RADIOSA): a randomised, open-label, phase 2 clinical trial

Giulia Marvaso, Giulia Corrao*, Mattia Zaffaroni, Maria Giulia Vincini, Chiara Lorubbio, Sara Gandini, Cristiana Fodor, Sofia Netti, Dario Zerini, Stefano Luzzago, Francesco Alessandro Mistretta, Konstantinos Venetis, Giulia Cursano, Tiziana Burla, Ketti Mazzocco, Federica Cattani, Giuseppe Petralia, Nicola Fusco, Gabriella Pravettoni, Gennaro Musi, Ottavio De Cobelli, Chad Tang, Piet Ost, David A Palma, Roberto Orecchia, Barbara Alicja Jereczek-Fossa*

Marvaso et al, Lancet Oncology 2025





Clinical PFS 15.1 mo vs 32.3 mo

Biochemical PFS 12.6 mo vs 26.8 mo

Marvaso et al, Lancet Oncology 2025

What about pelvic nodal oligomets – should we treat them differently?

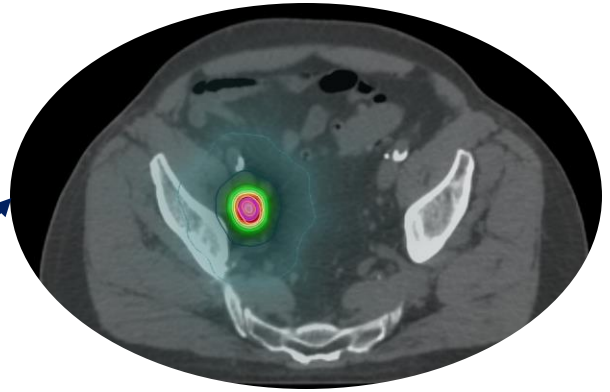
PEACE-V - STORM trial

Oligo Recurrent PCa, Normal T level, with ≤ 5 Pelvic Nodes on PET imaging

R 1:1

97 patients

MDT: 3 x 10 Gy SBRT or sLND (salvage lymph-node dissection)



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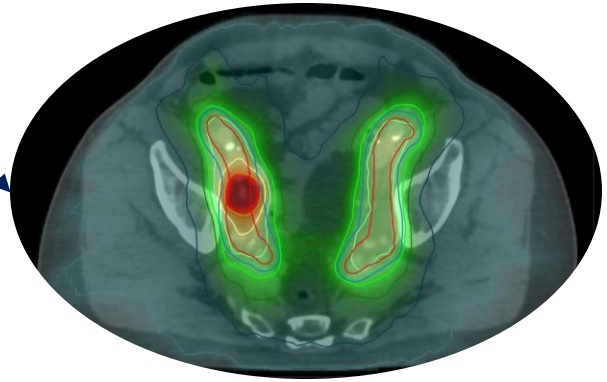
ADT: 6 months

93 patients



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ENRT: 25 x 1.8 Gy + SIB boost
sLND + ENRT without boost

ADT: 6 months

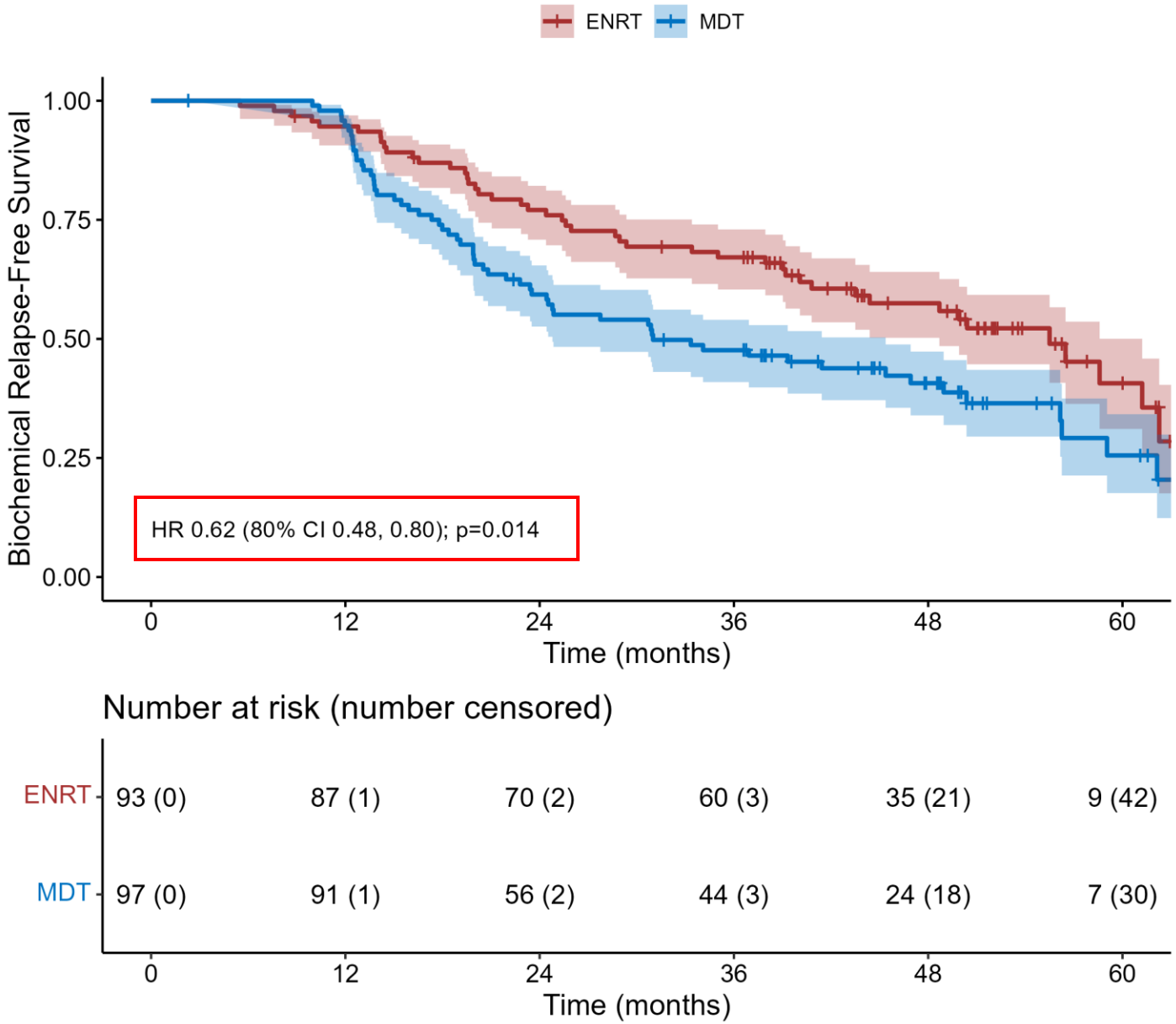
Median follow-up: 50 months (IQR 42-58)
6 months ADT given to all

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

Slide credit: Prof Thomas Zilli, ESTRO 2025

Results: biochemical relapse-free survival (bRFS)

