Avelumab first-line maintenance for locally advanced or metastatic urothelial cancer : treatment patterns and real-world outcomes in the US

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SCOPE

- **This observational study describes treatment patterns, sequencing, and real-world (rw) outcomes in patients with locally advanced or metastatic urothelial cancer (la/mUC) in the US, particularly those treated with avelumab first-line maintenance (1LM) therapy since its FDA approval in June 2020[1,2]**

CONCLUSIONS

- **Two-thirds of the treated patients received standard-of-care platinum-based chemotherapy (PBC) in the 1L treatment setting, consistent with guideline recommendations[3]**
- **Early uptake of avelumab 1LM was observed in patients with la/mUC that had not progressed on 1L PBC who had gone on to receive 1LM treatment. Future studies with longer follow-up may show increased use of avelumab 1LM and allow further assessment of rw overall survival (rwOS)**
- **High attrition was observed across lines of treatment; only 26% of patients received second-line (2L) treatment, and of those, 29% received third-line treatment; hence, there is a need for more effective treatments to be used in the front line treatment setting**
- **Our results complement those from the JAVELIN Bladder 100 phase 3 trial by describing clinical outcomes in a more heterogeneous patient population treated in rw oncology practices,[4] clinical outcomes are consistent with those from other recent rw studies[5-9]**
- **Our study also provides early evidence of the use and effectiveness of 2L enfortumab vedotin (EV) administered after the JAVELIN Bladder regimen of 1L PBC followed by avelumab 1LM**
- **As new regimens are approved and incorporated into clinical practice, further research is needed to refine sequencing options and outcomes in larger cohorts of patients with la/mUC in rw settings[10]**

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BACKGROUND

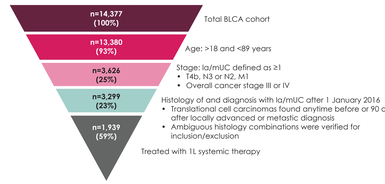
- UC (also known as transitional cell carcinoma) is a cancer that originates in cells lining the urinary tract, and may occur in the bladder, urethra, ureter, and renal pelvis; UC accounts for 90% of bladder cancer cases[11]
- The standard-of-care 1L treatment for la/mUC is PBC followed by avelumab 1LM in patients with disease that has not progressed with PBC[2,3]
- Treatment options for la/mUC have rapidly evolved over recent years with the approval of several immuno-oncology (IO) therapies, fibroblast growth factor receptor inhibitors, and antibody-drug conjugates, which has led to updates in clinical guidelines[3,10,13,14]
  - Recommended subsequent therapies after avelumab 1LM include EV, erdafitinib, and chemotherapy rechallenge[3]
- Given the addition of these novel therapies and the evolving treatment landscape, rw data may complement evidence from clinical trials and help guide clinical decision-making by providing information on the generalizability of treatments[12,13]
  - Evidence from rw clinical settings is lacking on how to incorporate these agents into the optimal treatment sequencing approach
- This retrospective study leveraged electronic health record (EHR) data collected during routine care in the US to provide a longitudinal view of patient experience with newly approved therapies as they enter clinical use
- In addition, this study provides insights into the rw use of EV after 1L PBC and avelumab 1LM since its US approval in 2019[14,15]

METHODS

Data source

- This study used the Tempus database, a nationwide, longitudinal EHR database comprising de-identified, patient-level structured and unstructured data that are curated by Tempus[16]
- The cohort comprised patients aged ≥18 years diagnosed with la/mUC (T4b, N2/3, and/or M1 or overall cancer stage III/IV) (index date) between 1 January 2016 and 13 March 2023 (**Figure 1**)
- The data cutoff for this analysis was 29 March 2023

Figure 1. Patient flow diagram

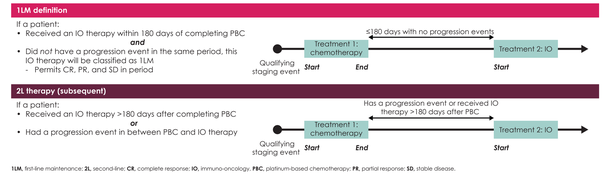


1LM, first-line maintenance; **BLCA**, bladder urothelial carcinoma; **la/mUC**, locally advanced or metastatic urothelial carcinoma.

