PARP inhibitors as first-line maintenance therapy in ovarian cancer: Using data from SGO 2022 to inform clinical best practice

Prof. Isabelle Ray-Coquard
Medical Oncologist
Centre Léon Bérard,
University Claude Bernard Lyon I,
Lyon, France

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Overview

PARP inhibitors as first-line maintenance therapy in ovarian cancer
SGO Hybrid Annual Meeting on Women's Cancer 2022

- **Part 1:** Describe efficacy data for PARP inhibitors in the first-line maintenance treatment of ovarian cancer
- **Part 2:** Recall safety data for PARP inhibitors in the first-line maintenance treatment of ovarian cancer
- **Part 3:** Evaluate how the latest data may impact the use of PARP inhibitors as first-line maintenance therapy in clinical practice

PARP, poly(adenosine diphosphate-ribose) polymerase; SGO, Society of Gynecologic Oncology.

SGO Hybrid Annual Meeting on Women's Cancer 2022

Latest efficacy data on PARP inhibitors in the first-line maintenance setting

PARP, poly(adenosine diphosphate-ribose) polymerase; SGO, Society of Gynecologic Oncology.

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PARPi 1LM approaches in AOC: Where are we now?

In patients with complete or partial response to first-line Pt-based CTx

Niraparib	Olaparib	Olaparib plus bevacizumab
irrespective of *BRCA*m HRD status[1,2]	with germline or somatic *BRCA*m[3,4]	HRD+ status defined as *BRCA*m ± genomic instability[3,4]
PRIMA[5]	SOLO-1[6]	PAOLA-1[7]
HR for disease progression or death		
HRD+ (incl. *BRCA*m+): HR 0.43 Total cohort: HR 0.62	Total cohort (all *BRCA*m+): HR 0.30	HRD+ *BRCA*m+: HR 0.33 *BRCA*m-: HR 0.43

1LM, first-line maintenance; AOC, advanced ovarian cancer; *BRCA,* breast cancer gene; *BRCA* m, *BRCA* mutation; CTx, chemotherapy; EMA, European Medicines Agency; FDA, US Food and Drug Administration; HR, hazard ratio; HRD, homologous recombination deficiency; PARPi, poly(adenosine diphosphate-ribose) polymerase inhibitor; Pt, platinum.

1. EMA SmPC: niraparib; 2. FDA PI: niraparib; 3. EMA SmPC: olaparib; 4. FDA PI: olaparib; 5. Gonzalez-Martin A, et al. *N Engl J Med*. 2019;381:2391–402; 6. Moore K, et al. *N Engl J Med*. 2018;379:2495–505; 7. Ray-Coquard I, et al. *N Engl J Med*. 2019;381:2416–28.
EMA SmPC and FDA PI available at: EMA www.ema.europa.eu/ and www.fda.gov/ (accessed 24 March 2022).

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Disease recurrence and poor survival rates remain challenging

Without maintenance therapy, PFS shortens with each recurrence in AOC[1]

mPFS (months)

Long-term follow-up data on survival benefit with PARPi maintenance are emerging[2,3]

SOLO-1 5-year follow-up[2]

	Olaparib		Placebo
Median PFS	56.0 months	vs	13.8 months

ENGOT-OV16/NOVA 6-year follow-up[3]

	with g*BRCA*m			without g*BRCA*m		
	Niraparib		Placebo	Niraparib		Placebo
Mean OS	45.9 months	vs	43.2 months	38.5 months	vs	39.1 months

AOC, advanced ovarian cancer; *BRCA*, breast cancer gene; g*BRCA*m, germline *BRCA* mutation; OS, overall survival; PARPi, poly(adenosine phosphate-ribose) polymerase inhibitor; mPFS, median progression-free survival.

1. Hanker LC, et al. *Ann Oncol.* 2012;23:2605–12; 2. Banerjee S, et al. *Lancet Oncol.* 2021;22:1721–31; 3. Matulonis U, et al. *Gynecol Oncol.* 2021;162(Suppl. 1):S24–5.

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OVARIO: Niraparib and bevacizumab in AOC

Hardesty MM, et al.

Phase II investigation of the safety and efficacy of combination niraparib and bevacizumab maintenance in newly diagnosed patients with AOC regardless of biomarker status

- **Primary**
  - PFS rate at 18 months
- **Selected secondary**
  - PFS
  - OS
  - Time to first subsequent therapy
  - Safety and tolerability

Endpoint assessment

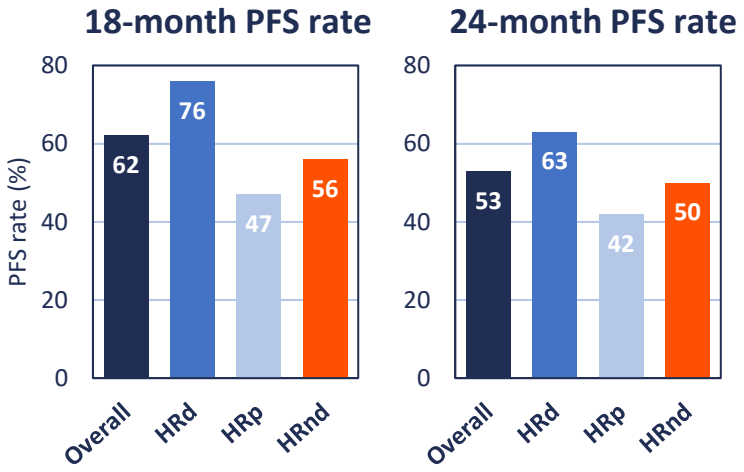
AOC, advanced ovarian cancer; CR, complete response; CTx, chemotherapy; HRD, homologous recombination deficiency; NED, no evidence of disease; OS, overall survival; PFS, progression-free survival; PR, partial response; Pt, platinum; QD, every day; Q3W, every 3 weeks; SGO, Society of Gynecologic Oncology.

