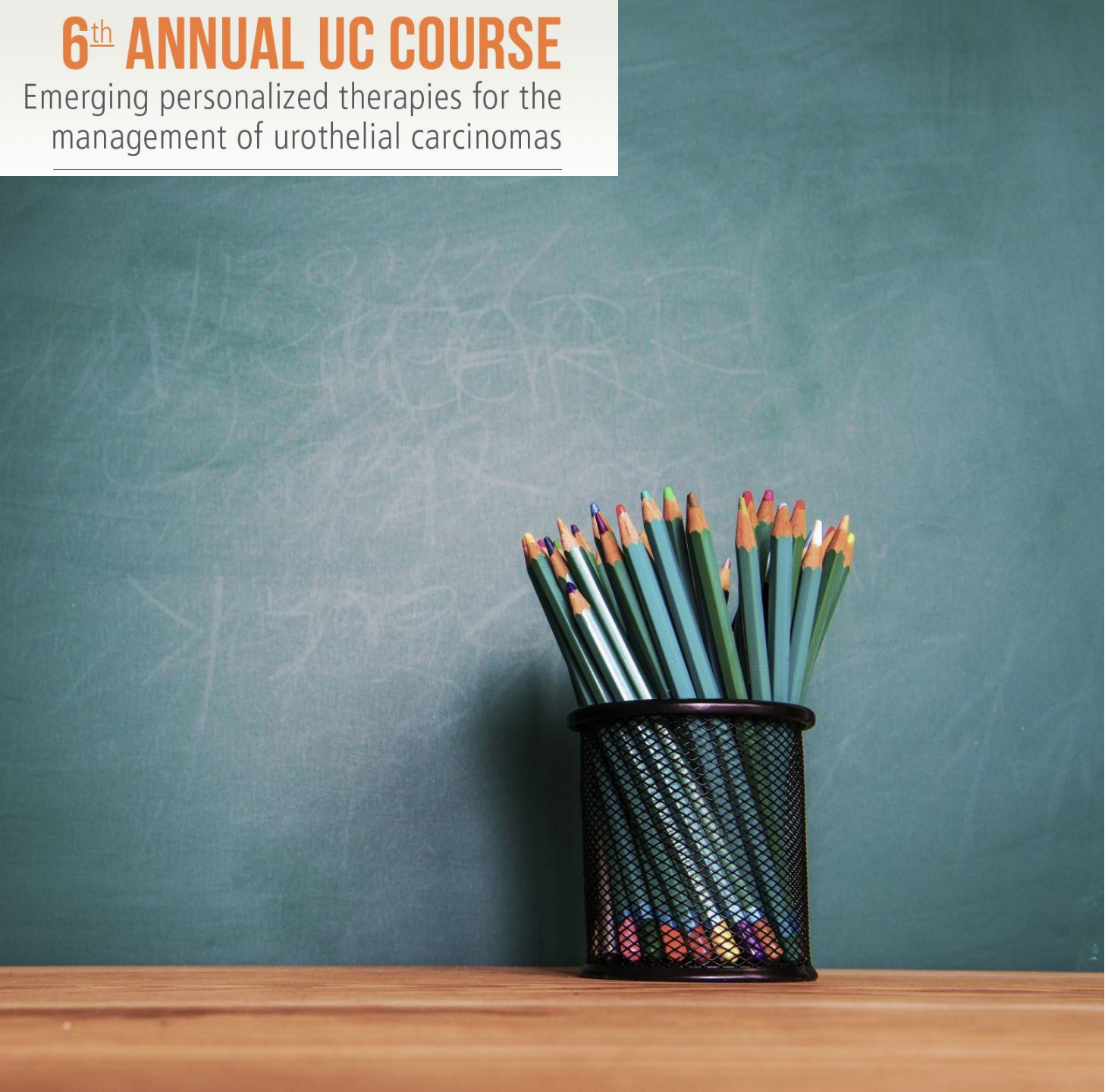
6th ANNUAL UC COURSE
Emerging personalized therapies for the management of urothelial carcinomas



New options for neoadjuvant systemic therapies

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My disclosures

- Advisory Boards:
  - MSD, BMS, Roche-Genentech, PYCYC, IPSEN, Novartis, Bayer, Astra-Zeneca
- Research Funding [institution]:
  - Roche-Genentech, Astra-Zeneca
- Travel expenses:
  - Roche-Genentech, IPSEN, Astra-Zeneca, Bayer
- Clinical Trials [collaboration]:
  - BMS, Roche-Genentech, PYCYC, EISAI, MSD, Tahio Oncology, Gilead, Exelixis, Bicycle Therapeutics,
- Lectures:
  - EUSA pharma, MSD, BMS, Roche-Genentech, IPSEN, Jansen, Astellas, Bayer, Astra-Zeneca
- Clinical trial [lead]: Gilead [PI of the PRISMA-1]

Outline

- The rationale of perioperative treatments
- NACT: The historical evidence and the recent addition
- Other neoadjuvant strategies: CPI as single agents or in combinations
- The perioperative approach: NIAGARA
- The upcoming strategies
- Conclusions

The rationale of perioperative tx

RADICAL CYSTECTOMY

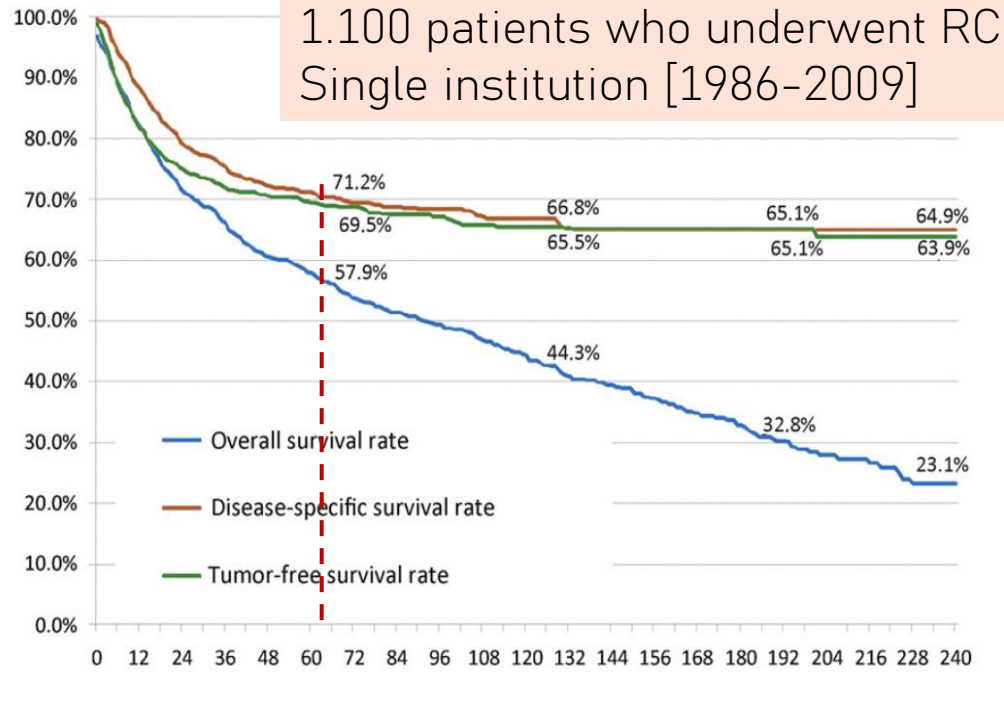
Neoadjuvant

Adjuvant

- The **aim** of any **perioperative treatment** (adjuvant or neoadjuvant) is to **decrease the risk of relapse [DFS]** and ultimately **the risk of death [OS/DSS]** of a localized tumor treated with surgery by **theoretically treating the micro metastatic disease**
- The associated risks [i.e. **toxicities**] with any perioperative treatment **need to be balanced** with the **potential improvement** in DFS and/or OS given that we are dealing with **potentially curable patients**

What is surgery alone able to achieve?

1.100 patients who underwent RC
Single institution [1986-2009]



Years	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20
Pat. (n)	1100	815	660	567	486	434	367	318	272	250	205	172	152	131	115	87	73	51	36	27	21

STAGE MATTERS TO PREDICT OUTCOMES

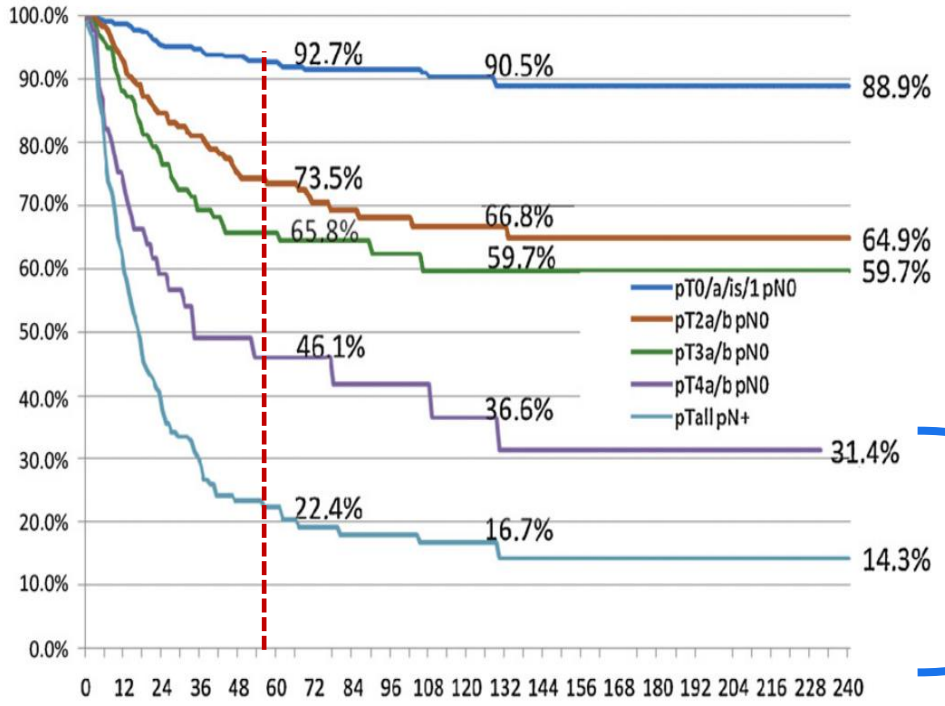
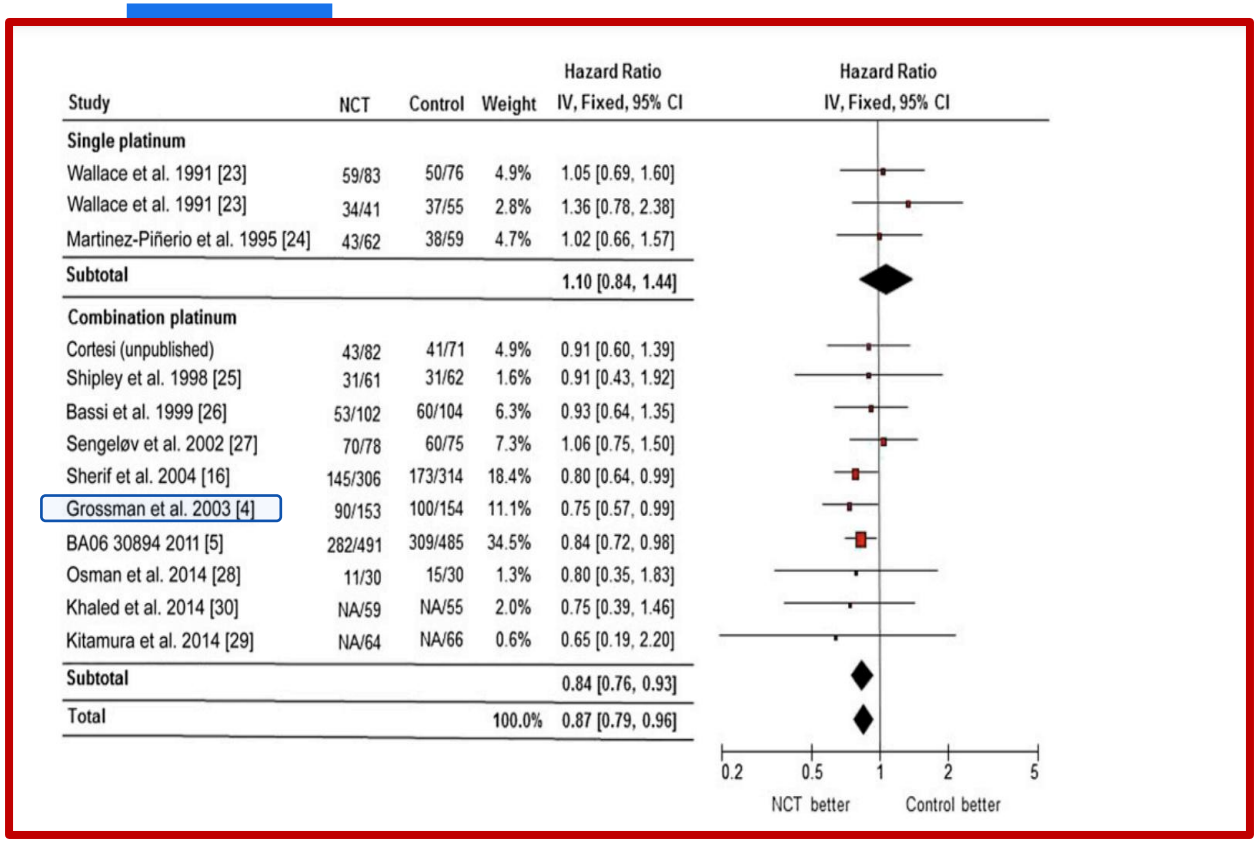


Fig. 2 – Disease-specific survival rates according to the tumor stage of the cystectomy specimen.

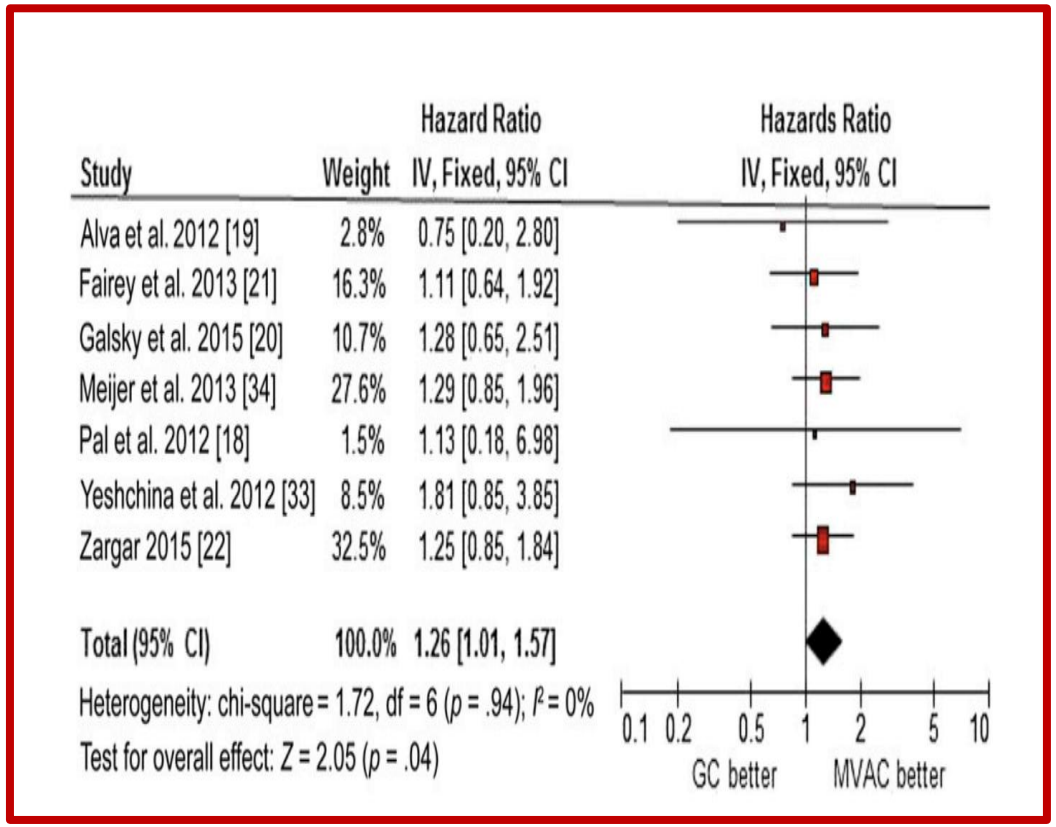
Some patients might achieve long and durable benefit only with surgery in historical series
But, overall, the OS abd DSS at 5 years remain a challenge [particularly in >pT2p and N+]

Hautmann RE, de Petriconi RC, Pfeiffer C, Volkmer BG. Radical cystectomy for urothelial carcinoma of the bladder without neoadjuvant or adjuvant therapy: long-term results in 1100 patients. Eur Urol. 2012 May;61(5):1039-47. doi: 10.1016/j.eururo.2012.02.028. Epub 2012 Feb 22. PMID: 22381169.

