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Prescribers and patients drive maintenance therapy patterns in a community oncology practice: National guidelines versus the real-world experience

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ABSTRACT

Objective: Previous studies have shown that first-line (1L) maintenance therapy (MT) with poly(ADP-ribose) polymerase inhibitors and/or bevacizumab improves outcomes among patients with advanced ovarian cancer (OC); however, these treatments are underutilized. This study aimed to provide a real-world understanding of MTs among patients with advanced OC who received 1L platinum-based chemotherapy (PBC).

Methods: A retrospective chart review using iKnowMed electronic health records to identify patients aged ≥18 years with advanced OC who initiated 1L PBC between January 1, 2018–December 31, 2020. Following 1L PBC, patients could have received MT or active surveillance (AS). Kaplan–Meier methods were used to estimate time to treatment discontinuation (TTD), real-world progression-free survival (rwPFS), and overall survival (OS).

Results: Of the 600 chart-reviewed patients included, 239 (39.8 %) received MT and 315 (52.5 %) received AS. Patients who were <65 years of age, or those with higher-stage disease or those who had received neoadjuvant treatment, were more likely to initiate MT than AS. Genetic testing rates were low across both cohorts. Median (95 % confidence interval [CI]) TTD for the MT cohort was 13.6 months (11.0, 21.2). Median (95 % CI) rwPFS was 26.9 months (21.3, not reached) and 11.3 months (9.5, 13.0) for the 1L MT and AS cohorts, respectively ($p < 0.0001$). OS at 36 months was 82.4 % in the 1L MT cohort and 58.0 % in the 1L AS cohort.

Conclusions: This study reinforces clinical trial findings that 1L MT improves outcomes in patients with advanced OC; however, genetic testing rates and 1L MT remained low.

1. Introduction

In 2023, Ovarian cancer (OC) was estimated to be the fifth leading cause of cancer-related death in women in the United States (USA) (Siegel et al., 2023). From 2013 to 2019, the 5-year relative survival rate among women with OC was estimated to be 50.8 % (National Cancer Institute, 2023). An estimated 19,710 new diagnoses and 13,270 deaths from OC were expected to occur in the USA in 2023 (American Cancer Society, 2023; Siegel et al., 2023).

Cytoreductive surgery and platinum-based chemotherapy (PBC) are the primary standard-of-care treatments for OC (National Comprehensive Cancer Network, 2024); however, a high proportion of patients relapse after positive response to initial treatment (Bartoletti et al., 2020; Gogineni et al., 2021; Luvero et al., 2019). Patients with stage III/IV OC have a 70–75 % rate of recurrence within 2 years of diagnosis, and treatments have been reported to be less effective at each recurrence (Gogineni et al., 2021).

The National Comprehensive Cancer Network guidelines recommend maintenance therapy (MT) following first-line (1L) treatment for patients with stage II–IV OC who show partial response, stable disease, or progression, whereas active surveillance (AS; i.e. close monitoring without treatment) is recommended for patients with stage II–IV disease who show a complete response (National Comprehensive Cancer Network, 2024). However, there is flexibility within these guidelines for certain patient groups. Multiple studies have shown that MT with targeted therapies such as poly(ADP-ribose) polymerase inhibitors

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(PARPis) and/or bevacizumab improve outcomes among patients with advanced OC following primary therapy (Bartoletti et al., 2020; Burger et al., 2011; Ibrahim et al., 2020; Tattersall et al., 2022).

PARPi therapies target DNA repair pathways (Smith and Pothuri, 2022), and there are currently two PARPi therapies that have been approved by the U.S. Food and Drug Administration as MTs following complete or partial response to 1L PBC among patients with advanced OC: olaparib (MT in 1L setting; olaparib monotherapy only for patients with a *BRCA* mutation) and niraparib (1L MT for OC in patients with a *BRCA* mutation) (O'Malley et al., 2023; U.S. Food and Administration, 2023; U.S. Food and Administration, 2024).

Bevacizumab is a monoclonal antibody that suppresses tumor growth and inhibits metastatic disease progression (Perren et al., 2011), and it is approved as a MT in the 1L setting for patients with advanced OC (U.S. Food and Administration, 2022; Vasudevan et al., 2023).

Despite being effective therapeutic strategies for OC, studies have shown that PARPi and bevacizumab may be underutilized for MT by physicians treating OC in clinical practice, and many patients instead continue to undergo AS (Chan et al., 2023; Turell et al., 2020). Real-world studies are important for demonstrating the value of such treatments in clinical practice and supporting clinical decision-making. The results of real-world oncology studies have also been shown to be concordant with clinical trials, and data from electronic health records (EHR) have been shown to help derive information on clinical outcomes (Huang Bartlett et al., 2020). Several observational studies have shown real-world PARPi and bevacizumab use to be associated with improvements in progression-free survival (PFS), symptoms, and quality-of-life outcomes (Chan et al., 2023; Demirkiran et al., 2023; Mahtani et al., 2022).

This study aimed to provide a real-world understanding of PARPi, bevacizumab, or PARPi and bevacizumab combination OC MTs by describing patient characteristics, treatment patterns, and clinical outcomes among patients with advanced OC who received 1L PBC in the US community oncology setting.

