PARP inhibitors as first-line maintenance treatment for ovarian cancer: Translating the latest data to clinical practice

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Overview

PARP inhibitors as first-line maintenance therapy in ovarian cancer
SGO Virtual Annual Meeting on Women's Cancer 2021

- **Part 1:** Update on PARP inhibitors as first-line maintenance therapy
- **Part 2:** Emerging real-world outcomes with PARP inhibitors
- **Part 3:** Factors guiding treatment decisions surrounding PARP inhibitors in first-line maintenance therapy

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

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Update on PARP inhibitors in the first-line maintenance setting

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

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PARP inhibitors approved as first-line maintenance for advanced ovarian cancer by EMA and FDA

- In patients with complete or partial response to first-line platinum-based chemotherapy:

Olaparib in patients with germline or somatic *BRCA* mutation[1,2]

Niraparib irrespective of *BRCA* mutation status or HRD status[3,4]

Olaparib plus bevacizumab for patients with HRD-positive status defined by either *BRCA* mutation and/or genomic instability[1,2]

BRCA, breast cancer gene; EMA, European Medicines Agency; FDA, US Food and Drug Administration; HRD, homologous recombination deficiency; PARP, poly (adenosine diphosphate-ribose) polymerase.
1. EMA SmPC: olaparib; 2. FDA PI: olaparib; 3. EMA SmPC: niraparib; 4. FDA PI: niraparib.
EMA SmPC and FDA PI available at: EMA www.ema.europa.eu/ and www.fda.gov/ (accessed 18 March 2021).

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PARP inhibitors as first-line maintenance: Key trials

				HR for disease progression/death	
SOLO-1[1] N=391	**Olaparib (n=260)** 300 mg BID **Placebo (n=131)**	**All patients** *BRCA*m+	Median follow-up **41 months**	**HR 0.30** 95% CI 0.23–0.41	
PRIMA[2] N=733	**Niraparib (n=487)** 200 or 300 mg QD **Placebo (n=246)**	**50.9% HRD+** **49.1% HRD-/nd** **HRD+:** *BRCA*m+ or high Myriad myChoice® score (≥42)	Median follow-up **13.8 months**	HRD+ (including *BRCA*m+) **HR 0.43** 95% CI 0.31–0.59	Overall population **HR 0.62** 95% CI 0.50–0.76
PAOLA-1[3] N=806	**Olaparib (n=537)** 300 mg BID **Placebo (n=269)** **+ bevacizumab** 15 mg/kg Q3W	**48% HRD+** **52% HRD-/nd**	Median follow-up **22.9 months**	HRD+ (*BRCA*m+) **HR 0.33** 95% CI 0.25–0.45	HRD+ (no *BRCA*m) **HR 0.43** 95% CI 0.28–0.66

BID, twice daily; BRCA, breast cancer gene; CI, confidence interval; HR, hazard ratio; HRD, homologous recombination deficient; HRD+, HRD status positive; HRD-/nd, HRD status negative or not defined; m, mutation; PARP, poly (adenosine diphosphate-ribose) polymerase; Q3W, every 3 weeks; QD, once daily.

1. Moore K, et al. *N Engl J Med*. 2018;379:2495–505; 2. Gonzalez-Martin A, et al. *N Engl J Med*. 2019;381:2391–402; 3. Ray-Coquard I, et al. *N Engl J Med*. 2019;381:2416–28.

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SOLO-1: 5-year follow-up data for olaparib

Bradley WH, et al.

PFS benefit with maintenance olaparib sustained beyond 2 year treatment cap in SOLO-1 trial

N=391

- Newly diagnosed high-grade serous or endometrioid stage III–IV ovarian, fallopian tube or primary peritoneal cancer
- Achieved CR or PR after Pt-based chemotherapy
- *BRCA* mutation positive: deleterious or suspected deleterious germline or somatic mutation on *BRCA1* and/or *BRCA2*

n=260 → Olaparib 300 mg BID

n=131 → Placebo

→ Up to 2 years or until disease progression

Overall efficacy at 5 years*

	Olaparib n=260	Placebo n=131	
Median PFS	56.0 months	13.8 months	HR 0.33 (95% CI 0.25–0.43)
Median PFS2	NR months	42.1 months	HR 0.46 (95% CI 0.33–0.65)

No new safety signals observed

- No additional cases of AML or MDS reported
- Incidence remained <1.5%

*Median 5-year follow-up; data cut-off 5 March 2020.