Neoadjuvant the preferred approach so far



Forest plot of overall survival in comparison of cisplatin-based neoadjuvant chemotherapy plus locoregional therapy versus locoregional therapy alone by randomized clinical trials.

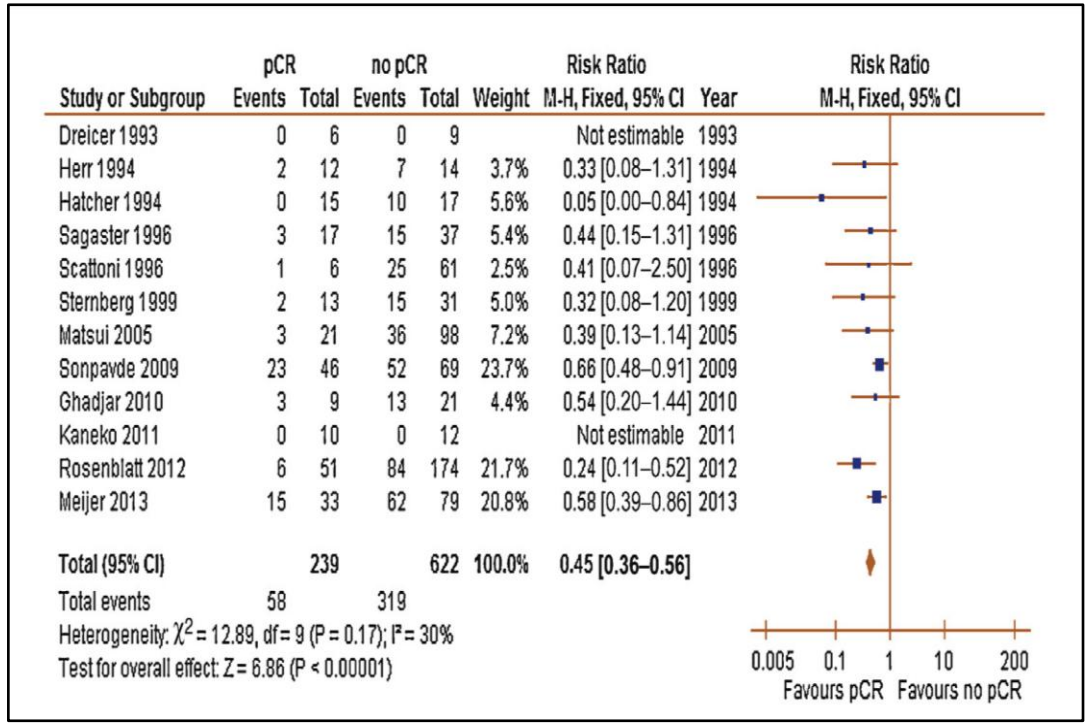


Forest plot of **overall survival in comparison of GC versus MVAC** by retrospective studies.

- The meta-analysis demonstrated that platinum-based combos administered <u>in the neoadjuvant setting</u> provide an OS benefit with an <u>absolute 8% improvement in 5y-OS</u> from 45 to 53% and a <u>16% reduction in the risk of death.</u>
- It also pointed to a greater benefit for MVAC vs GC

Yin M, Joshi M, Meijer RP, et al.. Neoadjuvant Chemotherapy for Muscle-Invasive Bladder Cancer: A Systematic Review and Two-Step Meta-Analysis. Oncologist. 2016 Jun;21(6):708-15

How can we "anticipate" greater benefit to NACT?



Study or Subgroup	pCR Events	pCR Total	no pCR Events	no pCR Total	Weight	Risk Ratio M-H, Fixed, 95% CI	Year
Dreicer 1993	0	6	0	9		Not estimable	1993
Herr 1994	2	12	7	14	3.7%	0.33 [0.08–1.31]	1994
Hatcher 1994	0	15	10	17	5.6%	0.05 [0.00–0.84]	1994
Sagaster 1996	3	17	15	37	5.4%	0.44 [0.15–1.31]	1996
Scattoni 1996	1	6	25	61	2.5%	0.41 [0.07–2.50]	1996
Sternberg 1999	2	13	15	31	5.0%	0.32 [0.08–1.20]	1999
Matsui 2005	3	21	36	98	7.2%	0.39 [0.13–1.14]	2005
Sonpavde 2009	23	46	52	69	23.7%	0.66 [0.48–0.91]	2009
Ghadjar 2010	3	9	13	21	4.4%	0.54 [0.20–1.44]	2010
Kaneko 2011	0	10	0	12		Not estimable	2011
Rosenblatt 2012	6	51	84	174	21.7%	0.24 [0.11–0.52]	2012
Meijer 2013	15	33	62	79	20.8%	0.58 [0.39–0.86]	2013
Total (95% CI)		**239**		**622**	**100.0%**	**0.45 [0.36–0.56]**	
Total events	58		319				

Heterogeneity: $\chi^2 = 12.89$, df = 9 (P = 0.17); $I^2 = 30\%$

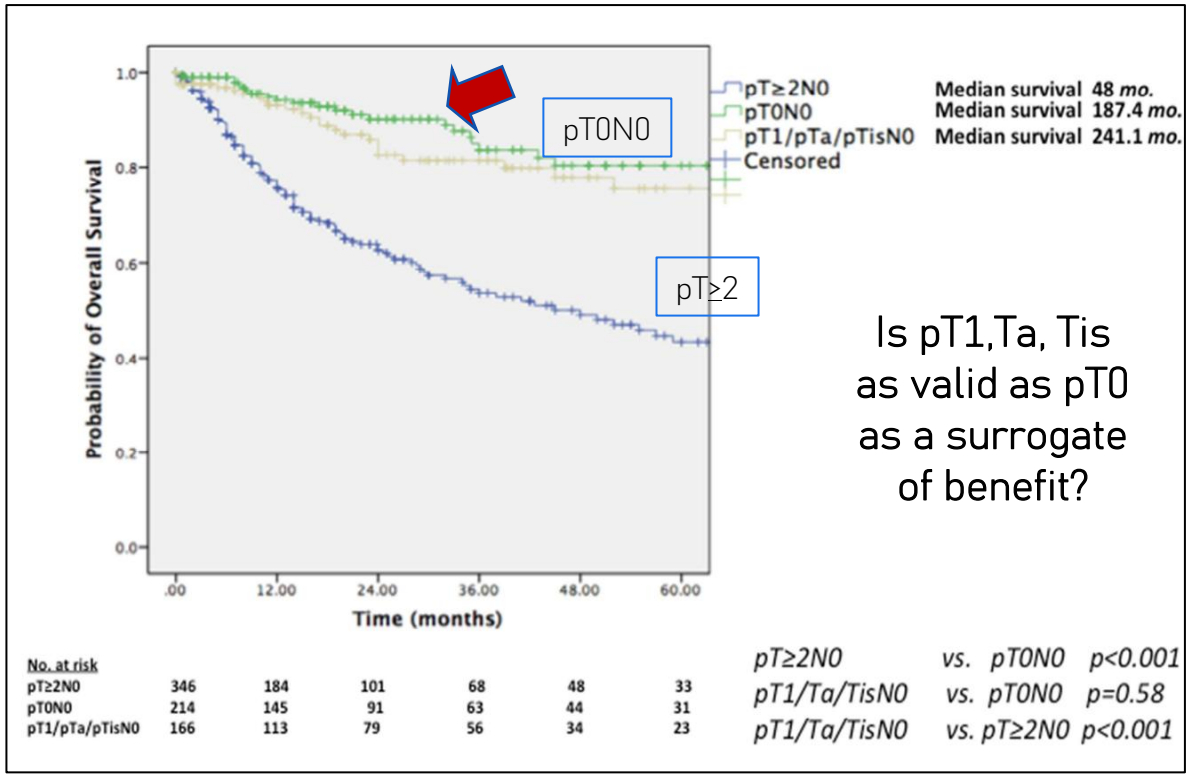
Test for overall effect: Z = 6.86 (P < 0.00001)

Risk Ratio M-H, Fixed, 95% CI

0.005 0.1 1 10 200

Favours pCR Favours no pCR

Pooled relative risk of OS from eligible studies reporting outcome associated with achieving pCR



Is pT1,Ta, Tis as valid as pT0 as a surrogate of benefit?

Estimated overall according to pathological response

pCR: Patients with MIBC who achieved pCR after platinum-based NCT have a better OS and RFS

pT0N0 and **pT1/Ta/TisN0 also associated with better** OS compared to patients who had pT≥2N0

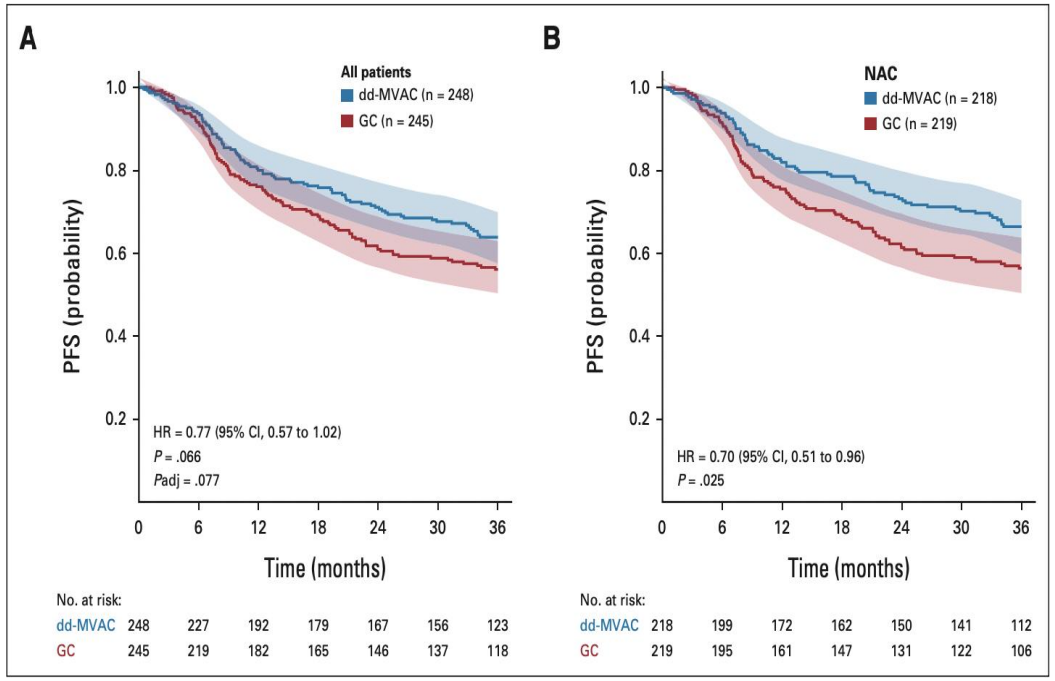
Petrelli F, et al. Eur Urol. 2014 Feb;65(2):350-7. Zargar H, et al.J Urol. 2016 Apr;195(4 Pt 1):886-93.

NCT, neoadjuvant chemotherapy; pCR, pathologic complete response. OS, overall survival.

More data to be discussed: The positivity of the negative

Perioperative dose-dense methotrexate, vinblastine, doxorubicin, and cisplatin in muscle-invasive bladder cancer (VESPER): survival endpoints at 5 years in an open-label, randomised, phase 3 study

Prof Christian Pfister, MD PhD [a,b] · Gwenaelle Gravis, MD [c] · Aude Flechon, MD [d] · Christine Chevreau, MD [e] · Hakim Mahammedi, MD [f] · Brigitte Laguerre, MD [g] · et al. Show more



At 3 years 66% of the patients were disease free in DD MVAC arm vs 56% in the GC arm [HR 0.70 (95% CI, 0.51-0.96), p=0.025 in the Neoadjuvant group .

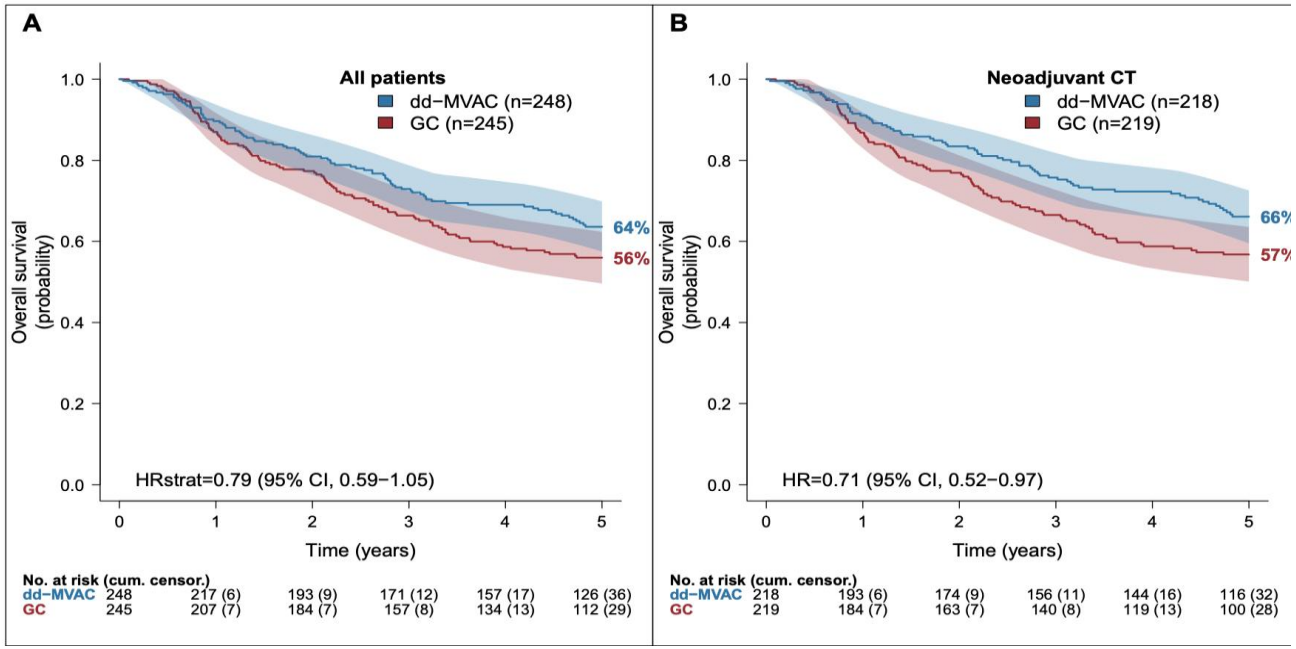
Arm A (standard) 4 cycles of **Gemcitabine** 1250 mg/m² d1 and d8 + **Cisplatin** 70 mg/m² d1

Arm B (experimental) **6 cycles of dd-MVAC**
Methotrexate 30 mg/m² d1, Vinblastine 3 mg/m² d2, Doxorubicin 30 mg/m² Cisplatin 70 mg/m² d2
+ G-CSF support

88% of patients were neoadjuvant

- Primary endpoint: PFS at 3 years

pCR: 42% vs 36%;
Downstaging: 63% vs 49%[1]



The 5-year OS-rate was 66% vs 57% HR 0.71 for the NACT cohort

Pfister C, Gravis G, Fléchon A et al. ; VESPER Trial Investigators. Randomized Phase III Trial of Dose-dense Methotrexate, Vinblastine, Doxorubicin, and Cisplatin, or Gemcitabine and Cisplatin as Perioperative Chemotherapy for Patients with Muscle-invasive Bladder Cancer. Analysis of the GETUG/AFU V05 VESPER Trial Secondary Endpoints: Chemotherapy Toxicity and Pathological Responses. Eur Urol. 2021 Feb;79(2):214-221. Pfister C, Gravis G, Fléchon A et al. VESPER Trial Investigators. Dose-Dense Methotrexate, Vinblastine, Doxorubicin, and Cisplatin or Gemcitabine and Cisplatin as Perioperative Chemotherapy for Patients With Nonmetastatic Muscle-Invasive Bladder Cancer: Results of the GETUG-AFU V05 VESPER Trial. J Clin Oncol. 2022 Jun 20;40(18):2013-2022. Pfister C, Gravis G, Flechon A, Chevreau C, Mahammedi H, Laguerre B, Guillot A, Joly F, Soulie M, Allory Y, Harter V, Culine S; VESPER Trial Investigators. Perioperative dose-dense methotrexate, vinblastine, doxorubicin, and cisplatin in muscle-invasive bladder cancer (VESPER): survival endpoints at 5 years in an open-label, randomised, phase 3 study. Lancet Oncol. 2024 Feb;25(2):255-264.

