Demographics and Survival Outcomes in Patients With Advanced or Recurrent Endometrial Cancer Following Platinum-Based Doublet in the English Real-World Setting

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Craig Knott[1], Kiera Heffernan[2], Fulya Sen Nikitas[2], Urmi Shukla[2], Helen Starkie Camejo[2*]

[1]Health Data Insight CIC, Cambridge, UK; National Cancer Registration and Analysis Service, Public Health England, London, UK; [2]GSK, Brentford, UK
**Affiliation at the time of study design and initiation*

Background

Endometrial cancer (EC) is the sixth most commonly diagnosed cancer among women globally, and the fourth most common in the United Kingdom (UK).[1,2]

Approximately 15%–20% of patients are diagnosed with advanced-stage disease, 10%–15% of women with any stage disease at diagnosis will have a recurrence, and prognosis is poor for these patients.[2–5]

Surgery and/or radiotherapy are recommended as upfront treatments for patients with advanced or recurrent EC according to UK and European Union (EU) guidelines.[6,7]

- Therapy with carboplatin and paclitaxel is recommended as first-line (1L) systemic anti-cancer therapy.[6]

Treatment options for patients who require second-line (2L) treatment are limited, with no clear standard of care or treatment pathway, and limited data to support recommendations.[8]

- Platinum-based chemotherapy is typically the most common 2L treatment in real-world settings; however, chemotherapy regimens in this setting have a limited duration of response.[9]
- The use of immune-checkpoint inhibitors (ICIs) has recently shown promising anti-tumour responses and duration of response in the 2L treatment of EC,[10,11] suggesting ICIs may be beneficial for this patient population.

There is limited real-world data on the current treatment landscape for advanced or recurrent EC in the relapsed setting in many countries, including in England, as well as a lack of clear guidelines, highlighting an unmet need in this patient population and for the clinicians who treat them.

Objective

The objectives of these analyses were to describe the treatment patterns, baseline demographics, disease characteristics, and clinical outcomes (overall survival [OS] and time to next treatment [TTNT]) for a cohort of patients with advanced or recurrent EC who progressed to 2L treatment (ICI-eligible 2L cohort) in a real-world setting in England.

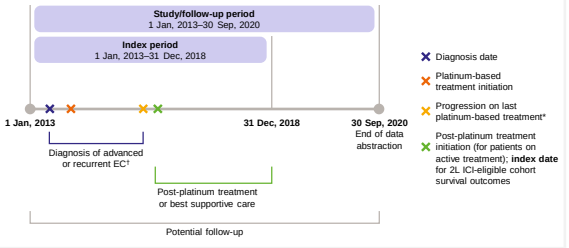
Methods

Study Design

This was a non-interventional, retrospective, descriptive, cohort study.

Routine patient-level data available through Public Health England's National Cancer Registration and Analysis Service (NCRAS) in England was used to identify patients with a primary diagnosis of EC between 1 January, 2013, and 31 December, 2018 (the "index period"), and who received a platinum-based regimen after the index date (first diagnosis of advanced or recurrent EC) (**Figure 1**).

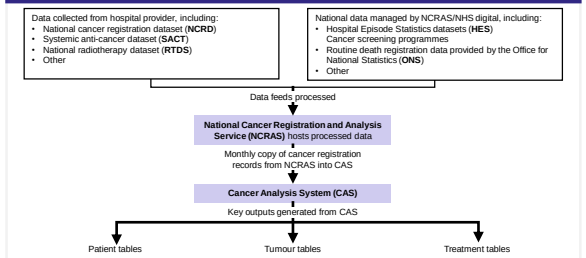
Figure 1. Study design



*Progression was not reported, but movement to a subsequent therapy was reported. †Patient was deemed recurrent if diagnosed at Stage I/II (blue X) and subsequently resumed treatment following a 90-day gap between 2 treatments of any kind, i.e. surgery or other (orange X).

The NCRAS pools patient data from a range of sources to create the Cancer Analysis System (CAS) (**Figure 2**).

Figure 2. NCRAS datasets



NHS, National Health Service.

