MasterClass in Bladder Cancer 2026

Bladder sparing options: past, present and future

Organized by:
HENDERE HEALTHCARE

#BladderMasterClass26

Hospital Universitario 12 de Octubre

Disclosures

Research support/PI	Johnson & Johnson, Pfizer, Taris, BMS, Roche, Seagen, AstraZeneca, Combat Medical, Cepheid, Fidia, Astellas, UroGen, MSD, enGene
Employee	SERMAS (Servicio Madrileño de Salud)
Consultant	Johnson & Johnson, Pfizer, Merck, Roche, Taris, Combat Medical, AstraZeneca, MSD, BMS, enGene, Nanobots Therapeutics, Gebro, Photocure
Stockholder	CG Oncology, Johnson & Johnson, Pfizer, Danae Urogenomics
Speaker bureau	Nucleix, MSD, Pfizer, Merck, BMS, AstraZeneca, Palex, Combat Medical, Johnson & Johnson, Recordati, Gebro
Travel	Pfizer, Recordati, Ipsen, Combat Medical, Alter, Salvat, Nucleix, AstraZeneca, Fidia, Johnson & Johnson
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Others	Co-founder of Danae Urogenomics

What are the current recommendations?

Findings

Neoadjuvant therapy

- **Chemotherapy**
  Recommended in cisplatin patients
- **Chemo-immunotherapy**
  Immunotherapy plus gemcitabine and cisplatin
- **Immunotherapy**
  Experimental, only in clinical trial setting
- **Radiotherapy**
  Not recommended

Radical cystectomy

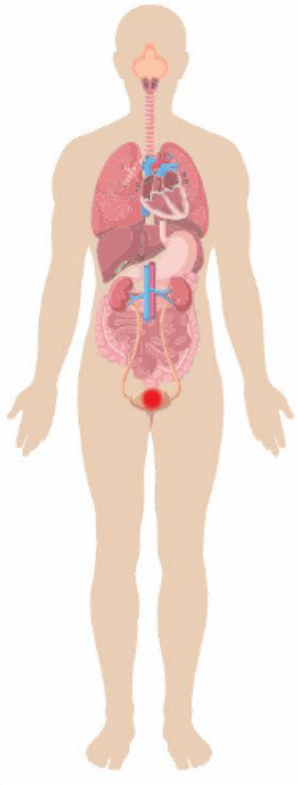
- A higher case load improves
- Perform sexual organ-preserving techniques in eligible women
- Only offer sexual-preserving techniques to eligible men highly motivated to preserve sexual function

Adjuvant therapy

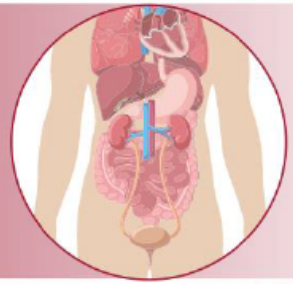
Offer if indicated adjuvant:

- Radiotherapy
- Chemotherapy
- Immunotherapy

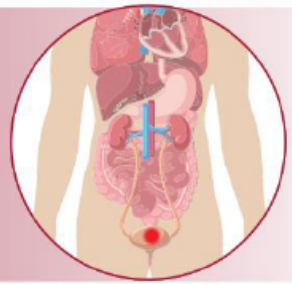
Current Standard of Care: Three Possible Scenarios



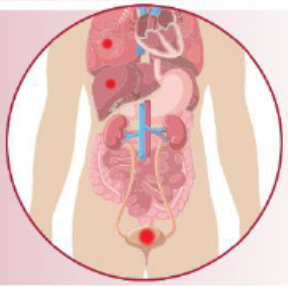
Systemic therapy



No residual disease (30-40%)

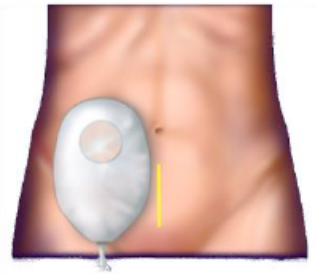


Residual disease in bladder



Subclinical Metastases beyond the bladder

Surgery for all



Strength rating
Strong

Strength rating
Strong

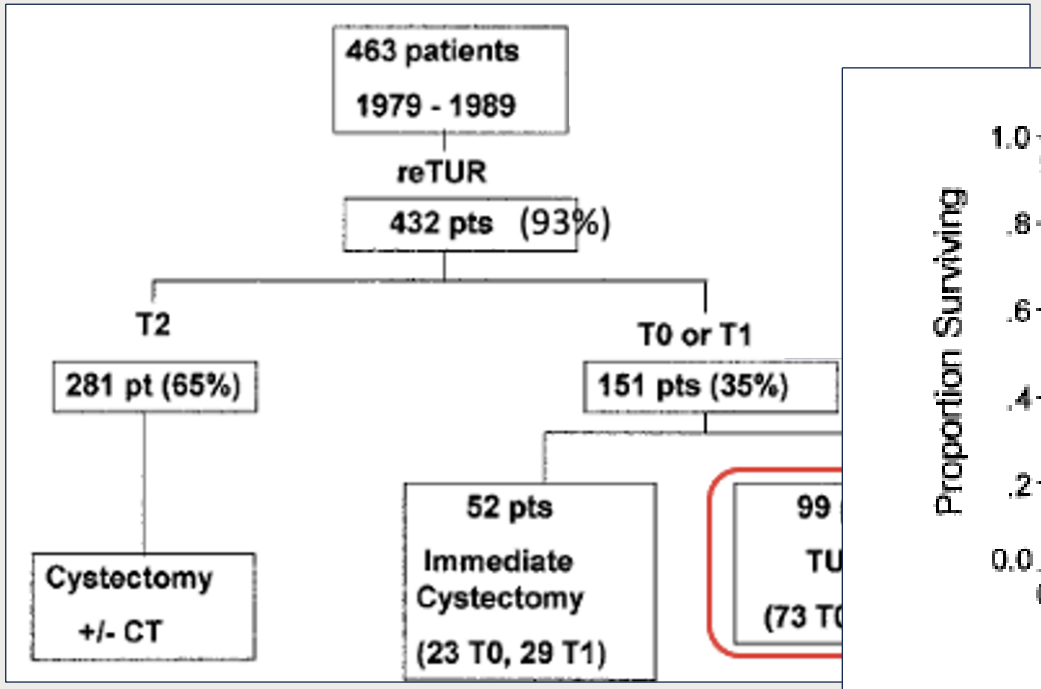
Strength rating
Strong
Strong

EAU Guidelines on MIBC and M1 2026; Plimack E, ESMO 2023

What is bladder preservation?

- TURBT alone
- TURBT + chemotherapy
- TURBT + radiotherapy
- TURBT + chemoradiotherapy
- New approaches

TURBT alone



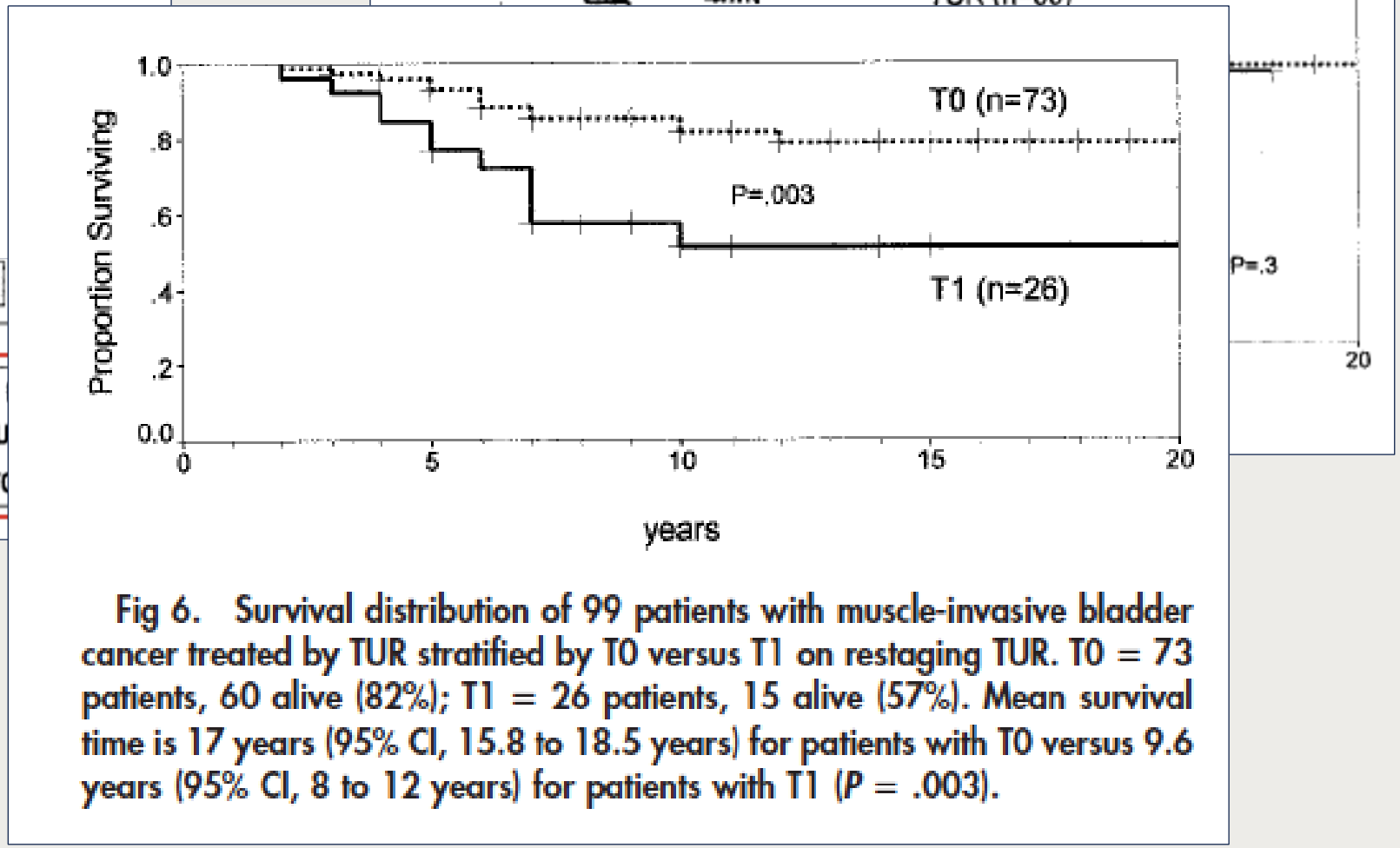


Fig 6. Survival distribution of 99 patients with muscle-invasive bladder cancer treated by TUR stratified by T0 versus T1 on restaging TUR. T0 = 73 patients, 60 alive (82%); T1 = 26 patients, 15 alive (57%). Mean survival time is 17 years (95% CI, 15.8 to 18.5 years) for patients with T0 versus 9.6 years (95% CI, 8 to 12 years) for patients with T1 (P = .003).

