Advancing the treatment of muscle-invasive bladder cancer: Updates on immunotherapy in the perioperative setting

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Exploring the potential of immunotherapy in the perioperative setting in MIBC

Dr Laura Mertens
Oncologic Urologist,
Netherlands Cancer Institute,
Amsterdam, The Netherlands

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What is the current standard of care for perioperative treatment of MIBC, and what are the unmet needs?

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Current neoadjuvant therapy guidelines for MIBC

NCCN 2024[1]

- Neoadjuvant cisplatin-based combination ChT
- Cystectomy alone for those not eligible to receive cisplatin-based ChT

EAU 2024[2]

- If eligible for cisplatin-based ChT, offer neoadjuvant cisplatin-based combination ChT (T2–T4a, cN0 M0)
- Do not offer neoadjuvant ChT to patients who are ineligible for cisplatin-based combination ChT
- Only offer neoadjuvant immunotherapy to patients within a clinical trial setting

ESMO 2021[3]

- Three to four cycles of cisplatin-based neoadjuvant ChT

ChT, chemotherapy; EAU, European Association of Urology; ESMO, European Society for Medical Oncology; M, metastasis; MIBC, muscle-invasive bladder cancer; N, node; NCCN, National Comprehensive Cancer Network; T, tumour.

1. NCCN Clinical Practice Guidelines in Oncology. Bladder Cancer. Version 5.2024. Available at: www.nccn.org/guidelines/ (accessed 6 November 2024); 2. EAU Guidelines on Muscle-invasive and Metastatic Bladder Cancer, 2024. Available at: https://uroweb.org/guidelines/muscle-invasive-and-metastatic-bladder-cancer (accessed 6 November 2024); 3. Powles T, et al. *Ann Oncol*. 2022;33:244–58.

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Current adjuvant therapy guidelines for MIBC

NCCN 2024[1]

- If no cisplatin neoadjuvant treatment given and pT3, pT4a, or pN+
  - Adjuvant cisplatin-based ChT should be discussed or consider adjuvant nivolumab
- If cisplatin neoadjuvant ChT given and ypT2–ypT4a or ypN+, consider nivolumab
- Consider adjuvant RT in selected patients (pT3–4, positive nodes/margins at time of surgery)

EAU 2024[2]

- If no neoadjuvant ChT has been given, offer adjuvant cisplatin-based combination ChT to patients with pT3/4 and/or pN+ disease
- If not eligible for, or declined, adjuvant cisplatin-based ChT, offer adjuvant nivolumab to selected patients with pT3/4 and/or pN+ disease

ESMO 2021[3]

- There is weak evidence to support the use of adjuvant cisplatin-based ChT in patients who did not receive neoadjuvant therapy. Neoadjuvant ChT is preferred

ChT, chemotherapy; EAU, European Association of Urology; ESMO, European Society for Medical Oncology; M, metastasis; MIBC, muscle-invasive bladder cancer; N, node; NCCN, National Comprehensive Cancer Network; p, pathologic; RT, radiotherapy; T, tumour; yp, pathological after neoadjuvant therapy.

1. NCCN Clinical Practice Guidelines in Oncology. Bladder Cancer. Version 5.2024. Available at: www.nccn.org/guidelines/ (accessed 6 November 2024); 2. EAU Guidelines on Muscle-invasive and Metastatic Bladder Cancer, 2024. Available at: https://uroweb.org/guidelines/muscle-invasive-and-metastatic-bladder-cancer (accessed 6 November 2024); 3. Powles T, et al. *Ann Oncol.* 2022;33:244–58.

What is the rationale for immunotherapy for MIBC in the perioperative setting?

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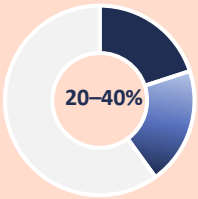
Cisplatin ineligibility in patients with MIBC



- Cisplatin-based NAC yields a 20–40% pCR rate at RC which correlates with improved overall survival.[1] However, less than 25% of patients with MIBC receive cisplatin-based NAC[2]
- A large proportion patients who are deemed cisplatin ineligible have residual disease after RC or patients can become cisplatin ineligible following surgery[3]

Under-utilization of cisplatin-based NAC often attributed to:

Inherent frailty[2]

Comorbidities[2]

Impaired renal function[2]

- Currently, no neoadjuvant systemic treatment options are available for patients with MIBC who are judged to be ineligible for cisplatin-based therapy[3]
- The introduction of ICIs has the potential to greatly expand therapeutic options available in the perioperative setting[4]

ICI, immune checkpoint inhibitor; MIBC, muscle-invasive bladder cancer; NAC, neoadjuvant chemotherapy; pCR, pathologic complete response; RC, radical cystectomy.