2. Materials and methods

2.1. Study design

This retrospective chart review study used The US Oncology Network iKnowMed electronic health records (EHR) to perform a targeted chart abstraction of structured and unstructured data from the records of 600 female patients who initiated 1L PBC following metastatic disease between January 1, 2018, and December 31, 2020 (study identification period). The study observation period was January 1, 2018, to September 30, 2021. The index date was defined as the date of initiation of 1L PBC, and the baseline period was the 6-month (180-day) period prior to and after the index date, during which demographic and clinical characteristics were assessed. Patients were followed until end of study period (September 30, 2021), date of last visit, or death, whichever occurred first.

2.1.1. Study population

To be included in this study, patients must have been female and aged ≥18 years with a diagnosis of stage III/IV and/or recurrent OC treated within The US Oncology Network (with >1 visit in addition to the index event visit). Recurrence was defined as metastatic disease after curative surgery with or without adjuvant chemotherapy. Patients were excluded from the study if they did not have a visit to a practice within The US Oncology Network within 90 days of the OC diagnosis, were enrolled in interventional clinical trials, or received treatment for another primary cancer following the index date and before the end of the study period. A chart review was conducted on a subset of patients who were most recently treated with 1L PBC. These 600 patients represented approximately 30 % of the eligible population (Table S1).

2.1.2. Cohort definitions and stratifications

Our study results focus on two cohorts: patients who received an MT and patients who underwent AS. The MT cohort included patients who received PARPi monotherapy, bevacizumab monotherapy, or PARPi plus bevacizumab within 120 days after the end of 1L PBC. The AS cohort included patients who received 1L PBC, did not have MT, and received second-line (2L) treatment (second line of anticancer chemotherapy for ovarian cancer), or patients who received 1L platinum-based therapy, did not have MT, did not receive 2L treatment, and had a last contact date of >42 days from the end date of the 1L platinum-based therapy. Response after 1L PBC was not considered in the definition of these cohorts.

2.1.3. Objectives

The primary objectives of this study were to assess the baseline demographic and clinical characteristics of the cohorts, evaluate real-world response rate (rwRR) of 1L PBC, and evaluate factors associated with initiation of 1L MT. rwRR was defined as the proportion of patients who achieved a complete response and response not otherwise specified, based on providers' assessments. The two measures of rwRR explored in this study were real-world overall response rate (calculated as the percentage of patients with a response rate within the duration of time from first documented response of complete response or partial response to the earliest date of first progression or recurrent disease, or date of death) and best overall response (the best response observed up to progression during the study observation time period). Using the best response observed meant that whether the patient responded to treatment or not before the progression could be defined. The number of patients with a complete, partial or mixed response were reported, as well as the number of patients with stable or progressive disease.

Exploratory objectives included time to discontinuation of MT (bevacizumab and/or PARPi), real-world PFS (rwPFS), overall survival (OS), reasons for treatment discontinuation, and maintenance switch patterns. Time to treatment discontinuation was defined as the interval between MT initiation and discontinuation. OS was defined as the interval between the end of 1L PBC and the date of death. For time to discontinuation and OS, patients were censored on the study end date or the last visit date available in the data set, whichever occurred first. rwPFS was measured from the end of 1L PBC to the earliest date of progression or death. Patients who were still alive at the end of the study observation and did not progress at the last visit date were censored.

2.2. Data source and collection

The iKnowMed EHR captures outpatient histories for patients who received care in community-based oncology practices within The US Oncology Network, including patient demographics, clinical information, and treatment information (e.g. line of therapy and treatment administration). The US Oncology Network includes 1,400 affiliated physicians practicing at >500 sites of care across the USA with approximately 1.2 million patients with cancer receiving care each year (The US Oncology Network).

Structured data fields within the iKnowMed EHR provided information needed to address most research questions; data were supplemented by additional unstructured data collected through chart review. Electronic chart review data were collected by means of a secure, web-based electronic case report form by healthcare professionals with oncology experience.

2.3. Data analysis

Descriptive analyses were conducted to evaluate the demographic, clinical, and treatment characteristics of the population. Categorical variables are reported as frequency and percentage, and continuous variables are reported as mean, standard deviation, median, and range (minimum, maximum). Kaplan–Meier estimates were used to describe

time to treatment discontinuation, rwPFS, and OS in patients who received MT and AS following 1L PBC. Log-rank p-values were used to identify significant results (with $p < 0.05$ considered statistically significant). Multivariate logistic regression was used to assess predictors of 1L MT, which were expressed as odds ratios with 95 % confidence intervals (CIs).

3. Results

3.1. Patient identification and characteristics

Of the 600 chart-reviewed patients, 239 (39.8 %) received MT (PARPi only, n = 135; bevacizumab only, n = 82; combination PARPi and bevacizumab, n = 22) and 315 (52.5 %) received AS (Table 1). Of the remaining 46 patients, 16 were platinum refractory, 13 were maintenance eligible, and 17 were lost to follow-up.

Across both MT and AS cohorts, most patients had stage IIIC disease (MT, n = 114/239, 47.7 %; AS, n = 165/315, 52.4 %) and over 85 % had received debulking surgery, the most common types being oophorectomy, omentectomy, and hysterectomy. The proportion of patients receiving surgery was similar between the MT and AS cohorts. *BRCA* testing (germline and somatic) rates were similar across MT and AS cohorts (MT, n = 137/239, 57.3 %; AS, n = 165/315, 52.4 %); however, a greater proportion of patients receiving MT had *BRCA* mutations (MT, n = 35/239, 14.6 %; AS, n = 7/315, 2.2 %). Homologous recombination deficiency testing rates were low across both cohorts (MT, n = 31/239, 13.0 %; AS, n = 19/315, 6.0 %).

