

Real-World Treatment Patterns and Outcomes in US Platinum-Resistant Ovarian Cancer Patients: Characterizing the Unmet Clinical Need

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Introduction

- Ovarian cancer (OC) is the second most frequently diagnosed gynecological malignancy in the United States (US) and has the highest mortality of all gynecological cancers.¹ Platinum-resistant ovarian cancers (PROC) are among the most aggressive and recurrent forms of gynecologic malignancies
- PROC is typically defined as progression within 180 days from the last dose of platinum.^{2,3} It is estimated that up to 80% of OCs become platinum-resistant at some point in the course of disease^{4,5}
- The National Comprehensive Cancer Network (NCCN) guidelines recommend use of nonplatinum chemotherapy monotherapy or in combination with targeted or hormonal agents or approved antibody drug conjugates (ADC) as preferred therapies¹⁰
- A prior real-world, retrospective US cohort analysis limited to PROC patients initiating guideline-preferred therapies demonstrated poor clinical outcomes, evidenced by short progression-free survival (rwPFS) (~3 months) and overall survival (rwOS) (7-10 months) and low real-world response rate (rwRR; 20%)⁷
- Rechallenging with platinum-based chemotherapies is becoming more prevalent, despite not being preferred in this setting^{9,10}
- As the PROC treatment landscape continues to evolve, this work aims to characterize a broad real-world PROC cohort utilizing any therapy, including platinum rechallenge and approved ADCs, to evaluate patient characteristics, treatment utilization, and outcomes in the US

Objectives

- In a broad real-world PROC cohort:
 - Evaluate clinical outcomes (overall survival (rwOS), time to next treatment (rwTTNT), and time to treatment discontinuation (rwTTD))
 - Describe index line of therapy (LOT) treatments, including platinum rechallenge
 - Describe patient and clinical characteristics
 - Assess biomarker testing patterns and status

Methods

Design

- Noninterventional, retrospective, observational study using US-based advanced ovarian cancer data from Flatiron Health, a longitudinal, oncology-specific, electronic health record-derived database, composed of deidentified patient-level data⁸
- Primary study cohort ("broad cohort"):**
 - Adult women with stage III/IV OC at initial diagnosis on or after 05/01/2020
 - Received first-line (1L) platinum-based chemotherapy (PBC)
 - Received a subsequent therapy
 - Met criteria for PROC at second line (2L), third line (3L), or fourth line (4L) (see **Figure 1** for the study cohort attrition)
 - Had at least 3 months of potential follow-up from index LOT initiation to data cutoff (02/28/2025)
- Secondary study cohort (guideline-preferred, "SOC cohort") additional criterion**
 - Received in the index line any of the following drugs as monotherapy or in combination with one another: doxorubicin, doxorubicin pegylated liposomal, paclitaxel, paclitaxel protein-bound, topotecan, gemcitabine, cyclophosphamide, docetaxel, etoposide, ifosfamide, irinotecan, ixabepilone, melphalan, pemetrexed, vinorelbine, bevacizumab, or mirvetuximab soravtansine-gynx
- PROC definition**
 - 2L index: Platinum-free interval (PFI) between 90 and 180 days (from last administration of platinum in 1L to start of next therapy)
 - 3L or 4L index: PFI <180 days (from last administration of platinum in prior line to start of next therapy)
 - Indexing approach: utilized the first-eligible LOT, the earliest eligible treatment line meeting PROC criteria, as the index LOT
- Index date was the start date of the index LOT

Measures

- Outcomes: Real-world time to treatment discontinuation or death (rwTTD), time to next treatment or death (rwTTNT), and overall survival (rwOS)

