Treatment Patterns and Clinical Outcomes In Patients with Metastatic Urothelial Carcinoma (mUC) in England: A Retrospective, Observational Study

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There is an urgent unmet need for newer treatments in the first and second-line settings to improve survival outcomes for mUC patients in England

A high attrition rate in systemic anti-cancer treatment (SACT) was observed with 63% of patients untreated from 2016-2021 followed up to 2023

The median overall survival (OS) was 5.4 months from diagnosis indicating a poor prognosis

Further real-world studies to explore the reasons behind poor survival in bladder cancer are required; underscoring the importance of a national bladder cancer audit

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This work uses data that has been provided by patients and collected by the NHS as part of their care and support. The datasets are collated, maintained and quality assured by the National Disease Registration Service, which is part of NHS England

- In England, platinum-based chemotherapy with or without an immune checkpoint inhibitor is the standard-of-care for patients diagnosed with metastatic urothelial carcinoma (mUC).
- However, treatment patterns following first-line therapy and outcomes in patients diagnosed with mUC remain unclear given the national clinical guidelines are outdated following recent marketing authorisations of medicines in mUC.
- There is a need to collect real-world data to enable an improved understanding of the clinical management of mUC in the National Health Service (NHS) and associated outcomes.

Objectives

- Retrospectively identify and follow-up patients diagnosed with mUC in England to provide insight into real-world clinical practice.
- Describe the baseline characteristics and distribution of patients diagnosed with mUC in England by:
  - Lines of systemic anti-cancer therapy and
  - Treatment with prior anti-PD-(L)-1 therapy to understand the patient treatment pathway in England
- Report a key treatment milestone, mainly overall survival, from the date of diagnosis and the initiation of subsequent systemic anti-cancer therapy

Methods

Data sources:

Routine patient data was obtained through the National Disease Registration Service (NDRS), which collects data from all patients diagnosed with cancer in England. Diagnoses were extracted for the period from January 2016 to December 2021, with follow-up to March 2023 to report treatment and progression.

Variables:

Patient baseline demographics, tumour characteristics, systemic anti-cancer therapy (SACT) and lines of treatment were obtained.

Outcomes:

- Distribution of patients by line of therapy
- Kaplan-Meier methods were used to calculate OS

Study population

- A total of 10,787 patients were diagnosed with mUC between January 2016 and December 2021 (**Table 1**)
- 3,942 patients (37%) of patients received SACT
- 1,376 mUC patients received an anti-PD-(L)1 treatment

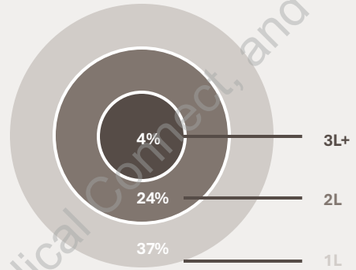
Table 1: Baseline characteristics

Characteristic	All patients N=10,787	PD-(L)1 exposed N = 1,376
Age in years, median (IQR)	75.0 (68.0–82.0)	70.0 (63.0-76.0)
Age category at diagnosis, n (%)		
18 to 34	21 (0.2)	5 (0.4)
35 to 49	275 (2.5)	59 (4.3)
50 to 64	1,657 (15.4)	333 (24.2)
65 and older	8,834 (81.9)	979 (71.1)
Male, n (%)	7,115 (66.0)	985 (71.6)
Year of initial diagnosis, n (%)		
2016	2,202 (20.4)	156 (11.3)
2017	2,458 (22.8)	295 (21.4)
2018	1,756 (16.3)	312 (22.7)
2019	1,353 (12.5)	185 (13.4)
2020	1,565 (14.5)	220 (16.0)
2021	1,453 (13.5)	208 (15.1)
Performance status at diagnosis, n (%)		
0	1,780 (16.5)	380 (27.6)
1	1,296 (12.0)	209 (15.2)
2	578 (5.4)	34 (2.5)
3	359 (3.3)	5 (0.4)
4	77 (0.7)	1 (0.1)
Null	6,697 (62.1)	747 (54.3)
Cisplatin ineligibility at diagnosis, n (%)		
Yes	3,409 (31.6)	341 (24.8)
No	7,378 (68.4)	1,035 (75.2)
Duration of follow-up from diagnosis		
Mean (standard deviation), months	11.8 (16.5)	16.9 (14.6)
Median (Q1 – Q3)	5.3 (1.9-14.1)	12.6 (6.6-22.0)

***Key**: N: count; %: proportion; IQR: interquartile range, Q: quartile*

- The mean age at diagnosis was 74 years (median 75 years)
- Male patients comprised 66% of the overall cohort
- Patients who received an anti-PD-(L)1 treatment were younger with mean age at diagnosis of 69 years (median 70 years)
- Of patients with a known performance status (PS), a higher proportion of patients who received an anti-PD-(L)1 had a PS of 0-1 compared to the overall cohort

Figure 1: SACT attrition rates



Note: Denominator is 3,942 (patients receiving a line of therapy)

Patient outcomes

- High attrition rates (**Table 2 and Figure 1**)
  - 37% of 10,787 patients received a first line treatment
  - 24% of 3,942 patients received a second line treatment
- Standard of care (**Table 2**)
  - Significant use of anti-PD-(L)1 inhibitors in the 1L setting
  - 5.6% of patients received carboplatin + gemcitabine driven by temporary COVID guidance[1]
  - Second-line and subsequent treatment after anti-PD-(L)1 is predominantly paclitaxel monotherapy or paclitaxel in combination with carboplatin
- Poor prognosis (**Table 3 and Figure 2**)
  - Median overall survival of 5.4 months for mUC patients from diagnosis
  - Median overall survival of 7 months for mUC patients on second- and third-line treatments

