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ORIGINAL RESEARCH

A Real-World Retrospective Observational Study of Patients with Advanced/Recurrent Endometrial Cancer Across England

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ABSTRACT

***Introduction*:** Robust real-world data (RWD) on endometrial cancer (EC) are lacking. In the United Kingdom (UK), molecular classification of EC based on tumour mismatch repair (MMR) status, either MMR-deficient (dMMR) or MMR-proficient (MMRp), has been recommended at diagnosis since 2020. This study characterised patients with advanced/recurrent EC, documented treatment pathways and evaluated clinical outcomes stratified by MMR status using RWD from National Health Service (NHS) trusts in England.

***Methods*:** This retrospective, observational study captured electronic health records (EHRs) from seven NHS trusts from 2000 to 2023. Clinical outcomes included overall survival (OS) and time to next treatment (TTNT).

***Results*:** Data were retrieved from 731 patients with EC (79% advanced, 21% recurrent). Overall, 56.63% of patients received systemic treatment; most received platinum-based chemotherapy in first line (1L). MMR status was identified for 166 patients, with 25.30% being dMMR. Overall, 1L median TTNT was 1.22 years (95% confidence interval [CI] 1.02–1.37). Median OS from the start of 1L was 1.80 years (95% CI 1.59–2.16) in the whole cohort, 4.25 years (95% CI 1.67–not reached [NR]) in the dMMR group, 2.36 years

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(95% CI 2.10–2.36) in the MMRp group and 1.64 years (95% CI 1.32–1.98) in the unknown MMR group.
Conclusions: Although interpretation is hampered by small sample sizes, this analysis is suggestive of a difference in outcomes between MMR subgroups, underlining the importance of biomarker testing for patients with EC. Historic recording of MMR status was low; consistent testing and improvements in linking EHRs to biomarker data are needed to examine the relationship between outcomes and MMR status.

Keywords: Endometrial cancer; DNA mismatch repair; Biomarker testing; Real-world data; Chemotherapy; Radiotherapy; Immunotherapy

Key Summary Points
Why carry out this study?
In the United Kingdom, mismatch repair (MMR) testing is recommended at diagnosis of endometrial cancer (EC) to inform prognosis and treatment strategies.
This real-world study using electronic health record data for the period 2000–2023 from selected National Health Service trusts in England characterised treatments and clinical outcomes in patients with advanced or recurrent EC by MMR status.
What was learned from the study?
The most common first-line treatment for advanced or recurrent EC at the time of this study was carboplatin plus paclitaxel.
Median overall survival was numerically longer in the MMR-deficient group than the MMR-proficient group, although not statistically significant.
However, given the low level of known biomarker status in the patients included in this analysis, further studies are needed to fully explore the relationship between outcomes and MMR status.

INTRODUCTION

Endometrial cancer (EC) is the most common gynaecological cancer in the United Kingdom (UK) [1]. There has been a 57% increase in new cases since early 1990, likely related to an ageing population and increased prevalence of obesity, as well as a reduction in hysterectomies for benign cases [1].

Immunohistochemistry can be used to classify mismatch repair (MMR) biomarker status as either MMR-deficient (dMMR) or MMR-proficient (MMRp) [2, 3]. These classifications help to inform EC prognosis and treatment strategies [3, 4], including the decision to use immunotherapy [5, 6], highlighting the importance of MMR testing at diagnosis as part of standard of care. There is a growing role for anti-programmed cell death protein 1 (anti–PD-1) and anti-programmed cell death ligand 1 (anti–PD-L1) immune checkpoint inhibitors in advanced/recurrent EC. In England, dostarlimab plus chemotherapy has recently been approved in the first-line (1L) setting for microsatellite instability-high (MSI-H)/dMMR advanced/recurrent EC [7]. The National Institute for Health and Care Excellence (NICE) is also currently reviewing recommendations on durvalumab plus platinum-based chemotherapy followed by maintenance with durvalumab monotherapy for primary advanced/recurrent dMMR EC [8]. Options in the second-line (2L) setting and beyond include dostarlimab monotherapy for MSI-H/dMMR disease and pembrolizumab plus lenvatinib irrespective of MMR status [7, 9, 10]. Clinical trials have shown promising outcomes for anti–PD-1 and anti–PD-L1 checkpoint inhibitors in patients with advanced/recurrent EC [2, 11–19]. However, there is a lack of information on the effectiveness of these treatments in the real-world setting.

A recent analysis of patients with advanced or recurrent EC in England revealed that treatments in the relapsed setting varied, and survival outcomes in those receiving 2L treatment were poor [20], highlighting the current unmet clinical need for these patients. MMR/microsatellite instability status was not included in

that study, owing to limited availability in the database [20].

This study characterises patients with advanced or recurrent EC, including their treatments and clinical outcomes by MMR status, using real-world data (RWD) collected from selected National Health Service (NHS) trusts in England. Specifically, this included summarising the classification by MMR status, treatment pathways concerning systemic anti-cancer therapies (SACT) received at 1L and 2L, and the sequencing and duration of these treatments.

METHODS

Study Design and Population

This retrospective, non-interventional, observational study used anonymised electronic health record (EHR) data from the UK Arcturis dataset for seven English NHS trusts (Fig. 1). These trusts cover approximately 5% of the 30.7 million female population in England and Wales [21]. Individual human subject data derived from anonymised EHRs from UK NHS trusts were collected in accordance with internal governance at each trust and adhered to the principles of UK General Data Protection Regulation (GDPR). No direct subject contact or primary collection of individual human subject data occurred. Individual patient consent and ethics committee or institutional review board approval were not necessary.