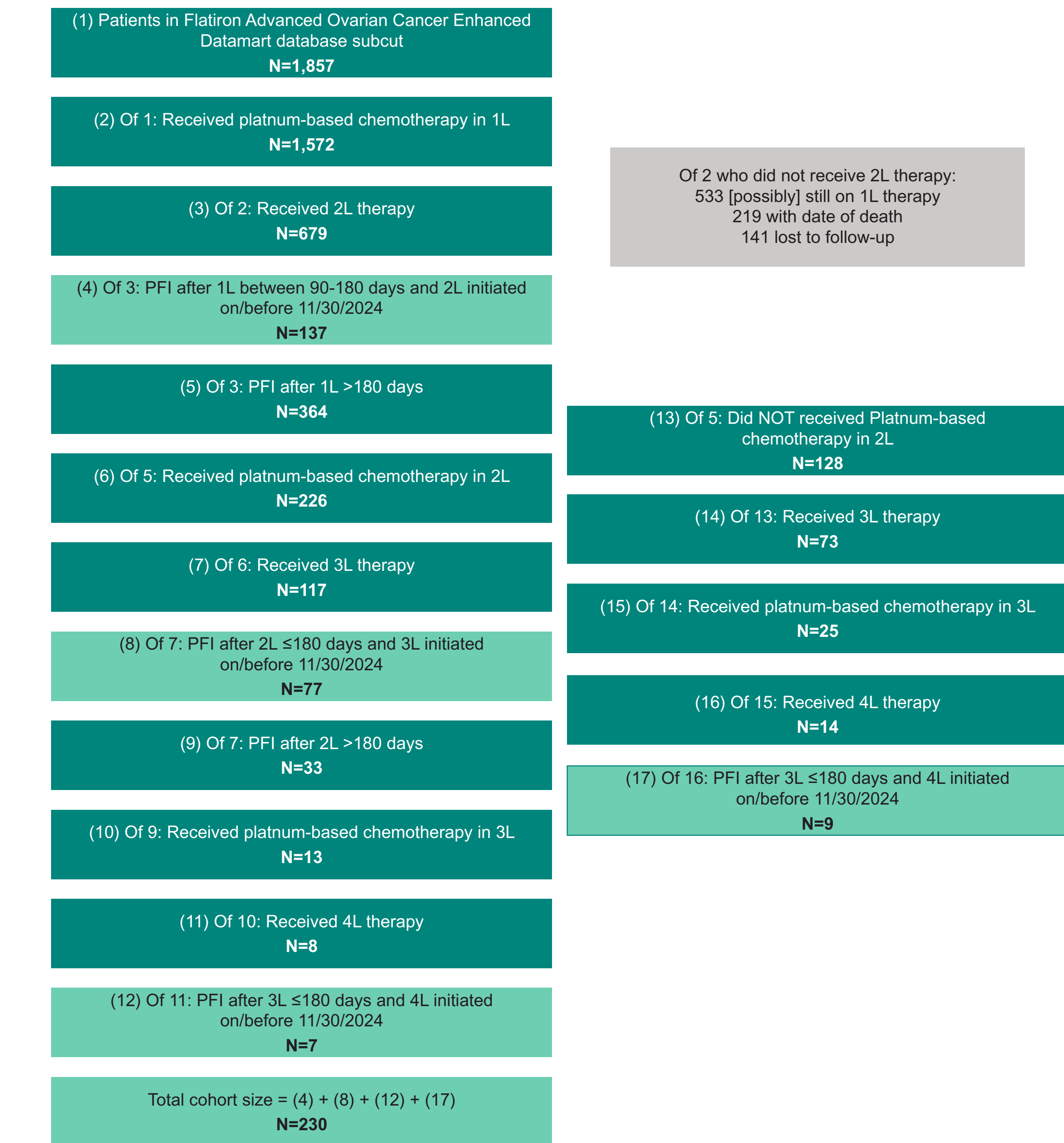
Analyses

- Descriptive statistics summarized demographics and clinical characteristics, index LOT treatments, and clinical outcomes
- Kaplan-Meier methods estimated real-world time-to-event outcomes

Results

- A total of 230 women with PROC were included in the broad cohort (**Figure 1**): 137 first-eligible at 2L (59.6%), 77 first-eligible at 3L (33.5%), and 16 first-eligible at 4L (7.0%). In the SOC cohort, 106 patients were included, with 50% of index LOTs in 2L, 44.3% in 3L, and 5.7% in 4L (**Table 1**)

Figure 1. Broad cohort attrition



1L, first-line; 2L, second-line; 3L, third-line; 4L, fourth-line; PFI, platinum-free interval.