1. Hinsenveld FJ, et al. *BMC Cancer*. 2021;21:1161; 2. Jiang DM, et al. *Nat Rev Urol.* 2021;18:104–14; 3. Singh A, et al. *Curr Treat Options Oncol.* 2023;24:1213–30; 4. Esteban-Villarrubia J, et al. *Cancers (Basel).* 2023;15:566.

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What are the key immunotherapy approaches currently being explored for MIBC in the perioperative setting?

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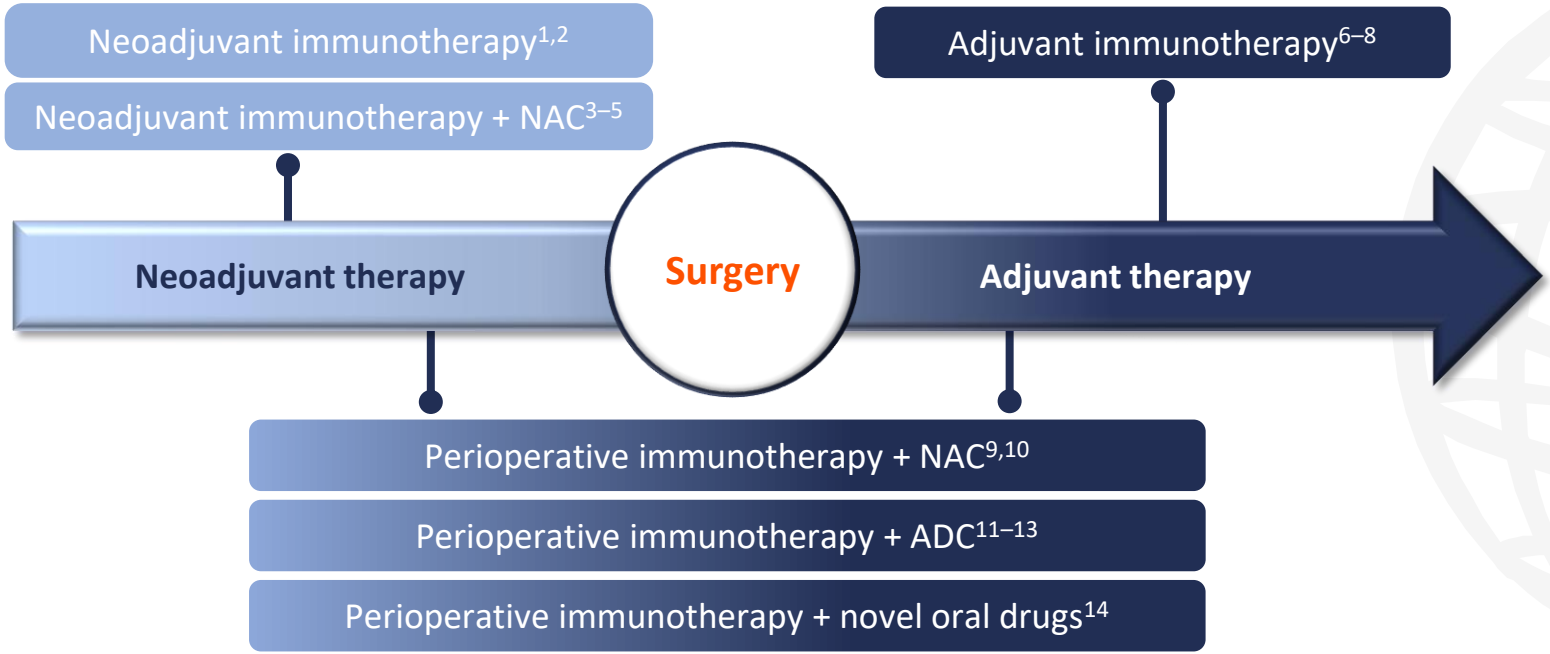
Immunotherapy in the perioperative setting

Current and emerging immunotherapy approaches within the perioperative setting



ADC, antibody–drug conjugate; NAC, neoadjuvant chemotherapy.

1. Basile G, et al. *Clin Cancer Res.* 2022;28:5107–14; 2. Szabados B, et al. *Eur Urol.* 2022;82:212–22; 3. Thibault C, et al. *Ann Oncol.* 2023;34:S1202; 4. Rose TL, et al. *J Clin Oncol.* 2021;39:3140–48; 5. Gupta S, et al. *J Clin Oncol.* 2020;38:439; 6. Bajorin DF, et al. *N Engl J Med.* 2021;384:2102–14; 7. Apolo AB, et al. *N Engl J Med.* 2024. doi:10.1056/NEJMoa2401726 (Online ahead of print); 8. Bellmunt J, et al. *Lancet Oncol.* 2021;22:525–37; 9. Powles T, et al. *N Engl J Med.* 2024;391:1773–86; 10. NCT03924856; 11. NCT04700124; 12. NCT03924895; 13. NCT04960709; 14. Sonpavde G, et al. *Future Oncol.* 2020;16:4359–68.
All NCT references from ClinicalTrials.gov. Available at: https://clinicaltrials.gov according to specific trial number (accessed 20 November 2024).