Hardesty MM, et al. Oral presentation at SGO 2022, 18–21 March 2022: #170B.

OVARIO: Niraparib and bevacizumab in AOC

Hardesty MM, et al.

Primary outcome



Selected secondary outcomes

PFS
- 19.6 months (95% CI, 16.5–25.1)

OS rate
- 23.8% (immature data collection)

Time to first subsequent therapy
- 17.5 months (95% CI, 14.5–20.7)

Safety and tolerability
- Safety consistent with the known profiles of niraparib and bevacizumab as monotherapies

PFS analysis showed clinical benefit in overall population and in the biomarker subgroups; Additionally, no new safety signals were observed

AOC, advanced ovarian cancer; CI, confidence interval; HRd, homologous recombination deficient; HRnd, homologous recombination not determined; HRp, homologous recombination proficient; OS, overall survival; PFS, progression-free survival; SGO, Society of Gynecologic Oncology.
Hardesty MM, et al. Oral presentation at SGO 2022, 18–21 March 2022: #170B.

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PRIME: Niraparib in newly diagnosed AOC

Li N, et al.

Phase III investigation of the efficacy and safety of niraparib with an ISD as 1LM in patients with newly diagnosed AOC after a response to first-line CTx, regardless of biomarker status and postoperative residual disease status

N=384 → Stratified randomization → Niraparib (ISD*) or placebo (2:1) → 36 months or until disease progression or unacceptable toxicity

- Status of g*BRCA* mutations (g*BRCA*m+/g*BRCA*m-)
- Tumour HRD status (66% HRD+)
- Receipt of neoadjuvant CTx
- Response to first-line Pt-based CTx (CR/PR)

Stratified randomization

- **Primary**
  - PFS by BICR in the ITT population

Endpoint assessment

*ISD was 200 mg for all patients except those with body weight ≥77 kg and platelet count ≥150,000 µL.

1LM, first-line maintenance; AOC, advanced ovarian cancer; BICR, blinded independent central review; CR, complete response; CTx, chemotherapy; g*BRCA*m, germline breast cancer gene mutation; HRD, homologous recombination deficiency; ISD, individualized starting dose; ITT, intention to treat; PFS, progression-free survival; PR, partial response; Pt, platinum; SGO, Society of Gynecologic Oncology.

Li N, et al. Oral presentation at SGO 2022, 18–21 March 2022: #244.

PRIME: Niraparib in newly diagnosed AOC

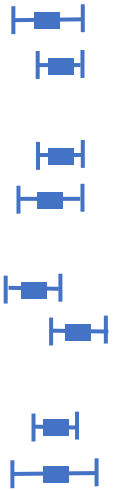
Li N, et al.

Primary outcome

mPFS (54.4% data maturity)

- Niraparib 24.8 months (95% CI, 19.2–NE)
- Placebo 8.3 months (95% CI, 7.3–11.1)

PFS benefit in pre-specified subgroups



	HR (95% CI)
g*BRCA* mutation status	
g*BRCA*+	0.40 (0.23–0.68)
g*BRCA*m-	0.48 (0.34–0.67)
HRD status	
Deficient	0.48 (0.34–0.68)
Proficient	0.41 (0.25–0.65)
Neoadjuvant CTx	
Yes	0.32 (0.21–0.48)
No	0.63 (0.42–0.94)
Response to first-line CTx	
CR	0.45 (0.32–0.61)
PR	0.45 (0.23–0.86)

PFS analysis showed clinical benefit in overall population and in the biomarker subgroups; Additionally, no new safety signals were observed

AOC, advanced ovarian cancer; CI, confidence interval; CR, complete response; CTx, chemotherapy; g*BRCA*, germline breast cancer gene; g*BRCA*m, mutated g*BRCA*; HR, hazard ratio; HRD, homologous recombination deficiency; mPFS, median PFS; NE, not estimable; PFS, progression-free survival; PR, partial response; SGO, Society of Gynecologic Oncology.

Li N, et al. Oral presentation at SGO 2022, 18–21 March 2022: #244.

ANNIE: Niraparib and anlotinib in Pt-resistant ovarian cancer

Liu G, et al.

Phase II investigation of the efficacy and safety of niraparib combined with anlotinib in patients with Pt-resistant recurrent ovarian carcinoma

N=40

No PARPi treatment history

Plasma samples collected continuously for ctDNA testing

Niraparib 300/200 mg* QD + anlotinib 10–12 mg QD†

- **Primary**
  - ORR
- **Selected secondary**
  - DCR
  - PFS
  - OS
  - Safety

Endpoint assessment

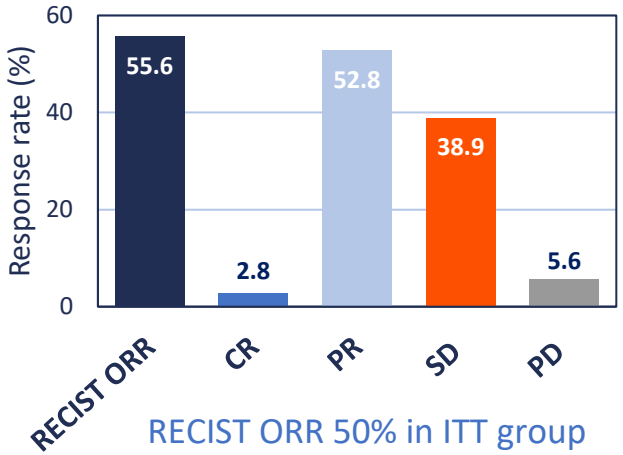
*200 mg for patients with body weight <77 kg or with platelet count <150,000/μL; †Due to toxicities observed in the first 23 patients, the initial dose was lowered to 10 mg.
ctDNA, circulating tumour DNA; DCR, disease control rate; ORR, overall response rate; OS, overall survival; PARPi, poly(adenosine diphosphate-ribose) polymerase inhibitor; PFS, progression-free survival; Pt, platinum; QD, every day; SGO, Society of Gynecologic Oncology.