Figure 2: Kaplan-Meier curves showing OS from the date of diagnosis and from the initiation of 1L, 2L and 3L+ SACT

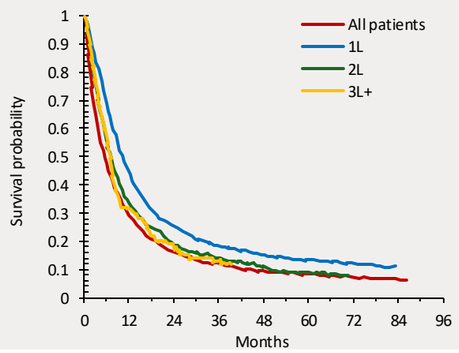


Table 2: SACT delivery among patients with mUC

Incident 'metastatic' cancer patients with derived lines of therapy, N (%)	3,942 (36.5)
Received at least one drug from the following classes and regimens, N (%)	
Alkylating agents	26 (0.7)
Anthracyclines	35 (0.9)
Antimetabolites	2,979 (75.6)
Cytotoxic antibiotics	129 (3.3)
Hormone treatments	18 (0.5)
Immune checkpoint inhibitors	1,376 (34.9)
Atezolizumab	563 (40.9)
Avelumab	147 (10.7)
Pembrolizumab	668 (48.5)
Immunomodulators	28 (0.7)
Monoclonal antibodies	12 (0.3)
Other cytotoxic agents	204 (5.2)
Platinum compounds	3,117 (79.1)
Targeted therapies	33 (0.8)
Taxanes	216 (5.5)
Patients who received 1L anti-PD-(L)1 therapy including maintenance avelumab	834 (7.7)
Common 2L regimens received following 1L anti-PD-(L)1 therapy, N (%)	
Carboplatin + Gemcitabine	47 (5.6)
Paclitaxel	30 (3.6)
Pembrolizumab	17 (2.0)
Atezolizumab	12 (1.4)
Patients who received 1L systemic therapy followed by 2L anti-PD-(L)1	515 (4.8)
Common 3L regimens received following 2L anti-PD-(L)1 therapy, N (%)	
Paclitaxel	24 (4.7)
Pembrolizumab	14 (2.7)
Carboplatin + Paclitaxel	12 (2.3)
Patients who received 1L platinum-based therapy with maintenance avelumab	127 (1.2)
Common 2L regimens received following 1L platinum-based therapy with avelumab, N (%)	
Paclitaxel	10 (7.9)

***Key**: N: number; %: proportion; 1L: first-line; 2L: second-line*
Note: 27 patients received anti-PD-(L)-1 at 3L+

Table 3: Overall survival for the entire cohort and for patients stratified by treatment line

	All patients	First line (1L)	Second line (2L)	Third line (3L)	Fourth line (4L)
Number of patients, N (%)	**10,787 (100.0)**	**3,942 (36.5)**	**959 (24.3)**	**158 (4.0)**	**19 (0.5)**
Months of follow-up, mean (SD)	11.8 (16.5)	16.7 (17.8)[#]	12.5 (15.1)[†]	12.0 (15.0)[£]	8.7 (10.5)[¥]
Failures during the study period	9,628	3,221	805	132	15
Median OS, months (95% CI)	5.4 (5.2, 5.6)	10.4 (10.0, 10.7)	7.0 (6.4, 7.7)	6.9 (6.1, 7.7)	*
Survival probability after 6, 12, 24, 36 and 60 months					
6 months (95% CI)	0.47 (0.46, 0.48)	0.70 (0.68, 0.71)	0.55 (0.52, 0.58)	0.58 (0.51, 0.67)	*
12 months (95% CI)	0.29 (0.28, 0.30)	0.45 (0.43, 0.46)	0.34 (0.31, 0.37)	0.30 (0.24, 0.39)	*
24 months (95% CI)	0.16 (0.15, 0.17)	0.26 (0.24, 0.27)	0.19 (0.16, 0.21)	0.18 (0.13, 0.26)	*
36 months (95% CI)	0.12 (0.11, 0.12)	0.18 (0.17, 0.20)	0.14 (0.12, 0.17)	0.13 (0.09, 0.21)	*
60 months (95% CI)	0.08 (0.07, 0.09)	0.13 (0.12, 0.15)	0.09 (0.07, 0.12)	*	*

***Key**: CI: confidence interval; SD: standard deviation; Asterix means not estimable.*
Months of follow-up are from diagnosis[#], 1L[†], 2L[£], and 3L[¥] initiation therapy to death, embarkation or end of the study.

Limitations

- The study timeline spanned the COVID-19 pandemic where NHS England issued guidance to prescribe atezolizumab in the 1L setting.[1]
- Pembrolizumab is not reimbursed in England
- Clinical guidelines do not endorse anti-PD-(L)1 retreatment[2,3]
- Lines of therapy were approximated via an algorithm; with a risk of misclassification

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3. Powles T, Bellmunt J, Comperat E et al. Bladder cancer: ESMO Clinical Practice Guideline interim update on first-line therapy in advanced urothelial carcinoma *Ann Oncol.* 2024;35(6):485-490.

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Presented by S Gill at ASCO-GU; February 13-15, 2024; San Francisco, California, United States