Recommendation from Guidelines [until recently]

Summary of evidence	LE
Neoadjuvant cisplatin-containing combination chemotherapy improves OS (5–8% at five years).	1a
Neoadjuvant treatment may have a major impact on OS in patients who achieve ypT0 or ≤ ypT2.	2a

Cisplatin-based NACT should be offered to patients with MIBC [T2-T4acN0cM0]

Recommendations	Strength rating
If eligible for cisplatin-based chemotherapy, offer neoadjuvant cisplatin-based combination chemotherapy to patients with muscle-invasive bladder cancer (T2-T4a, cN0 M0).	Strong
Do not offer NAC to patients who are ineligible for cisplatin-based combination chemotherapy.	Strong

EAU Guidelines. Edn. presented at the EAU Annual Congress Madrid 2025. ISBN 978-94-92671-29-5. Accessed March 2025

WHAT IS THE ROLE OF OTHER STRATEGIES IN THE NEOADJUVANT SETTING:

THE ROLE OF I.O

IO based tx in the neoadjv setting

- <u>NEOADJUVANT APPROACHES SINGLE AGENT</u>
  - ABACUS [Atezolizumab]
  - PURE [Pembrolizumab]
- <u>NEOADJUVANT APPROACHES I.O. COMBOS</u>
  - NABUCCO [IPI-NIVO diff doses]
  - DUTRENEO [Durva-Treme]
  - MD Anderson. [Durva-Treme]
- <u>CHEMOTHERAPY + CPI COMBOS</u>
  - DD-MVAC AVELU/CIS-GEM AVELU [AURA Cis-eleg]
  - TAXOL-GEM AVELU [AURA Cis-ineg]
  - GEM-CIS-ATEZO [MSKCC]
  - GEM-CIS-NIVO [BLASST]
  - GEM-CISspd-PEMBRO [Chapel Hill]
  - GEM-CIS-PEMRO/ GEM-PEMBRO [Duke]
  - DD-MVAC DURVA/DDMVAC DURVA-TREME [Nemio]

- Some signals were generated mostly from IO combinations [either with chemo or IO doublets] although data needs a careful interpretation
  - Determination of pCR rates variable
  - Small sample size
  - Short f/u

Oncology 40, no. 16_suppl (June 01, 2022) 4517Pfister C, et al. Oral presentation at ESMO 2021; abstract 6520.; Grossman HB, et al. N Engl J Med. 2003;349:859-66.. Martinez Chanza N, et al. Oral abstract presentation at ESMO 2021; abstract 659MO.. Funt S, et al. Poster presentation at ASCO 2021; abstract 4517.9. Rose TL, et al. J Clin Oncol. 2021.doi: 10.1200/JCO.21.01003.. Gupta S, et al. Oral presentation at ASCO 2020; abstract 439. Hoimes C et al Journal of Clinical Oncology 38, no. 15_suppl (May 20, 2020) 5047-5047.Cathomas R, Petrausch U, Hayoz S, Schneider M, Schardt JA, Seiler R, et al.Perioperative chemoimmunotherapy with durvalumab (Durva) in combinationwith cisplatin/gemcitabine (Cis/Gem) for operable muscle-invasive urothelial carcinoma (MIUC): Preplanned interim analysis of a single-arm phase II trial (SAKK 06/17). JCO 2020;38(6_suppl). 499-499. [Kaimakliotis HZ, Adra N, Kelly WK, Trabulsi EJ, Lauer RC, Picus J, et al. Phase II neoadjuvant (N-) gemcitabine (G) and pembrolizumab (P) for locally advanced urothelial cancer (laUC): Interim results from the cisplatin (C)-ineligible cohort of GU14-188. JCO 2020;38(15_suppl). 5019-5019. Martinez-Chanza N. Avelumab as the basis of neoadjuvant regimen in platinum-eligible and -ineligible patients with nonmetastatic muscle-invasive bladder cancer: AURA (Oncodistinct-004) trial. . Journal of Clinical ; Powles T, Kockx M, Rodriguez-Vida A, Duran I et al. Clinical efficacy and biomarker analysis of neoadjuvant atezolizumab in operable urothelial carcinoma in the ABACUS trial. Nat Med. 2019 Nov;25(11):1706-1714..; Necchi A, Raggi D, Gallina A, Madison R, Colecchia M, Luciano ` R, et al. Updated results of PURE-01 with preliminary activity of neoadjuvant pembrolizumab in patients with muscle-invasive bladder carcinoma with variant histologies. Eur Urol 2020 Apr;77(4):439-46.; Van Dijk *et al.*, Nat Med, 2020 Van Dorp J, et al. Oral presentation at ESMO 2021; abstract LBA31. Gao J, et al. Nature Medicine. 2020; 26: 1845-1851. Grande E et al. ASCO 2020. 2364MO Durvalumab (D) +/- tremelimumab (T) in combination with dose-dense MVAC (ddMVAC) as neoadjuvant treatment in patients with muscle-invasive bladder carcinoma (MIBC): Results of NEMIO, a randomized phase I-II trial Thibault, C. et al. Annals of Oncology, Volume 34, S1202

Guidelines 2025. I.O neoadjv[fresh]

Neoadjuvant immunotherapy with checkpoint inhibitors alone has demonstrated promising results.	-
There are still no reliable tools available to select patients who have a higher probability of benefitting from NAC. In the future, genomic markers in a personalised medicine setting might facilitate the selection of patients for NAC and differentiate responders from non-responders.	-

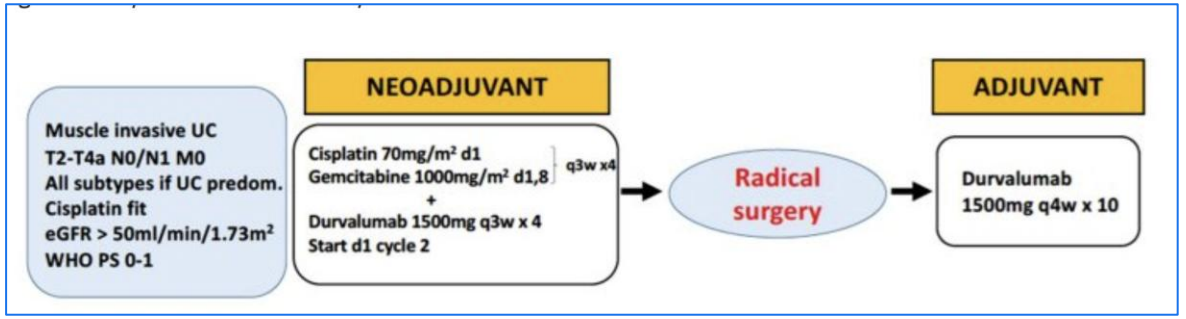
Only offer neoadjuvant immunotherapy with checkpoint inhibitors alone to patients within a clinical trial setting.	Strong

Chemo-IO periop

J Clin Oncol. 2023 Aug 17;JCO2300363. doi: 10.1200/JCO.23.00363. Online ahead of print.

Perioperative Chemoimmunotherapy With Durvalumab for Muscle-Invasive Urothelial Carcinoma: Primary Analysis of the Single-Arm Phase II Trial SAKK 06/17

Richard Cathomas [1], Sacha I Rothschild [2 3], Stefanie Hayoz [4], Lukas Bubendorf [5], Berna C Özdemir [6], Bernhard Kiss [7], Andreas Erdmann [3], Stefanie Aeppli [8], Nicolas Mach [9], Räto T Strebel [10], Boris Hadaschik [11], Dominik Berthold [12], Hubert John [13], Deborah Zihler [14], Mathias Schmid [15], Ilaria Alborelli [5], Martina Schneider [4], Jana Musilova [4], Martin Spahn [7 16 17], Ulf Petrausch [18]



Results: Sixty one patients were accrued at 12 sites. The full analysis set consisted of 57 patients, 54 (95%) had bladder cancer. Median follow-up was 40 months. The primary end point was met, with EFS at 2 years of 76% (one-sided 90% CI [lower bound], 67%; two-sided 95% CI, 62 to 85). EFS at 3 years was 73% (95% CI, 59 to 83). Complete pathologic response in resected patients (N = 52) was achieved in 17 patients (33%), and 31 (60%) had pathologic response <ypT2 ypN0. Overall survival (OS) was 85% (95% CI, 72 to 92) at 2 years and 81% (95% CI, 67 to 89) at 3 years. Grade 3 and 4 treatment-related adverse events (TRAEs) during neoadjuvant treatment occurred in 42% and 25%, respectively. TRAEs related to adjuvant durvalumab were grade 3 in 5 (11%) and grade 4 in 2 (4%) patients.

NIAGARA: Study Design

NIAGARA is the first global Phase 3 study to evaluate a perioperative immune checkpoint inhibitor, durvalumab, combined with NAC in cisplatin-eligible patients with MIBC

Perioperative

Study population
- Adults
- Cisplatin-eligible MIBC (cT2–T4aN0/1M0)
- UC or UC with divergent differentiation or histologic subtypes
- Evaluated and confirmed for RC
- CrCl of ≥40 mL/min

R 1:1

	Neoadjuvant (4 cycles)	Radical cystectomy	Adjuvant (8 cycles)
Durvalumab arm N=533	**Durvalumab** 1500 mg IV Q3W + **Gemcitabine + cisplatin**		**Durvalumab** 1500 mg IV Q4W
Comparator arm N=530	**Gemcitabine + cisplatin**		**No treatment**

Dual primary endpoints
- EFS*
- pCR**

Key secondary endpoint
- OS

Safety

Stratification factors

Clinical tumour stage (T2N0 vs >T2N0)

Renal function (CrCl ≥60 mL/min vs ≥40–<60 mL/min)

PD-L1 status (high vs low/negative expression)

Gemcitabine/cisplatin dosing

CrCl ≥60 mL/min: Cisplatin 70 mg/m^2 + gemcitabine 1000 mg/m^2 Day 1, then gemcitabine 1000 mg/m^2 Day 8, Q3W for 4 cycles

CrCl ≥40–<60 mL/min: Split-dose cisplatin 35 mg/m^2 + gemcitabine 1000 mg/m^2 Days 1 and 8, Q3W for 4 cycles

EFS was defined as:
- **Progressive disease that precluded RC**
- **Recurrence after RC**
- **Date of expected surgery in patients who did not undergo RC**
- **Death from any cause**

Other endpoints (not reported here): DFS, DSS, MFS, HRQoL, 5-year OS

First patient enrolled: Nov 2018
Last patient enrolled: Jul 2021
Last RC: Nov 2021

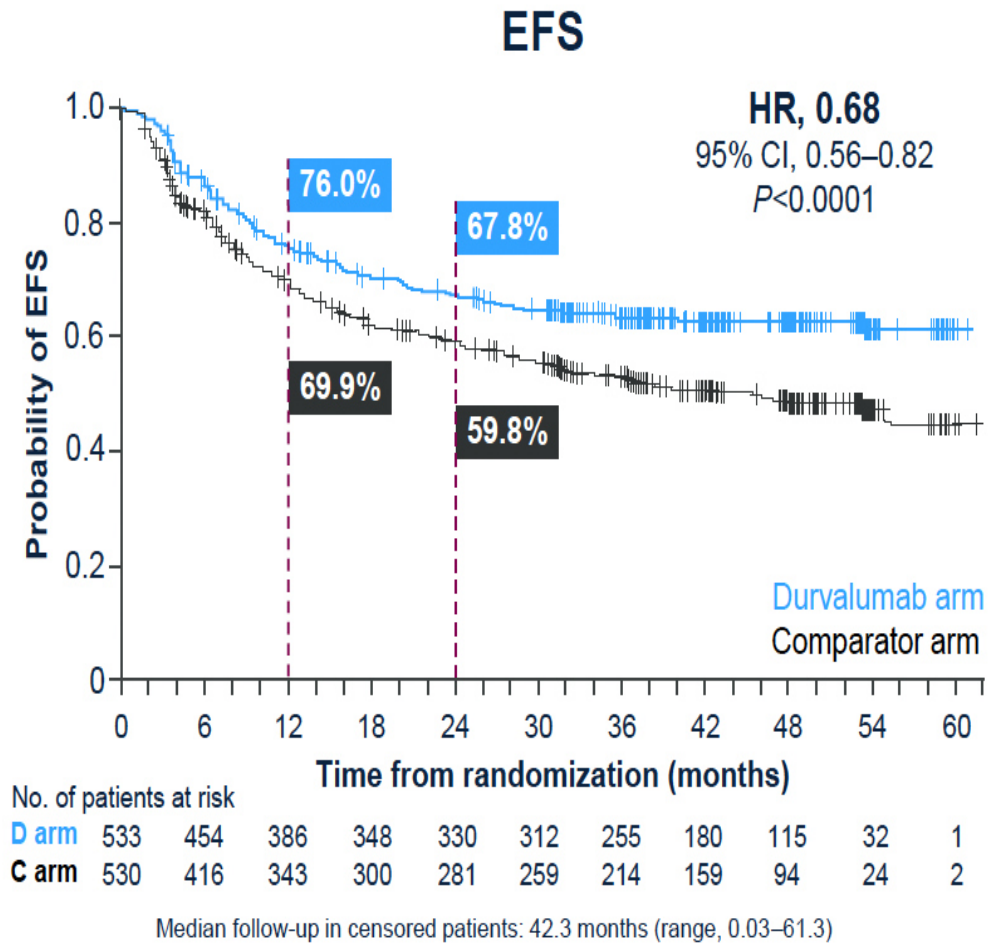
*Evaluated by blinded independent central review or central pathology review (if a biopsy was required for a suspected new lesion). **Evaluated by blinded central pathology review.
ClinicalTrials.gov, NCT03732677; EudraCT number, 2018-001811-59. CrCl, creatinine clearance; DFS, disease-free survival; DSS, disease-specific survival; EFS, event-free survival; HRQoL, health-related quality of life; IV, intravenous; MFS, metastasis-free survival; MIBC, muscle-invasive bladder cancer; OS, overall survival; pCR, pathologic complete response; PD-L1, programmed cell death ligand-1; Q3W, every 3 weeks; Q4W, every 4 weeks; R, randomised; RC, radical cystectomy; UC, urothelial carcinoma..