AML, acute myeloid leukaemia; BID, twice daily; BRCA, breast cancer gene; CI, confidence interval; CR, complete response; HR, hazard ratio; MDS, myelodysplastic syndrome; NR, not reached; PFS, progression-free survival; PFS2, time to second progression or death; PR, partial response; Pt, platinum.

Bradley WH, et al. Presented at the SGO 2021 Virtual Annual Meeting on Women's Cancer, 19–25 March 2021.

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SOLO-1: PFS in higher- and lower-risk subgroups

Bradley WH, et al.

PFS benefit with maintenance olaparib was consistent across higher- and lower-risk subgroups in an exploratory analysis by risk status

Median follow-up | **Olaparib** (n=260) **4.8 years** | **Placebo** (n=131) **5.0 years**

Higher-risk

- FIGO IV
- FIGO III with RD after PDS
- FIGO III + IDS

Baseline characteristics, %

	Olaparib n=146	Placebo n=73
IDS	64	59
CR to prior chemo	73	74
*BRCA1*m+	75	59
*BRCA2*m+	25	41
*BRCA1*m+/2m+	1	0

Median PFS*

Olaparib n=142	Placebo n=72
40.6 months	11.1 months

vs

HR 0.35

95% CI 0.25–0.49

*PFS analysis excludes five patients recruited in China

Lower-risk

- FIGO III without RD after PDS

Baseline characteristics, %

	Olaparib n=114	Placebo n=58
IDS	0	0
CR to prior chemo	93	91
*BRCA1*m+	72	83
*BRCA2*m+	26	17
*BRCA1*m+/2m+	2	0

Median PFS

Olaparib n=114	Placebo n=58
NR months	21.9 months

vs

HR 0.38

95% CI 0.25–0.59

BRCA, breast cancer gene; chemo, chemotherapy; CI, confidence interval; CR, complete response; FIGO; International Federation of Gynecology and Obstetrics Stage; HR, hazard ratio; IDS, interval debulking surgery; m, mutation; NR, not reached; PDS, primary debulking surgery; PFS, progression-free survival; RD, residual disease.

Bradley WH, et al. Presented at the SGO 2021 Virtual Annual Meeting on Women's Cancer, 19–25 March 2021.

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PRIMA: Niraparib efficacy by timing of surgery and residual disease

O'Cearbhaill RE, et al.

Evaluate impact of residual disease after interval or primary debulking surgery on niraparib efficacy

N=733

- Newly diagnosed patients with advanced, high-grade serous or endometrioid ovarian, primary peritoneal or fallopian tube cancer with a CR or PR to first-line Pt-chemotherapy

PRIMA included HIGH-RISK patients ONLY: stage IV, or PDS with RD, or received NACT and IDS

n=487
66.4%

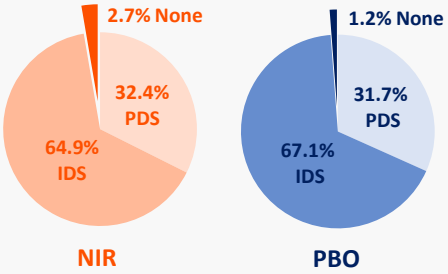
Niraparib
200 mg or 300 mg QD
200 mg: <77 kg ± platelet count <150,000/µL; 300 mg: all others

n=246
33.6%

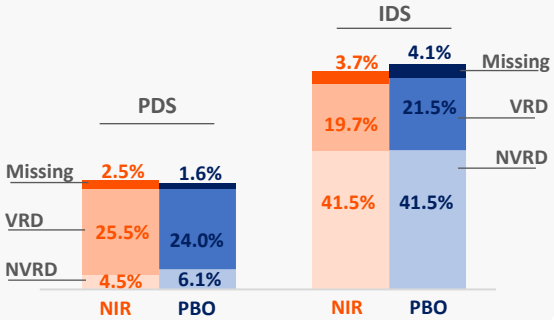
Placebo

Baseline characteristics (% patients)

Debulking surgery



Residual disease status after debulking surgery



CR, complete response; IDS, interval debulking surgery; NACT, neoadjuvant chemotherapy; NIR, niraparib; NVRD, no visible residual disease; PBO, placebo; PDS, primary debulking surgery; PR, partial response; Pt, platinum; QD, once daily; RD, residual disease; VRD, visible residual disease.

