Real-World Trends of PARPi Maintenance Treatment Uptake and Progression-Free Survival in Patients with Newly Diagnosed Advanced Ovarian Cancer in the United States

John K. Chan,[1] Jinan Liu,[2] Jinlin Song,[3] Cheryl Xiang,[4] Eric Wu,[4] Linda Kalilani,[5] Jean A. Hurteau,[6] Premal H. Thaker[7]

[1]California Pacific/Palo Alto Medical Foundation/Sutter Health, Palo Alto, CA, USA; [2]GlaxoSmithKline, Collegeville, PA, USA; [3]Analysis Group, Los Angeles, CA, USA; [4]Analysis Group, Boston, MA, USA; [5]GlaxoSmithKline, Durham, NC, USA; [6]GlaxoSmithKline, Waltham, MA, USA; [7]Department of Gynecologic Oncology, Washington University School of Medicine, St. Louis, MO, USA

Background

- In advanced ovarian cancer, maintenance treatment with poly(ADP-ribose) polymerase inhibitors (PARPi), such as niraparib and olaparib, is recommended for patients with a partial or complete response after first-line (1L) chemotherapy to delay disease recurrence[1]
- In patients with advanced ovarian cancer in the 1L maintenance setting[2–4]:
  - Niraparib monotherapy is approved for patients with advanced ovarian cancer across all biomarker subgroups
  - Olaparib monotherapy is approved only for patients with *BRCA* mutations (*BRCA*m)
  - Olaparib in combination with bevacizumab is indicated for patients with homologous recombination–deficient (HRd) status
- Despite strong evidence for the benefit of PARPi maintenance therapy from clinical trials, many patients with partial or complete response after 1L chemotherapy continue to undergo active surveillance instead of receiving maintenance treatment
- Evidence supporting the benefits of PARPi monotherapies in the real-world setting is lacking

Conclusions

- This real-world analysis shows that adoption of PARPi monotherapy in the 1L maintenance setting in patients with newly diagnosed advanced ovarian cancer has increased between 2017 and 2021
- PARPi use, when compared with active surveillance, was associated with significantly improved median progression-free survival (PFS) and was an independent predictor of improved PFS in patients with *BRCA*m or *BRCA* wild-type (*BRCA*wt) as well as patients with HRd or homologous recombination proficient (HRp)/homologous recombination deficiency (HRD) unknown status

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Presenting author email: chanjohn@sutterhealth.org

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Conflicts of Interest

Dr. Chan reports research, consulting, and speakers' bureau fees from Abbvie, Acerta, Aravive, AstraZeneca, Clovis, Eisai, GlaxoSmithKline, Merck, and Roche. **Ms. Xiang and Drs. Song and Wu** are employees of Analysis Group, which received funding from GlaxoSmithKline for the conduct of this study. **Dr. Thaker** reports institutional grants from GlaxoSmithKline and Merck; and personal fees from AstraZeneca, Celsion, GlaxoSmithKline, Iovance, Novocure, and Seagen. **Drs. Liu, Kalilani, and Hurteau** are employees of GlaxoSmithKline.

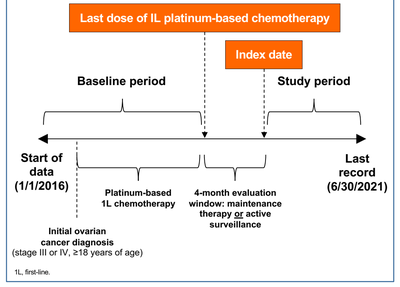
Objective

- The objective of the study was to compare real-world PFS (rwPFS) in patients with newly diagnosed advanced ovarian cancer who received PARPi monotherapy versus those who received active surveillance in the 1L maintenance treatment setting

Methods

- This was a real-world retrospective cohort study of electronic health records of patients with newly diagnosed advanced ovarian cancer derived from the Flatiron Health database
  - The Flatiron Health database is a longitudinal electronic health record-derived database consisting of deidentified 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 of patients in the database originate from community oncology practices
- Patients diagnosed with advanced ovarian cancer (stage III or IV) who had completed 1L platinum-based chemotherapy between January 1, 2017, and June 30, 2021, and received active surveillance or PARPi monotherapy in the 1L maintenance setting were included in the analysis (**Figure 1**)
  - The use of PARPi or active surveillance was identified during a 120-day period after the last dose of 1L chemotherapy; the end of the 1L maintenance treatment identification period was defined as the index date

Figure 1. Study Design



1L, first-line.