Liu G, et al. Oral presentation at SGO 2022, 18–21 March 2022: #223.

ANNIE: Niraparib and anlotinib in Pt-resistant ovarian cancer

Liu G, et al.

Primary outcome (efficacy-evaluable analysis set)



RECIST ORR 50% in ITT group

Selected secondary outcomes

PFS

- mPFS was 8.3 months (95% CI, 5.86–10.81)
- 6-month PFS rate was 81.2% (95% CI, 63.6–92.8)

Safety

- Most common TRAEs were hypertension (55.0%), leukopenia (45.0%), hand-foot syndrome (42.5%), thrombocytopenia (37.5%) and neutropenia (35.0%)

Niraparib in combination with anlotinib showed promising antitumour activity and tolerable toxicity in heavily treated patients with Pt-resistant recurrent ovarian cancer

CI, confidence interval; CR, complete response; ITT, intention to treat; mPFS, median PFS; ORR, objective response rate; PD, progressive disease; PFS, progression-free survival; PR, partial response; Pt, platinum; RECIST, Response Evaluation Criteria in Solid Tumours; SD, stable disease; SGO, Society of Gynecologic Oncology; TRAE, treatment-related adverse event.

Liu G, et al. Oral presentation at SGO 2022, 18–21 March 2022: #223.

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Summary

- Patients with ovarian cancer receiving niraparib maintenance therapy showed improvements in their outcomes regardless of their genetic status
- Novel combinations of niraparib with other agents show promise as new treatment modalities. However, data from longer follow-up of current studies and phase III trials to confirm current phase II results are needed
- Overall benefit to patient outcomes was higher in those who were HRD+ vs HRD-

HRD, homologous recombination deficiency.

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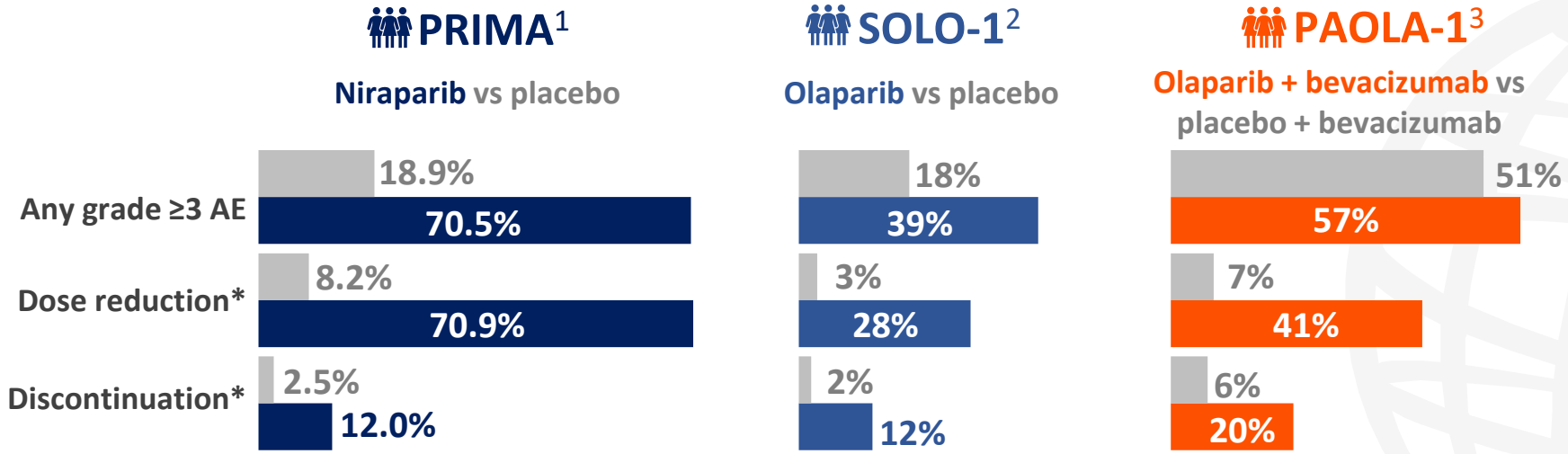
Latest safety data on PARP inhibitors in the first-line maintenance setting

PARP, poly(adenosine diphosphate-ribose) polymerase; SGO, Society of Gynecologic Oncology.

PARPi 1LM in AOC: What are the safety considerations?



Frequent AEs

- Fatigue
- Asthenia
- Nausea
- Anaemia
- Thrombocytopenia
- Neutropenia

*Dose reduction or treatment discontinuation due to AE.
1LM, first-line maintenance; AE, adverse event; AOC, advanced ovarian cancer; PARPi, poly(adenosine diphosphate-ribose) polymerase inhibitor.
1. Gonzalez-Martin A, et al. *N Engl J Med*. 2019;381:2391–402; 2. Moore K, et al. *N Engl J Med*. 2018;379:2495–505; 3. Ray-Coquard I, et al. *N Engl J Med*. 2019;381:2416–28.

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PARPi and HC-QoL in patients with AOC

Philip L, et al.

Patient-reported outcomes collected in a single gynaecologic oncology clinic

N=222

Patients with ovarian cancer were identified and data on PARPi use collected

General oncology and disease-site specific PROMs

HC-QoL compared pre- and post-PARPi therapy

Baseline characteristics

- **Stage**
  - 1: 14%
  - 2: 8%
  - 3: 55%
  - 4: 23%
- **Diagnosis**
  - Carcinosarcoma: 5%
  - Clear cell: 7%
  - Endometrioid: 8%
  - Granulosa cell: 2%
  - High-grade serous: 71%
  - Low-grade serous: 4%
  - Mucinous: 3%
- **PARPi use**
  - Yes: 34%
  - No: 66%
- **Treatment setting**
  - 1LM: 75%
  - Recurrent: 25%

1LM, first-line maintenance; AOC, advanced ovarian cancer; HC-QoL, health-care quality of life; PARPi, poly(adenosine diphosphate-ribose) polymerase inhibitor; PROM, patient-reported outcome measure; SGO, Society of Gynecologic Oncology.

