

Novel Bladder Cancer Therapies

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Disclosures

- Bayer and J&J Advisory
- OncLive and Targeted Oncology

Bladder Cancer Outcomes

5-year relative survival rates for bladder cancer

These numbers are based on people diagnosed with bladder cancer between 2014 and 2020.

SEER* Stage	5-year Relative Survival Rate
In situ alone	97%
Localized	72%
Regional	40%
Distant	9%
All SEER stages combined	78%

Localized Bladder Cancer

Management of Non-Muscle Invasive Bladder Cancer

- AUA Low Risk: Surveillance
- AUA Intermediate Risk: Intravesical therapy versus surveillance
- AUA High Risk: Cystectomy preferred if very-high risk, BCG if no very-high risk features

AUA Risk Stratification for Non-Muscle-Invasive Bladder Cancer*

Low Risk	Intermediate Risk	High Risk
<ul style="list-style-type: none"> • Papillary urothelial neoplasm of low malignant potential • Low grade urothelial carcinoma <ul style="list-style-type: none"> ▶ Ta and ▶ ≤3 cm and ▶ Solitary 	<ul style="list-style-type: none"> • Low grade urothelial carcinoma <ul style="list-style-type: none"> ▶ T1 or ▶ >3 cm or ▶ Multifocal or ▶ Recurrence within 1 year • High grade urothelial carcinoma <ul style="list-style-type: none"> ▶ Ta and ▶ ≤3 cm and ▶ Solitary 	<ul style="list-style-type: none"> • High grade urothelial carcinoma <ul style="list-style-type: none"> ▶ CIS or ▶ T1 or ▶ >3 cm or ▶ Multifocal • Very high risk features (any): <ul style="list-style-type: none"> ▶ BCG unresponsive^l ▶ Certain histopathologic subtypes^m ▶ Lymphovascular invasion ▶ Prostatic urethral invasion

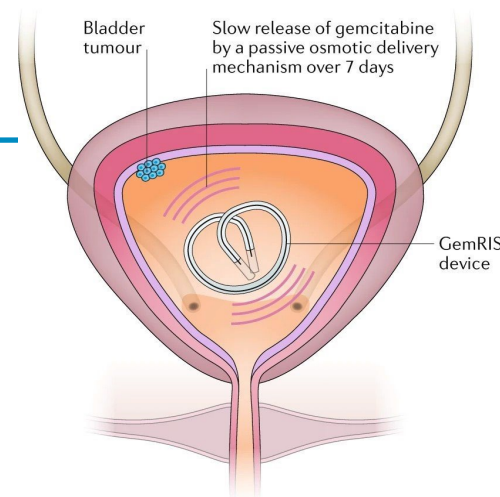
Localized Bladder Cancer

Management of Non-Muscle Invasive Bladder Cancer

- BCG unresponsive or intolerant:
 - Cystectomy
 - Intravesical chemotherapy: Mitomycin C, Gemcitabine, Valrubicin, Gem/Docetaxel
 - Pembrolizumab (2020) -> Phase II study, 46% CR at 12m
 - Systemic PD-1 inhibitor, Grade 3/4 AEs: 13%
 - Nadofaragene firadenovec-vcng (2023) -> Phase III study, 64% CR at 12m
 - Non-replicating adenovirus delivering IFN-2b, Grade 3/4 AEs: 4%
 - Nagopendekin alfa inbakicept-pmln + BCG (2024) -> Phase II/III study, 64% CR at 12m
 - IL-15 superantagonist, Grade 3/4 AEs: 3%

SunRise-1

- Tar-200 provides the highest single agent CR rate of 82.4%, 46% at 12m
- Grade 3/4 AEs: 13%
- *FDA Approval 9/9/2025 for BCG-unresponsive high risk MIBC with CIS*



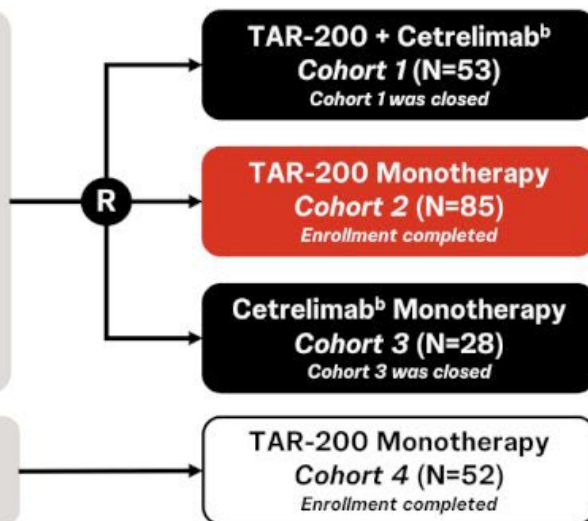
NCT04640623

Population:

- Aged ≥18 years
- Histologically confirmed HR NMIBC CIS (with or without papillary disease)
- ECOG PS of 0-2
- Persistent or recurrent disease within 12 months of completion of BCG
- Unresponsive to BCG^{1,2} and not receiving RC

Population:

- Papillary-only HR NMIBC (no CIS)^a



TAR-200 dosing:
Q3W (indwelling) for the first 24 weeks;
then Q12W through Week 96

Cohorts 1-3:

Primary end point

- Overall CR rate

Key secondary end points

- Duration of response
- Overall survival
- Safety
- Tolerability

Cohort 4:

Primary end point

- DFS rate at 12 months

MoonRISe-1

- Tar-210 Erdafitinib Intravesical Delivery System for intermediate risk NMIBC with FGFR 2/3 alterations
- FGFR 2/3 alteration prevalence in 50-80% low grade NMIBC
- Open and recruiting at Ochsner!

Key eligibility criteria

- Adults (aged ≥ 18 years)
- Histologically confirmed IR NMIBC:
 - Ta LG/grade 1
 - Recurrent or
 - Primary: Multifocal, or ≥ 3 cm
 - Ta LG/grade 2
 - Primary
 - Recurrent
- With ≥ 1 risk factor^a
- FGFR2/3 alterations by central or local tissue or urine testing

Stratification factors

- Anticipated choice of intravesical chemotherapy
- Newly diagnosed versus recurrent disease
- Cystoscopic assessment method (white light vs photodynamic diagnostics)

1:1
(N \approx 540)

R

TAR-210
(n \approx 270)
(Q12W for 1 year)

**Investigator's choice of intravesical
chemotherapy (n \approx 270)**
MMC or gemcitabine
(QW for 4 to 6 doses [induction]
and maintenance for 6 months to 1 year)