Patient and clinical characteristics

- Across the broad and SOC cohorts, the median age was 70 years. Patients were primarily White (70.0%-71.7%), with an ECOG performance score of 0-1 (59.4%-60.4%), and treated within community practices (74.3%-74.5%; **Table 1**)
- Slightly over half the sample was diagnosed between 2020 and 2021 (52.6%-57.5%). Serous histology was the most common (77.0%-78.3%), while patients were evenly split for stage at diagnosis (stage III: 50.4%-52.8%; stage IV: 47.2%-49.6%)
- The majority of patients had normal liver function (71.7%-73.0%). However, 63.5%-68.8% of patients had some level of renal impairment

Table 1. Demographic and clinical characteristics of real-world platinum-resistant ovarian cancer patients for the broad cohort and the SOC cohort

Demographic or clinical features	Broad cohort (N=230)	SOC cohort (N=106)
Age at index date, yrs		
Median (Q1, Q3)	70.0 (61.0, 76.0)	70.0 (61.0, 76.0)
Age group at index date, yrs		
31-54	22 (9.6%)	9 (8.5%)
55-64	59 (25.7%)	32 (30.2%)
65-74	79 (34.3%)	30 (28.3%)
≥75	70 (30.4%)	35 (33.0%)
Race, n (%)		
Asian	7 (3.0%)	≤5
Black or African American	16 (7.0%)	≤10
White	161 (70.0%)	76 (71.7%)
Other race	18 (7.8%)	≤10
Unknown	28 (12.2%)	13 (12.3%)
Ethnicity, n (%)		
Hispanic or Latino	18 (7.8%)	9 (8.5%)
Not Hispanic or Latino	158 (68.7%)	75 (70.8%)
Unknown	54 (23.5%)	22 (20.8%)
BMI, kg/m² at index date		
Median (Q1, Q3)	26.5 (22.4, 31.5)	25.5 (22.0, 29.4)
Geographic region, n (%)		
Midwest	16 (7.0%)	7 (6.6%)
Northeast	22 (9.6%)	9 (8.5%)
South	90 (39.1%)	47 (44.3%)
West	36 (15.7%)	12 (11.3%)
Unknown	66 (28.7%)	31 (29.2%)
Practice type, n (%)		
Academic	45 (19.6%)	20 (18.9%)
Community	171 (74.3%)	79 (74.5%)
Both	14 (6.1%)	7 (6.6%)
Socioeconomic status (SES) at index date, n (%)		
1 (lowest SES)	30 (13.0%)	11 (10.4%)
2	33 (14.3%)	12 (11.3%)
3	44 (19.1%)	20 (18.9%)
4	48 (20.9%)	23 (21.7%)
5 (highest SES)	54 (23.5%)	28 (26.4%)
Unknown	21 (9.1%)	12 (11.3%)
Histology at advanced diagnosis, n (%)		
Clear cell	6 (2.6%)	≤5
Endometrioid	≤5	≤5
Epithelial NOS	37 (16.1%)	16 (15.1%)
Serous	177 (77.0%)	83 (78.3%)
Unknown/not documented	≤5	≤5
Stage at advanced diagnosis, n (%)		
III	116 (50.4%)	56 (52.8%)
IV	114 (49.6%)	50 (47.2%)
Year of advanced diagnosis, n (%)		
2020-2021	121 (52.6%)	61 (57.5%)
2022-2024	109 (47.4%)	45 (42.5%)
ECOG at index date, n (%)		
0-1	139 (60.4%)	63 (59.4%)
2-4	28 (12.2%)	17 (16.1%)
Missing	63 (27.4%)	26 (24.5%)
Liver function at index date, n (%)		
Moderately impaired	≤5	≤5
Mildly impaired	22 (9.6%)	15 (14.2%)
Normal	168 (73.0%)	76 (71.7%)
No data in window	39 (17.0%)	14 (13.2%)
Renal function at index date, n (%)		
Severely impaired	6 (2.6%)	≤5
Moderately impaired	60 (26.1%)	33 (31.1%)
Mildly impaired	80 (34.8%)	38 (35.8%)
Normal	61 (26.5%)	28 (26.4%)
No data in window	23 (10.0%)	≤5
LOT number of index, n (%)		
2L	137 (59.6%)	53 (50.0%)
3L	77 (33.5%)	47 (44.3%)
4L	16 (7.0%)	6 (5.7%)

- Almost all patients were tested for BRCA mutation (**Table 2**; 93.5%), with 9.3% of those having record of any type of mutation. HRD testing occurred for over half the cohort (53.0%), with 36.9% of those having positive results. GIS status was largely unknown, as only 16.1% of patients were tested
- FRα testing was performed for 47.4% of patients, of whom 34.9% had high expression (percent staining ≥75% and stain intensity 2+; **Table 2**)

Table 2. Biomarker testing status of real-world platinum-resistant ovarian cancer patients for the broad and SOC cohorts