O'Cearbhaill RE, et al. Presented at the SGO 2021 Virtual Annual Meeting on Women's Cancer, 19–25 March 2021.

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PRIMA: Outcomes by timing of surgery and residual disease

O'Cearbhaill RE, et al.

Impact of residual disease on niraparib efficacy following primary/interval debulking surgery was similar across subgroups

	Intention-to-treat	No visible residual disease	Visible residual disease*
All patients† (n=733)			
HR (95% CI) **mPFS, months** (NIR vs PBO) **ΔmPFS, months**	**0.62** (0.50–0.76; p<0.0001) **13.8** vs **8.2** **5.6**	Not assessed	Not assessed
Primary debulking surgery‡ (n=236)			
HR (95% CI) **mPFS, months** (NIR vs PBO) **ΔmPFS, months**	**0.67** (0.468–0.964) **13.7** vs **8.2** **5.5**	**NE**§ **NE**§ **NE**§ **n=37**	**0.58** (0.391–0.864) **11.8** vs **7.8** **4.0** **n=183**
Interval debulking surgery/neoadjuvant chemotherapy¶ (n=481)			
HR (95% CI) **mPFS, months** (NIR vs PBO) **ΔmPFS, months**	**0.57** (0.441–0.731) **14.2** vs **8.2** **6.0**	**0.65** (0.461–0.91) **18.2** vs **10.9** **7.3** **n=304**	**0.41** (0.269–0.620) **11.1** vs **5.6** **5.5** **n=149**

*Residual disease defined as no visible residual disease (R0, NVRD) or visible residual disease (R1/R2, VRD) based on physician assessment on completion of primary surgery.
†16 patients did not undergo debulking surgery. §Subgroup too small for meaningful analysis. ‡16 and ¶28 patients had unknown residual disease status.
CI, confidence interval; HR, hazard ratio; mPFS, median progression-free survival; NE, not evaluable; NIR, niraparib; PBO, placebo.
O'Cearbhaill RE, et al. Presented at the SGO 2021 Virtual Annual Meeting on Women's Cancer, 19–25 March 2021.

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PRIMA: Outcomes by timing of surgery and residual disease

O'Cearbhaill RE, et al.

Impact of residual disease on niraparib efficacy following primary/interval debulking surgery was similar across subgroups

	Intention-to-treat	No visible residual disease	Visible residual disease*
All patients† (n=733)			
HR (95% CI)			Not assessed
mPFS, months (N			
ΔmPF			
Primary debulking			
H			0.58 (0.391–0.864)
mPFS, months (NIR vs PBO)	13.7 vs 8.2	NE‡	11.8 vs 7.8
ΔmPFS, months	5.5	NE§ n=37	4.0 n=183
Interval debulking surgery/neoadjuvant chemotherapy¶ (n=481)			
HR (95% CI)	0.57 (0.441–0.731)	0.65 (0.461–0.91)	0.41 (0.269–0.620)
mPFS, months (NIR vs PBO)	14.2 vs 8.2	18.2 vs 10.9	11.1 vs 5.6
ΔmPFS, months	6.0	7.3 n=304	5.5 n=149

Authors' conclusion

Patients with visible residual disease after interval debulking surgery showed greatest reduction in risk of disease progression

*Residual disease defined as no visible residual disease (R0, NVRD) or visible residual disease (R1/R2, VRD) based on physician assessment on completion of primary surgery.
†16 patients did not undergo debulking surgery. §Subgroup too small for meaningful analysis. ‡16 and ¶28 patients had unknown residual disease status.
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O'Cearbhaill RE, et al. Presented at the SGO 2021 Virtual Annual Meeting on Women's Cancer, 19–25 March 2021.

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OVARIO: Phase II trial of niraparib plus bevacizumab

Hardesty M, et al.