Primary end point

- Disease-free survival^b

Key secondary end points

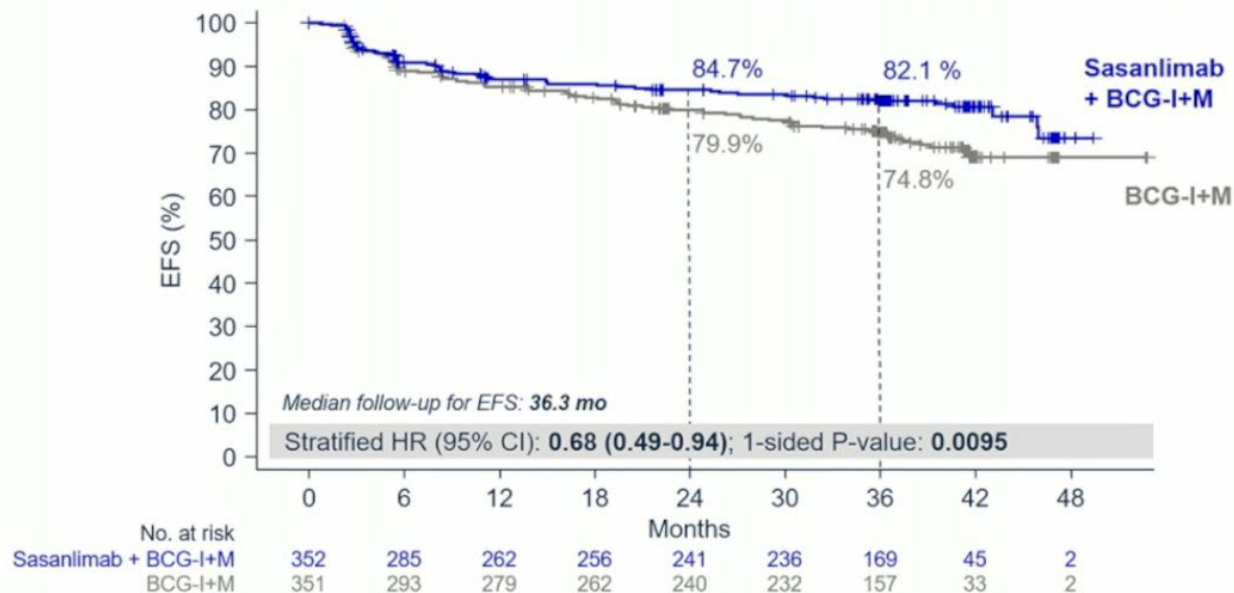
- Time to next treatment
- High grade recurrence-free survival
- Progression-free survival
- Rate of diagnostic and therapeutic urological interventions
- Safety and tolerability

CREST

- Sasanlimab, SubQ PD1 inhibitor, and BCG – *pending FDA approval*
- Complete response at 36 months: 92% (S+ BCG) vs 87.4% (BCG)
- S + BCG 32% lower EFS at 36 months, no OS benefit at 36 months
- Grade 3/4 AEs: 15%, primarily thyroid disorders, rash and hepatitis

Primary Endpoint EFS by Investigator: Arm A vs Arm C

The risk of experiencing an EFS event was 32% lower with sasanlimab + BCG-I+M vs BCG-I+M



ESMO 2025 – Late Breaking Abstracts

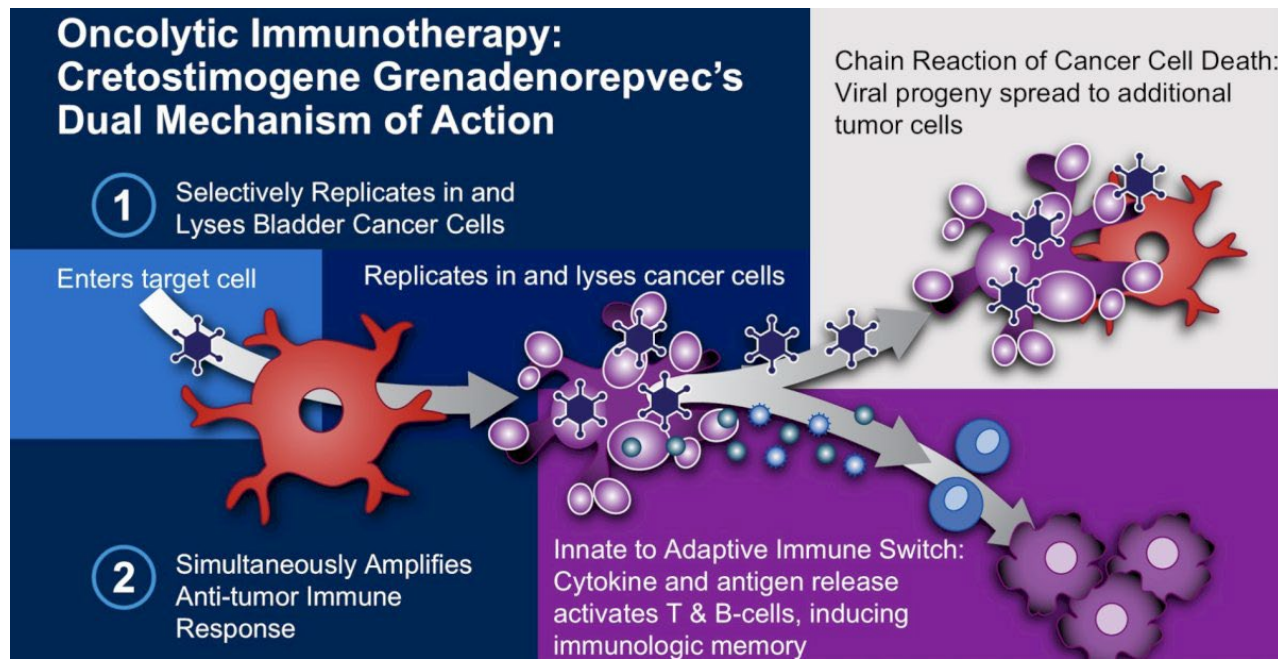
- POTOMAC: Phase III Durvalumab & BCG
 - Durvalumab q4w up to one year, primary endpoint EFS
 - Press release 5/2025 shows improved DFS
- ALBAN: Phase III Atezolizumab & BCG
 - Atezolizumab q3w up to one year, primary endpoint is EFS



ESMO 2025 Berlin 10/17 – 10/21/25

BOND-003

- Phase III single arm study of Cretostimogene Grandenorepvec for BCG-unresponsive NMIBC, *pending FDA approval*
- Conditionally replicating oncolytic serotype 5 adenovirus
- 46.3% CR at 12 months, Grade 3/4 AEs: 0
- CORE-008 Phase II for high risk non-muscle invasive bladder cancer open at Ochsner!



