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Starting dose of niraparib as first-line maintenance among patients with newly diagnosed advanced ovarian cancer in a real-world database

Poster No.352

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Background

- Ovarian cancer (OC) is the fifth leading cause of cancer death among women in the US.[1]
- Niraparib is the only poly(adenosine diphosphate-ribose) polymerase (PARP) inhibitor that is approved by the Food and Drug Administration as a first-line (1L) maintenance monotherapy for OC, regardless of biomarker status, with an individualized starting dose (ISD).[2]
- An ISD for niraparib was first recommended on April 29, 2020.[3]
- For patients weighing <77 kg (<170 lb) or with a platelet count <150,000/μL, the ISD recommendation is 200 mg taken orally once daily rather than the standard 300 mg dose.[2,3]
- The ISD of 200 mg compared with 300 mg niraparib, based on baseline body weight and platelet count, showed comparable efficacy and an improved safety profile in the phase III PRIMA trial.[4]

Objective

- To evaluate dose assignment and uptake of the ISD in patients from the US with OC who were receiving niraparib as 1L maintenance therapy, using real-world data from the Flatiron Health database.

Methods

Data source

- Data for this retrospective cohort study were from the nationwide, longitudinal Flatiron Health electronic health record-derived database, comprised of de-identified patient-level structured and unstructured data, curated via technology-enabled abstraction.[5,6]
- Date of index was defined as date of the last dose of 1L platinum-based chemotherapy (PBC).
- During the study period, the de-identified data originated from approximately 280 US cancer clinics.

Study population

- The study included patients receiving niraparib monotherapy as a 1L maintenance therapy with newly diagnosed Stage III/IV epithelial OC (between January 1, 2016, and February 28, 2021) and a last 1L PBC dose between January 1, 2017, and February 28, 2021.
- Patients were excluded if they had started a second-line chemotherapy treatment within 2 months of last 1L PBC dose.

Assessments

- Starting doses of niraparib, according to weight and platelet count, were assessed among patients receiving niraparib monotherapy as 1L maintenance therapy.

Results

Patient population

- Of the 3676 patients with a diagnosis of OC in the Flatiron Health database, 64 received niraparib as 1L maintenance therapy and were included in the study (**Figure 1**). Of these, 96.9% were from community practices and 3.1% were from academic practices.

Patient demographics and clinical characteristics

- Median (interquartile range [IQR]) age was 66 years (60–74) and 68.8% of patients were White (**Table 1**).
- Mean (standard deviation [SD]) weight was 70.2 kg (15.3); 73.4% of patients weighed <77 kg and 26.6% weighed ≥77 kg (**Table 1**).
- Median time from last 1L PBC dose to the initiation of maintenance therapy was 49 days (IQR: 38–77) (**Table 2**).

Figure 1. Data selection criteria

Step 1	Ovarian cancer diagnosis* N = 3676
Step 2	Stage III or IV ovarian cancer at diagnosis n = 2282 (62%)
Step 3	Aged ≥18 years at diagnosis n = 2282 (100%)
Step 4	Received 1L PBC† n = 1553 (68%)
Step 5	No early progression‡ n = 1392 (90%)
Step 6	Data completeness§ n = 1215 (87%)
Step 7	No evidence of pregnancy by ICD-9/10-CM n = 1214 (100%)
Step 8	With ≥60 days of follow-up data‖ n = 1016 (84%)
Step 9	No PARP inhibitor in 1L chemotherapy n = 1010 (99%)
Step 10	Received 1L maintenance therapy¶ n = 383 (38%)
Step 11	Received niraparib n = 64 (17%)

1L, first-line; 2L, second-line; ICD-9-CM, International Classification of Diseases, Ninth Revision, Clinical Modification; ICD-10-CM, International Classification of Diseases, Tenth Revision, Clinical Modification; PARP, poly(adenosine diphosphate-ribose) polymerase; PBC, platinum-based chemotherapy.
*Initial diagnosis during the data availability period (January 1, 2016, to February 28, 2021). †Patients received therapy on or after initial diagnosis with their last dose between January 1, 2017, and February 28, 2021. ‡Patients were excluded if they received 2L therapy within 60 days of the last dose of 1L PBC. §At least one record of patient-level confirmed activity (including patient visits [medication administrations, vitals, or labs] and abstracted treatment information [oral abstractions and other abstracted drug episodes]) within 90 days of initial diagnosis and before and after last dose of PBC. ‖Patients were excluded if the last confirmed patient-level activity or death was within 60 days of last dose of PBC. ¶Cohort assignment was determined during the 120-day period after the last dose of PBC.

Table 1. Patient demographics

Demographics*	Niraparib (N = 64)
Duration of follow-up (months), median (IQR)	9.3 (6.1–13.4)
Age at index (years), median (IQR)	66 (59.5–74.3)
Age category at index (years), n (%)	
18–54	7 (10.9)
55–64	18 (28.1)
65–74	23 (35.9)
75–84	16 (25.0)
Race, n (%)	
White	44 (68.8)
Other†	15 (23.4)
Unknown	5 (7.8)
Weight, kg	
Mean±SD	70.2±15.3
Median (IQR)	67.9 (58.0–79.0)
Proportion <77 kg, n (%)	47 (73.4)
Proportion ≥77 kg, n (%)	17 (26.6)

1L, first-line; IQR, interquartile range; PBC, platinum-based chemotherapy; SD, standard deviation.
*Demographics and clinical characteristics were assessed on or prior to the index date, defined as date of the last dose of 1L PBC. †Includes patients with Asian, Black or African American, Hispanic or Latino, or "Other Race" (as classified by Flatiron).