Herr HW, J Clin Oncol 2001

TURBT alone

Very well-selected patients

Complete fractionated TURBT

Negative cold-cup biopsies from

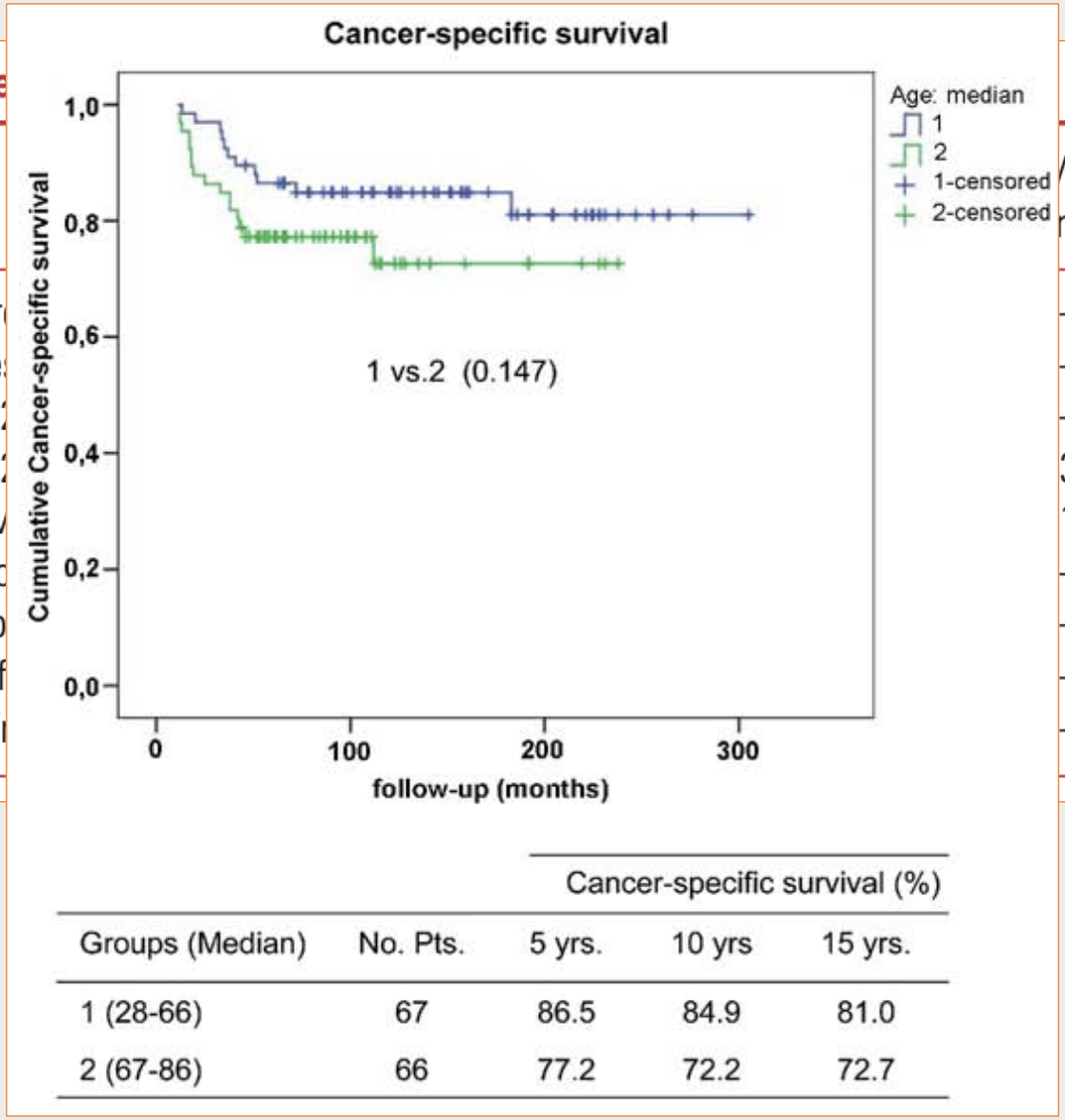
- Tumor bed
- Perivesical fat

Size < 3 cm

Negative CT/MRI

No hydronephrosis

CIS & multifocal tumors allowed



		Cancer-specific survival (%)		
Groups (Median)	No. Pts.	5 yrs.	10 yrs	15 yrs.
1 (28-66)	67	86.5	84.9	81.0
2 (67-86)	66	77.2	72.2	72.7

Solsona E, J Urol 2010

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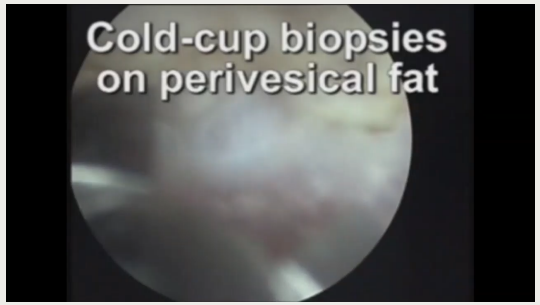
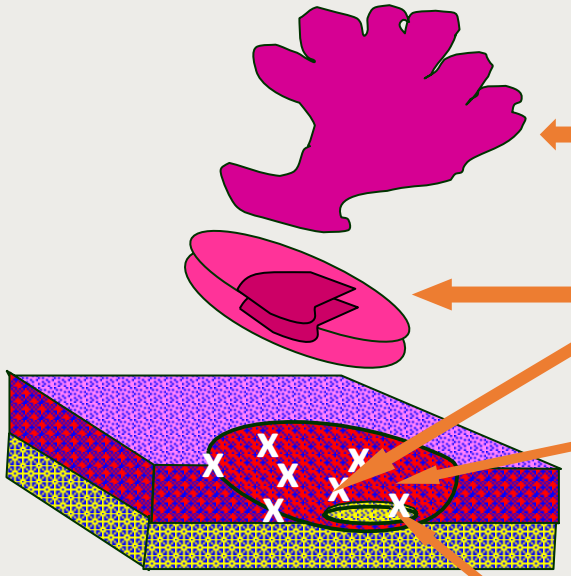
Complete fractionated TURBT





Exophytic part
(1st sample)

Endophytic part
(2nd sample)

Healthy-looking tumour bed biopsies
(3rd sample)

Perivesical fat cold-cup biopsies
(4th sample)

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Slide courtesy of Dr. José Rubio (Valencia, Spain)

TURBT alone

	Herr (RC)	Herr (TURBT)	Solsona (TURBT)
n	52	99	133
mFU	10y	10y	10y
10y CSS (%)	71	76	79.5
10y OS (%)	?	?	39.4
Local recurrence (%)	-	34	29.8
M1 (%)	?	8.08	5.5
Need RC (%)	100	53	45.3
Bladder preservation (%)	0	68	70.2

Herr HW, J Clin Oncol 2001; Solsona E, J Urol 2010

TURBT + chemotherapy

63 patients (57% cT2, 43% cT3-4) refusing RC after cCR to NAC

- Mostly MVAC
- 56% LVI; 32% > 5cm; 14% hydronephrosis
- At 5 years: 54% intact functioning bladder

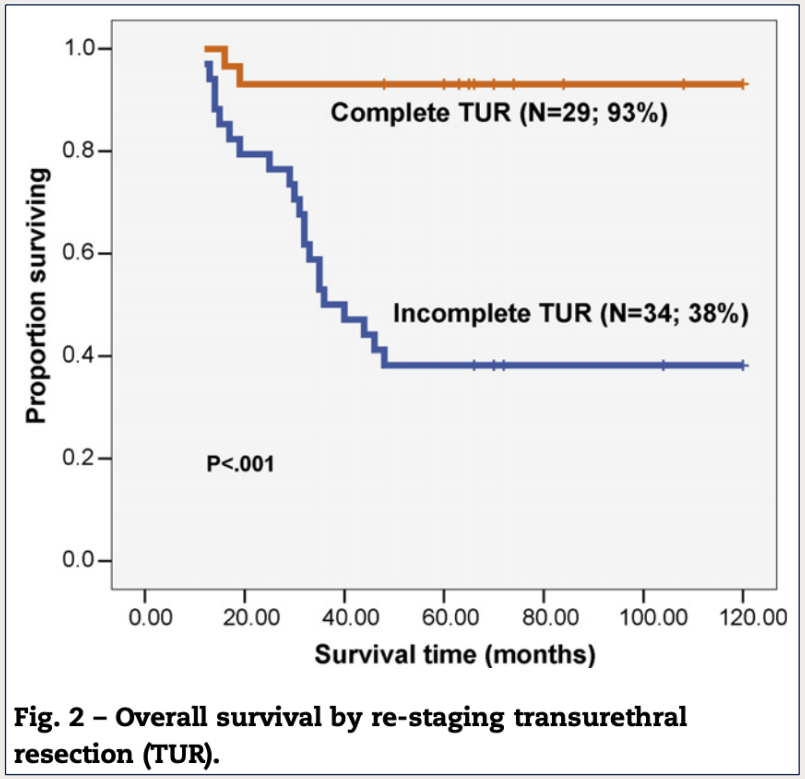


Fig. 2 – Overall survival by re-staging transurethral resection (TUR).

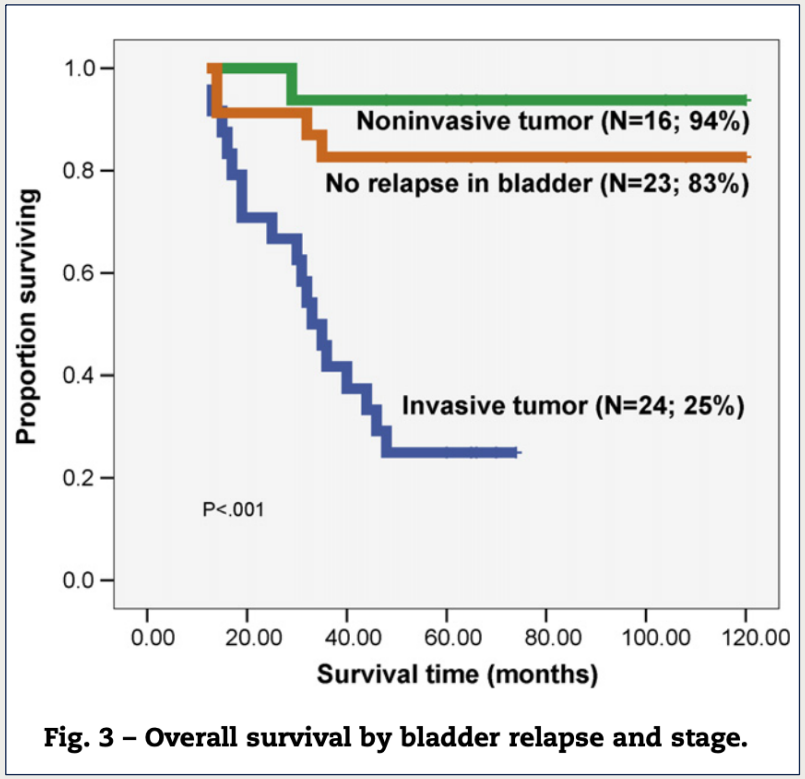
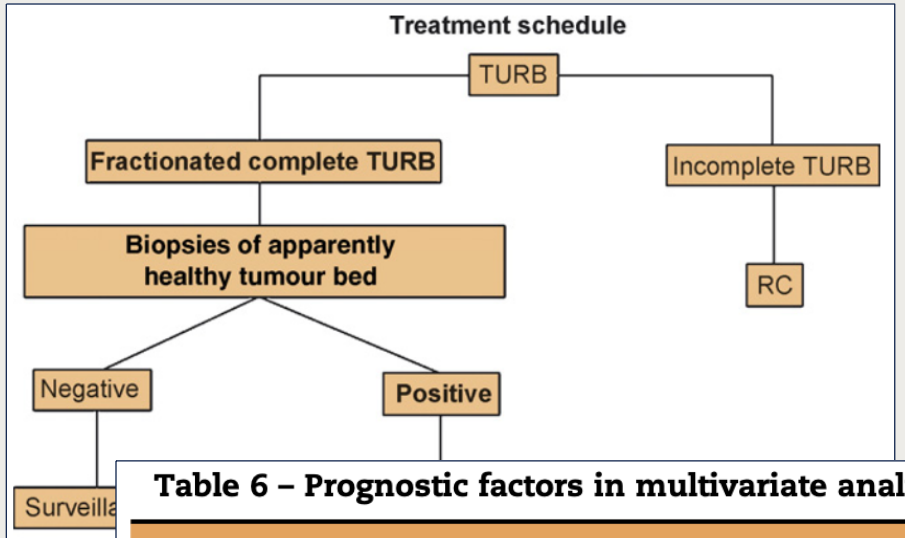


Fig. 3 – Overall survival by bladder relapse and stage.