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What are the latest key clinical trial data on perioperative immunotherapy as monotherapy for MIBC?

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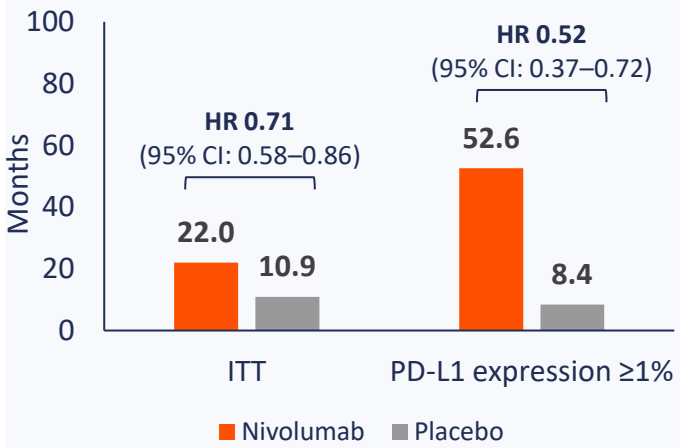
Adjuvant

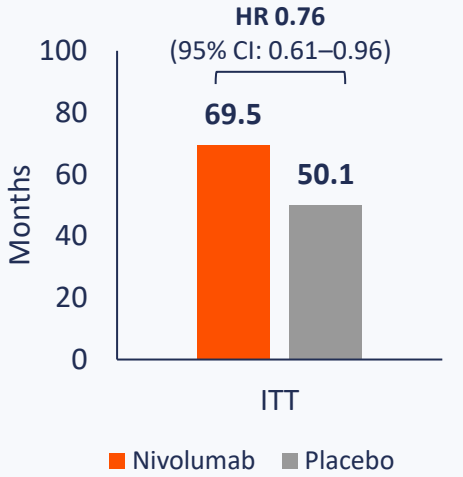
Phase III CheckMate 274 trial

- 709 patients with resected, high-risk MIUC (including MIBC) were randomized 1:1 to adjuvant **nivolumab** or **placebo**[1,2]
- **Primary endpoints:** DFS in ITT and in patients with PD-L1 expression ≥1%[1]

3-year median DFS



3-year median OS



PD-L1 expression ≥1% group:
NR vs **NR** (**HR 0.56**, 95% CI: 0.36–0.86)

Safety

- Overall, **TRAEs** occurred in **78.6%** receiving nivolumab and **56.0%** receiving placebo[2]
- **No new safety signals** were detected with the additional follow-up[2]

CI, confidence interval; DFS, disease-free survival; HR, hazard ratio; ITT, intention-to-treat; MIBC, muscle-invasive bladder cancer; MIUC, muscle-invasive urothelial carcinoma; NR, not reached; OS, overall survival; PD-L1, programmed death ligand 1; TRAE, treatment-related adverse event.

1. Bajorin DF, et al. *N Engl J Med*. 2021;384:2102–14; 2. Galsky MD, et al. *J Clin Oncol.* 2024. doi: 10.1200/JCO.24.00340 (Online ahead of print).

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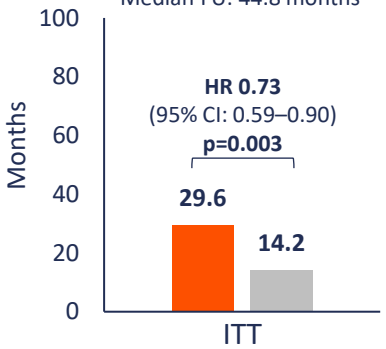
Phase III AMBASSADOR and IMvigor010 trials

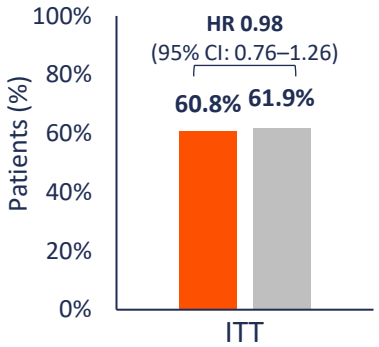
AMBASSADOR[1]

- 702 patients with high-risk resected MIUC were randomized 1:1 to adjuvant **pembrolizumab** or **observation**[1]
- **Co-primary endpoints:** DFS and OS[1]

Median DFS[1]



3-year OS[1]

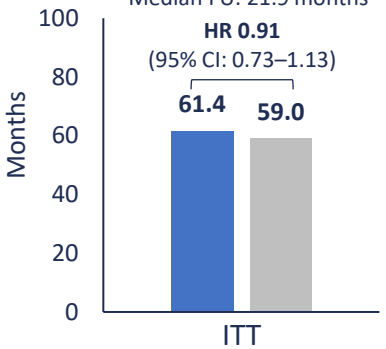


- Although **PD-L1 status was prognostic**, it was not predictive of DFS benefit[1]
- Grade 3+ AEs occurred in **50.6%** receiving pembrolizumab and **31.6%** in the observation group. Pembrolizumab's AE profile was consistent with what has been previously reported[1]

