Who Receives Maintenance Therapy After First-Line Chemotherapy? A Real-world Assessment of Patients with Ovarian Cancer Who Received Niraparib First-Line Maintenance Therapy in the United States

Presentation ID 618

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Background

- In the US, approximately 60% of patients with ovarian cancer (OC) have distant disease at diagnosis, and the estimated 5-year survival rate for these patients is 30% regardless of treatment[1]
- To delay recurrence and extend progression-free survival, the treatment landscape for OC has expanded to include maintenance therapies given after a response to first-line (1L) platinum-based chemotherapy[2,3]
- Niraparib, a poly(ADP-ribose) polymerase (PARP) inhibitor, was approved on 27 March 2017 in the US as once daily monotherapy for the maintenance treatment of patients with recurrent platinum-sensitive epithelial OC (EOC), regardless of biomarker status[4]
- Subsequently, niraparib was approved on 29 April 2020 in the US as once daily monotherapy for the 1L maintenance (1LM) treatment of patients with advanced EOC, regardless of biomarker status, who responded to 1L platinum-based chemotherapy; an individualised starting dose is recommended based on a patient's body weight and platelet count[5]
- In patients with OC, known risk factors for disease progression or death include advanced disease at diagnosis, greater volume of residual disease following surgery, and *BRCA* wild-type (*BRCA*wt) disease[1,6–8]
- Results also suggest that patients who have multiple high-risk factors for disease progression or death have worse outcomes than patients with fewer high-risk factors[9]
- Real-world data describing patients with EOC who received niraparib in the 1LM setting in clinical practice are lacking

Objective

- This observational study characterised real-world US patients with EOC prescribed niraparib 1LM therapy before and after US Food and Drug Administration approval

Conclusions

- This study is the first to describe the characteristics and risk profiles of real-world patients who initiated niraparib 1LM therapy based on niraparib's 1LM approval status in the US
- A variety of body weights and platelet count levels were observed among patients; these factors are important for determining the recommended individualised starting dose for niraparib 1LM therapy
- Results suggest that *BRCA* and homologous recombination deficiency (HRD) testing may have increased over time
  - The high proportion of patients with *BRCA*wt disease in the post-1LM approval cohort may reflect the fact that niraparib is the only PARP inhibitor approved in the US for 1LM regardless of *BRCA* status
- The optimal outcome after surgery for the initial OC diagnosis, no visible residual disease (NVRD), was reported for less than half of patients in both cohorts
- The majority (98.9%) of patients who received niraparib 1LM therapy had at least 1 high-risk factor for disease progression or death; the most common high-risk factor was *BRCA*wt disease

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Presented at the European Society of Gynaecological Oncology (ESGO) 2022 Congress; 27–30 October 2022; Berlin, Germany.

