

#guardsymposium2025
X @GuardConsortium



GUARD **INTERNATIONAL** **SYMPOSIUM**

GU-Alliance for Research and Development

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

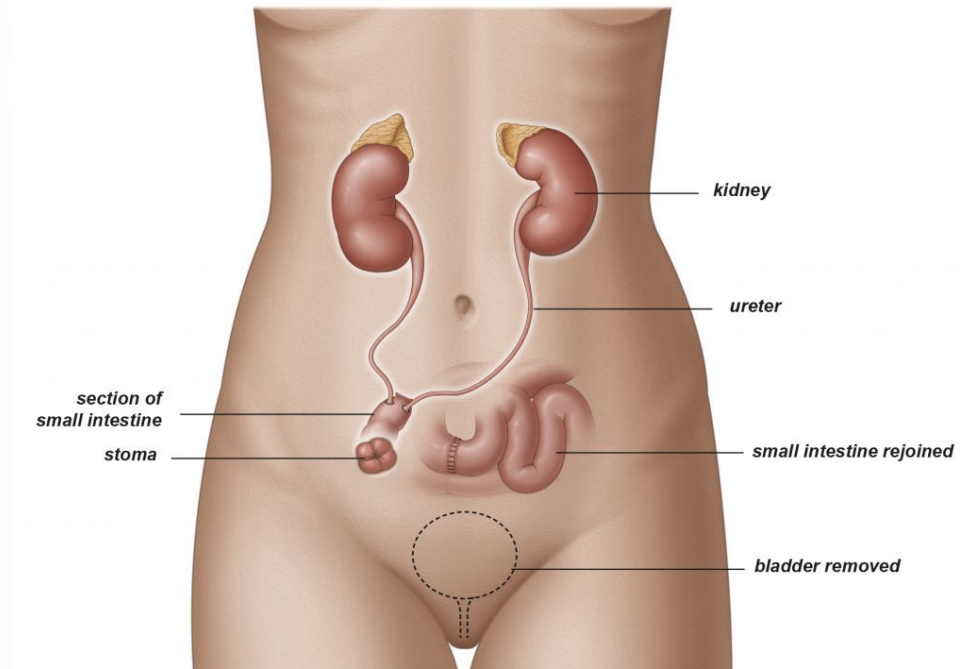
26-27 JUNIO 2025

Espacio Maldonado, Madrid

How to select patients in whom we preserve the bladder without local treatment?

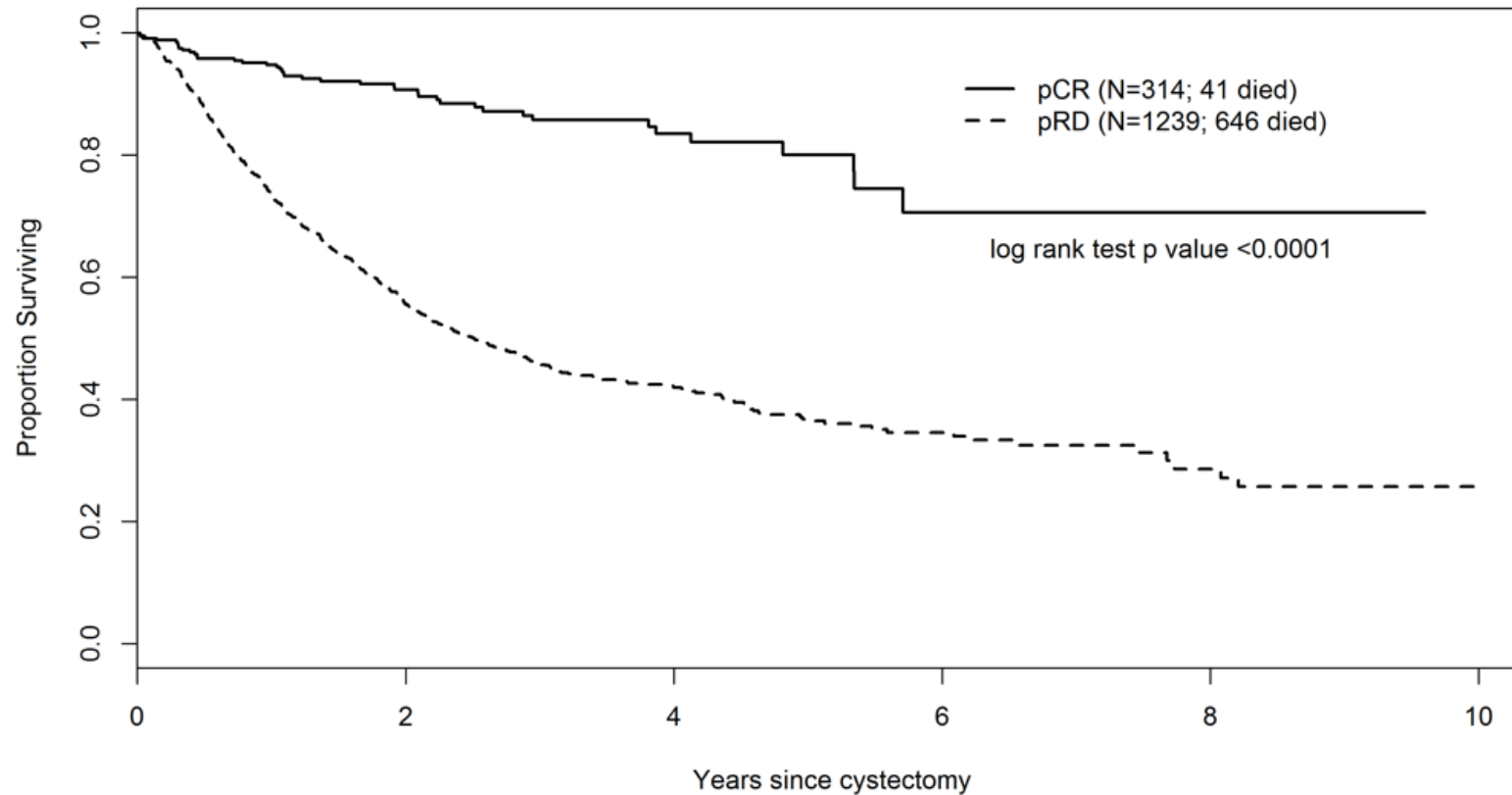
Matthew D. Galsky, MD
Icahn School of Medicine at Mount Sinai