Biomarker status ^{b,c}	Broad cohort (N=230)	SOC cohort (N=106)
BRCA tested, n (%)		
Yes	215 (93.5%)	103 (97.2%)
Any mutation	20 (9.3%)	7 (6.8%)
No mutation	185 (86.0%)	91 (88.3%)
Unknown	10 (4.7%)	≤5
HRD tested, n (%)		
Yes	122 (53.0%)	62 (58.5%)
HRD positive	45 (36.9%)	19 (30.6%)
HRD negative	68 (55.7%)	41 (66.1%)
Unknown	10 (8.2%)	≤5
GIS tested, n (%)		
Yes	37 (16.1%)	22 (20.8%)
GIS positive	10 (27.0%)	≤5
GIS negative	24 (64.9%)	15 (68.2%)
Unknown	≤5	≤5
FRα tested, n (%)		
Yes	109 (47.4%)	61 (57.5%)
FRα positive (any expression)	52 (47.7%)	31 (50.8%)
FRα high expression ^d	38 (34.9%)	18 (29.0%)
FRα negative	58 (53.2%)	30 (49.2%)
Unknown	≤5	≤5

^bBiomarker status was defined within the interval of ever before index date to +30 days of index date.

^cPresence of biomarker testing is on the patient level. N and percent specific results are on the test level; a patient may have more than 1 test result. N unique tests is larger than N patients.

^dHigh FRα expression defined as percent staining ≥75% and stain intensity 2+.

Index LOT treatments

- Index LOT distribution (**Table 3**):
 - Broad cohort: 59.6% of index LOTs were in 2L, 33.5% in 3L, and 7.0% in 4L
 - ≤SOC cohort index treatments were previously reported⁷

Table 3. Real-world index LOT treatments of broad cohort^a platinum-resistant ovarian cancer patients

Broad Cohort Index LOT	Overall (N=230)	2L (n=137)	3L (n=77)	4L (n=16)
Nonplatinum chemotherapy monotherapy	44 (19.1%)	19 (13.9%)	20 (26.0%)	5 (31.2%)
<i>Doxorubicin</i>	30 (68.2%)	13 (68.4%)	15 (75.0%)	2 (40.0%)
Nonplatinum chemotherapy + bevacizumab	43 (18.7%)	25 (18.2%)	16 (20.8%)	2 (12.5%)
<i>Doxorubicin + bevacizumab</i>	29 (67.4%)	17 (68.0%)	11 (68.8%)	1 (50.0%)
Mirvetuximab soravtansine-gynx-containing regimen	19 (8.3%)	4 (2.9%)	12 (5.6%)	3 (18.8%)
Platinum-containing regimen	53 (23.0%)	42 (30.7%)	9 (11.7%)	2 (12.5%)
Other	71 (30.9%)	47 (34.3%)	20 (26.0%)	4 (25.0%)

^aIndex LOT treatments for the SOC cohort were previously reported.⁷

Outcomes in the broad cohort^a

- Real-world outcomes for the broad cohort are presented in **Table 4**
- Outcomes for the SOC cohort were previously reported⁷

Table 4. Real-world outcomes of broad cohort platinum-resistant ovarian cancer patients

Outcome parameter	Broad Cohort (N=230)
rwTTD, median (95% CI), months	3.3 (2.9, 3.7)
rwTTNT, median (95% CI), months	5.6 (4.9, 6.9)
rwOS, median (95% CI), months	12.6 (10.7, 16.6)

Figure 2. Kaplan-Meier curve and estimates for real-world overall survival for patients with platinum-resistant ovarian cancer from the first-eligible index LOT in the broad cohort