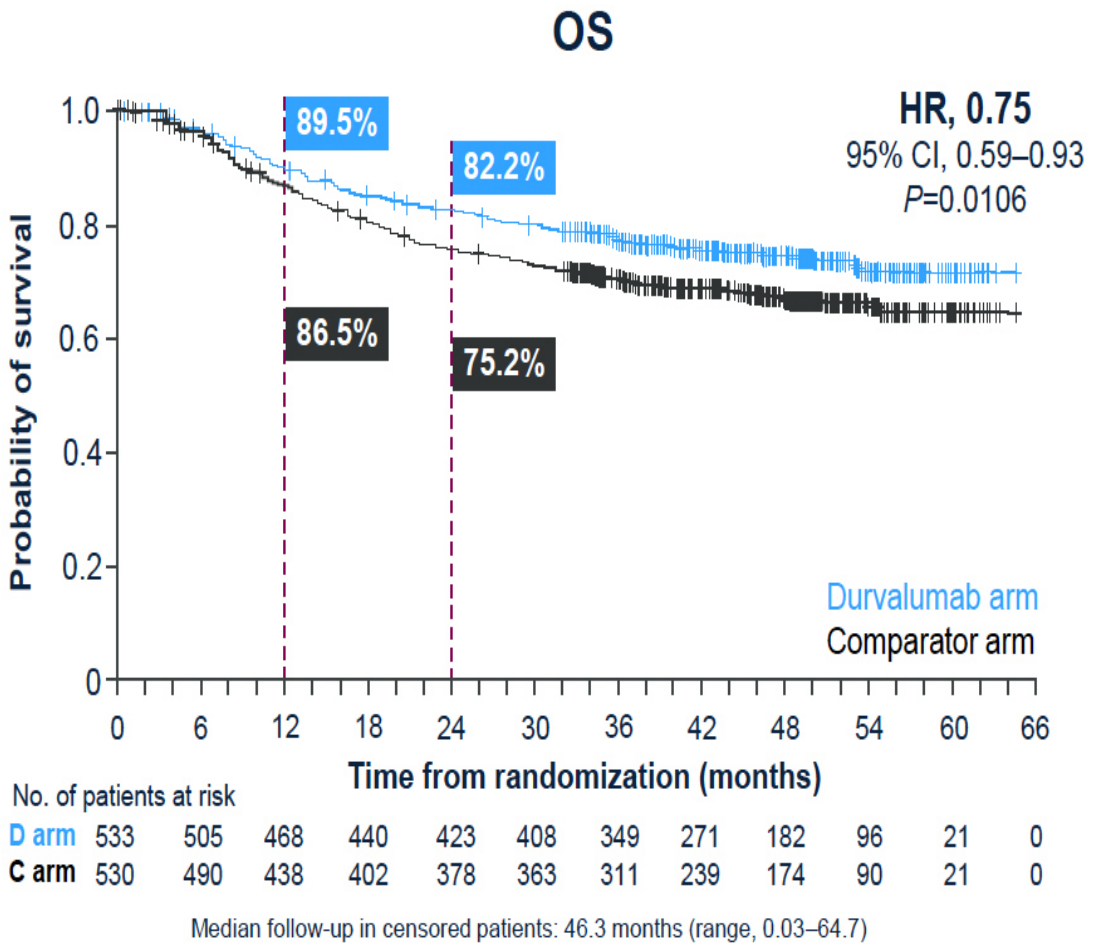
NIAGARA: Baseline Characteristics (ITT)

Characteristics		Durvalumab arm N=533	Comparator arm N=530
Age	Median, years (range)	65 (34–84)	66 (32–83)
Sex, %	Male	82	82
Race, %	White	66	68
	Asian	29	27
	Black/Other	2	1
	Not reported	3	4
ECOG PS, %	0	78	78
	1	22	22
Smoker, %	Yes (current or former)	71	75
Renal function, %	CrCl ≥60 mL/min	81	81
	CrCl ≥40–<60 mL/min	19	19
Tumour stage*, %	T2N0	40	40
	>T2N0	60	60
PD-L1 expression†, %	High	73	73
	Low/negative	27	27
Histology, %	UC	86	83
	UC with divergent differentiation or histologic subtypes	14	17
Regional lymph nodes, %	N0	95	94
	N1	5	6

*The study design capped recruitment of patients with tumour stage T2 at 40% and CrCl of <60 mL/min to 20%. †Assessed with the VENTANA PD-L1 (SP263) Assay using the TC/IC25% algorithm; high PD-L1 expression was defined as ≥25% of TCs with any membrane staining or ICs staining for PD-L1 at any intensity. Data cutoff 29 Apr 2024. CrCl, creatinine clearance; ECOG PS, Eastern Cooperative Oncology Group performance status; IC, immune cell; ITT, intent-to-treat population; PD-L1, programmed cell death ligand-1; TC, tumour cell; UC, urothelial carcinoma.

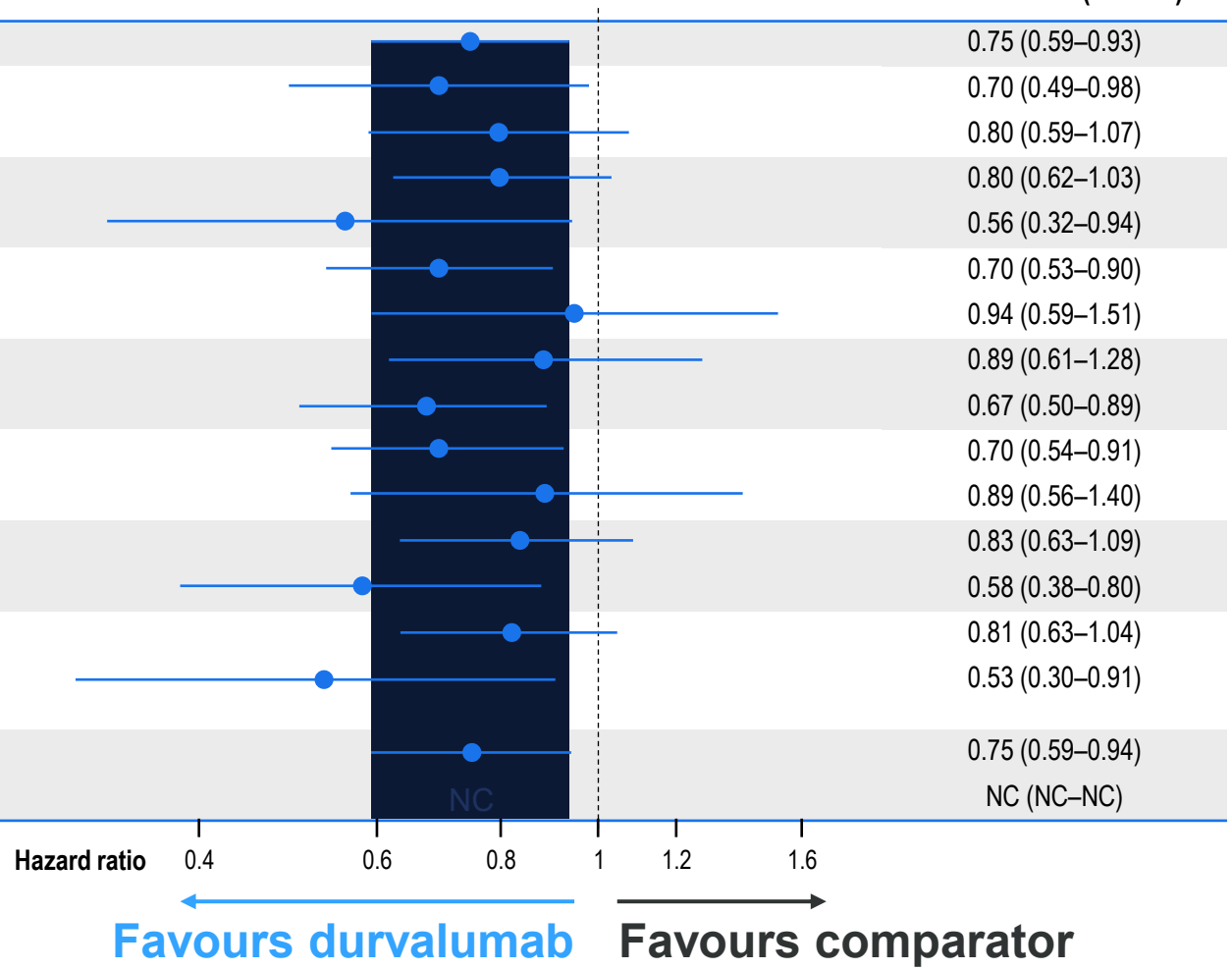
Perioperative durvalumab + NAC demonstrated statistically significant and clinically meaningful EFS and OS improvement





NIAGARA: Overall Survival Subgroup Analyses

Subgroup	Category	N	Hazard ratio (95% CI)
All patients		1063	0.75 (0.59–0.93)
Age at randomisation	<65 years	499	0.70 (0.49–0.98)
	≥65 years	564	0.80 (0.59–1.07)
Sex	Male	870	0.80 (0.62–1.03)
	Female	193	0.56 (0.32–0.94)
Race	White	712	0.70 (0.53–0.90)
	Non-White	315	0.94 (0.59–1.51)
Tumour stage at baseline	T2N0	428	0.89 (0.61–1.28)
	>T2N0	635	0.67 (0.50–0.89)
Renal function at baseline	CrCl ≥60 mL/min	862	0.70 (0.54–0.91)
	CrCl ≥40–<60 mL/min	201	0.89 (0.56–1.40)
PD-L1 expression at baseline*	High	777	0.83 (0.63–1.09)
	Low/negative	286	0.58 (0.38–0.80)
Histology at baseline	UC	898	0.81 (0.63–1.04)
	UC with divergent differentiation or histologic subtypes	165	0.53 (0.30–0.91)
Lymph node positive at baseline	N0	1005	0.75 (0.59–0.94)
	N1	58	NC (NC–NC)

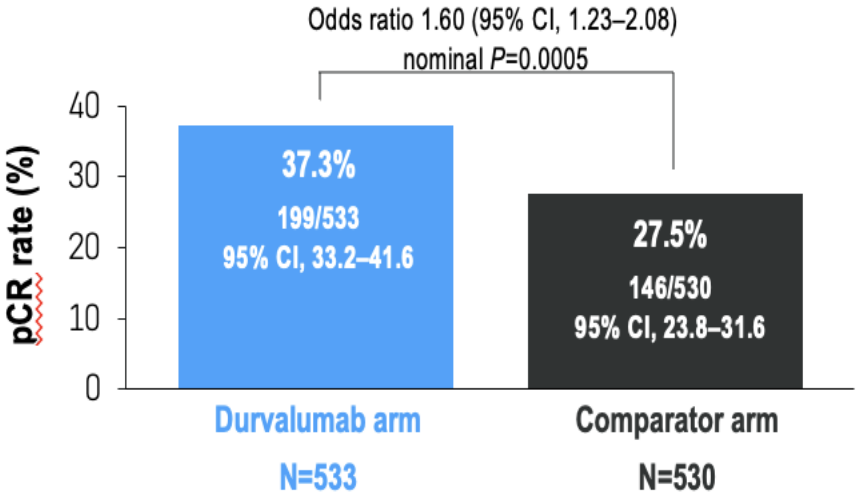


The plot is of hazard ratio and 95% CI. Tan-coloured band represents the 95% CI for the overall (all patients) hazard ratio. The subgroup analyses were performed using an unstratified Cox proportional hazard model, with treatment as only covariate and ties handled by Efron approach.
*Assessed using the VENTANA PD-L1 (SP263) Assay using the TC/IC25% algorithm; high PD-L1 expression was defined as ≥25% of TCs with any membrane staining or ICs staining for PD-L1 at any intensity.
Data cutoff 29 Apr 2024. CI, confidence interval; CrCl, creatinine clearance; IC, immune cell; NC, not calculated; PD-L1, programmed cell death ligand-1; TC, tumor cell; UC, urothelial carcinoma.

Pathological complete response: Has all been said?

ITT

(Apr 2024)

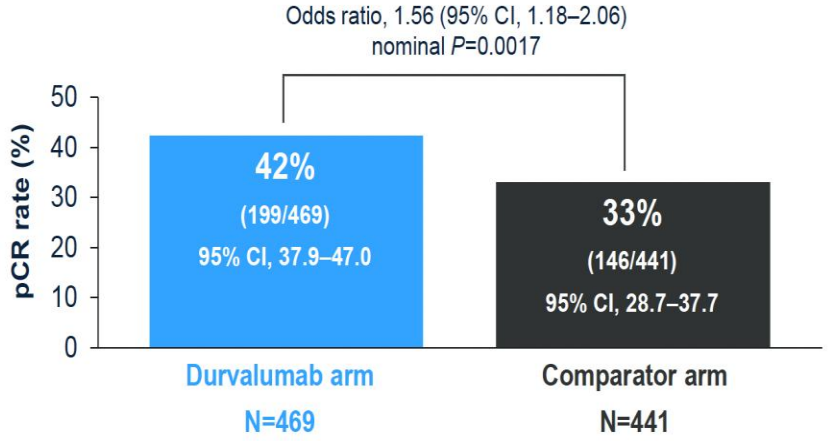


- The re-analysis showed nominal statistical significance in favour of the durvalumab arm
- This analysis includes the results of the 59 omitted samples (28 additional pCRs)*

RC POPULATION

pCR rate was 42% with perioperative durvalumab + NAC vs 33% with NAC alone in the RC population

pCR rate per central review (RC population)



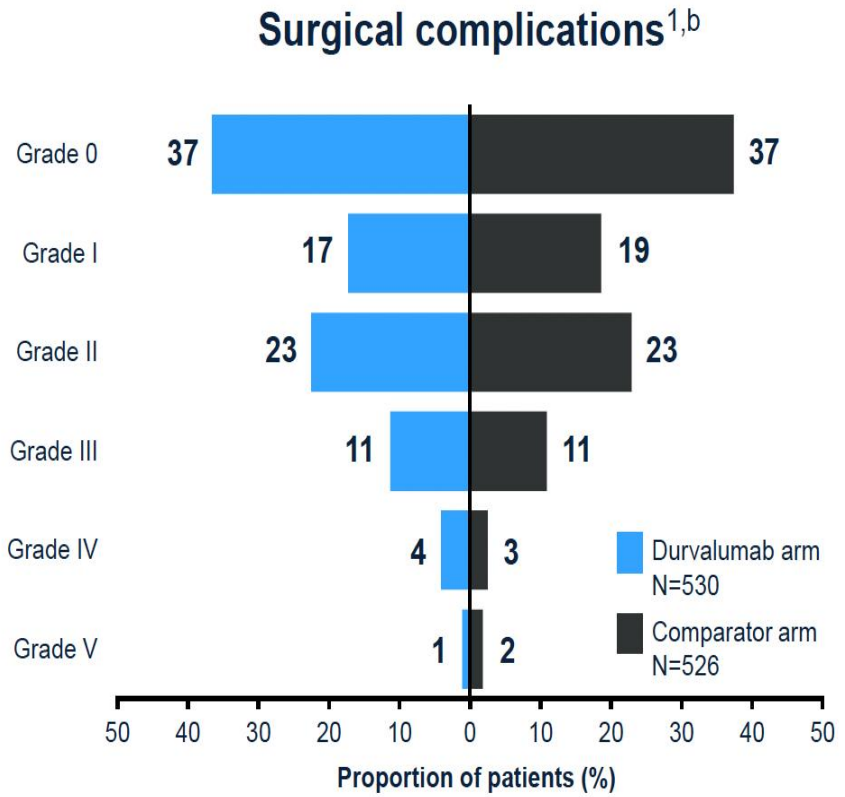
Data cutoff: 29 April 2024. Odds ratio and corresponding CI value were obtained using logistic regression adjusted for the stratification factors (renal function, tumor stage, and PD-L1 status). Pathologic staging of samples taken during RC was performed centrally; pCR was the proportion of patients with stage T0N0M0 at RC (American Joint Committee on Cancer 8th edition classification).
CI, confidence interval; NAC, neoadjuvant chemotherapy; pCR, pathological complete response; PD-L1, programmed cell death ligand-1; RC, radical cystectomy.

