Disease management and frontline treatment of locally advanced or metastatic urothelial carcinoma (la/mUC): the US Physician PARADIGM study

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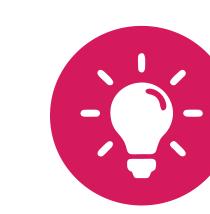
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SCOPE



 This study examined recent systemic anticancer treatment (tx) patterns in la/mUC using a targeted literature search (TLS), qualitative interviews (Qls), and a cross-sectional survey of US medical oncologists and urologists to understand motivations for first-line (1L) tx decisions and practice patterns

CONCLUSIONS



- Physicians in the Qls (N=15) reported higher tx rates than reported in the TLS
- Findings from the Qls reflect a more recent perspective and suggest that, over time, the proportion of pts with la/mUC in the US treated with or eligible for systemic tx has increased in 1L (including 10 maintenance) and subsequent lines of tx
- Qls and survey results showed that the regimen of choice is platinumcontaining chemo followed by avelumab maintenance for pts with la/ mUC who have not progressed following 1L tx with platinum-containing chemo
- Physician survey (N=150) estimated that 23% of pts never received systemic anticancer tx; top reasons included poor PS, pt refusal, advanced age, toxicity concerns, and limited pt/caregiver support
- Survey results indicated that among la/mUC pts who received systemic anticancer tx, 46% received 1L tx in the past 6 months. The reasons why eligible pts did not receive 1L IO maintenance differs by academic and community setting. Thus increased education for both physicians and pts with la/mUC is critical for optimal tx selection; guidelines play a significant role in 1L tx decision-making

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BACKGROUND

- While platinum-containing chemo is the standard of care (SOC) in la/mUC, the introduction of PD-1/PD-L1 inhibitors has led to changes in practice
- In June 2020, avelumab, a PD-L1 inhibitor, was first approved in the US as 1L maintenance tx for pts with Ia/mUC whose disease has not progressed following tx with platinum-containing chemo
- Prior studies have shown that 40%-65% of pts with la/mUC do not receive 1L tx,¹ and ≤40% of pts who receive 1L tx are not treated with platinum-containing chemo^{2,3,5-7}
- It is imperative to understand physician tx decision-making and practice patterns in the context of the changing tx landscape
- A TLS that reviewed abstracts published between January 2018 and March 2021 was conducted
- 60-minute QIs were conducted with 15 US medical oncologists and urologists in
- For the cross-sectional survey, 150 US medical and hematology oncologists completed a 35-minute online survey (September-October 2021)
- Physicians for both the QIs and survey were required to be in practice ≥1 year post fellowship, be a board-certified urologist (only for QI) or medical/ hematology oncologist, and manage ≥5 pts with Ia/mUC (1 pt with Ia/mUC for QI) who received 1L systemic tx in the past 6 months
- Post-study, physicians were defined as "high 1L prescribers" if they reported that >46% of their pts had been treated with 1L systemic tx in the past 6 months based on the median split (n=72; low prescriber, n=78)
- Similarly, physicians were defined as "high 1L IO maintenance prescribers" if they reported that >71% of their pts received IO maintenance tx based on the median split (n=71; low 1L IO maintenance prescribers, n=75)
- Results are reported descriptively

RESULTS

- Studies reported data on tx patterns for la/mUC pts during study periods ranging from 2000 to 2017
- 6 published US retrospective studies found relatively low use of 1L systemic tx; 42%-60% of pts with la/mUC were treated with systemic anticancer tx, and only 33-39% of pts with 1L tx received second-line (2L) tx (Table 1)

Table 1. TLS of US retrospective studies on tx patterns for pts with la/mUC

Author, publication year	Data source	Study period	Line of tx	Pts with la/mUC receiving 1L tx, %	Most common 1L agents or regimens (% of treated pts)	Pts with la/mUC receiving 2L tx, %
Aly, 2019	SEER-Medicare database (US)	2004-2011	1L, 3L	45	Gemcitabine + carboplatin (32) Gemcitabine + cisplatin (31)	39
Dinan, 2021*	SEER-Medicare database (US)	2008-2012	1L, 2L	48	Gemcitabine (81) Carboplatin (50) Cisplatin (38)	33
Doshi, 2018	US Oncology Network/ iKnowMed	2015-2017	1L, 3L	NR	Gemcitabine + carboplatin (28) Gemcitabine + cisplatin (26)	NR
Flannery, 2019	US Oncology Network/ iKnowMed	2010-2016	1L, 2L	60	Gemcitabine + carboplatin (28) Gemcitabine + cisplatin (26)	34
Galsky, 2018	SEER-Medicare database (US)	2004-2011	1L, 2L	42	Gemcitabine + carboplatin (32) Gemcitabine + cisplatin (21)	35
Simeone, 2018	Flatiron Health (US)	2011-2017	1L, 2L	NR	Gemcitabine + carboplatin (35) Gemcitabine + cisplatin (27)	NR