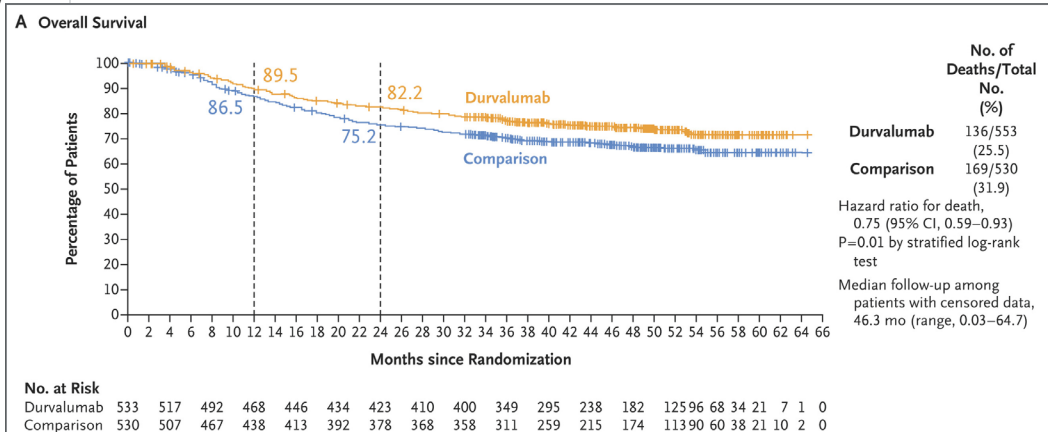
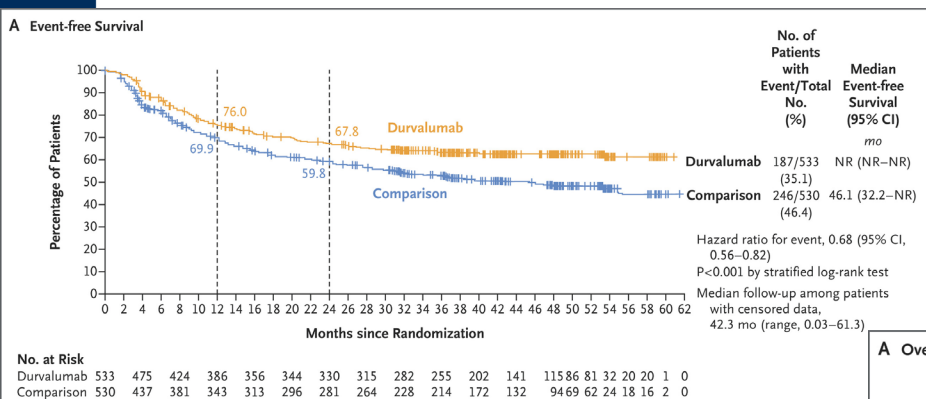
Localized Bladder Cancer

Management of Muscle Invasive Bladder Cancer

- Neoadjuvant Cisplatin-based chemotherapy if eligible -> Cystectomy
 - Adjuvant immunotherapy if eligible
 - VESPER study shows improved PFS with neoadjuvant ddMVAC x6 versus Gem/Doce x4 (2022)
- Bladder preservation with concurrent chemoRT after maximal TURBT
 - Ideally tumors <6 cm, no CIS, no hydronephrosis
 - Cisplatin, Gemcitabine or 5FU/Mitomycin as radiosensitizing agents

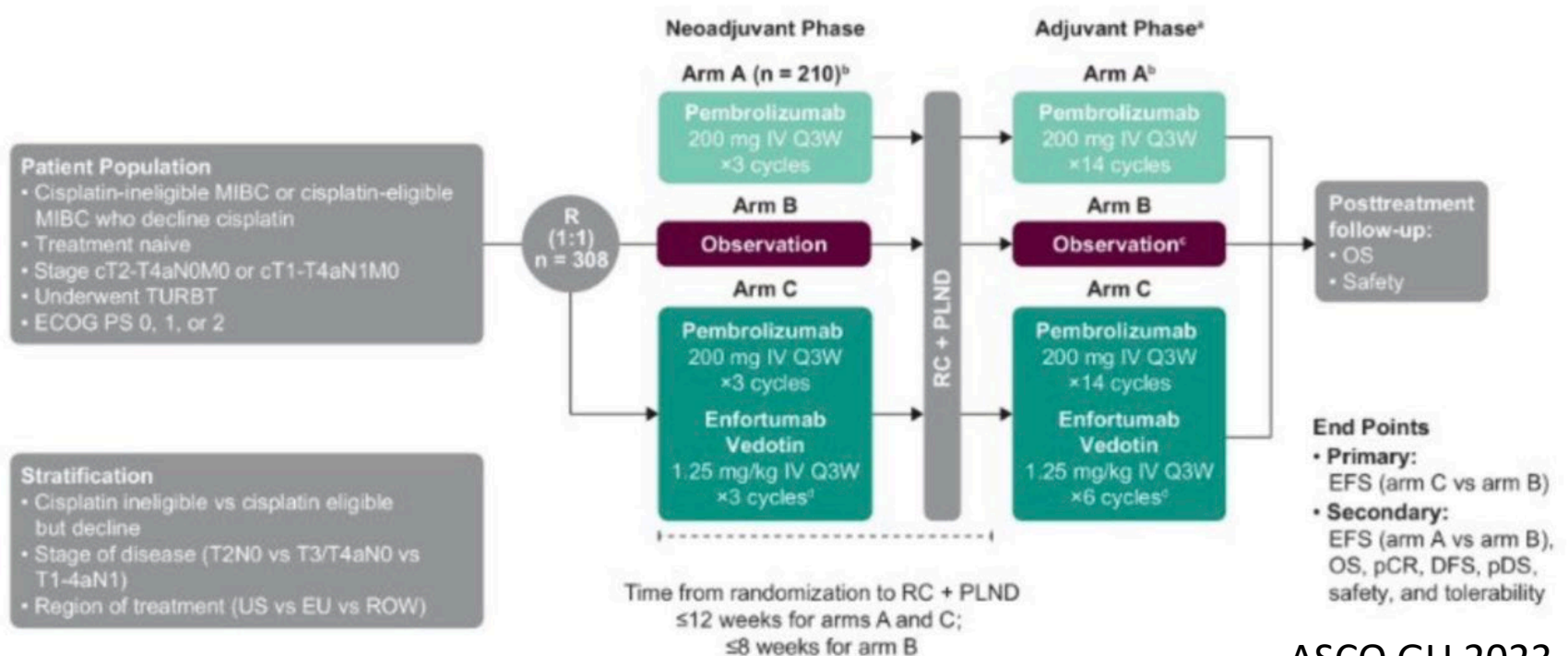
NIAGARA

- Neoadjuvant Gem/Cis/Durva -> Adjuvant Durvalumab **FDA 3/28/25**
- Key secondary endpoint shows improved OS by 25%, HR 0.75 with durvalumab arm. Grade 3/4 AEs: 40.6% G/C + D vs 40.9% G/C
- How does this fit with ddMVAC?
- Are we overtreating some patients with neoadjuvant IO?



