Real-world treatment patterns and sequencing in patients with locally advanced or metastatic urothelial cancer (la/mUC) in the US

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SCOPE



- This study aimed to describe baseline demographic and clinical characteristics, real-world treatment patterns, and treatment sequencing in patients with la/mUC in the US
- Characterizing the patient population to determine how avelumab's approval has impacted treatment sequencing was a key objective of this analysis

CONCLUSIONS



- The treatment patterns observed are consistent with known and evolving treatment paradigms in la/mUC¹
- 77% of patients received systemic anticancer treatment following la/mUC diagnosis; among them, most patients (62%) received guideline-recommended first-line (1L) platinum-based chemotherapy (PBC)
- The use of PBC has increased and the use of immuno-oncology (IO)
 therapy and non-PBC has decreased in the 1L setting from 2020 through
 February 2022 following updated clinical guidelines and FDA label
 changes for IO monotherapy in the 1L setting
- Post-avelumab approval, in patients receiving IO therapy as subsequent treatment to PBC, 80% received IO therapy as first-line maintenance (1LM), of which 84% received avelumab 1LM
- High attrition rates beyond 1L were observed with only 33% of patients receiving second-line (2L) therapy, indicating the persistence of high unmet treatment needs
- However, at the end of the follow-up period, 32% of patients remained on avelumab 1LM (post-approval)
- Enfortumab vedotin was the most commonly used 2L agent in patients who discontinued 1LM during the study period
- Future real-world studies could provide further insight into the optimal sequencing of targeted therapies in this disease

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BACKGROUND

- PBC is the preferred 1L treatment for patients with la/mUC followed by 1LM with avelumab, a programmed cell death ligand 1 (PD-L1)—blocking antibody and immune checkpoint inhibitor (ICI), in those whose disease does not progress on 1L PBC²
- Avelumab was approved as 1LM treatment for la/mUC by the FDA in June 2020, based on the seminal data from the JAVELIN Bladder 100 study^{3,4}
- Avelumab 1LM with best supportive care (BSC) significantly prolonged overall survival (OS) vs BSC alone in patients with la/mUC that had not progressed with 1L PBC (median OS, 21.4 vs 14.3 months; hazard ratio, 0.69 [95% CI, 0.56-0.86]; p=0.001)^{3,5}
- The treatment options for la/mUC have rapidly evolved over recent years with the approval of various ICIs, fibroblast growth factor receptor (FGFR) inhibitors, and antibody-drug conjugates (ADCs),⁶ which has led to updates in clinical guidelines^{1,2,7,8}

Data cources

METHODS

Data sources

 This retrospective observational study used the Tempus database, a nationwide longitudinal electronic health records (EHR) database, comprising de-identified patient-level structured and unstructured data, curated by Tempus⁹

Patient population

- Patients aged ≥18 years and diagnosed with la/mUC (T4b, N2/3, and/or M1 or overall cancer stage 3/4) (index date) between January 1, 2016, and February 23, 2022, were included
- Patients who completed 1L PBC and then received an IO therapy were categorized as 1LM or 2L, according to the algorithm in Figure 1

 These patients were further split into pre- and postgroups based on when they completed their 1L PBC treatment in relation to avelumab's 1LM US approval⁴ on June 30, 2020

Statistical analysis

 Demographic and clinical characteristics were summarized by descriptive statistics