Data analysis

- Patients who completed 1L PBC and then received an IO therapy were categorized as 1LM or 2L according to the algorithm in **Figure 2**
- 1LM was differentiated from 2L treatment based on recorded clinical intent or based algorithmically on initiation of IO therapy within 180 days of 1L PBC completion without recorded disease progression[17]
- Enhanced manual chart review was used to obtain rw outcomes, and reasons for avelumab 1LM discontinuation were obtained from unstructured data in physician notes; radiology, pathology, or biomarker reports, and other sources

Figure 2. Algorithm used to identify 1LM and 2L IO therapy



1LM, first-line maintenance; **2L**, second-line; **CR**, complete response; **IO**, immuno-oncology; **PBC**, platinum-based chemotherapy; **PR**, partial response; **SD**, stable disease.

Statistical analysis

- Patient demographics and clinical characteristics were summarized by descriptive statistics at the la/mUC diagnosis date (index date)
- Time-to-event outcomes, including rwOS, rw progression-free survival (rwPFS), and rw time on treatment, were estimated using the Kaplan-Meier method
- The observed follow-up was estimated from the initiation of 1L treatment for all 1L PBC–treated patients or initiation of 1LM treatment for all 1LM–treated patients until loss to follow-up using the Kaplan-Meier method

Ethics approval

- The study utilized retrospective, de-identified patient records and was exempt from IRB oversight and need for patient consent

RESULTS

Patient characteristics

- Of 3,299 patients with la/mUC, 59% (1,939) received 1L systemic treatment (**Figure 1**)
- Baseline demographic and clinical characteristics of the final treated la/mUC cohort (n=1,939) are reported in **Table 1**
  - Included patients were treated in academic centers (40%), community practices (26%), and other (33%)
  - Median age at diagnosis was 70 years; 74% of patients were male, 63% were White, and 88% had transitional cell carcinoma

Table 1. Baseline demographics and clinical characteristics of patients in the total treated cohort (n=1,939)

Characteristic	n=1,939
Follow-up from la/mUC diagnosis, median (range), months	19 (17-22)
Age at la/mUC diagnosis, median (range), years	70 (62-76)
Year of la/mUC diagnosis, n (%)	
2016	112 (6)
2017	161 (8)
2018	219 (11)
2019	381 (20)
2020	429 (22)
2021	431 (22)
2022	199 (10)
2023	7 (<1)
Sex, n (%)	
Male	1,431 (74)
Female	508 (26)
Race, n (%)	
White	1,212 (63)
Black or African American	100 (5)
Asian	39 (2)
American Indian or Alaska Native	6 (<1)
Native Hawaiian or Other Pacific Islander	2 (<1)
Other race	70 (4)
Unknown	510 (26)
Region, n (%)	
Midwest	337 (43)
South	203 (26)
West	175 (22)
Northeast	65 (8)
Unknown	1,159
Data source, n (%)	
Academic	567 (40)
Community	375 (26)
Other	474 (33)
Histology type, n (%)	
Transitional	1,713 (88)
Ambiguous carcinoma	152 (8)
Other	73 (4)
Comorbidities, n (%)	
1	347 (48)
2	142 (20)
3	74 (10)
4+	154 (21)
Unknown	1,222
Deceased records, n (%)	795 (41)

la/mUC, locally advanced or metastatic urothelial carcinoma.