3.2. Treatment patterns

Of the 118 patients who had 1L PBC with bevacizumab, 67.8 % (n = 80) underwent MT and 26.3 % (n = 31) were on AS. Of the 482 patients who received 1L PBC without bevacizumab, 33.0 % (n = 159) received 1L MT and 58.9 % (n = 284) were on AS (Table 1). A greater proportion of patients who received 1L PBC with bevacizumab (n = 44, 55.0 %) had bevacizumab maintenance monotherapy compared with patients who received 1L PBC without bevacizumab (n = 38, 23.8 %) (Table S2). There was also a greater proportion of patients with 1L PBC with bevacizumab who received PARPi plus bevacizumab MT compared with patients who had 1L PBC without bevacizumab (n = 16, 20.0 % with bevacizumab; n = 6, 3.8 % without bevacizumab). PARPi monotherapy was the most common MT regimen (n = 115, 72.3 %) among patients with 1L PBC without bevacizumab, whereas only 25.0 % (n = 20) of patients with 1L PBC with bevacizumab received PARPi monotherapy.

3.3. rwRR to 1L PBC

Of the 339 patients with a recorded response assessment, 69.6 % (n = 236) showed partial response and 22.1 % (n = 75) showed complete response to 1L PBC, yielding an overall response rate of 91.7 % (Table 2).

3.4. Factors associated with initiation of 1L MT

Multivariate logistic regression analysis showed older age (75–84 years compared with < 65 years) was associated with a reduced likelihood of initiating 1L MT (relative risk [RR] 0.528; 95 % CI 0.310, 0.899; p = 0.0186) (Table 3). Conversely, stage IV disease at diagnosis compared with stage IIIA–IIIB (RR 3.732 95 % CI 1.569, 8.878; p = 0.0029) and receipt of neoadjuvant treatment (RR 2.394; 95 % CI 1.187, 4.828; p = 0.0147) were associated with a higher likelihood of initiating 1L MT (Table 3).

3.5. Time to discontinuation of MT after 1L PBC

Median (95 % CI) time to MT discontinuation was 13.6 months (11.0,

Table 1
Baseline demographics and clinical characteristics.

	Overall population[a] (N = 600)	1L MT cohort (N = 239)	AS cohort (N = 315)
Mean (SD) age	64.7 (12.8)	62.4 (12.0)	65.8 (12.9)
≥65 years, n (%)	320 (53.3)	129 (54.0)	179 (56.8)
Race, n (%)			
White	398 (66.3)	150 (62.8)	223 (70.8)
African American	33 (5.5)	14 (5.9)	15 (4.8)
Asian	15 (2.5)	8 (3.3)	5 (1.6)
Other	24 (4.0)	15 (6.3)	7 (2.2)
Not documented	130 (21.7)	52 (21.8)	65 (20.6)
Mean (SD) BMI, kg/m^2	27.5 (6.8)	27.5 (6.9)	27.6 (6.8)
BMI category, n (%)			
Underweight (<18 kg/m^2)	26 (4.3)	11 (4.6)	14 (4.4)
Normal (18–24.9 kg/m^2)	220 (36.7)	86 (36.0)	111 (35.2)
Overweight (25–29.9 kg/m^2)	157 (26.2)	60 (25.1)	84 (26.7)
Obese (>30 kg/m^2)	178 (29.7)	75 (31.4)	95 (30.2)
Not documented	19 (3.2)	7 (2.9)	11 (3.5)
Payer type, n (%)			
PPO	159 (26.5)	73 (30.5)	77 (24.4)
Managed Medicare	112 (18.7)	45 (18.8)	59 (18.7)
Medicare	116 (19.3)	41 (17.2)	62 (19.7)
HMO	56 (9.3)	24 (10.0)	30 (9.5)
Medicaid	25 (4.2)	15 (6.3)	7 (2.2)
Oncology Care Model	50 (8.3)	14 (5.9)	33 (10.5)
Managed Medicaid	16 (2.7)	7 (2.9)	9 (2.9)
Commercial	9 (1.5)	NR	NR
Other	14 (2.3)	NR	11 (3.5)
Not documented	43 (7.2)	15 (6.3)	23 (7.3)
Median (min, max) duration of follow-up from initial OC diagnosis or recurrence to end of observation, months	19.2 (0.1, 44.2)	20.0 (4.4, 44.2)	20.1 (2.2, 43.3)
Median (min, max) time from initial OC diagnosis or recurrence to initiation of PBC, months	1.1 (0.0, 18.7)	1.1 (0.1, 4.3)	1.1 (0.0, 18.7)
Initial stage III/IV diagnosis or stage of initial diagnosis among patients with recurrent disease, n (%)			
I/II	5 (0.8)	<5	<5
IIIA	74 (12.3)	29 (12.1)	43 (13.7)
IIIB	56 (9.3)	21 (8.8)	35 (11.1)
IIIC	299 (49.8)	114 (47.7)	165 (52.4)
III (NOS)	10 (1.7)	<5	6 (1.9)
IVA	41 (6.8)	20 (8.4)	13 (4.1)
IVB	73 (12.2)	32 (13.4)	32 (10.2)
IV (NOS)	42 (7.0)	18 (7.5)	17 (5.4)
Patients who received debulking surgery, n (%)			
Yes	501 (83.5)	205 (85.8)	270 (85.7)
Not documented	99 (16.5)	34 (14.2)	45 (14.3)
Surgery outcome[b], n (%)			
Complete (R0)	258 (51.5)	119 (58.0)	126 (46.7)
Partial (R1, R2)	133 (26.5)	53 (25.9)	72 (26.7)
Not documented	118 (23.6)	38 (18.5)	75 (27.8)
1L PBC, n (%)			
With bevacizumab	118 (19.7)	80 (67.8)	31 (26.3)