Herr HW, Eur Urol 2008

TURBT + chemotherapy



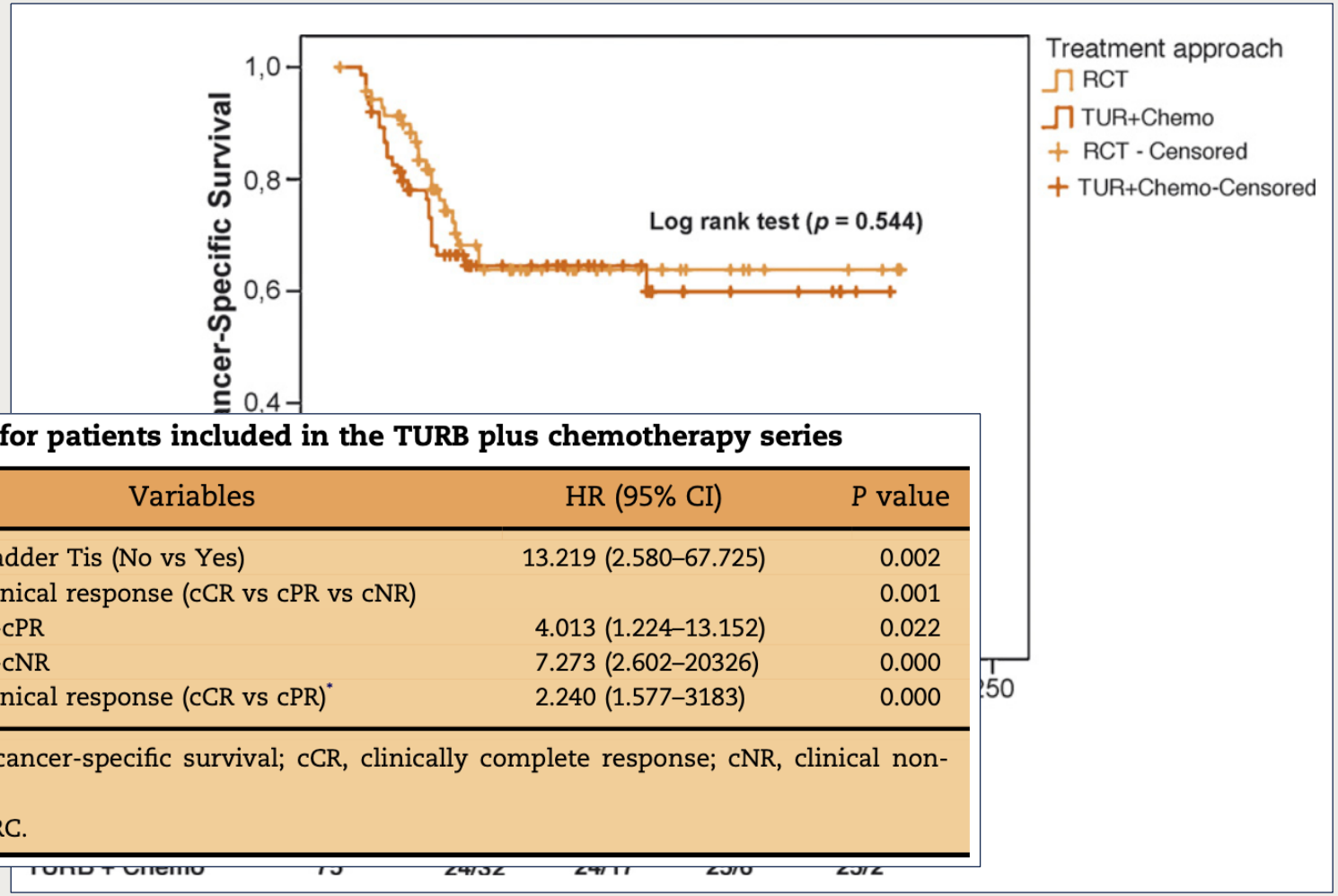


Table 6 – Prognostic factors in multivariate analysis for patients included in the TURB plus chemotherapy series

Outcome tested	Variables	HR (95% CI)	P value
cPR	Bladder Tis (No vs Yes)	13.219 (2.580–67.725)	0.002
CSS	Clinical response (cCR vs cPR vs cNR)		0.001
	-cPR	4.013 (1.224–13.152)	0.022
	-cNR	7.273 (2.602–20326)	0.000
Pogression-free survival plus bladder preservation	Clinical response (cCR vs cPR)*	2.240 (1.577–3183)	0.000

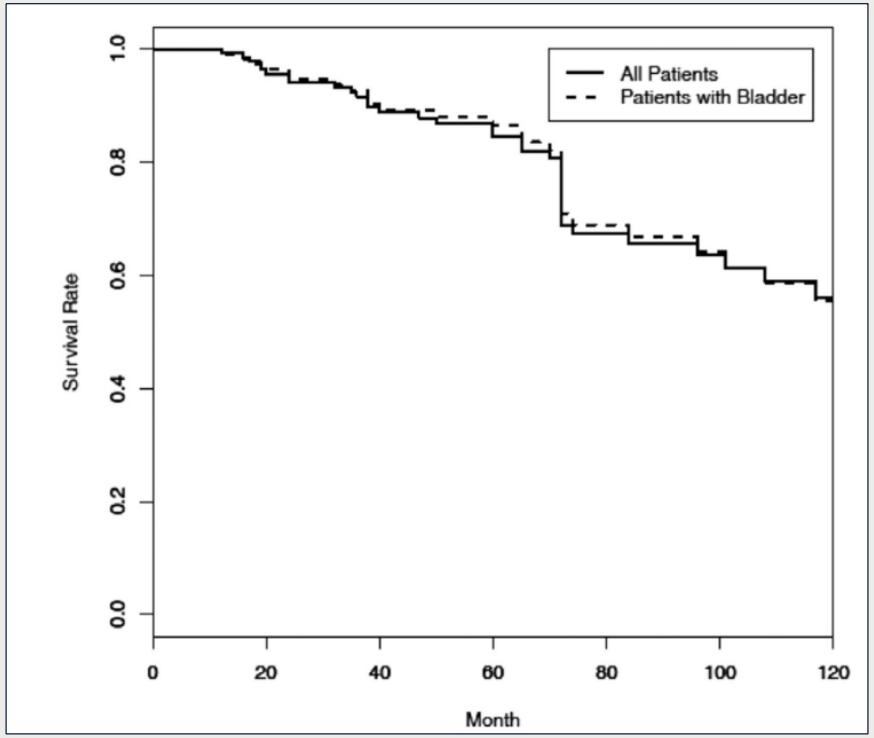
CI, confidence interval; cPR, clinical partial response; CSS, cancer-specific survival; cCR, clinically complete response; cNR, clinical non-response; RC, radical cystectomy.

* Patients with cNR were excluded, as they were to undergo RC.

Solsona E, Eur Urol 2009

TURBT + chemotherapy

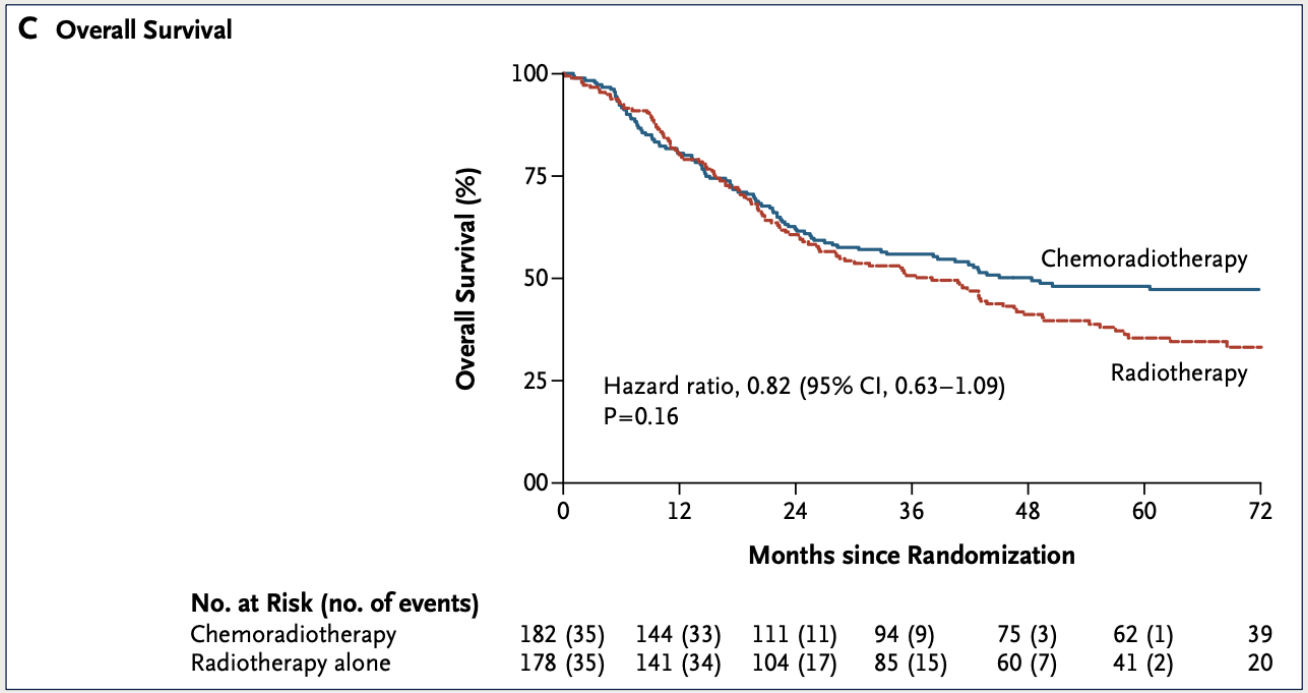
cT2, < 5 cm, cTURBT (negative reTURBT) → NAC → cCR who refuse radical cystectomy (n = 148)

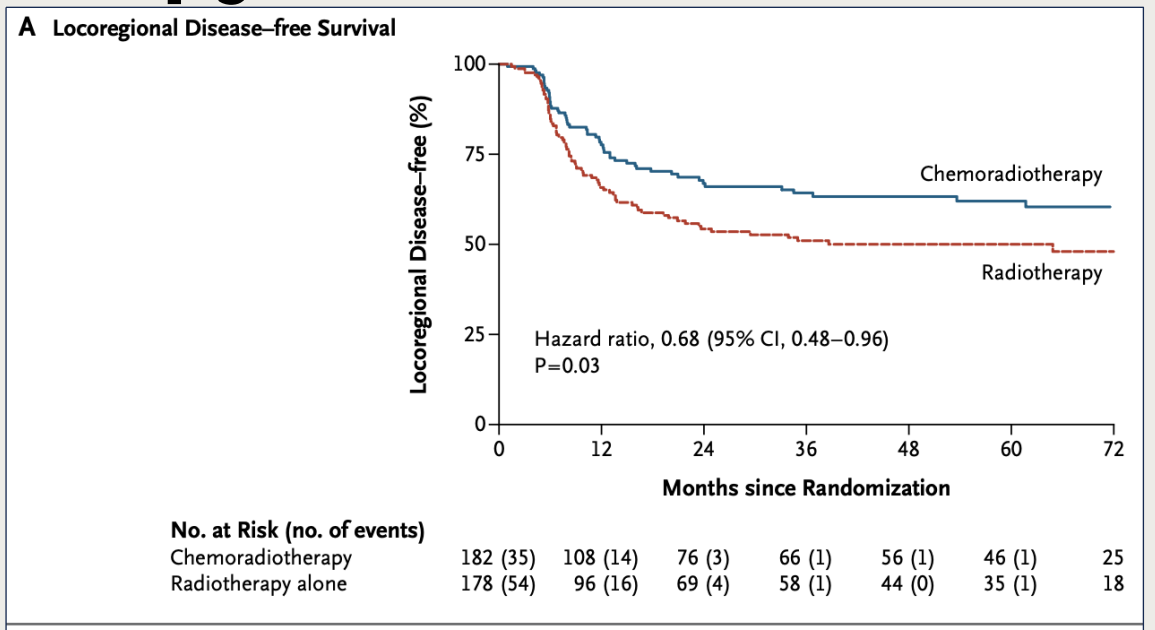


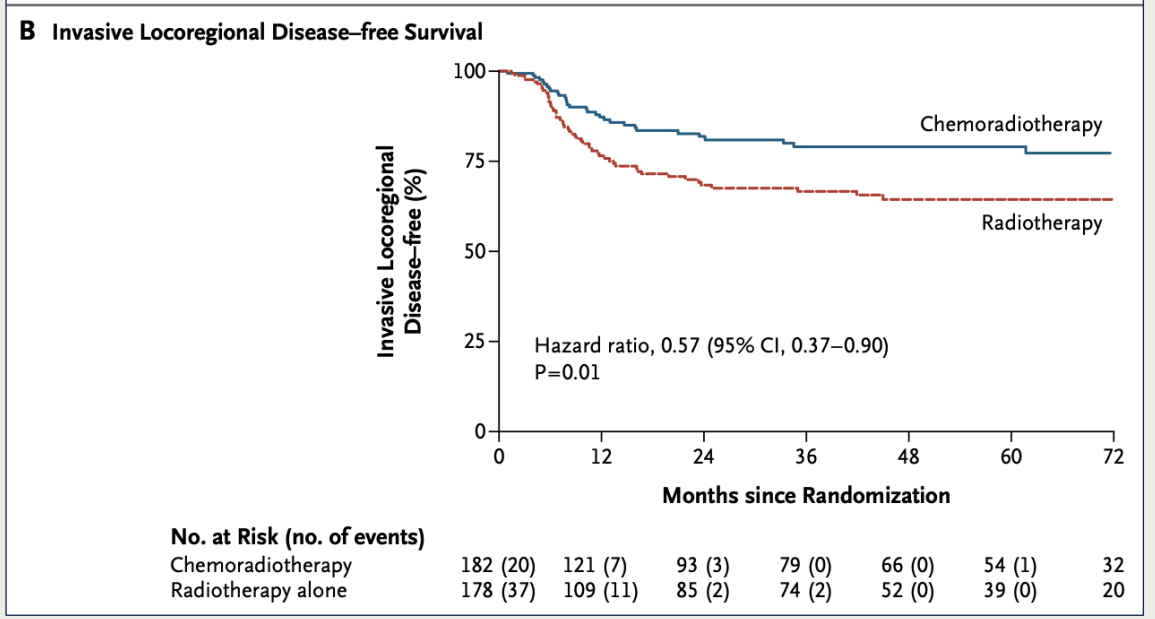
Endpoint	%
5y CSS	90
5y OS	86
Bladder preservation	76
5y RFS	64
Local recurrence	48 (11 MIBC vs 37 NMIBC)
Distant recurrence	2.7