ESMO 2025

- EV-303 / Keynote-905: Neoadjuvant EV/P -> Adjuvant EV/P
- 8/12/25 Press Release: EV/P has improved PFS, OS and pCR rates vs surgery alone
- How will pCR and OS compare to NIAGRA? Pembro only arm?
- EV-304/Keynote-B15 for Cisplatin eligible patients

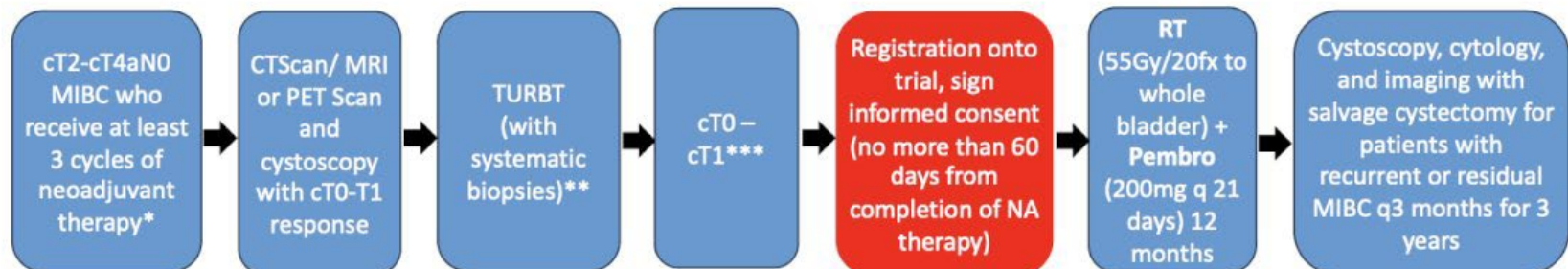


Bladder Sparing Approaches

- Some patients opt against surgery after neoadjuvant chemotherapy
- Paucity of prospective studies.
 - Does cT0 = pT0? Biomarkers? Does salvage/delayed surgery = upfront?
- GU 15-257(2023): Nivo/Gem/Cis x4 -> If CR Nivo q2w x8 cycles
 - 46% CR, clinical complete response for 2-year metastasis free survival was 0.97

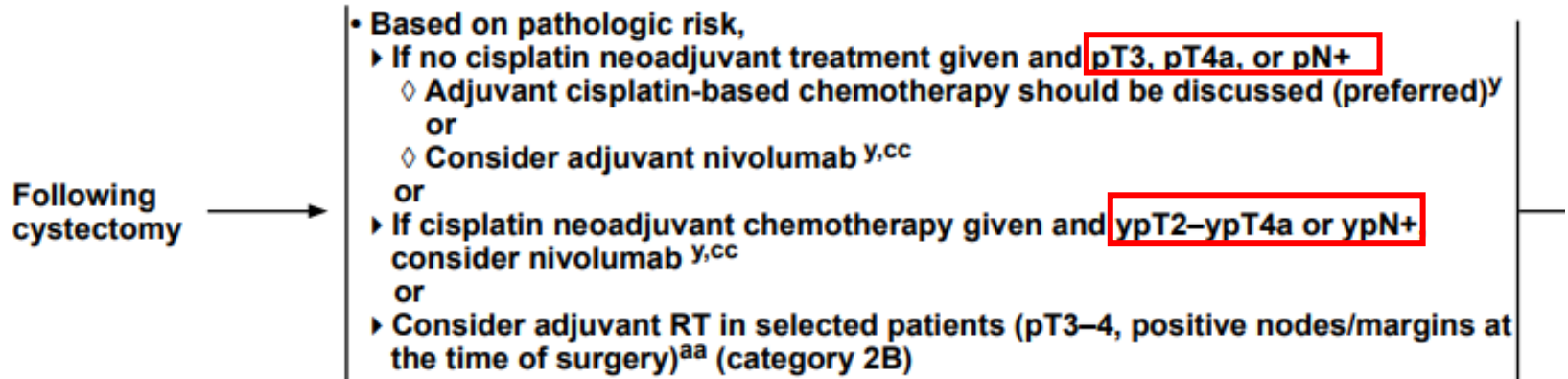
Schema

S2427 BRIGTH trial



Localized Bladder Cancer

Guidelines for Adjuvant Therapy

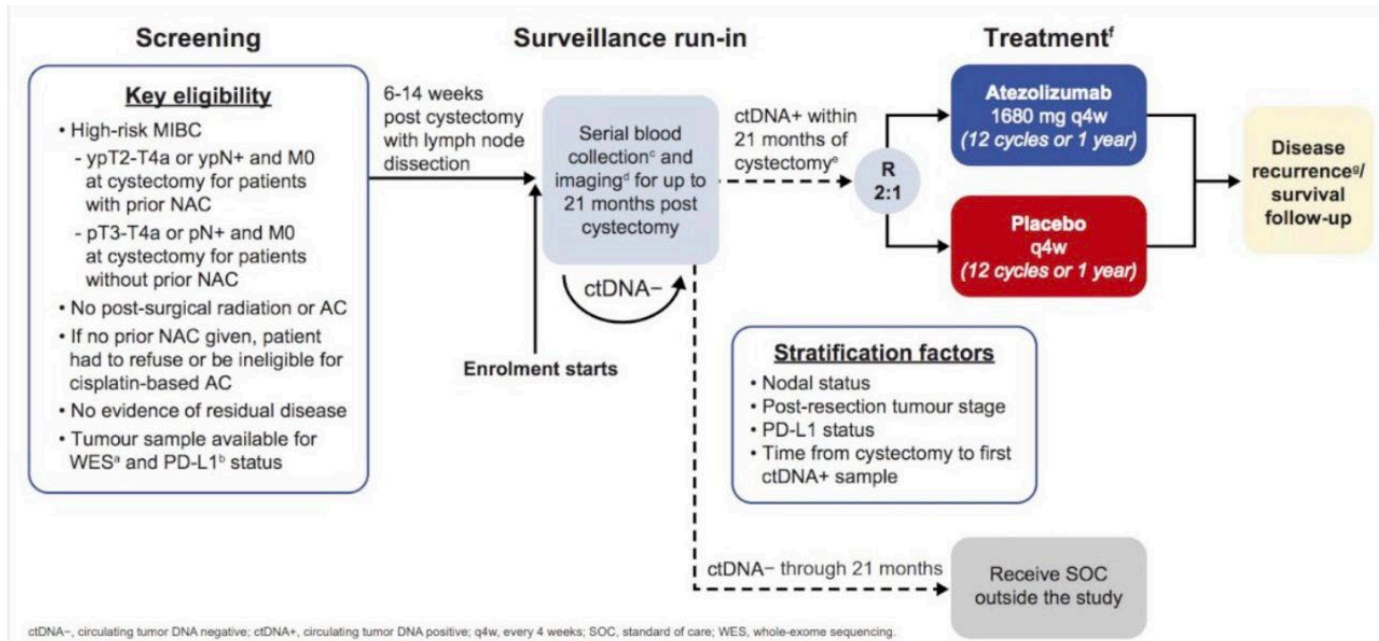


NCCN Bladder Cancer Guidelines

- CheckMate-274 – Adjuvant Nivolumab: DFS 22 months, OS 69.5 months (HR 0.76 [95% CI, 0.61 to 0.96]). Grade 3/4 AEs: 17.9% vs 7.2% (2021)
- AMBASSADOR – Adjuvant Pembrolizumab: DFS 29 months, OS immature but trend towards insignificant (HR: 0.98, 95% CI: 0.76 – 1.26, p=0.88). Grade 3/4 AEs: 48% vs 31% (2024)
 - Significant cross-over from placebo -> Nivolumab