(*continued on next page*)

Table 1 (*continued*)

	Overall population[a] (N = 600)	1L MT cohort (N = 239)	AS cohort (N = 315)
Without bevacizumab	482 (80.3)	159 (33.0)	284 (58.9)
BRCA[c] testing results (*BRCA*1 or 2), n (%)			
Negative	279 (46.5)	102 (42.7)	158 (50.2)
Positive	44 (7.3)	35 (14.6)	7 (2.2)
Not documented	277 (46.2)	102 (42.7)	150 (47.6)
Homologous recombination deficiency testing result, n (%)			
Positive	39 (6.5)	25 (10.5)	13 (4.1)
Negative	13 (2.2)	6 (2.5)	6 (1.9)
Inconclusive	<5	0 (0.0)	0 (0.0)
Not documented	547 (91.2)	208 (87.0)	296 (94.0)

Numbers smaller than five are suppressed for patient privacy reasons.
1L, first-line; AS, active surveillance; BMI, body mass index; HMO, health maintenance organization; Min, minimum; Max, maximum; MT, maintenance therapy; NOS, not otherwise specified; NR, not reported; OC, ovarian cancer; PBC, platinum-based chemotherapy; PPO, preferred provider organization; R, residual disease; SD, standard deviation.

[a] Of the 600 chart-reviewed patients included in the overall population, 554 received MT or AS; of the remaining 46 patients, 16 were platinum refractory, 13 were maintenance eligible but did not receive MT or AS, and 17 were lost to follow-up.

[b] Patients could have received more than one surgery and surgery outcome was reported for each surgery.

[c] *BRCA* testing included both germline and somatic testing.

Table 2
Real-world response rates to 1L PBC.

Total patient count	600
Number of patients with no documentation/not evaluated	261
Patients with response assessment	339
Patients experiencing an event (complete response or partial response)	311
Overall response rate[a] including evaluated patients (patients with response assessment as denominator), % (95 % CI)	91.7 (88.7, 94.8)
Patients experiencing an event (complete response, partial response, stable disease)	326
Overall disease control rate including evaluated patients (patients with response assessment as denominator), % (95 % CI)	96.2 (94.1, 98.2)
Best overall response[b]	
Patients with response assessment, n (%)	339
Complete response	75 (22.1)
Partial response	236 (69.6)
Mixed response	<5
Stable disease	15 (4.4)
Progressive disease	11 (3.2)

Numbers smaller than five are suppressed for patient privacy reasons.
1L, first-line; CI, confidence interval; PBC, platinum-based chemotherapy.

[a] Overall response rate was calculated as the percentage of patients with a response rate within the duration of time from first documented response of complete response or partial response to the earliest date of first progression or recurrent disease, or date of death.

[b] Best overall response was defined as the best response observed up to progression during the study observation time period. This approach enabled us to define whether or not the patient responded to treatment before the progression.

21.2). Probability of treatment discontinuation at 12 months after MT initiation was 52.4 % (Table 4). A total of 162/239 (67.8 %) patients receiving 1L MT had documented reasons for MT discontinuation (Table S3). Among these patients, the most common reasons for

Table 3
Factors associated with initiation of 1L MT: multivariate logistic regression model.

Variable	Number (N = 595)[a]	Event (n)	Relative risk (95 % CI)	p-value
Age at initial stage III/IV diagnosis				
<65 years (reference)	277	128	–	–
65–74 years	193	78	0.762 (0.505, 1.150)	0.1959
75–84 years	106	28	0.528 (0.310, 0.899)	**0.0186**
≥85 years	19	<5	0.405 (0.123, 1.339)	0.1387
Race				
White (reference)	395	149	–	–
Black or African American	33	14	1.304 (0.587, 2.897)	0.5151
Asian	15	8	1.819 (0.594, 5.564)	0.2946
Other[b]	24	15	2.897 (1.155, 7.269)	0.0234
Unknown	128	52	1.173 (0.744, 1.848)	0.4916
Practice region				
West (reference)	291	117	–	–
Midwest	139	60	1.135 (0.691, 1.865)	0.6179
Northeast	7	<5	0.520 (0.078, 3.465)	0.4992
South	158	59	0.925 (0.564, 1.516)	0.7578
Stage at diagnosis[c]				
IIIA–IIIB (reference)	140	54	–	–
IIIC	299	114	1.113 (0.701, 1.768)	0.6494
IV	156	70	3.732 (1.569, 8.878)	**0.0029**
Metastatic site count				
1 (reference)	134	51	–	–
2	38	13	0.584 (0.247, 1.378)	0.2194
3+	25	13	1.608 (0.602, 4.291)	0.3433
Not documented	398	161	2.295 (1.062, 4.962)	0.0347
ECOG PS score at diagnosis				
0 (reference)	112	58	–	–
1	265	104	0.718 (0.435, 1.187)	0.1965
2+	84	26	0.536 (0.262, 1.095)	0.0870
Not documented	134	50	0.755 (0.414, 1.377)	0.3594
*BRCA*1/2 status				
Negative (reference)	275	101	–	–
Positive	44	35	2.767 (0.952, 8.045)	0.0616
Not documented	276	102	1.174 (0.798, 1.727)	0.4149
Derived homologous recombination deficiency status				
Negative (reference)	13	6	–	–
Positive	74	53	2.038 (0.531, 7.823)	0.2996
Not documented	508	179	0.748 (0.231, 2.420)	0.6275