Treatment patterns

- For the 50.2% of patients (974/1,939) who completed 1L treatment post avelumab 1LM approval, PBC was the most common 1L treatment (66% [644/974]; **Table 2**)
  - Of these patients, 61% received cisplatin (n=391), 35% received carboplatin (n=226), 3% received both carboplatin and cisplatin (n=19), 1% received oxaliplatin (n=7), and 0.2% received an unknown platinum compound (n=1)
  - 89% of patients (574/644) had no evidence of disease progression after completion of 1L PBC; of these, 38% (219/574) had a recorded 1LM treatment, with 62% (135/219) receiving avelumab. These patients had a median follow-up from 1LM start of 8.9 months
- After avelumab 1LM, 35% of patients (47/135) received 2L treatment
  - The most common 2L treatment was EV (70% [33/47])

Table 2. Treatment classes by line of therapy in patients who completed 1L treatment post avelumab approval

Treatment setting	Patients n/N (%)	Most common treatment, n (%)
1L	974/974 (100)	Cisplatin + gemcitabine: 297 (30) Carboplatin + gemcitabine: 200 (21) Pembrolizumab: 154 (16) MVAC: 60 (6) Nivolumab: 36 (4) Other: 227 (23)
1LM	219/644 (34)*	Avelumab: 135 (62) Other IO therapy: 84 (38)
2L	258/974 (26)	EV: 70 (27) Pembrolizumab: 47 (18) Carboplatin + gemcitabine: 34 (13) Cisplatin + gemcitabine: 17 (7) Nivolumab: 17 (7) Erdafitinib: 10 (4) Gemcitabine: 10 (4) Other: 53 (20)
3L	74/258 (29)	EV: 15 (20) Pembrolizumab: 10 (14) Avelumab: 10 (14) Erdafitinib: 9 (12) Sacituzumab govitecan: 7 (10) Atezolizumab†: 4 (5) Carboplatin + gemcitabine: 4 (5) Other: 15 (20)

1L, first-line; **1LM**, first-line maintenance; **2L**, second-line; **3L**, third-line; **EV**, enfortumab vedotin; **IO**, immuno-oncology; **MVAC**, methotrexate + vinblastine + doxorubicin + cisplatin.

*Percentage calculated from patients who received 1L platinum-based chemotherapy. †Atezolizumab is no longer approved in the US to treat patients with locally advanced or metastatic urothelial carcinoma following the manufacturer's decision to withdraw its indication after consulting with the FDA. The withdrawal was made in accordance with the FDA's Accelerated Approval Program after results from the phase 3 IMvigor130 trial (NCT02807636) failed to meet the postmarketing requirement necessary to convert the accelerated approval for atezolizumab into regular approval.

Clinical outcomes: PBC-treated patients

- Median follow-up from 1L PBC start was 10.2 months
- Median rwOS was 13.6 months
- 89% of patients (574/644) had no evidence of disease progression after completion of 1L PBC

Clinical outcomes: avelumab 1LM–treated patients

- The most common 1LM treatment was avelumab (62% [135/219]); these patients had a median follow-up from 1LM start of 8.9 months
- A rwOS landmark analysis from 1LM start showed that 80% of patients treated with avelumab 1LM were still alive at 6 months; 63% were alive at 12 months (**Table 3**)
- Median rwPFS from 1LM start was 6.4 months; median time on treatment was 3.85 months (**Table 3**)

Table 3. Clinical outcomes in patients treated with 1L PBC and avelumab 1LM

	1L PBC (n=644)	Avelumab 1LM (n=135)
Time on treatment, median (95% CI), months	2.73 (2.53-2.96)	3.85 (2.76-4.96)
rwOS (95% CI), %		
6-month landmark	82 (78-87)	80 (72-90)
12-month landmark	56 (50-63)	63 (52-75)
18-month landmark	42 (36-50)	43 (31-59)
rwPFS		
Median (95% CI), months	3.5 (3.3-4.1)	6.4 (4.6-NR)
3-month landmark (95% CI), %	65 (57-74)	73 (64-83)
6-month landmark (95% CI), %	10 (6-17)	52 (42-65)
12-month landmark (95% CI), %	2 (1-7)	40 (30-54)

Avelumab 1LM–treated patients are a subset of 1L PBC–treated patients. Analyses are anchored on 1L PBC start for 1L PBC patients (N=644) and anchored on avelumab 1LM initiation for avelumab 1LM–treated patients (n=135).