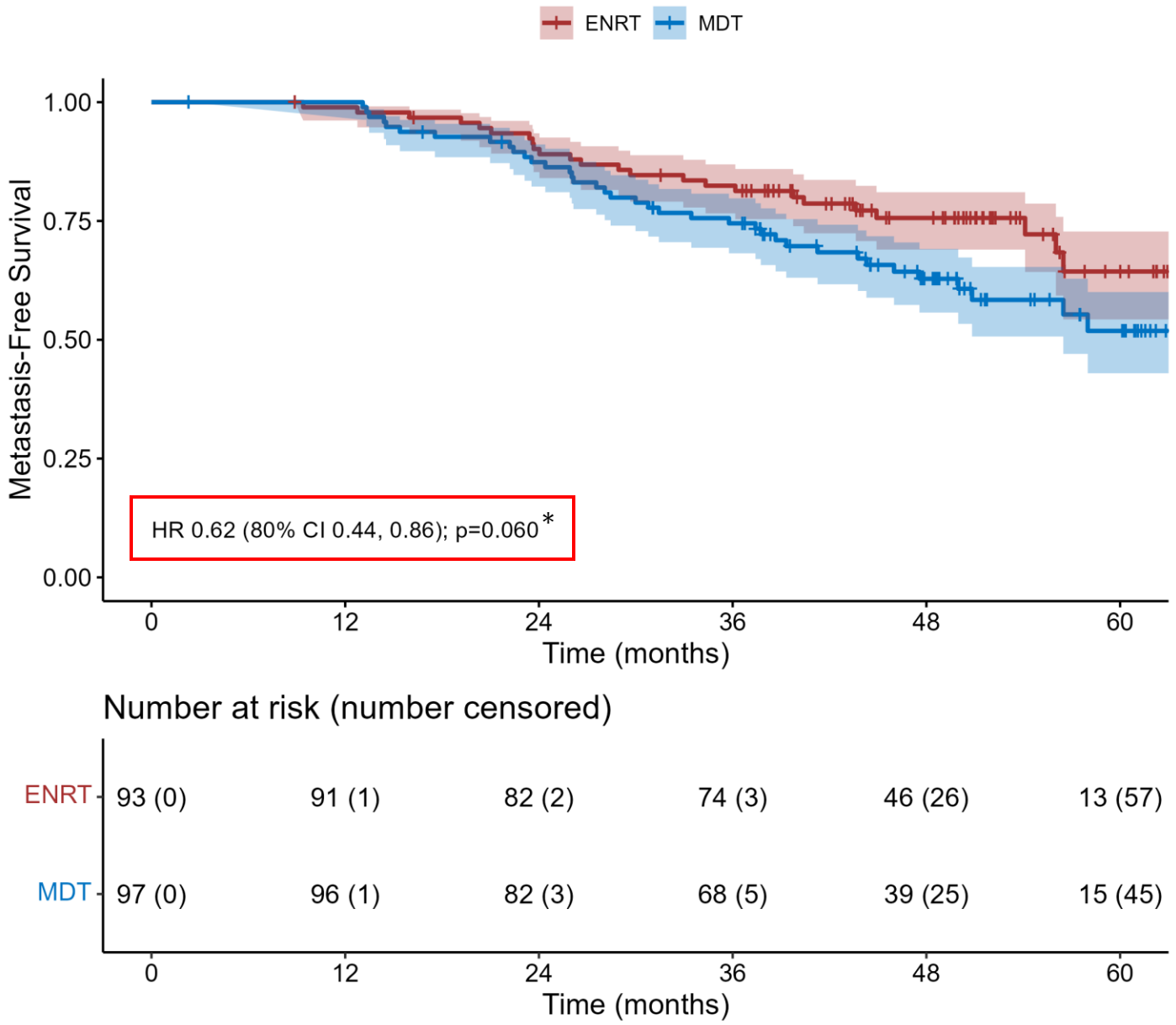
Slide credit: Prof Thomas Zilli, ESTRO 2025



4-year bRFS:

- MDT = **41%** [80% CI:0.34-0.47]
- ENRT = **57%** [80% CI:0.50-0.64]

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



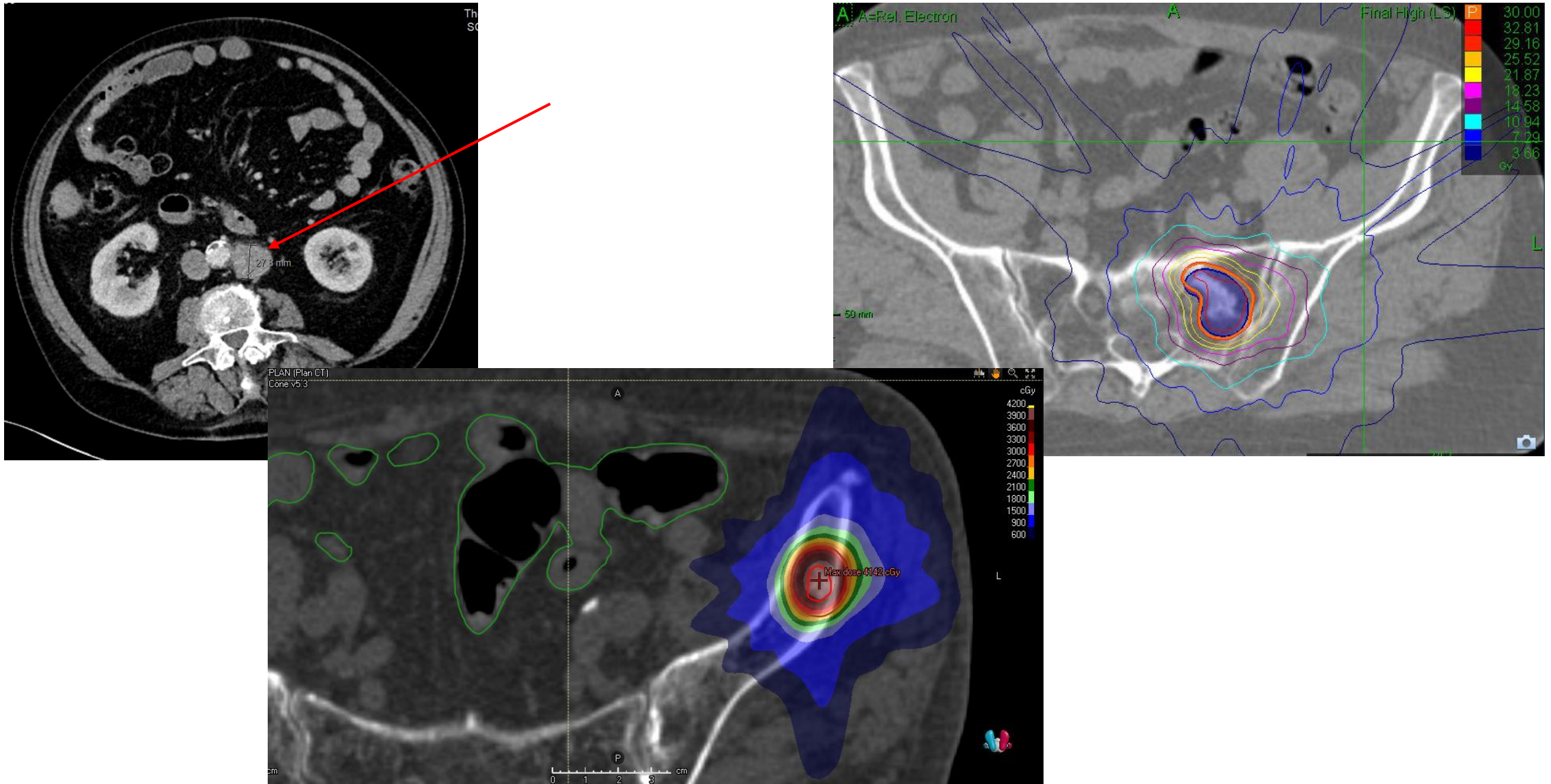
4-year MFS:

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

Slide credit: Prof Thomas Zilli, ESTRO 2025

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

So how to treat oligomets?