Radical cystectomy is standard treatment for MIBC but has major disadvantages

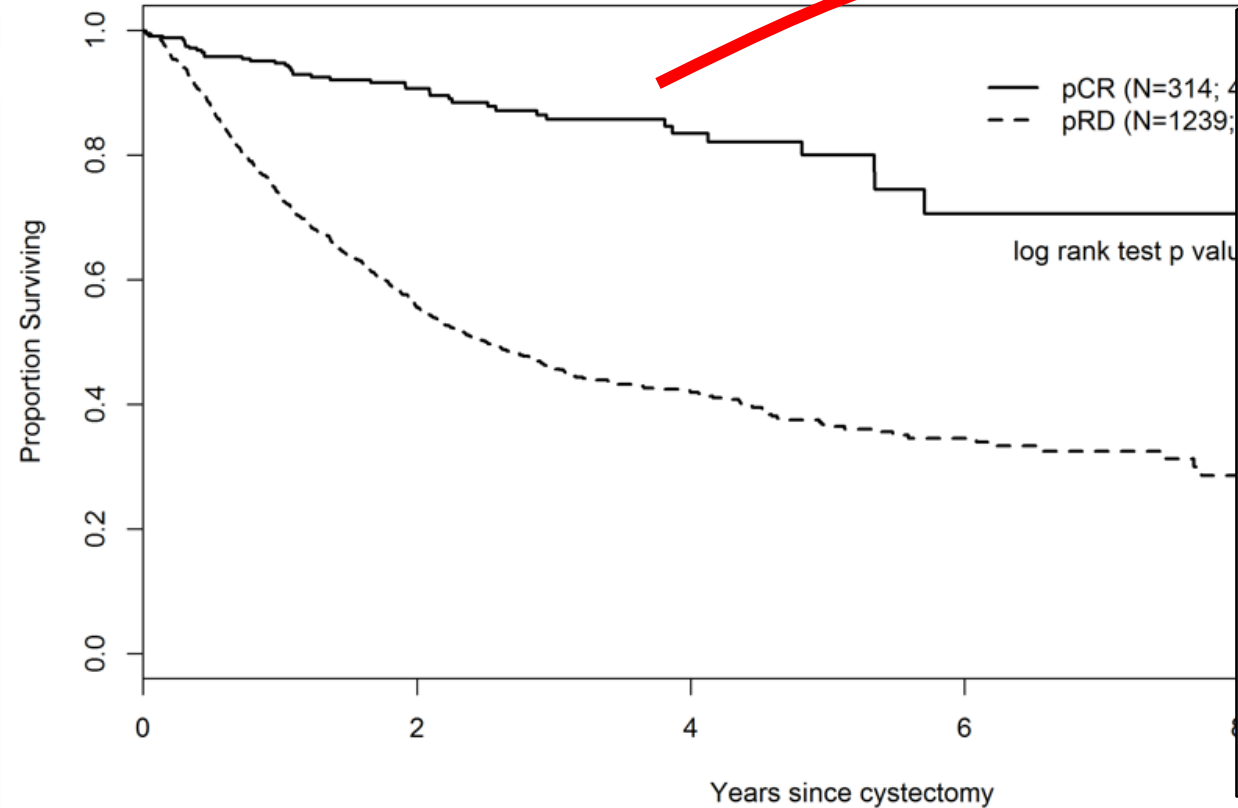


Not everyone *can* have it, not everyone *should* have it, not everyone *wants* it

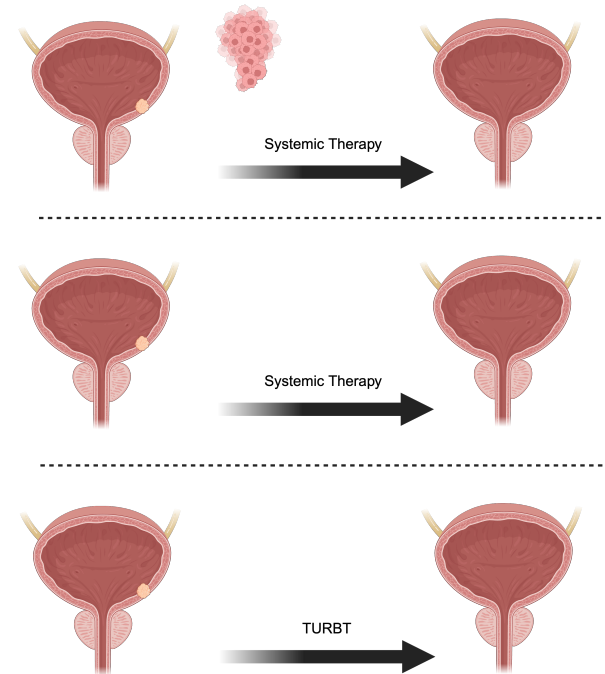
The Framework



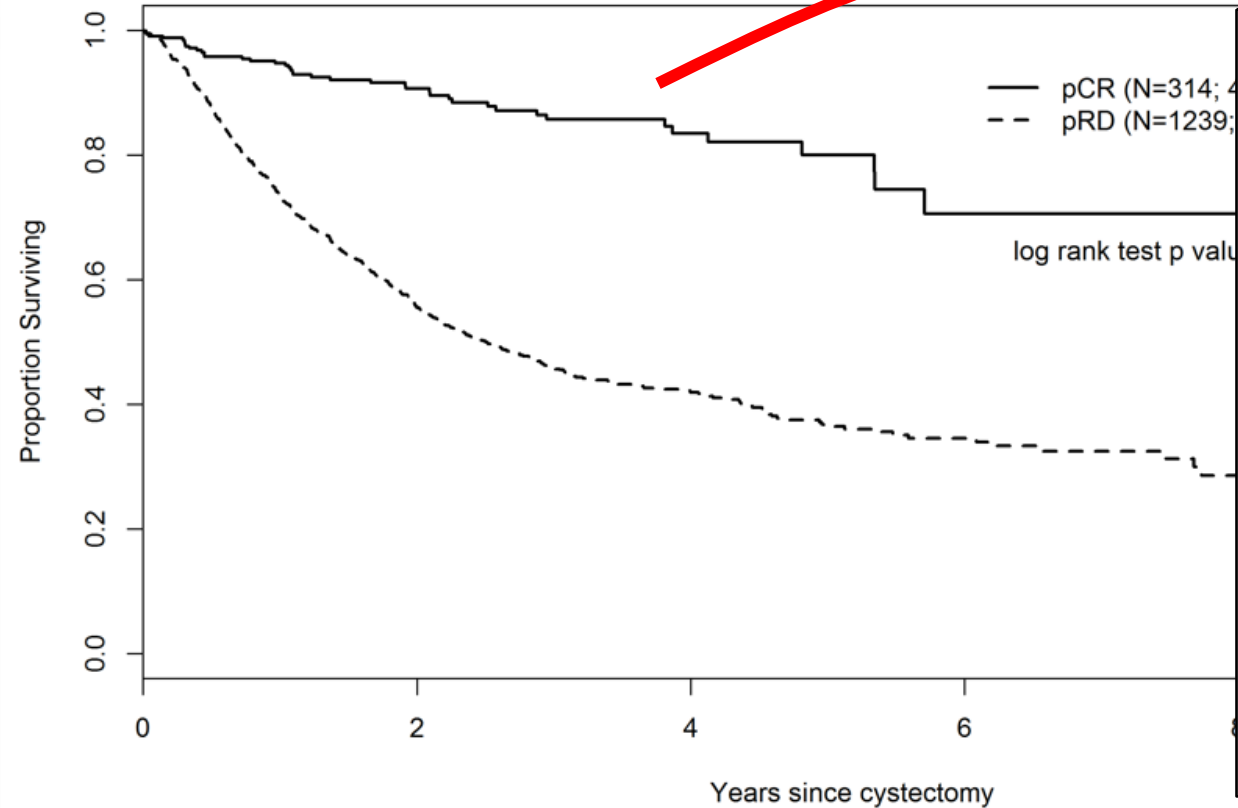
The Framework



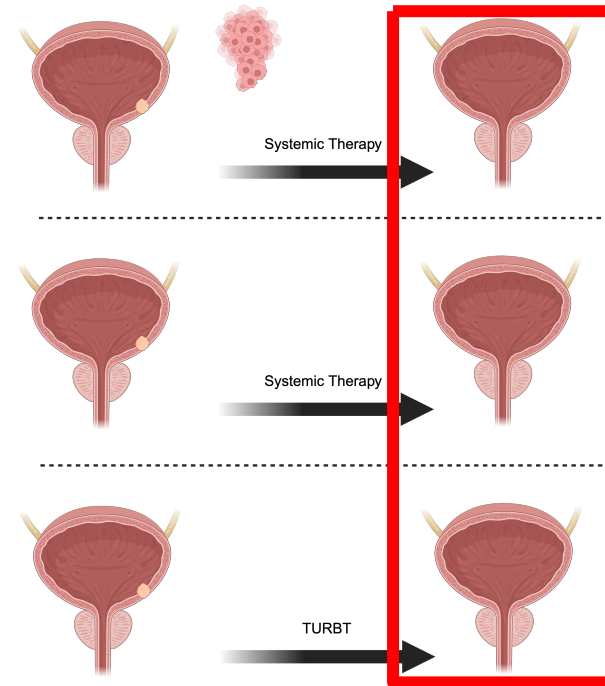
Who are these patients?



