Real-world treatment patterns and clinical outcomes in patients with metastatic urothelial carcinoma (mUC) receiving first-line (1L) treatment: results from IMPACT UC

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SCOPE

- The objective of IMPACT UC was to assess treatment patterns and clinical outcomes in patients with mUC enrolled in Medicare Fee-for-Service (FFS) treated with chemotherapy or immuno-oncology monotherapy (IO mono) in the 1L setting

CONCLUSIONS

- This study is one of the first descriptive real-world studies using Medicare FFS to assess real-world treatment patterns and clinical outcomes in the post-IO approval time frame
- Patients who received chemotherapy tended to be younger than IO-treated patients and those not receiving chemotherapy. Also, those who received cisplatin-containing chemotherapy (cis) appear to have baseline clinical characteristics that may be associated with improved clinical outcomes
- Among patients receiving 1L treatment, unadjusted real-world overall survival (OS) was longer in patients receiving 1L cis compared with those receiving other 1L treatments
- While the median follow-up time in the 1L treatment cohorts was similar, the time on treatment was variable
- More than 50% of Medicare FFS beneficiaries with a diagnosis of mUC had no identified 1L treatment
- With the mUC treatment landscape evolving with the introduction of avelumab as the 1L maintenance treatment, future studies should assess the latest treatment patterns and clinical outcomes. Additionally, these studies should evaluate patient characteristics and unmet needs in patients with untreated mUC

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BACKGROUND

- UC is the most common malignancy involving the urinary system
  - According to projections in the 2021 Surveillance, Epidemiology, and End Results Program report, an estimated 83,730 adults in the US will be diagnosed with UC, and an estimated 17,200 deaths will occur due to UC[1]
- Although advances in the regimens to manage mUC have led to substantial increases in survival, treatment regimens for mUC remained relatively unchanged until the emergence of PD-(L)1 immune checkpoint inhibitors[2]
- The standard of care 1L treatment for patients with mUC remains platinum-containing therapy [3-5]
- Real-world data related to treatment patterns and OS in patients with mUC are limited since IO introduction, and this descriptive study fills that gap

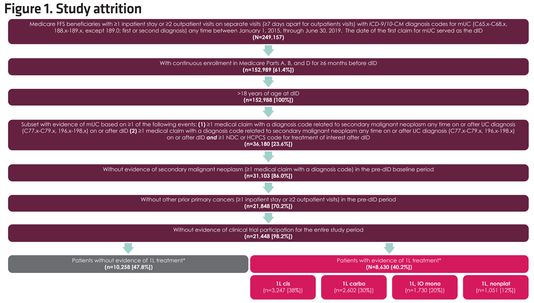
METHODS

- A descriptive retrospective study was conducted using deidentified Centers for Medicare & Medicaid Services; sample sourced from Medicare FFS Parts A, B, and D claims.[6] Institutional review board review for this study was not required per Title 45 Code of Federal Regulations Part 46; this research was exempt because it involved the study of existing data, and the information was recorded in such a manner that the individuals could not be identified directly or through identifiers linked to individuals[7]
- Patients ≥18 years old with ≥1 inpatient or ≥2 outpatient visits (≥7 days apart) with an International Classification of Diseases (ICD) ICD-9/10 code for UC (188.x-189.x, except 189.0, C65.x-C68.x) were identified between January 1, 2015, and June 30, 2019 (first UC visit = diagnosis index date [dID]). Patients were required to have continuous enrollment for ≥6 months pre-dID (baseline) (**Figure 1**) and were followed up from 1L treatment through end of study time period, disenrollment, or death (**Figure 2**)
- Patients with ≥1 diagnosis code related to secondary malignant neoplasm and ≥1 National Drug Code or Healthcare Common Procedure Coding System code for 1L treatments post dID (first treatment date = treatment index date [tID]) were defined as treated patients
- Patients with evidence of other cancers or prior systemic or IO therapies pre-dID were excluded; those with clinical trial participation at any time were also excluded
- Patient cohorts were categorized by type of 1L treatment received: cis, carboplatin-containing chemotherapy (carbo), IO mono, and non–platinum-containing chemotherapy (nonplat)*
- Unadjusted median OS (Kaplan-Meier), time on treatment (TOT), defined as time between initiation and end of 1L therapy, and time to next treatment (TTNT), defined as the time from start of 1L therapy to start of second-line (2L) therapy, were estimated and presented by type of 1L treatment (**Tables 3** and **4**, **Figure 3**) and presented in months

*Nonplat did not include any IO.

