Adoption of New First-line Maintenance Strategies Among Patients with Primary Advanced Ovarian Cancer After Food and Drug Administration Approval (#507)

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Background

- Approximately 60% of patients with ovarian cancer (OC) have distant disease at diagnosis, and the 5-year survival rate in these patients is approximately 30% regardless of treatment[1]
- To help extend progression-free survival in patients with advanced OC at diagnosis, maintenance treatment with poly(ADP-ribose) polymerase (PARP) inhibitors, alone or in combination with bevacizumab, is recommended for patients with a complete or partial response after first-line (1L) chemotherapy[2]
- The US FDA approved two 1L maintenance treatments for primary advanced OC in 2020
  - Niraparib was approved on April 29, 2020, for patients regardless of tumor biomarker status[3]
  - Olaparib + bevacizumab combination was approved on May 8, 2020, for patients with homologous recombination–deficient tumors[4]
- Data on the use of these maintenance therapies in real-world clinical practice are lacking

Objective

- To evaluate the use of niraparib and olaparib + bevacizumab 1L maintenance therapy 1 year after their approval among real-world patients with advanced OC who were treated within the Flatiron Health Network

Conclusions

- Use of PARP inhibitor 1L maintenance therapy, both monotherapy and combination, increased following the 2020 approvals of niraparib monotherapy and olaparib + bevacizumab combination therapy for patients with advanced OC
- Although PARP inhibitor use increased, nearly 14% of patients with *BRCA*-mutated (*BRCA*m) disease and 40% of patients with *BRCA* wild-type (*BRCA*wt) disease who were treated after the approvals in 2020 did not receive maintenance therapy

Presentation #507

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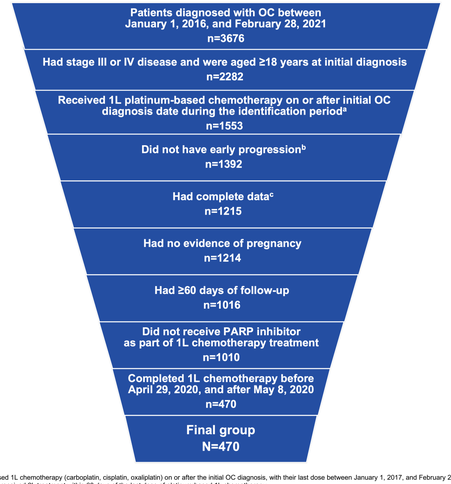
Methods

- This was a real-world retrospective cohort study of electronic health records of patients with newly diagnosed advanced OC, derived from the Flatiron Health database
  - The Flatiron Health database is a longitudinal electronic health record–derived database consisting of de-identified patient-level structured and unstructured data that are curated via technology-enabled abstraction from approximately 280 cancer clinics (≈800 sites of care) representing patients with cancer in the United States nationwide[5,6]; of note, the majority (≈80%) of patients in the database originate from community oncology practices
- Patients aged ≥18 years diagnosed with advanced OC (stage III or IV) who received 1L platinum-based chemotherapy between January 1, 2017, and February 28, 2021, and had ≥60 days of follow-up were included in the analysis (Figure 1). Patients were excluded from the analysis if they were pregnant, experienced early progression (received second-line treatment within 60 days of the last dose of 1L platinum-based chemotherapy), had incomplete data, or received a PARP inhibitor as part of 1L chemotherapy treatment
- To study maintenance therapy use before and after approval, patients who completed 1L chemotherapy before April 29, 2020, and after May 8, 2020, were further selected
  - Patients were divided into 2 groups: patients who received the last dose of 1L chemotherapy within 12 months before April 29, 2020, and patients who received the last dose of 1L chemotherapy on or within 12 months after May 8, 2020
  - The use of maintenance therapy was identified during a 120-day period after the last dose of 1L chemotherapy
  - The index date was defined as the completion date of 1L chemotherapy
- Patient demographics, clinicopathological characteristics, and maintenance treatment patterns were summarized in a descriptive analysis

Results

- In total, 470 patients with advanced OC who received 1L platinum-based chemotherapy within the specified period met all inclusion criteria and were included in the analysis (Figure 1)

Figure 1. Study Attrition



[a]Patients received platinum-based 1L chemotherapy (carboplatin, cisplatin, oxaliplatin) on or after the initial OC diagnosis, with their last dose between January 1, 2017, and February 28, 2021.
[b]Patients were excluded if they received 2L treatment within 60 days of the last dose of platinum-based 1L chemotherapy.
[c]Patients were required to have ≥1 record of patient-level confirmed activity within 90 days after the initial OC diagnosis and to have ≥1 record within 90 days before and ≥1 record within 90 days after the date of last dose for platinum-based 1L chemotherapy. Patient-level confirmed activity included patient visits (medication administrations, vitals, or labs) and abstracted treatment information (oral abstractions and other abstracted drug episodes).
1L, first-line; 2L, second-line; OC, ovarian cancer; PARP, poly(ADP-ribose) polymerase.