- Descriptive statistics for patient demographics, clinic-pathological characteristics, and 1L treatment patterns were calculated
- Time to next treatment was used as a proxy for rwPFS and was defined as time from the index date to the next therapy or death
  - Patients who did not experience either event were censored on the date of the last clinical activity
- Kaplan-Meier methods and Cox models were used to analyze rwPFS
- rwPFS evaluations were also conducted for the *BRCA*m or *BRCA*wt and HRd or HRp/unknown HRD status subgroups

Results

- Of the 705 patients included in the study, 539 underwent active surveillance (76.5%) and 166 received PARPi monotherapy (23.5%) after completion of 1L chemotherapy (**Table 1**)
  - Of the 103 *BRCA*wt patients receiving PARPi monotherapy, 53.4% received niraparib, 38.8% received olaparib, and 7.8% received rucaparib
- In the PARPi monotherapy cohort, 31.3% of patients had *BRCA*m and 43.4% were HRd compared with 7.6% and 10.0% of patients, respectively, in the active surveillance cohort
- Trend analysis over the 4-year study period showed PARPi monotherapy use increased from 6.4% in 2017 to 53.2% in 2021

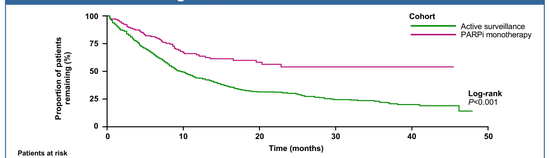
Results *(cont'd)*

- Overall, the median time to progression or death was 9.5 months for patients on active surveillance versus not reached for those receiving PARPi monotherapy (*P*<0.001; **Figure 2**)
- Among patients with *BRCA*m, median time to progression or death was 11.4 months for patients on active surveillance and not reached for patients receiving PARPi monotherapy (*P*<0.001; **Figure 3**)
- Among patients with *BRCA*wt, median time to progression or death was 9.1 months for patients on active surveillance and 13.5 months for patients receiving PARPi monotherapy (*P*<0.01; **Figure 4**)
- 1L maintenance treatment with PARPi was an independent predictor for improved PFS when compared with active surveillance in all patients, including both the *BRCA*m and *BRCA*wt subgroups (**Figure 5**)
  - Stage IV disease at initial diagnosis, no debulking surgery, residual disease status, 1L bevacizumab use, and *BRCA*wt status were associated with poorer PFS in all patients
- Among patients with HRd status, median time to progression or death was 10.2 months for patients on active surveillance and not reached for patients receiving PARPi monotherapy (*P*<0.001; **Figure 6**)
- Among patients with HRp/unknown HRD status, median time to progression or death was 9.3 months for patients on active surveillance and 13.5 months for patients receiving PARPi monotherapy (*P*<0.05; **Figure 7**)
- 1L maintenance treatment with PARPi was an independent predictor for improved PFS when compared with active surveillance in all patients, regardless of HRD status (**Figure 8**)
  - Debulking surgery and residual disease status were associated with improved PFS in patients with HRp/unknown HRD status, whereas 1L bevacizumab use and stage IV disease at initial diagnosis were associated with poorer PFS

Limitations

- Study population is distinct from the general advanced ovarian cancer population because of the required 120-day follow-up to define the active surveillance and PARPi monotherapy cohorts. Consequently, those patients experiencing an event or those who were lost to follow-up were excluded from the analysis. It is assumed that this potential bias was nondifferential

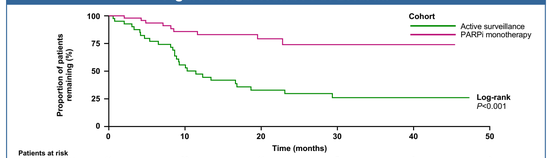
Figure 2. Real-World PFS: Overall



	Active surveillance n=539	PARPi monotherapy n=166	All patients N=705
Progression event, n (%)	354 (65.7)	53 (31.9)	407 (57.7)
Median time to event (95% CI), mo	9.5 (8.4–11.2)	NR (19.5–NR)	11.1 (9.8–13.5)
1-month retention rate, %	92.3	97.0	93.4
3-month retention rate, %	81.3	88.5	83.0
6-month retention rate, %	65.8	81.0	69.1
12-month retention rate, %	43.7	64.6	48.0

Retention rate is defined as the number of patients who did not experience either next therapy or death as of the designated time point as a proportion of the total number of participants who were identified at the index date.
NR, not reached; PARPi, poly(ADP-ribose) polymerase inhibitor; PFS, progression-free survival.