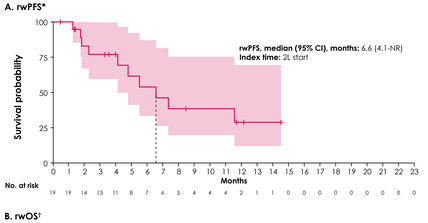
1LM, first-line maintenance; **PBC**, platinum-based chemotherapy; **NR**, not reached; **rwOS**, real-world overall survival; **rwPFS**, real-world progression-free survival.

Clinical outcomes: avelumab 1LM followed by 2L EV

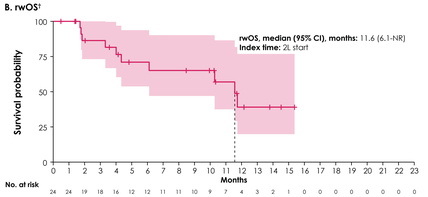
- All 33 patients who received EV were diagnosed with la/mUC in 2020 or later (**Table 4**)
- Median rwPFS from 2L EV start was 6.6 months (**Figure 3A**)
- Median rwOS from 2L EV start was 11.6 months (**Figure 3B**)

Figure 3. Patients receiving 2L EV after PBC and avelumab 1LM sequence

A. rwPFS*



B. rwOS†



Patients were not included if they had next-generation sequencing and thus entered the Tempus database after their last known clinical follow-up date or if their progression date or 2L EV treatment initiation date was missing.

1LM, first-line maintenance; **2L**, second-line; **EV**, enfortumab vedotin; **NR**, not reached; **PBC**, platinum-based chemotherapy; **rwOS**, real-world overall survival; **rwPFS**, real-world progression-free survival.

*This rwPFS analysis included 29 of 33 patients receiving 2L EV after PBC and avelumab 1LM sequence. Not all 20 patients were at risk at time 0 due to the risk-set adjustment methodology.

†This rwOS analysis included 26 of 33 patients receiving 2L EV after PBC and avelumab 1LM sequence. Not all 26 patients were at risk at time 0 due to the risk-set adjustment methodology.

Table 4. Baseline demographics and clinical characteristics of patients treated with avelumab 1LM who received 2L EV (n=33)

Characteristic	n=33
Follow-up from la/mUC diagnosis, median (range), months	22 (21-27)
Age at la/mUC diagnosis, median (range), years	70 (63-77)
Year of la/mUC diagnosis, n (%)	
2020	17 (52)
2021	14 (42)
2022	2 (6)
Sex, n (%)	
Male	22 (67)
Female	11 (33)
Race, n (%)	
White	19 (58)
Asian	1 (3)
Black or African American	1 (3)
Other race	2 (6)
Unknown	10 (30)
Region, n (%)	
Midwest	5 (36)
South	4 (29)
West	3 (21)
Northeast	2 (14)
Unknown	19
Data source, n (%)	
Community	12 (50)
Academic	11 (46)
Other	1 (4)
Unknown	9
Histology type, n (%)	
Transitional	29 (88)
Ambiguous Carcinoma	3 (9)
Other	1 (3)
No. of comorbidities, n (%)	
1	6 (46)
2	1 (8)
3	5 (38)
4+	1 (8)
Unknown	20
Deceased records, n (%)	10 (30)

1LM, first-line maintenance; **2L**, second-line; **la/mUC**, locally advanced or metastatic urothelial carcinoma.

