Review

Special Topic: Advances in Bladder Cancer Research

Current Urology

OPEN

Immune checkpoint inhibitor therapy as a neoadjuvant treatment for muscle-invasive bladder carcinoma: A narrative review

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Abstract: Immunotherapy has become a standard treatment for patients with advanced urothelial carcinoma, and neoadjuvant immunotherapy is currently being extensively explored. This review highlights the initial findings and key clinical therapeutic insights on immune checkpoint inhibitors in the early treatment of muscle-invasive bladder cancer across diverse patient populations. Most available literature consists of clinical investigations involving small sample, single-arm phase II trials, with the primary endpoint being the pathologic complete response rate. Early results of immune checkpoint inhibitors in the neoadjuvant treatment of bladder cancer have demonstrated promising efficacy. However, these findings require confirmation in large phase III clinical trials, with particular emphasis on long-term survival benefits and identifying patients who respond to treatment.

Keywords: Muscle-invasive bladder cancer; Immune checkpoint inhibitor; Tislelizumab; Neoadjuvant immunotherapy

1. Introduction

Urothelial cancer, an aggressive malignancy, is the most prevalent cancer of the urinary tract, with more than 90% of cases arising from the bladder. Approximately 20% to 40% of patients with bladder cancer present with muscle-invasive bladder cancer (MIBC). Although surgical procedures such as radical cystectomy (RC) and pelvic lymph node dissection are effective in treating localized MIBC lesions, up to 50% of patients eventually develop distant metastases due to occult micrometastases.[1,2] Therefore, appropriate perioperative treatment requires a combination of local and systemic therapies to improve long-term patient survival. Starting in the 1980s, the search for an effective neoadjuvant chemotherapy for treating bladder cancer spanned 3 decades, culminating in the cisplatin-based neoadjuvant chemotherapy being considered the standard of care for cT2–4aN0M0 bladder cancer. Meta-analyses[3] have shown that cisplatin-based neoadjuvant chemotherapy reduces the risk of death by 13%, providing an absolute 5-year survival benefit of 5%.[4]

However, several challenges hinder clinical application—approximately 50% of patients cannot tolerate cisplatin-based chemotherapy, and the downstaging rates of neoadjuvant chemotherapy vary across different regimens.[5] Therefore, new compounds are required to address unmet treatment needs.

Immune checkpoint inhibitors (ICIs) are validated as a second-line option following chemotherapy failure.[6] Programmed death 1/programmed death ligand 1 (PD-1/PD-L1) inhibitors, such as pembrolizumab and nivolumab, have been approved in the United States and other countries for the treatment of bladder cancer. Tislelizumab, a humanized immunoglobulin G4 monoclonal antibody that targets PD-1, has been approved by the National Medical Products Administration as the first novel ICI for the treatment of urothelial carcinoma in China. Recently, there has been a surge in exploratory studies on PD-1/PD-L1 analogs in the neoadjuvant setting for urothelial cancer, enriching the portfolio of neoadjuvant regimens. This review explores the current status and biomarkers of immunotherapy in the neoadjuvant treatment of urothelial cancer.

Immunological mechanisms

Immune checkpoint therapy targets regulatory pathways in T cells to enhance antitumor immune responses, not by activating the immune system to attack specific tumor cell targets, but by removing inhibitory pathways that block effective antitumor T-cell responses.[7] Using the PD-1 inhibitor as an example, the Fab segment serves as the antigen-binding site, primarily binding to PD-1. The clinical effectiveness of antibodies as therapeutic molecules is largely due to the high binding affinity and specificity of their interactions. In addition, modifications to the Fc segment are becoming increasingly important in the development of new drugs. Tislelizumab is an investigational humanized immunoglobulin G4 monoclonal antibody with high affinity and binding specificity for PD-1. Its engineering aims to reduce binding to FcγR on macrophages, thereby limiting antibody-dependent phagocytosis, a mechanism that could potentially lead to resistance to anti–PD-1 therapy.[8] Neoadjuvant therapy targets the primary tumor and leverages higher levels of primary tumor antigens to enhance T-cell activation, inducing the emergence of tumor-specific T cells into the systemic circulation and exerting both local and distal antitumor effects. Compared with adjuvant therapy, neoadjuvant treatment promotes T-cell receptor epitope expansion.[9] Recent preclinical data support the superior activity of T-cell checkpoint blockade when administered prior to surgery.[10] Tumor-draining lymph nodes play an important role in