ESMO 2025

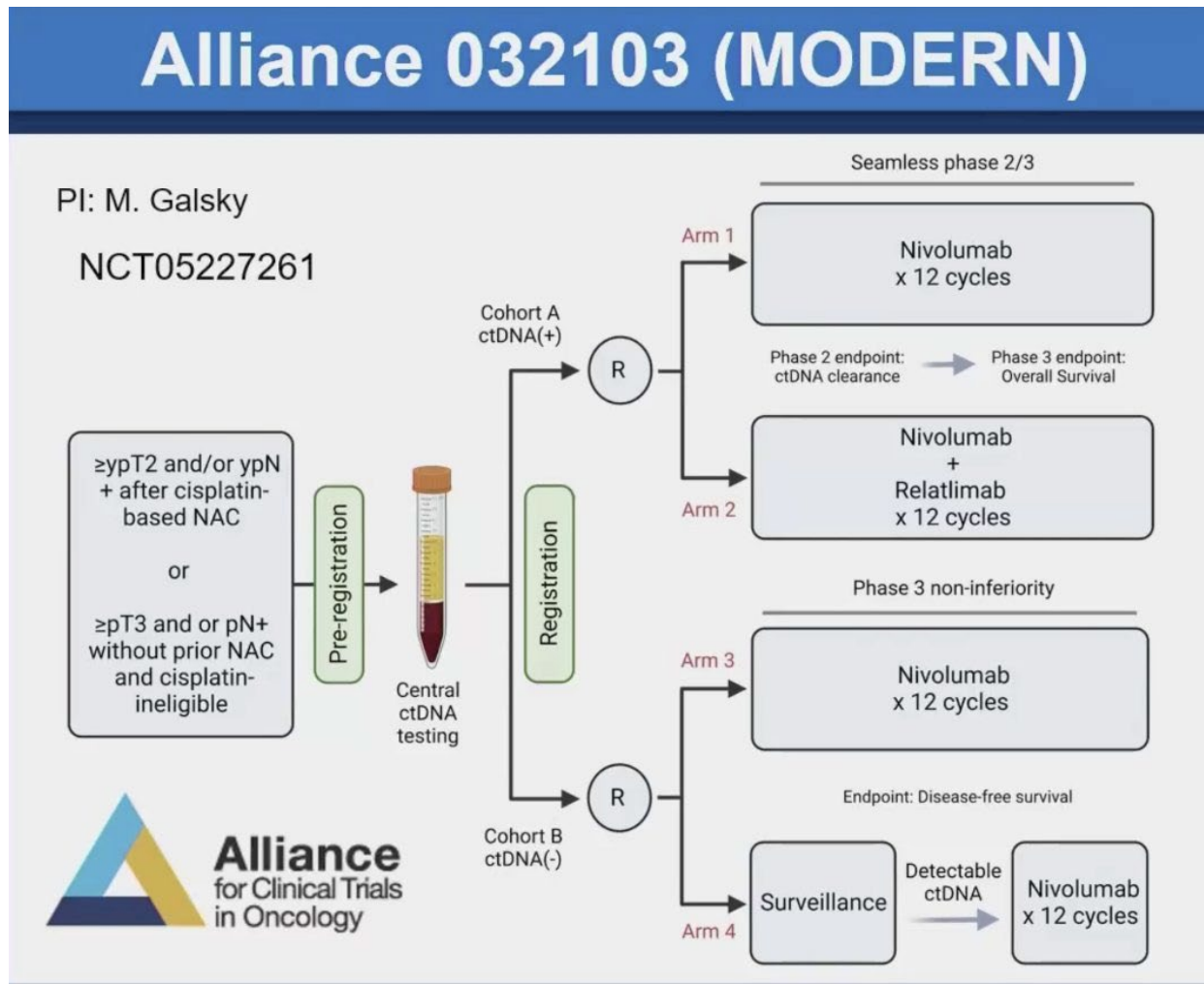
- Imvigor011: Adjuvant Atezolizumab in ctDNA+ post-cystectomy patients
- Imvigor010 Adjuvant – No DFS / OS improvement
 - Difference between PD-1 and PD-L1 inhibition?
 - Updated results shows DFS/OS benefit in ctDNA (+) population



ctDNA-, circulating tumor DNA negative; ctDNA+, circulating tumor DNA positive; q4w, every 4 weeks; SOC, standard of care; WES, whole-exome sequencing.
^a Evaluable WES data for development of a personalised multiplex PCR (mPCR) ctDNA assay from post-surgical blood samples (Signatera assay) are required.
^b Per the VENTANA SP142 IHC assay.
^c Every 6 weeks up to 36 weeks and q12w (every 12 weeks) up to 21 months.
^d q12w up to Week 84 or until 21 months from date of cystectomy, whichever occurs first.
^e ctDNA positivity is defined as ≥ 2 mutations per ctDNA mPCR assay. Patients will be randomised to treatment at the first ctDNA+ sample; full recovery from cystectomy and no evidence of disease recurrence within 28 days of treatment initiation is required.
^f Imaging and blood draws q9w (every 9 weeks) starting at Week 9 up to Week 54.
^g Assessed q9w up to Year 3; less often up to Year 6.

MODERN STUDY

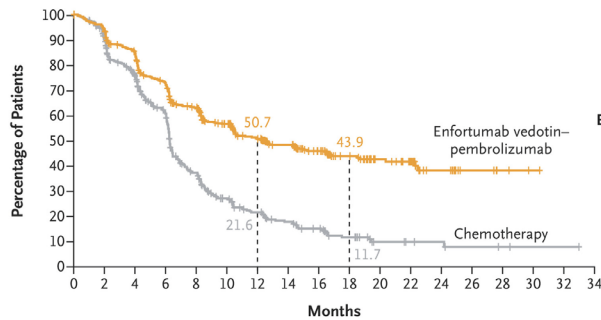
- Currently recruiting at Ochsner!