What OAR constraints?

ARTICLE IN

Clinical Oncolog

Contents lists avail

Clinical

journal homepage: www.

ELSEVIER

UK 2022 Consensus on Normal Tissue D Oligometastatic, Primary Lung and Hepa Stereotactic Ablative Radiotherapy

P. Diez [*], G.G. Hanna [†‡], K.L. Aitken [§¶], N. van As [¶‖], A E.M. Dunne [§§], D.J. Eaton [*¶¶‖‖], K.N. Franks [***], J.S. Gc M.A. Hawkins [§§§¶¶¶], S. Jain [†‡], F. McDonald [¶‖], R. Pat A. Tree [§¶], L. Murray [*******]

Table 3
Abdominal constraints

Structure (standard nomenclature)	Metric	One fraction		Three fractions		Five fractions		End point (if available)
		Optimal	Mandatory	Optimal	Mandatory	Optimal	Mandatory	
BileDuct_Common	$D_{0.1cc}$		30 Gy [25]	50 Gy		50 Gy [2,4]		
Bowel_Small	$D_{0.1cc}$		15.4 Gy [18,25]		25.2 Gy [18,25]	30 Gy	35 Gy [18,25]	Grade 3+ enteritis/ obstruction
	D_{5cc}		11.9 Gy [18,25]		17.7 Gy [18,25]			
	D_{10cc}					25 Gy [25]		
Duodenum	$D_{0.1cc}$		12.4 Gy [18,25]		22.2 Gy [18,25]	33 Gy	35 Gy [2,4]	Grade 3+ ulceration
	D_{10cc}		9 Gy [18,25]		11.4 Gy [18,25]	25 Gy [2,4]		
Kidney_Cortex (individual/ combined)	D_{mean}			8.5 Gy[†] [25]		10 Gy [2,4]		Grade 3+ renal function dysfunction
Kidney_Cortex (combined)	$D_{\geq 200cc}$		8.4 Gy [18,25]		16 Gy [18,25]		17.5 Gy [18,25]	
If solitary kidney or one Kidney_Cortex D_{mean} constraint exceeded[‡]	V_{10Gy}		33% [40]		33% [40]	10% [2,4]	45% [2,4]	
Liver (non-liver lesions) and Liver-GTV (liver lesions)*	$D_{\geq 700cc}$		9.1 Gy [18,25]	15 Gy [23,25]	17 Gy [23]	15 Gy [23]		Grade 3+ liver function dysfunction
	V_{10Gy}					70% [2,4]		
	D_{mean}			13 Gy [23]	15 Gy [23]	13 Gy [2]	15.2 Gy [2,25]	Radiation-induced liver disease (classic or non-classic)
Spleen	D_{mean}		Report		Report		Report	
Stomach	$D_{0.1cc}$		12.4 Gy [18,25]		22.2 Gy [18,25]	33 Gy [2,4,25]	35 Gy [2,4]	Grade 3+ ulceration/fistula
	D_{10cc}		11.2 Gy [18,25]		16.5 Gy [18,25]	25 Gy [2,4,25]		
	D_{50cc}					12 Gy [2,4]		

What to contour?

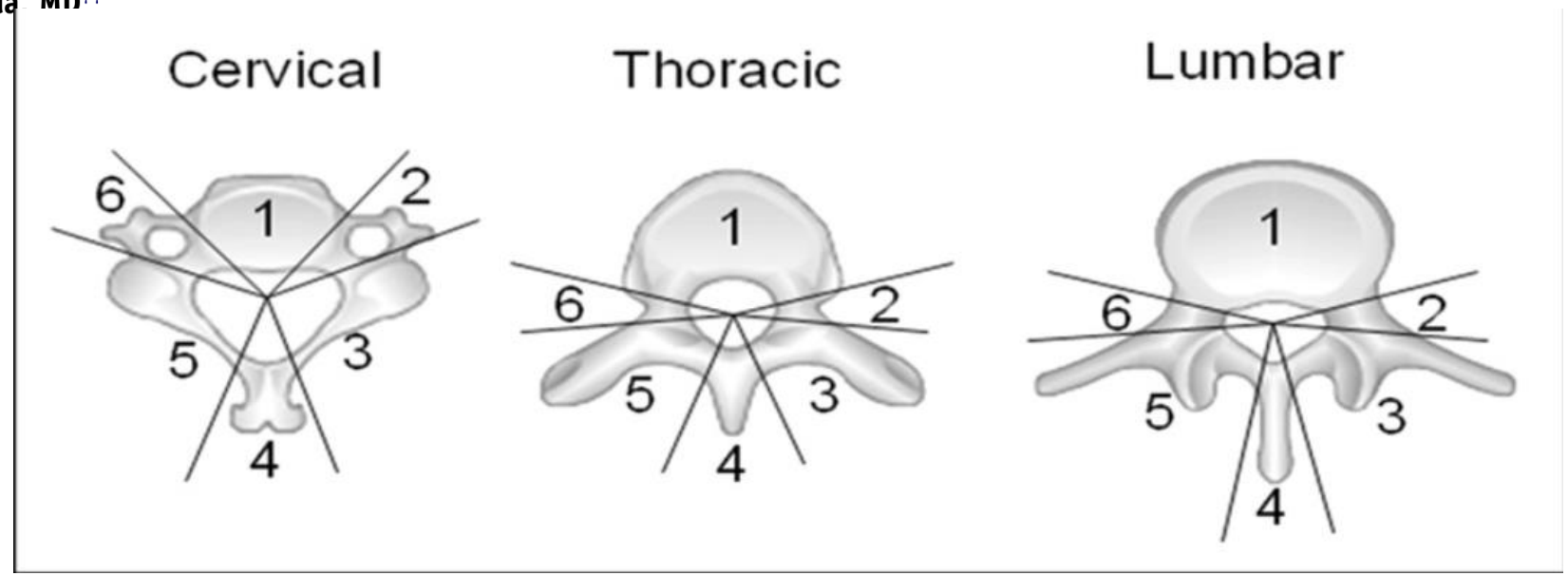
- GTV
- CTV (intra-osseous)
- PTV

International Journal of Radiation Oncology biology • physics
www.redjournal.org

Clinical Investigation: Central Nervous System Tumor

International Spine Radiosurgery Consortium Consensus Guidelines for Target Volume Definition in Spinal Stereotactic Radiosurgery

