Contemporary Treatment Patterns of Patients with Muscle-Invasive Bladder Cancer Undergoing Radical Cystectomy: A Retrospective Analysis of German Claims Data

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Background

Muscle-invasive bladder cancer (MIBC) accounts for approximately 25% of all bladder tumors and infiltrates the muscular layer of the bladder wall, exhibiting a higher propensity for metastasis and progression.[1] The standard treatment for MIBC is radical cystectomy (RC) with pelvic lymphadenectomy, involving surgical removal of the bladder and surrounding organs or tissues that may harbor cancer cells.[2] Despite therapeutic advances in MIBC, patients experience high recurrence rates and overall poor prognosis.[3] Adjuvant nivolumab received EMA (European Medicines Agency) approval in March 2022 for certain patients with high recurrence risk, but subsequent uptake is unknown.

Objective

- To describe characteristics and contemporary, real-world treatment patterns of patients with MIBC receiving RC in Germany

Methods

Patient selection

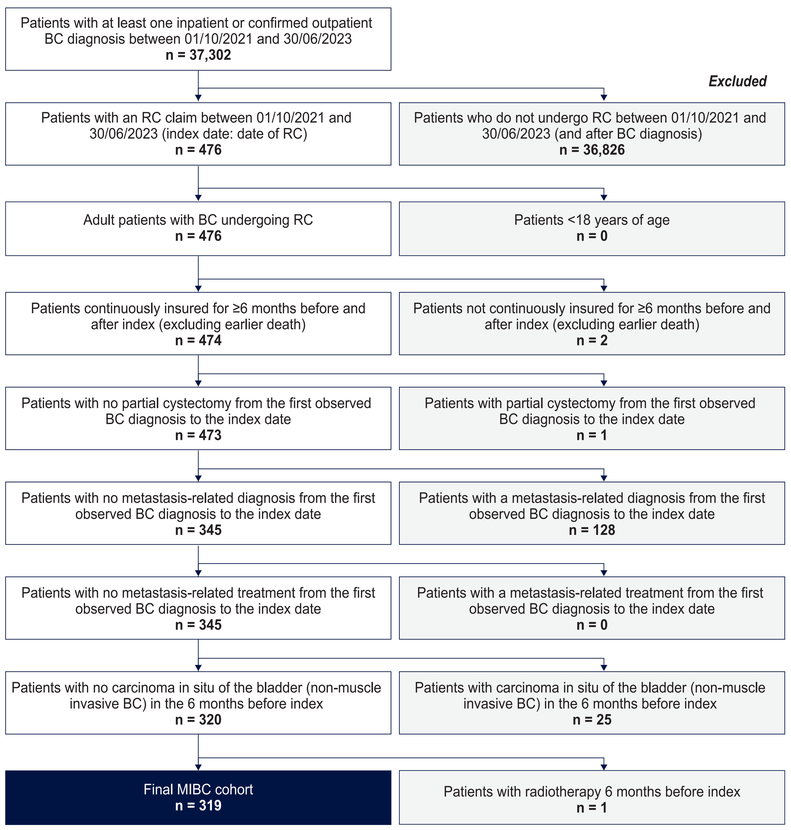
Adult patients (≥18 years of age) with ≥1 inpatient or outpatient specialist diagnosis (non-GP) for bladder cancer (BC; ICD-10-GM: C67.-) from 01 January 2010 to 30 June 2023 and a subsequent RC procedure (OPS: 5-576.2 to 5-576.7) from 01 October 2021 (6 months prior to EMA approval of adjuvant nivolumab) to 30 June 2023 were identified from the German AOK PLUS claims dataset, which covers >3.4 million insured individuals in the regions of Saxony and Thuringia (**Figure 1**). Index was defined as the date of RC.

As diagnostic codes for MIBC are not available, RC following BC diagnosis and exclusion of metastatic or in situ disease indicators were used to proxy for MIBC. Patients were excluded if they had evidence of partial cystectomy, secondary malignant neoplasms, or immunotherapies used for metastatic disease between the first BC diagnosis and RC as well as bladder carcinoma in situ or radiotherapy 6 months before RC. Moreover, continuous insurance for at least 6 months pre- and post-index (RC) was required (excluding cases of earlier death).