(*continued on next page*)

Table 3 (*continued*)

Variable	Number (N = 595)[a]	Event (n)	Relative risk (95 % CI)	p-value
Physician speciality				
Gynecologic oncology/ obstetrics & gynecology (reference)	274	98	–	–
Hematology & medical oncology & internal medicine	300	131	1.460 (0.971, 2.195)	0.0689
Other[d]	21	9	1.653 (0.595, 4.597)	0.3352
Neoadjuvant treatment				
No (reference)	512	202	–	–
Yes	83	36	2.394 (1.187, 4.828)	**0.0147**
Surgery outcomes within 4 months prior to the index date				
Complete (R0, no gross residual, optimal) (reference)	199	92	–	–
Partial (R1, R2, residual disease)	107	42	0.742 (0.437, 1.260)	0.2690
Not documented	289	104	0.489 (0.297, 0.806)	**0.0050**
Surgery outcomes within 6 months on or after the index date				
Complete (R0, no gross residual, optimal) (reference)	45	22	–	–
Partial (R1, R2, residual disease)	24	10	0.813 (0.362, 1.824)	0.8393
Not documented	526	206	0.891 (0.291, 2.726)	0.6149

Numbers smaller than five are suppressed for patient privacy reasons.
p-values in bold indicate statistically significant results.
1L, first-line; CI, confidence interval; ECOG PS, Eastern Cooperative Oncology Group performance status; MT, maintenance therapy.
[a] Of the 600 chart-reviewed patients included in this study, five patients with stage I–II disease were excluded from this analysis.
[b] Other race includes American Indian or Alaska native, or people with a mixed ethnic background.
[c] Five patients with stage I–II were eliminated from this analysis.
[d] Other specialties include radiation oncologist, physician/general surgery, physician/urology, pain medicine.

Table 4
Time to discontinuation of MT after 1L PBC.

TTD	All patients who received 1L MT: N = 239
Events, n (%)	123 (51.5)
Mean (SE), months	15.4 (0.7)
Median (95 % CI), months	13.6 (11.0, 21.2)
Q1, Q3	5.1, 26.9
TTD probability, % (95 % CI)	
6 months	73.4 (67.3, 78.6)
12 months	52.4 (45.2, 59.1)
18 months	45.7 (38.2, 52.9)
24 months	36.5 (27.9, 45.1)
30 months	19.0 (9.4, 31.1)

TTD was defined as the interval between the initiation of MT (bevacizumab or PARPi) and discontinuation for any cause. Patients who did not discontinue treatment during the study observation period were censored on the study end date or the last visit date available in the data set, whichever occurred first.
1L, first-line; CI, confidence interval; MT, maintenance therapy; PARPi, poly (ADP-ribose) polymerase inhibitor; PBC, platinum-based chemotherapy; Q, quartile; SE, standard error; TTD, time to treatment discontinuation

treatment discontinuation were disease progression (n = 80, 49.4 %), adverse events (n = 45, 27.8 %), and completed planned treatment (n = 30, 18.5 %).

3.6. rwPFS from end of 1L PBC

Kaplan–Meier analyses of rwPFS were conducted among patients receiving 1L MT and 1L AS. rwPFS was significantly longer for 1L MT compared with 1L AS (log-rank $p < 0.0001$) (Table 5; Fig. 1A). Median rwPFS was 26.9 (95 % CI 21.3, not reached) and 11.3 (95 % CI 9.5, 13.0) months for the 1L MT and 1L AS cohorts, respectively. A total of 49.1 % (95 % CI 39.8, 57.7) of patients were still alive without disease progression at 36 months in the 1L MT cohort, compared with 24.5 % (95 % CI 18.1, 31.4) in the 1L AS cohort.

3.7. OS from end of 1L PBC

OS was also compared between patients receiving 1L MT and 1L AS. Median OS was not reached for either the 1L MT or 1L AS cohort; however, OS was significantly longer in the 1L MT cohort than in the 1L AS cohort (log-rank $p < 0.0001$) (Table 5; Fig. 1B). At 36 months, probability of survival was 82.4 % (95 % CI 72.2, 89.1) in the 1L MT cohort and 58.0 % (95 % CI 46.0, 68.2) in the 1L AS cohort.

4. Discussion

Previous studies have shown that MT with PARPi and/or bevacizumab are effective treatment strategies for patients with advanced OC; however, previous research has demonstrated that they may be underutilized by physicians (Chan et al., 2023; Turell et al., 2020). This study builds upon existing real-world evidence of the benefits of 1 l MT in stage III/IV OC. Additionally, it sought to provide a comprehensive understanding of treatment patterns and biomarker testing, and used multivariable analyses to determine clinical predictors of MT use among patients who received 1L PBC in the US community oncology setting. Our findings showed that 1L MT with PARPi and/or bevacizumab was associated with better survival outcomes compared with 1L AS. However, fewer than 50 % of patients in this study received 1L MT following 1L PBC, despite guideline recommendations and previous studies demonstrating effectiveness in patients with advanced OC (Bartoletti et al., 2020; Burger et al., 2011; Ibrahim et al., 2020; National Comprehensive Cancer Network, 2024; Tattersall et al., 2022).