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Current Urology, (2025) 19, 1, 39–42

Received January 16, 2024; Accepted October 9, 2024.

http://dx.doi.org/10.1097/CU9.0000000000000263

immunotherapy, as dendritic cells loaded with tumor antigenic signals stimulate the generation of tumor-specific effector T cells, which subsequently enter the bloodstream and migrate to the tumor site.[11] Neoadjuvant immunotherapy has been clinically validated in Phase III trials for lung cancer and triple-negative breast cancer, demonstrating promising results.[12,13]

2. Neoadjuvant immune checkpoint inhibitor therapy for muscle-invasive bladder carcinoma

2.1. Neoadjuvant immunotherapy for cisplatin-ineligible patients

A previous study[14] has shown that nearly 50% of MIBC cases are ineligible for cisplatin chemotherapy. For these patients, RC remains the standard of care. In the neoadjuvant treatment of cisplatin-ineligible patients, various regimens have been investigated, including ICI alone, ICI in combination with other nonplatinum chemotherapeutic agents, and PD-1 inhibitors in combination with cytotoxic T lymphocyte antigen 4 inhibitors. Regarding the pCR, the proportion of patients exhibiting pT0 on RC specimens varies considerably between studies, ranging from 17% to 46%. Overall, ICI monotherapy resulted in a relatively limited rate of stage reduction. In ABACUS,[15] 95 patients received 2 cycles of atezolizumab before RC. The study met its primary endpoint with a pathologic complete response (pCR) rate of 31% (27/88; 95% confidence interval [CI], 21%–41%). Among patients who tested positive for PD-L1, the pCR rates were 37% and 75%, respectively. No significant correlation was observed between PD-L1 expression and the clinical outcome. Therapy-related adverse events (TRAEs) occurred in 52% of patients for any grade, with Grade 3–4 adverse events (AEs) reported in 10 of 95 patients (11%). The final follow-up data[16] showed that the 2-year disease-free survival (DFS) rate for all patients was 68%, whereas those who achieved a pCR had a 2-year DFS of 85%. The 2-year overall survival (OS) rate was 77%.

The combination of nonplatinum chemotherapeutic agents resulted in a further increase in the pCR rate. HCRN GU14-188[17] was divided into cisplatin-eligible (Cohort 1) and cisplatin-ineligible (Cohort 2) groups. Cohort 2 included patients with T2–4aN0M0 tumors who received 5 doses of pembrolizumab and 3 cycles of gemcitabine prior to cystectomy. The primary endpoint was the pathologic muscle-invasive response rate (≤ypT1N0), which occurred in 51.6% (16/31) of patients. Extended follow-up data[18] revealed that 38 evaluable patients had a 36-month OS rate of 65.7%. In contrast, the AURA study[19] demonstrated similar clinical staging for enrolled patients but reported that the avelumab + gemcitabine + paclitaxel arm had a pCR rate of 36%, with a ≤ ypT1N0 rate of 39%. This difference may be related to the observed poor efficacy of PD-L1 inhibitors in bladder cancer.

2.2. Neoadjuvant immunotherapy for cisplatin-eligible patients

The PURE-01 study[20] included 155 patients with clinical (c)-T2–3bN0M0 stage disease, regardless of their eligibility for cisplatin. Patients received pembrolizumab 200 mg for 3 cycles prior to RC, with a median patient age of 66 years. The primary endpoint, pCR rate, was achieved in 36.8% of patients. The 3-year event-free survival rate was 74.4% in the intention-to-treat population. These results are not substantially different from the ypT0N0 response rates reported in recent prospective trials of standard chemotherapy, such as VESPER.[6] All types of AEs had an incidence of less than 10%, with only 6% of patients experiencing Grade 3–4 AEs. The PURE-01 study confirmed that a significant proportion of patients with nonmetastatic MIBC can safely receive ICI monotherapy preoperatively, including those eligible for cisplatin treatment.