The Framework



Who are these patients?



The Framework

Neoadjuvant Chemotherapy and Bladder-Sparing Surgery for Invasive Bladder Cancer: Ten-Year Outcome

By Harry W. Herr, Dean F. Bajorin, and Howard I. Scher

Purpose: To evaluate the 10-year outcome of patients with invasive (T2-3N0M0, staged according to the tumor, node, metastasis system) bladder cancer who responded completely to a combination of methotrexate, vinblastine, adriamycin, and cisplatin (MVAC) chemotherapy followed by bladder-sparing surgery.

Patients and Methods: Of 111 surgical candidates who received neoadjuvant MVAC, 60 (54%) achieved a complete clinical response (T0) on transurethral resection (TUR) of the primary tumor site. Of these, 28 requested follow-up with TUR alone, 15 had a partial cystectomy, and 17 elected a radical cystectomy. The patients were followed up for a median of 10 years (range, 8 to 13 years).

Results: Of 43 patients who had bladder-sparing surgery, 32 (74%) are alive, which includes 25 (58%)

with an intact functioning bladder. Twenty-four patients (56%) developed bladder tumor recurrences from 5 to 96 months, which were invasive in 13 (30%) and superficial in 11 (26%). Thirteen patients required a salvage cystectomy, of whom 6 died, which includes 4 (9%) from a new invasive neoplasm. Of the 17 patients who had radical cystectomy, 11 (65%) are alive.

Conclusion: The majority of patients with invasive bladder tumors who achieve T0 status after neoadjuvant MVAC chemotherapy preserve their bladders for up to 10 years with bladder-sparing surgery. The bladder remains at risk for new invasive tumors. Cystectomy salvages the majority, but not all, of relapsing patients.

J Clin Oncol 16:1298-1301. © 1998 by American Society of Clinical Oncology.

The Framework

Neoadjuvant Chemotherapy and Bladder-Sparing Surgery for Invasive Bladder Cancer: Ten-Year Outcome

Retrospective studies and anecdotes tell us what can be achieved but not necessarily if it *should* be achieved or how it should be achieved

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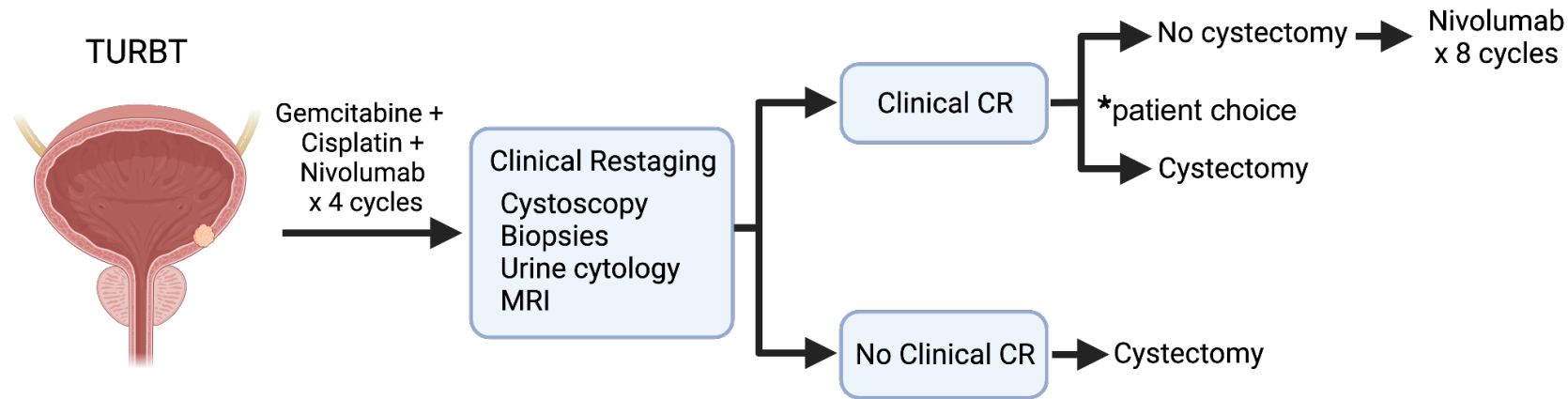
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J Clin Oncol 16:1298-1301. © 1998 by American Society of Clinical Oncology.

Historical barriers to TURBT + systemic therapy as definitive treatment for MIBC

1. Paucity of prospective studies.
2. Lack of rigorous methods to measure and define *clinical* complete response.
3. Limited understanding of the role of “delayed” cystectomy in patients with local recurrence.
4. Suboptimal systemic therapeutic regimens.
5. Absence of biomarkers to refine decision making.

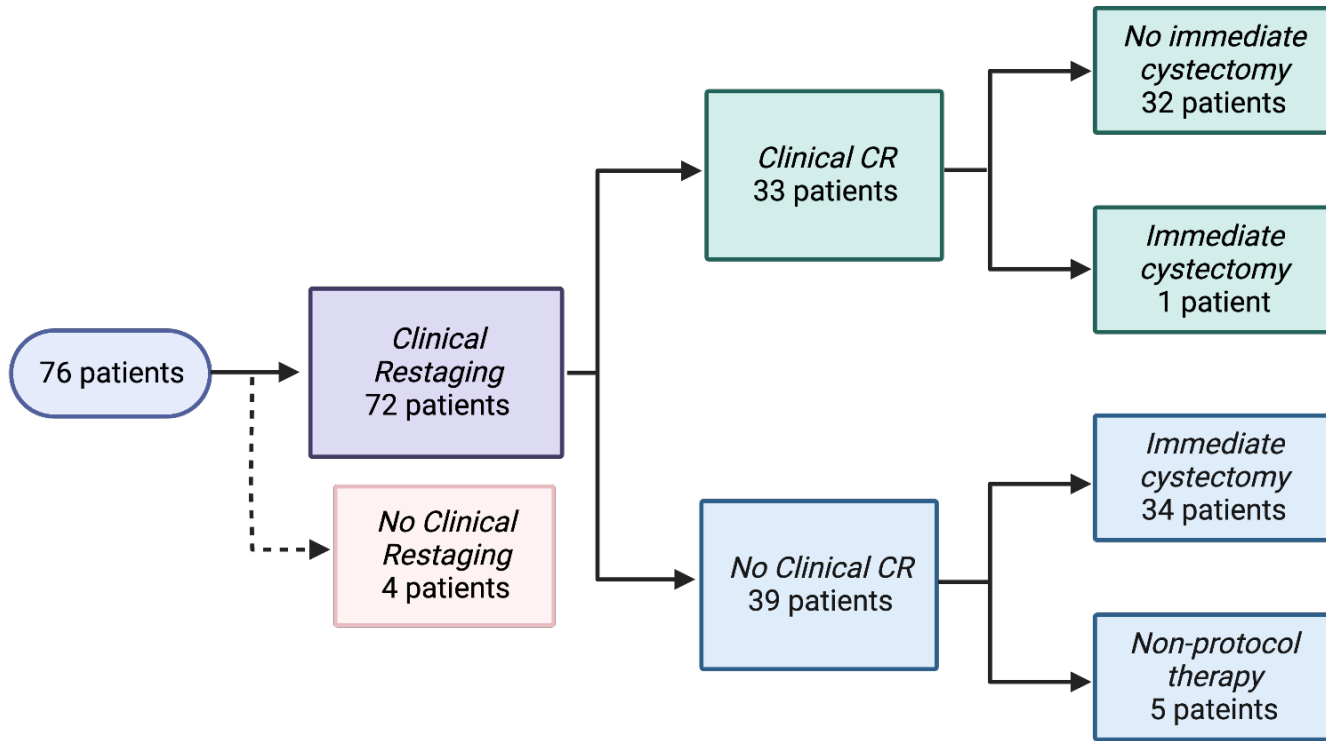
HCRN GU16-257: Response-guided bladder sparing