Adult female patients with a first primary diagnosis of EC, defined as the presence of an International Classification of Diseases, Tenth Revision code for malignant neoplasm of corpus uteri (C54.0, C54.1, C54.3, C54.8 or C54.9), were included. Further details on the definition of advanced/recurrent EC in this study can be found in the Supplemental Methods. The cohort was stratified by MMR status (dMMR or MMRp) detailed in the EHR. MMR status was determined retrospectively by accessing existing immunohistochemistry data in which loss of MutS homolog 2 (MSH2), MutS homolog 6 (MSH6), MutL homolog 1 (MLH1), or post-meiotic segregation increased 2 (PMS2) expression had been recorded. Patients without an available MMR classification were included in a third 'unknown MMR' subgroup.

The study period was from 1 January 2000 to 29 September 2023. Details for the cohort entry date for patients with advanced EC and the index date for patients with recurrent EC can be found in the Supplemental Methods and Supplemental Figs. 1 and 2. All analyses were descriptive and were performed with R version 4.0.2 [22].

Clinical Outcomes

Clinical outcomes included time to next treatment (TTNT) and overall survival (OS). All outcomes were analysed from initiation of 1L therapy in the advanced/recurrent setting, and from initiation of 2L therapy, where relevant. As progression based on Response Evaluation Criteria in Solid Tumors (RECIST) is not routinely recorded in EHRs, TTNT served as a proxy for progression-free survival (PFS). Reasons for treatment discontinuation were not assessed, as they were not included in the dataset.

An additional sensitivity analysis for TTNT and OS was performed in patients with an index treatment date on or after 1 January 2019. This analysis was performed to observe outcomes after the publication of NICE guidelines for routine testing of Lynch syndrome in patients with EC and explicitly to assess whether there were any differences between the known and unknown MMR subgroups potentially attributable to increases in MMR testing [23].

To derive lines of therapy from SACT data provided by the NHS partner trusts, an algorithm was used to identify both the start and end dates of exposure, as well as the therapeutic agents that defined each line of therapy (Supplemental Methods).

RESULTS

A total of 5504 adult patients with a diagnosis of EC were identified (Fig. 1 and Supplemental Fig. 3). Of patients with a record of EC-related treatment available ($n = 3731$; Fig. 1), staging

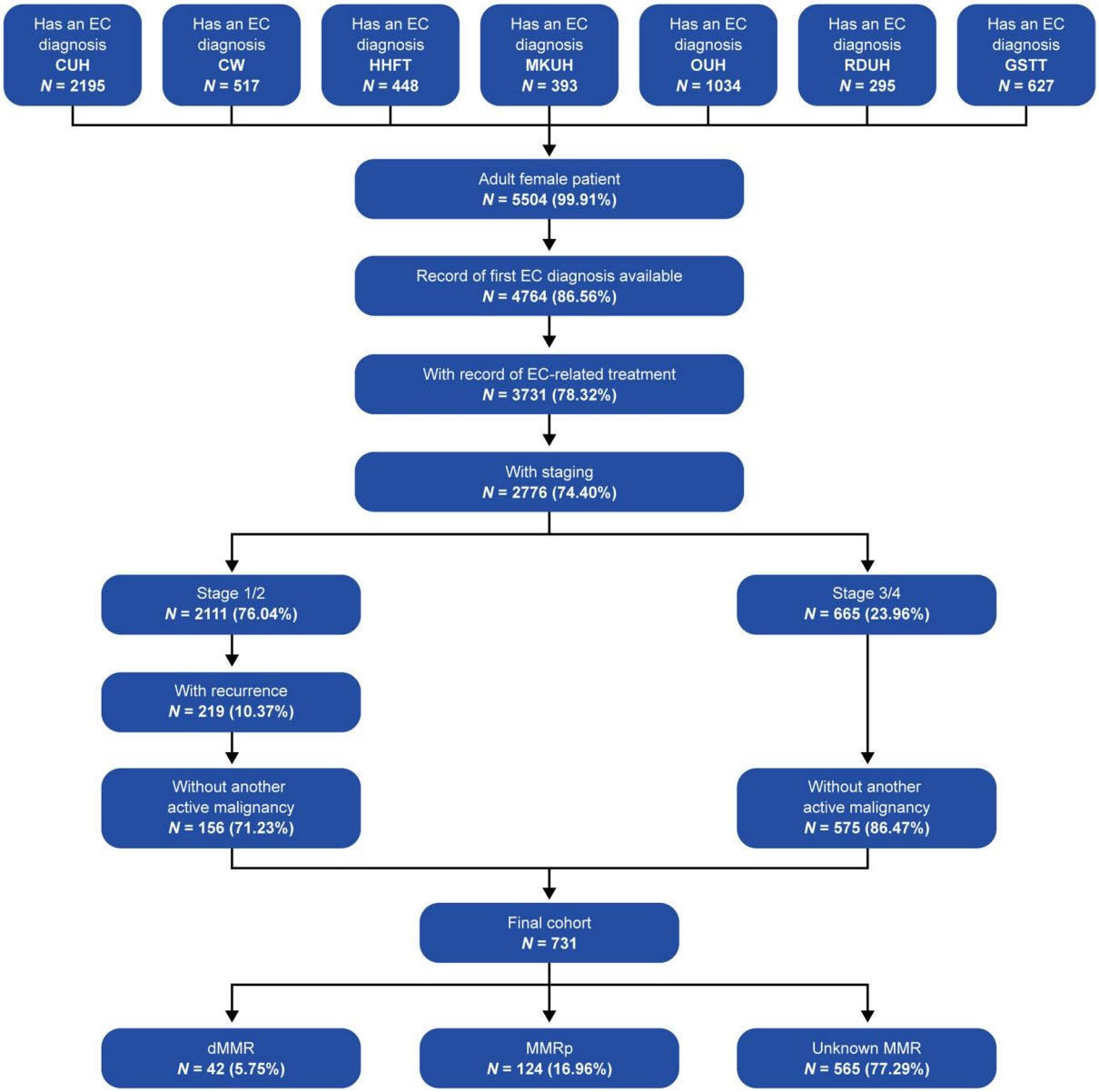

Fig. 1 Flowchart of patients with EC through each of the inclusion and exclusion criteria used to define study cohorts. *CUH* Cambridge University Hospital NHS Foundation Trust; *CW* Chelsea and Westminster NHS Foundation Trust; *dMMR* mismatch repair-deficient; *EC* endometrial cancer; *GSTT* Guy's and St Thomas' NHS Foundation Trust; *HHFT* Hampshire Hospitals NHS Foundation Trust; *MKUH* Milton Keynes University Hospital NHS Trust; *MMR* mismatch repair; *MMRp* mismatch repair-proficient; *OUH* Oxford University Hospitals NHS Foundation Trust; *non-dMMR* non-mismatch repair-deficient; *RDUH* Royal Devon University Hospital Foundation Trust

