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Has the introduction of poly(ADP-ribose) polymerase inhibitors changed the advanced ovarian cancer treatment pathway? A bird's-eye view of the English advanced ovarian cancer treatment landscape

This study demonstrated that the introduction of PARPis in the 1LM setting transformed the advanced OC treatment landscape in England, with patients diagnosed in 2018 and later being twice as likely to receive a 1LM treatment than those diagnosed before 2018

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INTRODUCTION

- Because of the nonspecific presenting symptoms of ovarian cancer (OC), patients are most typically diagnosed with advanced disease (International Federation of Gynecology and Obstetrics [FIGO] stage III and IV), and in developed countries, OC has the highest mortality rate among all gynaecologic cancers[1–3]
  - In the UK, the 5-year survival rate for patients with stage I disease is 87%, compared with only 14% with stage IV disease[2]
- Standard treatment for advanced OC is a combination of surgery and platinum-based chemotherapy[4]
- Maintenance therapies were first used in routine care of advanced OC in 2013, beginning with bevacizumab[5]
- Poly(ADP-ribose) polymerases (PARPs) are a family of proteins involved in cellular processes such as DNA repair[6]
- PARP inhibitors (PARPis) as first-line maintenance (1LM) have demonstrated improved clinical outcomes,[7–9] including prolonged survival[7–8]
- The first PARPi approval in the 1LM setting in 2019 provided a new frontline treatment option for patients with advanced OC in the UK,[10] and 3 agents are currently approved: niraparib, olaparib, and rucaparib[11]
- Real-world data can complement and extend clinical trial findings by documenting the extent of PARPi usage and the characteristics of patients who receive PARPis in routine care. However, data are limited on real-world 1LM PARPi use in the UK

AIM

The objective of this real-world study was to describe patient characteristics and treatment patterns before and after 2018 to examine how the introduction of 1LM PARPis changed the advanced OC treatment landscape in England

