Treatment patterns and clinical outcomes in patients with locally advanced or metastatic urothelial cancer in England: results of a longitudinal observational cohort study

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SCOPE

- **The objective of this study was to evaluate treatment patterns and clinical outcomes in patients with newly diagnosed, locally advanced or metastatic urothelial cancer (UC) in England**

CONCLUSIONS

- **Given the low percentage of patients who receive systemic treatment, a need exists to treat patients with locally advanced or metastatic UC with the most effective and tolerable frontline agents that can be administered by a broad range of treating physicians**
- **Newer and more efficacious treatments are currently under regulatory review; these may alleviate the unmet need in this elderly population with significant comorbidities and poor outcomes**
- **This study can serve as a useful benchmark for future real-world studies in locally advanced or metastatic UC, thereby enabling clinicians to better understand the utilization of and outcomes associated with newer systemic agents**

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BACKGROUND

- Bladder cancer accounts for approximately 1 in every 30 new cancer diagnoses each year in the UK and is the 10th most common cancer in the UK[1]
  - In 2017, 8,686 new patients were diagnosed with bladder cancer in England[2]
  - It is a life-threatening condition with a 1-year age-standardised survival rate of 35.7% for stage IV disease in England[2]
- UC is most common in the bladder (approximately 90% of cases)[3]
- Platinum-containing combination chemotherapy (PBC) remains the standard first-line (1L) treatment for patients with locally advanced or metastatic UC
  - Although response rates to PBC regimens are high (70%), durable responses are uncommon, and most patients will ultimately experience disease progression
- The goal of treatment for patients with advanced UC is to prevent disease progression, maintain health-related quality of life, provide relief from cancer symptoms, and extend life

METHODS

Design

- A descriptive, noninterventional study of a real-world cohort of patients with advanced UC as defined using routine patient-level data hosted by the National Cancer Registration and Analysis Service (NCRAS) in England:
  - Incident primary cases of locally advanced or metastatic UC (stage III/IV) were captured from January 2013 to December 2018, inclusive
  - Patients were followed up until the earliest of death, loss to follow-up, or end of study period (December 2019)

Statistical analyses

- Descriptive statistics were used to describe baseline characteristics and treatment patterns
- Overall survival (OS) data were analysed from diagnosis and the start of 1L systemic therapy using Kaplan-Meier survival curves

Inclusion criteria

- Resident of England at the date of diagnosis
- Aged ≥18 years at the date of diagnosis
- ≥1 incident primary diagnosis (index) of advanced or metastatic UC (stage III/IV), dated between 1 January 2013 and 31 December 2018

Exclusion criteria

- No recorded date or stage of diagnosis
- No recorded age at diagnosis
- Cases identified via death certificate only
- Receipt of a nonsponsor systemic therapy funded through the Cancer Drugs Fund (CDF)
- Participation in a clinical trial

RESULTS

Table 1. Patient characteristics

	N=14,548
Age at diagnosis, years	
Mean (SD)	73.2 (11.0)
Median (Q1-Q3)	74.0 (67.0-81.0)
Sex, n (%)	
Male	9,569 (65.8)
Female	4,979 (34.2)
Stage at diagnosis, n (%)	
III	5,084 (34.9)
IV	9,464 (65.1)
Duration of follow-up from diagnosis, months*	
Mean (SD)	16.7 (18.8)
Median (Q1-Q3)	9.7 (3.2-22.7)
Modified Deyo-Charlson Comorbidity Index score at baseline†	
Mean (SD)	3.4 (1.7)
Median (Q1-Q3)	3.0 (2.0-4.0)

* Follow-up period was defined from the date of advanced or metastatic UC diagnosis to the date of death, loss to follow-up, or end of the observation period, whichever came first
† Baseline = between 3 and 27 months prior to index date (ie, date of diagnosis)

Comorbidities

- In the overall population, ie, patients with stage III/IV disease (N=14,548; **Table 1**), the most frequently occurring comorbidities documented during the baseline period (between 3 and 27 months prior to index date) were hypertension (23.5%), type 2 diabetes without complications (7.9%), and unspecified hematuria (6.8%)

Treatment patterns

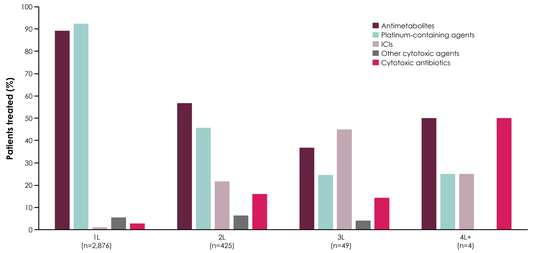
Patients with stage III/IV disease (N=14,548)