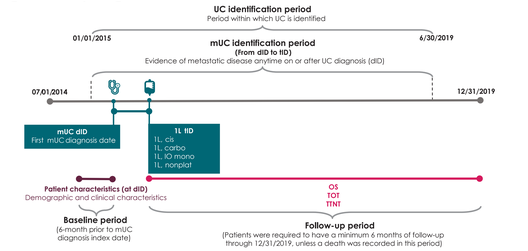
RESULTS

Figure 1. Study attrition



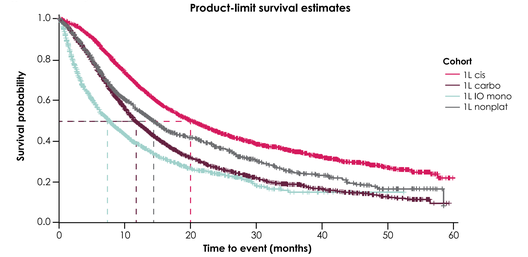
*Without evidence of prior IO mono (avelumab, pembrolizumab, nivolumab, atezolizumab, durvalumab) in the pre-dID baseline period
Atezolizumab and durvalumab applications for 2L indication in locally advanced UC and mUC were recently withdrawn.[3]
1L, first-line; carbo, carboplatin-containing chemotherapy; **cis**, cisplatin-containing chemotherapy; **dID**, diagnosis index date; **HCPCS**, Healthcare Common Procedure Coding System; **IO mono**, immune-oncology monotherapy; **mUC**, metastatic urothelial carcinoma; **NDC**, National Drug Code; **nonplat**, non–platinum-containing chemotherapy.

Figure 2. Study design



1L, first line; **carbo**, carboplatin-containing chemotherapy; **cis**, cisplatin-containing chemotherapy; **dID**, diagnosis index date; **IO mono**, immune-oncology monotherapy; **mUC**, metastatic urothelial carcinoma; **nonplat**, non–platinum-containing chemotherapy; **OS**, overall survival; **tID**, treatment index date.

Figure 3. Unadjusted OS



carbo, carboplatin-containing chemotherapy; **cis**, cisplatin-containing chemotherapy; **IO mono**, immune-oncology monotherapy; **nonplat**, non–platinum-containing chemotherapy.

Table 1. Baseline demographic characteristics

	1L cis (n=3,247)	1L carbo (n=2,602)	1L IO mono (n=1,730)	1L nonplat (n=1,051)	No identified 1L treatment (n=10,258)
Year, n (% of all 1L treated by year)					
2015	969 (35.4)	987 (36.0)	347 (12.7)	438 (16.0)	3,734 (35.5)
2016	756 (37.7)	670 (33.4)	321 (16.0)	260 (13.0)	2,569 (25.0)
2017	665 (37.8)	468 (26.6)	449 (25.5)	177 (10.1)	1,932 (18.8)
2018	593 (39.0)	344 (22.6)	452 (29.8)	130 (8.6)	1,416 (13.8)
2019*	264 (43.7)	133 (22.0)	161 (26.7)	46 (7.6)	607 (5.9)
Age at index, median (IQR)	76 (72-76)	75 (70-81)	79 (73-84)	78 (72-83)	78 (72-85)
Sex, n (%)					
Male	2,287 (70.4)	1,830 (70.3)	1,199 (69.3)	763 (72.6)	6,887 (67.1)
Race/ethnicity, n (%)					
White	2,951 (90.9)	2,334 (89.7)	1,556 (89.9)	959 (91.2)	9,128 (89.0)
Black	139 (4.3)	136 (5.2)	80 (4.6)	46 (4.4)	638 (6.2)
Hispanic or Latino	37 (1.1)	25 (1.0)	14 (0.8)	<11 (NR)	129 (1.3)
Other	38 (1.2)	45 (1.7)	41 (2.4)	18 (1.7)	175 (1.7)
Unknown	82 (2.5)	62 (2.4)	39 (2.3)	21 (2.0)	188 (1.8)
Geographic region, n (%)					
Midwest	826 (25.4)	662 (25.4)	410 (23.7)	272 (25.9)	2,586 (25.2)
Northeast	750 (23.1)	595 (22.9)	403 (23.3)	279 (26.5)	2,594 (25.3)
South	1,119 (34.5)	959 (36.9)	596 (34.5)	339 (32.3)	3,419 (33.3)
West	547 (16.8)	383 (14.7)	320 (18.5)	160 (15.2)	1,648 (16.1)
Dual-eligible (Medicaid) status, n (%)	538 (16.6)	425 (16.3)	282 (16.3)	184 (17.5)	2,214 (21.6)
Original reason for entitlement to Medicare, n (%)					
Age	2,699 (83.1)	2,190 (84.2)	1,513 (87.5)	892 (84.9)	8,476 (82.6)
Disability and/or ESRD	548 (16.9)	412 (15.8)	217 (12.5)	159 (15.1)	1,782 (17.4)

1L, first line; **carbo**, carboplatin-containing chemotherapy; **cis**, cisplatin-containing chemotherapy; **ESRD**, end-stage renal disease; **IO mono**, immune-oncology monotherapy; **IQR**, interquartile range; **nonplat**, non–platinum-containing chemotherapy.
*Note that identification period for patients was up to June 30, 2020; consequently, fewer patients fall into this category.