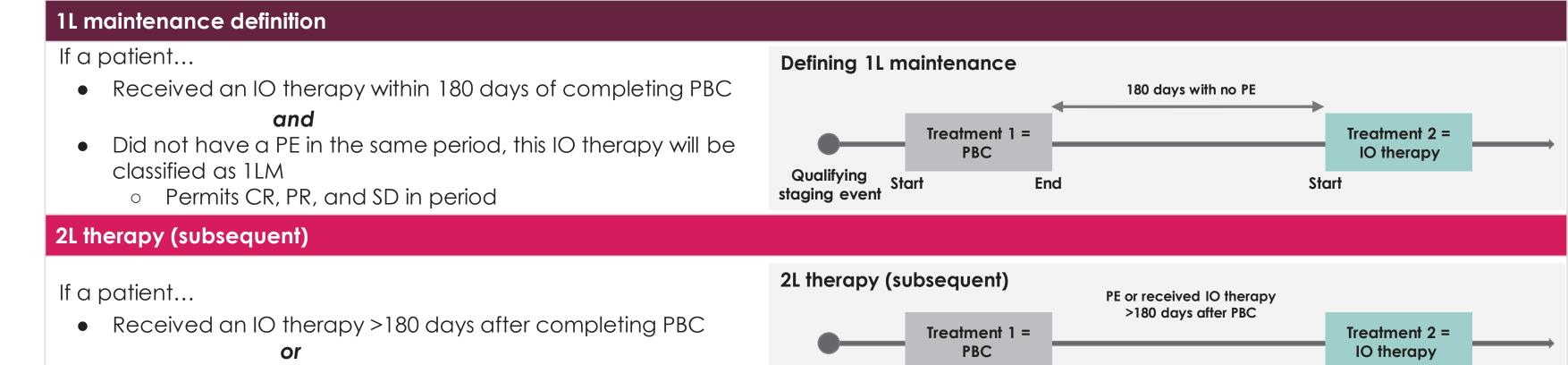
Ethics approval

 As the study used de-identified patient records, it was exempt from review and approval by ethics committees and the need for patient informed consent

Figure 1. Algorithm to define 1LM and 2L IO therapy

Had a PE between PBC and IO therapy

 1LM was differentiated from 2L treatment based on a stated clinical intent of 1LM or initiation of IO therapy within 180 days of 1L PBC completion without disease progression in the Tempus data



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

RESULTS

Patient population

- A total of 821 patients were included (**Figure 2**) from community centers (21%), academic centers (27%), and ASCO CancerLinQ network sites (52%)
- Baseline demographic and clinical characteristics in the final la/mUC cohort are reported in **Table 1**
- The median age at diagnosis was 69 years (interquartile range, 62-76 years), 73% of patients were male, 63% were White, 80% had transitional cell carcinoma, and 44% had a documented smoking history (**Table 1**)

Figure 2. Study population

Characteristic

Sex, n (%)

Race, n (%)

Data source, n (%)

Academic centers

Community centers

IQR, interquartile range; Ia/mUC, locally advance metastatic urothelial carcinoma.

Systemic treatment, n (%)

Year of la/mUC diagnosis, n (%)