Biomarker testing is critical for identifying patients most likely to benefit from MT and to guide treatment decisions (O'Malley et al., 2023). Generally, biomarker test rates were low in the study population. The PARPi MT cohort had the highest proportions of patients testing positive for *BRCA* mutation (14.6 %); however, a large proportion of patients in each cohort were not tested. This may be because homologous recombinant deficiency and *BRCA* testing results were only available in the unstructured data field. During the unstructured data abstraction, patients' medical records were searched for homologous recombinant deficiency and *BRCA* testing. However, it is possible that a patient received NGS testing but their results were not captured, their NGS results were not scanned in or available on or prior to the end of the study observation period and therefore unknown to the oncologist. It is also possible that the tests were performed, and the results were known to the oncologist, supporting appropriate clinical decisions. However, in this study, both *BRCA* 1/2 positive status and derived homologous recombinant deficiency status were associated with a slightly increased likelihood of 1L maintenance therapy initiation. Other real-world database studies have found MT to be more common among patients with a *BRCA* mutation (Garofalo et al., 2019; Moss et al., 2021). Homologous recombination deficiency testing in our study cohort was at very low rates, with approximately 90 % of the study patients lacking documented homologous recombination deficiency results. Although the large proportion of patients without genetic testing results may have

Table 5
Kaplan–Meier estimates of rwPFS and OS from end of 1L PBC among patients overall and stratified by 1L MT and 1L AS.

Variable	Overall (N = 554[a])	1L MT cohort (N = 239)	AS cohort (N = 315)	Log-rank p-value	Hazard ratio (95 % CI)[b]
rwPFS				**<0.0001**	**0.45 (0.35, 0.58)**
Events, n (%)	286 (51.6)	87 (36.4)	199 (63.2)		
Mean (SE), months	17.5 (0.5)	19.8 (0.6)	14.8 (0.6)		
Median (95 % CI), months	16.1 (13.4, 19.8)	26.9 (21.3, NR)	11.3 (9.5, 13.0)		
Q1, Q3	7.6, NR	11.1, NR	5.3, 29.7		
PFS probabilities, % (95 % CI)					
6 months	81.9 (78.4, 84.8)	92.5 (88.3, 95.2)	73.8 (68.5, 78.3)		
12 months	57.8 (53.4, 62.0)	73.0 (66.5, 78.4)	46.6 (40.7, 52.2)		
18 months	47.1 (42.4, 51.6)	62.0 (54.5, 68.6)	36.2 (30.5, 42.0)		
24 months	39.6 (34.6, 44.5)	52.4 (43.7, 60.3)	30.3 (24.5, 36.3)		
30 months	34.5 (28.9, 40.2)	49.1 (39.8, 57.7)	24.5 (18.1, 31.4)		
36 months	34.5 (28.9, 40.2)	49.1 (39.8, 57.7)	24.5 (18.1, 31.4)		
OS				**<0.0001**	**0.36 (0.22, 0.59)**
Events, n (%)	94 (17.0)	21 (8.8)	73 (23.2)		
Mean (SE), months	29.6 (0.5)	26.5 (0.4)	28.0 (0.7)		
Median (95 % CI), months	NR (NR, NR)	NR (NR, NR)	NR (34.4, NR)		
Q1, Q3	30.9, NR	NR, NR	24.6, NR		
OS probabilities, % (95 % CI)					
6 months	95.8 (93.7, 97.2)	98.7 (96.1, 99.6)	93.5 (90.1, 95.8)		
12 months	90.1 (87.2, 92.5)	95.7 (91.9, 97.8)	85.9 (81.3, 89.4)		
18 months	84.5 (80.7, 87.6)	91.5 (86.0, 94.9)	79.3 (73.8, 83.8)		
24 months	78.6 (73.8, 82.6)	88.3 (81.5, 92.7)	71.5 (64.7, 77.3)		
30 months	74.3 (68.5, 79.2)	82.4 (72.2, 89.1)	68.4 (60.8, 74.8)		
36 months	67.3 (58.3, 74.7)	82.4 (72.2, 89.1)	58.0 (46.0, 68.2)		

1L, first-line; AS, active surveillance; CI, confidence interval; MT, maintenance therapy; NR, not reached; OS, overall survival; PBC, platinum-based chemotherapy; PFS, progression-free survival; Q, quartile; rwPFS, real-word progression-free survival; SE, standard error.
Values in bold indicate statistically significant results.
[a] Of the 600 chart-reviewed patients included in this study, 554 received MT or AS; this is presented as overall here.
[b] 1L AS cohort was the reference group.

