Real-World Adjuvant Nivolumab Utilization in Surgically Treated Muscle-Invasive Bladder Cancer Patients Within US Community Oncology Practice

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Background

- In 2025, bladder cancer is expected to account for approximately 84,870 new cancer cases and 17,420 deaths in the United States (US)[1]
- Muscle-invasive bladder cancer (MIBC) represents approximately 25% of newly diagnosed bladder cancer cases.[2] Radical cystectomy (RC) with pelvic lymph node dissection is the gold-standard treatment for patients with MIBC[3] and has been shown to improve overall survival (OS)[4,5]
- Guidelines recommend neoadjuvant cisplatin-based chemotherapy for eligible patients, followed by adjuvant treatment with cisplatin-based chemotherapy, nivolumab, or radiotherapy, based on pathological risk and prior neoadjuvant therapy
- Nivolumab received approval in August 2021 for the treatment of patients with urothelial carcinoma at high risk of recurrence following RC in the adjuvant setting[6]; however, the current real-world utilization patterns remain unclear

Objective

- This contemporary study aimed to describe adjuvant nivolumab utilization among surgically treated MIBC patients in the US community oncology setting

Methods

Study design

- Retrospective observational study using structured data and curated progress notes from US electronic medical record (EMR) data

Data source

- The ConcertAI Patient360™ Bladder Cancer Dataset is a US-based, deidentified, patient-level dataset from the ConcertAI network that contains human abstracted variables from unstructured records in patients' oncology EMR
- The majority of practice sites in the ConcertAI dataset are community-based practices

Eligibility

- Adult patients with confirmed MIBC (T2-T4aN0M0, T1-T4aN1M0) who underwent RC between February 19, 2021 (6 months prior to nivolumab approval), and October 31, 2023. Data was collected through April 30, 2024, to allow for a potential 6 months of follow-up after RC to adequately assess adjuvant treatment regimens
- Patients with previous history of another primary cancer, non-bladder systemic antineoplastic therapies, prior partial cystectomy, or neoadjuvant radiation were excluded

Study variables

- Patients were considered at high risk of recurrence if they met one of two criteria:
  - Received neoadjuvant cisplatin-based therapy and pT2-T4a or pN+
  - Did not receive neoadjuvant cisplatin-based therapy and pT3-4a or pN+

Statistical methods

- Descriptive statistics were used to quantify demographics, clinical characteristics, and treatment patterns. Treatment patterns were described among all RC-treated MIBC patients as well as among those with high risk of recurrence

Results

Demographics and clinical characteristics

- A total of 138 patients met the eligibility criteria (**Figure 1**)
- The median age was 69 years; 71% were male; 88% were White; 82% presented with de novo MIBC; and 93% had urothelial histology (**Table 1**)

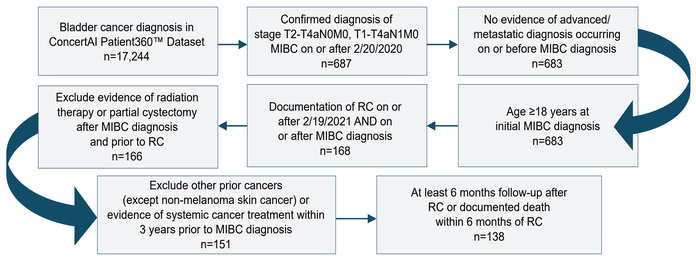
Table 1. Patient demographics and clinical characteristics (N=138)