*pCR was statistically tested as the final analysis in Jan 2022 (formal analysis). The results of 59 evaluable samples were omitted due to applying the DCO to the date of central review, rather than date of surgery. The re-analysis is a descriptive analysis of pCR rate and associated odds ratios that includes all samples from the formal pCR analysis and applies the DCO to the date of surgery for all samples. Alpha spend for the multiple testing procedure is associated with the formal pCR analysis only. pCR statistical significance was set at a threshold of 0.001.
95% CIs for the pCR rate are calculated using the Clopper-Pearson method. Odds ratio, corresponding CI, and *P* value are obtained using logistic regression adjusted for the stratification factors (renal function, tumour stage, and PD-L1 status). Pathological staging of samples taken during RC was performed centrally; pCR was the proportion of patients with stage T0N0M0 at RC (American Joint Committee on Cancer 8th edition classification). CI, confidence interval; DCO, data cutoff; ITT, intent-to-treat population; pCR, pathologic complete response; RC, radical cystectomy.

Safe and not a major delay cause

Time to radical cystectomy and rate of surgical complications were similar between treatment arms

	Durvalumab arm	Comparator arm
Median time from randomization to RC,[1,a] (IQR), weeks	16.3 (14.7–18.4)	16.1 (14.3–18.3)
Median time from last dose of neoadjuvant therapy to RC,[2] (range), weeks	5.6 (1.1–16.9)	5.4 (1.7–47.6)
Time to RC after last dose of therapy,[1,2] % (n/N)		
≤56 days	90 (424/533)	90 (399/530)
≤70 days	96 (450/533)	95 (424/530)
Time from RC to starting adjuvant therapy		
Median (range), weeks	**8.0 (4.0–64.3)**	–
>120 days, % (n/N)	**2 (9/383)**	–



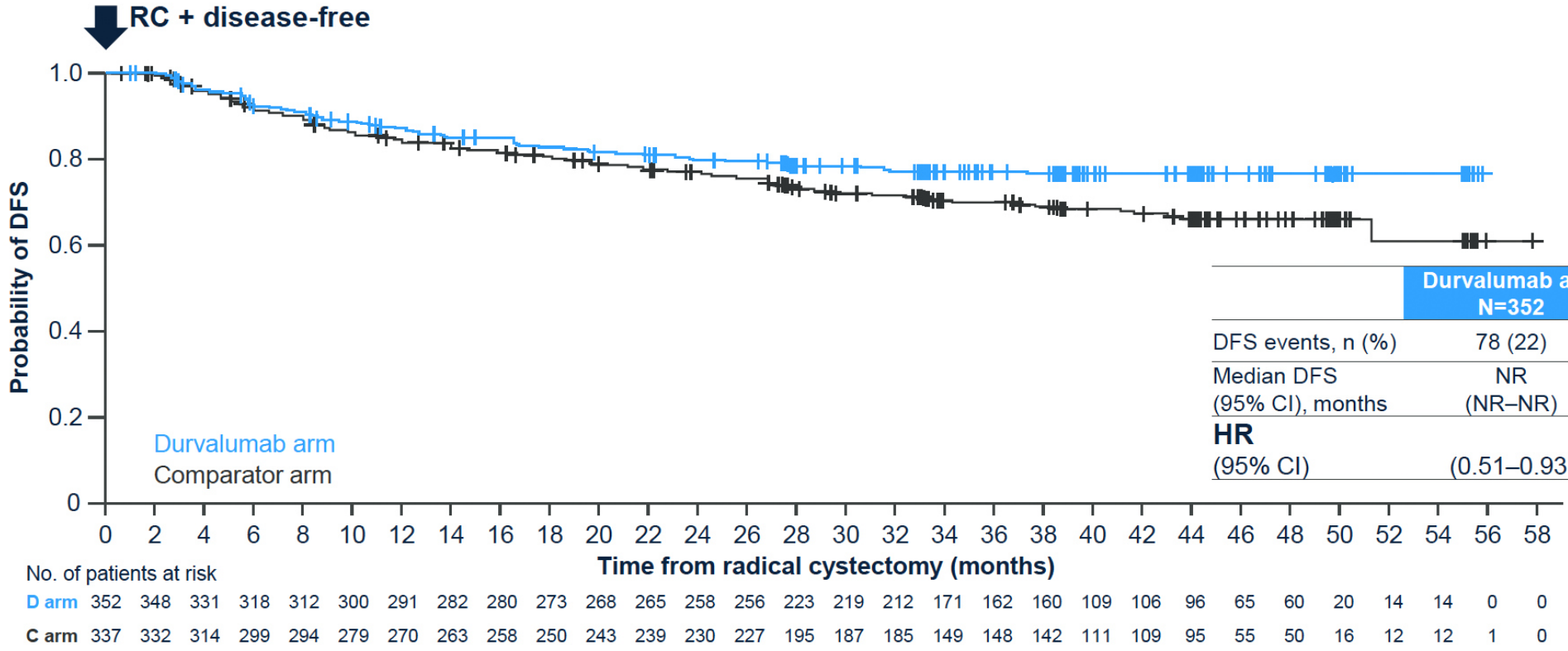
From Catto JWF, et al. Presented at: EAU Congress; March 21–24, 2025; Madrid, Spain; Abst #AM25-6261. Copyright © (2025) European Association of Urology. Reprinted with permission from European Association of Urology.

1. Catto JWF, et al. Presented at: EAU Congress; March 21–24, 2025; Madrid, Spain; Abst #AM25-6261. 2. Powles T, et al. *N Engl J Med*. 2024;391:1773–1786.
Data cutoff: 29 April 2024. [a]Calculated using the Kaplan–Meier technique. [b]Per Clavien–Dindo classification.
IQR, interquartile range; RC, radical cystectomy.

Meeks J et al. AUA 2025

DFS improved after radical cystectomy

Perioperative durvalumab + NAC reduced the risk of recurrence or death post-RC by 31%



	Durvalumab arm N=352	Comparator arm N=337
DFS events, n (%)	78 (22)	102 (30)
Median DFS (95% CI), months	NR (NR–NR)	NR (51.3–NR)
HR (95% CI)	**0.69** (0.51–0.93); nominal *P*=0.0143	

Data cutoff: 29 April 2024. HR based on Cox proportional hazard model adjusted for the stratification factors (tumor stage, renal function, and PD-L1 status), with ties handled by the Efron approach. DFS is the time from date of RC to first recurrence of disease post-RC, or death due to any cause, whichever occurs first. RC population included all randomized patients who underwent RC and were disease-free at adjuvant baseline per blinded independent central review. C, comparator; CI, confidence interval; D, durvalumab; DFS, disease-free survival; HR, hazard ratio; NAC, neoadjuvant chemotherapy; NR, not reached; PD-L1, programmed cell death ligand-1; RC, radical cystectomy.

TAKE HOME MESSAGE FROM NIAGARA

- For the first time a phase III trial testing a combo of chemo+ immunotherapy in the perioperative setting shows IMPROVEMENT in EFS, OS and DFS and does not seem to have a negative impact in SAFETY and time and complications related to SURGERY
- pCR was NOT statistically significant different although numerically superior in ITT but showed an SF benefit in the RC population
- Chemo + IO appears as a new SOC in the MIBC setting

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Perioperative Durvalumab with Neoadjuvant Chemotherapy in Operable Bladder Cancer

T. Powles, J.W.F. Catto, M.D. Galsky, H. Al-Ahmadie, J.J. Meeks, H. Nishiyama, T.Q. Vu, L. Antonuzzo, P. Wiechno, V. Atduev, A.G. Kann, T.-H. Kim, C. Suárez, C.-H. Chang, F. Roghmann, M. Özgüroğlu, B.J. Eigl, N. Oliveira, T. Buchler, M. Gadot, Y. Zakharia, J. Armstrong, A. Gupta, S. Hois, and M.S. van der Heijden, for the NIAGARA Investigators*

SEP 2024

FDA approves durvalumab for muscle invasive bladder cancer

On March 28, 2025, the Food and Drug Administration approved durvalumab (Imfinzi, AstraZeneca) with gemcitabine and cisplatin as neoadjuvant treatment, followed by single agent durvalumab as adjuvant treatment following radical cystectomy, for adults with muscle invasive bladder cancer (MIBC).

Full prescribing information for Imfinzi will be posted on Drugs@FDA.

SUMMER 2025?

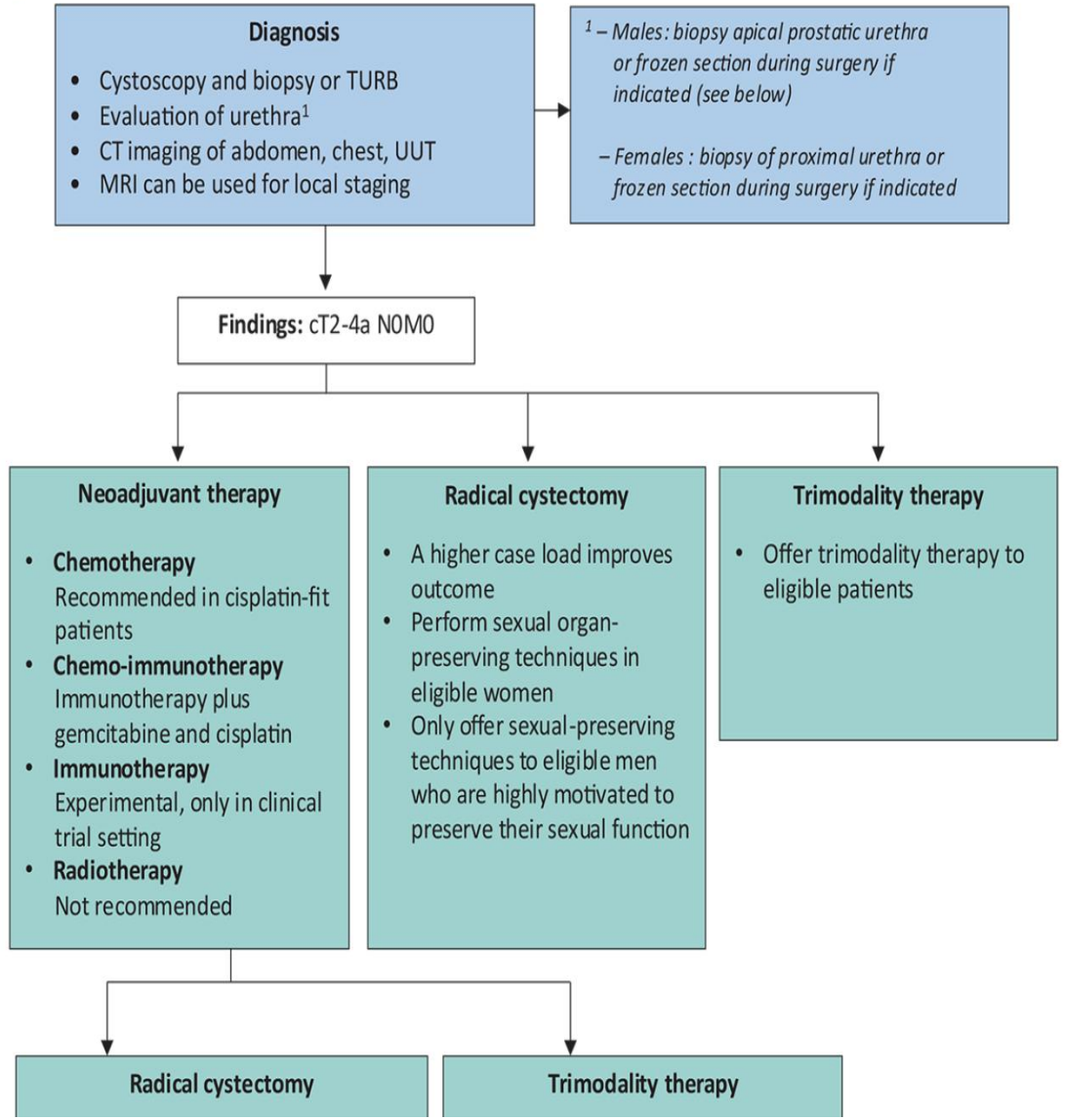
EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

GUIDELINES EAU 2025

Peri-operative durvalumab plus neoadjuvant gemcitabine and cisplatin improves EFS and OS compared to neoadjuvant gemcitabine and cisplatin alone.	1b

Recommendations	Strength rating
If eligible for cisplatin-based chemotherapy, offer neoadjuvant cisplatin-based combination chemotherapy to patients with muscle-invasive bladder cancer (T2-T4a, cN0 M0).	Strong

Figure 7.1: Flow chart for the management of T2–T4a N0M0 urothelial bladder cancer



Is all crystal clear?

- Some questions always arise after the reading of any study that are open to debate?
  - How valid is cisplatin split dose as a regime in the neo adj setting? How relevant is in clinical practice?
  - How relevant is the lack of statistically significant diff in pCR in ITT? Is not a good surrogate endpoint for IO?
  - How many patients do we overtreat with a perioperative approach? Do all patients need to be treated after surgery?
  - Do we have any means to select for patients most likely to relapse?
  - Are there any patient populations that might not benefit as much based on the study population and subgroup analysis [i.e. T2, N1] ?

A glimpse into the future

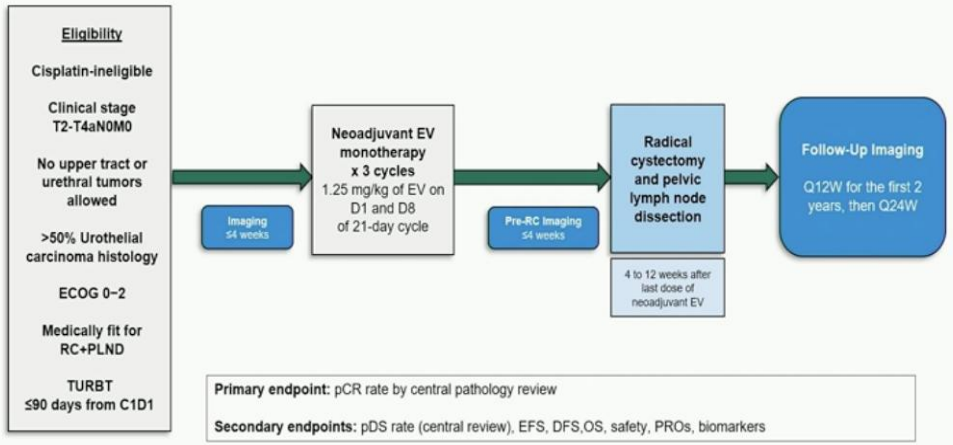
- ADC have shown some activity in this context
    - As single agent
    - In combos

ASCO Genitourinary Cancers Symposium

Study EV-103 Cohort H: Antitumor activity of neoadjuvant treatment with enfortumab vedotin monotherapy in patients with muscle invasive bladder cancer (MIBC) who are cisplatin-ineligible

Daniel P. Petrylak, Yale University, New Haven, CT; Thomas
Nataliya Mar, UC Irvine, Irvine, CA; Theodore S. Gourdin, Hol
Sandy Srinivas, Stanford University Medical Center, Palo Alto
New York, NY; Marla Guseva, Astellas Pharma Inc., Northbro
Bothell, WA; Christopher J. Holmes, Duke University, Duke C

EV-103 Cohort H Study Design



Primary endpoint: pCR rate by central pathology review

Secondary endpoints: pDS rate (central review), EFS, DFS,OS, safety, PROs, biomarkers

DFS: Disease-free survival; ECOG: Eastern Cooperative Oncology Group; EFS: Event-free survival; EV: Enfortumab vedotin; OS: Overall survival; pCR: pathological Complete Response rate; pDS: pathological Downstaging; RC+PLND: radical cystectomy + pelvic lymph node dissection; PROs: Patient-reported outcomes; TURBT: transurethral resection of bladder tumor