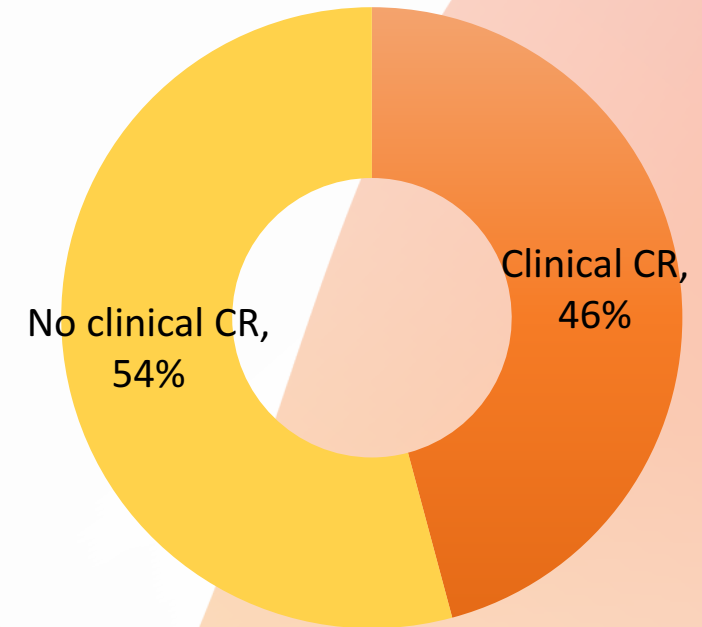
- Co-primary endpoints {
- Clinical complete response (CR) rate
 - Performance of clinical CR in predicting treatment *benefit*:
 - ❖ 2 year metastasis free if no cystectomy
 - ❖ pCR in immediate cystectomy

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HCRN GU16-257: Response-guided bladder sparing



Clinical CR rate = 43% (95% CI: 32%, 55%)



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Measuring and defining clinical complete response

Cystoscopy and biopsies
Imaging (MRI)
Urine cytology

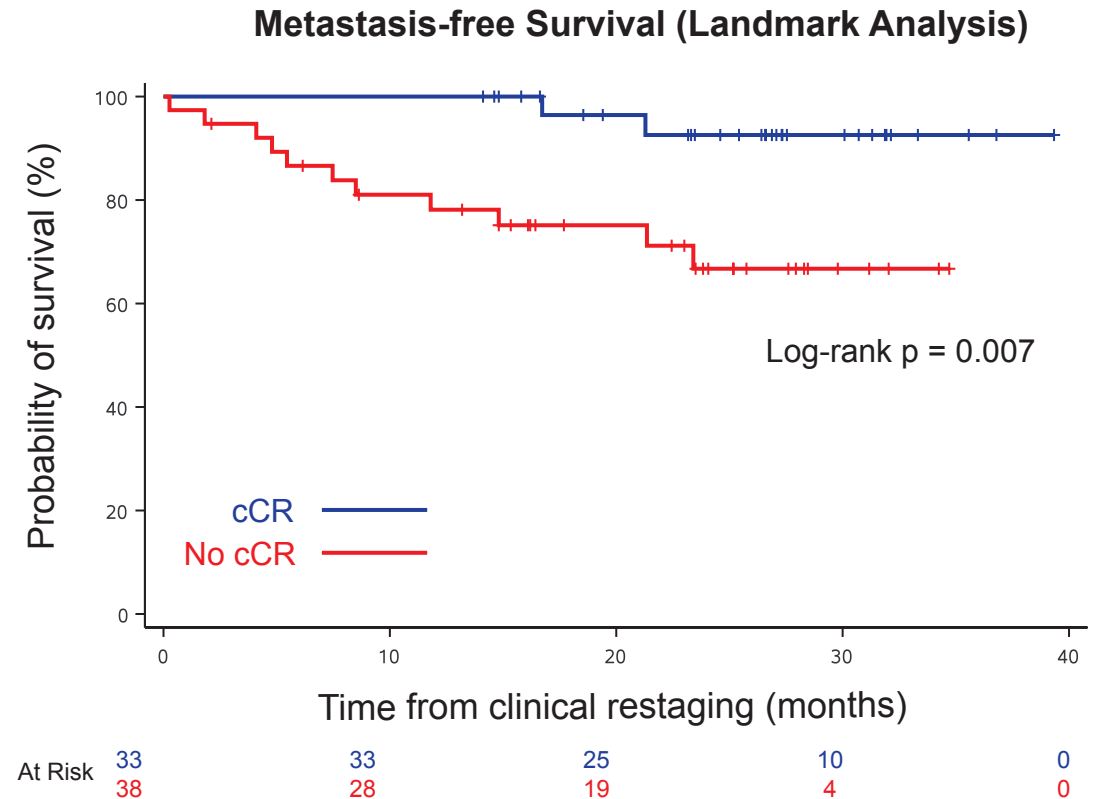
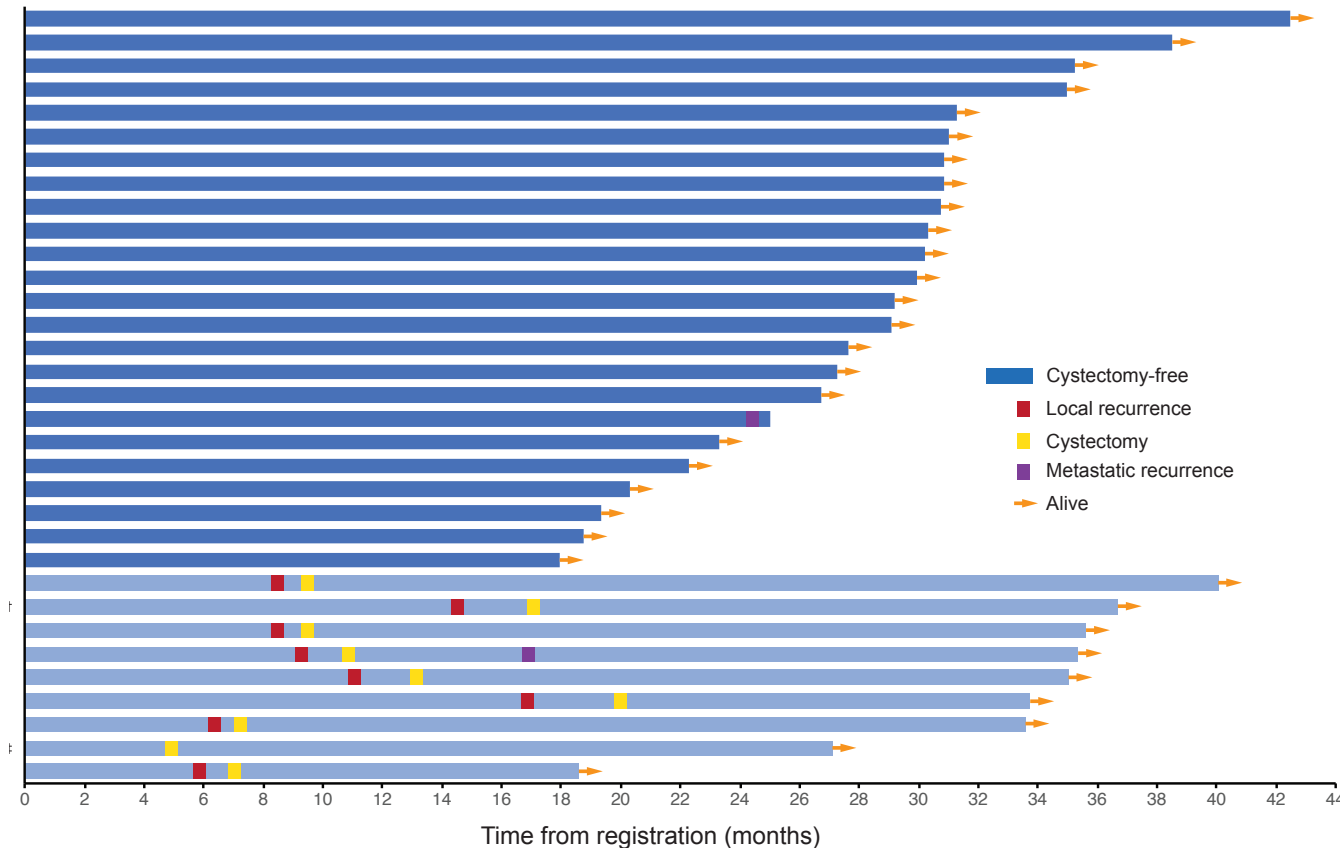
Clinical complete response:

- no evidence of high-grade malignancy on biopsy
- no malignant cells on urine cytology
- no definitive evidence of local or metastatic disease on cross-sectional imaging

Cystoscopic assessment of bladder tumors

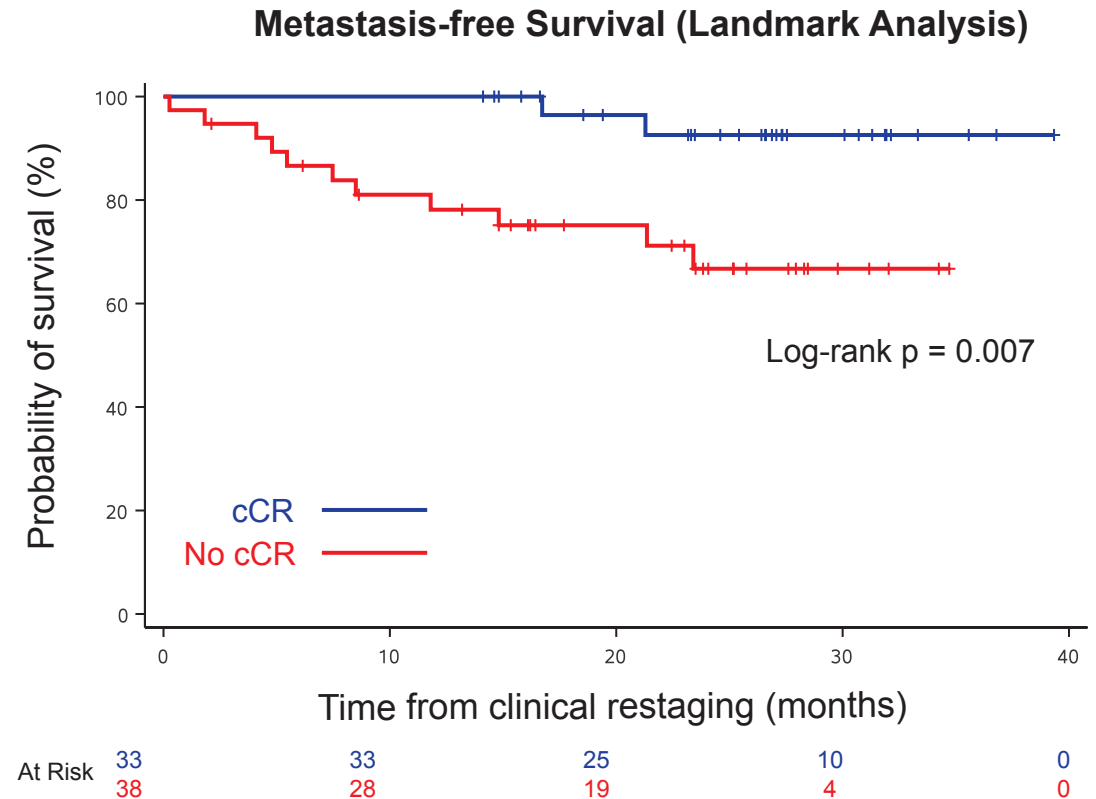
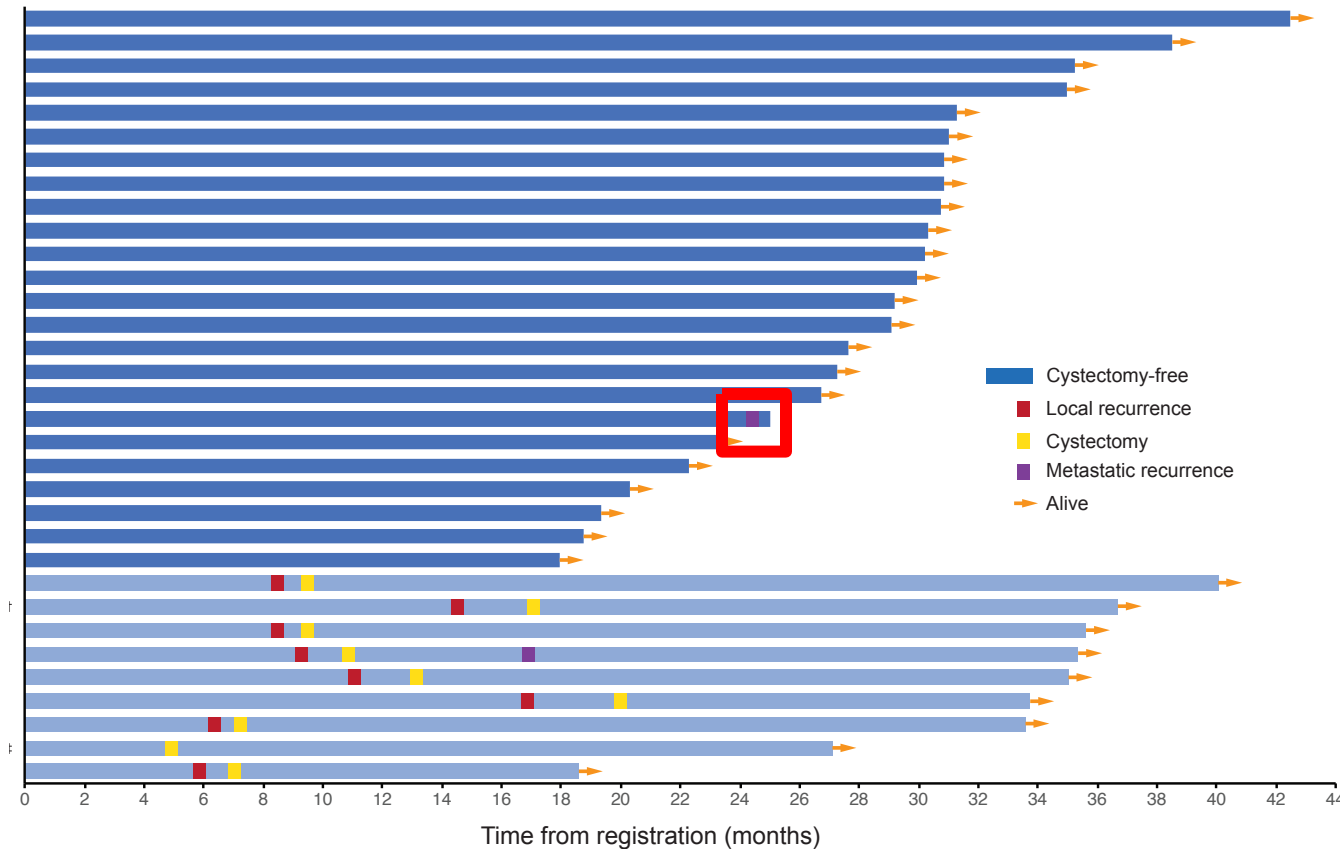
Site	# of biopsies	Lesion score	Lesion Subscript	Comments
Prior tumor site/scar				
Trigone				
Left				
Right				
Anterior				
Posterior				
Dome				
Prostatic urethra				