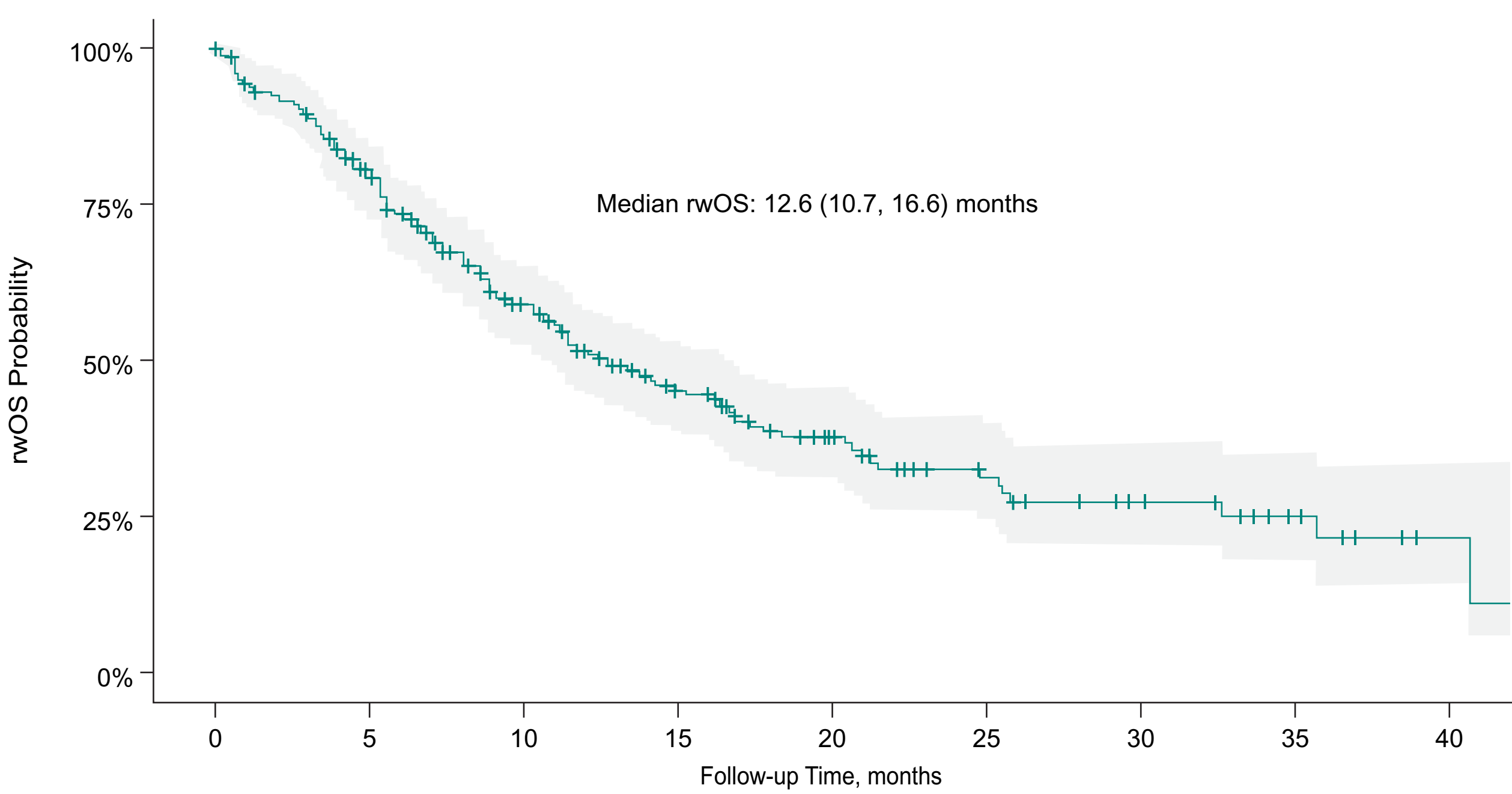


Figure 3. Kaplan-Meier curve and estimates for real-world time to next treatment for "patients with platinum-resistant ovarian cancer from the first-eligible index LOT in the broad cohort"