information was identified for 2776 (74.40%) patients (Fig. 2). After excluding patients with other prior malignancies in the 3 years preceding the index date, the final cohort comprised 731 patients with advanced (n=575) or recurrent EC (n=156). Patients were classified as dMMR (n=42, 5.75%), MMRp (n=124, 16.96%) or with unknown MMR status (n=565, 77.29%; Fig. 1).

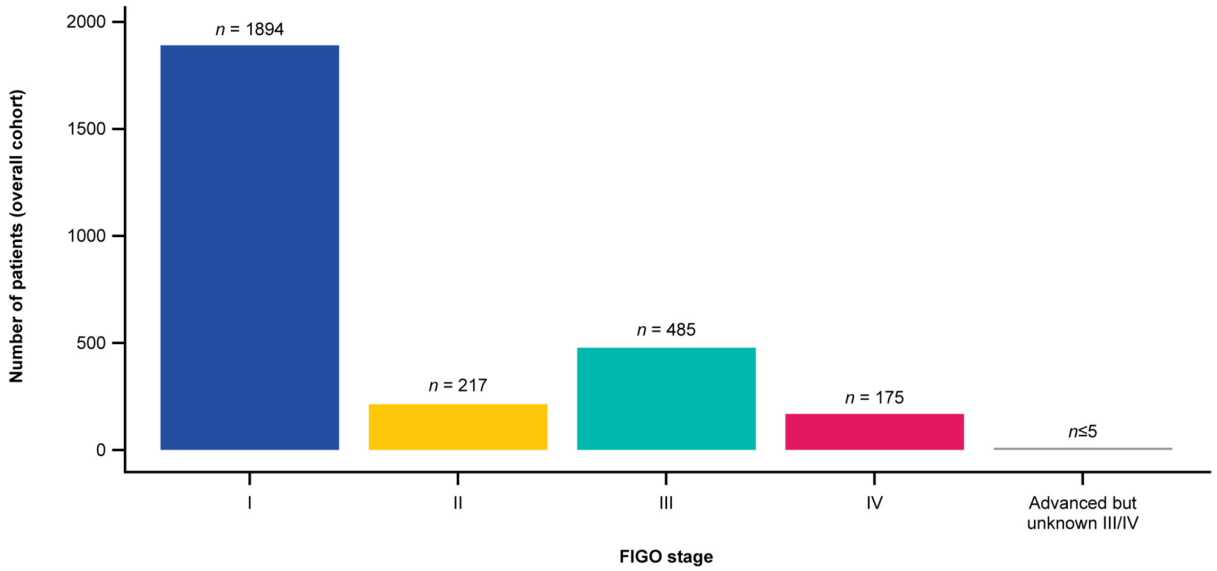

Fig. 2 FIGO staging information available for patients across all seven English NHS trusts. *FIGO* Fédération Internationale de Gynécologie et d'Obstétrique; *NHS* National Health Service

The prevalence of dMMR among patients with known MMR status was 25.30%.

Patient Characteristics

The overall average age at index date was 68.26 years (standard deviation [SD] 10.66); 64.68 years (SD 12.31) for patients with dMMR, 65.47 years (SD 11.17) for patients with MMRp and 69.14 years (SD 10.27) for patients with unknown MMR status. Ethnicity data were available for around 70% of the overall cohort; 81.66% were of White ethnicity. Among the dMMR cohort, ethnicity data were available for 29 out of 42 patients, the majority of whom were of White ethnicity. Among patients with reported anthropometric data, the mean body mass index (BMI) was 30.81 kg/m^2 (SD 7.69 kg/m^2; median [interquartile range] 29.55 [25.20–35.51]; Table 1).

Disease Characteristics

In the final cohort, 433 (59.23%) patients had stage III and 137 (18.74%) had stage IV disease at diagnosis (Table 1). By MMR status, 32 (76.19%) patients in the dMMR group, 70 (56.45%) patients in the MMRp group and 331 (58.58%) patients in the unknown MMR group had stage III disease (Table 1).

Treatment Patterns

A total of 473 (64.71%), 390 (53.35%) and 276 (37.76%) patients had records of receiving surgery, SACT (chemotherapy) and radiotherapy, respectively, as their index treatment for advanced/recurrent EC. The most common treatment modalities for patients with dMMR and MMRp were surgery ($n=13$, 30.95%) and chemotherapy with surgery ($n=30$, 24.19%), respectively (Fig. 3A and 3B).