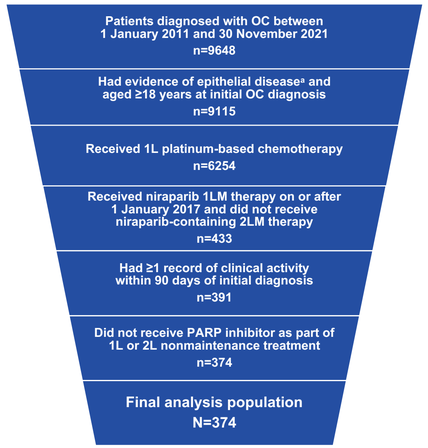
Methods

- This retrospective cohort study used the US nationwide Flatiron Health electronic health record–derived database, a longitudinal database consisting of de-identified, patient-level structured and unstructured data, curated via technology-enabled abstraction.[10,11] During the study period of 1 January 2011 and 30 November 2021, the data originated from approximately 280 cancer clinics (≈800 sites of care); of note, the majority (≈80%) of patients in the database originate from community oncology practices
  - The study included adult patients diagnosed with EOC, including ovarian, fallopian tube, and primary peritoneal cancer, during the study period
  - Eligible patients received 1L platinum-based treatment followed by niraparib 1LM monotherapy, initiated on or after 1 January 2017
  - Patients were excluded if they had an incomplete medical history (no clinical activity within 90 days of initial diagnosis) or had received a PARP inhibitor as part of 1L or 2L nonmaintenance treatment or subsequently received niraparib-containing 2L maintenance therapy
- The index date was defined as the initiation date of niraparib 1LM therapy
- Demographic and clinical characteristics of the study cohort were assessed using descriptive statistics in the overall population and by index date
  - Patients were stratified by index date: before 29 April 2020 (niraparib pre-1LM approval cohort) or on/after 29 April 2020 (niraparib post-1LM approval cohort)
- In the overall population, patients were grouped according to the number of high-risk factors for disease progression and death present in their records: (1) *BRCA*wt or unknown, (2) stage IV disease, (3) visible residual disease (VRD) or no surgery, and (4) interval debulking surgery (IDS) or no surgery
  - Patients who had unknown disease stage at diagnosis or had surgery but unknown residual disease status were excluded from risk factor classification

Results

- A total of 374 patients with advanced EOC who received niraparib 1LM therapy met all inclusion criteria and were included in the analysis (Figure 1)

Figure 1. Patient Attrition

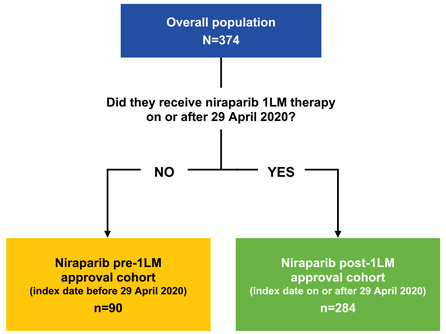


[a]Evidence of epithelial disease included the following histologies: serous, clear cell, mucinous, endometrioid, transitional cell, epithelial not otherwise specified, and unknown.
1L, first-line; 1LM, first-line maintenance; 2L, second-line; 2LM, second-line maintenance; OC, ovarian cancer; PARP, poly(ADP-ribose) polymerase.

Results *(cont'd)*

- 24.1% of patients were in the niraparib pre-1LM approval cohort, and 75.9% of patients were in niraparib post-1LM approval cohort (Figure 2)

Figure 2. Cohort Assignment Based on Index Date



1L, first-line; 1LM, first-line maintenance.

- Patient demographics are detailed in Table 1
- In the overall population, the median age at index was 68 years, and most patients were White (65.8%)
- Most patients were treated in community practices (88.8%)
- Patient demographics were generally similar in the niraparib pre- and post-1LM approval cohorts (Table 1)

Table 1. Patient Demographics[a]

	Overall population (N=374)	Niraparib pre-1LM approval cohort (index date before 29 April 2020) (n=90)	Niraparib post-1LM approval cohort (index date on or after 29 April 2020) (n=284)
Age at index, years			
Median (Q1, Q3)	68.0 (62.0, 75.0)	67.5 (62.0, 75.0)	68.0 (61.0, 75.0)
Race, n (%)			
White	246 (65.8)	62 (68.9)	184 (64.8)
Black or African American	28 (7.5)	5 (5.6)	23 (8.1)
Other	67 (17.9)	15 (16.7)	52 (18.3)
Unknown	33 (8.8)	8 (8.9)	25 (8.8)
Ethnicity, n (%)			
Hispanic or Latino	20 (5.3)	5 (5.6)	15 (5.3)
Unknown	354 (94.7)	85 (94.5)	269 (94.7)
Region of residence, n (%)[b]			
Midwest/Northeast	79 (21.1)	18 (20.0)	61 (21.5)
South	182 (48.7)	41 (45.6)	141 (49.6)
West	48 (12.8)	12 (13.3)	36 (12.7)
Other/unknown	65 (17.4)	19 (21.1)	46 (16.2)
Practice type, n (%)[c]			
Academic	60 (16.0)	17 (18.9)	43 (15.1)
Community	332 (88.8)	81 (90.0)	251 (88.4)
Median follow-up time (Q1, Q3), months	9.6 (4.6, 15.0)	21.6 (9.6, 34.9)	8.3 (4.0, 12.6)

[a]Results with counts less than 5 were masked by combining categories or were not reported to protect patient confidentiality.
[b]Midwest/Northeast: CT, ME, MA, NH, RI, VT, NJ, NY, PA, IL, IN, MI, OH, WI, IA, KS, MN, MO, NE, ND, SD; South: DE, FL, GA, MD, NC, SC, VA, DC, WV, AL, KY, MS, TN, AR, LA, OK, TX; West: AZ, CO, ID, MT, NV, NM, UT, WY, AK, CA, HI, OR, WA; other/unknown: Puerto Rico or missing. Patients from academic practices had unknown geographic region.
[c]Patients with records in academic and community practices were counted in both categories; therefore, patient counts and percentages may sum to more than 100%.
1LM, first-line maintenance; Q1, quartile 1; Q3, quartile 3.