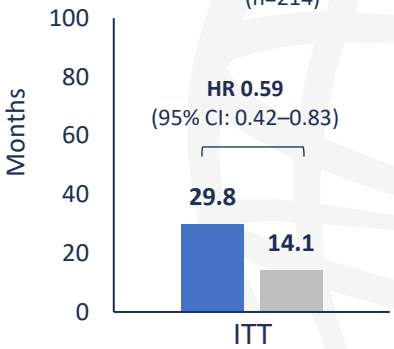
IMvigor010[2,3]

- 809 patients with high-risk resected MIUC were randomized 1:1 to adjuvant **atezolizumab** or **observation**[3]
- **Primary endpoint not met** (mDFS 19.4 vs 16.6 months, p=0.24)[3]

Median OS[2]



OS for ctDNA+ patients[2]



- AEs occurred in **94%** receiving atezolizumab and **79%** in the observation group[3]
- Safety was generally consistent with that observed in previous atezolizumab monotherapy studies[3]

AE, adverse event; CI, confidence interval; ctDNA, circulating tumour DNA; DFS, disease-free survival; FU, follow-up; HR, hazard ratio; ITT, intention-to-treat; m, median; MIUC, muscle-invasive urothelial carcinoma; OS, overall survival.

1. Apolo AB, et al. *N Engl J Med*. 2024. doi: 10.1056/NEJMoa2401726 (Online ahead of print); 2. Powles T, et al. *Eur Urol*. 2024;85:114–22;
3. Bellmunt J, et al. *Lancet Oncol.* 2021;22:525–37.

What are the latest key clinical trial data on combination perioperative immunotherapy for MIBC?

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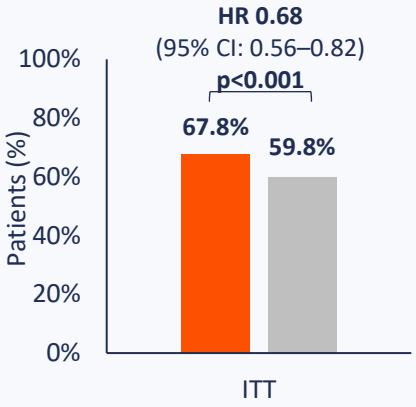
Phase III NIAGARA trial

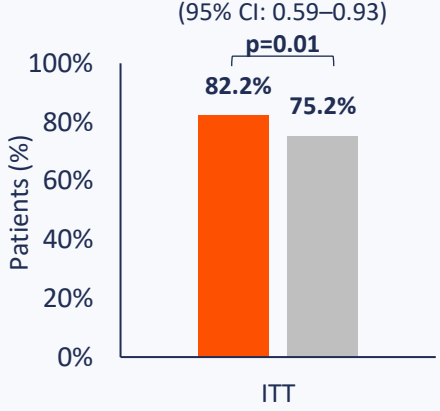
- 1,063 patients with MIBC were randomized 1:1 to neoadjuvant durvalumab + cisplatin–gemcitabine followed by RC + adjuvant durvalumab **(durvalumab group)** vs neoadjuvant cisplatin–gemcitabine followed by RC alone **(comparator group)**
- **Primary endpoints:** pCR and EFS

Median EFS: NR vs 46.1 months

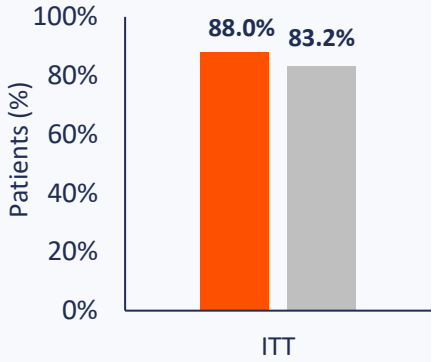
24-month EFS



24-month OS



RC rate



Safety

- **TRAEs** occurred in **94.7%** and **92.6%** in durvalumab and comparator groups, respectively
- **Safety profile** in the durvalumab group was **consistent with individual safety profiles** for durvalumab and cisplatin–gemcitabine

CI, confidence interval; EFS, event-free survival; HR, hazard ratio; MIBC, muscle-invasive bladder cancer; NR, not reached; OS, overall survival; pCR, pathologic complete response; RC, radical cystectomy; TRAE, treatment-related adverse event.

Powles T, et al. *N Engl J Med*. 2024;391:1773–86.

Integrating perioperative immunotherapy-based treatment options in clinical practice

Prof. Thomas Powles
Director and Professor of
Genitourinary Oncology,
Barts Cancer Centre,
London, UK

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What do the available data tell us about the potential role of immunotherapy in the perioperative setting for MIBC?