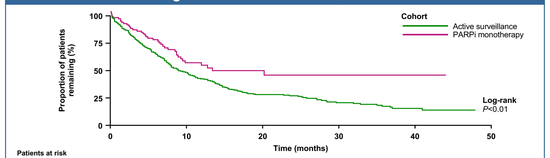
Figure 3. Real-World PFS: *BRCA*m



	Active surveillance n=41	PARPi monotherapy n=52	All patients N=93
Progression event, n (%)	27 (65.9)	9 (17.3)	36 (38.7)
Median time to event (95% CI), mo	11.4 (8.8–23.0)	NR (NR–NR)	29.2 (16.8–NR)
1-month retention rate, %	95.1	100.0	97.8
3-month retention rate, %	90.2	98.0	94.5
6-month retention rate, %	77.0	93.5	86.0
12-month retention rate, %	47.4	83.1	66.0

Retention rate is defined as the number of patients who did not experience either next therapy or death as of the designated time point as a proportion of the total number of participants who were identified at the index date.
m, mutation; NR, not reached; PARPi, poly(ADP-ribose) polymerase inhibitor; PFS, progression-free survival.

Figure 4. Real-World PFS: *BRCA*wt



	Active surveillance n=361	PARPi monotherapy n=103	All patients N=464
Progression event, n (%)	245 (67.9)	39 (37.9)	284 (61.2)
Median time to event (95% CI), mo	9.1 (7.9–11.2)	13.5 (9.3–NR)	9.9 (8.6–12.0)
1-month retention rate, %	91.9	95.1	92.6
3-month retention rate, %	80.3	84.6	81.2
6-month retention rate, %	65.0	76.0	67.3
12-month retention rate, %	42.3	56.1	44.8

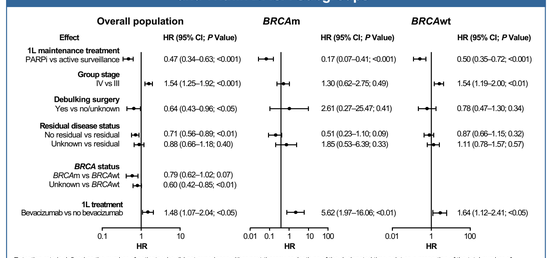
Retention rate is defined as the number of patients who did not experience either next therapy or death as of the designated time point as a proportion of the total number of participants who were identified at the index date.
NR, not reached; PARPi, poly(ADP-ribose) polymerase inhibitor; PFS, progression-free survival; wt, wild-type.

Table 1. Demographics and Baseline Characteristics

	Active surveillance N=539	PARPi monotherapy N=166	*P* Value
Age at index, years Mean (StDev) Median (IQR)	66.6 (11.3) 68.0 (59.0–75.0)	63.8 (11.4) 65.0 (56.0–72.8)	<0.01
Duration of follow-up, months Mean (StDev) Median (IQR)	21.8 (13.6) 20.6 (9.6–34.0)	13.7 (10.5) 10.9 (5.0–21.0)	<0.001
Index year, n (%) 2017 2018 2019 2020 2021[a]	117 (21.7) 180 (33.4) 129 (23.9) 84 (15.6) 29 (5.4)	8 (4.8) 16 (9.6) 43 (25.9) 66 (39.8) 33 (19.9)	<0.001
Initial diagnosis year, n (%) 2016 2017 2018 2019 2020	85 (15.8) 183 (34.0) 136 (25.2) 87 (16.1) 48 (8.9)	4 (2.4) 18 (10.8) 37 (22.3) 62 (37.3) 45 (27.1)	<0.001
Region, n (%) Midwest Northeast South West Unknown/other	69 (12.8) 60 (11.1) 228 (42.3) 96 (17.8) 86 (16.0)	27 (16.3) 14 (8.4) 69 (41.6) 39 (23.5) 17 (10.2)	0.14
Practice type, n (%) Academic Community	68 (12.6) 471 (87.4)	11 (6.6) 155 (93.4)	0.03
ECOG performance score, n (%) 0–1 2–4 Unknown	390 (72.4) 49 (9.1) 100 (18.6)	133 (80.1) 10 (6.0) 23 (13.9)	0.13
Group stage at initial diagnosis, n (%) III IV	383 (71.1) 156 (28.9)	103 (62.0) 63 (38.0)	<0.05
Debulking surgery before index, n (%) Yes No/unknown	492 (91.3) 47 (8.7)	154 (92.8) 12 (7.2)	0.66
Residual disease status, n (%) No residual disease Residual disease Unknown	245 (45.5) 150 (27.8) 144 (26.7)	78 (47.0) 51 (30.7) 37 (22.3)	0.50
BRCA status, n (%) *BRCA*m *BRCA*wt Unknown	41 (7.6) 361 (67.0) 137 (25.4)	52 (31.3) 103 (62.0) 11 (6.6)	<0.001
HRD status, n (%) HRd HRp Unknown	54 (10.0) 28 (5.2) 457 (84.8)	72 (43.4) 7 (4.2) 87 (52.4)	<0.001
Time to maintenance therapy, days Mean (StDev) Median (IQR)	— —	54.2 (24.6) 48.5 (35.0–69.8)	—
1L maintenance treatment, n (%) Niraparib Olaparib Rucaparib	— — —	65 (39.2) 89 (53.6) 12 (7.2)	NA