Mazza P, J Urol 2018

TURBT + radiotherapy







James ND, NEJM 2012

TURBT + radiochemotherapy

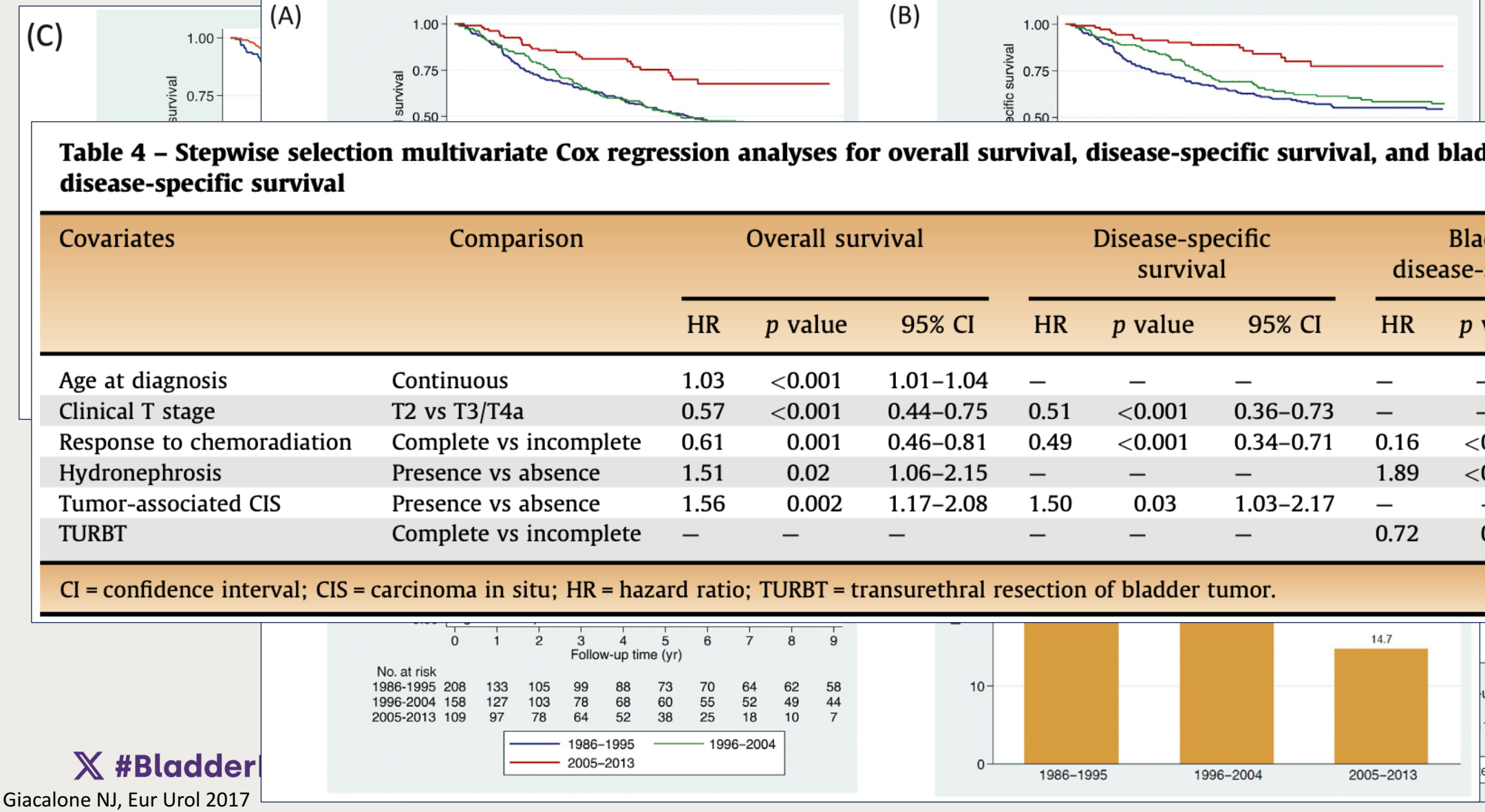


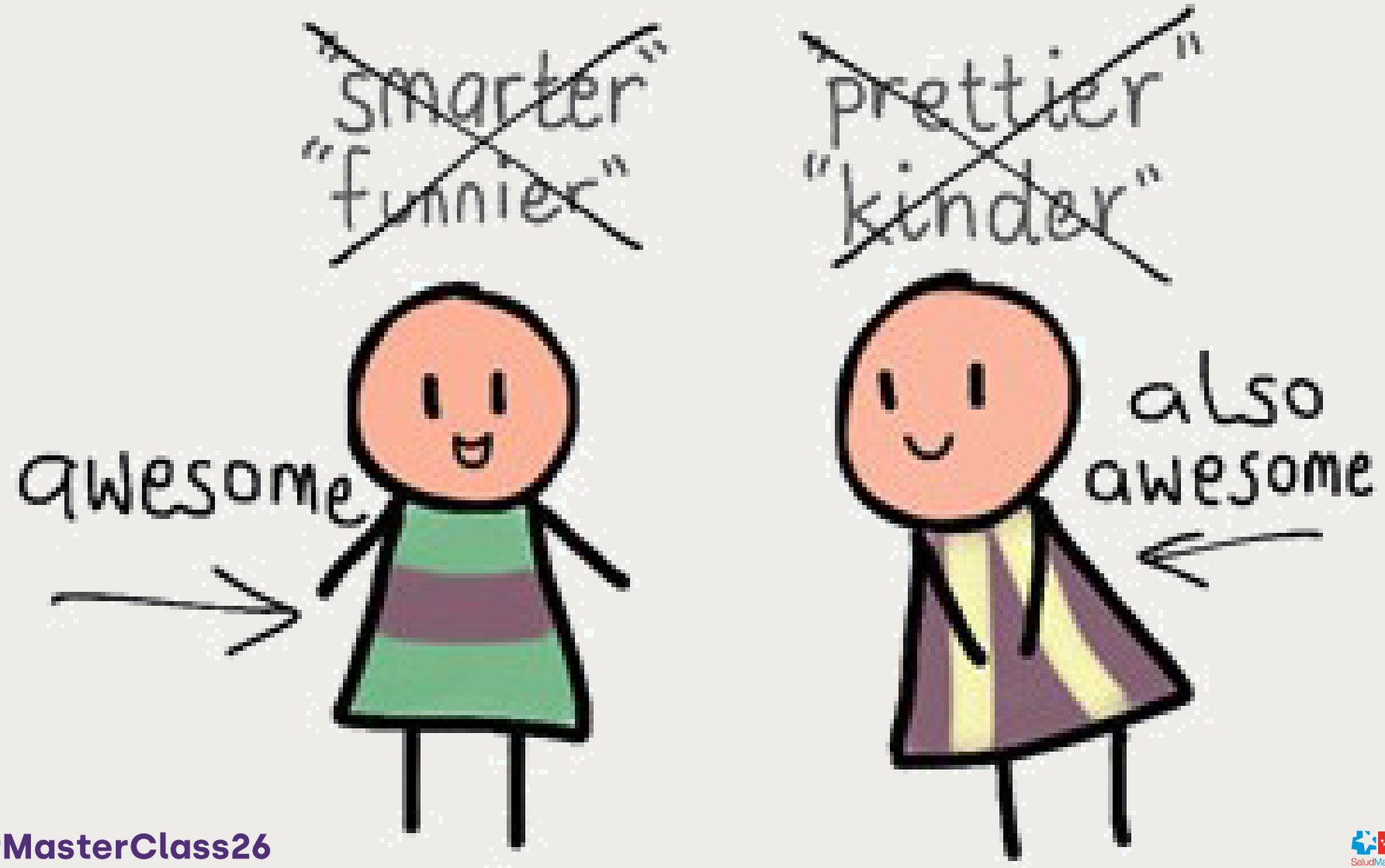
Table 4 – Stepwise selection multivariate Cox regression analyses for overall survival, disease-specific survival, and bladder-intact disease-specific survival

Covariates	Comparison	Overall survival			Disease-specific survival			Bladder-intact disease-specific survival		
		HR	*p* value	95% CI	HR	*p* value	95% CI	HR	*p* value	95% CI
Age at diagnosis	Continuous	1.03	<0.001	1.01–1.04	–	–	–	–	–	–
Clinical T stage	T2 vs T3/T4a	0.57	<0.001	0.44–0.75	0.51	<0.001	0.36–0.73	–	–	–
Response to chemoradiation	Complete vs incomplete	0.61	0.001	0.46–0.81	0.49	<0.001	0.34–0.71	0.16	<0.001	0.12–0.21
Hydronephrosis	Presence vs absence	1.51	0.02	1.06–2.15	–	–	–	1.89	<0.001	1.33–2.63
Tumor-associated CIS	Presence vs absence	1.56	0.002	1.17–2.08	1.50	0.03	1.03–2.17	–	–	–
TURBT	Complete vs incomplete	–	–	–	–	–	–	0.72	0.02	0.55–0.96

CI = confidence interval; CIS = carcinoma in situ; HR = hazard ratio; TURBT = transurethral resection of bladder tumor.

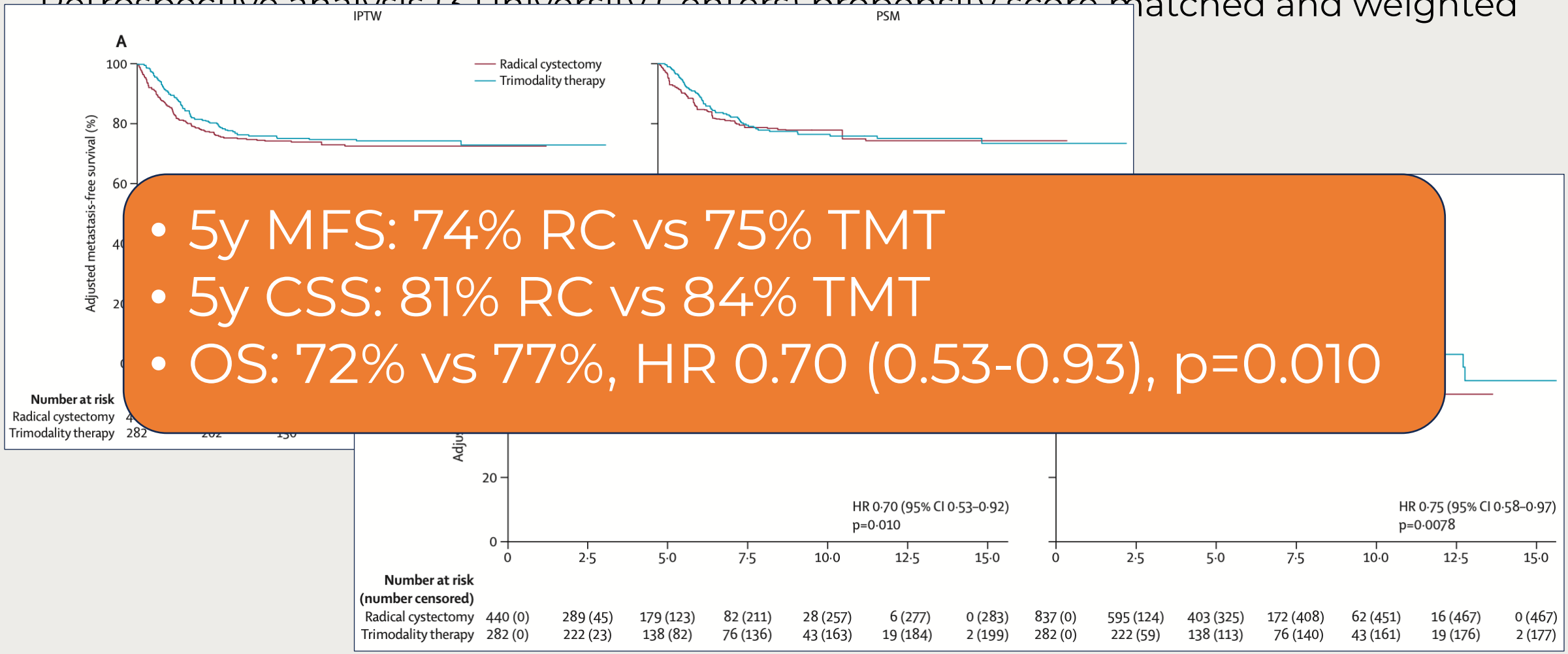
Giacalone NJ, Eur Urol 2017

Let's compare...