Of 414 (56.63%) patients with a record of receiving SACT for the treatment of EC at any time during their treatment pathway, the 1L chemotherapy combination of carboplatin plus paclitaxel (75.10% of all 1L treatments) was most common, and this was administered for a median duration of 105 days (range: 0–280). A total of 108 (14.77%) patients went on to receive 2L SACT (median duration 68 days (range: 0–719)), and 25 (3.42%) patients progressed to

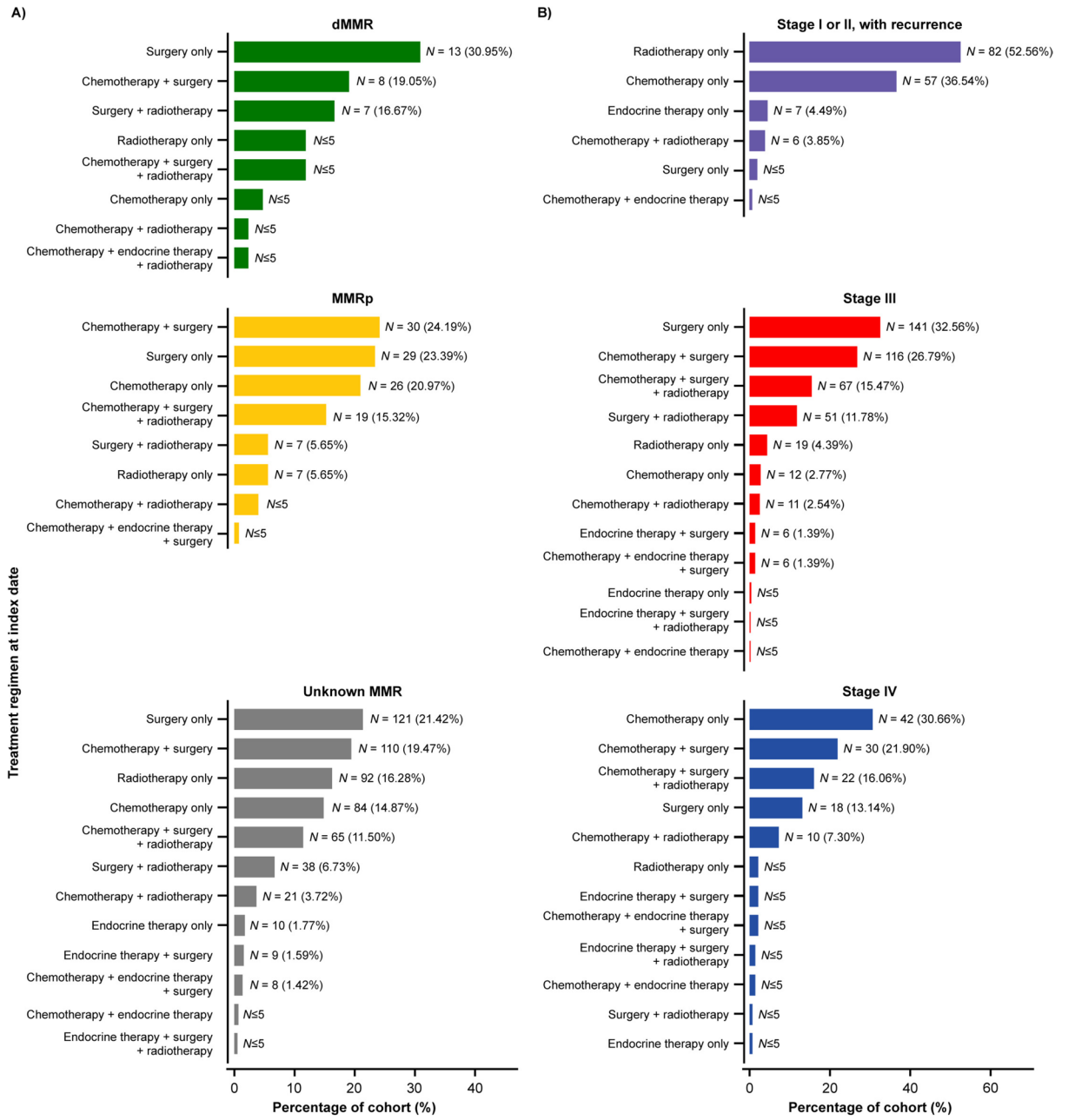

Fig. 3 Distribution of treatment regimens at index date received for advanced or recurrent EC stratified by MMR status (**A**) and by FIGO staging (**B**) at index. *Index* treatment would be 1L for patients with advanced EC and 2L for patients with recurrent EC. *Note*: where patients accessed treatment at alternative centres, their full treatment pathway was not captured. *1L* first line; *2L* second line; *dMMR* mismatch repair-deficient; *EC* endometrial cancer; *FIGO* Fédération Internationale de Gynécologie et d'Obstétrique; *MMR* mismatch repair; *MMRp* mismatch repair-proficient

third-line (3L) therapy (median duration 84 days [range: 0–198]), all of whom were in the MMRp and unknown MMR subgroups. Data on the lines of therapy for individual subgroups are presented in Supplemental Table 1.

Table 1 Baseline summary statistics stratified by MMR status

Variable	Overall (*N* = 731)	Deficient MMR status (*N* = 42)	Proficient MMR status (*N* = 124)	Unknown MMR status (*N* = 565)
Demographics				
Age (years), mean (SD)	68.26 (10.66)	64.68 (12.31)	65.47 (11.17)	69.14 (10.27)
Median (IQR)	69.14 (61.09–76.06)	62.72 (56.09–76.49)	65.92 (58.34–74.31)	69.98 (62.07–76.26)
Ethnicity (%)				
Asian	20 (3.94)	0 (0.00)	≤ 5	15–20
Black	55 (10.85)	0 (0.00)	17 (22.97)	38 (9.41)
Other	18 (3.55)	≤ 5	≤ 5	10–15
White	414 (81.66)	24–28	53–57	333 (82.43)
Missing	224 (30.64)	13 (30.95)	50 (40.32)	161 (28.50)
BMI (kg/m^2), mean (SD)	30.81 (7.69)	30.54 (7.22)	30.22 (7.14)	30.94 (7.84)
Median (IQR)	29.55 (25.20–35.51)	31.03 (23.81–34.05)	28.78 (25.74–33.64)	29.59 (25.28–35.95)
Patient history (years), mean (SD)	2.20 (3.24)	2.33 (3.68)	2.29 (3.23)	2.17 (3.21)
Median (IQR)	0.57 (0.09–3.59)	0.20 (0.08–3.50)	0.47 (0.08–3.32)	0.59 (0.09–3.59)
Follow up (years), mean (SD)	1.56 (1.72)	1.43 (1.86)	1.30 (1.33)	1.63 (1.79)
Median (IQR)	0.85 (0.37–2.22)	0.63 (0.27–1.35)	0.77 (0.35–1.73)	0.92 (0.39–2.27)
Diagnosis year, median (IQR)	2018 (2017–2021)	2021 (2019–2022)	2021 (2019–2022)	2018 (2016–2020)
Disease characteristics				
ECOG status[a] (%)				
0	163 (49.54)	14 (63.64)	25 (54.35)	124 (47.51)
1	124 (37.69)	≤ 5	20–25	95–100
2	34 (10.33)	≤ 5	0 (0.00)	30–35
3	8 (2.43)	0 (0.00)	0 (0.00)	8 (3.07)
4	0 (0.00)	0 (0.00)	0 (0.00)	0 (0.00)
FIGO stage at diagnosis (%)				
I[b]	126 (17.23)	≤ 5	15–20	105–110
Ia	70 (55.56)	≤ 5	5–10	55–60
Ib	50 (39.68)	≤ 5	5–10	40–45