American Indian or Alaska Native

Black or African American

Follow-up from la/mUC diagnosis, median, months

Age at la/mUC diagnosis, median (IQR), years

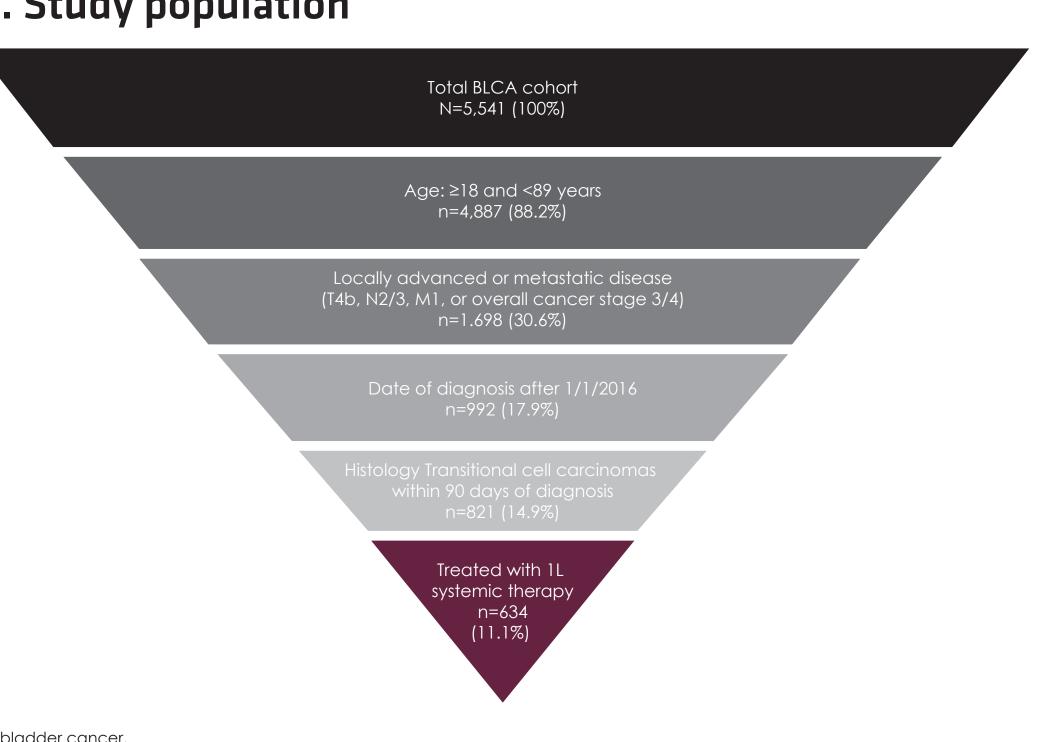


Table 1. Baseline demographic and clinical characteristics in patients in the overall la/mUC cohort (N=821)

9.20 (3.71-18.80)

69 (62, 76)

221 (27)

53 (6.5)

519 (63)

426 (52)

Treatment patterns

Characteristic (cont)

Smoking status, n (%)

Histology type, n (%)

Comorbidities, n (%)

Death records, n (%)

PD-L1 status, n (%)

Unknowr

Ambiguous carcinoma

Histopathology grade, n (%)

Grade 2 (moderately differentiated)

Grade 3 (poorly differentiated)

Grade 4 (undifferentiated)

History of smoking

- A total of 634 patients (77%) received 1L systemic treatment; of those, 62% (395/634) received PBC, 24% (155/634) received IO monotherapy, 7% (45/634) received non-PBC, and 6% (39/634) received other regimens* (Table 2)
- Among all patients who received 1L PBC, the majority received cisplatin (63.8%; 252/395), and most of the remaining patients received carboplatin (35.7%; 141/395)
- Among all patients who received 1L treatment, 33.1% (210/634) had evidence of receiving a 2L treatment. The most common 2L therapies included pembrolizumab (27.1%), enfortumab vedotin (16.7%), and carboplatin plus gemcitabine (9.0%)
- Among all patients who received 2L treatment, 31.0% (65/210) had evidence of receiving a third-line (3L) treatment. The most common 3L therapies included enfortumab vedotin (21.5%), pembrolizumab (20.0%), and atezolizumab[†] (10.8%) (Table 2)
- The distribution of systemic 1L therapy initiated according to treatment class is summarized by 6-month time intervals in Figure 3
- In the 1L setting, the use of PBC has increased and the use of IO monotherapy and non-PBC has decreased since 2020

*Other regimens included: ADCs, ADC combinations with IO therapy, chemotherapy or IO therapy + chemotherapy, IO therapy combinations, hormone + targeted therapy, tyrosine kinase inhibitors, and unlabeled investigational new drugs. †Atezolizumab is no longer approved in the US to treat patients with la/mUC 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.

N=821 (cont)

361 (63)

212 (37)

131 (16)

2 (0.2)

658 (80)

8 (1.6)

67 (14)

1 (0.2)