TMT vs RC

Retrospective analysis (7 University Centers) propensity score matched and weighted



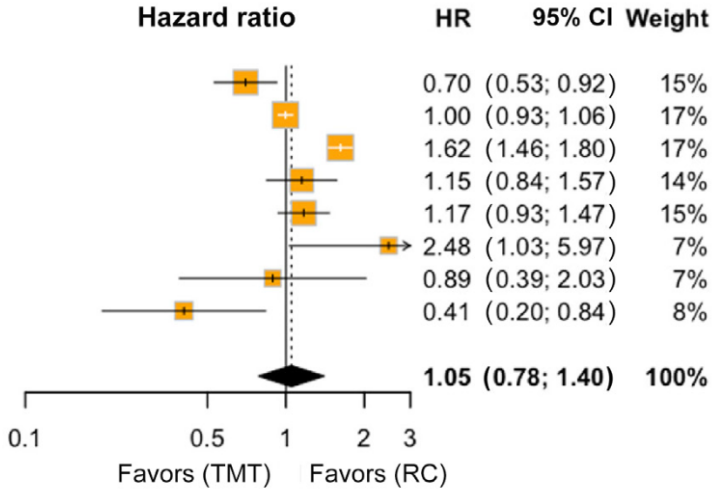
- 5y MFS: 74% RC vs 75% TMT
- 5y CSS: 81% RC vs 84% TMT
- OS: 72% vs 77%, HR 0.70 (0.53-0.93), p=0.010

Zlotta AR, Lancet Oncol 2023

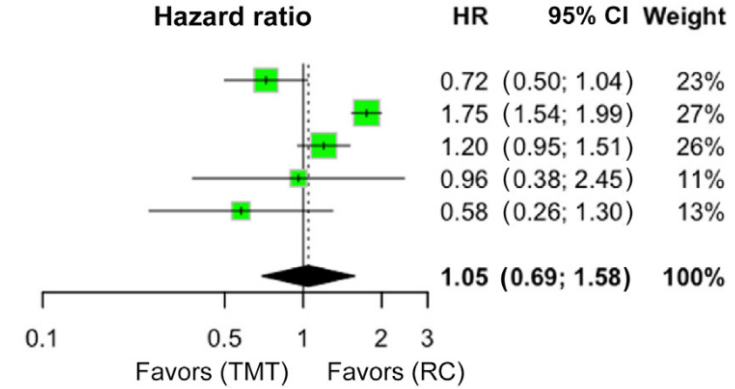
TMT vs RC

- 88 studies (n=28,387)
  - 3 randomized controlled trials
  - 42 prospective nonrandomize
  - 43 retrospective studies (n=25

(A) OS



(B) CSS



Matsukawa A, Eur Urol Focus 2025

NAC + RC vs NAC + observation

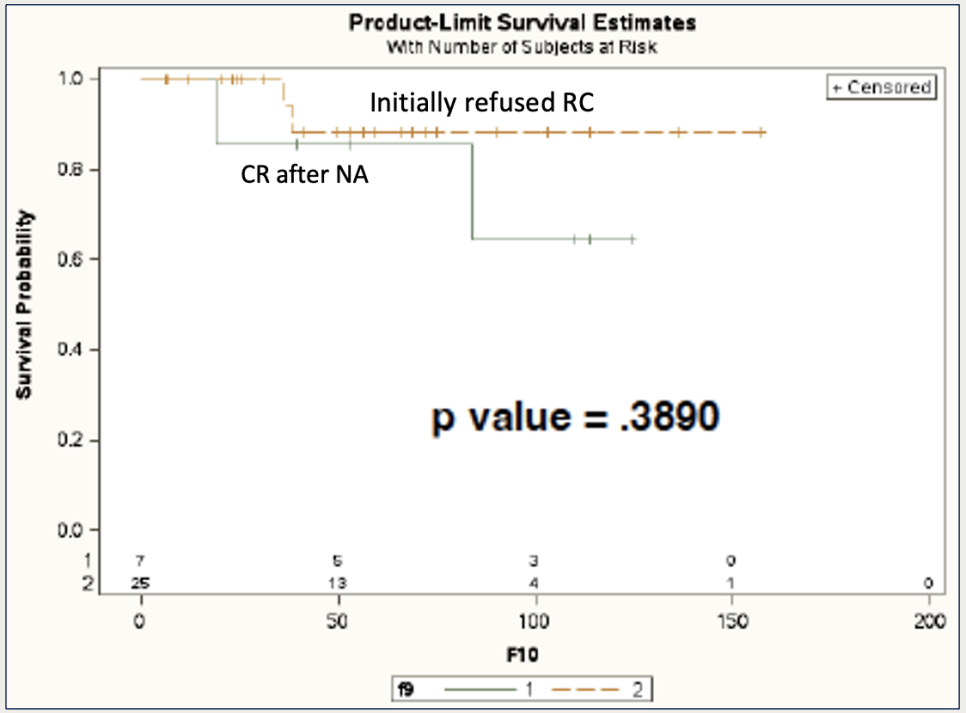
cT2-T4 → NAC → cCR

- 7 radical cystectomy
- 25 observation (refused RC): 7 (28%) relapses → radical cystectomy

5 years CSS (mFU = 54.5 months)

- Radical cystectomy: 88.2%
- Observation ± rescue radical cystectomy: 88.3%

5 years bladder preservation rate = 72%



Meyer A, J Urol 2014

“Cheap” comparisons

Institution	Inclusion criteria	Pts	Schedule: cTURB + …	5-yr OS
IVO	cTURB, R0, cT2	133	Surveillance	73.8%
Erlangen University	cTURB, R0, cT1 (23%), cT2-3 (69%), cT4 (7%)	142	TMT	72%

Are we <u>overtreating</u> with chemo or radiotherapy?

Herr HW, J Clin Oncol 2001; Solsona E, J Urol 2008; Mazza P, J Urol 2018; Krause FS, Anticancer Res 2011

And what about new approaches?

Evolution of clinical trials in MIBC

Classical approach (neo vs adjuvant)

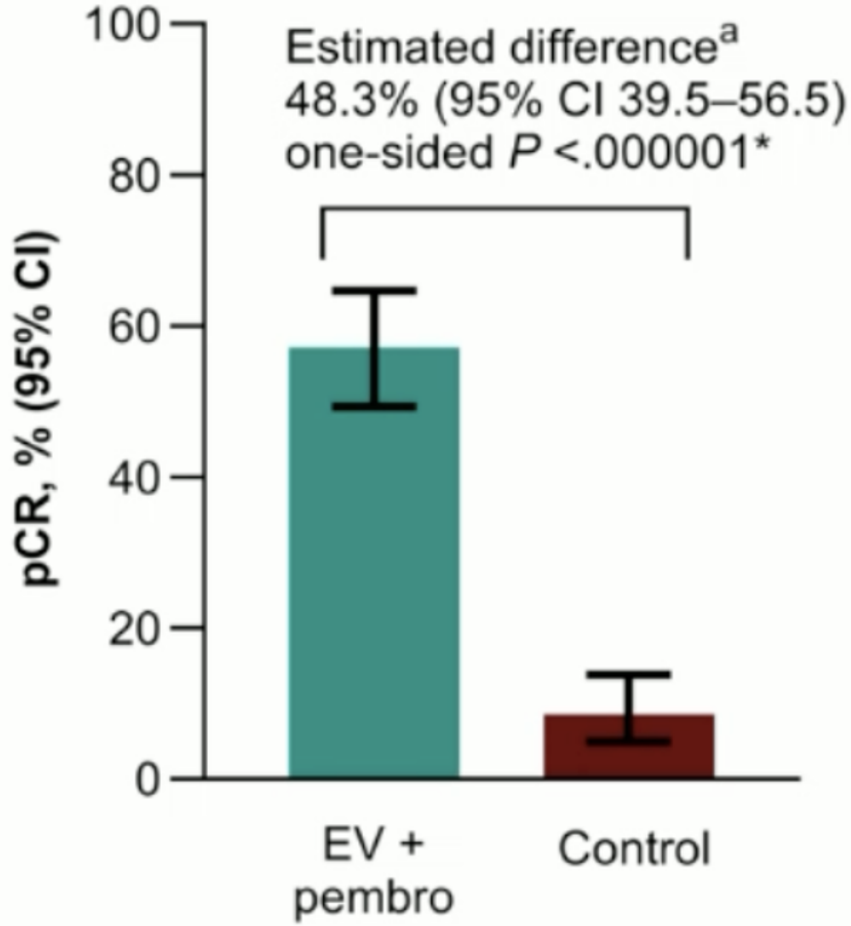
Perioperative approach

Dynamic approach

BIOMARKERS

Why bladder preservation in MIBC?

Just an example: EV-303/KN-905 trial

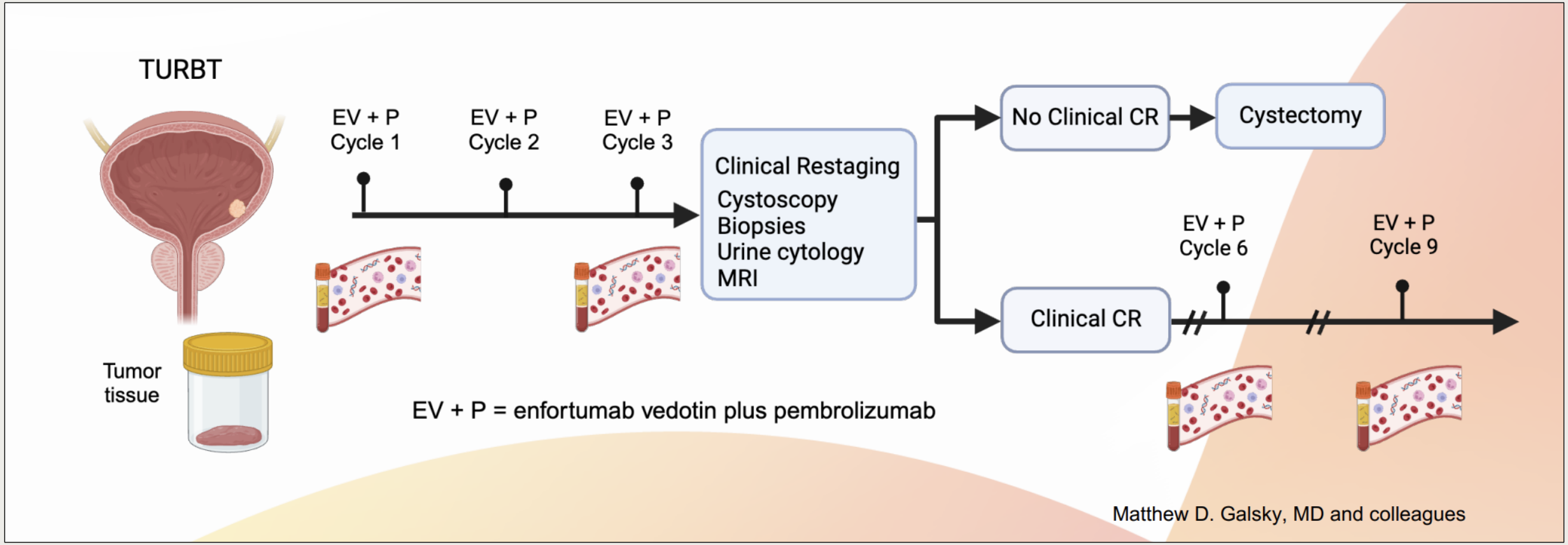


	EV + pembro (N = 170)	Control (N = 174)
pCR, n	97	15
pCR rate, % (95% CI)	57.1 (49.3–64.6)	8.6 (4.9–13.8)