Table 1 continued

Variable	Overall (*N* = 731)	Deficient MMR status (*N* = 42)	Proficient MMR status (*N* = 124)	Unknown MMR status (*N* = 565)
I with unspecified subcode	6 (4.76)	0 (0.00)	0 (0.00)	6 (5.66)
II[b]	30 (4.10)	≤ 5	10–15	15–20
III	433 (59.23)	32 (76.19)	70 (56.45)	331 (58.58)
IIIa	143 (33.03)	10 (31.25)	25 (35.71)	108 (32.63)
IIIb	49 (11.32)	≤ 5	5–10	35–40
IIIc1	148 (34.18)	11 (34.38)	22 (31.43)	115 (34.74)
IIIc2	78 (18.01)	7 (21.88)	13 (18.57)	58 (17.52)
IIIc with unspecified subcode	≤ 5	≤ 5	0 (0.00)	≤ 5
III with unspecified subcode	13 (3.00)	0 (0.00)	≤ 5	11 (3.32)
IV	137 (18.74)	≤ 5	20–25	105–110
IVa	6 (4.38)	0 (0.00)	≤ 5	≤ 5
IVb	123 (89.78)	≤ 5	20–25	95–100
IV with unspecified subcode	8 (5.84)	0 (0.00)	≤ 5	7 (6.48)
Advanced but unknown III/IV	≤ 5	≤ 5	≤ 5	≤ 5
Disease subgroup				
Endometrioid—low-grade	87 (16.89)	11 (36.67)	23 (24.73)	53 (13.52)
Endometrioid—high-grade	40 (7.76)	≤ 5	5–10	25–30
Endometrioid—unknown-grade	80 (15.53)	5–10	≤ 5	70 (17.86)
Uterine carcinosarcoma	78 (15.15)	≤ 5	15–20	60–65
Clear cell	18 (3.50)	≤ 5	5–10	10–15
Serous—high-grade	152 (29.51)	≤ 5	30–35	120–125
Other	60 (11.65)	≤ 5	5–10	45–50
BRCA wild-type = yes (%)	≤ 5	0 (0.00)	≤ 5	≤ 5
ER-positive = yes (%)	47 (65.27)	≤ 5	10–15	30–35

Table 1 continued

Variable	Overall ($N=731$)	Deficient MMR status ($N=42$)	Proficient MMR status ($N=124$)	Unknown MMR status ($N=565$)
PR-positive = yes (%)	33 (57.89)	≤ 5	5–10	20–25
TP53 wild type = yes (%)	42 (65.63)	≤ 5	15–20	20–25
POLE mutation = yes (%)	–	–	–	–
Comorbidities ($n \geq 6$)				
Charlson Comorbidity Index, median (IQR)	0 (0–0)	0 (0–0)	0 (0–0)	0 (0–0)
Chronic obstructive pulmonary disease = yes (%)	24 (4.86)	≤ 5	≤ 5	15–20
Rheumatoid disease = yes (%)	12 (2.43)	0 (0.00)	0 (0.00)	12 (2.97)
Diabetes without complications = yes (%)	44 (8.91)	≤ 5	≤ 5	30–35
Renal disease = yes (%)	10 (2.02)	≤ 5	≤ 5	5–10

Note that precise values are obscured to maintain data protection

[a]On index date or within a 180-day period either side of the index date

[b]With subsequent treatment for disease recurrence

– represents data missing

BMI body mass index; *BRCA* breast cancer gene; *ECOG* Eastern Cooperative Oncology Group; *ER* oestrogen receptor; *FIGO* Fédération Internationale de Gynécologie et d'Obstétrique; *IQR* interquartile range; *MMR* mismatch repair; *POLE* polymerase epsilon; *PR* progesterone receptor; *SD* standard deviation

Time to Next Treatment

Overall median TTNT for patients who received a 1L therapy ($n=414$, 562.02 person-years) was 1.22 years (95% confidence interval [CI] 1.02–1.37) (Fig. 4A and Supplemental Table 2). Median TTNT was 1.17 years (95% CI 0.88–not reached [NR]) in the dMMR group, 1.03 years (95% CI 0.90–1.49) in the MMRp group and 1.26 years (95% CI 1.00–1.40) in the unknown MMR group (Fig. 4B).

Overall median TTNT for patients who received a 2L therapy ($n=108$, 70.59 person-years) was 0.66 years (95% CI 0.62–0.82) (Supplemental Table 2). Median TTNT at 2L was 0.78 years (95% CI 0.63–1.11) in the MMRp group and 0.63 years (95% CI 0.50–0.75) in the unknown MMR group. No patients with dMMR received 3L treatment (Supplemental Table 2).