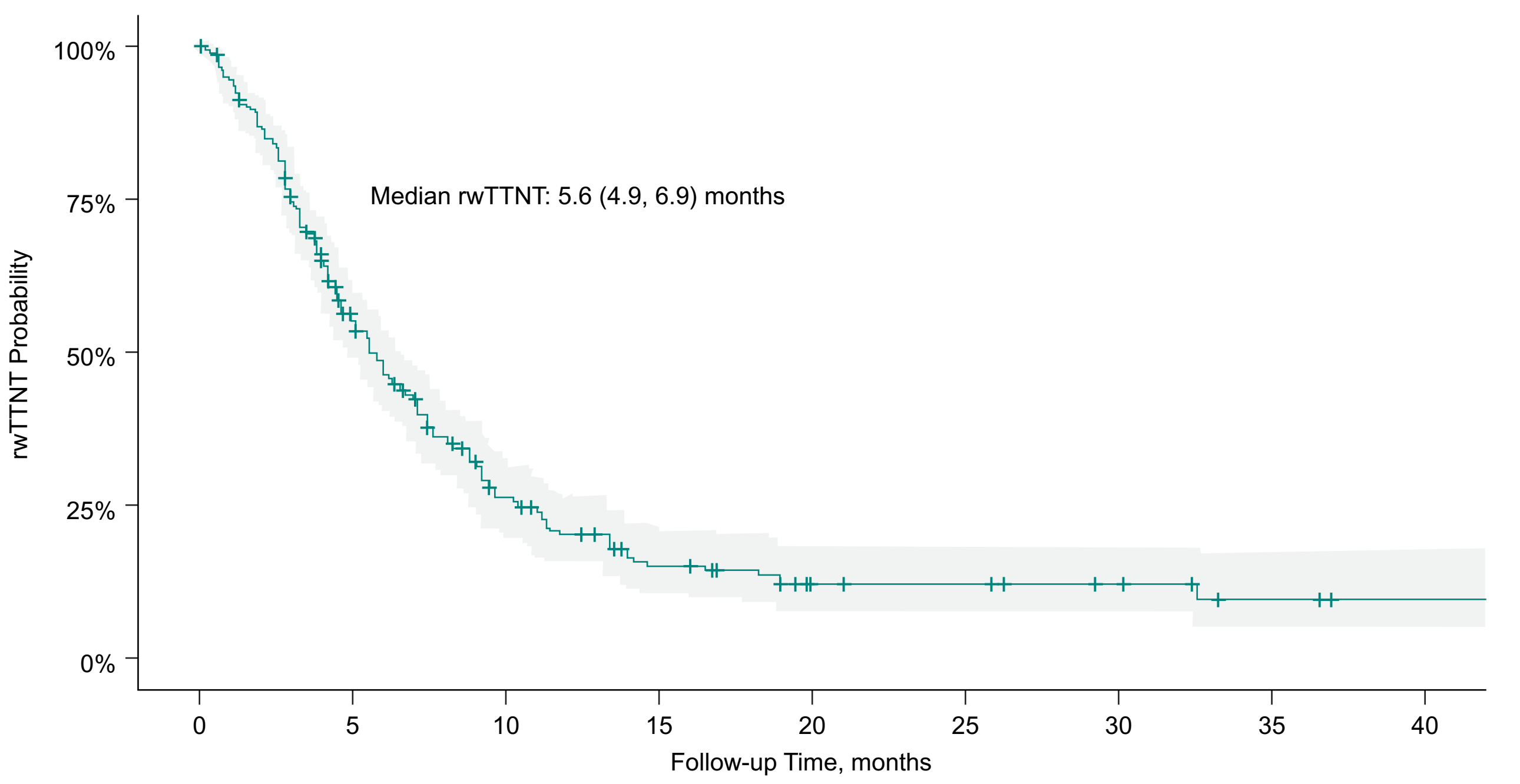
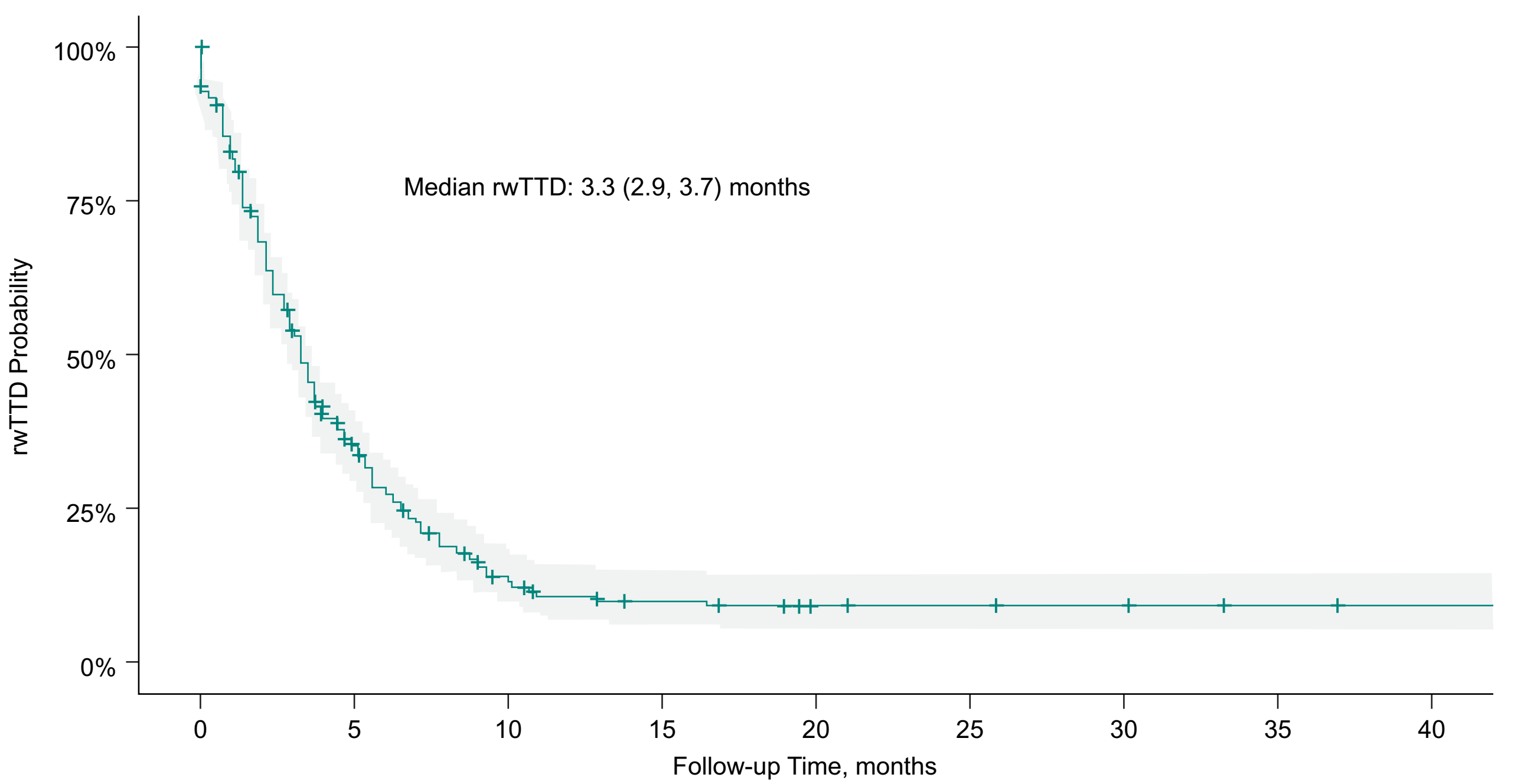


