Real-World Average Dose of PARP Inhibitors Used as Maintenance Therapy for Platinum-Sensitive Recurrent Ovarian Cancer

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Background

- Up to 85% of women with ovarian cancer will eventually relapse after primary cytoreductive surgery and platinum-based chemotherapy[1]
- There is a need to extend the progression-free interval with maintenance treatment while maintaining health-related quality of life (QoL)
- The poly(ADP-ribose) polymerase inhibitors (PARPi) niraparib, olaparib, and rucaparib are approved in the United States and Europe for maintenance treatment of platinum-sensitive recurrent ovarian cancer (PSROC)[2,3]
- Modifications to the recommended doses may occur due to adverse reactions, co-morbidities, and the use of concomitant medication

Objectives

- The primary objective of this study was to determine the real-world average doses of PARPi therapies used in the PSROC maintenance setting
- The secondary objective was to determine the average starting maintenance dose

Methods

- This retrospective, real-world study utilized the Flatiron Health electronic health record (EHR)-derived de-identified oncology database representing more than 280 cancer clinics and 2.2 million patients from throughout the United States
  - The breakdown of patients by practice type is ~80% community and ~20% academic
  - Lines of therapy are oncologist-defined and rule-based
- Patients diagnosed with invasive ovarian, fallopian tube, and/or primary peritoneal cancer (collectively referred to as ovarian cancer) from January 1, 2011 to August 31, 2019 who received PARPi maintenance therapy in the second line (2L) or later (2L+) after completing ≥2 platinum-based lines of therapy (LOT) and were platinum sensitive at the start of the subsequent platinum-based LOT were included in the study
- Niraparib, olaparib, and/or rucaparib were considered maintenance therapy when all of the non-maintenance drugs in the combination were dropped or PARPi was added within 90 days after the non-maintenance drug(s) in the LOT were stopped
- Patients were excluded from the study if they were missing PARPi start or end dates in the 2L+ setting, had >1 PARPi drug in the same maintenance LOT, or received olaparib capsules (started olaparib therapy prior to the tablet FDA approval date of August 17, 2017 or took an olaparib dose of 400 mg twice a day)
- Dose per day over the course of maintenance therapy was calculated per patient as dose * dose administration * days on drug
  - Dose per day was weighted by days on each dose
  - If there were gap days during the qualifying maintenance line, days off drug were weighted with a dose of zero
  - Patients with missing or a non-specific dose or dosing schedule were excluded from the average dose analyses

Results

- Recommended daily doses for niraparib, olaparib, and rucaparib are 300 mg, 600 mg, and 1200 mg respectively (representing "standard" recommended doses)
- Results of this analysis are reported for 2L, 2L+, and third line or later (3L+)
- 142 patients were included: 75 received niraparib, 38 received olaparib, and 29 received rucaparib (**Table 1**)
- Patient characteristics and baseline demographics are shown in **Table 2**
- Average daily doses over the course of treatment are shown in **Figure 1**
- Average starting doses are shown in **Figure 2**

Table 1. Study Attrition

Patient Population	Overall N (%)	Niraparib N (%)	Olaparib N (%)	Rucaparib N (%)
Patients with ovarian cancer initial diagnosis from January 1, 2011 to August 31, 2019	6571 (100)			
Patients with ≥2 lines of platinum-containing therapy	1222 (18.6)			
Patients who demonstrate platinum-sensitive disease in the subsequent platinum chemo course (subsequent line starts ≥6 months after last dose of prior line of platinum chemo)	941 (14.3)			
Patients with PARPi (niraparib, olaparib, rucaparib) maintenance in 2L+	153 (2.3)	76 (100)	47 (100)	30 (100)
Excluded patients with missing PARPi oral start or end dates in 2L+ maintenance or >1 PARPi drug for maintenance in same line of therapy	151 (2.3)	75 (99)	47 (100)	29 (97)
Excluded olaparib patients likely on capsule formulation – restrict to patients who started olaparib after August 17, 2017 or did not have a dose of 400 mg twice a day[a]	142 (2.2)	75 (99)	38 (81)	29 (97)
Final study population	142 (100)	75 (53)	38 (27)	29 (20)

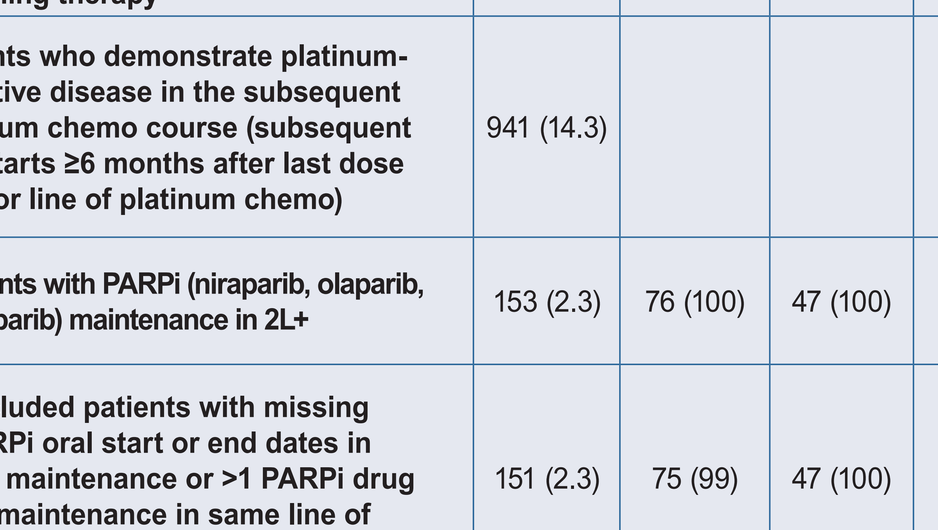
[a]August 17, 2017 is the date of FDA approval for the tablet formulation of olaparib.
2L+=second line or later; PARPi=poly(ADP-ribose) polymerase inhibitors.