Philip L, et al. Poster presentation at SGO 2022, 18–21 March 2022: #468.

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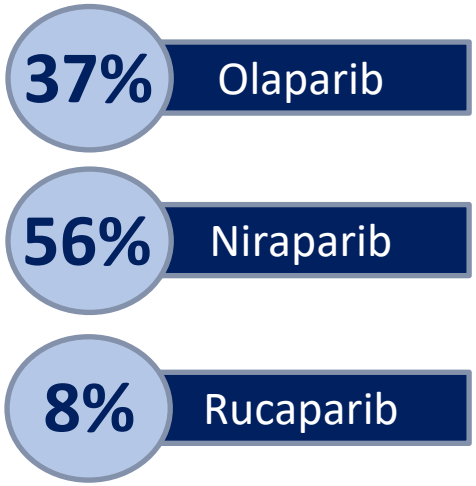
PARPi and HC-QoL in patients with AOC

Philip L, et al.



HC-QoL rating*

Treatment group	Pre-PARPi/ surgery	Immediately post-PARPi/ surgery	One year post-PARPi/ surgery
PARPi maintenance	~5.5	<5.0	>6.0
PARPi post-surgery	>5.0	~4.5	~5.5
No PARPi post-surgery	<5.0	~4.5	~5.5

PARPi use was associated with an initial temporary reduction in HC-QoL. In patients receiving 1LM PARPi, HC-QoL was equal to that of patients not receiving PARPi by 1 year post-surgery

*Evaluated by EORTC QLQ-C30 summary score, where a higher score indicates better HC-QoL.

AOC, advanced ovarian cancer; EORTC QLQ-C30; European Organisation for Research and Treatment of Cancer 30-item Quality of Life Questionnaire; HC-QoL, health-care quality of life; PARPi, poly(adenosine diphosphate-ribose) polymerase inhibitor; SGO, Society of Gynecologic Oncology.

Philip L, et al. Poster presentation at SGO 2022, 18–21 March 2022: #468.

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Impact of *BRCA*/HRD status on toxicity of PARPi in women with epithelial ovarian cancer

Wield A, et al.

Single institution, retrospective review of patients with epithelial ovarian cancer receiving PARPi from 1/3/2014 to 31/5/2021

N=230

Patients with epithelial ovarian cancer were identified

Medical records were reviewed for patient details and toxicity

Toxicities were graded using CTCAE version 5.0 and coded by organ system

- Clinicopathologic data
- Genetic status
- PARPi agent
- Indication
- Toxicity

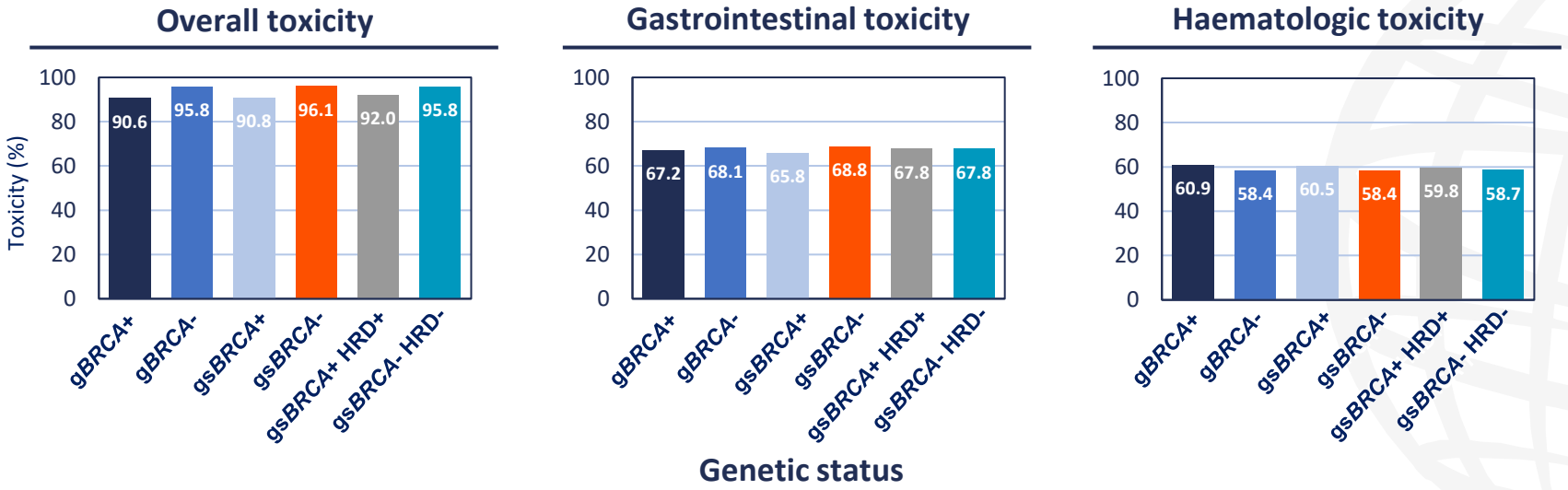
Collected patient and treatment characteristics

BRCA, breast cancer gene; CTCAE, Common Terminology Criteria for Adverse Events; HRD, homologous recombination deficiency; PARPi, poly(adenosine diphosphate-ribose) polymerase inhibitor; SGO, Society of Gynecologic Oncology.

Wield A, et al. Poster presentation at SGO 2022, 18–21 March 2022: #479.

Impact of *BRCA*/HRD status on toxicity of PARPi in women with epithelial ovarian cancer

Wield A, et al.