Figure 4. Kaplan-Meier curve and estimates for real-world time to treatment discontinuation for patients with platinum-resistant ovarian cancer from the first-eligible index LOT in the broad cohort



Conclusions

- Real-world PROC cohorts initiating SOC only and broad cohort initiating any therapy (including platinum rechallenge) have similar clinical and demographic characteristics
- Biomarker testing is widespread, regardless of therapy choice; nearly all PROC patients were BRCA tested, while over half were tested for HRD and FRα
- Despite preferred guideline recommendations, more than half of the broad cohort utilized a platinum-based therapy or "other" therapy, highlighting provider and patient willingness to utilize non-SOC treatments, possibly due to limitations with available options in a real-world setting
- The previously reported SOC cohort outcomes demonstrated short rwPFS and rwOS and low rwRR.⁷ This broad cohort analysis similarly highlights a short duration of index treatment and overall survival, suggesting that utilization of non-SOC therapies (ie, platinum rechallenge) may not improve outcomes at a population level
- Regardless of therapy initiated in the PROC setting, a high unmet need persists, highlighting the need for improved treatment options

Limitations

- Patients diagnosed at early stages whose disease later advanced were not included
- Limited ability to assess uptake of FRα testing and mirvetuximab soravtansine-gynx, which was approved in November 2022, halfway through the study period
- Analyses not designed to test differences across treatment regimens

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Disclosure

KMM, HD, KM, and MM are employees of Merck Sharp & Dohme LLC, a subsidiary of Merck & Co., Inc., Rahway, NJ, USA, who may own stock and/or hold stock options in Merck & Co., Inc., Rahway, NJ, USA. OT, SV, CN, YX, EM, and BG are employees of Daiichi Sankyo, Inc., Basking Ridge, NJ, USA, who may own stock and/or hold stock options in Daiichi Sankyo, Inc., Basking Ridge, NJ, USA. RS and KNM have received consulting fees from Merck Sharp & Dohme LLC, a subsidiary of Merck & Co., Inc., Rahway, NJ, USA.