Inclusion criteria

Eligibility criteria for the ICI-eligible cohort included:

- A diagnosis of advanced or recurrent EC between the index period, defined as:
  - Patients with at least one diagnosis of malignant neoplasm of corpus uteri (International Classification of Diseases [ICD] code C54; including malignant neoplasms of the myometrium [ICD code C54.2])[12]
  - Recurrent disease: Patients with Stage I/II disease and a gap >90 days between consecutive treatments.
  - Advanced disease: Stage III/IV disease.
- Receipt of a platinum-based doublet regimen after the index date
- Aged ≥18 years at index date
- No prior receipt of any anti-programmed cell death protein 1 (PD-1), -programmed death-ligand 1 and 2 (-PD-L1[2]) therapies
- No other primary malignancies recorded (with the exception of non-melanoma skin cancer (ICD code C44) and cervical carcinoma in situ (ICD code D06)[12] after or up to 18 months from the index date
- Histology that excluded endometrial sarcoma and carcinosarcoma
- Eastern Cooperative Oncology Group performance status (ECOG PS) <1

Patients in the ICI-eligible cohort who progressed to 2L treatment were then included in the ICI-eligible 2L cohort

Data Analysis

Baseline demographics, disease characteristics, and treatments received were descriptively summarised, which included stratification by line of therapy.

OS and TTNT (a proxy for progression-free survival due to a lack of data on progression in the NCRD) were evaluated by line of therapy for the ICI-eligible 2L cohort using Kaplan-Meier methodology.

OS and TTNT from 2L were calculated from the initiation of 2L therapy to the earliest of all-cause death or censoring.

Results

Patient population

The patient populations are shown in **Figure 3**; there were 999 patients in the ICI-eligible 2L cohort.

Baseline demographics and disease characteristics

Patient baseline demographics and disease characteristics for the ICI-eligible 2L cohort are summarised in **Table 1**.

Treatments

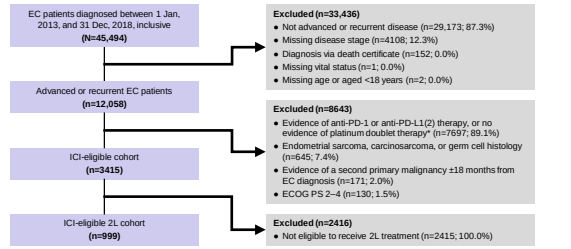
1L: In the ICI-eligible 2L cohort, 98.6% of patients received a platinum-doublet regimen as their 1L treatment, with the majority of patients (93.2%) receiving carboplatin + paclitaxel.

2L: The most common types of drug class received at 2L were platinum compounds (68.2%), taxanes (41.8%), and anthracyclines (39.4%).

Systemic treatment regimens received by the ICI-eligible 2L cohort are described in **Table 2**.

Results

Figure 3. Patient flow diagram



*Prior treatment with hormone therapies was acceptable but did not count towards lines of therapy.

Table 1. Baseline patient demographics and disease characteristics

Demographic or characteristic	ICI-eligible 2L (n=999)	Demographic or characteristic	ICI-eligible 2L (n=999)
Year of diagnosis – n (%)		**Grade at diagnosis – n (%)**	
2013	153 (15.3)	Data available (% of ICI-eligible cohort)	759 (76.0)
2014	170 (17.0)	1	104 (13.7)
2015	190 (19.0)	2	170 (22.4)
2016	184 (18.4)	3	389 (51.3)
2017	149 (14.9)	Could not be assessed†	96 (12.6)
2018	153 (15.3)		
Mean age – years (SD)	65.5 (8.6)	**Histology – n (%)**	
Age at diagnosis, years – n (%)		Endometrioid	424 (42.4)
<65	428 (42.8)	Serous	401 (40.1)
65–74	454 (45.4)	Non-specific carcinoma	74 (7.4)
≥75	117 (11.7)	Clear cell carcinoma	46 (4.6)
		Mixed carcinoma	33 (3.3)
Ethnicity – n (%)		Dedifferentiated/undifferentiated carcinoma	7 (0.7)
Data available (% of ICI-eligible cohort)	976 (98.0)	Neuroendocrine	6 (0.6)
White	841 (86.2)	Squamous	5 (0.5)
Black	57 (5.8)	Mucinous	2 (0.2)
Asian	46 (4.7)	Non-specific	1 (0.1)
Other	32 (3.3)		
FIGO Stage at diagnosis* – n (%)		**ECOG PS at diagnosis – n (%)**	
I	183 (18.3)	Recorded (% of ICI-eligible cohort)	501 (50.2)
II	38 (3.8)	0	320 (63.9)
III	415 (41.5)	1	181 (36.1)
IV	363 (36.3)	Missing‡ (% of ICI-eligible cohort)	498 (49.8)
Median duration of follow-up from advanced diagnosis or recurrence – months (range)			27.4 (3.5–91.1)