Study outcomes

Patient characteristics were described during baseline (6 months pre-index/index) and treatment was evaluated in the neoadjuvant (NAT, 6 months pre-index) and adjuvant settings (AT, 6 months post-index to study end [31 December 2023] or occurrence of metastatic/recurrence-related event or death, if earlier).

Figure 1. Patient attrition chart



Results

Patient characteristics

- The analysis included 319 MIBC patients overall, presenting with a median follow-up (FU) of 14.0 months (**Table 1**)
- Patients had a mean age of 71.4 ± 9.7 years, with 76.2% male patients. The mean age among patients with NAT or AT only was lower, at 66.0 and 69.1 years, respectively
- The majority of patients across all groups (>70%) had open surgery, with >18% undergoing laparoscopic RC
- The mean Charlson Comorbidity Index (CCI) was 7.0 ±3.0 among the overall cohort, lowest among patients with NAT only (mean 5.9)
- Cardiovascular disease was the most prevalent comorbidity presenting in 83.4% of patients overall with 78.7% of patients presenting with hypertension

Table 1. Baseline characteristics among the overall MIBC cohort and select treatment subgroups

Characteristic	Overall N = 319	NAT only N = 37	AT only N = 37	Neither NAT/AT N = 242
Demographics				
Age, mean (SD) | median	71.37 (9.71) | 72.0	65.97 (8.67) | 68.0	69.05 (8.88) | 68.0	72.64 (9.68) | 73.0
Male, n (%)	243 (76.18)	29 (78.38)	27 (72.97)	184 (76.03)
Index year, n (%)				
2021	41 (12.85)	3 (8.11)	5 (13.51)	33 (13.64)
2022	197 (61.76)	22 (59.46)	27 (72.97)	147 (60.74)
2023	81 (25.39)	12 (32.43)	5 (13.51)	62 (25.62)
FU length, mean (SD) | median	13.95 (7.14) | 13.6	12.62 (6.88) | 12.8	15.80 (6.85) | 15.8	13.93 (7.22) | 13.4
Clinical characteristics				
CCI, mean (SD) | median	6.97 (3.00) | 7	5.89 (2.75) | 5	7.11 (2.97) | 7	7.16 (3.02) | 7
Surgical approach, n (%)				
Laparoscopic	65 (20.38)	10 (27.03)	9 (24.32)	45 (18.60)
Robotic-assisted	45 (14.11)	9 (24.32)	7 (18.92)	29 (11.98)
Open	250 (78.37)	27 (72.97)	28 (75.68)	193 (79.75)
Other	4 (1.25)	0 (0.00)	0 (0.00)	4 (1.65)
Comorbidities, n (%)				
Cardiovascular disease	266 (83.39)	29 (78.38)	30 (81.08)	205 (84.71)
Hypertension	251 (78.68)	24 (64.86)	30 (81.08)	195 (80.58)
Renal disease	110 (34.48)	8 (21.62)	16 (43.24)	86 (35.54)
Chronic pulmonary disease	79 (24.76)	9 (24.32)	11 (29.73)	58 (23.97)
Diabetes	113 (35.42)	8 (21.62)	14 (37.84)	90 (37.19)
Other malignancies	118 (36.99)	11 (29.73)	13 (35.14)	93 (38.43)
Depression/anxiety	81 (25.39)	10 (27.03)	12 (32.43)	59 (24.38)

Treatment patterns

- Surgery without NAT/AT was the most frequent treatment type (75.9%, **Figure 2**). Overall, 40 patients (12.5%) received NAT, 40 (12.5%) received AT, and 3 (0.9%) received both (**Figure 2**)
- Of note, 3.8% of all RC-treated MIBC patients received adjuvant nivolumab (**Figure 3**)
- Among adjuvant-treated patients (N = 40), 27 received chemotherapy, 12 nivolumab, and 7 radiotherapy
- The mean time from start of NAT to RC was 98.4 ±29.2 days, whereas mean duration of NAT was 60.2 ±28.5 days
- The mean time from RC to start of adjuvant therapy was 80.0 ±35.3 days, consistent among patients initiating chemotherapy or immunotherapy