In the sensitivity analysis of patients with an index date post-2019, 208 patients (16 dMMR, 68 MMRp and 124 unknown MMR) had SACT detailed in their records. TTNT from initiation of 1L therapy was 0.98 years (95% CI 0.68–NR) in patients with dMMR, 0.93 years (95% CI 0.80–1.49) in patients with MMRp and 1.28 years (95% CI 0.90–1.60) in patients with unknown MMR (see Supplemental Fig. 4 and Supplemental Table 2). However, censoring was high, given there was limited time available for an event to occur, and the sample size of the known MMR subgroups was small.

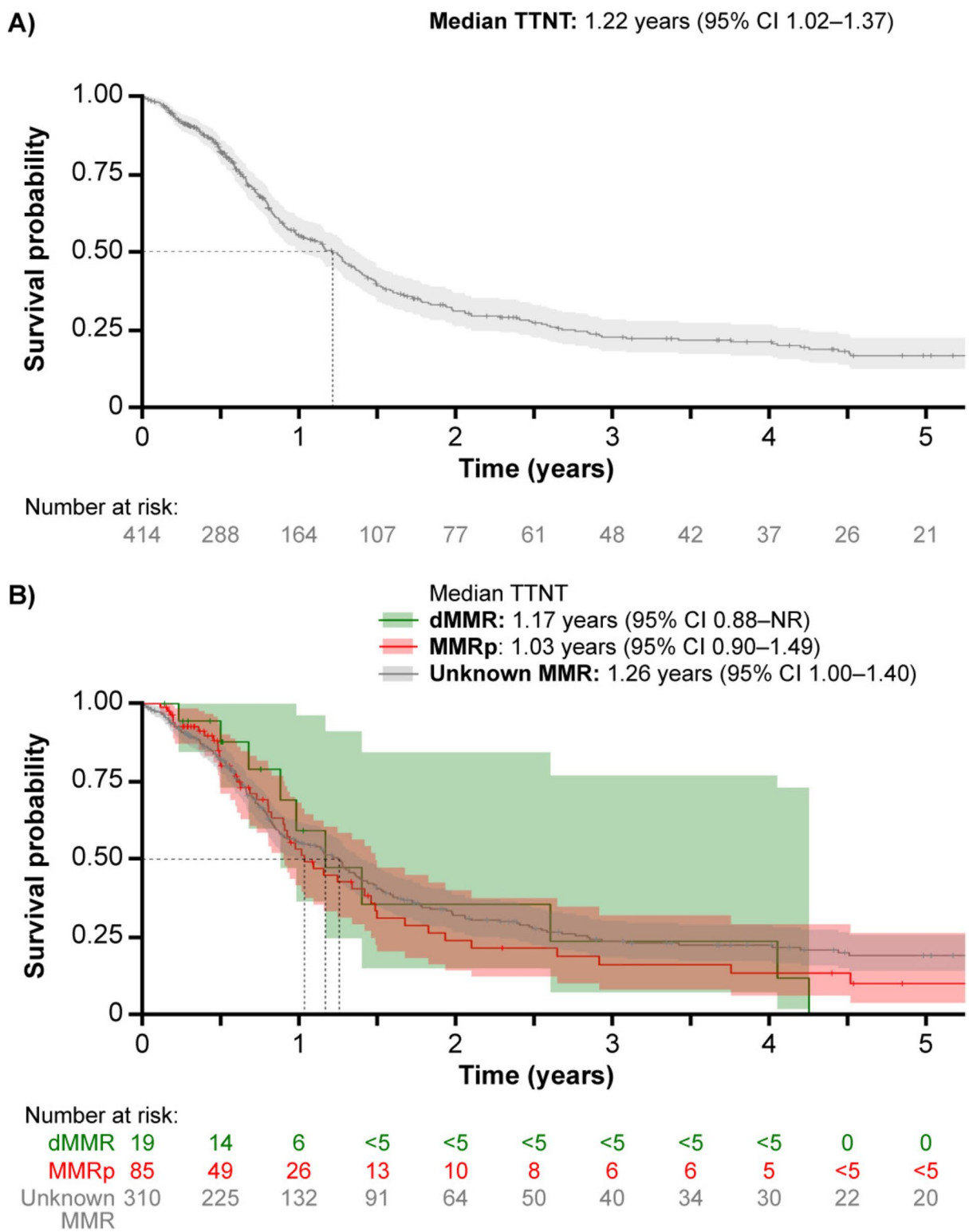

Fig. 4 TTNT following initiation of 1L therapy for the whole cohort (**A**) or stratified by MMR status (**B**). *1L* first line; *CI* confidence interval; *dMMR* mismatch repair-deficient; *MMR* mismatch repair; *MMRp* mismatch repair-proficient; *NR* not reached; *TTNT* time to next treatment

Overall Survival

In the overall cohort, median OS of patients who received a 1L therapy ($n=414$, 654.10 person-years) was 1.80 years (95% CI 1.59–2.16) (Fig. 5A and Supplemental Table 3). The 2-year and 5-year survival rates were 46.9% and 21.0%, respectively. Median OS was 4.25 years (95% CI 1.67–NR), 2.36 years (95% CI 2.10–2.36) and 1.64 years (95% CI 1.32–1.98) in the dMMR, MMRp and unknown MMR groups, respectively (Fig. 5B).

Among 108 patients who received a 2L therapy, there were 72 events and a total of 92.09 person-years available (Supplemental Table 3). Median time to event from 2L therapy was 0.75 years (95% CI 0.63–1.15). Median OS at 2L was not reached in the dMMR group, 1.31 years (95% CI 0.63–NR) in the MMRp group and 0.65 years (95% CI 0.61–0.87) in the unknown MMR group (Supplemental Table 3).