Table 2. Baseline clinical characteristics

	1L cis (n=3,247)	1L carbo (n=2,602)	1L IO mono (n=1,730)	1L nonplat (n=1,051)	No identified 1L treatment (n=10,258)
Charlson Comorbidity Index, median (IQR)	3 (2-5)	4 (2-6)	4 (3-7)	4 (2-6)	4 (2-6)
Cerebrovascular disease, n (%)	295 (9.1)	323 (12.4)	221 (12.8)	146 (13.9)	1,500 (14.6)
Chronic obstructive pulmonary disease, n (%)	873 (26.9)	741 (28.5)	499 (28.8)	297 (28.3)	3,249 (31.7)
Congestive heart failure, n (%)	259 (8.0)	339 (13.0)	270 (15.6)	152 (14.5)	1,822 (17.8)
Diabetes without complications, n (%)	888 (27.3)	932 (35.8)	571 (33.0)	349 (33.2)	3,439 (33.5)
Diabetes with complications, n (%)	274 (8.4)	378 (14.5)	283 (16.4)	166 (15.8)	1,573 (15.3)
Peripheral vascular disease, n (%)	631 (19.4)	625 (24.0)	484 (28.0)	257 (24.5)	2,751 (26.8)
Renal disease, n (%)	388 (11.9)	737 (28.3)	584 (33.8)	273 (26.0)	3,102 (30.2)

1L, first line; **carbo**, carboplatin-containing chemotherapy; **cis**, cisplatin-containing chemotherapy; **IO mono**, immune-oncology monotherapy; **IQR**, interquartile range; **nonplat**, non–platinum-containing chemotherapy.

Table 3. Unadjusted treatment patterns and OS

	1L cis (n=3,247)	1L carbo (n=2,602)	1L IO mono (n=1,730)	1L nonplat (n=1,051)
OS, median (IQR), months	20.0 (9.6-53.7)	11.4 (5.8-26.0)	7.6 (2.6-22.2)	14.3 (6.0-35.2)
6-Month OS rate, %	87.4	73.8	55.3	74.9
12-Month OS rate, %	67.1	48.7	38.4	54.9
24-Month OS rate, %	44.6	26.8	23.8	37.1
TOT, median (IQR), months	4.0 (2.6-10.8)	4.3 (2.3-9.2)	3.4 (1.6-7.8)	2.5 (1.6-6.7)
TTNT, median (IQR), months	3.1 (2.1-4.8)	3.7 (2.1-7.3)	3.3 (2.3-9.0)	3.5 (2.3-8.3)

carbo, carboplatin-containing chemotherapy; **cis**, cisplatin-containing chemotherapy; **IO mono**, immune-oncology monotherapy; **IQR**, interquartile range; **nonplat**, non–platinum-containing chemotherapy; **OS**, overall survival; **TOT**, time on treatment; **TTNT**, time to next treatment.

- 18,888 patients met selection criteria: 8,630 (45.7%) of the patients had an identified 1L systemic treatment, and 10,258 (54.3%) had no identified 1L treatment
  - Among patients receiving 1L, most had cis (37.6%) or carbo (30.2%), followed by IO mono (20.0%) and nonplat (12.2%) (**Figure 1**)
- Median age across the treated cohorts varied between 75 years (carbo) and 79 years (IO mono); the majority of the treated cohorts were male and White (**Table 1**)
- Patients who received cis had a median Charlson Comorbidity Index Score of 3, whereas the other cohorts had a score of 4 (**Table 2**)
  - Renal disease was present in 33.8% of patients with IO mono, with slightly lower percentages with carbo (28.3%), nonplat (26.0%), and cis (11.9%) (**Table 2**)
- Patients receiving cis and carbo had a median duration of 4 months of treatment, while patients receiving IO and nonplat had approximately 3 months (**Table 3**)
- Time between start of 1L and 2L treatment ranged from 3 to 4 months, with cis being the shortest and carbo the longest (**Table 3**)
- Survival was longest in patients with a 1L treatment with cis, with a median of 20 months compared with those with nonplat (14 months), carbo (11 months), and IO (8 months) (**Figure 3** and **Table 3**)

Limitations

- This study used data from the Medicare FFS population; hence, generalizability of results of this study to other populations may be limited
- Clinical conditions were identified using *ICD-9/10* codes with potential for miscoding
- Algorithms were used to identify lines of therapy based on administrative claims, which may not reflect the definitions of lines of therapy used in clinical practice
- Clinical information regarding the rationale for treatment discontinuation/switch is not available in claims data
- This was a descriptive study; therefore, no statistical tests were performed, and interpretation of the results should be done accordingly
- No information was available in the database regarding potential reasons why patients did not receive 1L systemic treatment. It is important to recognize that both physician and patient factors could have contributed to the choice of these treatments for older patients with mUC

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