Chemotherapy not only exerts a direct killing effect on tumor cells but also promotes an immune response against tumors.[21] Many studies have shown that combining an ICI with chemotherapy can further improve the pathologic muscle-invasive response rate in neoadjuvant treatment. The HCRN GU14-188 trial (Cohort 1)[22] evaluated the efficacy of pembrolizumab in combination with neoadjuvant GC chemotherapy. The cohort included 43 patients with MIBC, with a median age of 65 years. Among the 36 patients with known disease stage, 17 had clinical stage cT2, whereas 19 had disease stage cT3/T4. Cohort 1's results revealed a pCR rate of 44.4%, with 61.1% of patients downstaging to non–muscle-invasive disease. There was a simultaneous increase in the incidence of AEs following combination therapy. Specifically, 60% of patients experienced Grade 3/4 hematological AEs, and 30% experienced Grade 3/4 nonhematological AEs.

BLASST-1[23] was a single-arm Phase II study evaluating the efficacy of neoadjuvant gemcitabine and cisplatin in combination with nivolumab. The study reported a pathological downstaging rate of 66% (27/41), with a pCR in 49% of patients. Among the 39 specimens analyzed, 15 (39%) were PD-L1–positive. Notably, among the PD-L1–positive patients, 10 of 15 (67%) achieved pathological downstaging. In contrast, among the PD-L1–negative patients, the rate of pathological descent was 71% (17/24). There was no significant correlation between tumor PD-L1 expression and pathological descent. The incidence of Grade 3–4 AEs was 20%, and 1 patient developed postoperative Guillain-Barré syndrome; however, no mortality was reported.

Another representative study conducted in China, BGB-A317-2002,[24] is a multicenter, single-arm, Phase II clinical trial investigating the efficacy of tislelizumab combined with gemcitabine and cisplatin as neoadjuvant therapy for cT2–T4aN0M0 patients with MIBC. The treatment regimen consisted of tislelizumab 200 mg (D1), cisplatin 70 mg/m^2 (D2), and gemcitabine 1000 mg/m^2 (D1 and D8) for a total of 4 cycles. The primary endpoint of the study was a pCR (pT0N0M0). Of 63 patients enrolled, 55 underwent RC, with 27 (49.1%; 90% CI, 37.4%–60.9%) achieving pCR. In addition, 41 (74.5%; 95% CI, 61.0%–85.3%) patients reached pDS (pathologic downstaging rate, defined as ≤pT1N0). The most common neoadjuvant TRAEs observed were hematologic toxicity (88.9%), nausea (77.8%), and vomiting (50.8%). The incidence of Grade ≥3 TRAEs was 60.3%, with the majority attributed to hematologic toxicity (58.7%).

2.3. Biomarkers of neoadjuvant immunotherapy

A potential major challenge with neoadjuvant immunotherapy is the clinical deterioration of nonresponders and the occurrence of serious immune-related AEs that interfere with curative surgery. Several readily available and easily measured blood biomarkers appear to improve the selection of patients most likely to benefit from neoadjuvant therapy. These biomarkers include PD-L1 expression, tumor mutational burden, CD8 expression, DNA damage repair/BR1 mutations, absence of fibroblast growth factor receptor mutations, luminal infiltration, and fibroblast activation protein, among others. However, the predictive properties of these biomarkers are inconsistent.[25–27]

A central pathology review was performed on all available tissue collected at baseline (n = 92) and cystectomy (n = 84) in the ABACUS study.[16] A correlation between recurrence-free survival and high baseline stromal CD8$^+$ expression was observed for pretreatment

biomarkers (risk ratio, 0.2; 95% CI, 0.12–0.71; p = 0.01). Programmed death ligand 1 expression or tumor mutational burden did not correlate with recurrence. Posttreatment biomarker expression showed that the presence of fibroblast activation protein in the tumor microenvironment was associated with poor outcomes (risk ratio, 3.3; 95% CI, 1.2–9.3; p = 0.02). High FOXP3 expression correlated with treatment response; however, no association was observed between baseline FOXP3 levels and relapse. The obesity paradox has also been observed in neoadjuvant immunotherapy, as demonstrated by the Pure-01 study.[28] In this study, 57 patients (40%) achieved pCR, of whom 39 (68%) had a body mass index (BMI) of ≥25 kg/m^2. Multivariable analysis identified BMI as a predictor of pCR, with patients with a BMI ≥25 kg/m^2 exhibiting a higher likelihood of achieving pCR with neoadjuvant immunotherapy (odds ratio, 2.45; 95% CI, 1.09–5.51; p = 0.03). Although there were no differences in the percentage of CD8$^+$ infiltration in the transurethral resection specimens between the low- and high-BMI groups, BMI was associated with a higher rate of CD8$^+$ lymphocyte infiltration (p = 0.045).