Brett W. Cox, MD,[*,1] Daniel E. Spratt, MD,[*,1] Michael Lovelock, PhD,[†] Mark H. Bilsky, MD,[‡] Eric Lis, MD,[§] Samuel Ryu, MD,[‖] Jason Sheehan, MD,[¶] Peter C. Gerszten, MD, MPH,[**] Eric Chang, MD,[††] Iris Gibbs, MD,[‡‡] Scott Soltys, MD,[‡‡] Arjun Sahgal, MD,[§§] Joe Deasy, PhD,[†] John Flickinger, MD,[‖‖] Mubina Quader, PhD,[‖‖] Stefan Mindea, MD,[¶¶] and Yoshiya Yamada MD[‡‡]



Cox et al, IJROBP 2012

Radiotherapy and Oncology 205 (2025) 110717

Contents lists available at ScienceDirect

Radiotherapy and Oncology

journal homepage: www.thegreenjournal.com

Review Article

Stereotactic body radiotherapy for non-spine bone metastases: A *meta*-analysis and international stereotactic radiosurgery society (ISRS) clinical practice guidelines

Timothy K. Nguyen [a,*], Alexander V. Louie [b], Rupesh Kotecha [c], Anshul Saxena [d], Yanjia Zhang [d], Matthias Guckenberger [e], Mi-Sook Kim [f], Marta Scorsetti [g], Ben J. Slotman [h,i], Simon S. Lo [j], Arjun Sahgal [b], Alison C. Tree [k,l]

Suggested dose fractionation schedules include: 18–24 Gy/1, 27–30 Gy/3, and 30–35 Gy/5.

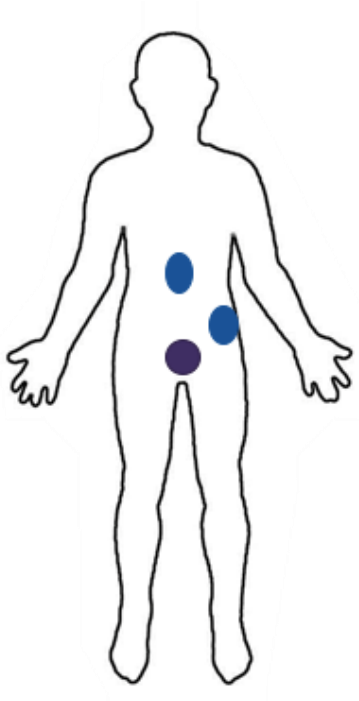
When the GTV is delineated based on MRI+/- PET/CT fusion, a CTV margin is recommended as a 0–5 mm expansion of the GTV within contiguous bone.

When the GTV is delineated based on CT alone, a CTV margin is recommended as a 5–10 mm expansion of the GTV within contiguous bone.

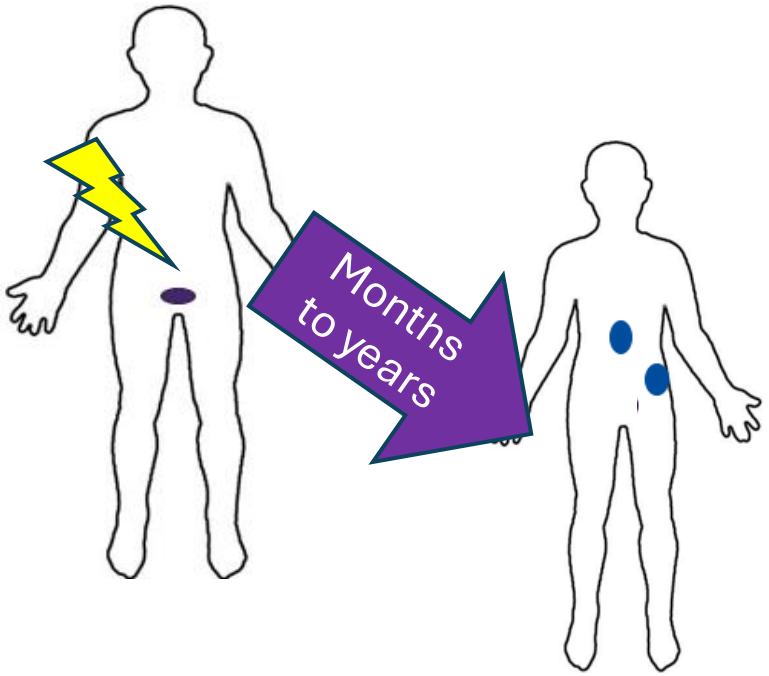
A 2–5 mm PTV should be generated and is dependent on the specific immobilization used and local institutional policies.