- **pCR:** absence of viable tumor (pT0N0) in examined tissue from RC + PLND
- Pts who did not undergo surgery, including those with clinical complete response after neoadjuvant therapy, were considered non-responders

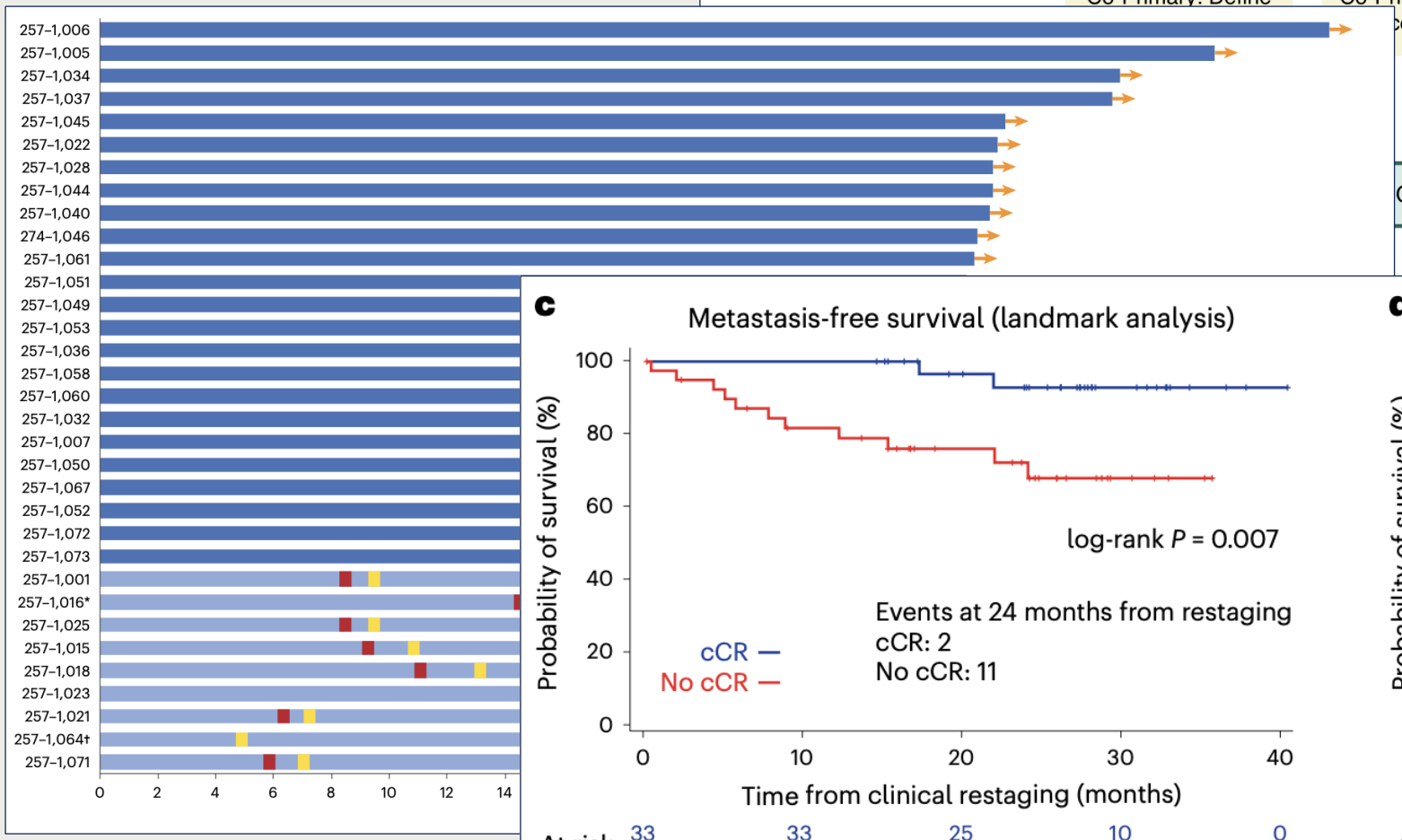
Vulsteke C, ESMO 2025

Coming from EV-303/KN-905 trial...



Galsky MD, NCT06809140

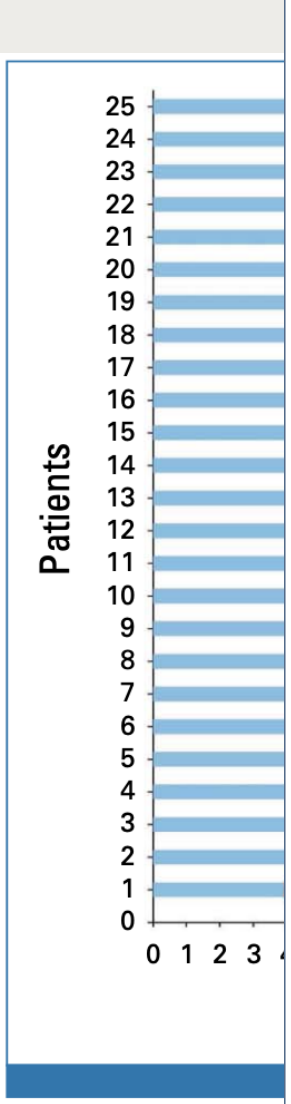
A new concept... HCRN GU16-257

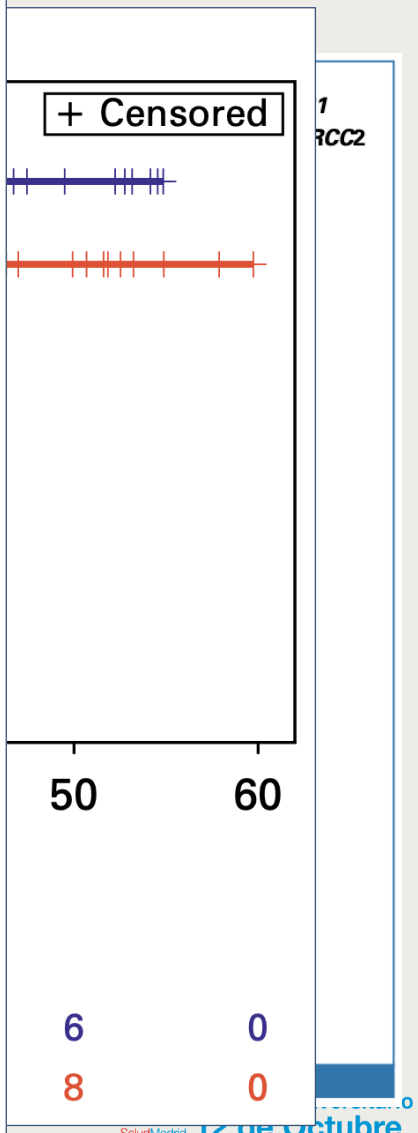


Galsky MD, Nat Med 2023

RETAIN-1

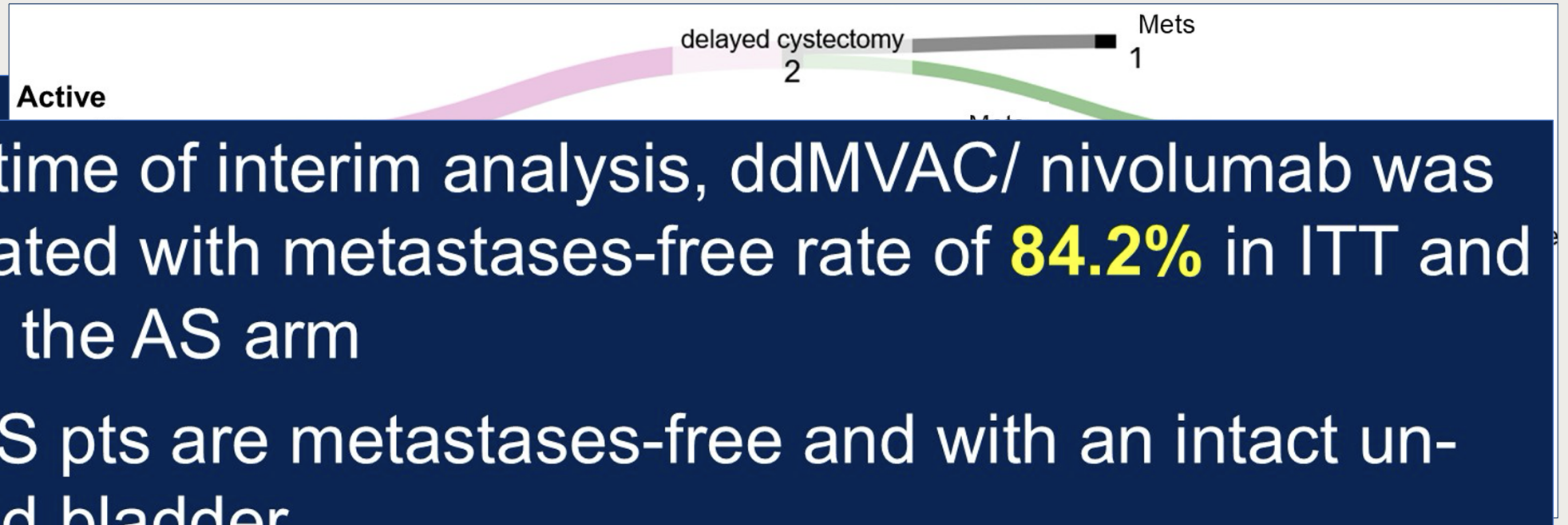
In summary, we conducted a phase II trial to assess the efficacy of NAC followed by a risk-adapted approach to bladder preservation in patients with muscle-invasive urothelial cancer of the bladder. We demonstrated a 24-month MFS in all evaluable patients of 72.9% with 17% (12/70) alive and free of metastases with an intact, nonradiated bladder. These results, on par with recent trials of NAC with a cystectomy-for-all approach, as well as the rapid rate of accrual to this trial, show that this approach, unprecedented at the time we launched this trial, is both feasible and promising. Riding the tide of support gained among clinicians, patients, and our partners in drug and biomarker development in this space, we hope to retain that momentum with the next generation of trials that optimize all aspects of a risk-adapted approach for MIBC.





Geynisman DM, J Clin Oncol 2025

RETAIN-2



Major Inclusion Criteria:

- cT
- Pr
  Ca
- EC

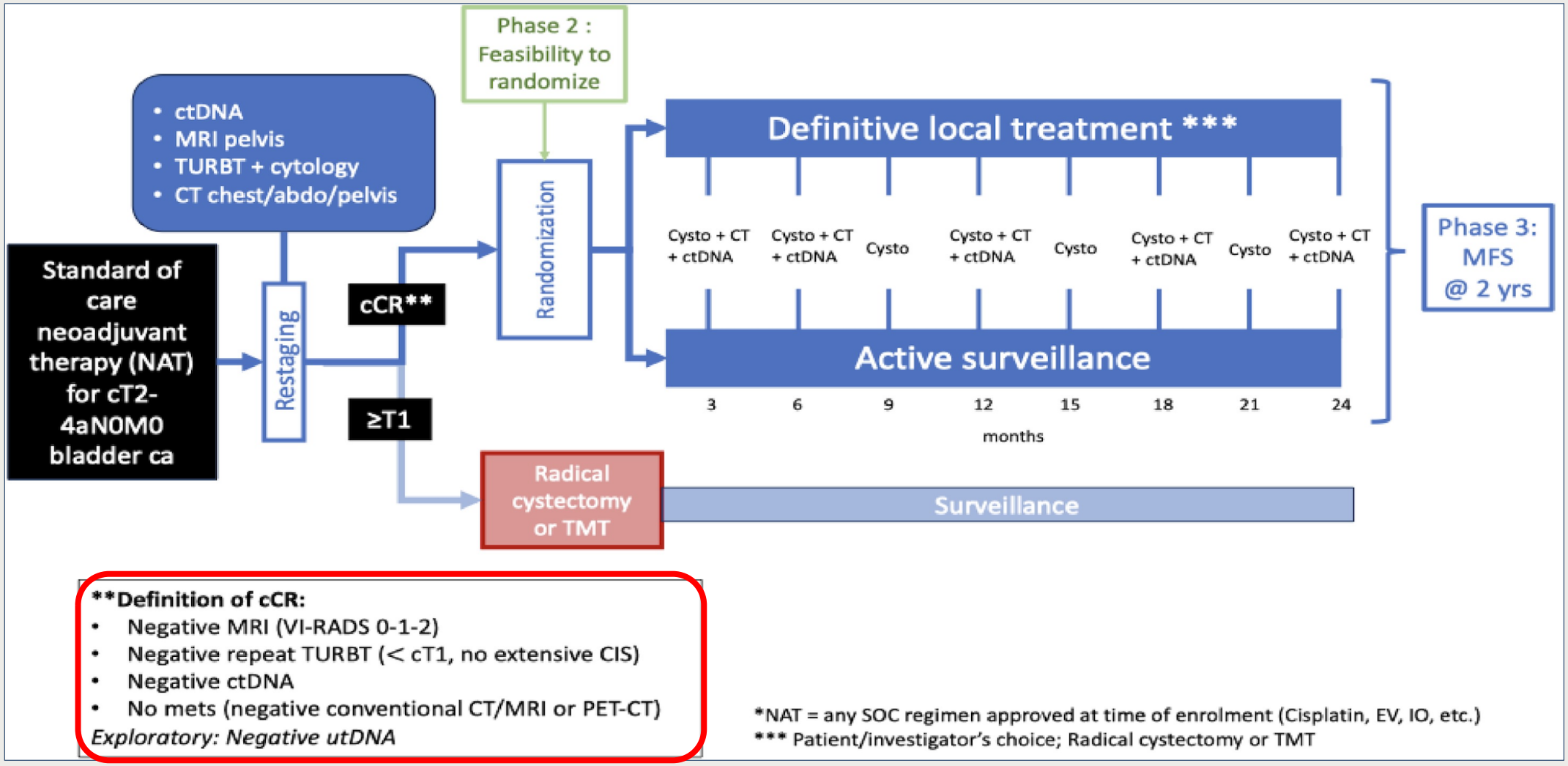
NGS
posi
alter
ATM

Meta
clinic

- At the time of interim analysis, ddMVAC/ nivolumab was associated with metastases-free rate of **84.2%** in ITT and **82%** in the AS arm
- **60%** AS pts are metastases-free and with an intact un-radiated bladder
- Compared to RETAIN-1 the ypT0 rate was higher at **40%** and rate of ypT0 + cCR of **54%** in RETAIN-2 suggesting additive benefit of adding nivolumab to ddMVAC

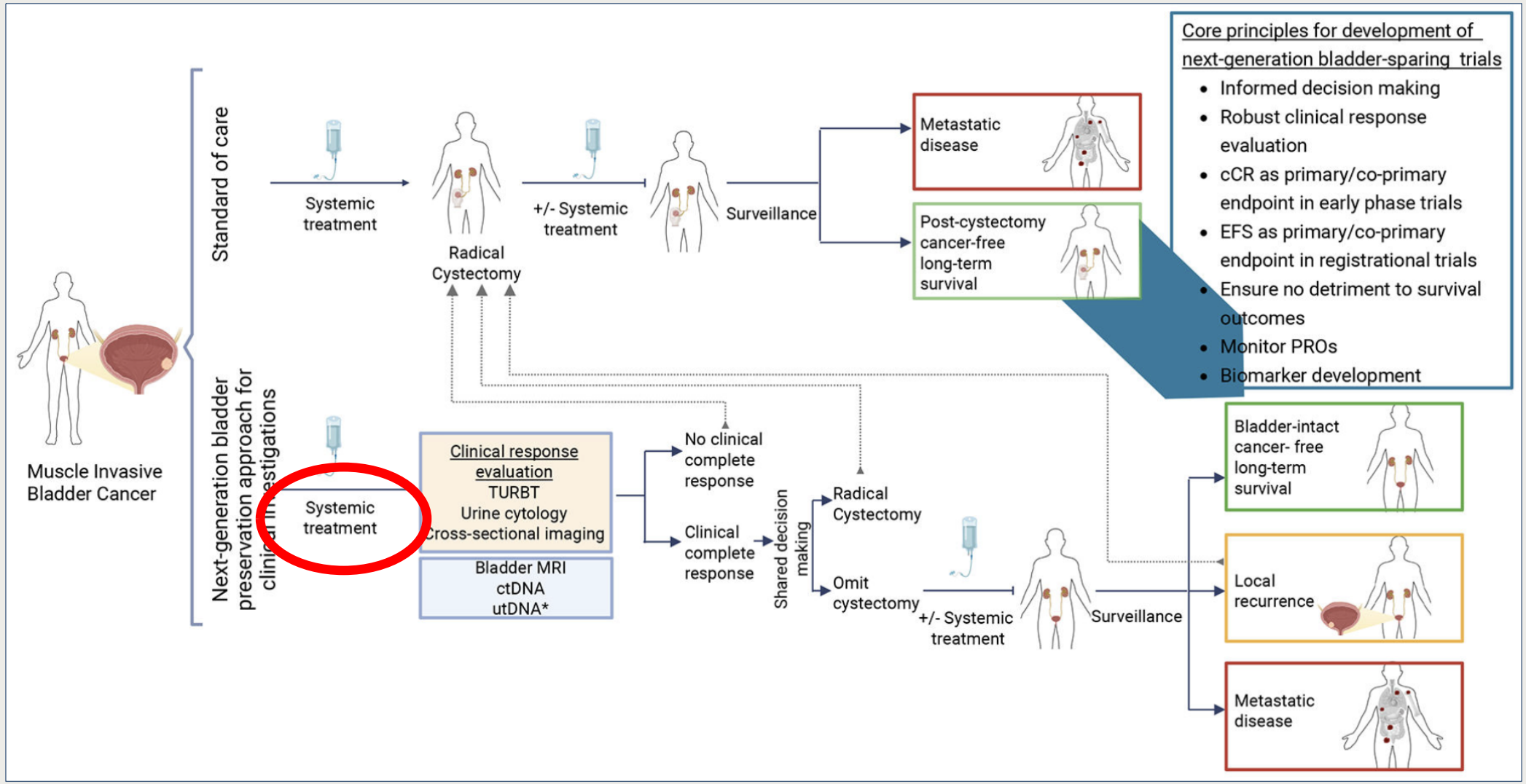
Ghatalia P, ASCOGU 2025

What else is coming? NEO-BLAST



St Laurent MP, ASCOGU 2025

What about the future?

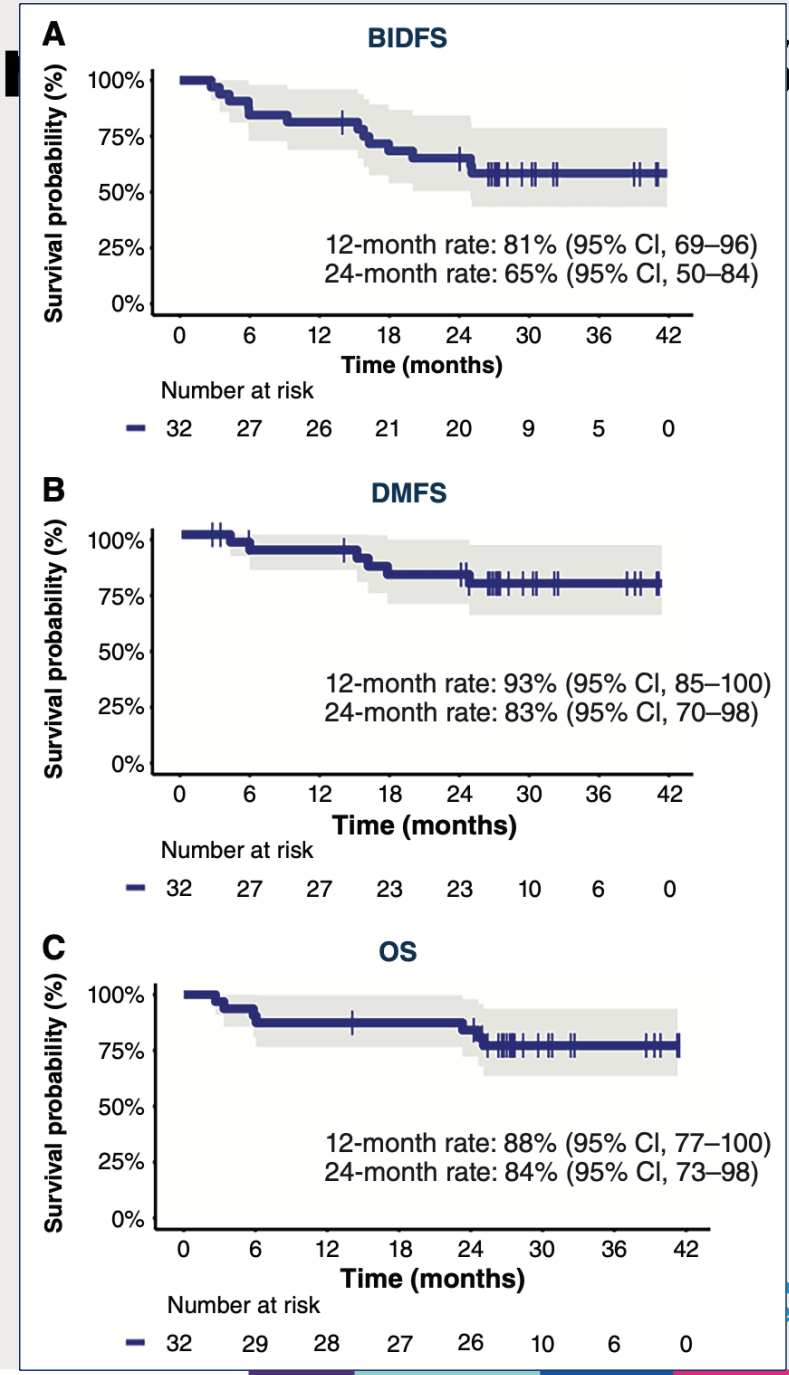


Necchi A, J Clin Oncol 2025

What about the futu ERVE

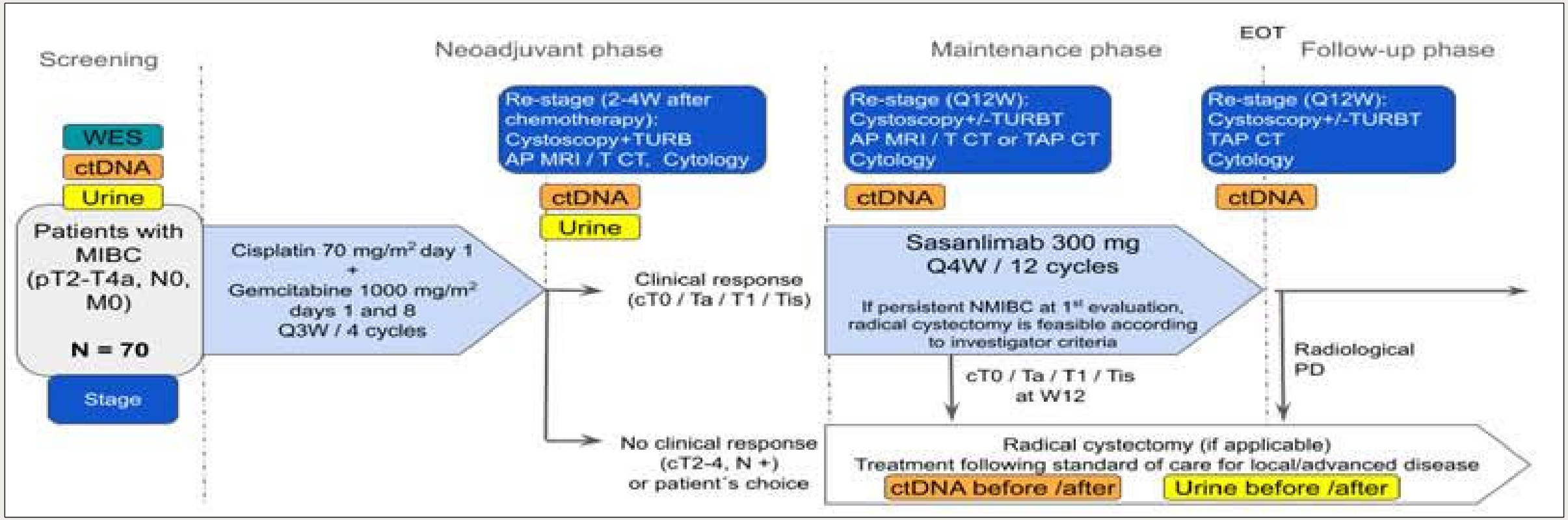
Table 2. Pathologic response rate.