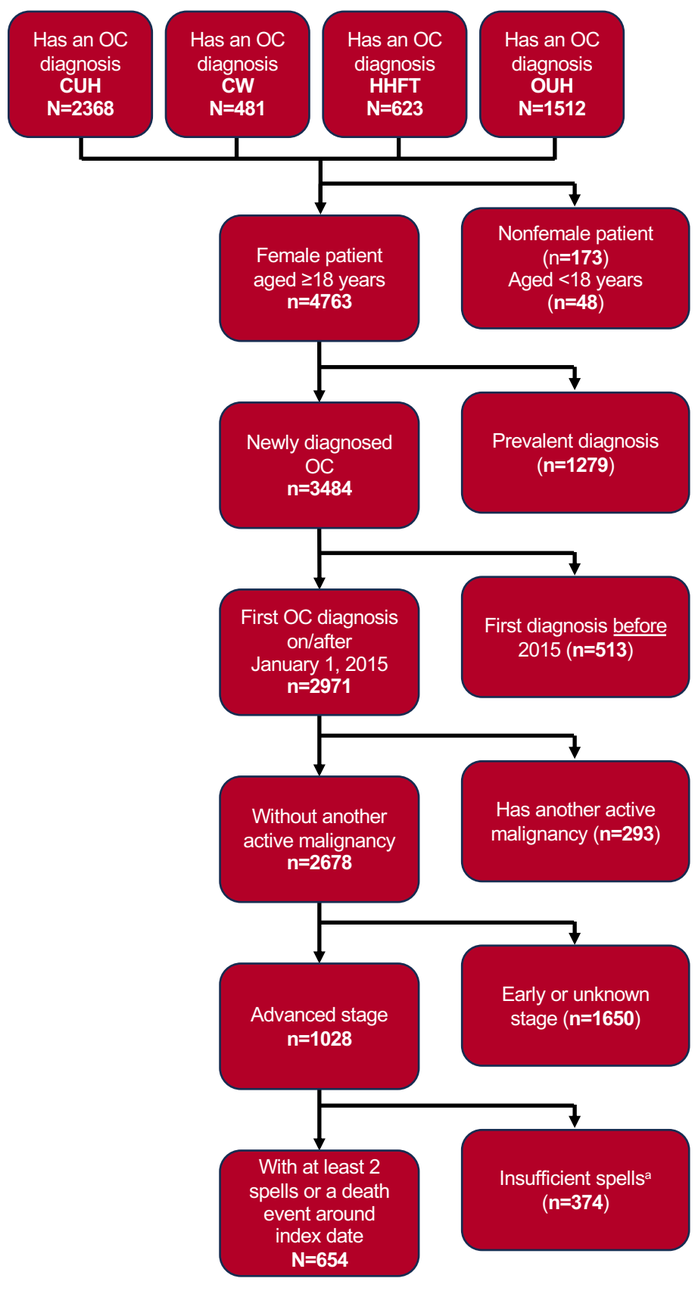
METHOD

- This retrospective study used anonymised electronic health record–derived data from the UK Arcturis data set of 4 National Health Service (NHS) trusts across England (Chelsea and Westminster Hospital NHS Foundation Trust, Oxford University Hospitals NHS Foundation Trust, Hampshire Hospitals NHS Foundation Trust, and Cambridge University Hospitals NHS Foundation Trust)
- Eligible patients were female (aged ≥18 years) with newly diagnosed FIGO stage III or IV OC (recorded 1 January 2015–23 July 2023) with no other active malignancies and ≥2 recorded spells (ie, an inpatient or outpatient visit to one of the participating NHS trusts within 60 days on either side of the index date or a record of death within 60 days of the index date (defined as the first diagnosis of advanced OC)
  - OC was defined as a primary diagnosis of malignant neoplasm of the ovary, fallopian tube, or retroperitoneum and peritoneum (*International Classification of Diseases*, 10th revision [ICD-10]: C56x, C57.0x, or C48x)
- Exclusion criteria included a diagnosis of another malignancy in the 3 years prior to index; recorded chemotherapy at any point between 180 days and 3 years prior to index; diagnosis of secondary malignant neoplasm of ovary or retroperitoneum and peritoneum (ICD-10: C78.6x, C79.6x) any time prior to index; or a first-recorded treatment regimen of bevacizumab, PARPi, immune checkpoint inhibitor monotherapy, or fluorouracil
- The start and end dates of exposure and the constituent therapeutic agents were identified through a line-of-therapy algorithm to define each line of therapy
- Data were stratified by patient diagnosis date at the study period midpoint (before vs on or after 1 January 2018)
  - Data relating to 5 or fewer patients were censored to ≤5 to protect patient privacy
- All analyses were descriptive

RESULTS

- A total of 4984 OC patient records were available for evaluation; after inclusion and exclusion criteria were applied, 654 records remained (**Figure 1**)

Figure 1: Patient record attrition and inclusion at each stage of cohort selection



[a]A hospital spell is an inpatient or outpatient visit to a participating NHS trust. CUH, Cambridge University Hospitals NHS Foundation Trust; CW, Chelsea and Westminster Hospital NHS Foundation Trust; HHFT, Hampshire Hospitals NHS Foundation Trust; NHS, National Health Service; OC, ovarian cancer; OUH, Oxford University Hospitals NHS Foundation Trust.

- Baseline demographic and clinical characteristics are shown in **Table 1**
  - Patients whose data were included in the analysis had a mean age of 66.5 years (SD, 12.2 years), and 97.9% of those with known ethnicity data were White
- The pre-2018 group included 346 patients (52.9%), and the post-2018 group included 308 patients (47.1%)
  - While both groups were similar demographically, the post-2018 group had more confirmed stage IV disease (29.2% vs 18.2% pre-2018 group) and high-grade serous histology (86.5% vs 79.5% pre-2018 group)

Table 1: Baseline summary statistics for the total cohort and stratified by the date of diagnosis