Insights from clinical trials: Adjuvant ICI monotherapy

CheckMate 274[1]	AMBASSADOR[2]	IMvigor010[3,4]
Nivolumab (n=353) vs placebo (n=356)	**Pembrolizumab (n=354)** vs observation (n=348)	**Atezolizumab (n=406)** vs observation (n=403)
• **Prior NAC*** (ypT2–ypT4a or ypN+) • **No prior NAC*** (pT3–pT4a or pN+)	• **Prior NAC** (≥ypT2, ypN+, microscopic +ve margins†) • **No prior NAC** (≥pT3, pN+, microscopic +ve margins†)	• **Prior NAC** (ypT2–4a, ypN+, **or** ypT2–4 or ypN+ for UTUC) • **No prior NAC** (pT3–4a, pN+, **or** pT3–4 or pN+ for UTUC)
3-year median DFS • **ITT: 22.0** vs 10.9 months HR 0.71 (0.58–0.86) • **PD-L1 ≥1%: 52.6** vs 8.4 months HR 0.52 (0.37–0.72)	**Median DFS** • **ITT: 29.6** vs 14.2 months HR 0.73 (0.59–0.90); p=0.003	**Median DFS** • **ITT: 19.4** vs 16.6 months HR 0.89 (0.74–1.08); p=0.24
3-year median OS • **ITT: 69.5** vs 50.1 months HR 0.76 (0.61–0.96) • **PD-L1 ≥1%: NR** vs NR HR 0.56 (0.36–0.86)	**3-year OS rate** • **ITT: 60.8%** vs 61.9% of patients HR 0.98 (0.76–1.26)	**Median OS** • **ctDNA positive status:** 29.8 vs 14.1 months HR 0.59 (0.42–0.83)
• Safety profile was consistent with previous trials and no new signals were identified	• Safety profile was consistent with previous trials and no new signals were identified	• Atezolizumab was generally tolerable and no new safety signals were identified

95% confidence intervals shown in brackets following HR. *Cisplatin-based NAC. †Presence of individual factors or a combination were allowed.
ctDNA, circulating tumour DNA; DFS, disease-free survival; HR, hazard ratio; ITT, intention-to-treat; N, node, NAC, neoadjuvant chemotherapy; NR, not reached; OS, overall survival; p, pathologic; PD-L1, programmed cell death ligand 1; pts, patients; T, tumour; UC, urothelial carcinoma; UTUC, upper tract UC; yp, pathological after neoadjuvant therapy.

1. Galsky MD, et al. *J Clin Oncol.* 2024. doi: 10.1200/JCO.24.00340 (Online ahead of print); 2. Apolo AB, et al. *N Engl J Med*. 2024. doi: 10.1056/NEJMoa2401726 (Online ahead of print); 3. Powles T, et al. *Eur Urol.* 2024;85:114–22; 4. Bellmunt J, et al. *Lancet Oncol.* 2021;22:525–37.

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Insights from clinical trials: Perioperative ICI

NIAGARA

NAC* + **durvalumab**, then RC + adjuvant **durvalumab (n=533)** vs NAC* then RC alone (**comparator; n=530**)

- Histological or cytological MIBC, T2, T3, or T4a, N0 or N1, and M0, and eligible for cisplatin-based chemotherapy

Durvalumab group

1. Neoadjuvant therapy: 4 IV cycles administered every 3 weeks
- Durvalumab at 1,500 mg
- Cisplatin at 70 mg/m^2 BSA (day 1)
- Gemcitabine at 1,000 mg/m^2 BSA (days 1 and 8)

2. RC

3. Adjuvant therapy: up to 8 IV cycles administered every 4 weeks
- Durvalumab at 1,500 mg

Comparator group

1. Neoadjuvant therapy: same gemcitabine–cisplatin regimen

2. RC

2-year EFS rate
- **ITT:** 67.8% vs 59.8% of patients

HR 0.68 (0.56–0.82); P<0.001

2-year OS rate
- **ITT:** 82.2% vs 75.2% of patients

HR 0.75 (0.59–0.93); P=0.01

pCR rate
- **ITT:** 33.8% vs 25.8% of patients

RR 1.30 (1.09–1.56); P=0.004

RC rate
- **ITT:** 88.0% vs 83.2% of patients

Safety profile of perioperative **durvalumab + NAC*** was **consistent** with **individual** safety profiles for durvalumab and gemcitabine–cisplatin

Surgical-related AEs leading to death in <90 days after RC:
- 2.1% vs 1.8%

95% confidence intervals shown in brackets following HR or RR. *NAC consisted of cisplatin–gemcitabine therapy.

AE, adverse event; BSA, body surface area; EFS, event-free survival; HR, hazard ratio; ITT, intention-to-treat; IV, intravenous; M, metastasis; MIBC, muscle-invasive bladder cancer; N, node; NAC, neoadjuvant chemotherapy; OS, overall survival; pCR, pathologic complete response; RC, radical cystectomy; RR, risk ratio; T, tumour.