Epidemiology, and End Results; TLS, targeted literature search; tx, treatmen * Patients received gemcitabine as part of their initial chemotherapy regimen

- QI respondents were community oncologists (n=8), academic oncologists (n=4), and community urologists (n=3)
- Physicians estimated that ≥75% of pts were being treated with systemic tx
- 73% of respondents reported that the proportion of pts receiving systemic tx increased in recent years given the availability of IO
- Poor PS was the most commonly cited reason why pts with la/mUC were not treated with systemic tx (73%)
- Others included old age (67%), pt preference (53%), comorbidities (47%), and frailty (33%)

Physician-reported criteria for cisplatin eligibility include: Physician-reported criteria for platinum eligibility include:

- >50 mL/min creatinine clearance
- Good PS (ECOG 0/1)
- No major comorbidities or contraindications (cardiac lung, neuropathy, hearing loss)
- No specific creatinine clearance criteria; dosing accounts for renal function
- Decent PS (not bedbound)
- No extreme frailty or significant comorbidities
- No major cytopenias

Drug regimen utilization in 1L la/mUC

- Physicians' regimen of choice was platinum-containing chemo followed by 1L IO maintenance with avelumab for pts with la/mUC that has not progressed following 1L tx with platinum-containing chemo
- 1L IO monotherapy was typically reserved for pts who were considered platinum ineligible or who refused chemo
- 10 oncologists reported that 60%-80% of pts who received 1L tx for la/mUC received 2L systemic tx
- From QI respondents (n=12 oncologists), platinum-containing chemo continued to be the SOC in 1L la/mUC, with similar cisplatin and carboplatin-containing chemo utilization rates
- Carboplatin-containing chemo (41%), cisplatin-containing chemo (37%), single-agent IO (18%), and nonplatinum chemo (4%)
- All oncologists reported prescribing 1L IO maintenance with avelumab to eligible pts (n=10 prescribing avelumab

Cross-sectional survey (N=150)

METHODS

- The cross-sectional survey included 150 medical/hematology oncologists (**Table 2**)
- In the previous 6 months, physicians estimated 23% of their patients did not receive systemic tx for la/mUC. Of those who received tx, 46% were treated in 1
- Top 5 factors for not treating la/mUC pts with 1L systemic tx are shown in Figure 1
- Physicians estimated that on average 69% of pts with la/mUC eligible for 1L IO maintenance received 1LIO maintenance (median, 71%)
- Top 5 reasons for pts with la/mUC not receiving 1L IO maintenance among those whose disease has not progressed are shown in Figure 2
 - Physician-reported barriers to prescribing avelumab as 1L IO maintenance for pts with la/mUC (academic vs community):
 - Pts want a tx break/are unwilling to agree to 1L IO maintenance: 53% vs 36% Logistical issues with getting pts infusions every 2 weeks: 29% vs 14%
 - Prior immunotherapy (neoadjuvant/adjuvant): 29% vs 12%