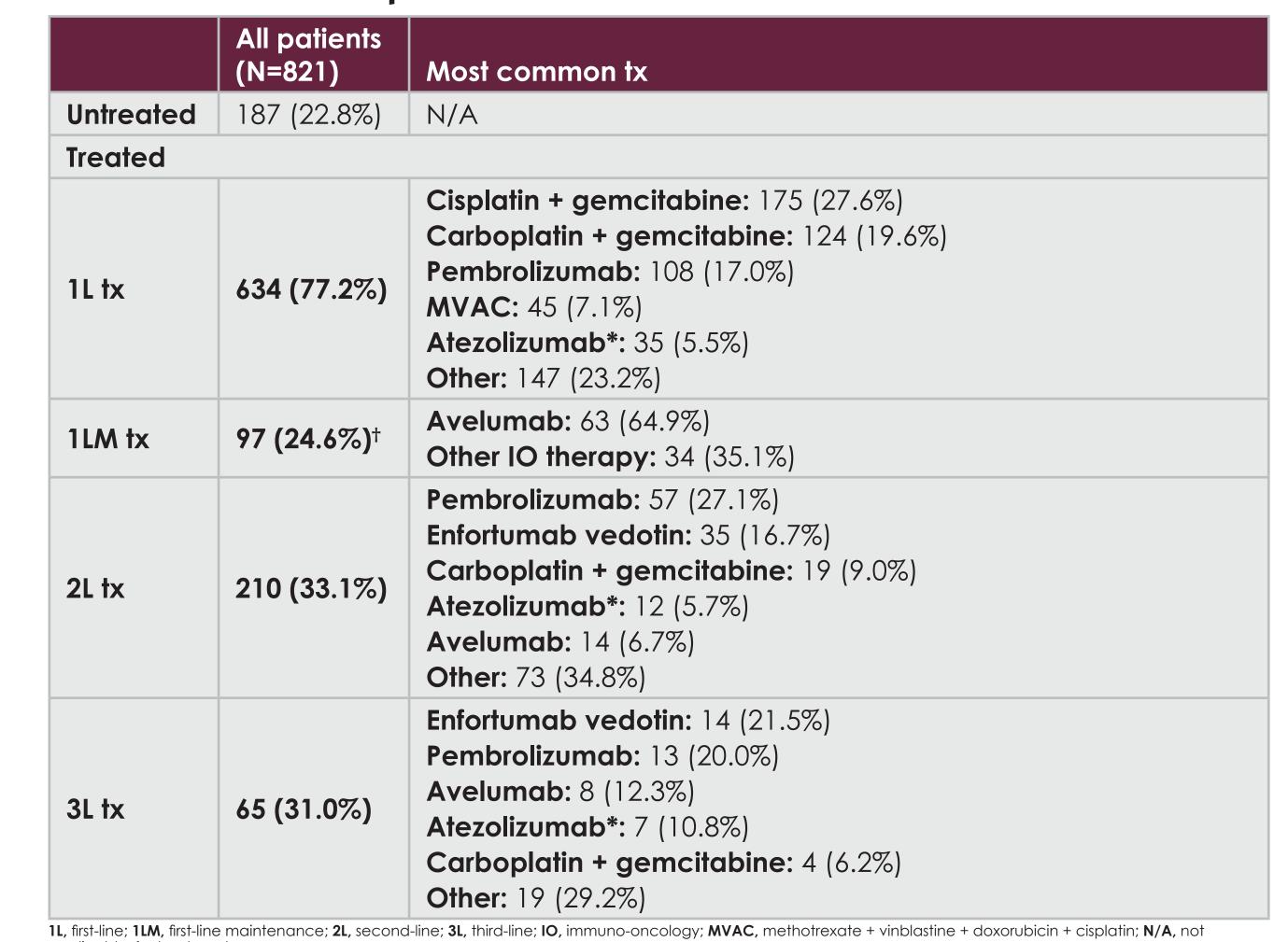
416 (84)

147 (37)

305 (37)