Powles T, et al. *N Engl J Med*. 2024;391:1773–86.

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Which factors may help guide the use of immunotherapy in the perioperative setting and what is the potential role of biomarkers?

Potential biomarkers for immunotherapy in MIBC

Neoadjuvant

PD-L1

CD8+ T-cell infiltration

TMB

ctDNA

ABACUS trial[1]

- Pretreatment **CD8+** expression and **serial ctDNA** levels **correlated with RFS** with **atezolizumab** therapy
- **No significant correlation** was found between **PD-L1** or **TMB** and **relapse**

PURE-01 trial[2]

- **PD-L1** expression and **TMB** were related to **pCR** with **pembrolizumab** therapy

Adjuvant

ctDNA

IMvigor010 trial[3]

- **ctDNA positivity** identified patients with an **OS** benefit **favouring atezolizumab** vs observation

Currently no established biomarkers to identify patients that will benefit from perioperative immunotherapy[4]

ctDNA, circulating tumour DNA; OS, overall survival; MIBC, muscle-invasive bladder cancer; pCR, pathologic complete response; PD-L1, programmed death ligand 1; RFS, recurrence-free survival; TMB, tumour mutation burden.

1. Szabados B, et al. *Eur Urol.* 2022;82:212–22; 2. Basile G, et al. *Clin Cancer Res.* 2022;28:5107–14; 3. Powles T, et al. *Eur Urol.* 2024;85:114–22; 4. Esteban-Villarrubia J, et al. *Cancers.* 2023;15:566.

What are some of the practical considerations for utilizing immunotherapies perioperatively for MIBC?

Aspects to consider for perioperative treatment

Eligibility for platinum-based chemotherapy[1]

Surgical considerations include patient preference for cystectomy and fitness to undergo the procedure[2,3]

Cautions for ICI use in certain patients e.g., those with active autoimmune disease, currently receiving immunosuppressive therapy[4]

ICI, immune checkpoint inhibitor.

1. Alfred Witjes J, et al. *Eur Urol*. 2024;85:17–31; 2. Desai A, et al. *Bladder Cancer*. 2024;10:145–55; 3. Chesnut GT, et al. *J Urol*. 2021;205:400–6;
4. Brahmer JR, et al. *J Immunother Cancer*. 2021;9:e002435.

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What do you think the future directions for perioperative immunotherapies in MIBC might be?

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Ongoing phase III clinical trials

Perioperative

KEYNOTE-866 (NCT03924856)[1]
- UC or MIBC (T2–T4aN0M0 or T1–T4aN1M0) with ≥50% urothelial histology or non-metastatic BC (N≤1 M0)
- Pembrolizumab + cisplatin–gemcitabine + surgery **vs** placebo + cisplatin–gemcitabine + surgery

VOLGA (NCT04960709)[2]
- MIUC; MIBC (T2–T4aN0/1M0) or UC of bladder (T1N1M0);* participants ineligible for/declined cisplatin therapy
- Tremelimumab + durvalumab + EV **vs** durvalumab + EV **vs** no therapy
- Post-surgical tremelimumab + durvalumab or durvalumab + EV

KEYNOTE-905/EV-303 (NCT03924895)[3]
- UC or MIBC (cT2–T4aN0M0 or T1–T4aN1M0) with ≥50% urothelial histology; participants ineligible for cisplatin therapy
- Pembrolizumab + surgery **vs** pembrolizumab + EV + surgery **vs** surgery alone

KEYNOTE-B15/EV-304 (NCT04700124)[4]
- UC or MIBC (T2–T4aN0M0 or T1–T4aN1M0) with ≥50% urothelial histology or non-metastatic BC (N≤1 M0)
- EV + pembrolizumab + surgery **vs** cisplatin–gemcitabine + surgery

ENERGIZE (NCT03661320)[5]
- Previously untreated MIBC
- Cisplatin–gemcitabine **vs** nivolumab + cisplatin–gemcitabine **or** nivolumab + BMS-986205
- Post-surgical nivolumab **or** nivolumab + BMS-986205

Neoadjuvant

SWOG GAP S2011 (NCT04871529) – currently suspended[6]
- MIBC, UTUC, or mixed with ≥50% urothelial histology (T2–T4aN0M0); participants ineligible for cisplatin therapy
- Avelumab + gemcitabine–carboplatin **vs** no neoadjuvant therapy prior to surgery

*Participants with transitional cell and mixed transitional/non-transitional cell histologies may be included.
BC, bladder cancer; EV, enfortumab vedotin; MIBC, muscle-invasive BC; MIUC, muscle-invasive UC; UC, urothelial carcinoma; UTUC, upper tract UC.
1. NCT03924856; 2. NCT04960709; 3. NCT03924895; 4. NCT04700124; 5. NCT03661320; 6. NCT04871529. All available at https://clinicaltrials.gov (accessed 28 November 2024).