Results *(cont'd)*

- Of 470 patients included in the study, 240 (51.1%) patients received their last dose of chemotherapy within the 12 months preceding April 29, 2020, and 230 (48.9%) patients received their last dose of chemotherapy on or within 12 months after May 8, 2020
- The median age of patients was 67.0 years in patients who received their last dose of 1L chemotherapy within 12 months prior to April 29, 2020, and 68.0 years in patients who received their last dose of chemotherapy on or within 12 months after May 8, 2020 (Table)

Table. Demographics and Clinical Characteristics at Index

	Received last dose of 1L chemotherapy	
	Within 12 months prior to April 29, 2020 (n=240)	On or within 12 months after May 8, 2020 (n=230)
Median age at initial diagnosis (IQR), years	67.0 (58.0–75.0)	68.0 (60.3–73.0)
Race, n (%)		
Black or African American	16 (6.7)	13 (5.7)
White	145 (60.4)	132 (57.4)
Other	57 (23.8)	50 (21.7)
Not documented	22 (9.2)	35 (15.2)
Disease stage at initial diagnosis, n (%)		
III	153 (63.8)	133 (57.8)
IV	87 (36.3)	97 (42.2)
BRCA status, n (%)		
*BRCA*m	32 (13.3)	22 (9.6)
*BRCA*wt	167 (69.6)	166 (72.2)
Unknown	41 (17.1)	42 (18.3)
HRD status, n (%)		
HRd	46 (19.2)	49 (21.3)
HRp	12 (5.0)	31 (13.5)
Unknown	182 (75.8)	150 (65.2)
Receipt of debulking surgery before index, n (%)		
Yes	187 (77.9)	171 (74.3)
No/unknown	53 (22.1)	59 (25.7)
Residual disease status, n (%)		
No residual disease	104 (43.3)	101 (43.9)
Residual disease	55 (22.9)	63 (27.4)
Unknown	81 (33.8)	66 (28.7)
Median duration of follow-up (IQR), months	18.0 (14.5–21.4)	7.4 (4.5–10.2)

1L, first-line; *BRCA*m, *BRCA* mutated; *BRCA*wt, *BRCA* wild-type; HRD, homologous recombination deficiency; HRd, homologous recombination deficient; HRp, homologous recombination proficient; IQR, interquartile range.

Overall population (N=470)

- Within 1 year after May 8, 2020, 1L maintenance therapy use increased from 53.3% to 60.0%
- PARP inhibitor monotherapy use increased from 22.9% to 28.3% and bevacizumab + PARP inhibitor combination therapy use increased from 6.2% to 10.9% (Figure 2)
  - Niraparib monotherapy use increased from 6.7% to 17.8%
  - Olaparib + bevacizumab use increased from 2.9% to 7.4%
  - Olaparib monotherapy use decreased from 15.0% to 9.6%

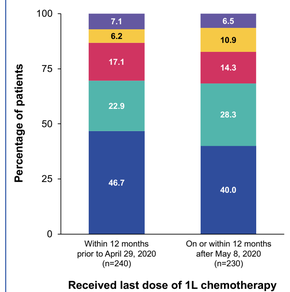
Patients with *BRCA*m disease (n=54)

- Most patients with *BRCA*m disease received some type of 1L maintenance therapy regardless of treatment timing (90.6% of patients who received the last dose of 1L chemotherapy within 12 months before April 29, 2020, and 86.4% of patients who received the last dose of 1L chemotherapy on or within 12 months after May 8, 2020)
- Within 1 year after May 8, 2020, PARP inhibitor use (monotherapies and combination) increased from 75.0% to 81.8% (Figure 3)
  - Olaparib monotherapy use decreased from 53.1% to 50.0%
  - Olaparib + bevacizumab use increased from 3.1% to 22.7%

Patients with *BRCA*wt disease (n=333)