HCRN GU16-257: Clinical Outcomes



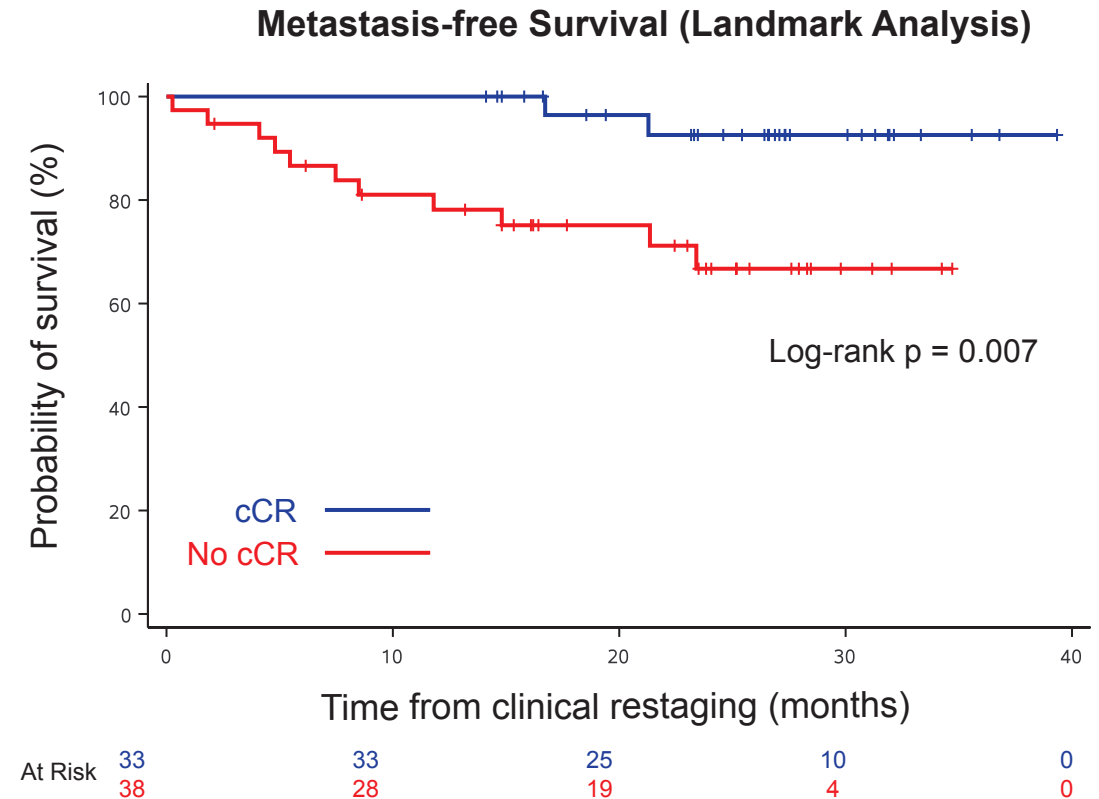
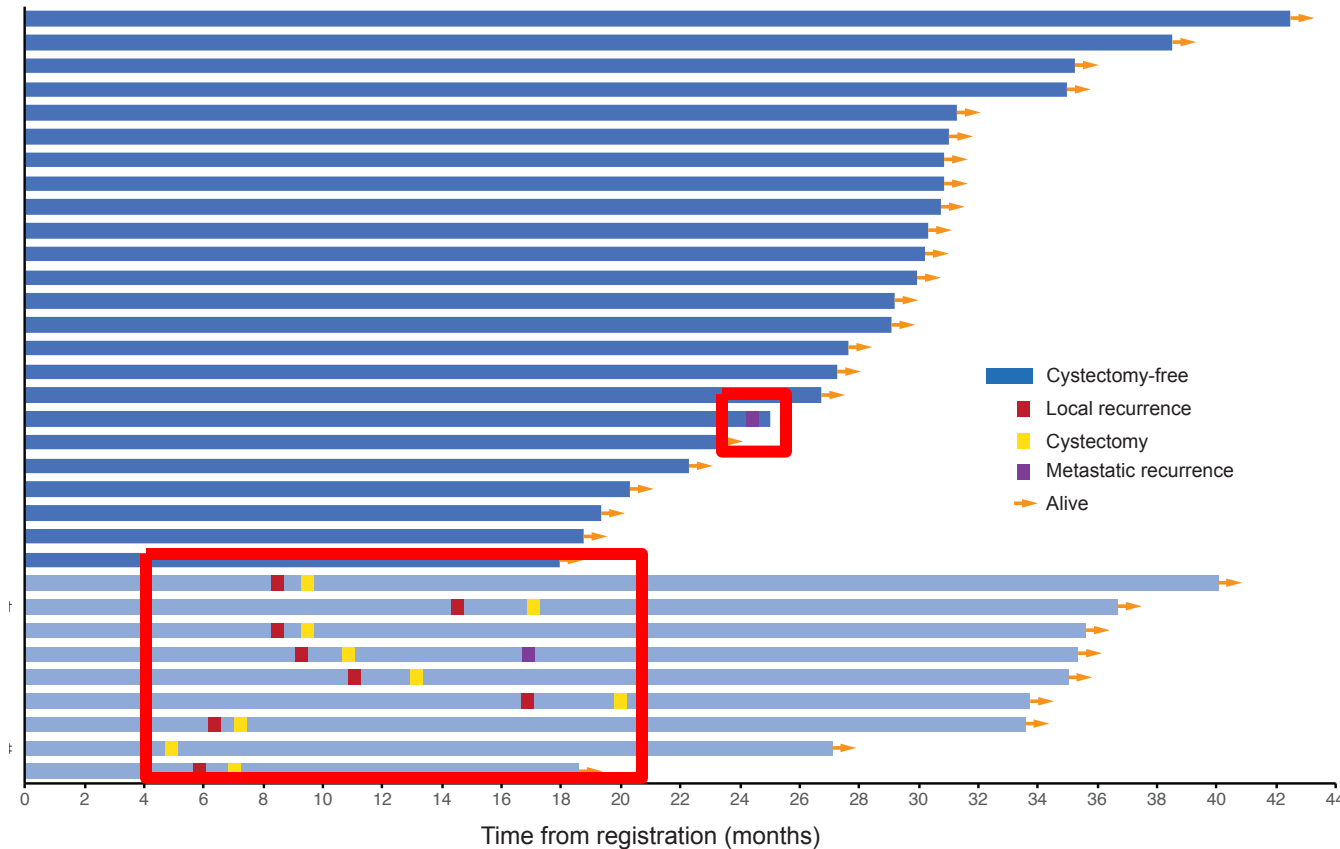
Galsky et al Nature Medicine 2023