Metastatic Bladder Cancer – 1L EV/Pembro

- EV 103: Enfortumab Vedotin & Pembrolizumab versus platinum based chemotherapy in cisplatin-ineligible patients (4/2023)
 - Grade 3/4 AEs: 55.9% EV/P vs 69.5% chemotherapy
- EV 302: Enfortumab Vedotin & Pembrolizumab versus platinum based chemotherapy in untreated bladder cancer patients (12/2023)

A Progression-free Survival



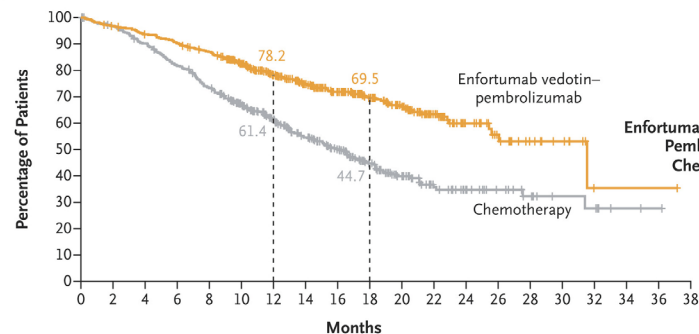
	No. of Events/ No. of Patients	Median Progression- free Survival (95% CI) mo
Enfortumab Vedotin– Pembrolizumab	223/442	12.5 (10.4–16.6)
Chemotherapy	307/444	6.3 (6.2–6.5)

Hazard ratio, 0.45 (95% CI, 0.38–0.54)
Two-sided P<0.001

No. at Risk

Months	0	2	4	6	8	10	12	14	16	18	20	22	24	26	28	30	32	34
Enfortumab vedotin–pembrolizumab	442	409	361	303	253	204	167	132	102	73	45	33	17	6	3	1		
Chemotherapy	444	380	297	213	124	78	56	41	30	19	8	6	5	3	2	1	1	

A Overall Survival



	No. of Events/ No. of Patients	Median Overall Survival (95% CI) mo
Enfortumab Vedotin– Pembrolizumab	133/442	31.5 (25.4–NE)
Chemotherapy	226/444	16.1 (13.9–18.3)

Hazard ratio, 0.47 (95% CI, 0.38–0.58)
Two-sided P<0.001

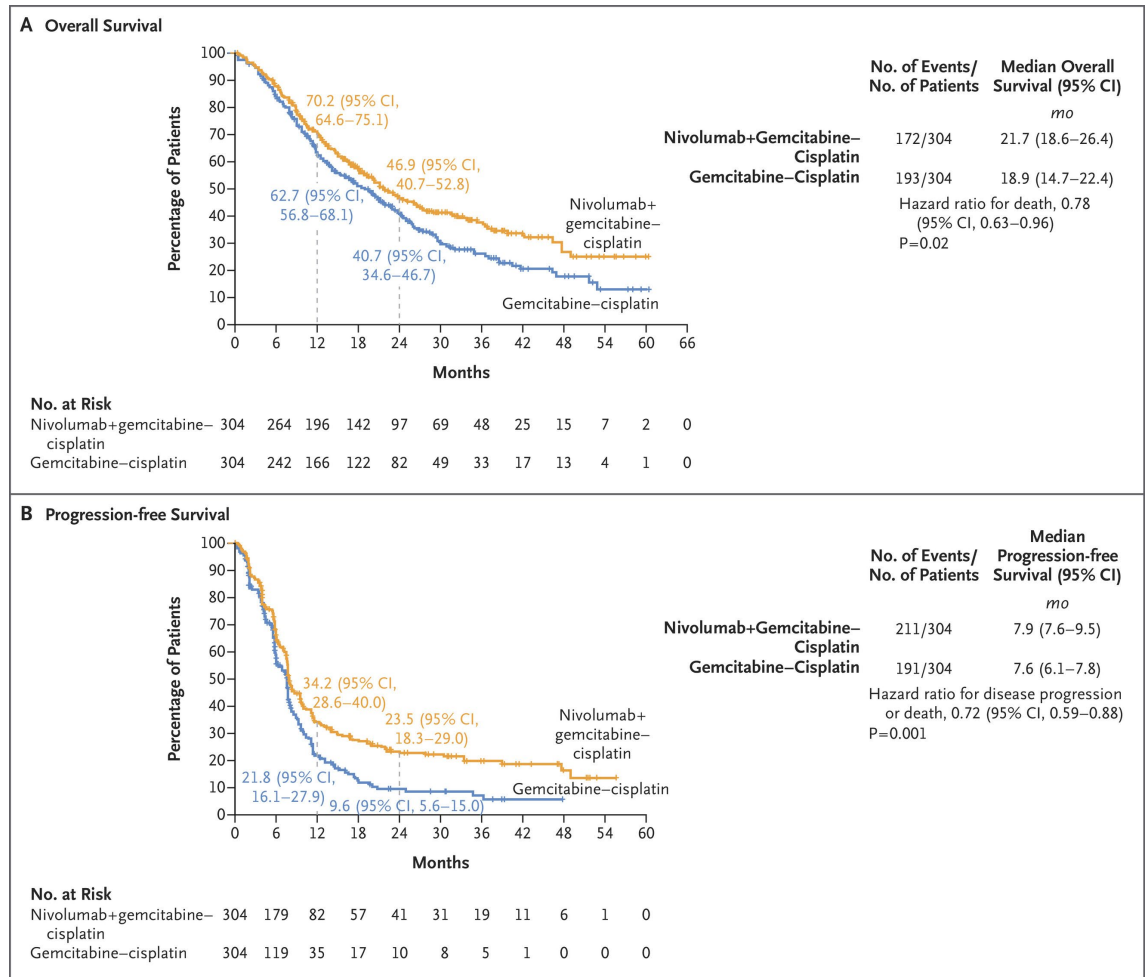
No. at Risk

Months	0	2	4	6	8	10	12	14	16	18	20	22	24	26	28	30	32	34	36	38
Enfortumab vedotin–pembrolizumab	442	426	409	394	376	331	270	222	182	141	108	67	36	22	12	8	1	1	1	
Chemotherapy	444	423	393	356	317	263	209	164	125	90	60	37	25	18	12	7	6	2	1	

Metastatic Bladder Cancer – 1L

Gem/Cis/Nivo

- CheckMate 901 - *FDA Approval 3/2024*
- Grade 3/4 AEs: 61.8% Nivo + G/C vs 51.7% G/C
- Included more histologic variants including adenocarcinoma, SqCC if predominate urothelial histology



Metastatic Bladder Cancer – ESMO 2025

- 1L Disitamab Vedotin + Toripalimab– Phase III 1st line therapy for HER2+
- Press Release 2/2025: Positive for PFS/OS

RC48-C016 Study Design

(NCT05302284)