	All eligible patients (N=654)	Grouped by index date[a]	
		Before 2018 (n=346)	After 2018 (n=308)
Age, mean (SD), years	66.5 (12.2)	66.1 (12.1)	67.0 (12.4)
Ethnicity, n (%)[b]			
Missing	167 (25.5)	—	—
Available	487 (74.5)	—	—
White	477 (97.9)	233 (97.5)	244 (98.4)
Black	≤5	≤5	0
Asian	≤5	≤5	≤5
Other	≤5	≤5	≤5
Body mass index, mean (SD), kg/m^2	27.4 (9.7)	27.9 (12.3)	27.0 (5.6)
ECOG performance status, n (%)			
Missing	148 (22.6)	—	—
Available	506 (77.4)	—	—
0	230 (45.5)	111 (42.5)	119 (48.6)
1	198 (39.1)	112 (42.9)	86 (35.1)
2	60 (11.9)	28 (10.7)	32 (13.1)
3	18 (3.6)	10 (3.8)	8 (3.3)
4	0	0	0
FIGO stage, n (%)			
III	316 (48.3)	164 (47.4)	152 (49.4)
IV	153 (23.4)	63 (18.2)	90 (29.2)
Advanced but unknown III/IV	185 (28.3)	119 (34.4)	66 (21.4)
Disease histology, n (%)			
Missing	235 (35.9)	—	—
Available	419 (64.1)	—	—
Clear cell	6 (1.4)	≤5	≤5
Endometrioid	6 (1.4)	≤5	≤5
Mucinous	6 (1.4)	≤5	≤5
Other	18 (4.3)	12 (5.5)	6 (3.0)
Serous, cystadenoma	≤5	≤5	0
Serous, high-grade	347 (82.8)	174 (79.5)	173 (86.5)
Serous, low-grade	22 (5.3)	13 (5.9)	9 (4.5)
Serous, unknown-grade	≤5	0	≤5
Serous, borderline	12 (2.9)	6 (2.7)	6 (3.0)
Charlson Comorbidity Index, median (IQR)[c]	0.0 (0.0–0.0)	0.0 (0.0–0.0)	0.0 (0.0–0.0)
Follow-up, median (IQR), years	1.9 (0.8–3.6)	2.2 (0.9–4.5)	1.6 (0.7–3.0)

[a]Number of missing and available were only calculated for the entire cohort, and not by subgroup, to avoid possible reidentification if sample sizes were ≤5. [b]Ethnicity was defined by the NHS data dictionary. [c]Calculated using all recorded comorbidities in the year prior to diagnosis of OC. ECOG, Eastern Cooperative Oncology Group; FIGO, International Federation of Gynecology and Obstetrics; NHS, National Health Service; OC, ovarian cancer.

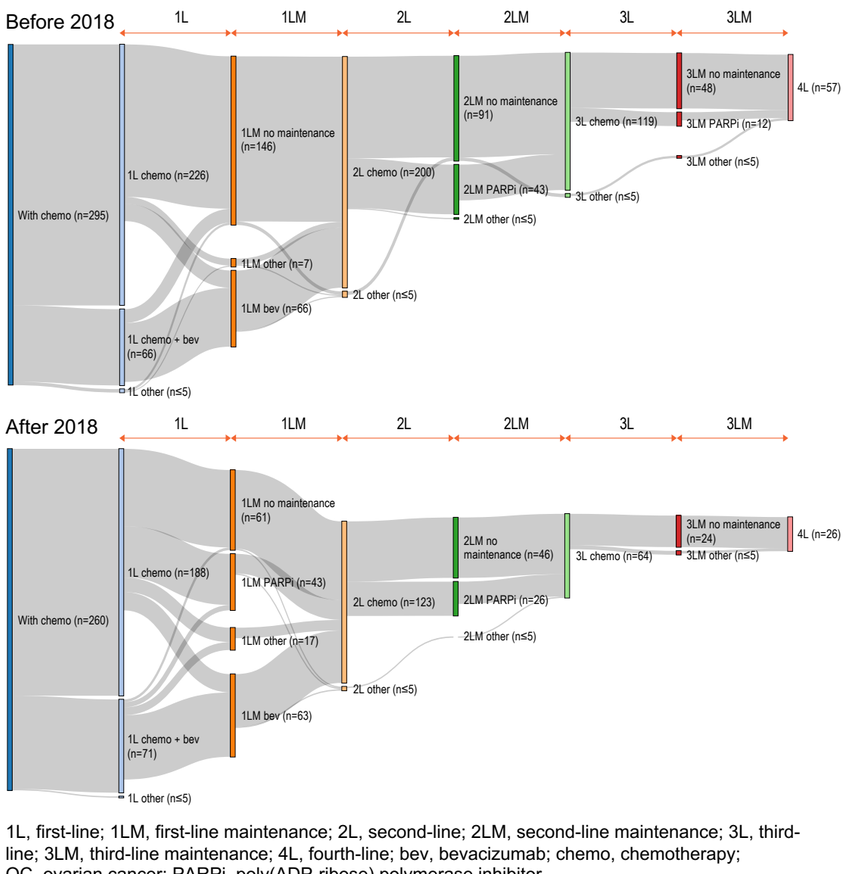
- Lines of therapy are summarised in **Table 2**
  - Most patients received first-line (1L) systemic anticancer therapies (overall, 84.9%; before 2018, 85.3%; after 2018, 84.4%), which consisted primarily of platinum-based regimens (551/555; 99.3%)
- Treatment patterns before and after 2018 are shown in **Figure 2**
  - A higher proportion of patients who received 1L treatment received 1LM treatment in the post-2018 group (47.3%) than in the pre-2018 group (24.7%)
  - There was a shift in PARPi use after 2018, as evidenced by greater 1LM PARPi use (before 2018, <1%; after 2018, 35.0%)