Variables, n (%)	
Age (years) at MIBC diagnosis	
Median (range)	69 (31-79)
Sex	
Male	98 (71.1%)
Race	
Number of patients with documented race[a]	127
White	112 (88.2%)
Black or African American	4 (3.1%)
Other or unknown race	11 (8.7%)
Setting of care at MIBC diagnosis	
Community setting	114 (82.6%)
ECOG performance status at MIBC diagnosis	
Number of patients with documented ECOG[b]	128
0	83 (64.8%)
1	40 (31.3%)
2+	5 (3.9%)
Year of RC	
2021	78 (56.5%)
2022	48 (34.8%)
2023	12 (8.7%)
TNM groups prior to RC	
T2N0M0	108 (78.3%)
T3-4N0M0	18 (13.0%)
T1-T4N1M0	12 (8.7%)
MIBC diagnosis presentation classification	
De novo MIBC	113 (81.9%)
Previous history of NMIBC	25 (18.1%)
Smoking status at MIBC diagnosis	
Number of patients with documented smoking status	135
Current smoker	43 (31.9%)
Former smoker	58 (43.0%)
Never smoker	34 (25.2%)
Tumor histology at MIBC diagnosis[c]	
Number of patients with documented tumor histology[d]	136
Pure urothelial[e]	112 (82.4%)
Variant urothelial[f]	14 (10.3%)
Non-urothelial	10 (7.4%)
Top comorbidities at MIBC diagnosis[g]	
Diabetes	24 (17.4%)
Chronic obstructive pulmonary disease, unspecified	18 (13.0%)
Weighted comorbidity index score[g] distribution at MIBC diagnosis	
0	86 (62.3%)
1	36 (26.1%)
2+	16 (11.6%)
High risk of recurrence after RC[h]	
High risk	57 (52.7%)
Non-high risk	51 (47.2%)

[a]11 patients did not have a documented race. [b]10 patients did not have a documented ECOG performance status. [c]2 patients did not have a documented tumor histology. [d]Histology closest to MIBC diagnosis. [e]Cancer that has differentiated exclusively from urothelial cells. [f]Conventional urothelial carcinoma with variant morphology. [g]Based on Charlson Comorbidity Index. [h]Among those with pathological staging (T and N) information available at RC; 30 patients did not have pathological staging at RC.

ECOG, Eastern Cooperative Oncology Group; MIBC, muscle-invasive bladder cancer; NMIBC, non-muscle-invasive bladder cancer; RC, radical cystectomy.

Figure 1. Study attrition



Treatment patterns among all MIBC patients with RC

- Approximately 25.4% (35/138) of MIBC patients received RC alone (ie, without neoadjuvant or adjuvant treatments)
- Most (72%; 100/138) MIBC patients received neoadjuvant therapy (**Table 2**)
  - 55% (55/100) received cisplatin + gemcitabine, with median time on treatment of 2.3 months
  - 36% (36/100) received methotrexate + vinblastine + doxorubicin + cisplatin (MVAC), with median time on treatment of 1.4 months
  - 65% patients had pathologic staging available at RC. Of these, 30.8% (20/65) achieved pathological complete response (pCR)
- Only 15% (21/138) of MIBC patients received adjuvant therapy (**Table 3**)
- 13% (18/138) received adjuvant nivolumab, with median time on treatment of 6.8 months
- About 13% (18/138) of MIBC patients received both neoadjuvant and adjuvant therapies

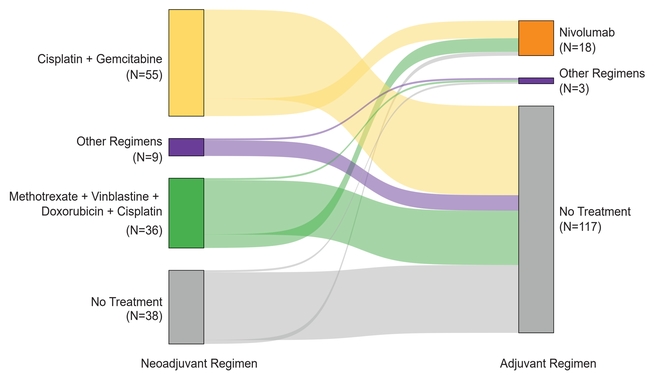
Table 2. Neoadjuvant therapy characteristics among all MIBC patients with RC (n=100)

Neoadjuvant therapy regimen, n	
Cisplatin + gemcitabine	55
Methotrexate + vinblastine + doxorubicin + cisplatin (MVAC)	36
Other regimens[a]	9
Neoadjuvant time on treatment (all regimens), months	
Mean (SD)	1.9 (0.75)
Median	2.3

[a]2 patients received cisplatin + gemcitabine then switched to carboplatin + gemcitabine; 2 patients received carboplatin + gemcitabine then switched to cisplatin + gemcitabine; 2 patients received carboplatin + gemcitabine; 1 patient each received the following regimens: a. carboplatin + cisplatin + etoposide; b. cisplatin + gemcitabine + pembrolizumab; c. pembrolizumab.