628

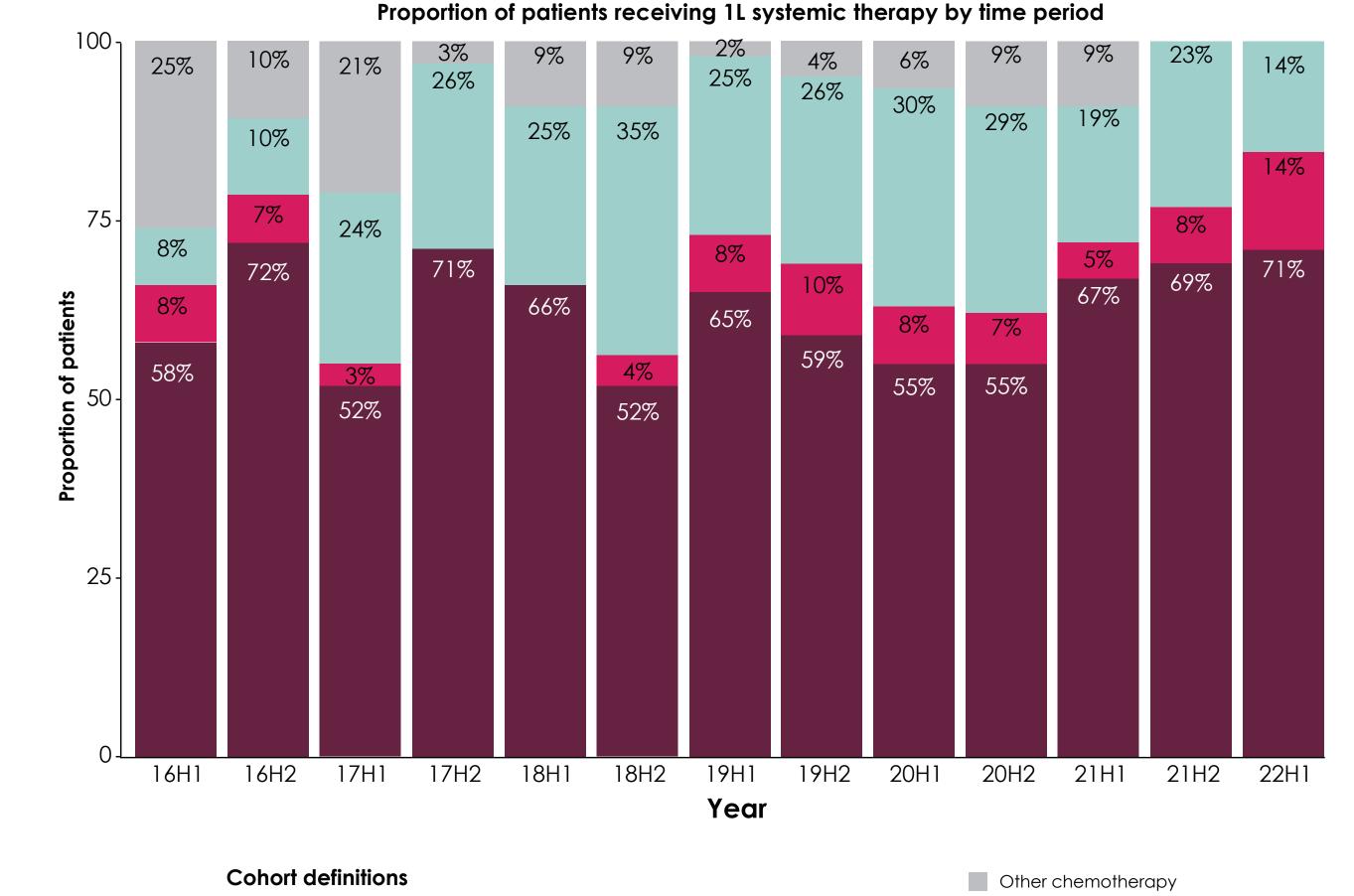
Table 2. Treatment patterns across lines of treatment

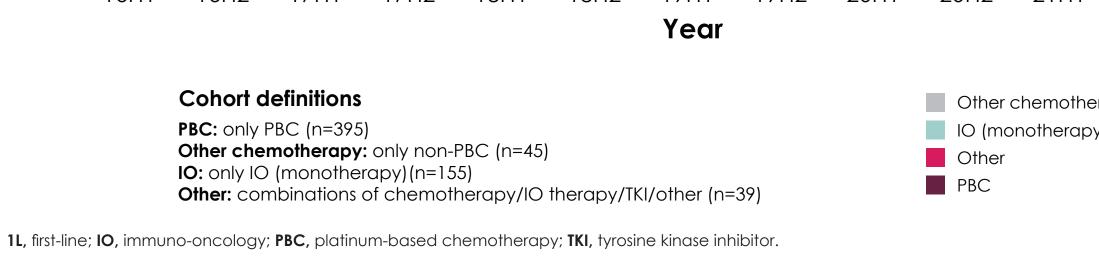


1L, first-line; 1LM, first-line maintenance; 2L, second-line; 3L, third-line; IO, immuno-oncology; MVAC, methotrexate + vinblastine + doxorubicin + cisplatin; N/A, not applicable; tx, treatment.

*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 IMvigor 130 trial (NCT02807636) failed to meet the postmarketing requirement necessary to convert the accelerated approval for atezolizumab into regulapproval. Percentage calculated from patients that received 1L platinum-based chemotherapy (n=395).