At present, research on tumor biomarkers is predominantly conducted using indirect methods such as gene sequencing and immunohistochemistry. In recent years, organoids have emerged as a new 3-dimensional structural model for *in vitro* culture, capable of simulating the structure and function of human organs. These organoids can screen for sensitivity to antitumor drugs and verify their efficacy.[29,30] Neal et al.[31] applied an air-liquid interface method to expand patient-derived organoids, demonstrating that patient-derived organoids tumor-infiltrating lymphocytes accurately retained the original tumor T-cell receptor spectrum. This method also enabled the modeling of immune checkpoint blockade with anti–PD-1 and/or anti–PD-L1 therapies, resulting in the expansion and activation of tumor antigen-specific TILs and triggering tumor cytotoxicity.

3. Clinical considerations for implementation of neoadjuvant immunotherapy

Immune checkpoint inhibitors have emerged as the new standard of care for advanced urothelial cancer, driving more selective perioperative treatment. However, suitable biomarkers for accurate patient stratification remain elusive. Liquid biopsy approaches and several readily available blood-based biomarkers, including circulating tumor DNA, hold promise for improving patient selection.[32] Improvements in high-throughput technology and novel artificial intelligence–based analysis tools are aiding in the identification of clinical biomarkers, whereas next-generation sequencing is emerging as an adjunctive diagnostic tool for precision medicine.[33] Notably, a combination of diverse biomarkers is more likely to yield higher predictive value than any single marker alone. In addition, when considering the clinical implementation of biomarkers, it is crucial to evaluate factors such as time, cost, and ease of access, alongside their predictive efficacy.

Neoadjuvant immunotherapy has not increased TRAEs or added surgical risks. In the ABACUS trial,[15] 39 of 87 (45%) patients experienced Grade 1–2 surgical complications, including urinary tract infections (26%), paralytic ileus (7%), and anemia (6%). The Grade ≥3 complication rate was 17%, with wound dehiscence being the most common (6%). Grade ≥ 3 TRAEs occurred in 11% of patients. The 2-year progression-free survival and OS were 68% and 77%, respectively. The 39-month follow-up data[34] of PURE-01 revealed a 3-year event-free survival rate of 74.4% and a 3-year OS rate of 83.8% in the intention-to-treat population. The results support the use of immunological monotherapy as a reliable therapeutic strategy for the neoadjuvant treatment of MIBC. However, most of the available data stem from Phase Ib–II clinical trials, where the primary endpoints focus on short-term efficacy indicators, such as pathological response rates, with limited long-term survival data published. Furthermore, there has been a lengthy historical discourse surrounding perioperative trials and the potential role of intermediate endpoints, such as DFS or recurrence-free survival, as surrogates for OS. It is essential to approach the clinical significance of these preliminary exploratory results with caution, ensuring a careful balance between treatment benefits and associated risks. Careful selection of patients suitable for neoadjuvant therapy is crucial. Further follow-up on long-term survival data is also necessary.

Finally, the optimal approach for combined treatment remains to be determined. For patients resistant to cisplatin, platinum-based chemotherapy combined with ICIs can further improve pathological downstaging rates. For those intolerant to cisplatin, the advent of ICIs offers additional options for neoadjuvant therapy. Given the increasing number of therapeutic options, caution is necessary when interpreting data from these trials, along with careful consideration of clinical toxicity and financial factors.

4. Conclusions

Enhancing efficiency and identifying nonresponding patients are two fundamental strategies for improving neoadjuvant therapy. Immune checkpoint inhibitors may offer a new alternative for the preoperative treatment of cisplatin-ineligible patients. For cisplatin-eligible patients, combining ICIs with chemotherapeutic agents could further improve the downstaging rate. Ongoing research is focused on the safety of drug combinations and the precise selection of patient populations likely to benefit. In addition, longer follow-up is necessary to assess the long-term survival benefits of different drug combinations.

Acknowledgments

None.

Statement of ethics

Not applicable.

Conflict of interest statement

JL is an associate editor of *Current Urology*. SD is an editorial board member of *Current Urology*. This article was accepted after normal external review.

Funding source

This study was supported by Shandong Provincial Natural Science Foundation (ZR2023LZL005) and Jinan Science and Technology Development Foundation.