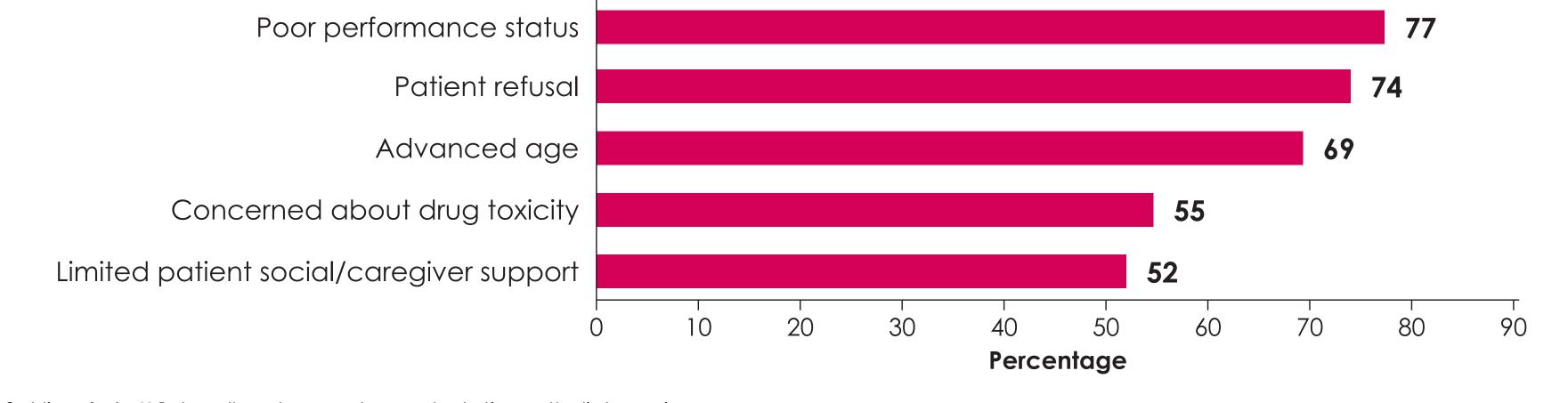
Table 2. Physician demographics and tx/practice patterns

(cross-sectional survey)	(cross-sectional survey)			
	Medical/ hematology oncologists (N=150)	Poor perfo		
Male, %	81	Concerned abo		
Practice setting, %	Limited patient social/car			
Community	63			
Academic	37			
Practice type, %	1L, first line; la/mUC, locally advanced or			
Comprehensive integrated health system	49	Figure 2. Top 5 physician la/mUC who have not pro		
Outpatient medical group	17	la/illoc willo llave ilot pro		
Independent or standalone practice	27	Poor porfe		
Other	8	Poor perfo		
Time in practice, median (SD), years	15 (2-31)	Tolero		
Pts with la/mUC prescribed a systemic drug re (past 6 months), $\%$	Issues with reimbursem			
1L	46			
2L	32	1L, first line; IO, immuno-oncology; la/mU		
≥3L	22	Figure 3. Impact of instit		
Tx philosophy and practices: "The guidelines/institution/practice impact my tx decisions in	tx decisions based on 1L survey)			
Agree somewhat	47	Physician agreement that in tx decisions among hig		
Agree completely	17	60.0 – 56		
Neither agree nor disagree	17	50.0 - 40.0 - 30.0 -		
Disagree completely	11	30.0 – 20.0 –		

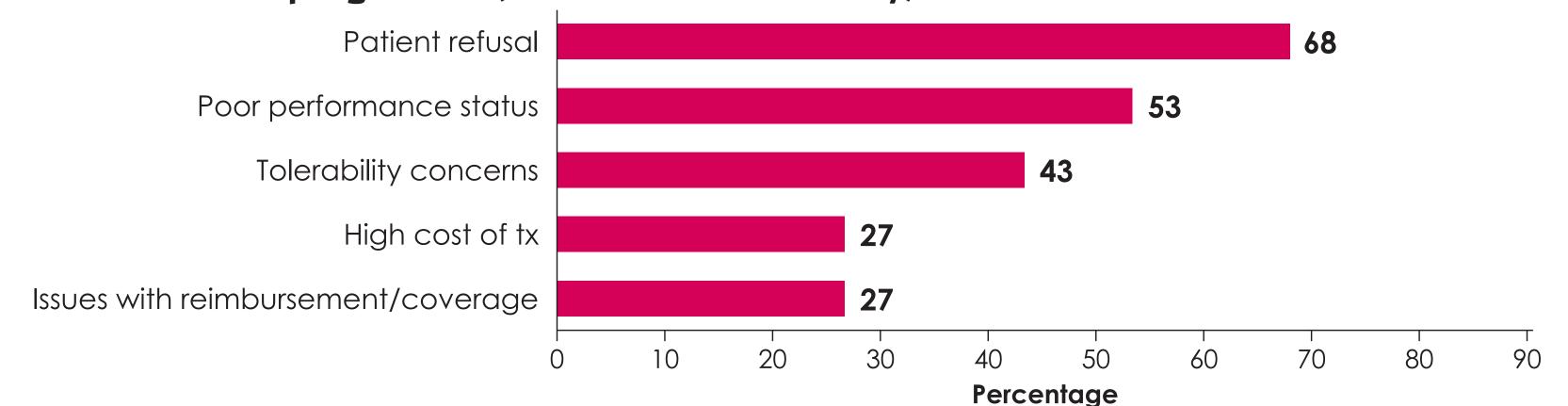
systemic regimen to at least 46% of their pts **1L**, first line; **pt**, patient; **tx**, treatment.