- 31.1% (n=4,525) underwent ≥1 surgical resection, 31.1% (n=4,519) received radiation therapy, and 30.2% (n=4,400) received systemic therapy during follow-up

Patients with stage IV disease (n=9,464; Figure 1)

- Only 30.4% (n=2,876) received ≥1 line of systemic therapy
  - Of these, platinum-containing agents (92.3%) and antimetabolites (89.2%) were the most commonly administered drug classes in the 1L
  - In the second line (2L), the most frequently administered agents were antimetabolites (56.7%), platinum-containing agents (45.6%), and immune checkpoint inhibitors (ICIs; 26.6%)

Figure 1. Treatment classes received by patients with stage IV disease who received any systemic treatment by line of therapy

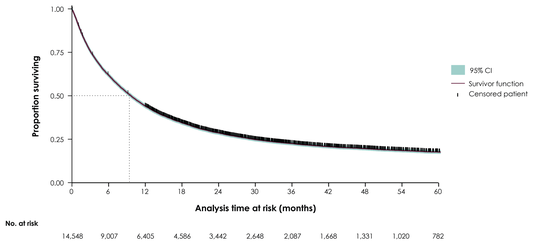


Patients could have received multiple classes of drug within a single line; National Institute for Health and Care Excellence (NICE) recommendation for 2L ICIs were published in mid 2018; systemic therapies funded through the CDF are excluded
3L, third line, **4L**, fourth line

OS

- In the overall population (N=14,548), there were 11,293 (77.6%) deaths following diagnosis, resulting in a median OS of 9.7 months (95% CI: 9.4-10.0 months) from diagnosis; the 12-month OS rate was 44.1% (95% CI: 43.3%-44.9%) and the 24-month OS rate was 28.7% (95% CI: 27.9%-29.4%; **Figure 2A**)
- From the initiation of 1L systemic therapy (n=4,400), there were 3,000 deaths (68.2%) during follow-up, resulting in a median OS of 14.0 months (95% CI: 13.4-14.7 months); the 12-month OS rate was 55.6% (95% CI: 54.1%-57.1%) and the 24-month OS rate was 34.9% (95% CI: 33.4%-36.4%; **Figure 2B**)

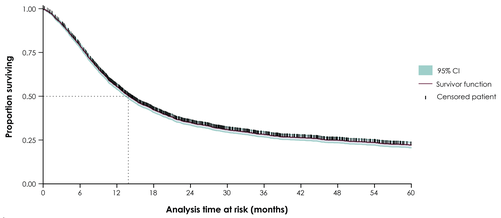
Figure 2A. Kaplan-Meier curve of OS from diagnosis (N=14,548)



No. at risk

14,548	9,007	6,405	4,586	3,442	2,648	2,087	1,668	1,331	1,020	782

Figure 2B. Kaplan-Meier curve of OS from initiation of 1L systemic therapy (n=4,400)



No. at risk

4,400	3,450	2,295	1,527	1,103	836	659	515	390	305	214

Strengths

- A national cancer registry in England with linkage to other relevant data sets
- Comprehensive real-world data, with records for every patient with a diagnosis of or treatment for locally advanced or metastatic UC provided or funded by the UK National Health Service (NHS)
- Standardised recording reduced the risk of misclassification
- Full continuum of care in all NHS-funded settings documented and longitudinal tracking of patient information

Limitations

- Lack of information on disease-specific outcomes, such as cancer recurrence and disease progression
- Systemic anti-cancer therapy (SACT) data set contains data for systemic therapy administered in secondary but not primary or private care settings
- Drugs funded through the CDF not included
- Lines of systemic therapy were derived using an algorithm
- Incompleteness of data items such as International Classification of Diseases, 10th revision (ICD-10) diagnosis codes and OPCS Classification of Interventions and Procedures version 4 (OPCS-4) procedure codes in Hospital Episode Statistics

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DISCLOSURES: MK, FXL, and **PV** are employees of Merck KGaA, Darmstadt, Germany. **AA** is an employee of Merck Serono Ltd, Feltham, UK; an affiliate of Merck KGaA, Darmstadt, Germany. **JH** was an employee of Pfizer at the time the research was conducted. **CK** is an employee of Health Data Insight, which received funding from Merck KGaA and Pfizer. **ACKNOWLEDGMENTS:** The authors would like to thank Health Data Insight for its analytical support and Public Health England (PHE) for providing access to the data. Data for this study are based on patient-level information collected by the NHS as part of the care and support of patients with cancer in the UK. The data are collated and maintained, and quality is assured by the NCRAS, which is part of PHE. This study was sponsored by Merck KGaA, Darmstadt, Germany, and is part of an alliance between Merck KGaA and Pfizer. Editorial support was provided by ClinicalThinking, and funded by Merck KGaA and Pfizer.

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