Safety: Treatment Emergent Adverse Events

EV-related TEAEs seen in ≥20% patients by preferred term	EV Mono (N=22)
Overall (all Grades)	22 (100)
Fatigue	10 (45.5)
Alopecia	8 (36.4)
Dysgeusia	8 (36.4)
Diarrhea	6 (27.3)
Nausea	6 (27.3)
Peripheral sensory neuropathy	6 (27.3)
Dry eye	5 (22.7)
Rash maculo-papular	5 (22.7)

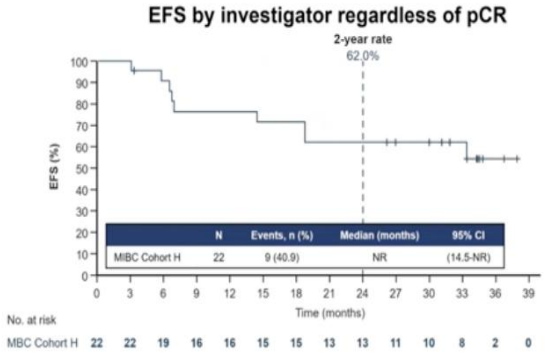
- Overall, 4 (18%) patients had Grade ≥3 EV-related TEAEs
  - Grade 3 EV-related TEAEs included: asthenia, dehydration, erythema multiforme, hyperglycemia, post procedural urine leak, rash maculo-papular, small intestinal obstruction
- No EV-related Grade 4 TEAEs or deaths were observed
- 3 deaths occurred on the study:
  - Acute kidney injury
  - Cardiac arrest (related to RC+PLND)
  - Pulmonary embolism (related to RC+PLND)

Efficacy: Central Pathology Review

Pathological Response	Central Pathology Results (N=22) n (%) [95% Confidence Interval]
Pathological Complete Response Rate (defined as absence of any viable tumor tissue: ypT0 and N0)	**8 (36.4%)** [17.2–59.3]
Pathological Downstaging Rate (defined as presence of ypT0, ypTis, ypTa, ypT1, and N0)	**11 (50.0%)** [28.2–71.8]

Event-Free Survival

In the overall population, median EFS has not been reached and EFS rate at 2 years was 62.0% (95% CI: 38.2-78.9)



- 8 patients (36.4%) achieved pCR following neoadjuvant treatment with EV; 6 continue to be disease free at data cutoff

Data cutoff: November 20, 2023.
EV, enfortumab vedotin; EFS, event-free survival; pCR, pathological complete response; NR, not reached.

Update in ASCO 2025

Study EV-103 cohort H: Neoadjuvant treatment with enfortumab vedotin (EV) monotherapy in cisplatin (cis)-ineligible patients (pts) with muscle invasive bladder cancer (MIBC)—3-year efficacy results.

N MAR Poster

ASCO Genitourinary Cancers Symposium

Abstract number: 665

Neoadjuvant treatment with disitamab vedotin plus perioperative toripalimab in patients with muscle-invasive bladder cancer (MIBC) with HER2 expression: updated efficacy and safety results from the phase II RC48-C017 trial

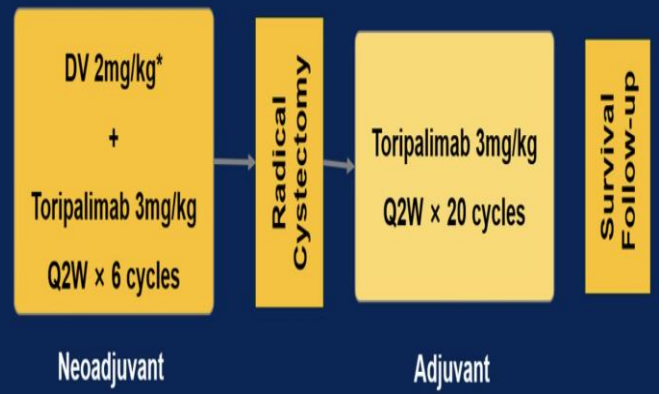
Xinan Sheng[1]*, Cuijian Zhang[2], Peng Du[3], Kaiwei Yang[2], Yongpeng Ji[3], Li Zhou[1], Benkui Zou[4], Hang Huang[5], Yonghua Wang[6], Xue Bai[7], Dan Feng[7], Yong Yang[3], Jiasheng Bian[4], Zhixian Yu[5], Haitao Niu[6], Jianmin Fang[8], Zhisong He[2], **Jun Guo[1]****

*presenting author **corresponding author

[1] Department of Genitourinary Oncology, Peking University Cancer Hospital & Institute, Beijing, China. [2] Department of Urology, Peking University First Hospital, Beijing, China. [3] Department of Urology, Peking University Cancer Hospital, Beijing, China. [4] Shandong Cancer Hospital and Institute, Beijing, China. [5] The First Affiliated Hospital of Wenzhou Medical University, Wenzhou, China. [6] The Affiliated Hospital of Qingdao University, Qingdao, China. [7] RemeGen Co., Ltd., Yantai, China. [8] School of Life Science and Technology, Tongji University, Shanghai, China.

- HER2-targeting ADCs such as disitamab vedotin(DV) and trastuzumab deruxtecan (T-DXd) have emerged as effective treatment options for HER2 positive mUC who failed to chemotherapy and immunotherapy.[1-2]
- Disitamab vedotin(DV) plus Toripalimab (an anti-PD-1 inhibitor) has shown encouraging efficacy (confirmed objective response rate: 76.3%) in patients with HER2 expression (IHC 1+, 2+ or 3+) in a phase 1b/2 trial (RC48-C014).[3]
- The single-arm phase II RC48-C017 trial (NCT05297552) was conducted to evaluate the efficacy and safety of neoadjuvant DV plus perioperative toripalimab in patients with HER2-expression (IHC 1+, 2+ or 3+) MIBC.

- Histologically confirmed urothelial carcinoma;
- MIBC at stage of cT2-T4a, N0-1, and M0;
- Eligible for radical cystectomy (RC) + pelvic lymph node dissection (PLND);
- HER2 expression: IHC 1+, 2+, or 3+.



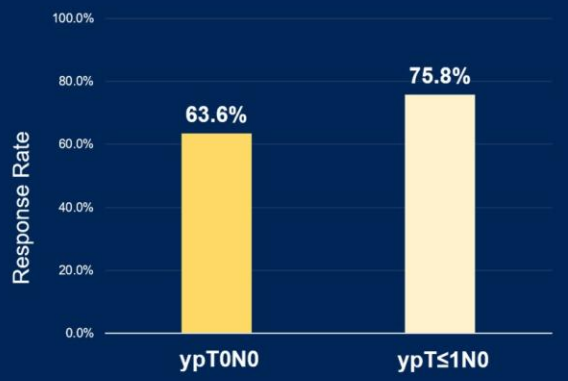
- **Primary endpoint:** Pathologic complete response (pCR, defined as ypT0N0) rate.
- **Secondary endpoints:** Pathological response rate (defined as ≤ypT1N0M0)#; event-free survival (EFS); overall survival (OS)^; adverse events.

Pathological response

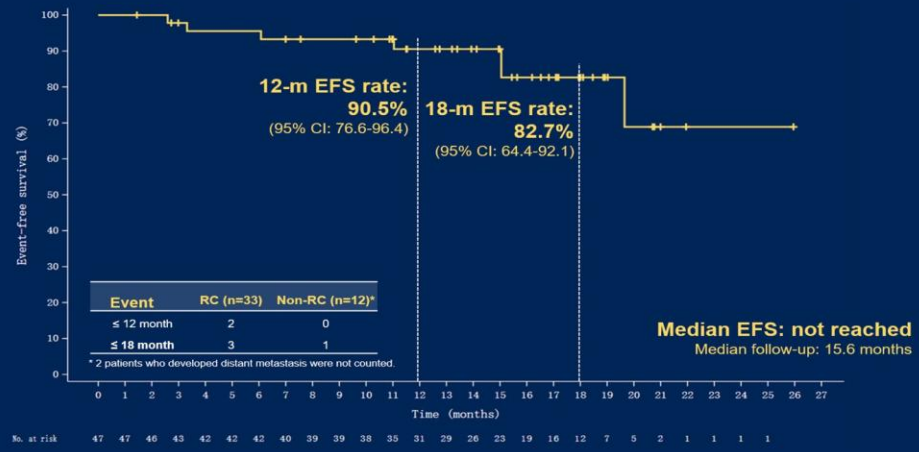
- Median time from end of neoadjuvant treatment to RC: 5.0 weeks (range: 2.6-13.1)

	Patients Received RC N=33
Pathological response	
pCR (ypT0N0), n (%)	**21 (63.6)**
95% CI	45.1-79.6
Pathological response (≤ypT1N0M0), n (%)	**25 (75.8)**
95% CI	57.7-88.9
Pathological staging, n (%)	
ypT0N0	21 (63.6)
ypT≤1N0	4 (12.1)
ypTisNx*	1 (3.0)
ypT2N0	4 (12.1)
ypT3N0	3 (9.1)
ypT4 or ypTanyN+	0

Pathological tumor response was assessed by the local pathologists based on the postoperative pathology.
*Pelvic lymph-node dissection was not performed.



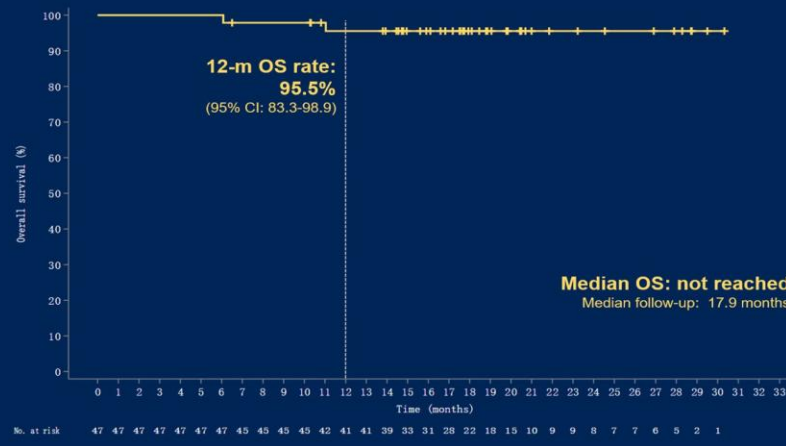
Event-free survival in ITT patients



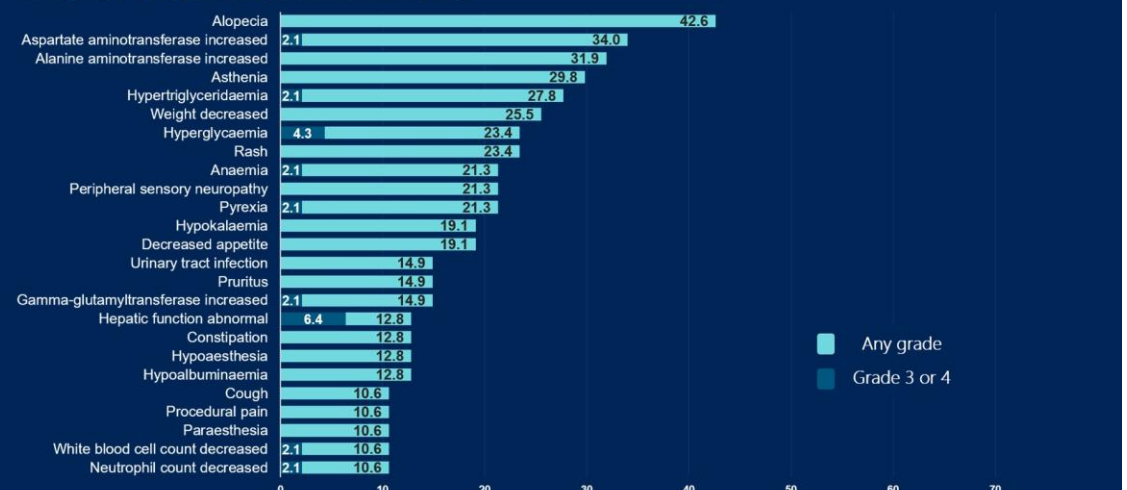
Event	RC (n=33)	Non-RC (n=12)*
≤ 12 month	2	0
≤ 18 month	3	1

* 2 patients who developed distant metastasis were not counted.

Overall survival in ITT patients



Most common TEAEs



The most common TEAEs occurring in ≥10% patients during the overall study period are listed. Abbreviations: TEAEs=treatment-emergent adverse events.

Conclusion

- RC48-017 is the first prospective study showing that ADC in combination with a PD-1 inhibitor as perioperative treatment provided prominent outcomes in operable MIBC.
  - pCR rate: 63.6% (95% CI: 45.1-79.6)
  - 12-month EFS rate: 92.5% (95% CI: 72.8- 98.1)
- Neoadjuvant DV plus toripalimab did not delay RC procedures or impact patients' ability to undergo RC. Safety profile was manageable with no new safety signals.
- The results indicated that neoadjuvant DV plus perioperative toripalimab had promising efficacy and acceptable safety in patients with HER2-expressing MIBC, warranting further investigation.

A glimpse into the future

- ~~ADC have shown some activity in this context~~
  - ~~As single agent~~
  - ~~In combos~~
- A number of me too studies and some new comers
  - CIS ELEGIBLE

The field is very active and 2025-26 might be a year of many news in MIBC

Cis-eligible MIBC (peri-operative)

KEYNOTE-866
Phase III, pembrolizumab + CTx → surgery → pembrolizumab
Changed primary endpoint: EFS (demoted pCR)

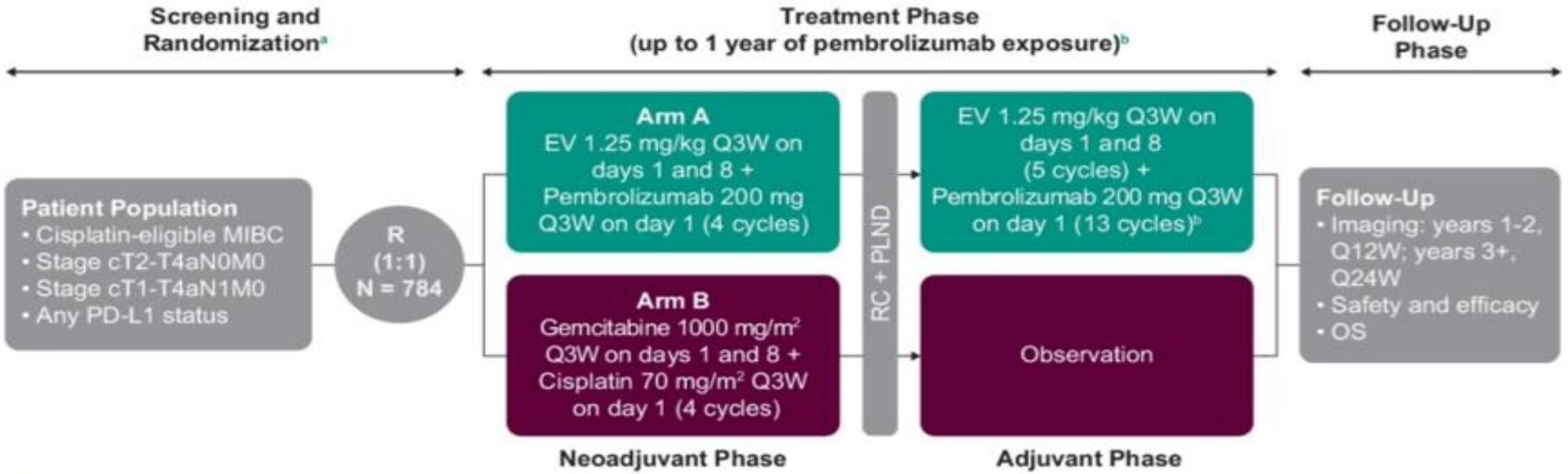
ENERGIZE
Phase III, nivolumab ± ~~IDO~~ + CTx → surgery → nivolumab ± ~~IDO~~
Removed IDO combination arm

KEYNOTE-B15 / EV-304
Phase III, pembrolizumab + EV → surgery → pembrolizumab + EV
Changed primary endpoint: EFS (demoted pCR)

ESMO 2025?