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How might a multidisciplinary team collaborate effectively to implement perioperative immunotherapies for MIBC?

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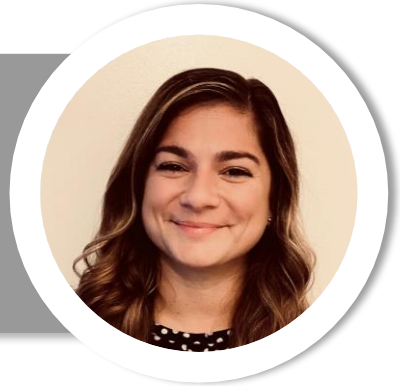
Collaborating on the safe use of immunotherapy-based treatments in the perioperative setting

Ms Lindsay Diamond
Genitourinary Oncology Nurse Practitioner,
Mount Sinai Hospital,
New York, NY, USA



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What are the key safety considerations for the use of immunotherapy in the perioperative setting for patients with MIBC?

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Immunotherapy safety considerations

- It is important that patients and caregivers receive up-to-date education on possible irAEs to support early identification and management[1]
- Immunotherapy works differently than traditional chemotherapy and elicits unique therapeutic responses and corresponding irAEs[1]
- IrAEs can affect any organ/system,[1] e.g. skin, endocrine, GI, respiratory, musculoskeletal, nervous system, cardiac, vascular, renal, ocular, blood/lymphatic[2]
- Timing of irAEs with immunotherapies is less predictable than with ChT, with the potential for events to occur and persist long after cessation of treatment[3]

ChT, chemotherapy; GI, gastrointestinal; irAE, immune-related adverse event.

1. Schneider BJ, et al. *J Clin Oncol.* 2021;39:4073–126; 2. Haanen J, et al. *Ann Oncol.* 2022;33:1217–38; 3. Brahmer JR, et al. *J Immunother Cancer.* 2021;9:e002435.

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Most common AEs with ICIs from key MIBC clinical trials*

Monotherapy

CheckMate274[1]

Nivolumab

N=351

Any grade	n (%)
Pruritus	81 (23)
Fatigue	61 (17)
Diarrhoea	59 (17)
Grade ≥3	**n (%)**
↑ lipase level	18 (5)
↑ amylase level	13 (4)
Diarrhoea	3 (1)

IMvigor010[2]

Atezolizumab

N=390

Any grade	n (%)
Pruritus	75 (19)
Fatigue	63 (16)
Diarrhoea	37 (9)
Grade ≥3	**n (%)**
Arthralgia	5 (1)
ALT increased	4 (1)
Colitis	4 (1)

AMBASSADOR[3]

Pembrolizumab

N=330

Any grade	n (%)
Fatigue	156 (47)
Pruritus	74 (22)
Diarrhoea	68 (21)
Grade 3/4	**n (%)**
↑ lipase level	15 (5)
Diarrhoea	10 (3)
Fatigue	8 (2)

Combination therapy

NIAGARA[4†]

Durvalumab + ChT

N=530

Any grade	n (%)
Nausea	284 (54)
Anaemia	205 (39)
Constipation	205 (39)
Grade 3/4	**n (%)**
Neutropenia	76 (14)
UTI	75 (14)
Anaemia	73 (14)

*Some percentages are the same with different n numbers due to rounding. †AEs of any cause.

AE, adverse event; ALT, alanine aminotransferase; ChT, chemotherapy; ICI, immune checkpoint inhibitor; MIBC, muscle-invasive bladder cancer; UTI, urinary tract infection.

1. Bajorin DF, et al. *N Engl J Med.* 2021;384:2102–14; 2. Bellmunt J, et al. *Lancet Oncol.* 2021;22:525–37; 3. Apolo AB, et al. *N Engl J Med.* 2024. doi: 10.1056/NEJMoa2401726 (Online ahead of print); 4. Powles T, et al. *N Engl J Med.* 2024;391:1773–86.

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What strategies can be used to identify possible irAEs at the earliest opportunity in patients with MIBC?

Strategies to support early identification of possible irAEs

Education

- Patient education is an essential element of toxicity management[1,2]
- Enhanced awareness of the expected and possible irAEs improves coping skills and resilience in patients[2]
- Patients must be informed that irAEs can occur at any time and even after treatment cessation[2]

Monitoring

- Routine screening before ICI initiation is advised[2]
- There should be suspicion that new symptoms are treatment related[1]
- Tests to be performed prior to and during ICI therapy include CBC with differential, CMP, TSH, fT4[3]
- Urinalysis should be considered to evaluate for baseline kidney disease[3]

Presentation

- Side effects may involve any system of the body but GI, dermatologic, hepatic, endocrine and pulmonary toxicities predominate[1]
- irAEs to be aware of include rash, diarrhoea, abdominal pain, cough, fatigue, headaches, vision changes[1]

CBC, complete blood count; CMP, comprehensive metabolic panel; fT4, free thyroxine; GI, gastrointestinal; ICI, immune checkpoint inhibitor; irAE, immune-related adverse event; TSH, thyroid-stimulating hormone.