LIMITATIONS

- Data were collected primarily in the oncology clinical practice setting through routine clinical care; therefore, nonrandom missingness may be present for several variables of interest
- Complete medical history outside of the Tempus database was not captured, which may lead to underreporting of treatments received
- Algorithms used to identify 1LM and 2L agents may not reflect the definitions used in clinical practice. In addition, there was potential for misclassification based on the algorithms used
- Patients who initiated 1L systemic therapy later in the study period may not have had enough follow-up for 2L and subsequent treatment rates to be observed

REFERENCES 1. US Food and Drug Administration. FDA approves avelumab for urothelial carcinoma maintenance treatment. Accessed September 27, 2023. https://www.fda.gov/drugs/drug-approvals-and-databases/fda-approves-avelumab-urothelial-carcinoma-maintenance-treatment **2.** Bavencio (avelumab). Prescribing information. EMD Serono, Inc., Rockland, MA, USA, an affiliate of Merck KGaA; 2022. **3.** NCCN Clinical Practice Guidelines in Oncology. Bladder Cancer. V3.2023. **4.** Powles T, et al. N Engl J Med. 2020;383(13):1218-30. **5.** Grivas P, et al. J Clin Oncol. 2023;41(Suppl 6):Abstract 465. **6.** Kirker M, et al. J Clin Oncol. 2023;41(Suppl 6):Abstract 468. **7.** Barthelemy P, et al. J Clin Oncol. 2023;41(Suppl 6):Abstract 471. **8.** Antonuzzo L, et al. J Clin Oncol. 2023;41(Suppl 6):Abstract 469. **9.** Bakaloudi DR, et al. Clin Genitourin Cancer. Published online June 20, 2023. **10.** Lavoie JM, et al. Oncologist. 2021;26(8):e1381-94. **11.** American Society of Clinical Oncology. Bladder Cancer: Introduction. Accessed September 27, 2023 https://www.cancer.net/cancer-types/bladder-cancer/introduction **12.** Siefker-Radtke AO, et al. J Clin Oncol. 2023;41(25):4084-86. **13.** Geynisman DM, et al. Urol Oncol. 2022;40(5):195.e1-11. **14.** US Food and Drug Administration. FDA grants regular approval to enfortumab vedotin-ejfv for locally advanced or metastatic urothelial cancer. Accessed September 27, 2023. https://www.fda.gov/drugs/resources-information-approved-drugs/fda-grants-regular-approval-enfortumab-vedotin-ejfv-locally-advanced-or-metastatic-urothelial-cancer#:~:text=FDA%20granted%20accelerated%20approval%20in%20December%202019%20to,in%20the%20neoadjuvant%2Fadjuvant%2C%20locally%20advanced%20or%20metastatic%20setting **15.** Padcev (enfortumab vedotin-ejfv). Prescribing information. Agensys, Inc. and Seagen Inc; 2023. **16.** Tempus. AI-enabled precision medicine. Accessed September 27, 2023. https://www.tempus.com/ **17.** Kearney M, et al. J Clin Oncol. 2023;41(Suppl 6):Abstract 572. **DISCLOSURES K. Carson** reports prior employment with Tempus Labs, Inc. and has other ownership interests in Tempus Labs, Inc. **S.H. Mahmoudpour** is an employee of Merck Healthcare KGaA, Darmstadt, Germany. **C. Ike** is an employee of EMD Serono, Inc., Rockland, MA, USA, an affiliate of Merck KGaA and also has stock ownership in Merck **S. Monzon** is an employee of Tempus, Chicago, IL, USA, and holds restricted stock units in Tempus. **S. Fragkogianni** is an employee of Tempus, Chicago, IL, USA, and holds restricted stock units in Tempus. **J. Ferrer** is an employee of Tempus, Chicago, IL, USA, and holds restricted stock units in Tempus. **M. Kearney** is an employee of Merck Healthcare KGaA, Darmstadt, Germany, and holds stock and other ownership interests in Merck, Novartis, and UCB. **ACKNOWLEDGMENTS** This study was sponsored by Merck (CrossRef Funder ID: 10.13039/100009945) and was previously conducted under an alliance between Merck and Pfizer. Editorial support was provided by Clinical Thinking and was funded by Merck.

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