HCRN GU16-257: Clinical Outcomes



Galsky et al Nature Medicine 2023

HCRN GU16-257: Clinical Outcomes

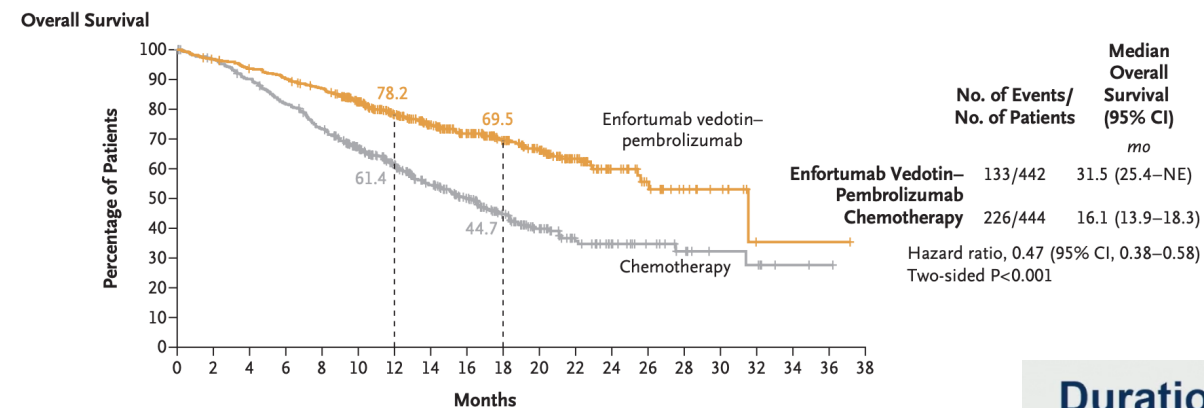


Galsky et al Nature Medicine 2023

How do we improve upon this paradigm?

- Integrate systemic therapies that are more generalizable
- Integrate systemic therapies that are more effective
- Discover biomarkers to refine out ability to identify patients who could most safely forgo cystectomy
- Define mechanisms of intrinsic resistance to guide development of next-generation regimens

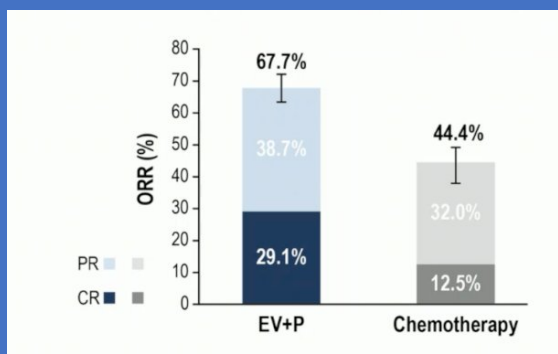
EV + Pembrolizumab in metastatic UC



No. at Risk
Enfortumab vedotin–pembrolizumab
Chemotherapy

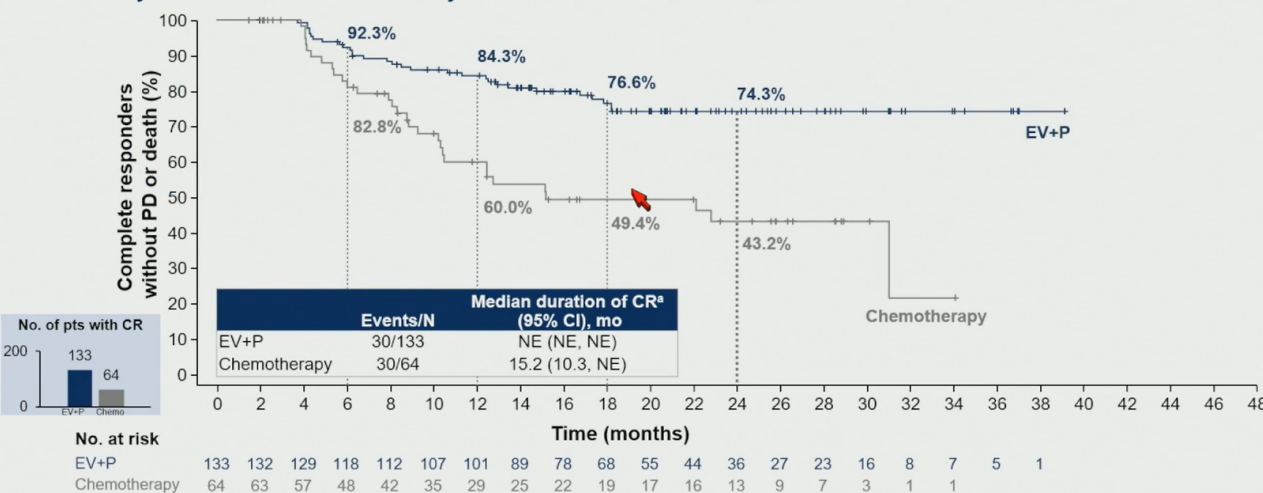
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444 423 404 385 366 347 328 309 290 271 252 233 214 195 176 157 138 119 100 81 62 43 24 5 0