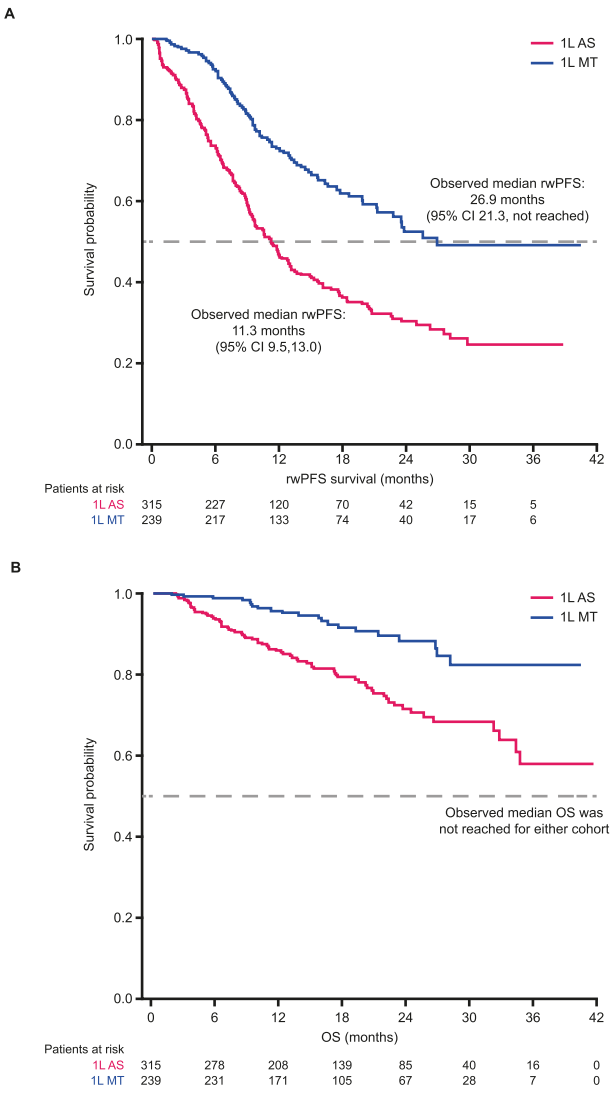

Fig. 1. Kaplan–Meier curve for (a) rwPFS and (b) OS among patients who received AS or MT following 1L PBC. rwPFS and OS were from the end date of 1L PBC. 1L, first-line; AS, active surveillance; CI, confidence interval; MT, maintenance therapy; OS, overall survival; PBC, platinum-based chemotherapy; rwPFS, real-world progression-free survival.

affected the generalizability of the study, missing data is a common limitation of EHR studies. Therefore, in this study, it was not possible to determine if the lack of documented biomarker results was due to an absence of testing or if the testing was performed but just not recorded in the EHR. Low rates of homologous recombination deficiency testing has been observed in another study in the real-world setting (Chase et al., 2023). These findings highlight the need for better integration of tumor and genetic testing results in EHRs to reduce the number of patients with undocumented results. They also highlight the need for further studies with higher documented *BRCA* and homologous recombinant deficiency testing results to identify if there is a stronger association between genetic testing and 1L MT initiation.

Approximately half (52.5 %) of patients with OC in this study

underwent AS instead of receiving guideline-recommended MT in the 1L setting. In a recent US real-world evidence study, it was shown that 76.5 % (n = 539/705) of patients with stage III or IV OC who completed 1L PBC had received AS, whereas 23.5 % (n = 166/705) received PARPi MT (Chan et al., 2023). Other US-based real-world studies have reported rates of between 37 % and 78 % of women with OC not receiving 1L MT, despite potentially benefiting and despite National Comprehensive Cancer Network guideline recommendations (Chase et al., 2023; Garofalo et al., 2019).

Older age (75–84 years) was found in our multivariate regression analysis to be associated with a lower likelihood of receiving 1L MT. Similarly, a retrospective study of patients with recurrent OC by Moss et al. found MT in the real-world setting to be more common in younger patients (Moss et al., 2021). This may in part be due to elderly patients with cancer receiving multiple medications for comorbidities, which need to be considered when planning treatment (National Comprehensive Cancer Network, 2023). Despite a previous study demonstrating effectiveness of MT in older patients (aged ≥65 years old) (Sabatier et al., 2023), this population remains undertreated. Investigations of larger populations of elderly patients from real-world settings are needed to better support recommendations for MT.

Our analysis also indicated that patients with stage IV disease (versus IIIA–IIIB) and patients receiving neoadjuvant treatment had a higher probability of initiating 1L MT. Real-world studies and a recent meta-analysis have suggested that stage IV disease, receipt of neoadjuvant therapy, visible residual disease following surgery, and *BRCA* wild-type status are associated with poorer prognosis in OC (Chan et al., 2023; Chase et al., 2023; Kim et al., 2023). In our study, the results for patients with stage IV OC who received 1L MT are consistent with National Comprehensive Cancer Network recommendations (National Comprehensive Cancer Network, 2024) and also with improved outcomes seen in clinical trials evaluating MT versus placebo (e.g. PRIMA and PRIME trials of niraparib monotherapy) (González-Martín et al., 2019; Li et al., 2022) and the PAOLA-1 trial of olaparib in combination with bevacizumab (Ray-Coquard et al., 2019).

In this study, disease progression was the most reported reason for discontinuation of 1L MT (n = 80/162, 49.4 %), after a median time to discontinuation of 13.6 months. Additionally, 27.8 % (n = 45/162) of patients discontinued their MT due to an adverse event, which is higher than in previous clinical studies (Friedlander et al., 2023). However, it is not unexpected to have differing rates of adverse events in real-world studies compared with clinical trials, as patients in real-world studies are typically older and have more comorbidities (Friedlander et al., 2023).