Three main scenarios

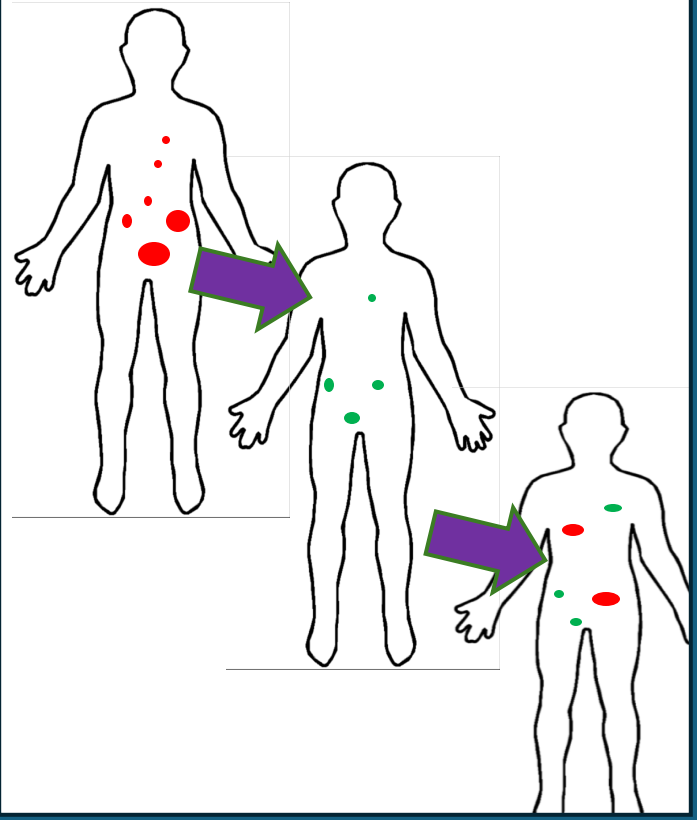
Synchronous oligometastases



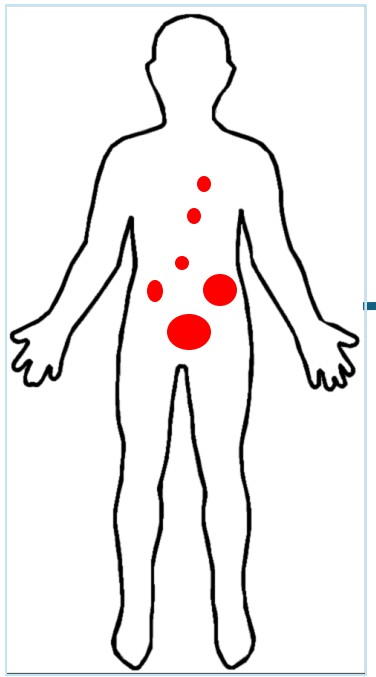
Metachronous oligometastases



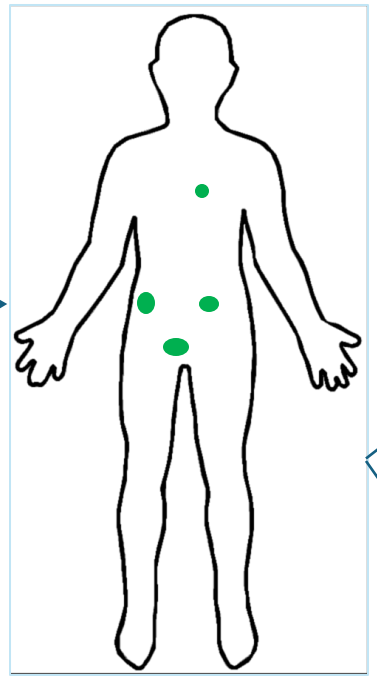
Oligoprogression



CRPC patients on ARPI

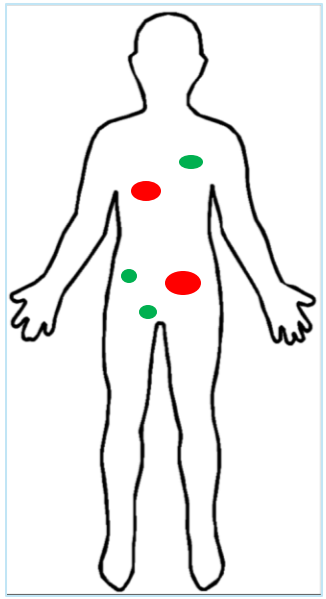


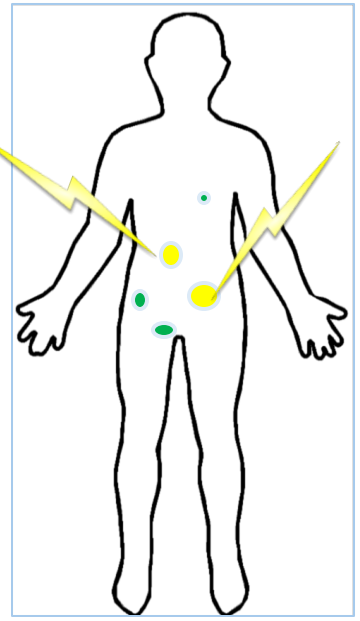
Abi/
Enza



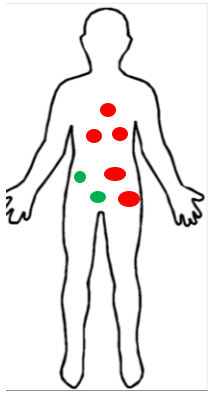
Response

Oligoprogressive disease





Reversal of treatment resistance



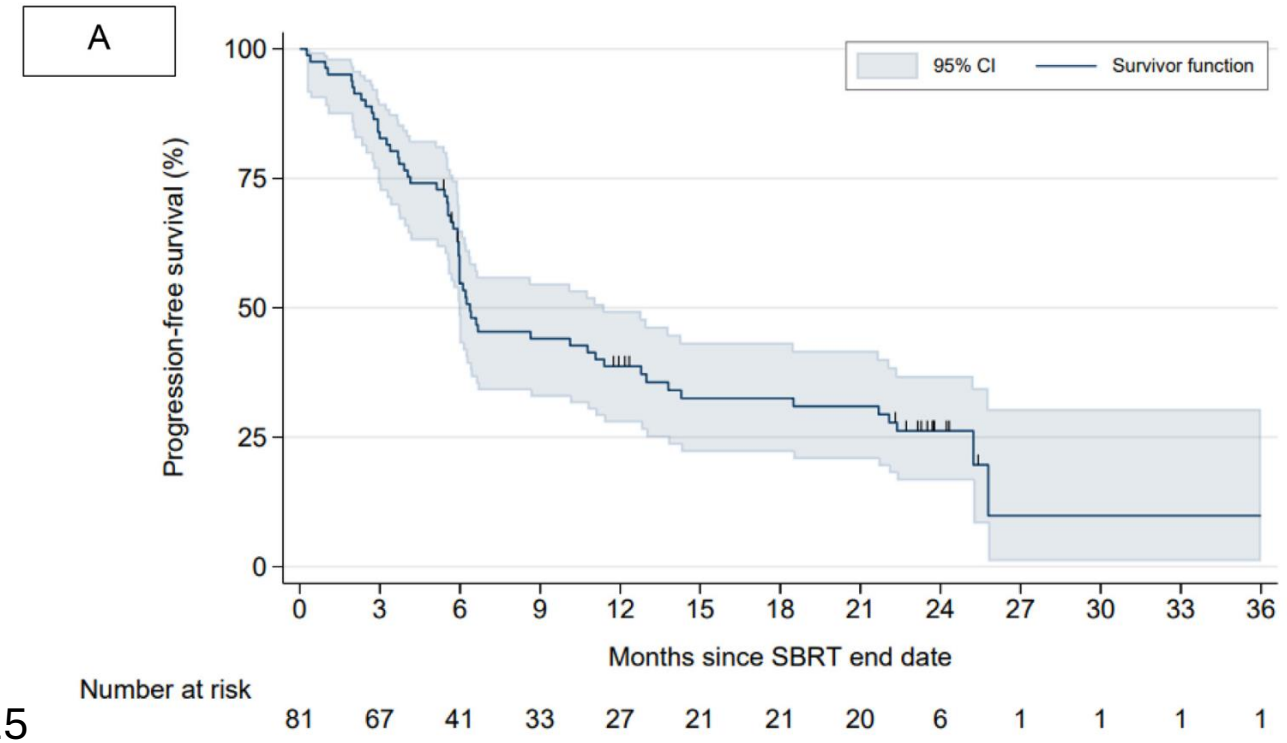
Widespread progression of disease

Key:

- Progressing
- Responding
- Irradiated lesions

Patel et al, IJROBP 2025

SBRT >6 months PFS in CRPC



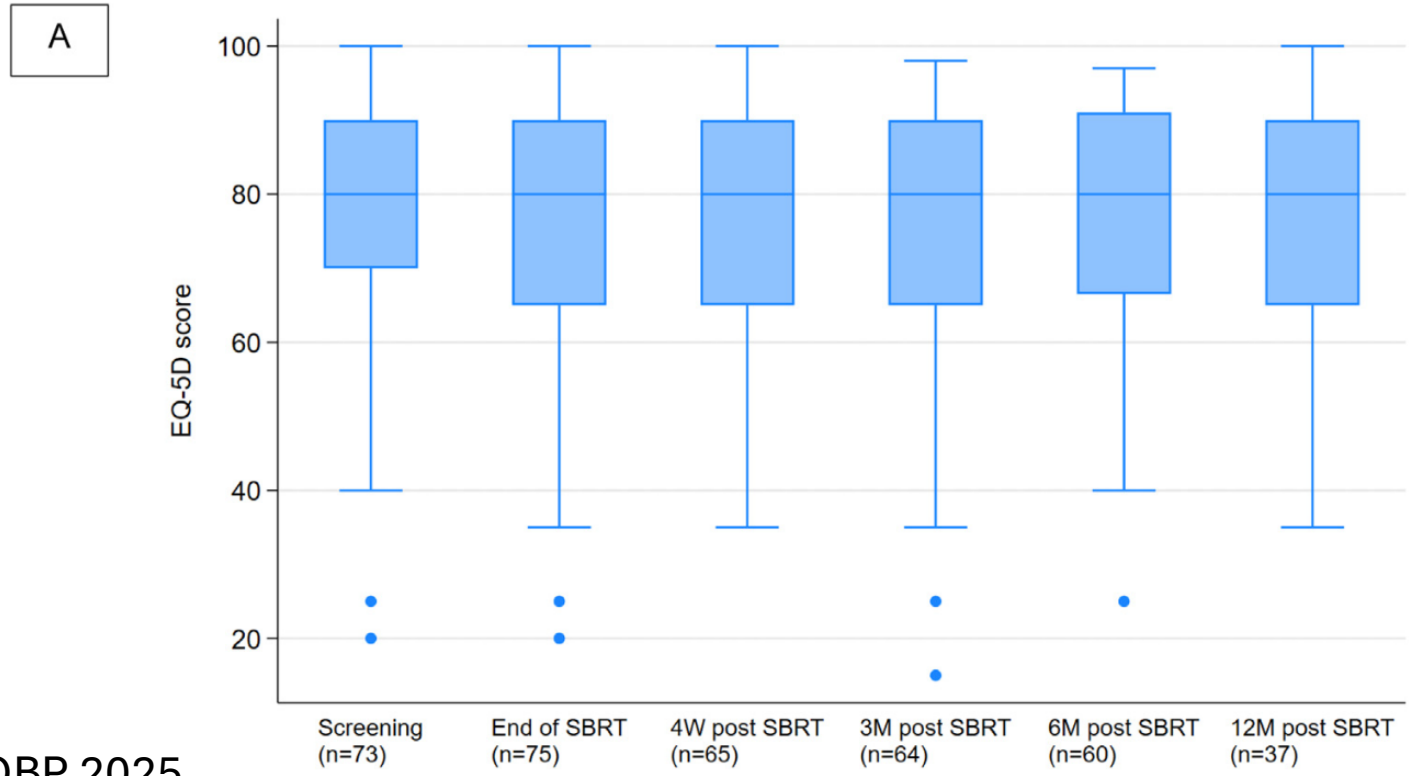
Median PFS 6.4 months

39% progression-free at 12 months

Patel et al, IJROBP 2025

Patel et al, IJROBP 2025

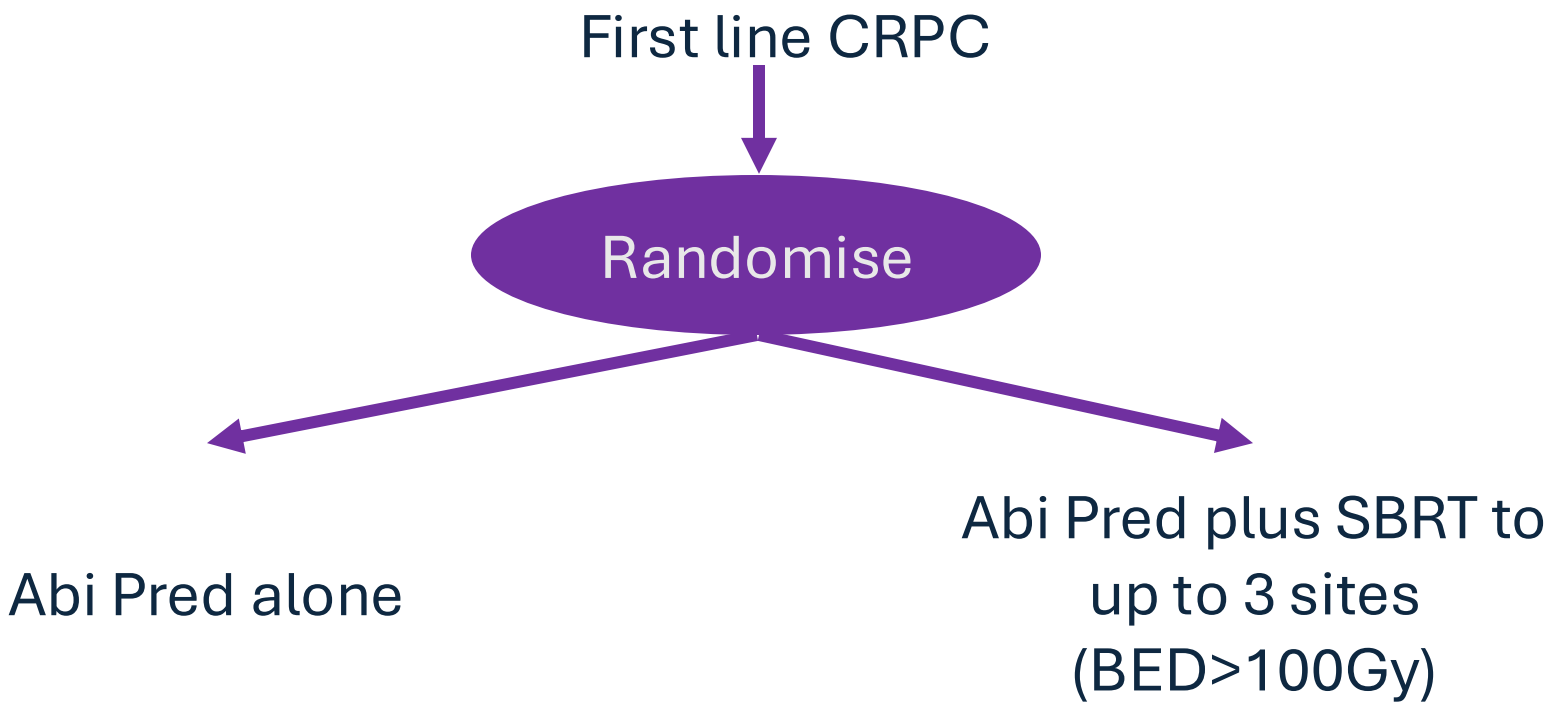
SBRT has no detriment on QOL



Patel et al, IJROBP 2025

Patel et al, IJROBP 2025

The ARTO trial



Francolini et al, JCO 2023

ARTO trial oligoprogression

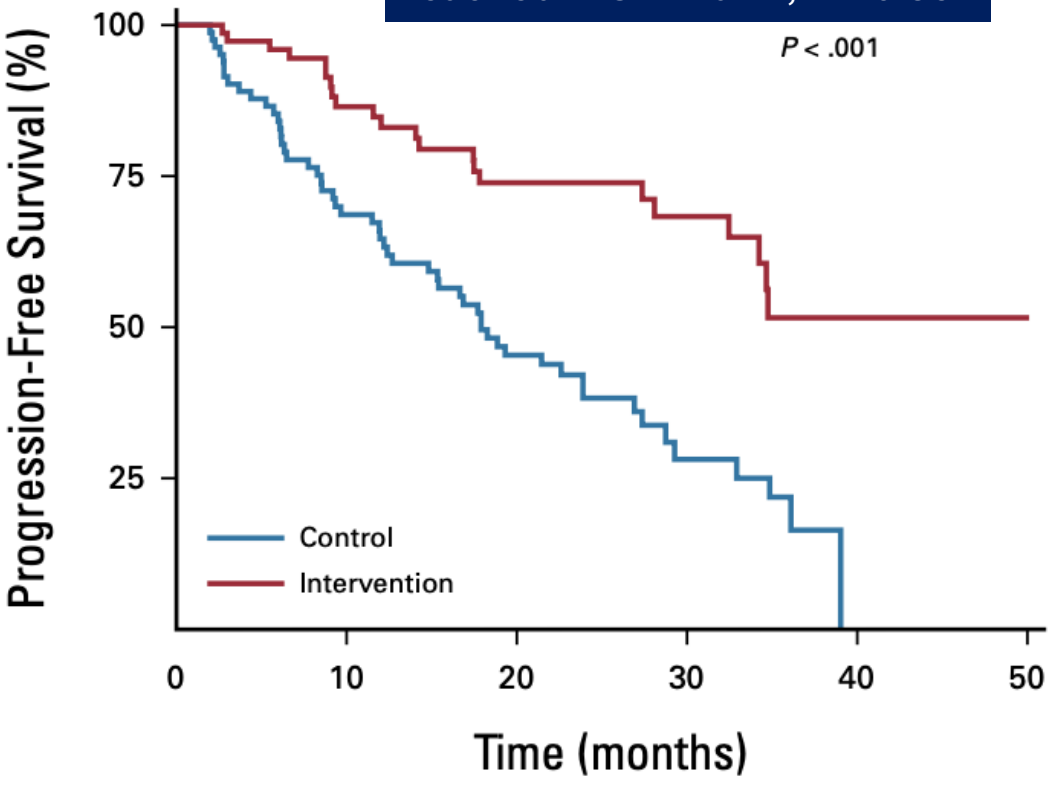
- 157 patients, minimum follow up 6 months, med FU 24.9 months
- Multi-centre (Italy)