Table 2: Lines of therapy for the total cohort and stratified by the date of diagnosis

Regimen	All eligible patients (N=654)	Before 2018 (n=346)	After 2018 (n=308)
	n (%) of cohort	n (%) of cohort	n (%) of cohort
1L	**555 (84.9)**	**295 (85.3)**	**260 (84.4)**
Chemo	414 (74.6)	226 (76.6)	188 (72.3)
Chemo + bev	137 (24.7)	66 (22.4)	71 (27.3)
Other[a]	4 (0.7)	3 (1.0)	1 (0.4)
1LM	**196 (30.0)**	**73 (21.1)**	**123 (39.9)**
Bev	129 (65.8)	66 (90.4)	63 (51.2)
PARPi	44 (22.5)	—	43 (35.0)
ICI	6 (3.1)	—	—
Other[a]	17 (8.7)	7 (9.6)	17 (13.8)
2L	**331 (50.6)**	**205 (59.2)**	**126 (40.9)**
Chemo	323 (97.6)	200 (97.6)	123 (97.6)
Chemo + bev[b]	6 (1.8)	—	—
Other[a]	2 (0.6)	5 (2.4)	3 (2.4)
2LM	**71 (10.9)**	**44 (12.7)**	**27 (8.8)**
PARPi	69 (97.2)	43 (97.7)	26 (96.3)
Other[a]	2 (2.8)	1 (2.3)	1 (3.7)
3L	**186 (28.4)**	**122 (35.3)**	**64 (20.8)**
Chemo	183 (98.4)	119 (97.5)	64 (100.0)
Other[a]	3 (1.6)	3 (2.5)	—
3LM	**17 (2.6)**	**14 (4.0)**	**3 (1.0)**
PARPi	15 (88.2)	12 (85.7)	—
Other[a]	2 (11.8)	2 (14.3)	3 (100.0)

[a]Other denotes pooled results for regimens administered to ≤5 patients. [b]Chemo + bev is not reimbursed in England.
1L, first-line; 1LM, first-line maintenance; 2L, second-line; 2LM, second-line maintenance; 3L, third-line; 3LM, third-line maintenance; bev, bevacizumab; chemo, chemotherapy; ICI, immune checkpoint inhibitor; PARPi, poly(ADP-ribose) polymerase inhibitor.

Figure 2: Sankey plots depicting 1L and 1LM treatment patterns for patients who were diagnosed with advanced OC before and after 2018



1L, first-line; 1LM, first-line maintenance; 2L, second-line; 2LM, second-line maintenance; 3L, third-line; 3LM, third-line maintenance; 4L, fourth-line; bev, bevacizumab; chemo, chemotherapy; OC, ovarian cancer; PARPi, poly(ADP-ribose) polymerase inhibitor.

CONCLUSIONS

- This study provided valuable insights on the advanced OC treatment landscape in England before and after PARPi approvals in the 1LM setting
- Relative to patients diagnosed before 2018, patients diagnosed after 2018 were twice as likely to receive 1LM treatments, driven by increased PARPi use in 1LM
- Additional research is needed to assess the impact of PARPi use in the 1LM setting on long-term patient outcomes

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CONFLICTS OF INTEREST

Jamie Wallis, **Federica Picariello**, 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. **Zsofia Kiss**, **Barbara Mascialino**, **Amanda Golembesky**, and **Nichola Roebuck** are employees of GSK. **Rene Roux** received consulting fees/honorarium from AstraZeneca, Clovis, GSK, Lilly, and Pfizer and participated on advisory boards for Clovis and Tesaro.