Outcome, *n* (%)	Number of patients (*N* = 32)	95% CI; binomial estimate
CR (≤T1)	26 (81)	(64–93)
T0	25 (78)	—
Non-MIBC (T1, Ta, and Tis)	1 (3)	—
Nonresponse (MIBC)	2 (6)	(1–21)
Not evaluated	4 (13)	(4–29)
Consent withdrawal	1 (3)	—
Clinical deterioration	1 (3)	—
Death from COVID-19	1 (3)	—
Toxic death from peritonitis	1 (3)	—



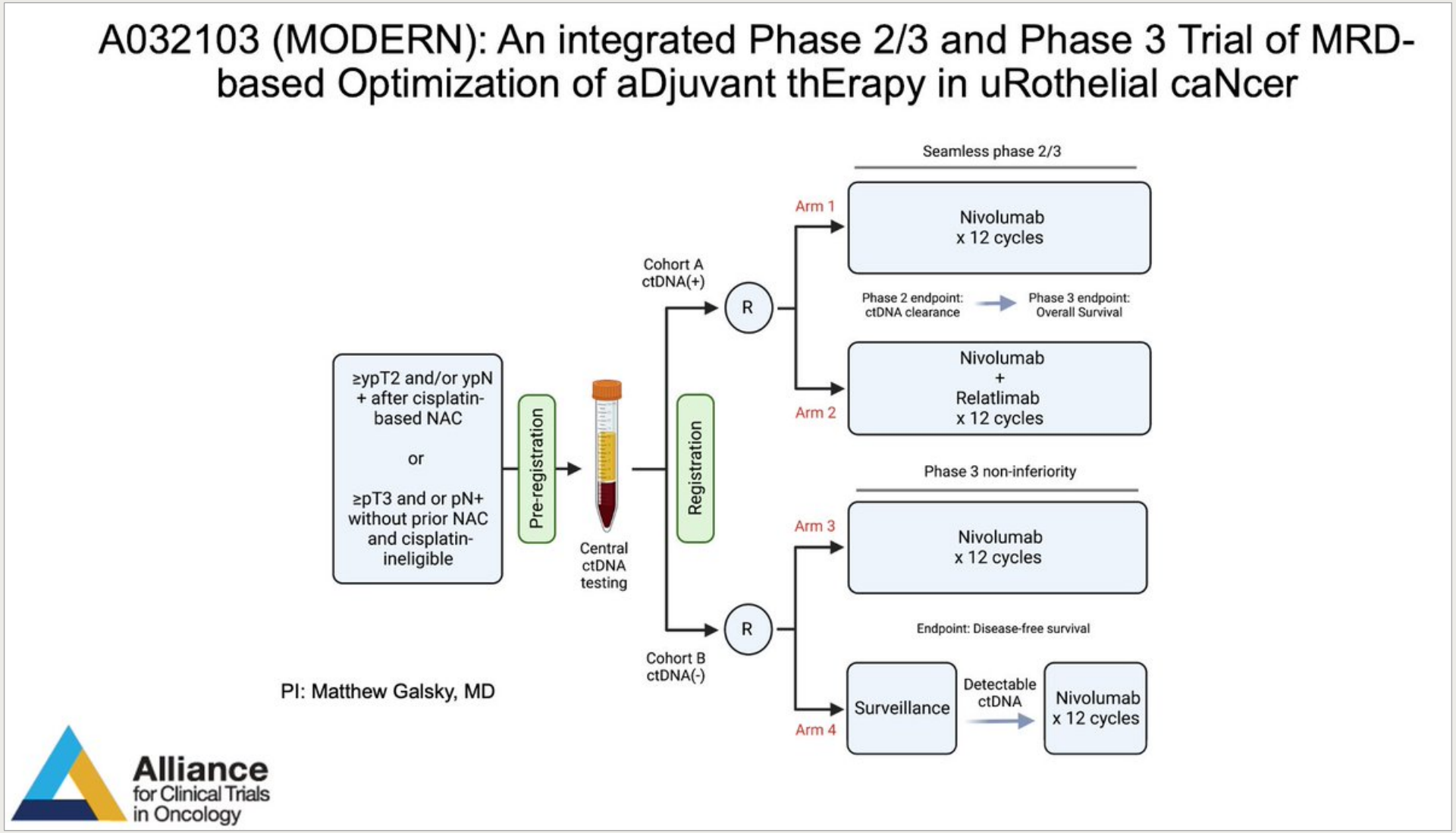
García del Muro X, Clin Cancer Res 2025

What about the future? SASAN-SPARE



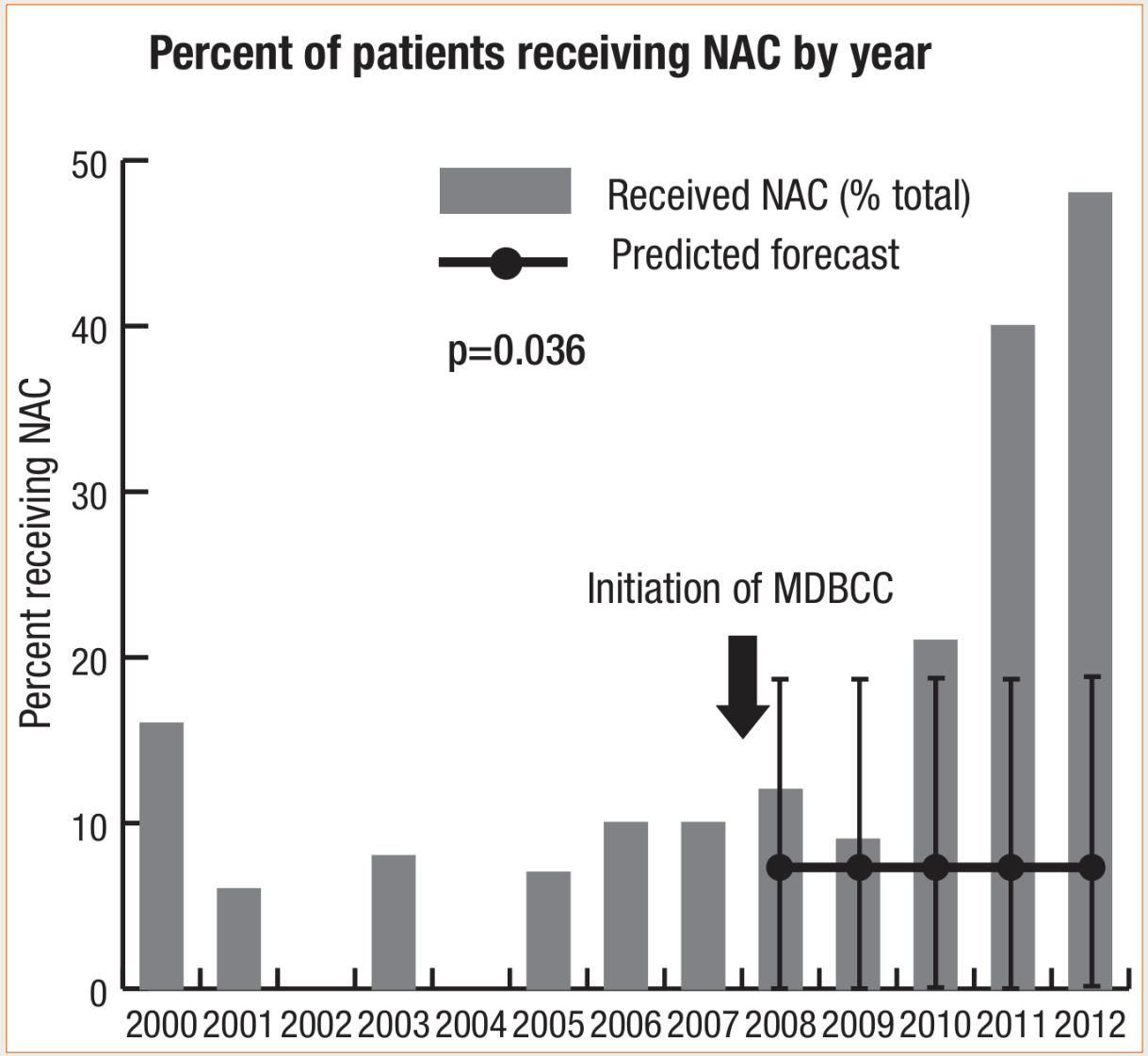
Sevillano E, ASCO 2026

What about the future? MODERN



Galsky M, ASCO-GU 2024

MDT is mandatory



Nayan M, Can Urol Assoc J 2016

MDT is mandatory

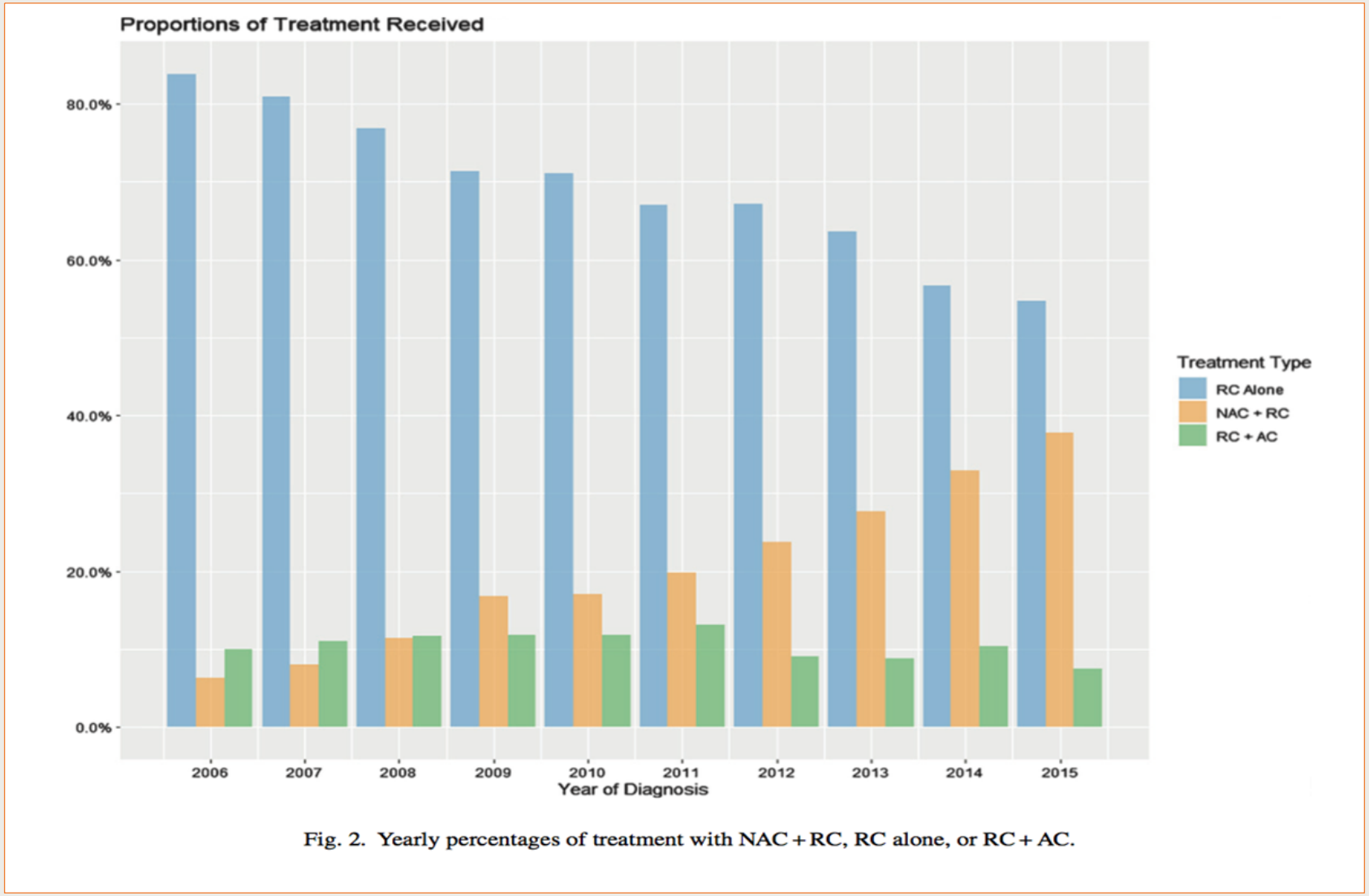


Fig. 2. Yearly percentages of treatment with NAC + RC, RC alone, or RC + AC.

Pfail JL, Bladder Cancer 2020

Take home messages

Bladder preservation is a real option

But… select the RIGHT patients

Low level of evidence, but…

- Some patients may be right
- Different ways of bladder preservation

In the near future: clinical trials

In the medium-long term: less cystectomies

Always within MDT

We need biomarkers!!!

MasterClass in Bladder Cancer 2026

¡GRACIAS!

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#BladderMasterClass26

Hospital Universitario 12 de Octubre