- Men presenting with CRPC for the first time
- Three or less identifiable sites of disease, excluding visceral disease

  (could be CT, bone scan or PET)

Francolini et al, JCO 2023

SBRT for oligoprogression delays need for chemotherapy

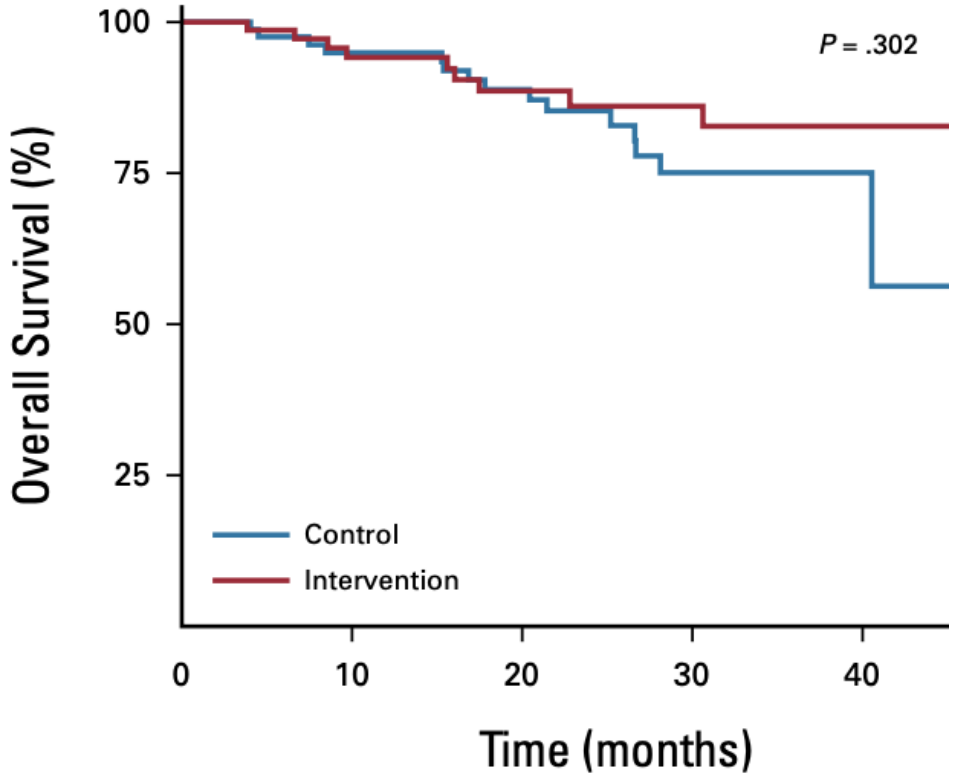
SOC arm 17 months vs not reached in SBRT arm, HR 0.35



sk:						
rm = control	82	52	32	10	0	0
rm = intervention	75	51	37	22	6	1

B

OS not significant

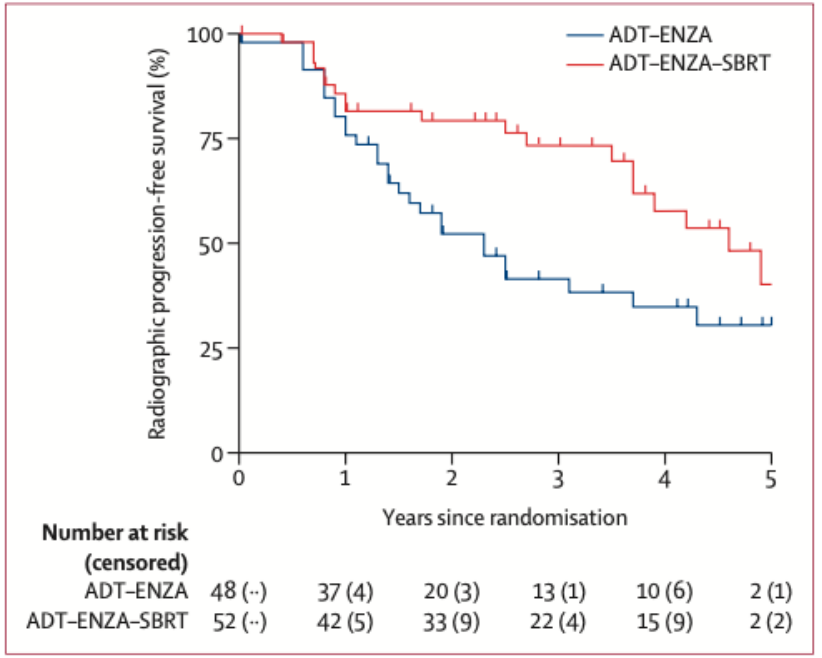


No. at risk:						
Study arm = control	82	70	55	23	5	
Study arm = intervention	75	59	45	27	10	