Figure 2. Neo- and adjuvant therapy utilization

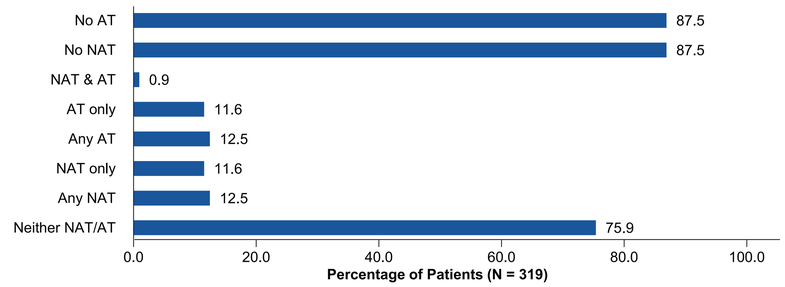
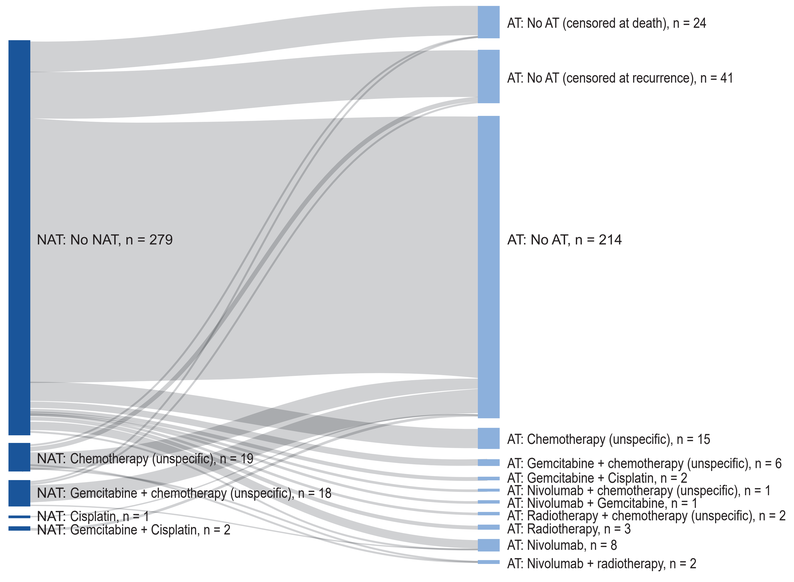


Figure 3. Patient flow from the neoadjuvant to adjuvant treatment setting



Strengths and limitations

This study utilized a large, population-based health insurance fund. Given uniform healthcare regulations, data entry requirements and access to health resources across Germany, a representative cohort of patients with MIBC was identified, free of study site/selection bias.

As a diagnosis code for MIBC was not available using ICD-10-GM, identification of MIBC relied on the combination of a BC diagnosis and RC procedure code, which may lead to some degree of misclassification, including patients with high-risk, non-muscle invasive disease undergoing surgery. Moreover, claims data includes complete treatment information in the outpatient setting; however, only partial in the inpatient setting (ie, for therapies subject to procedural coding or unspecific codes for chemotherapies).

Conclusions

Among contemporary German patients undergoing RC for MIBC, there was low neoadjuvant and adjuvant therapy use, including low adjuvant nivolumab uptake, suggesting underutilization of available systemic therapies.

References

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Disclosures

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Abbreviations

AT, adjuvant therapy; EMA, European Medicines Agency; CCI, Charlson Comorbidity Index; FU, follow-up; GP, general practitioner; ICD-10-GM, International Classification of Diseases, 10th revision, German Modification; MIBC, muscle-invasive bladder cancer; NAT, neoadjuvant therapy; OPS, Operation and Procedure Codes; RC, radical cystectomy

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