- In patients with *BRCA*wt disease, active surveillance was the most common choice following 1L treatment in both subgroups (received last dose of 1L chemotherapy within 12 months before April 29, 2020, 51.5%; received last dose of 1L chemotherapy on or within 12 months after May 8, 2020, 40.4%)
- Within 1 year after May 8, 2020, 1L maintenance therapy use increased from 48.5% to 59.6%
- PARP inhibitor monotherapy use increased from 18.6% to 29.5% (Figure 4)
  - Niraparib use increased from 8.4% to 21.7%
  - Olaparib + bevacizumab use increased from 3.0% to 6.6%

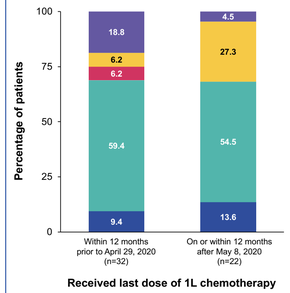
Figure 2. Treatment Distribution, Overall Population (N=470)



1L maintenance therapy type, n (%)	Received last dose of 1L chemotherapy: Within 12 months prior to April 29, 2020 (n=240)	On or within 12 months after May 8, 2020 (n=230)
Other therapy	17 (7.1)	15 (6.5)
Bevacizumab + PARP inhibitor combination therapy	15 (6.2)	25 (10.9)
Bevacizumab + niraparib	7 (2.9)	7 (3.0)
Bevacizumab + olaparib	7 (2.9)	17 (7.4)
Bevacizumab + rucaparib	1 (0.4)	1 (0.4)
Bevacizumab monotherapy	41 (17.1)	33 (14.3)
PARP inhibitor monotherapy	55 (22.9)	65 (28.3)
Niraparib	16 (6.7)	41 (17.8)
Olaparib	36 (15.0)	22 (9.6)
Rucaparib	3 (1.2)	2 (0.9)
Active surveillance	112 (46.7)	92 (40.0)

1L, first-line; PARP, poly(ADP-ribose) polymerase.

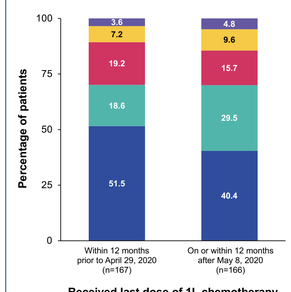
Figure 3. Treatment Distribution, *BRCA*m (n=54)



1L maintenance therapy type, n (%)	Received last dose of 1L chemotherapy: Within 12 months prior to April 29, 2020 (n=32)	On or within 12 months after May 8, 2020 (n=22)
Other therapy	6 (18.8)	1 (4.5)
Bevacizumab + PARP inhibitor combination therapy	2 (6.2)	6 (27.3)
Bevacizumab + niraparib	1 (3.1)	1 (4.5)
Bevacizumab + olaparib	1 (3.1)	5 (22.7)
Bevacizumab + rucaparib	0	0
Bevacizumab monotherapy	2 (6.2)	0
PARP inhibitor monotherapy	19 (59.4)	12 (54.5)
Niraparib	2 (6.2)	1 (4.5)
Olaparib	17 (53.1)	11 (50.0)
Rucaparib	0	0
Active surveillance	3 (9.4)	3 (13.6)

1L, first-line; *BRCA*m, *BRCA* mutated; PARP, poly(ADP-ribose) polymerase.

Figure 4. Treatment Distribution, *BRCA*wt (n=333)



1L maintenance therapy type, n (%)	Received last dose of 1L chemotherapy: Within 12 months prior to April 29, 2020 (n=167)	On or within 12 months after May 8, 2020 (n=166)
Other therapy	6 (3.6)	8 (4.8)
Bevacizumab + PARP inhibitor combination therapy	12 (7.2)	16 (9.6)
Bevacizumab + niraparib	6 (3.6)	4 (2.4)
Bevacizumab + olaparib	5 (3.0)	11 (6.6)
Bevacizumab + rucaparib	1 (0.6)	1 (0.6)
Bevacizumab monotherapy	32 (19.2)	26 (15.7)
PARP inhibitor monotherapy	31 (18.6)	49 (29.5)
Niraparib	14 (8.4)	36 (21.7)
Olaparib	15 (9.0)	11 (6.6)
Rucaparib	2 (1.2)	2 (1.2)
Active surveillance	86 (51.5)	67 (40.4)

1L, first-line; *BRCA*wt, *BRCA* wild-type; PARP, poly(ADP-ribose) polymerase.