SD, standard deviation.

Figure 2. Sankey diagram of neoadjuvant and adjuvant treatment sequences among all MIBC patients with RC (n=138)



Treatment patterns among MIBC patients at high risk of recurrence following RC

- Of all 138 MIBC patients, 108 patients (78.2%) had pathologic staging data available at RC. Of these, approximately half were at high risk of recurrence (52.8%; 57/108), including 39 patients who received neoadjuvant cisplatin-based therapy and had stage pT2-pT4a or pN1/2/3 disease at RC and 18 patients who did not receive neoadjuvant cisplatin-based therapy and had stage pT3-pT4a or pN1/2/3 disease at RC
  - 28.1% (16/57) of high-risk MIBC patients received RC alone
  - 68% (39/57) of high-risk MIBC patients received neoadjuvant treatment
    - 53.9% (21/39) who received neoadjuvant therapy received cisplatin + gemcitabine
  - 28.1% (16/57) of high-risk MIBC patients received adjuvant treatment
    - 26.3% (15/57) of high-risk MIBC patients received adjuvant nivolumab
    - 24.6% (14/57) of high-risk MIBC patients received both a neoadjuvant and adjuvant therapy
      - 50.0% (7/14) received cisplatin+gemcitabine in the adjuvant setting and nivolumab in the adjuvant setting
      - 50.0% (7/14) received MVAC in the adjuvant setting and nivolumab in the adjuvant setting

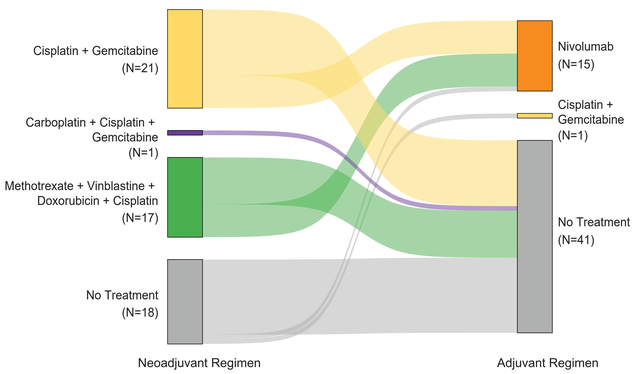
Table 3. Adjuvant therapy characteristics among all MIBC patients with RC (n=21)

Adjuvant therapy regimen	
Nivolumab	18
Other regimens[a]	3
Adjuvant time on treatment (all regimens), months	
Mean (SD)	5.6 (3.83)
Median	4.6

[a]1 patient each received the following regimens: a. cisplatin + gemcitabine; b. pembrolizumab; c. methotrexate.

SD, standard deviation

Figure 3. Sankey diagram of neoadjuvant and adjuvant treatment sequences among MIBC patients at high risk of recurrence following RC (n=57)



Limitations

- The results of the study should be interpreted with regard to its retrospective design; the accuracy and completeness of the data were enhanced through human curation of comprehensive medical records, which included detailed clinical and pathological staging information, despite minor missingness in the pathological staging data
- Findings may not be generalizable to populations not represented in the ConcertAI network
- Sample sizes are relatively limited; consequently, subgroups should be interpreted with caution

Conclusions

- In the era of adjuvant nivolumab, most RC-treated MIBC patients received neoadjuvant therapy, with cisplatin + gemcitabine being the most common regimen
- Conversely, adjuvant therapy use was low in this patient population. Following US FDA approval, adjuvant nivolumab utilization was limited among radically resected MIBC patients as well as among those with high risk of recurrence

References

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