Key Inclusion criteria

- No prior systemic treatment for unresectable locally advanced or metastatic UC
- Central lab-confirmed HER2 IHC 1+, 2+, or 3+
- Measurable disease per RECIST v1.1
- Eligible for cisplatin or carboplatin
- ECOG PS 0 or 1

N=243

R
1 : 1

N=241

Disitamab vedotin (2.0 mg/kg) a
+
Toripalimab (3.0 mg/kg)
IV Q2W

Gemcitabine (1000mg/m² d1, d8) +
Cisplatin (70mg/m², d1) / Carboplatin
(AUC=4.5, d1)
IV Q3W

Primary endpoints:

- PFS assessed by BIRC as per RECIST v1.1
- OS

Select secondary endpoints:

- PFS assessed by investigators
- ORR, DCR, and DoR assessed by both BIRC and investigators
- Safety

Stratification factors

- Cisplatin-eligibility (eligible vs ineligible)
- HER2 expression status (1+ vs 2+/3+)
- Visceral metastases (present vs absent)

• Treatment continued until disease progression/death, intolerable toxicity, or content withdraw.

• In the Chemo group, assignment of cisplatin or carboplatin were protocol-defined. Chemo was administered for a maximum of 6 cycles.

• Statistical plan for analysis: the first planned analysis was performed after approximately 278 PFS (final) and 183 OS events (interim); if OS was positive at interim, the OS interim analysis was considered final.

Metastatic Bladder Cancer –2L Chemo

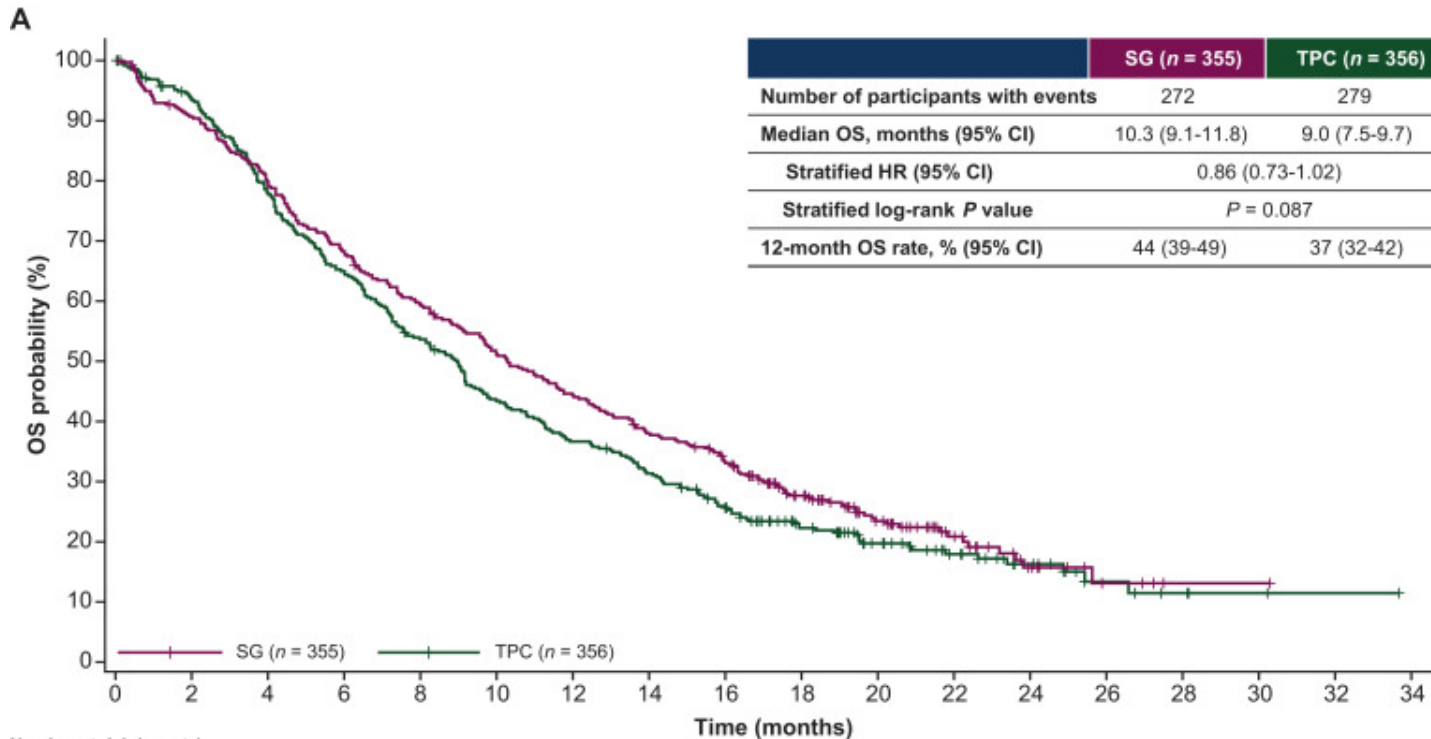
- Retrospective study out of Memorial Sloan Cancer Institute on outcomes of platinum-based chemotherapy after EV-Pembro
- Median PFS was 4.4 months, and median OS was 12 months

Disease response with platinum-based chemotherapy after enfortumab vedotin and pembrolizumab.

	N=38 (%)	95% CI
Observed response rate	17 (50%)	34%, 66%
Complete response	1 (2.9%)	0.15%, 17%
Partial response	16 (47%)	30%, 65%
Stable disease	6 (18%)	7.4%, 35%
Progressive disease	11 (32%)	18%, 50%