In this cohort, genetic variant status did not predict worse toxicity to PARPi

BRCA, breast cancer gene; CTCAE, Common Terminology Criteria for Adverse Events; g*BRCA*, germline *BRCA*; gs*BRCA*, germline and somatic *BRCA*; HRD, homologous recombination deficiency; PARPi, poly(adenosine diphosphate-ribose) polymerase inhibitor; s*BRCA*, somatic *BRCA;* SGO, Society of Gynecologic Oncology.
Wield A, et al. Poster presentation at SGO 2022, 18–21 March 2022: #479.

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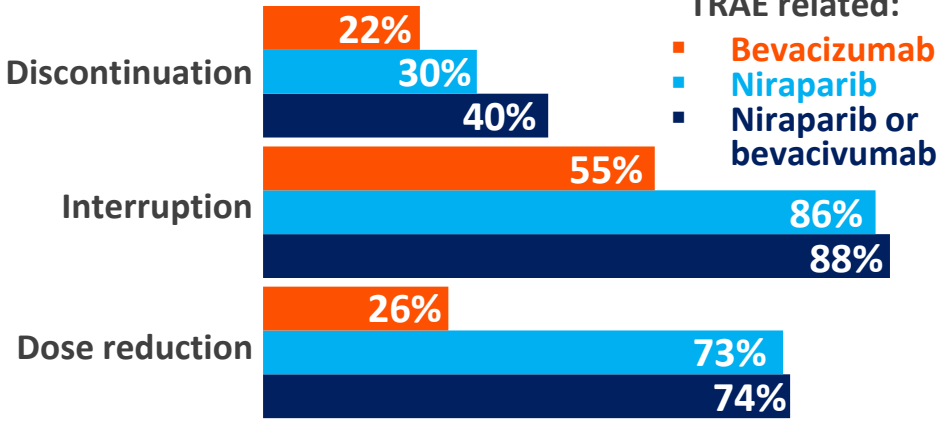
OVARIO: Niraparib and bevacizumab in AOC

Hardesty MM, et al.

N=105

- Safety findings consistent with previous profiles for niraparib or bevacizumab as monotherapies
- No new safety signals observed



Grade ≥3 TRAEs related to niraparib or bevacizumab

- Thrombocytopenia (39%)
- Anaemia (34%)
- Hypertension (27%)
- Neutropenia (12%)

<10% patients

- Fatigue
- Headache
- Proteinuria
- Nausea

Treatment discontinuation rates higher in combination therapy vs monotherapy, but were consistent with other studies evaluating PARPi plus bevacizumab regimens

AOC, advanced ovarian cancer; PARPi, poly(adenosine diphosphate-ribose) polymerase inhibitor; SGO, Society of Gynecologic Oncology; TRAE, treatment-related adverse event.

Hardesty MM, et al. Oral presentation at SGO 2022, 18–21 March 2022: #170B.

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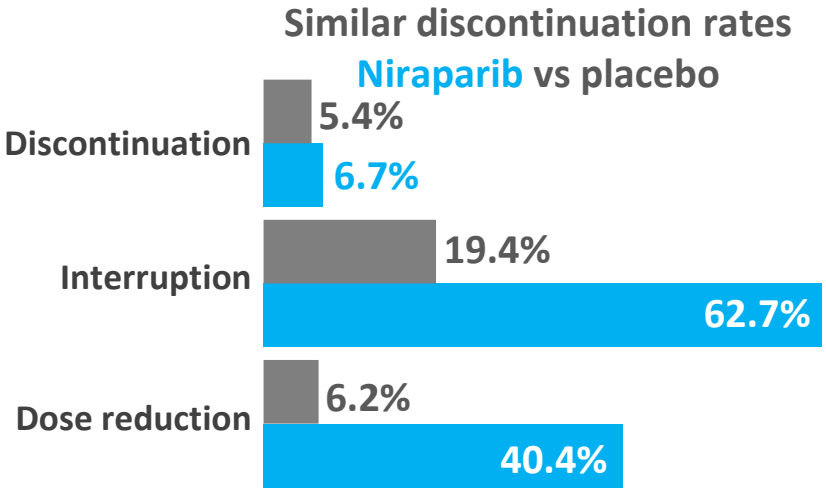
PRIME: Niraparib in newly diagnosed AOC

Li N, et al.

N=384

- Lower proportion of patients receiving niraparib required dose reduction (vs NOVA and PRIMA)
- No new safety signals identified for niraparib



Most common TEAEs

Haematological

Gastrointestinal

NIR cohort: Secondary malignancies

- 1 case of AML (died due to secondary malignancy AE)
- 1 case of MDS

- Individualized starting dose applied prospectively improved NIR safety profile
- TEAEs manageable and consistent with PARPi class

AE, adverse event; AML, acute myeloid leukaemia; AOC, advanced ovarian cancer; MDS, myelodysplastic syndrome; PARPi, poly (adenosine diphosphate-ribose) polymerase inhibitor; PBO, placebo; SGO, Society of Gynecologic Oncology; TEAE, treatment-emergent AE.

Li N, et al. Oral presentation at SGO 2022, 18–21 March 2022: #244.

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Summary

- Real-word evidence suggests that patients with AOC receiving PARPi 1LM may initially have a reduced quality of life but that this improves over time
- Patient genetic status does not appear to impact the toxicity of PARPi therapy
- Clinical trials investigating niraparib alone and in combination reported manageable safety profiles

1LM, first-line maintenance; AOC, advanced ovarian cancer; PARPi, poly(adenosine diphosphate-ribose) inhibitor.

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How could the latest data impact the use of PARP inhibitors in the first-line maintenance treatment of ovarian cancer in clinical practice?

PARP, poly(adenosine diphosphate-ribose) polymerase; SGO, Society of Gynecologic Oncology.

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Impact of *BRCA*/HRD status on clinical and survival outcomes in patients with AOC

Sims TT, et al.