1. Schneider BJ, et al. *J Clin Oncol.* 2021;39:4073–126; 2. Haanen J, et al. *Ann Oncol.* 2022;33:1217–38; 3. Brahmer JR, et al. *J Immunother Cancer.* 2021;9:e002435.

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How can potential side effects of immunotherapy for patients with MIBC be best managed?

Management strategies for side effects of immunotherapy

Guidelines for management of immunotherapy toxicities are available e.g. SITC[1], ASCO[2] and ESMO[3]

- **Systemic corticosteroids are commonly used as a first-line treatment[1]**
- **Some refractory cases may require other immunosuppressive therapy[2]**
- **Treatment interruption is recommended for grade 2 toxicities[1,2]**
- **Patients should be referred to a specialist when they experience toxicities of grade ≥3[1]**
- **In general, permanent discontinuation of treatment is recommended with grade 4 toxicities[2]**

- Effective management of severe irAEs depends on early recognition and prompt initiation of immune suppression[3]
- Supportive care for some patients will involve an MDT (e.g. endocrinologist, pulmonologist, gastroenterologist) to address specific symptoms[2]

ASCO, American Society of Clinical Oncology; ESMO, European Society for Medical Oncology; irAE, immune-related adverse event; MDT, multidisciplinary team; SITC, Society for Immunotherapy of Cancer.

1. Brahmer JR, et al. *J Immunother Cancer.* 2021;9:e002435; 2. Schneider BJ, et al. *J Clin Oncol.* 2021;39:4073–126; 3. Haanen J, et al. *Ann Oncol.* 2022;33:1217–38.

How can multidisciplinary expertise be utilized to optimally support patients with MIBC?

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How can perioperative immunotherapy treatments be best discussed with patients with MIBC?

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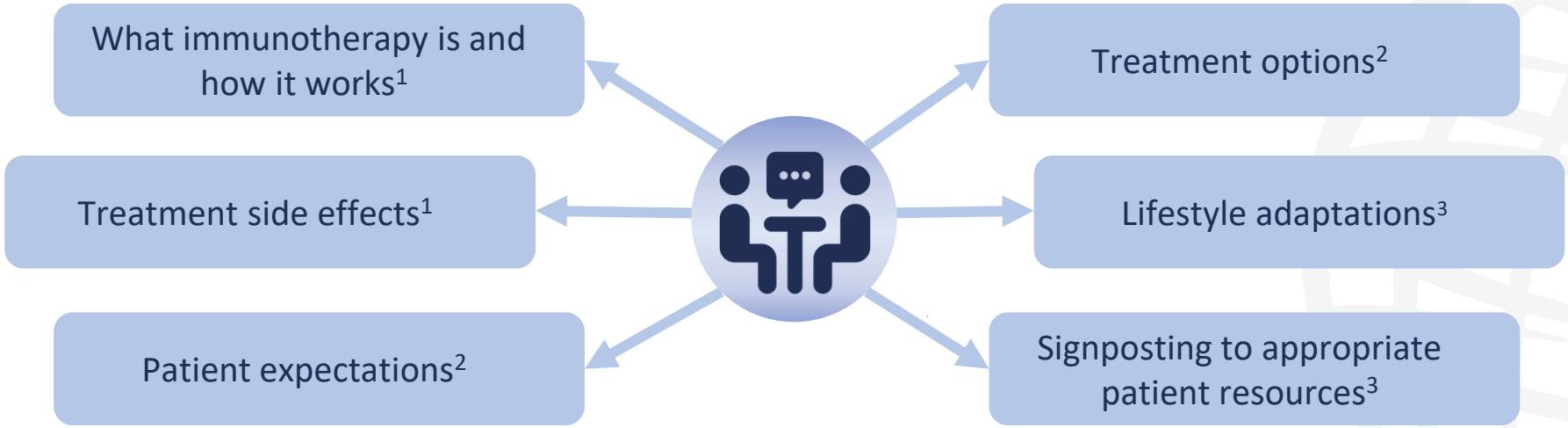
Key topics for discussing immunotherapy with patients



Reinforce importance of patients reporting side effects to their care team[3]

1. Schneider BJ, et al. *J Clin Oncol.* 2021;39:4073–126; 2. British Association of Urological Surgeons. MDT guidance for managing bladder cancer. 2nd edition. January 2013. Available at: https://bit.ly/3BmS4oi (accessed 25 November 2024); 3. The Christie NHS Foundation Trust. Immunotherapy. A guide for patients and their carers. Available at: https://bit.ly/4fb7V7k (accessed 25 November 2024).

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