Adj=adjuvant; ctDNA=circulating tumour DNA; CTx=chemotherapy; EV=enfortumab vedotin; MIBC=muscle invasive bladder cancer.

EV 304



AE, adverse event; BICR, blinded independent central review; CT, computed tomography; MOW, most of world; MRI, magnetic resonance imaging; Q3W, every 3 weeks; Q12W, every 12 weeks; Q24W, every 24 weeks; R, randomization.

[a]All patients will undergo baseline imaging studies (CT or MRI) for clinical staging (evaluated by BICR before randomization) and central pathology confirmation for pathologic stage pT2-T4a or pT1 (only if N1), urothelial histology, and PD-L1 expression.

[b]Until unacceptable AEs, intercurrent illness preventing further treatment administration, or investigator or patient decision to withdraw.

[c]CPS is the number of PD-L1–staining cells (tumor cells, lymphocytes, macrophages) divided by the total number of viable tumor cells, multiplied by 100.

A glimpse into the future

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  - ~~CIS ELEGIBLE~~
  - CIS INELEGIBLE

The field is very active and 2025-26 might be a year of many news in MIBC

Cis-ineligible/Cis-refusal MIBC (peri-operative)

~~**Nivolumab + NKTR-214**~~
~~Phase III, nivolumab ± NKTR-214 → surgery → nivolumab ± NKTR-214~~
Program closed

KEYNOTE-905 / EV-303
Phase III, pembrolizumab ± EV → surgery → pembrolizumab ± EV
Changed primary endpoint: EFS (demoted pCR)

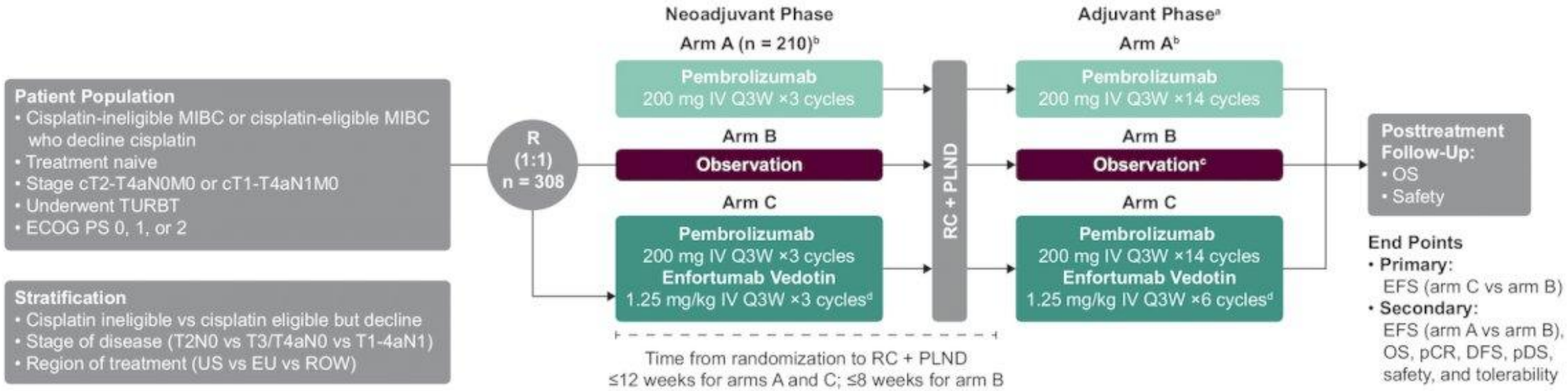
VOLGA (AZ)
Phase III, durvalumab ± tremelimumab + EV → surgery → durvalumab ± tremelimumab
Changed primary endpoints: EFS (demoted pCR)

THE ARRIVAL OF EV-PEMBO TO THE PERIOPERATIVE SETTING

THE ARRIVAL OF THE TRIPLETS?

EV-303

Study design



A glimpse into the future

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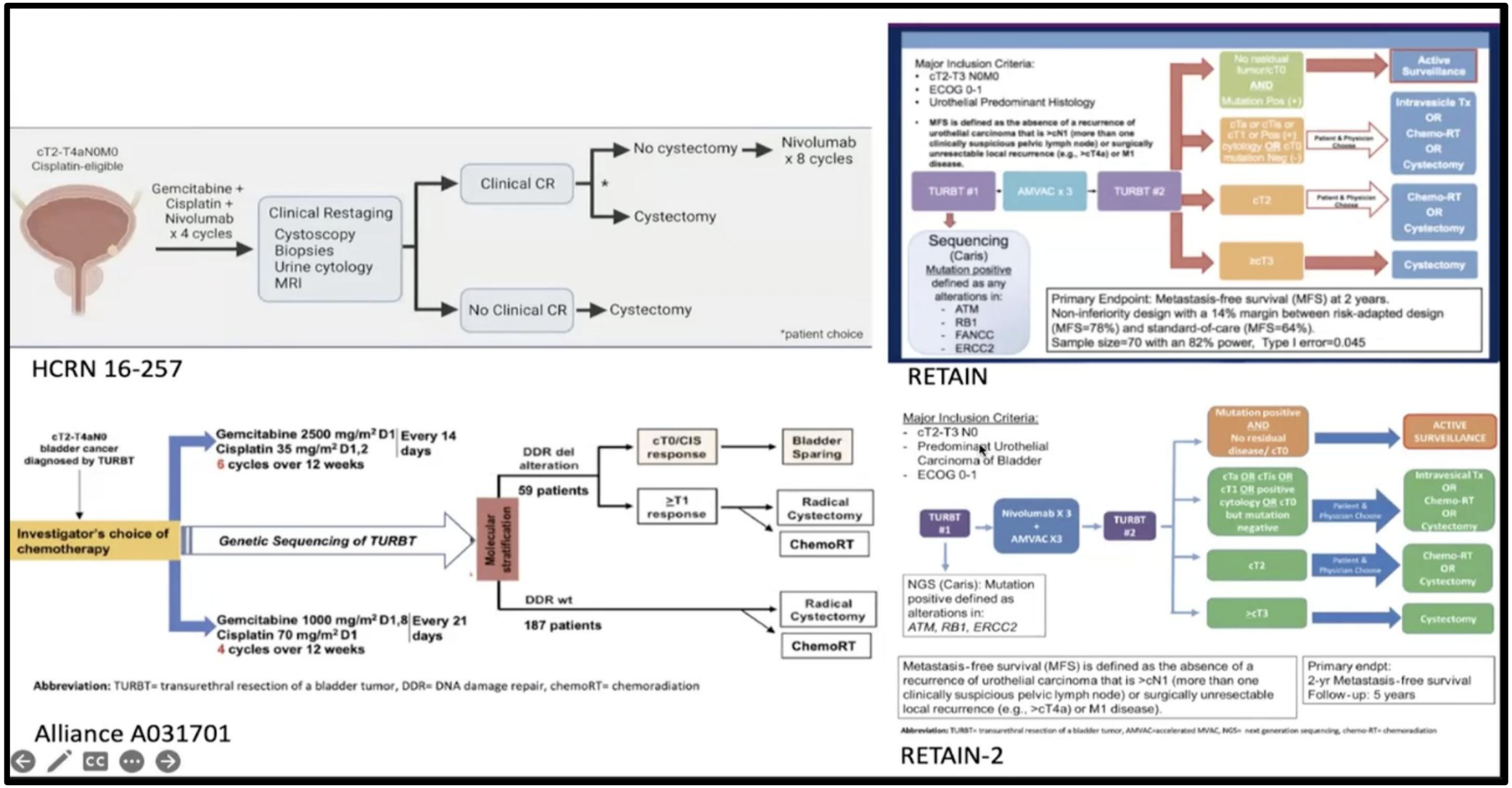
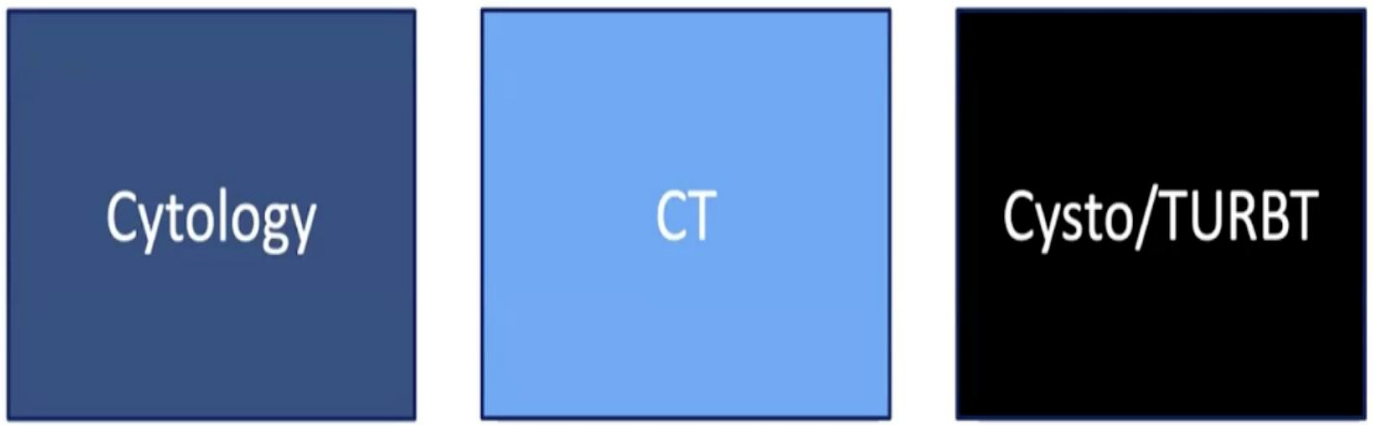
- ~~A number of me too studies and some new comers~~
  - ~~CIS ELEGIBLE~~
  - ~~CIS INELEGIBLE~~
- A new approach
  - Considering bladder. preservation

Clinical Complete Response and bladder preservation: Is it fair? Is it safe?

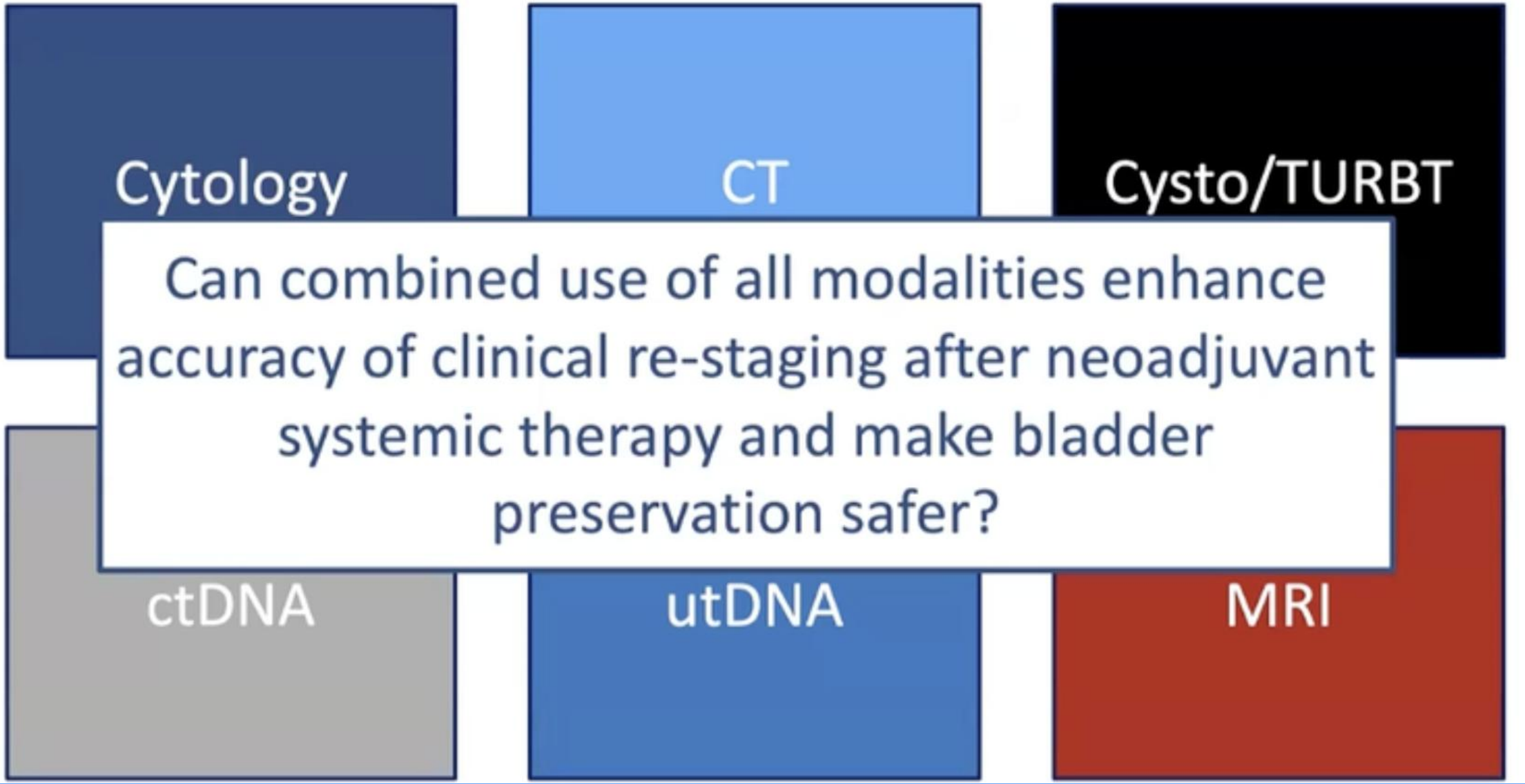


•Daniel M. Geynisman et al.Phase II Trial of Risk-Enabled Therapy After Neoadjuvant Chemotherapy for Muscle-Invasive Bladder Cancer (RETAIN 1). *JCO* **43**, 1113-1122(2025). Galsky MD, Daneshmand S, Izadmehr S, et al. Gemcitabine and cisplatin plus nivolumab as organ-sparing treatment for muscle-invasive bladder cancer: a phase 2 trial. Nature Medicine; Published online 2 October 2023.; Geynisman DM, Abbosh P, Ross EA, et al. Phase II trial of risk-enabled therapy after neoadjuvant chemotherapy for muscle-invasive bladder cancer (RETAIN 1). J Clin Oncol. 2025;43(5):396-408.