*Stage at the time of registry diagnosis. This is derived by cancer registration staff and based primarily on FIGO staging information provided by the diagnosing trust via the multidisciplinary team. †Reasons may include: no histological confirmation; biopsy too small to assign a grade; grading not formally recommended for that tumour at that site (e.g. squamous cell carcinoma of lung); and grade not being useful discriminator. ‡Patients with ECOG PS >1 were not included in the ICI-eligible cohort; therefore, missing ECOG PS data are assumed to be ≤1.
FIGO, International Federation of Gynaecology and Obstetrics.

Table 2. Systemic treatments for the ICI-eligible 2L cohort

Most commonly occurring distinct regimens, n (%)	2L (N=999)
Carboplatin + paclitaxel	279 (27.9)
Carboplatin + liposomal doxorubicin	141 (14.1)
Liposomal doxorubicin monotherapy	130 (13.0)
Paclitaxel monotherapy	116 (11.6)
Carboplatin monotherapy	93 (9.3)
Other*	146 (14.6)

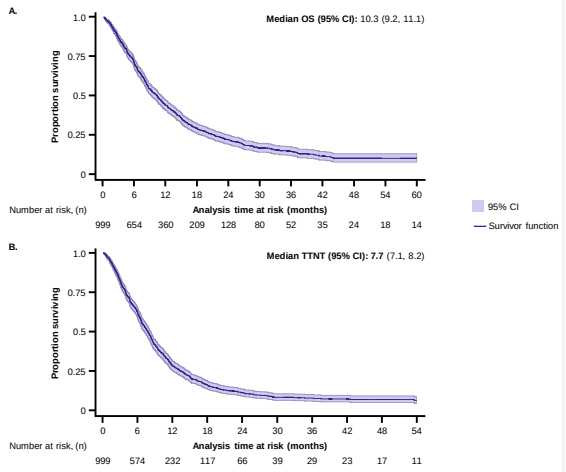
*Other includes cisplatin + doxorubicin, doxorubicin, cisplatin, carboplatin + gemcitabine, carboplatin + doxorubicin, which were given to >1%–<5% of patients.

Clinical outcomes

Median OS for the ICI-eligible 2L cohort was 10.3 months (95% confidence interval [CI]: 9.2, 11.1) (**Figure 4A**), with an OS estimate at 24 months of 21.5% (95% CI: 18.6, 24.4).

Median TTNT for the ICI-eligible 2L cohort was 7.7 months (95% CI: 7.1, 8.2) (**Figure 4B**).

Figure 4. Kaplan-Meier estimate of (A) OS and (B) TTNT for ICI-eligible 2L cohort



Conclusions

Whilst the majority of ICI-eligible patients received 1L standard-of-care carboplatin + paclitaxel (94.3%), a range of drug classes and treatment regimens were received in the 2L—with carboplatin + paclitaxel being the most frequent regiment received, consistent with real-world evidence from the US.[9]

Survival outcomes (OS and TTNT) at 2L were poor for the ICI-eligible population.

This study highlights the unmet need for both a defined standard of care and treatments that are more effective than current chemotherapy options in the 2L recurrent/advanced setting.

Durable and clinically meaningful responses have been observed with anti-PD-1 inhibitors dostarlimab and pembrolizumab in the 2L advanced or recurrent EC cohort in the Phase I GARNET[10] and Phase III KEYNOTE-775[11] trials, respectively, suggesting that ICIs may improve survival outcomes in future ICI-eligible 2L populations.

Disclosures

KH, **FSN**, and **US** are employees of GSK. **HSC** is a former employee of GlaxoSmithKline (GSK). **CK** has no conflicts of interest to declare.

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Author email address: craig.knott@phe.gov.uk

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