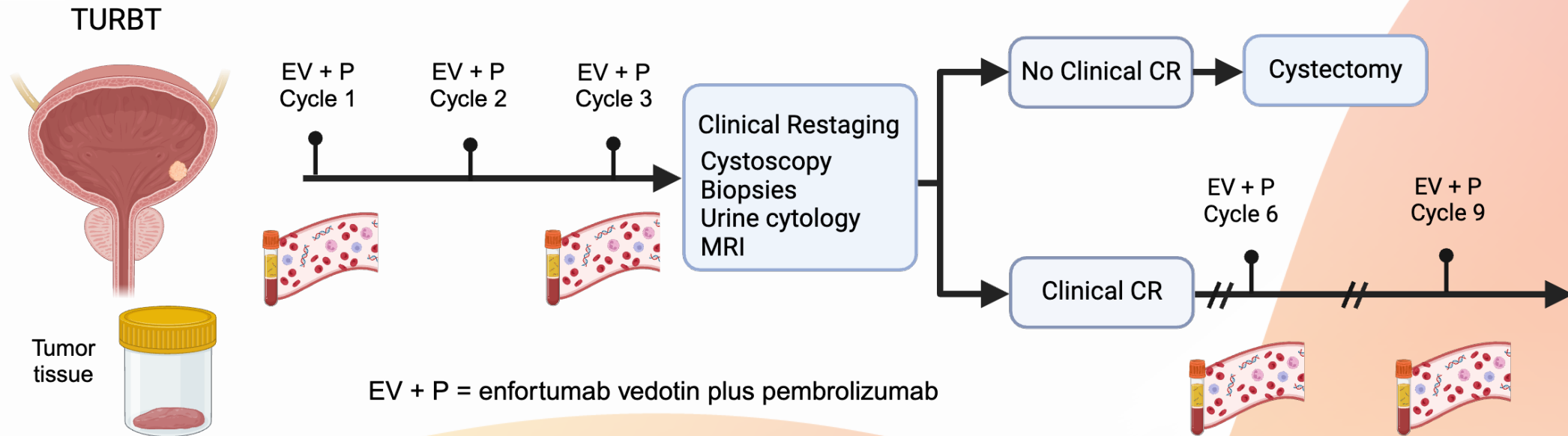


Duration of CR: Patients with best response of CR^{1,2}

Probability of maintained CR at 2 years was 74.3% with EV+P

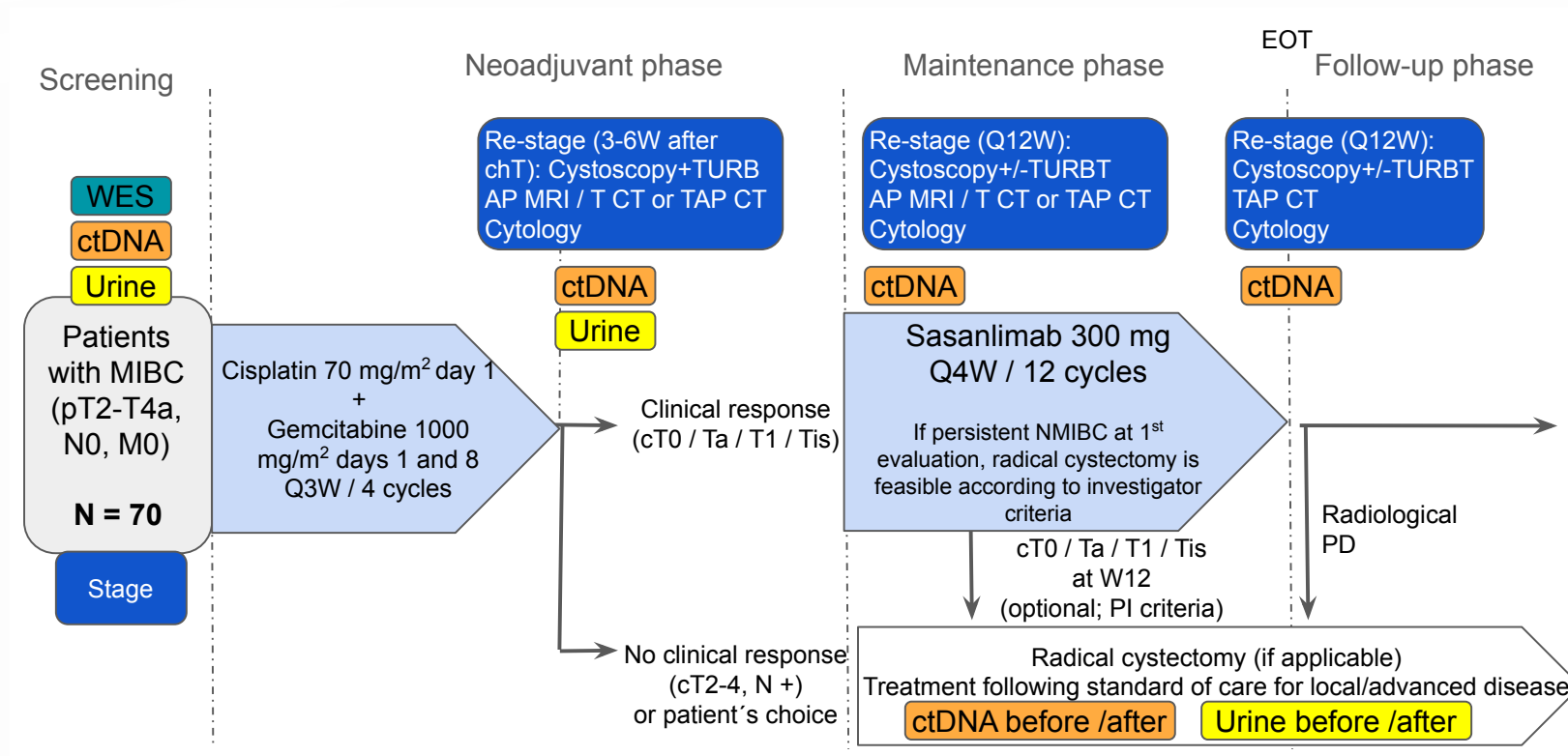


HCRN GU22-598: Response-guided bladder-sparing with EV + pembrolizumab (NCT06809140)



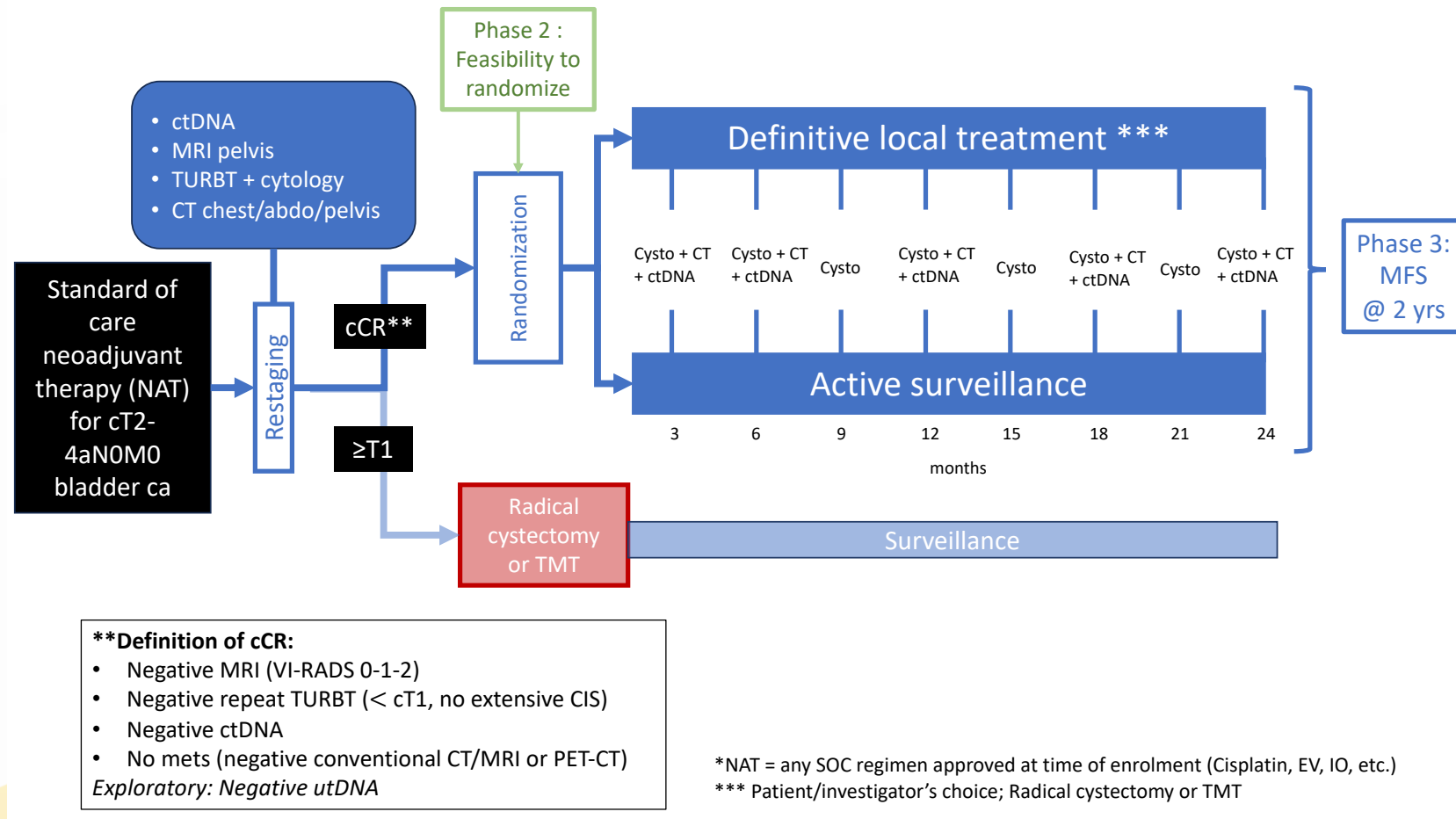
Matthew D. Galsky, MD and colleagues

Sasanlimab as bladder-sparing maintenance treatment after neoadjuvant chemotherapy in patients with muscle invasive bladder cancer (MIBC): The phase 2, HM-8788561 Trial



Elena Sevillano Fernández, MD PhD, Guillermo de Velasco, MD PhD, and colleagues

NEO-BLAST (NCT06537154)



The next decade will witness an unprecedented convergence of powerful therapeutics, precise biomarkers, and risk-adapted strategies creating a watershed moment to redefine muscle-invasive bladder cancer care.



@MattGalsky

¡Gracias!