Author contributions

SD: Writing of the main manuscript text;
JL: Conceived and designed the experiments, revised the manuscript, project administration;
SD, CW, JC: Collected and analyzed the data;
All authors: Review of the manuscript.

Data availability

All data generated or analyzed during this study are included in this published article [and its supplementary information files].

References

[1] Stein JP, Lieskovsky G, Cote R, et al. Radical cystectomy in the treatment of invasive bladder cancer: Long-term results in 1054 patients. *J Clin Oncol* 2001;19(3):666–675.

[2] Yafi FA, Aprikian AG, Chin JL, et al. Contemporary outcomes of 2287 patients with bladder cancer who were treated with radical cystectomy: A Canadian multicentre experience. *BJU Int* 2011;108(4):539–545.

[3] Vale CL. Neoadjuvant chemotherapy in invasive bladder cancer: Update of a systematic review and meta-analysis of individual patient data: Advanced Bladder Cancer (ABC) Meta-analysis Collaboration. *Eur Urol* 2005;48(2):202–205 discussion 205–206.

[4] Grossman HB, Natale RB, Tangen CM, et al. Neoadjuvant chemotherapy plus cystectomy compared with cystectomy alone for locally advanced bladder cancer. *N Engl J Med* 2003;349(9):859–866.

[5] Zaid HB, Patel SG, Stimson CJ, et al. Trends in the utilization of neoadjuvant chemotherapy in muscle-invasive bladder cancer: Results from the National Cancer Database. *Urology* 2014;83(1):75–80.

[6] Galsky MD, Guan X, Rishipathak D, et al. Immunomodulatory effects and improved outcomes with cisplatin- versus carboplatin-based chemotherapy plus atezolizumab in urothelial cancer. *Cell Rep Med* 2024;5(2):101393.

[7] Sharma P, Allison JP. The future of immune checkpoint therapy. *Science* 2015;348(6230):56–61.

[8] Desai J, Deva S, Lee JS, et al. Phase IA/IB study of single-agent tislelizumab, an investigational anti–PD-1 antibody, in solid tumors. *J Immunother Cancer* 2020;8(1):e000453.

[9] Blank CU, Rozeman EA, Fanchi LF, et al. Neoadjuvant versus adjuvant ipilimumab plus nivolumab in macroscopic stage III melanoma. *Nat Med* 2018;24(11):1655–1661.

[10] Liu J, Blake SJ, Yong M CR, et al. Improved efficacy of neoadjuvant compared to adjuvant immunotherapy to eradicate metastatic disease. *Cancer Discov* 2016;6(12):1382–1399.

[11] Topalian SL, Taube JM, Pardoll DM. Neoadjuvant checkpoint blockade for cancer immunotherapy. *Science* 2020;367(6477):eaax0182.

[12] Schmid P, Cortes J, Pusztai L, et al. Pembrolizumab for early triple-negative breast cancer. *N Engl J Med* 2020;382(9):810–821.

[13] Godoy LA, Chen J, Ma W, et al. Emerging precision neoadjuvant systemic therapy for patients with resectable non–small cell lung cancer: Current status and perspectives. *Biomark Res* 2023;11(1):7.

[14] Hermans TJN, Voskuilen CS, van der Heijden MS, et al. Neoadjuvant treatment for muscle-invasive bladder cancer: The past, the present, and the future. *Urol Oncol* 2018;36(9):413–422.

[15] Powles T, Kockx M, Rodriguez-Vida A, et al. Clinical efficacy and biomarker analysis of neoadjuvant atezolizumab in operable urothelial carcinoma in the ABACUS trial. *Nat Med* 2019;25(11):1706–1714.

[16] Szabados B, Kockx M, Assaf ZJ, et al. Final results of neoadjuvant atezolizumab in cisplatin-ineligible patients with muscle-invasive urothelial cancer of the bladder. *Eur Urol* 2022;82(2):212–222.

[17] Kaimakliotis HZ, Adra N, Kelly WK, 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. *J Clin Oncol* 2020;38(15suppl):5019.

[18] Brown J, Kaimakliotis HZ, Kelly WK, et al. HCRN GU14-188: Phase Ib/II study of neoadjuvant pembrolizumab and chemotherapy for T2–4aN0M0 urothelial cancer. *J Clin Oncol* 2023:41(6_suppl):448.