Figure 3. Trends in 1L therapy over the study period (2016-2022) for the 1L-treated cohort (n=634)





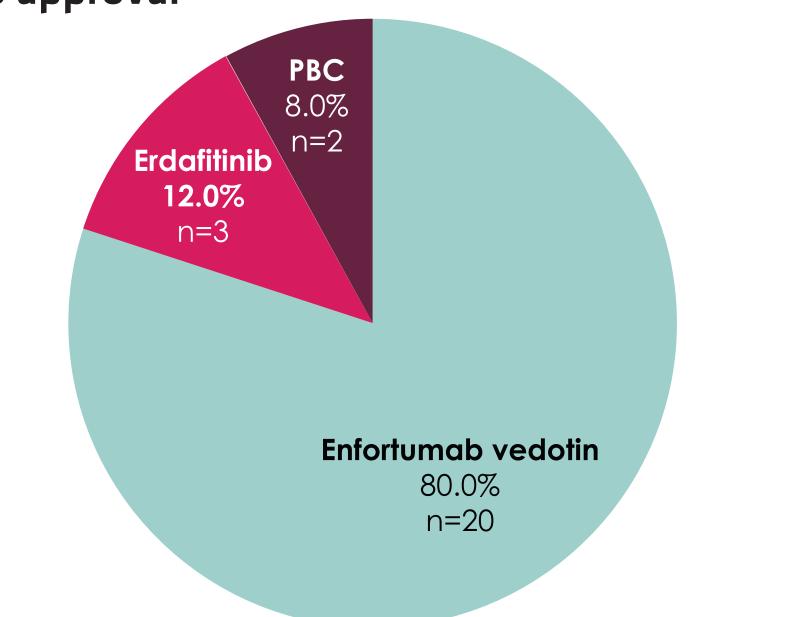
Treatment sequencing patterns

- Treatment sequencing for a group of patients who discontinued 1L
 PBC pre- and post-avelumab 1LM approval is shown in Table 3
- Of those receiving IO therapy (n=84) as subsequent treatment post-avelumab approval, 80% (67/84) received an IO therapy as 1LM, of which 84% (56/67) received avelumab 1LM
- Of the 25 patients who received 2L treatment after progression on IO 1LM therapy post-avelumab approval, enfortumab vedotin was the most commonly used 2L agent (80%; 20/25) (Figure 4)

Table 3. Treatment sequencing

	1L PBC end date pre-avelumab 1LM approval (n=243) n/N (%)	1L PBC end date post-avelumab 1LM approval (n=152) n/N (%)
Received IO therapy as 2L or 1LM following 1L PBC	87/243 (36)	84/152 (55)
Received IO therapy as 2L	59/87 (68)	17/84 (20)
Received IO therapy as 1LM	28/87 (32)	Avelumab: 56/67 (84) (18/56 patients (32%) were still receiving avelumab at the end of the follow-up period) Other: 11/67 (16)
Received 2L tx after progression on IO 1LM	9/28 (32) Enfortumab vedotin: 4/9 (44) PBC: 5/9 (56)	25/67 (37) Enfortumab vedotin: 20/25 (80) Erdafitinib: 3/25 (12) PBC: 2/25 (8)
Did not receive IO therapy after 1L PBC but received 2L or later tx	110/243 (45)	34/152 (22)

Figure 4. Breakdown of 2L treatments after progression on IO 1LM post-avelumab approval



11.M first-line maintenance: 21 second-line: PRC platinum-based chemotherapy: 10 immuno-oncoloc

Strength and limitations

Strengths

- Data from the Tempus real-world database came from the ASCO CancerLinQ network, which includes >300 community health systems, 2,500 oncologists, and >2 million patients across the US
- This study is one of the first real-world studies showing the integration of 1LM therapy in patients with mUC in the US

Limitations

- Data were collected primarily in the oncology clinical practice setting through routine clinical care and not for research purposes; therefore, nonrandom missingness may be present for several variables of interest, and data on healthcare received outside of the Tempus network of practices are not available
- Complete medical history outside of the oncology EHR 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
- Patients who initiated 1L systemic therapy later in the study period may not have had enough follow-up time to observe 2L and subsequent treatment rates, which may have led to underestimates in these lines of treatment
- Similarly, the study was limited in its ability to comprehensively understand the use of avelumab in 1LM as it was approved by the FDA³ on June 30, 2020

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