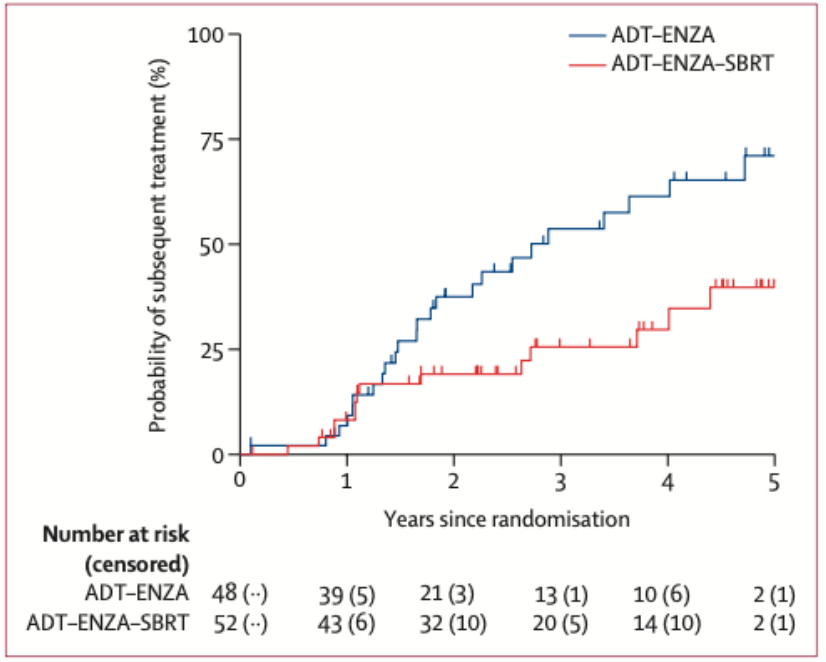
Francolini et al, JCO 2023

GROUQ-PCS 9

- Multicentre Phase 2 randomised trial in oligomet CRPC
- **Conventional imaging**
- ADT+Enza vs ADT+Enza+SBRT
- 100 patients



SBRT doubled rPFS 4.6 years vs 2.3 years

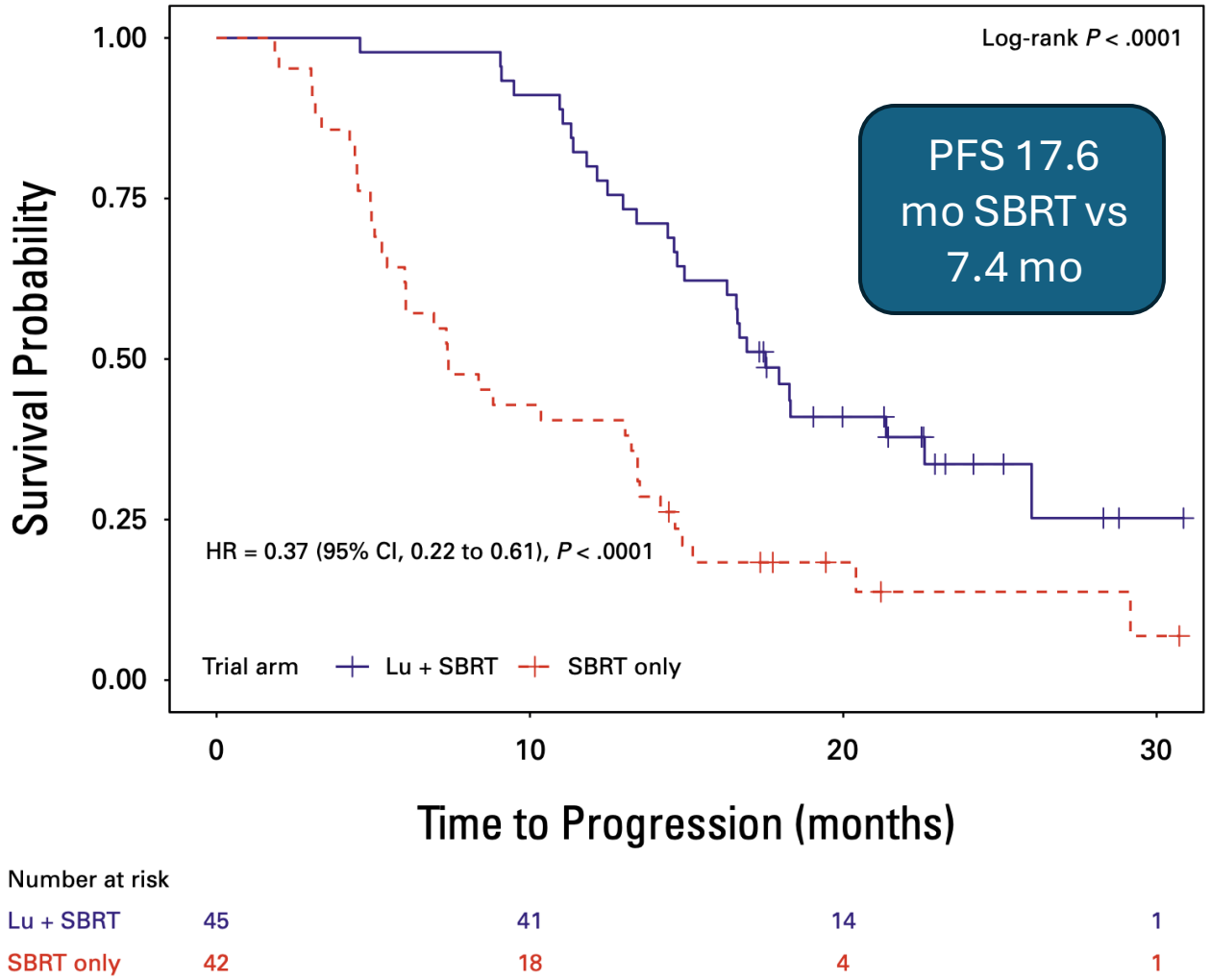


Increased time to subsequent therapy 5.1 years SBRT vs 3.8 years SOC

Niazi et al, Lancet Oncol 2025

LUNAR trial

- Single centre randomised Ph2 trial
- 1-5 metachronous oligometastases **on PET**
- Randomised to SBRT alone vs SBRT+2 cycles of Lutetium PSMA 6.8GBq
- 87 evaluable patients
- Median FU 22 months



Kishan et al, JCO 2025

Conclusions

- Level 1 evidence supporting use of prostate radiotherapy in de novo M1 hormone sensitive prostate cancer
- SBRT to metachronous/oligorecurrent oligomets improves PFS, delays time to next therapy
- SBRT to oligoprogressive/oligoactive CRPC also improves PFS, delays time to next therapy
- OS benefits not well proven, but not the only endpoint of importance
- Combining SBRT with novel therapies under development

Thanks for your attention

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