In the sensitivity analysis of those with an index date post-2019, median OS from initiation of 1L therapy was NR (95% CI 1.67–NR) in the dMMR group, 2.36 years (95% CI 1.59–NR) in the MMRp group and 1.74 years (95% CI 1.58–2.56) in the unknown MMR group (Supplemental Fig. 5 and Supplemental Table 3).

DISCUSSION

This large retrospective study with RWD used EHR data from seven NHS trusts in England to characterise patients with advanced or recurrent EC, including their treatments and outcomes in clinical practice. The study was conducted according to the historic standard of care in England, prior to the routine use of immune checkpoint inhibitors in the 1L treatment of primary advanced/recurrent EC.

Although testing and recording of MMR status in patients with EC is recommended in international guidelines and in the recent NICE recommendations for Lynch syndrome screening in EC [3, 23], a record of MMR status was available for only 22.71% of patients. The study period for this analysis was from 2000 to 2023; therefore, MMR status was more commonly recorded for patients with an indexed diagnosis of EC after the publication of NICE guidelines relating to routine testing of Lynch syndrome in late 2020 [23]. According to EHRs included in this study, 53.35% of patients received 1L SACT. This is likely to be under-reported because, when patients had received 1L SACT in a centre outside of the NHS trust, their treatment would not have been documented in their EHRs.

OS from 1L therapy in the overall cohort was 1.80 years, reflecting poor outcomes for patients initiating typical 1L treatments for EC. Carboplatin plus paclitaxel was the most commonly used 1L form of chemotherapy during the timeframe of this study. OS for those who received 2L therapy reflects the historic lack of effective 2L treatment options. The mortality rate and median OS following 2L treatment in our study were similar to some published literature not stratified by MMR status [20, 24]; survival outcomes were still very poor.

Low patient numbers and short follow-up time, given the recency of the NICE guidelines, means that the Kaplan–Meier OS results in patients with known MMR status are difficult to interpret in our study. While acknowledging this limitation and noting these findings are inconclusive, observed OS was numerically longer in the MMRp group (2.36 years) than the unknown MMR group (1.64 years), and the dMMR data were suggestive of prolonged OS (median 4.25 years from initiation of 1L therapy). There was a trend for extended OS in the dMMR subgroup diagnosed post-2019 after the publication of NICE guidelines requiring routine MMR testing in advanced/recurrent EC, although the follow-up time in this sensitivity analysis was short. The potential trend towards more favourable outcomes in dMMR subgroups highlights the importance of MMR testing in advanced/relapsed EC. RWD in the United States show favourable outcomes with biomarker-specific therapies [4].

This is one of several studies in patients with EC in Europe and demonstrates similarities and differences in EC care RWD when compared with published trials. In a recent study in the UK, all patients had received chemotherapy and must have been eligible to receive 2L therapy,