low 1L systemic regimen prescribers (n=78) "agree completely" that the guidelines/ tx decisions in 1L therapy

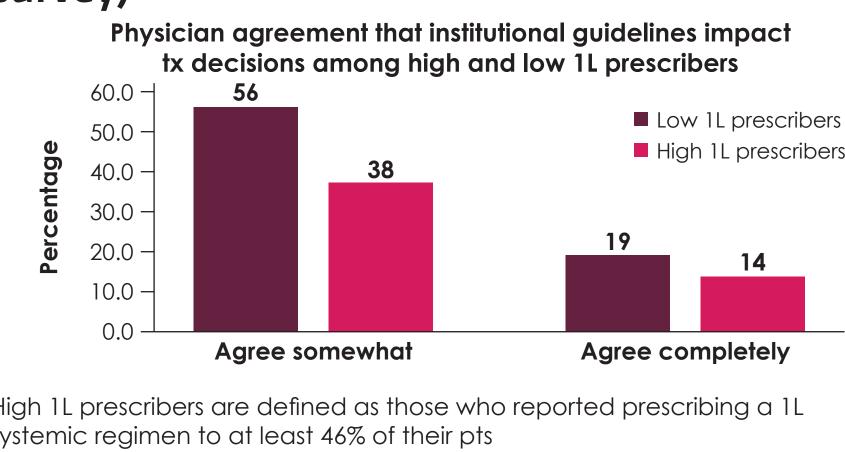




n-reported reasons for not receiving 1L IO maintenance among pts with rogressed (cross-sectional survey)

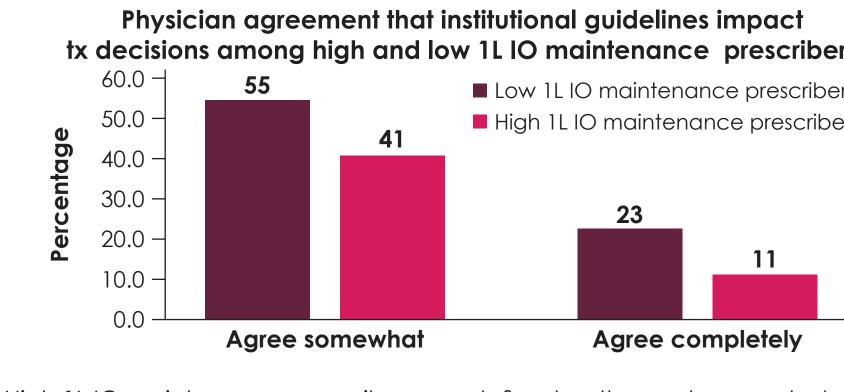


itutional guidelines on _ use (cross-sectiona



 Compared with high 1L systemic regimen prescribers (n=72), a greater percentage of indicated that they "agree somewhat" or pathways of my institution/practice impact my

Figure 4. Impact of institutional guidelines on tx decisions based on 1L IO maintenance prescribers (cross-sectional survey)



prescribing 1L IO maintenance to at least 71% of eligible la/mUC pts

 A higher proportion of low 1L IO maintenance prescribers (n=75) "agree somewhat" or "agree completely" that the guidelines/pathways of my institution/practice impact my tx decisions in 1L therapy compared with high 1L IO maintenance prescribers (n=71)

LIMITATIONS

Disagree somewhat

Clinical guidelines followed, %

Local institutional guidelines

cological Association; **ESMO**, European Society for Medical Oncology; **Ia/mUC**, locally advanced or netastatic urothelial carcinoma; **NCCN**, National Comprehensive Cancer Network; **tx**, treatment.

- Results from this study were obtained from 3 sources (TLS, QIs, and cross-sectional survey) conducted at different time periods, which may explain the differences in tx patterns/rates
- Results may not generalizable since the sample size from the QIs was small. Additionally, since the cross-sectional survey relied on convenience sampling methods, it is possible that certain subgroups of physicians may be over-represented and that the results may not be generalizable to all physicians managing pts with la/mUC
- Cross-sectional survey results are limited in that they analyze data at a single point in time. Therefore, recall bias could be a possibility since physicians were asked about tx decisions in the past 6 months

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