- Patient clinical and tumour characteristics are detailed in Table 2
- In the overall population
  - 50.3% of patients had stage III and 34.8% had stage IV disease at diagnosis
  - 80.5% of patients had serous histology
  - 10.2% of patients had *BRCA*-mutated (*BRCA*m) disease
- ECOG performance score, histology, and platelet count results were generally similar in the niraparib pre- and post-1LM approval cohorts (Table 2)
- The proportion of patients with stage III or stage IV disease at initial diagnosis differed across the niraparib pre- and post-1LM approval cohorts (Table 2)
  - The proportion of patients with stage III disease was 36.7% in the pre-1LM approval cohort and 54.6% in the post-1LM approval cohort
  - The proportion of patients with stage IV disease was 48.9% in the pre-1LM approval cohort and 30.3% in the niraparib post-1LM approval cohort
- The proportion of patients with *BRCA* mutation status data was 84.4% in the pre-1LM approval cohort and 96.8% in the post-1LM approval cohort
  - The proportion of patients with *BRCA*wt disease was 63.3% in the pre-1LM approval cohort and 90.1% in the post-1LM approval cohort
- The proportion of patients with HRD status data was 15.6% in the pre-1LM approval cohort and 36.6% in the post-1LM approval cohort

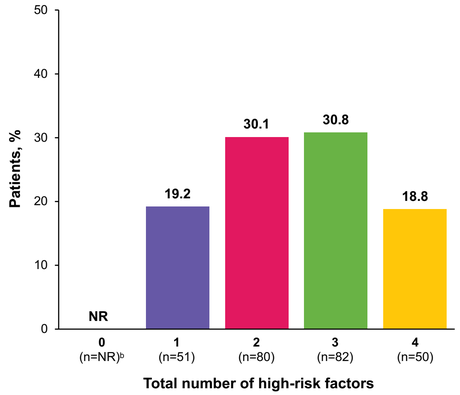
Table 2. Patient Clinical Characteristics[a]

	Primary study population (N=374)	Niraparib pre-1LM approval cohort (index date before 29 April 2020) (n=90)	Niraparib post-1LM approval cohort (index date on or after 29 April 2020) (n=284)
Body weight, n (%)			
<77 kg	269 (71.9)	62 (68.9)	207 (72.9)
≥77 kg	103 (27.5)	28 (31.1)	75 (26.4)
Platelet count, n (%)			
<150,000/µL	71 (19.0)	17 (18.9)	54 (19.0)
≥150,000/µL	259 (69.3)	65 (72.2)	194 (68.3)
Unknown	44 (11.8)	8 (8.9)	36 (12.7)
ECOG performance score, n (%)			
0–1	297 (79.4)	73 (81.1)	224 (78.9)
2–4	42 (11.2)	8 (8.9)	34 (12.0)
Unknown/missing	35 (9.4)	9 (10.0)	26 (9.2)
Stage at initial diagnosis, n (%)			
I/II	20 (5.3)	5 (5.6)	15 (5.3)
III	188 (50.3)	33 (36.7)	155 (54.6)
IV	130 (34.8)	44 (48.9)	86 (30.3)
Unknown/not documented	36 (9.6)	8 (8.9)	28 (9.9)
Epithelial histology, n (%)			
Serous	301 (80.5)	67 (74.4)	234 (82.4)
Epithelial NOS, other	53 (14.2)	NR	NR
Endometrioid	13 (3.5)	NR	NR
Unknown	7 (1.9)	NR	NR
BRCA mutation status, n (%)[b]			
*BRCA*m	38 (10.2)	19 (21.1)	19 (6.7)
*BRCA*wt	313 (83.7)	57 (63.3)	256 (90.1)
Unknown	23 (6.1)	14 (15.6)	9 (3.2)
HRD status, n (%)			
HRd	59 (15.8)	8 (8.9)	51 (18.0)
HRp	59 (15.8)	6 (6.7)	53 (18.7)
Unknown	256 (68.4)	76 (84.4)	180 (63.4)
Residual disease status after surgery for initial OC diagnosis, n (%)			
No surgery	62 (16.6)	24 (26.7)	38 (13.4)
NVRD	148 (39.6)	33 (36.7)	115 (40.5)
VRD	82 (21.9)	22 (24.4)	60 (21.1)
Unknown	82 (21.9)	11 (12.2)	71 (25.0)
Duration of 1L platinum-based chemotherapy, months			
Median (Q1, Q3)	4.6 (3.7, 5.6)	4.8 (3.9, 5.7)	4.6 (3.7, 5.6)
Time from initial diagnosis to 1LM, months			
Median (Q1, Q3)	7.3 (6.4, 8.5)	7.8 (6.5, 9.2)	7.2 (6.3, 8.3)