Metastatic Bladder Cancer – Sacituzumab

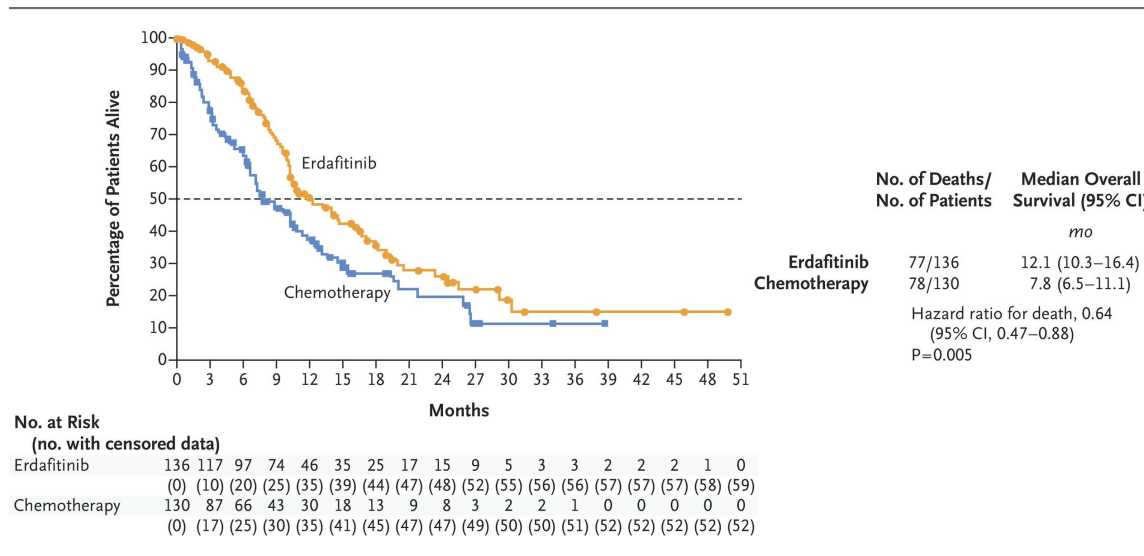
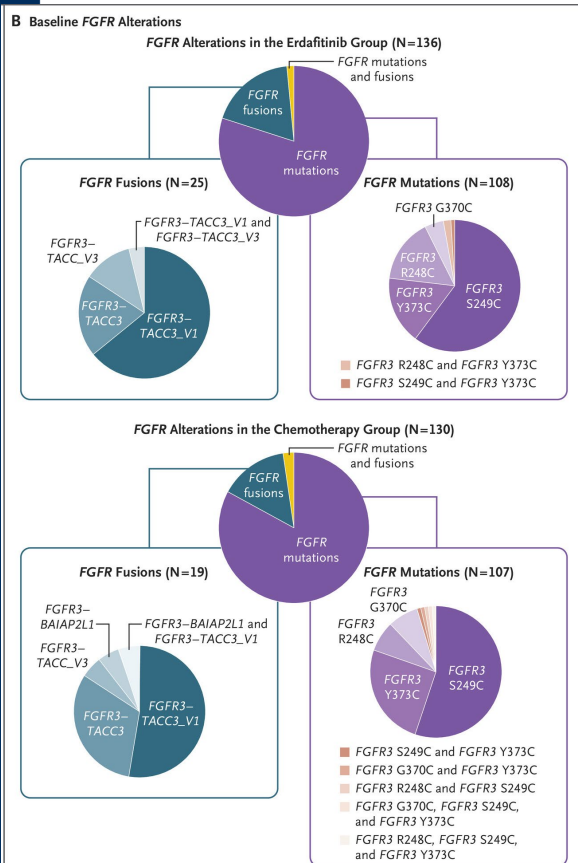
- TROPICS-04 Study, FDA Approval 2021. Withdrawn **10/2024**
- Sacituzumab vs 2L Investigator Choice Chemotherapy: ORR 28%
- 35% Grade 3 neutropenia, 12% febrile neutropenia, 12% G5 neutropenia
 - Low g-CSF rate



Annals of
Oncology
5/2025

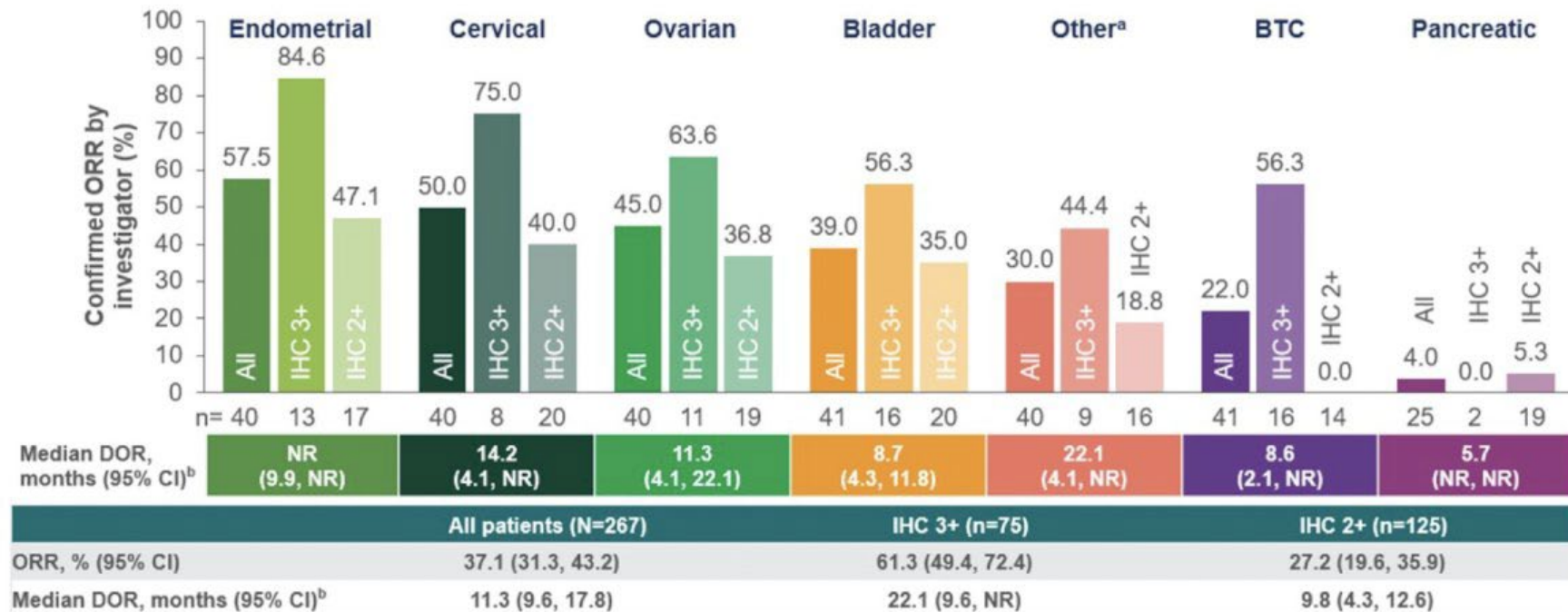
Metastatic Bladder Cancer –2L Erdafitinib

- THOR Study – Erdafitinib vs Chemotherapy. *FDA Approval 1/2024*
 - FGFR3 mutation in 10-20% advanced bladder cancer
 - Grade 3/4 AEs: 45.9% Erdafitinib, 46.4% chemotherapy
- Median OS – 12.1 months vs 7.8 months, HR 0.64



Metastatic Bladder Cancer –2L

- DESTINY-PanTumor02, Phase II – Phase II T-DXD for Her2 2+/3+ expressing locally advanced or metastatic cancer after prior therapy or without alternative. *FDA Approval 4/2024 for Her2 3+*
- Grade 3/4 AEs: 40.8%, neutropenia and anemia



Future Directions for Bladder Cancer

- Need for early molecular testing and histologic staining
- Utilization of biomarkers to evaluate early response to treatment
- SBRT for oligo-progression
- Bladder conserving approaches

Thank you!