Single institution, retrospective review of patients with high-grade ovarian cancer receiving PARPi from April 2013 to March 2021

N=352

Patients with known germline *BRCA* and HRD status were identified

Medical records were reviewed for clinical outcomes

Clinical outcomes were analyzed and stratified by *BRCA* and HRD status

- g*BRCA+* (n=139)
- s*BRCA+*/HRD+ (n=69)
- *BRCA-*/HRD- (n=143)

- 1LM PARPi (n=29)
- Recurrent PARPi maintenance (n=51)

Collected patient and treatment characteristics

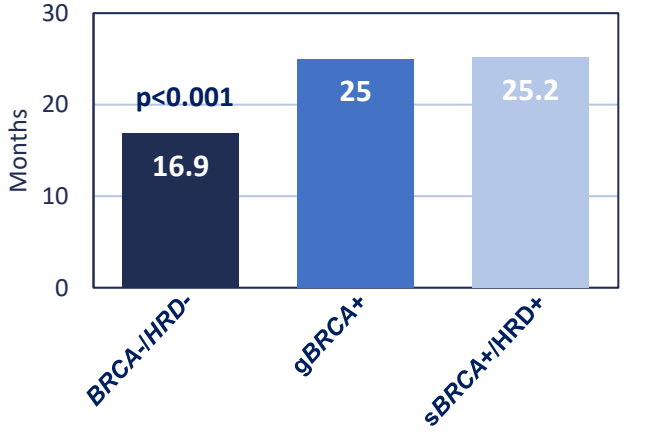
AOC, advanced ovarian cancer; g*BRCA*, germline breast cancer gene; HRD, homologous recombination deficiency; PARPi, poly(adenosine diphosphate-ribose) polymerase inhibitor; sBRCA, somatic breast cancer gene; SGO, Society of Gynecologic Oncology.

Sims TT, et al. Poster presentation at SGO 2022, 18–21 March 2022: #187.

Impact of *BRCA*/HRD status on clinical and survival outcomes in patients with AOC

Sims TT, et al.

PFS



Survival probabilities of patients on 1LM PARPi

6-month
- 1.00 (95% CI, NE)

12-month
- 0.82 (95% CI, 0.59–0.93)

Regardless of germline *BRCA*+ or somatic *BRCA*+/HRD+ status

Significant PFS HRs of patients on 1LM PARPi

Age
- 1.02 (95% CI, 1.00–1.03)

Advanced stage
- 5.02 (95% CI, 1.21–20.94)

R0 resection
- 0.40 (95% CI, 0.23–0.69)

***BRCA*-/HRD- status**
- 1.74 (95% CI, 1.20–2.51)

***BRCA*-/HRD- status was a poor prognostic factor for survival in high-grade ovarian cancer; 1LM PARPi therapy was associated with improved PFS in patients who were candidates for therapy**

AOC, advanced ovarian cancer; CI, confidence interval; g*BRCA*, germline breast cancer gene; HR, hazard ratio; HRD, homologous recombination deficiency; NE, not estimable; PARPi, PARP, poly(adenosine diphosphate-ribose) polymerase inhibitor; PFS, progression-free survival; R0, no residual tumour; s*BRCA*, somatic breast cancer gene; SGO, Society of Gynecologic Oncology.

Sims TT, et al. Poster presentation at SGO 2022, 18–21 March 2022: #187.

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OPINION: Clinical and molecular characteristics of patients with short- and long-term PFS receiving 1LM olaparib

Lheureux S, et al.

Characterization of the clinical and molecular characteristics of patients with short- and long-term PFS in the phase IIIb OPINION study of 1LM olaparib for Pt-sensitive relapsed ovarian cancer without g*BRCA*m

N=279

Patients in CR/PR to their last Pt-based CTx

Olaparib (300 mg BID) until disease progression or unacceptable toxicity

Post hoc subgroup analysis of clinical and molecular characteristics

- **Long-term PFS**
  - >18 months from first dose to PFS event, censored PFS event, study discontinuation or patient progression
  - Patients progression-free at analysis were also included
- **Short-term PFS**
  - <4 months from first dose to PFS event or censored PFS event

Patient stratification

BID, twice a day; CR, complete response; CTx, chemotherapy; g*BRCA*m, germline breast cancer gene mutation; PFS, progression-free survival; PR, partial response; Pt, platinum; SGO, Society of Gynecologic Oncology.

Lheureux S, et al. Poster presentation at SGO 2022, 18–21 March 2022: #306.

OPINION: Clinical and molecular characteristics of patients with short- and long-term PFS receiving 1LM olaparib

Lheureux S, et al.

HRD, t*BRCA*m and non-*BRCA HRR*m status

Characteristic	Long-term PFS	Short-term PFS	Neither long- or short-term PFS
HRD+ tumours	70%	40%	39%
t*BRCA*m	22%	8%	12%
Non-*BRCA HRR*m	22%	8%	10%

Objective response to last Pt-based CTx

Complete response
- Long-term PFS 51%
- Short-term PFS 18%

Partial response
- Long-term PFS 49%
- Short-term PFS 80%

Stable disease
- Short-term PFS 2%

Patients with long-term PFS (>18 months) in the OPINION study more commonly had HRD+ tumours than patients with short-term PFS (<4 months)

BRCA, breast cancer gene; CTx, chemotherapy; HRD, homologous recombination deficiency; *HRR*m, homologous recombination repair gene mutation; PFS, progression-free survival; PT, platinum; SGO, Society of Gynecologic Oncology; t*BRCA*m, tumour *BRCA* mutation.

Lheureux S, et al. Poster presentation at SGO 2022, 18–21 March 2022: #306.

PAOLA-1/ENGOT-ov25: Comparison of the predictive value of platforms for analysing HRD status

Loverix L, et al.