[a]Results with counts less than 5 were masked by combining categories to protect patient confidentiality.
[b]Data do not differentiate between somatic and germline mutations.
1L, first-line; 1LM, first-line maintenance; *BRCA*m, *BRCA* mutated; *BRCA*wt, *BRCA* wild-type; ECOG, Eastern Cooperative Oncology Group; HRD, homologous recombination deficiency; HRd, homologous recombination–deficient; HRp, homologous recombination–proficient; IQR, interquartile range; NOS, not otherwise specified; NR, not reported; NVRD, no visible residual disease; OC, ovarian cancer; Q1, quartile 1; Q3, quartile 3; VRD, visible residual disease.

- 79.7% of patients had at least 2 high-risk factors, and 49.6% of patients had at least 3 high-risk factors (Figure 3)
- Fewer than 5 patients had no high-risk factors

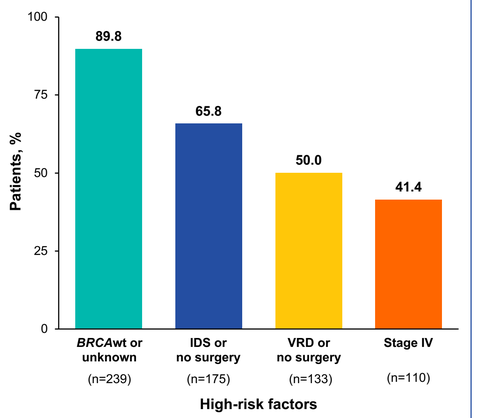
Figure 3. Distribution of Patients by Total Number of High-Risk Factors Among Patients with Complete Data for Risk Factor Classification (n=266)[a]



[a]Percentages calculated out of 266 patients with complete data for risk factor classification. Patients who had unknown disease stage at diagnosis or who had surgery but unknown residual disease status were excluded from the risk factor classification.
[b]Results with fewer than 5 patients masked to protect patient confidentiality.
NR, not reported.

- The most common high-risk factor was *BRCA*wt or unknown *BRCA* status, present in 89.8% of patients; the least common high-risk factor was stage IV disease at diagnosis, present in 41.4% of patients (Figure 4)

Figure 4. Distribution of High-Risk Factors Among Patients with Complete Data for Risk Factor Classification (n=266)[a]



[a]Percentages calculated out of 266 patients with complete data for risk factor classification. Patients who had unknown disease stage at diagnosis or who had surgery but unknown residual disease status were excluded from the risk factor classification.
*BRCA*wt, *BRCA* wild-type; IDS, interval debulking surgery; VRD, visible residual disease.

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Acknowledgments

This study (OneCDP 217870) was funded by GSK (Waltham, MA, USA). The authors thank Ramsanjay RK and Sachi Mehra of GSK for their statistical programming support. Writing and editorial support, funded by GSK and coordinated by Hasan Jamal, MSc, of GSK, were provided by Betsy C. Taylor, PhD, CMPP, and Jennifer Robertson, PhD, of Ashfield MedComms, an Inizio company (Middletown, CT, USA).