Table 2. Patient Characteristics and Baseline Demographics

Characteristic	Niraparib N=75	Olaparib N=38	Rucaparib N=29
Mean age, years (median)	67.2 (68.0)	68.0 (70.0)	67.2 (66.0)
Age, n (%)			
18–65 years	34 (45)	12 (32)	13 (45)
66–75 years	21 (28)	16 (42)	8 (28)
>75 years	20 (27)	10 (26)	8 (28)
Race, n (%)			
White	56 (75)	26 (68)	22 (76)
Other or missing	19 (25)	12 (32)	7 (24)
Practice type,[a] n (%)			
Community	64 (85)	37 (97)	26 (90)
Stage at diagnosis, n (%)			
I–II	5 (7)	2 (5)	3 (10)
III	50 (67)	18 (47)	19 (66)
IV	12 (16)	13 (34)	5 (17)
Unknown	8 (11)	5 (13)	2 (7)
Total lines of therapy until most recent PARPi maintenance, n (%)			
2	41 (55)	25 (66)	15 (52)
3+	34 (45)	13 (34)	14 (48)
BRCA status, n (%)			
BRCA mutated	10 (13)	11 (29)	12 (41)
BRCA wild type	46 (61)	18 (47)	17 (59)
BRCA unknown or missing	19 (25)	9 (24)	0
Mean platelets,[b] x10^9/L (median)	183.7 (176.0)	171.2 (170.0)	170.2 (173.0)
Mean weight, kg (median)	75.9 (70.2)	68.8 (66.5)	68.3 (62.6)
Time from initial OC diagnosis, years, mean (median)	2.9 (2.7)	3.3 (2.7)	2.6 (2.3)

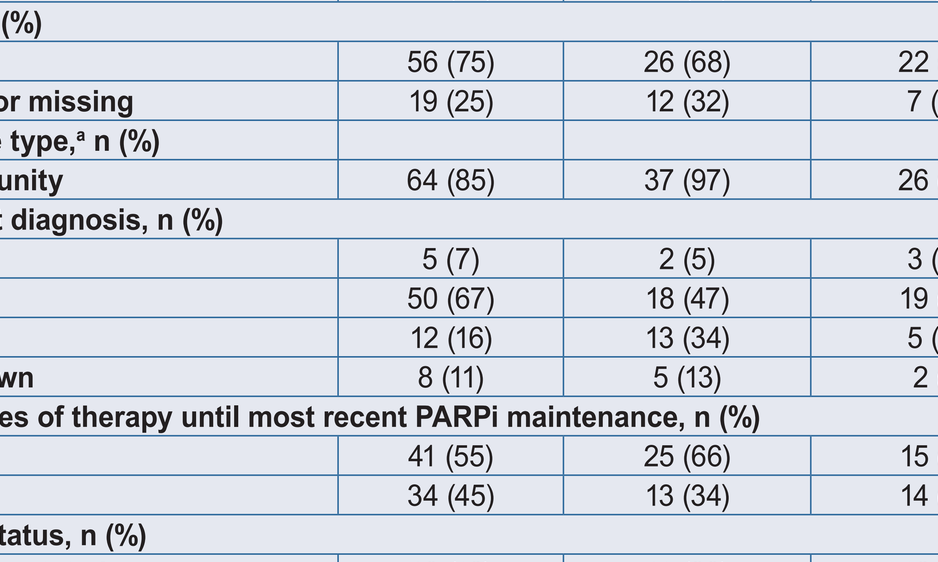
[a]Practice type is either community or academic; [b]22% of patients in the study were missing platelets.
OC=ovarian cancer; PARPi=poly(ADP-ribose) polymerase inhibitors.

Figure 1. Mean Dose Per Day



2L=second line; 2L+=second line or later; 3L+=third line or later.

Figure 2. Mean Starting Maintenance Dose



2L=second line; 2L+=second line or later; 3L+=third line or later.

Conclusions

- The data for niraparib and olaparib suggest that the average doses are slightly lower for the later lines of maintenance therapy compared with 2L
  - For rucaparib, the converse is true, but the difference is small
- In all cases except for 2L olaparib, the average dose during maintenance treatment was lower than the average starting dose
- The results should be interpreted with caution given the small patient numbers

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