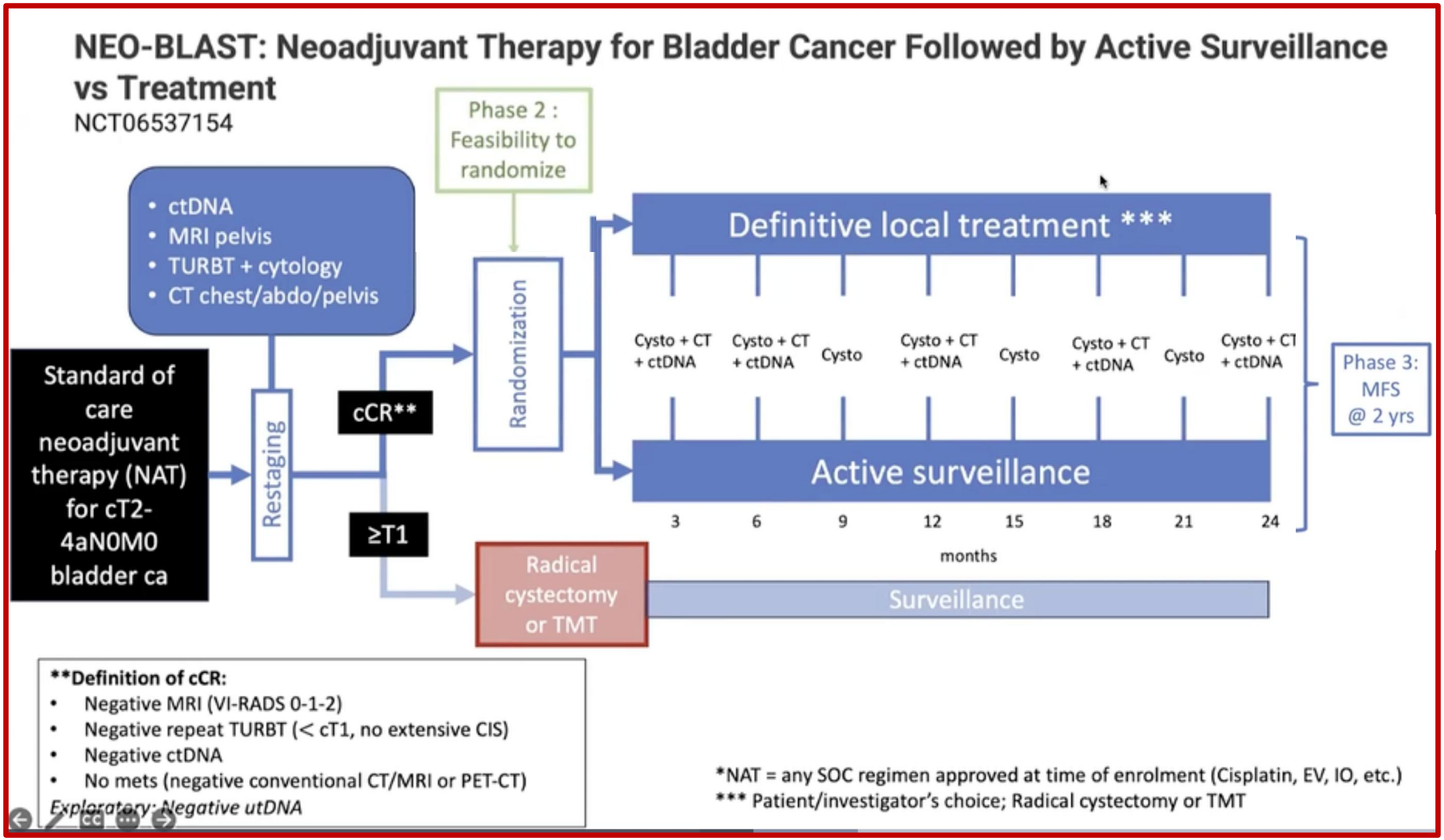
Current Re-Staging Methods Inadequate



Multiple studies demonstrate that clinical staging prior to RC misses residual MIBC in 20-30% of cases


Cytology
CT
Cysto/TURBT
Can combined use of all modalities enhance accuracy of clinical re-staging after neoadjuvant systemic therapy and make bladder preservation safer?
ctDNA
utDNA
MRI

A NEW APPROACH



A glimpse into the future

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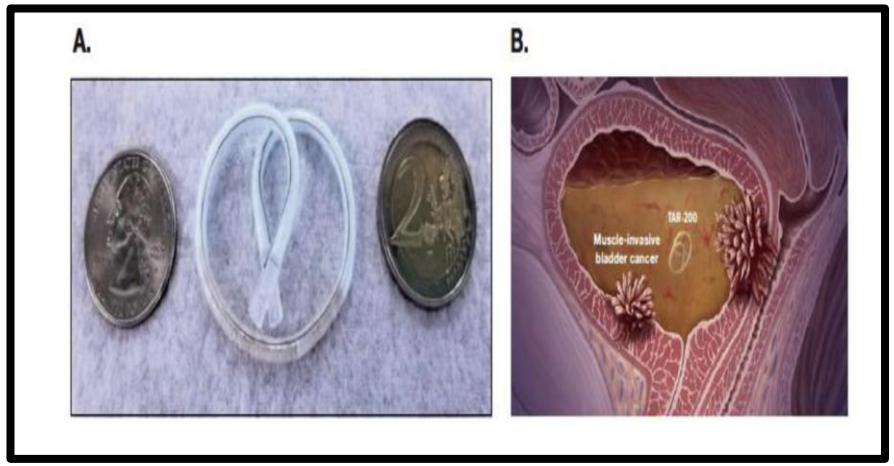
  - ~~CIS ELEGIBLE~~
  - ~~CIS INELEGIBLE~~
- ~~A new approach~~
  - ~~Considering bladder. preservation~~
- Intravesical devices
  - SUNRISE

Upcoming strategies



TAR-200, a gemcitabine-releasing intravesical system, forming a "pretzel"-like configuration within the bladder.

The sunrise program: TAR-200

A Study of TAR-200 in Combination With Cetrelimab and Cetrelimab Alone in Participants With Muscle-Invasive Urothelial Carcinoma of the Bladder (SunRISe-4)

SunRISe-4: Conclusions

- The combination of neoadjuvant **TAR-200 + cetrelimab** showed pCR and pOR rates of **42%** and **60%**, respectively, in patients with MIBC
  - In the cT2 subgroup, **48%** of patients treated with TAR-200 + cetrelimab achieved pCR, and **68%** were downstaged to ≤T1 at RC
- **Cetrelimab monotherapy** provided pCR and pOR rates of **23%** and **35%**, respectively
- **TAR-200 + cetrelimab** had a manageable safety profile in the neoadjuvant setting
  - Most TRAEs with TAR-200 + cetrelimab were low grade
  - The rate of discontinuations due to TRAEs was low at **13%**

SunRISe-4 demonstrates for the first time a benefit of the addition of TAR-200, an intravesical targeted releasing system, to checkpoint inhibition as neoadjuvant treatment in patients with MIBC

ESMO 2024

Presented by A Necchi at ESMO; September 13-17, 2024; Barcelona, Spain

A glimpse into the future

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  - ~~As single agent~~
  - ~~In combos~~
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  - ~~CIS ELEGIBLE~~
  - ~~CIS INELEGIBLE~~
- ~~A new approach~~
  - Considering bladder. preservation
- Intravesical devices
  - SUNRISE
- Alternative drug combos
  - SACITUZUMAB GOVITECAN + IO
  - OTHERS

STAY TUNED for ASCO 2025

First results of SURE-02: A phase 2 study of neoadjuvant sacituzumab govitecan (SG) plus pembrolizumab (Pembro), followed by response-adapted bladder sparing and adjuvant pembro, in patients with muscle-invasive bladder cancer (MIBC).

WORK IN PROGRESS

Phase 2 study of perioperative sacituzumab govitecan in combination with zimberelimab and domvanalimab for patients with muscle invasive bladder cancer ineligible or who refuse cisplatin-based chemotherapy: The PRISMA-1 Study

PRISMA-1 FUPOCAN oncología

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Background

- Neoadjuvant cisplatin-based chemotherapy (**NACT**) has demonstrated a 5-8%[1] improvement in 5-year overall survival (OS) in patient with muscle invasive bladder cancer (MIBC), **but its routine implementation is still low** due to concerns about toxicity/efficacy and **about 50% of patients** are considered **cisplatin ineligible**.
- Immune-checkpoint inhibitors (ICI) and antibody drug conjugates (ADC) have demonstrated separately clinical activity in the perioperative setting and remarkable efficacy of ADC-ICIs combos in patients with advanced urothelial cancer has been shown: **New combos in the perioperative setting seem an interesting approach.**[2-3]
- PRISMA-1 will evaluate **safety and efficacy** of the **Trop-2 directed ADC**, sacituzumab govitecan (SG) in combination with the **anti-PD1** zimberelimab (Z) and the **anti-TIGIT** domvanalimab (D) in MIBC.
- Additionally, **predictive biomarkers of response will be searched and the role of ctDNA will be evaluated in the perioperative setting** to better select for patients who need post operative treatment.

Eligibility

Key Inclusion criteria:
- Muscle invasive urothelial carcinoma of the bladder stage cT2-T4cN0-1cM0, fit and planned for cystectomy.
- Refusal of neoadjuvant cisplatin-based chemotherapy or patients in whom neoadjuvant cisplatin-based therapy is not appropriate.

Key Exclusion criteria:
- Known or suspected autoimmune disease or primary immunodeficiency.
- Receiving treatment with inhibitors/inducers UGT1A1.
- Other malignancy (low-risk prostate cancer are allowed).
- Patients on dialysis.
- Invasive catheters (i.e. percutaneous nephrostomy).

Objectives

Primary endpoint:
- Efficacy: Pathological complete response (pCR) rate.

Secondary endpoints:
- Downstaging rate.
- Relapse free survival and OS.
- Safety profile.
- Predictive biomarkers.
- ctDNA clearance.

Biomarker analysis

Tissue Samples
T1: Diagnosis tissue from TURBT.
T2: Cystectomy.

Blood Samples
All patients:
B1 (SCR) + B2 (after neoadjuvant tx) + B3 (after surgery).

FU Cohort (pCR and negative ctDNA after surgery):
B4-B7 (+B8).

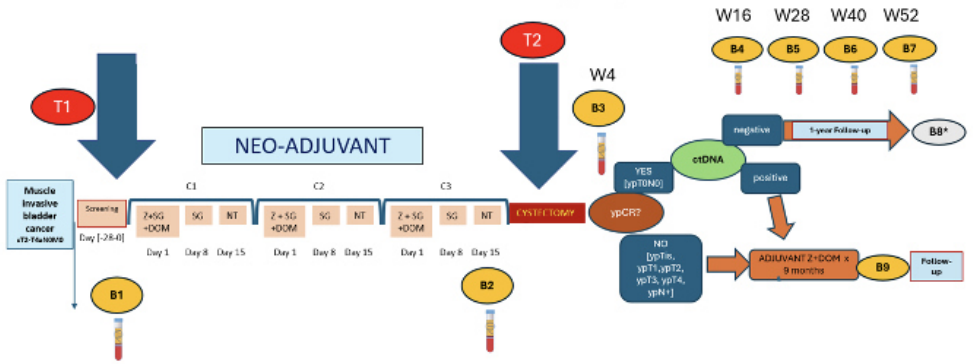
Adjuvant Cohort:
B9 (after adjuvant).

Study Design

Phase 2, single arm, multicenter, open-label
cT2-T4cN0-1cM0
ECOG PS 0-2
Non eligible or refuse NACT

Recruitment in two stages:
1st Stage: **8 patients SG+Z**
2nd Stage:. **8 patients SG+Z+D,**
if safe : Recruitment up to 70 patients

Central laboratory:
Hospital Universitario Marqués de Valdecilla



- **Three Q3W neoadjuvant cycles of Z (360mg D1) + D (1200mg D1) + SG (7,5mg/m2 D1&8) followed by cystectomy.**
- **After surgery: Only patients with no pCR or pCR but still positive ctDNA: 12 cycles of adjuvant Z+D.**
- **The remaining (FU cohort) will be followed with serial ctDNA and imaging.**

References

1.Stein JP, Lieskovsky G, Cote R, Groshen S, Feng AC, Boyd S, et al. Radical Cystectomy in the Treatment of Invasive Bladder Cancer: Long-Term Results in 1,054 Patients. J Clin Oncol. 1 feb 2001;19(3):666-75; 2. Powles T, Kockx M, Rodriguez-Vida A, Duran I, Crabb SJ, Van Der Heijden MS, et al. Clinical efficacy and biomarker analysis of neoadjuvant atezolizumab in operable urothelial carcinoma in the ABACUS trial. Nat Med. Nov. 2019;25(11):1706- 14.; 3. ASCO 2024 meeting Cigliola A et al. J Clin Oncol 42, 2024 (suppl 17; abstr LBA4517).

Acknowledgments

This study was supported by Gilead Sciences.
The authors thank APICES for its support with the study setup, project management and medical writing.

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A glimpse into the future

- ~~ADC have shown some activity in this context~~
  - ~~As single agent~~
  - ~~In combos~~
- ~~A number of me too studies and some new comers~~
  - ~~CIS ELEGIBLE~~
  - ~~CIS INELEGIBLE~~
- ~~A new approach~~
  - ~~Considering bladder. preservation~~
- ~~Intravesical devices~~
  - ~~SUNRISE~~
- Alternative drug combos
  - ~~SACITUZUMAB GOVITECAN + IO~~
  - OTHERS

Other combos

CLONEVO: Preoperative abemaciclib for cisplatin-ineligible muscle-invasive bladder cancer (MIBC) with molecular response assessment.

B FALTAS. Rapid oral

Pathologic response and safety of neoadjuvant pembrolizumab with or without entinostat in muscle-invasive urothelial cancer (MIUC).

T ROSE. Poster

Other interesting data to be presented at ASCO 2025

Updated results from a phase II study of perioperative disitamab vedotin (RC48-ADC) plus cadonilimab (AK104) for HER2-expressing muscle-invasive bladder cancer (MIBC).

S. HAN. Poster

Microbiota proteomics profiles in muscle-invasive bladder carcinoma related to response to neoadjuvant chemotherapy.

A. PINTO. Poster

MRI radiomics to predict outcome of neoadjuvant chemotherapy in patients with muscle invasive bladder cancer undergoing radical cystectomy.

L Schwartz Poster

Take home message

- Proper management of patients with MIBC requires the integration of multiple disciplines/strategies to maximize benefit and increase chances of long term disease control and OS
- Durvalumab + cisplatin-gemcitabine neoadjuvant followed by adjuvant durvalumab has recently demonstrated and improvement in EFS and OS and should be considered as a new SOC
- Yet, new approaches are being developed including different drug combinations and strategies that prioritize a bladder sparing approach
- At ASCO 2025 some interesting data will be presented about progress in this field

Thanks

Coming up at ASCO 2025

First results of SURE-02: A phase 2 study of neoadjuvant sacituzumab govitecan (SG) plus pembrolizumab (Pembro), followed by response-adapted bladder sparing and adjuvant pembro, in patients with muscle-invasive bladder cancer (MIBC).

A. NECHHI. Rapid oral

CLONEVO: Preoperative abemaciclib for cisplatin-ineligible muscle-invasive bladder cancer (MIBC) with molecular response assessment.

B FALTAS. Rapid oral

Pathologic response and safety of neoadjuvant pembrolizumab with or without entinostat in muscle-invasive urothelial cancer (MIUC).

T ROSE. Poster

First survival outcomes and biomarker results of SURE-01: Neoadjuvant sacituzumab govitecan (SG) monotherapy, followed by radical cystectomy (RC), in patients with muscle-invasive urothelial bladder cancer (MIBC).

B MAIORANO. Poster

Correlation of circulating tumor DNA (ctDNA) dynamics with clinical response in muscle-invasive bladder cancer (MIBC) patients (pts) undergoing trimodality therapy (TMT).

I EPSTEIN. Poster

Coming up at ASCO 2025

Updated results from a phase II study of perioperative disitamab vedotin (RC48-ADC) plus cadonilimab (AK104) for HER2-expressing muscle-invasive bladder cancer (MIBC).

S. HAN. Poster

Microbiota proteomics profiles in muscle-invasive bladder carcinoma related to response to neoadjuvant chemotherapy.

A. PINTO. Poster

MRI radiomics to predict outcome of neoadjuvant chemotherapy in patients with muscle invasive bladder cancer undergoing radical cystectomy.

L Schwartz Poster

Study EV-103 cohort H: Neoadjuvant treatment with enfortumab vedotin (EV) monotherapy in cisplatin (cis)-ineligible patients (pts) with muscle invasive bladder cancer (MIBC)—3-year efficacy results.

N MAR Poster

Coming up at ASCO 2025

Overall survival and biomarker results of NURE-Combo: A phase 2 study of neoadjuvant nivolumab (NIVO) and nab-paclitaxel (ABX) followed by postsurgical adjuvant NIVO in patients (pts) with muscle-invasive bladder cancer (MIBC).

C. MARCINELLI. Poster

Neoadjuvant stereotactic radiotherapy and enfortumab vedotin: A phase I/II study for localized, cisplatin ineligible, muscle invasive bladder cancer (STAR-EV).

T. ZANG Poster