Patients who received MT in the 1L setting showed improved outcomes compared with the 1L AS cohort. Receipt of MT in the 1L setting was associated with significantly longer PFS compared with 1L AS (26.9 months versus 11.3 months; $p < 0.0001$), as well as significantly higher probability of PFS at 1, 2, and 3 years and a 55 %-reduced risk of disease progression versus 1L AS. These findings are consistent with another retrospective real-world analysis, which observed significantly improved rwPFS among patients with advanced OC who received 1L PARPi monotherapy compared with 1L AS (median rwPFS not reached for PARPi; 9.5 months for AS; $p < 0.001$) (Chan et al., 2023). The 12-month rwPFS rates in Chan et al. were 64.6 % for the PARPi monotherapy cohort and 43.7 % for the AS cohort (Chan et al., 2023) – similar to the 12-month PFS probabilities observed in our study. Consistent with the reduced risk of disease progression observed in the 1L MT cohort in our study, maintenance with PARPi in Chan et al. was shown to be an independent predictor for improved rwPFS compared with AS (adjusted hazard ratio 0.47; 95 % CI 0.34, 0.63; $p < 0.001$) (Chan et al., 2023).

Patients in the 1L MT cohort also demonstrated better OS outcomes than patients in the 1L AS cohort, including higher OS probabilities at 1, 2, and 3 years and a 64 %-reduced risk of death. Previous studies have had conflicting findings regarding the ability of PARPi to prolong OS, with some clinical trials reporting little or no benefit versus placebo in patients with recurrent OC (Coleman et al., 2022; Matulonis et al., 2023). A 7-year follow-up of patients in the SOLO1/GOG 3004 trial showed a clinically meaningful (but non-statistically significant) improvement in OS with olaparib MT among patients with advanced OC (DiSilvestro et al., 2023). In our study, both cohorts did not reach median OS during a median 19.2-month follow-up; a longer follow-up period would be warranted to observe long-term OS effects. However, the Phase 3 PRIMA clinical trial reported similar OS rates at 24 months among patients with advanced OC receiving MT compared to our study (84 % versus 88 %) (González-Martín et al., 2019).

Data for this study were captured from the oncology-specific iKnowMed EHR and supplementary chart abstraction. However, the iKnowMed EHR used in this study contains EHR data that are collected for clinical practice rather than research purposes; therefore, a missingness of data is anticipated. The data collection methods and reporting practices of the physician may not be standardized across all practices using the EHR system. Additionally, as with all administrative databases, iKnowMed data are subject to coding errors, which may introduce some level of misclassification bias. Furthermore, due to the retrospective nature of this study, response assessments were only determined and captured based on a chart review. Unfortunately, these data were not available for many patients. Additionally, The US Oncology Network iKnowMed EHR contains information on patients only when they are seen by a US Oncology Network physician; therefore, if a patient also saw a physician outside of The US Oncology Network, access to these records would be limited. In addition, not all community oncology practices are included in the database; therefore, the study may not represent all patients across the network. The US Oncology Network encourages use of evidence-based treatment guidelines. Therefore, practices that participate in The US Oncology Network may be different from other community oncology practices in the patient population. The Kaplan-Meier estimates used in this study to describe rwPFS and OS did not account for confounding factors identified in the multivariate logistic regression model; therefore, future studies should consider also using a Cox proportional hazard model including the variables that were significant in the logistic regression model, to reduce confounding.

5. Conclusions

The findings from our study demonstrate that patients aged >65 years, specifically 75–84 years, were less likely to receive 1L MT than patients aged <65 years. Additionally, despite clinical evidence and guideline recommendations, rates of MT in the 1L setting were low, and a considerable proportion of patients were not tested for biomarkers associated with PARPi efficacy. Our findings also suggest that 1L MTs may improve rwPFS and OS in patients with advanced or recurrent OC, compared with patients who receive AS. These results demonstrate that there is a gap in patient care in clinical practice and a need to further emphasize the option for maintenance therapy among this patient population. There is a need to better understand provider preferences and/or challenges in the prescribing of MTs, to help to understand the uptake of MTs in this patient population.

Ethics statement

No direct subject contact or primary collection of individual human subject data has occurred in this study; therefore, informed consent, ethics committee or Institutional Review Board approval were not required.

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CRediT authorship contribution statement

Dana M. Chase: Writing – review & editing, Writing – original draft, Supervision, Investigation, Formal analysis, Conceptualization. **Laura Iadeluca:** Writing – review & editing, Writing – original draft, Supervision, Project administration, Methodology, Investigation, Formal analysis. **Jonathan Lim:** Writing – review & editing, Writing – original draft, Supervision, Methodology, Investigation. **Wan-Yu Tseng:** Writing – review & editing, Project administration, Methodology. **Purva Bulsara:** Writing – review & editing, Project administration, Methodology, Formal analysis. **Gregory Patton:** Writing – review & editing, Project administration.

Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: The authors declare the following real or perceived conflicts of interest during the past 3 years: Dana M. Chase reports personal fees from AstraZeneca, Eisai, GSK, Immunogen, and Seagen/Genmab. Laura Iadeluca and Jonathan Lim are employees of, and/or hold stocks/shares in, GSK. Wan-Yu Tseng, Purva Bulsara, and Gregory Patton are employees of Ontada (a subsidiary of McKesson) and may hold stocks/shares in McKesson.

Data availability

In accordance with the journal's guidelines, we will provide our data for independent analysis by a team selected by the Editorial Team for the purposes of additional data analysis or for the reproducibility of this study in other centers, if such is requested.

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Appendix A. Supplementary material

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