Table 2. Patient clinical characteristics

Clinical characteristics*	Niraparib (N = 64)
1L treatment details	
1L treatment, n (%)†	
Carboplatin-based chemotherapy	64 (100.0)
Bevacizumab-based chemotherapy	14 (21.9)
Time to 1L chemotherapy (days), median (IQR)‡	28 (15.8–41.0)
Number of chemotherapy cycles, median (IQR)	6 (6.0–7.0)
Time to maintenance therapy (days), median (IQR)§	49 (38.3–77.0)
Blood counts	
Platelet count (count/μL), median (IQR)	178,500 (127,500–252,000)
Platelet count (count/μL), mean±SD	209,296±120,096
Platelet count, n (%)‖	
≥150,000/μL	40 (62.5)
<150,000/μL	20 (31.3)
Unknown	4 (6.3)
Hemoglobin count (g/dL), median (IQR)	10.6 (9.7–11.4)
Hemoglobin count (g/dL), mean±SD	10.6±1.2
Hemoglobin count, n (%)‖	
≥10 g/dL	42 (65.6)
<10 g/dL	22 (34.4)
Unknown	0 (0.0)
Neutrophil count (count/μL), median (IQR)	3550 (2025–5091)
Neutrophil count (count/μL), mean±SD	4290±2821
Neutrophil count, n (%)‖	
≥1500/μL	46 (71.9)
<1500/μL	4 (6.3)
Unknown	14 (21.9)

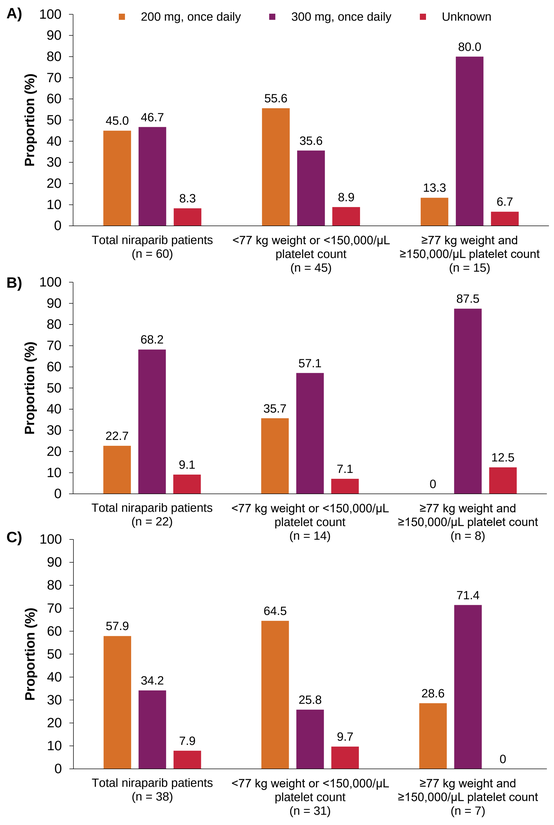
1L, first-line; IQR, interquartile range; PBC, platinum-based chemotherapy; SD, standard deviation.
*Demographics and clinical characteristics were assessed on or prior to the index date, defined as date of the last dose of 1L PBC. †It was possible for patients to receive more than one 1L therapy. ‡Time-to-1L chemotherapy was defined as the time from disease diagnosis to the start of 1L chemotherapy. §Time to maintenance therapy was defined as the time from the index date to the start date of 1L maintenance therapy. ‖Blood cell counts (platelets, hemoglobin, and neutrophils) reported were the measurement on, or closest to and before, the index date. Average blood cell counts were reported if multiple measurements were taken on the same day.

- Of the 60 patients who had platelet count information available, 20 (33.3%) had counts <150,000/μL (**Table 2**).
- Median (IQR) and mean (SD) platelet counts were 178,500/μL (127,500–252,000) and 209,296/μL (120,096), respectively (**Table 2**).

Assessment of niraparib starting dose information

- Dosing information was available for 60 patients and missing for 4 patients.
- Among those patients who met the criteria for the lower dose (n = 45), 25 (55.6%) initiated niraparib at the correct dose of 200 mg and 16 (35.6%) initiated niraparib at 300 mg (**Figure 2A**).
- Among the 15 patients who weighed ≥77 kg and had a platelet count of ≥150,000/μL, 12 (80.0%) initiated niraparib at the correct dose of 300 mg and 2 (13.3%) initiated at 200 mg (**Figure 2A**).
- After the ISD recommendation (April 29, 2020), the use of the 200 mg dose increased from 22.7% to 57.9% in the overall group (**Figure 2B, 2C**) and from 35.7% to 64.5% in those who met the weight and platelet count criteria for the lower dose (**Figure 2B, 2C**).

Figure 2. Starting dose of niraparib A) overall, B) before April 29, 2020, and C) after April 29, 2020



Conclusions

- Of the 60 patients with dosing information, 45 were eligible for the lower dose of niraparib (200 mg).
- Use of the lower dose among eligible patients increased from 35.7% to 64.5% after the ISD recommendation on April 29, 2020.
- Despite the benefits, over 25% of OC patients who were eligible were not receiving the lower dose after the ISD recommendation.
- This study is limited by its small sample size (N = 64).
- Further studies are needed to better understand and educate oncologists about the option of personalized dosing of PARP inhibitors.

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