Comparison of Leuven HRD testing in correlation with PFS in the phase III PAOLA-1/ENGOT-ov25 trial vs Myriad myChoice PLUS status

N=468

All samples were first tested with Myriad myChoice platform as part of the PAOLA-1/ENGOT-ov25 trial

Remaining DNA analysed in development of new, academic HRD assay

Capture-based probe design for targeted sequencing developed at University of Leuven

- Evaluated first-line standard therapy including bevacizumab in advanced high-grade ovarian cancer with the addition of maintenance olaparib or placebo
- Significant improved PFS was observed in HRD+ tumours, with or without *BRCA*m, tested with Myriad myChoice PLUS, but not in HRD- tumours

PAOLA-1/ENGOT-ov25 trial

BRCA, breast cancer gene; m*BRCA,* mutated *BRCA*; HRD, homologous recombination deficient; PFS, progression-free survival; SGO, Society of Gynecologic Oncology.

Loverix L, et al. Oral presentation at SGO 2022, 18–21 March 2022: #245.

PAOLA-1/ENGOT-ov25: Comparison of the predictive value of platforms for analysing HRD status

Loverix L, et al.

HRD+ status (all, including *BRCA*m)

	Olaparib	Placebo	Olaparib	Placebo
Events	44%	71%	43%	73%
mPFS (months)	44.8	20.7	44.8	20.1
PFS (24 months)	71%	36%	71%	36%
HR (95% CI)	0.404 (0.288–0.568)		0.373 (0.262–0.532)	
	Leuven HRD test		Myriad myChoice PLUS	

Agreement rates between assays

	Positive agreement	Negative agreement	Overall agreement
Overall HRD status	94%	86%	91%
***BRCA* analysis**	95%	99.6%	98%
HRD GIS scoring	88%	86%	87%

The Leuven HRD test showed a similar impact of olaparib on PFS as the Myriad myChoice PLUS test

BRCA, breast cancer gene; *BRCA*m, mutated *BRCA*; GIS, genomic instability score; HR, hazard ratio; HRD, homologous recombination deficient; mPFS, median progression-free survival; PFS, progression-free survival; SGO, Society of Gynecologic Oncology.

Loverix L, et al. Oral presentation at SGO 2022, 18–21 March 2022: #245.

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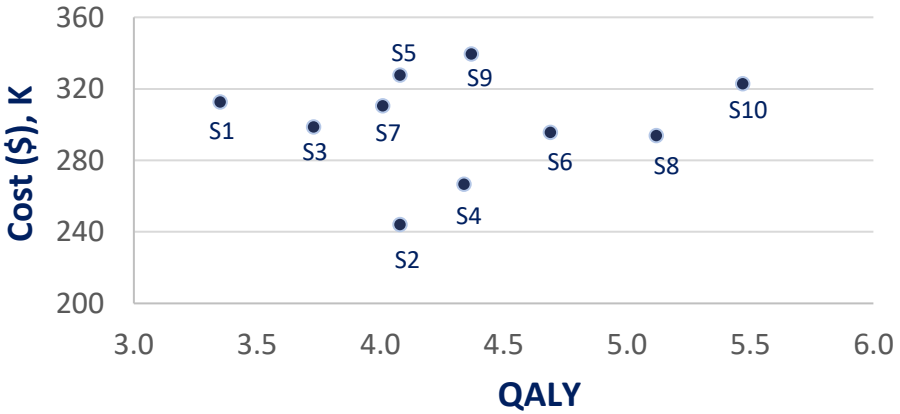
Biomarker testing to guide PARPi 1LM for patients with AOC: Cost-effectiveness study

Fan L, et al.

Comparison of 10 testing and treatment strategies involving three biomarker testing options (none, *BRCA* and HRD) and four treatment options (B, O, N and O+B) depending on the testing results



S	Test	Popn	Tx
1	None	All	N
2	None	All	B
3	*BRCA*	*BRCA*+ *BRCA*-	O N
4	*BRCA*	*BRCA*+ *BRCA*-	O B
5	*BRCA*	*BRCA*+ *BRCA*-	O+B N
6	*BRCA*	*BRCA*+ *BRCA*-	O+B N
7	HRD	HRD+/*BRCA*+ HRD+/*BRCA*- HRD-	O O+B N
8	HRD	HRD+/*BRCA*+ HRD+/*BRCA*- HRD-	O O+B B
9	HRD	HRD+ HRD-	O+B N
10	HRD	HRD+ HRD-	O+B B

HRD biomarker-guided strategy with O+B for HRD+ and B for HRD- patients (S10) resulted in the best health outcomes with longest QALYs

1LM, first-line maintenance; AOC, advanced ovarian cancer; B, bevacizumab; *BRCA*, breast cancer gene; B, bevacizumab; HRD, homologous recombination deficiency; N, niraparib; O, olaparib; PARPi, poly(adenosine diphosphate-ribose) polymerase inhibitor; QALY, quality-adjusted life year; SGO, Society of Gynecologic Oncology; S, strategy; TX, therapy.

Fan L, et al. Poster presentation at SGO 2022, 18–21 March 2022: #382.

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1LM PARPi: Emerging impacts on AOC in clinical practice

Moore KN, et al.

Increased PARPi monotherapy use in the real world, but unmet needs remain

Over half received 1LM

More patients with *BRCA*m received 1LM PARPi compared with *BRCA*wt

1LM PARPi use was highest in the USA

Antiangiogenic 1LM use decreased

Nearly 1/5 of patients with stage III/IV disease did not receive genetic testing

Improved treatment planning to support uptake of approved therapies is needed to optimize long-term outcomes in AOC

1LM, first-line maintenance; AOC, advanced ovarian cancer; *BRCA*, breast cancer gene; *BRCA*m, mutated *BRCA*; *BRCA*, wild-type *BRCA*; PARPi, poly(adenosine diphosphate-ribose) polymerase inhibitor; SGO, Society of Gynecologic Oncology.