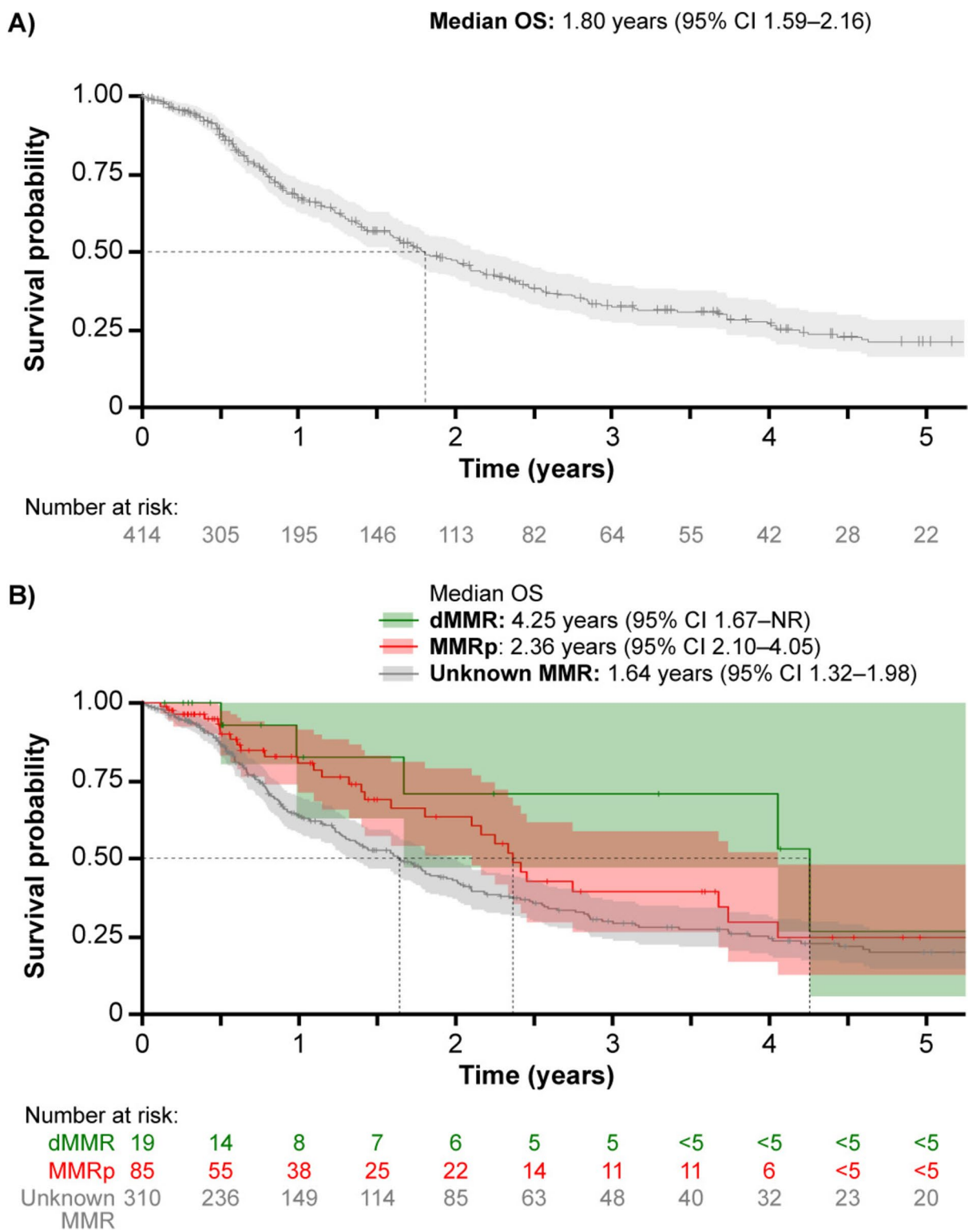

Fig. 5 OS following initiation of 1L therapy for the whole cohort (**A**) or stratified by MMR status (**B**). *1L* first line; *CI* confidence interval; *dMMR* mismatch repair-deficient; *MMR* mismatch repair; *NR* not reached; *OS* overall survival; *MMRp* mismatch repair-proficient

but this criterion was not applied to our analysis and may partially account for the shorter observed follow-up duration [20]. Of those with MMR status recorded in this analysis, the proportion of patients with dMMR tumours identified (25%) is in line with recent retrospective analyses in EC (25–28%) [25, 26]. When considering contemporary anti–PD-1 clinical trials that have led to shifts in globally approved treatment options for EC, the overall average age, BMI and ethnicity of patients with advanced/recurrent EC included in this analysis are broadly similar [13, 27].

The small sample size and short follow-up of the MMR subgroups have already been noted as limitations of this study. Staging information was not readily available in the EHRs for one-quarter of patients. Clinical progression data were not available; however, TTNT is broadly considered a suitable proxy for PFS, as a new line of treatment is considered an indication of disease progression. TTNT has been used as a proxy for PFS in other real-world EC studies [28, 29]. In addition, ethnicity data were available for approximately 70% of the cohort. While the ethnicity breakdown in this analysis is in line with expectations of the areas covered by the NHS trusts involved, the high proportion of patients with a White ethnic background may be indicative of disparities in care. In the UK, Black patients are more likely to be diagnosed with advanced EC and have worse outcomes compared with White patients [30, 31], suggesting possible inequities in access to care between ethnic groups. However, missing ethnicity data can be more common among minority ethnic groups [32].

As testing of MMR status was integrated into routine clinical practice following NICE guidance in 2020 [23], there was a short timeframe in this study period with available data on MMR status. This has affected the number of patients with MMR status recorded and the amount of follow-up time available for these patients. Therefore, the limited data on MMR status impact the interpretation of this analysis. Further research into real-world outcomes stratified by MMR status is needed following widespread adoptions of MMR testing across the UK to better inform the appropriate selection of immunotherapy treatment within the management of advanced/recurrent EC. In addition, there is a need to introduce a robust, consistent and auditable method of recording MMR testing in patient health records.

Although the female population served by the trusts included in this study represents approximately 5% of females in England and Wales, these data, including age and broad ethnic groups, are similar to another real-world study of patients with EC [33]. We examined a large and well-defined cohort of patients using anonymised, patient-level data from routinely recorded NHS EHRs obtained directly from NHS trusts across England. These results benchmark real-world practice and clinical outcomes and can support an understanding of the management of advanced/recurrent EC in the UK and countries with similar standards of care and data recording practices. Finally, this study included data collated during the years of the coronavirus disease 2019 pandemic, which may have influenced data recording, diagnosis and treatment regimens.

CONCLUSIONS

This large study of patients with advanced/recurrent EC from selected NHS trusts in England benchmarked treatment patterns and outcomes, and confirmed previous findings in the published literature. Although this analysis is suggestive of a difference in outcomes between MMR subgroups, attainment of MMR status was low, and further research comparing real-world outcomes based on molecular profile, including MMR subgroups, is warranted. As recent NICE guideline recommendations are implemented across the UK, which support MMR testing for patients with EC [23], future studies could explore these differences further. Additional research into the impact of other biomarkers, such as p53, would also be of interest. Understanding differences in outcomes is particularly pertinent given the recent approvals for immunotherapies, such as pembrolizumab and dostarlimab, in advanced/recurrent EC globally [7, 34] and highlights the importance of knowing

biomarker status to better inform treatment decision-making.

DATA AVAILABILITY STATEMENT

Data used for this publication were curated and analysed by Arcturis Data. For access to anonymised subject-level data, please contact Arcturis Data.

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Declarations

Conflicts of Interest. Jamie Wallis, Shammi Luhar, Filipa Tunaru and Lewis Carpenter are employees of Arcturis Data, the entity that received payments for the conduct of this study. Lewis Carpenter additionally received personal consulting fees from Pfizer and participated in the safety monitoring board for the George Institute for Global Health. Anthony Wesselbaum, Dirk Schneider, Kiera Heffernan and Barbara Mascialino are employees of GSK and hold financial equities in GSK. Joo Ern Ang has received fees for lectures and presentations from AstraZeneca and GSK. Laura Tookman has served on advisory boards for AstraZeneca, Clovis Oncology and GSK; has received consulting fees and fees for lectures and presentations from Tesaro, AstraZeneca, GSK, MSD and Clovis; travel and congress attendance support from MSD; and was part of the NICE technology appraisal committee for dostarlimab with carboplatin and paclitaxel. Kathryn Graham has served on advisory boards for GSK and MSD. Rene Roux has received advisory and consultation fees for GSK, AstraZeneca, Clovis, pharma& and Tesaro; and speaker fees for Pfizer, Lilly and Daiichi Sankyo.

Ethical Approval. Individual human subject data derived from anonymised EHRs from UK NHS trusts were collected in accordance with internal governance at each trust and adhered to the principles of the UK GDPR. No direct subject contact nor primary collection of data occurred.

Therefore, individual patient informed consent, ethics committee or institutional review board approval was not necessary.

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