[19] Martinez Chanza N, Carnot A, Barthelemy P, et al. 659MO Avelumab (A) as the basis of neoadjuvant chemotherapy (NAC) regimen in platinum eligible and ineligible patients (pts) with non-metastatic muscle invasive bladder cancer (NM-MIBC). *Ann Oncol* 2021;32(Supplement 5):S683.

[20] Necchi A, Anichini A, Raggi D, et al. Pembrolizumab as neoadjuvant therapy before radical cystectomy in patients with muscle-invasive urothelial bladder carcinoma (PURE-01): An open-label, single-arm, Phase II study. *J Clin Oncol* 2018;36(34):3353–3360.

[21] Galluzzi L, Buqué A, Kepp O, Zitvogel L, Kroemer G. Immunological effects of conventional chemotherapy and targeted anticancer agents. *Cancer Cell*. 2015;28(6):690–714.

[22] Hoimes CJ, Adra N, Fleming MT, et al. Phase Ib/II neoadjuvant (N-) pembrolizumab (P) and chemotherapy for locally advanced urothelial cancer (laUC): Final results from the cisplatin (C)-eligible cohort of HCRN GU14–188. *J Clin Oncol* 2020;38(15_suppl):5047.

[23] Gupta S, Sonpavde G, Weight CJ, et al. Results from BLASST-1 (Bladder Cancer Signal Seeking Trial) of nivolumab, gemcitabine, and cisplatin in muscle invasive bladder cancer (MIBC) undergoing cystectomy. *J Clin Oncol* 2020;38(suppl 6):439.

[24] Li K, Zhong W, Fan J, et al. Neoadjuvant gemcitabine-cisplatin plus tislelizumab in persons with resectable muscle-invasive bladder cancer: A multicenter, single-arm, phase 2 trial. *Nat Cancer* 2024;5(10):1465–1478.

[25] Rouanne M, Bajorin DF, Hannan R, et al. Rationale and outcomes for neoadjuvant immunotherapy in urothelial carcinoma of the bladder. *Eur Urol Oncol* 2020;3(6):728–738.

[26] Plimack ER, Dunbrack RL, Brennan TA, et al. Defects in DNA repair genes predict response to neoadjuvant cisplatin-based chemotherapy in muscle-invasive bladder cancer. *Eur Urol* 2015;68(6):959–967.

[27] Van Allen EM, Mouw KW, Kim P, et al. Somatic ERCC2 mutations correlate with cisplatin sensitivity in muscle-invasive urothelial carcinoma. *Cancer Discov* 2014;4(10):1140–1153.

[28] Martini A, Raggi D, Marandino L, et al. The paradoxical role of body mass index in patients with muscle-invasive bladder cancer receiving neoadjuvant immunotherapy. *Eur Urol Oncol* 2022;5(3):370–372.

[29] Guo A, Ding S. Progress in the establishment and application of organoids of bladder cancer. *J Shandong Univ (Health Sci)* 2023;61(11):20–26.

[30] Jiang Y, Sun X, Song X, et al. Patient-derived bladder cancer organoid model to predict sensitivity and feasibility of tailored precision therapy. *Curr Urol* 2023;17(4):221–228.

[31] Neal JT, Li X, Zhu J, et al. Organoid modeling of the tumor immune microenvironment. *Cell* 2018;175(7):1972–1988.e16.

[32] Laukhtina E, Pradere B, Lemberger U, Karakiewicz PI, Fajkovic H, Shariat SF. Molecular biomarkers to help select neoadjuvant systemic therapy for urothelial carcinoma of the bladder. *Curr Opin Urol* 2022; 32(5):561–566.

[33] Miron B, Hoffman-Censits JH, Anari F, et al. Defects in DNA repair genes confer improved long-term survival after cisplatin-based neoadjuvant chemotherapy for muscle-invasive bladder cancer. *Eur Urol Oncol* 2020; 3(4):544–547.

[34] Padua TCD, Basile G, Bandini M, et al. $_{173}$8P Three-year follow-up update and survival outcomes of the PURE-01 study. *Ann Oncol* 2022;33 (Supplement 7):S1331–S1332.

How to cite this article: Ding S, Wu C, Cao J, Lyu J. Immune checkpoint inhibitor therapy as a neoadjuvant treatment for muscle-invasive bladder carcinoma: a narrative review. *Curr Urol* 2025;19(1):39–42. doi: 10.1097/CU9.0000000000000263