Moore KN, et al. Oral presentation at SGO 2022 Annual Meeting on Women's Cancer, Phoenix, AZ, USA; 18–21 March 2022: #103.

1LM PARPi use in patients with newly diagnosed AOC: Real-world evidence

Liu J, et al.

Investigation of the use of 1LM therapies and the predictors of 1LM PARPi use among eligible patients with ovarian cancer in a real-world setting

N=1,010

Flatiron Health electronic health record-derived de-identified database

Identify patients with newly diagnosed AOC

Identify predictors of 1LM PARPi monotherapy use vs active surveillance

- **Active surveillance (62.1%)**
- **1LM (37.9%)**
  - PARPi: 42.3%
  - Bevacizumab: 31.9%
  - Bevacizumab + PARPi: 8.6%
  - Other: 17.2%

- **PARPi**
  - Olaparib: 54.3%
  - Niraparib: 39.5%
  - Rucaparib: 6.2%

Treatment distribution

1LM, first-line maintenance; AOC, advanced ovarian cancer; PARPi, poly(adenosine diphosphate-ribose) polymerase inhibitor; SGO, Society of Gynecologic Oncology.
Liu J, et al. Poster presentation at SGO 2022, 18–21 March 2022: #351.

1LM PARPi use in patients with newly diagnosed AOC: Real-world evidence

Liu J, et al.

Predictors of PARPi monotherapy use

	Odds ratio (95% CI)	P value		Odds ratio (95% CI)	P value
Age at index date	0.98 (0.97–1.00)	0.064	Academic vs community	0.38 (0.17–0.86)	**<0.05**
Index year 2018 vs 2017	1.74 (0.84–3.59)	0.135	*BRCA* mutated vs not mutated	7.49 (4.21–13.31)	**<0.001**
Index year 2019 vs 2017	7.57 (3.86–14.86)	**<0.001**	Unknown vs not *BRCA* mutated	0.76 (0.45–1.29)	0.318
Index year 2020 vs 2017	14.99 (7.61–29.53)	**<0.001**	Number of CTx cycles	1.24 (1.09–29.53)	**<0.001**

Patients who received a PARPi were more likely to be treated in a community setting, have *BRCA* mutation and receive more CTx cycles than those who were under active surveillance

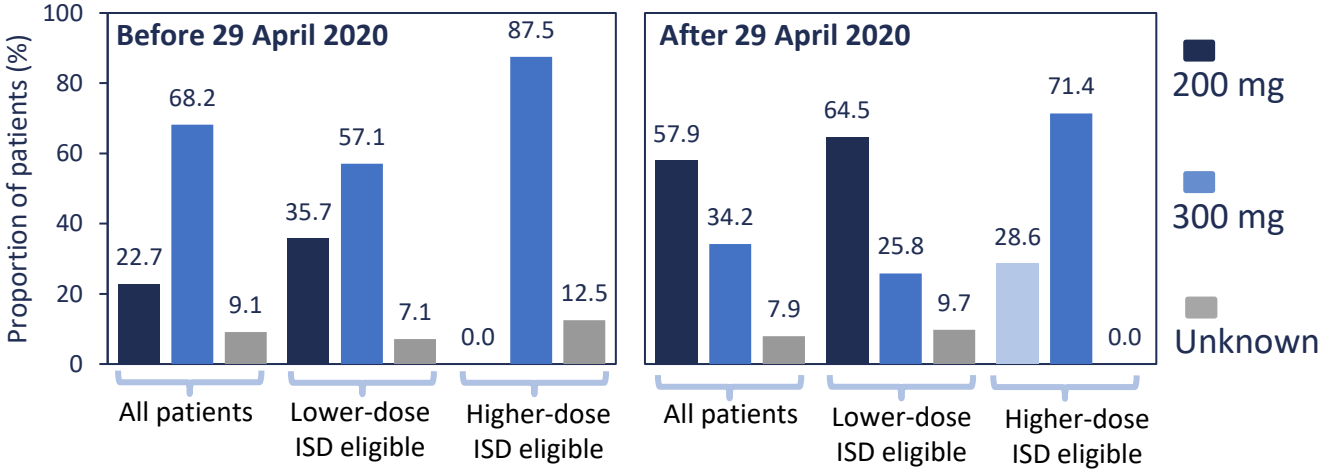
1LM, first-line maintenance; AOC, advanced ovarian cancer; CI, confidence interval; CTx, chemotherapy; PARPi, poly(adenosine diphosphate-ribose) polymerase inhibitor; SGO, Society of Gynecologic Oncology.

Liu J, et al. Poster presentation at SGO 2022, 18–21 March 2022: #351.

Starting dose of niraparib as 1LM among patients with newly diagnosed AOC

Liu J, et al.

Real-world database evaluation of dose assignment and uptake of the ISD in patients from the US who were receiving niraparib as 1LM therapy (n=64)



ISD

- **200 mg:** <77 kg or <150,000/µL platelet count
- **300 mg:** ≥77 kg and ≥150,000/µL platelet count

Over 25% of patients who were eligible were not receiving the lower dose after the ISD recommendation

1LM, first-line maintenance; AOC, advanced ovarian cancer; ISD, individualized starting dose; SGO, Society of Gynecologic Oncology.

Liu J, et al. Poster presentation at SGO 2022, 18–21 March 2022: #352.

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Summary

- Real-world evidence shows that first-line PARPi maintenance therapy is associated with improved outcomes for patients with advanced ovarian cancer
- *BRCA* mutations and HRD tumour status are useful biomarkers for good responses to 1LM PARPi
- PARPi monotherapy, or in combination with bevacizumab, are not used similarly in the different countries in clinical practice

HRD, homologous recombination deficient; PARPi, poly (adenosine diphosphate-ribose) polymerase inhibitor.

SGO Hybrid Annual Meeting on Women's Cancer 2022

Thank you for watching!

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