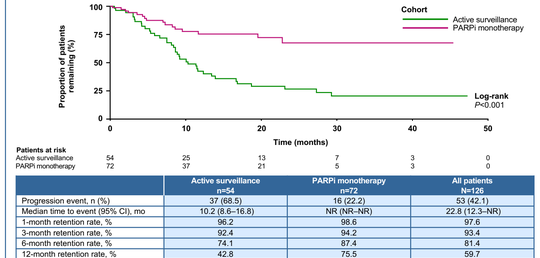
[a]Data for 2021 are incomplete and are only through June 30, 2021.
1L, first-line; ECOG, Eastern Cooperative Oncology Group; HRd, homologous recombination deficient; HRD, homologous recombination deficiency; HRp, homologous recombination proficient; IQR, interquartile range; m, mutation; NA, not applicable; PARPi, poly(ADP-ribose) polymerase inhibitor; StDev, standard deviation; wt, wild-type.

Figure 5. Real-World Predictors of PFS in the Overall Population and Within *BRCA* Subgroups[a]



Retention rate is defined as the number of patients who did not experience either next therapy or death as of the designated time point as a proportion of the total number of participants who were identified at the index date.
[a]Multivariate Cox regression analysis.
1L, first-line; HR, hazard ratio; m, mutation; PARPi, poly(ADP-ribose) polymerase inhibitor; PFS, progression-free survival; wt, wild-type.

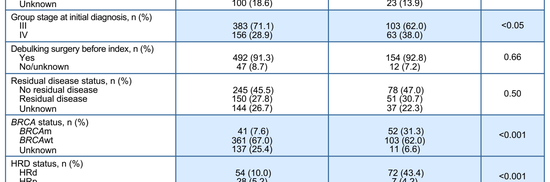
Figure 6. Real-World PFS: HRd



	Active surveillance n=54	PARPi monotherapy n=72	All patients N=126
Progression event, n (%)	37 (68.5)	16 (22.2)	53 (42.1)
Median time to event (95% CI), mo	10.2 (8.6–16.8)	NR (NR–NR)	22.8 (12.3–NR)
1-month retention rate, %	96.2	98.6	97.6
3-month retention rate, %	92.4	94.2	93.4
6-month retention rate, %	74.1	87.4	81.4
12-month retention rate, %	42.8	75.5	59.7

Retention rate is defined as the number of patients who did not experience either next therapy or death as of the designated time point as a proportion of the total number of participants who were identified at the index date.
HRd, homologous recombination deficient; NR, not reached; PARPi, poly(ADP-ribose) polymerase inhibitor; PFS, progression-free survival.

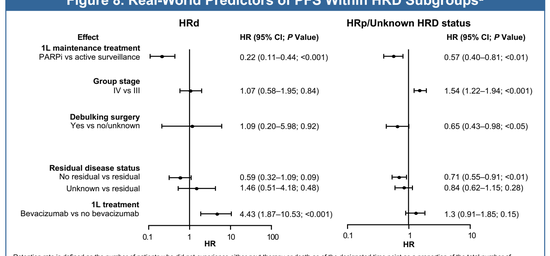
Figure 7. Real-World PFS: HRp and Unknown HRD Status



	Active surveillance n=485	PARPi monotherapy n=94	All patients N=579
Progression event, n (%)	317 (65.4)	37 (39.4)	354 (61.1)
Median time to event (95% CI), mo	9.3 (8.1–11.2)	13.5 (9.3–NR)	10.0 (8.8–12.0)
1-month retention rate, %	91.9	95.7	92.5
3-month retention rate, %	80.1	84.0	80.7
6-month retention rate, %	64.8	76.0	66.5
12-month retention rate, %	43.9	55.7	45.5

Retention rate is defined as the number of patients who did not experience either next therapy or death as of the designated time point as a proportion of the total number of participants who were identified at the index date.
HRD, homologous recombination deficiency; HRp, homologous recombination proficient; NR, not reached; PARPi, poly(ADP-ribose) polymerase inhibitor; PFS, progression-free survival.

Figure 8. Real-World Predictors of PFS Within HRD Subgroups[a]



Retention rate is defined as the number of patients who did not experience either next therapy or death as of the designated time point as a proportion of the total number of participants who were identified at the index date.
[a]Multivariate Cox regression analysis.
1L, first-line; HR, hazard ratio; HRD, homologous recombination deficiency; HRd, homologous recombination deficient; HRp, homologous recombination proficient; PARPi, poly(ADP-ribose) polymerase inhibitor; PFS, progression-free survival.