Evaluate NIR plus BEV maintenance in AOC after response to first-line Pt-based chemotherapy plus BEV

- Newly diagnosed high-grade serous or endometrioid stage IIIB–IV epithelial ovarian, fallopian tube or primary peritoneal cancer
- Achieved CR, PR or NED result following first-line Pt-based chemotherapy plus bevacizumab

N=105

n=82 — **78%** — **200 mg QD NIR + 15 mg/kg Q3W BEV** (<77 kg ± platelet count <150,000/µL)

n=23 — **22%** — **300 mg QD NIR + 15 mg/kg Q3W BEV** (all others)

Baseline characteristics (% patients)

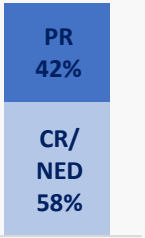
Histological subtype

- 95% serous
- 4% endometrioid
- 1% undifferentiated

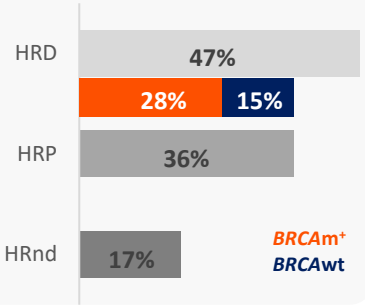
Debulking surgery

- 37% PDS
- 63% NACT/IDS

Response after surgery/chemotherapy



Biomarker status



AOC, advanced ovarian cancer; BEV, bevacizumab; BRCA, breast cancer gene; CR, complete response; HRD, homologous recombination deficient; HRnd, homologous recombination not defined; HRP, homologous recombination proficient; IDS, interval debulking surgery; m, mutation; NACT, neoadjuvant chemotherapy; NED, no evidence of disease; NIR, niraparib; PDS, primary debulking surgery; PR, partial response; Pt, platinum; Q3W, every three weeks; QD, once daily; wt, wild-type.

Hardesty M, et al. Presented at the SGO 2021 Virtual Annual Meeting on Women's Cancer, 19–25 March 2021.

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OVARIO: 18-month PFS and safety

Hardesty M, et al.

OVARIO[1] reported favourable results for upfront maintenance therapy in a lower-risk AOC population versus PRIMA[2]

62% of patients remained progression-free at 18 months

18-month PFS rate*

Overall	N=105	62% (95% CI 52–71)
HRD	n=49	76% (95% CI 61–87)
HRP	n=38	47% (95% CI 31–64)
HRnd	n=18	56% (95% CI 31–78)

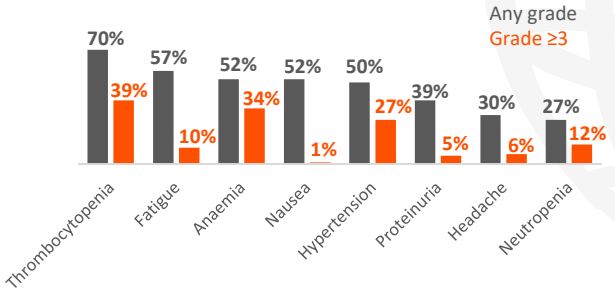
27% of patients discontinued NIR due to TEAEs

TEAEs leading to dose modifications or discontinuations (% patients)

Overall N=105

- 85% treatment interruption
- 73% dose reduction
- 27% treatment discontinuation

Most frequent TEAEs (% patients)



*Last patient enrolled 14 February 2019. Data cut-offs: 14 August 2019; 14 February 2020; 14 August 2020. Median follow-up: 8.6, 12.8 and 16.0 months.
AOC, advanced ovarian cancer; CI, confidence interval; HRD, homologous recombination deficient; HRnd, homologous recombination not defined; HRP, homologous recombination proficient; NIR, niraparib; PFS, progression-free survival; TEAE, treatment-related treatment-emergent adverse event.
1. Hardesty M, et al. Presented at the SGO 2021 Virtual Annual Meeting on Women's Cancer, 19–25 March 2021; 2. Gonzalez-Martin A, et al. *N Engl J Med*. 2019;381:2391–402.

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PAOLA-1: CA-125 surveillance with olaparib plus bevacizumab

Hietanen S, et al.

Evaluate progression by RECIST/CA-125 to determine role of CA-125 surveillance in PAOLA-1

N=806

- Newly diagnosed patients with advanced high-grade serous or endometrioid ovarian, fallopian tube and/or primary peritoneal cancer with NED, CR or PR to first-line Pt-taxane-based chemotherapy
- First-line upfront or interval surgery and ≥2 cycles of bevacizumab

Randomized by *BRCA*m status and first-line treatment outcome

- n=537 ▶ 66.6% **Olaparib 300 mg BID**
- n=269 ▶ 33.4% **Placebo**

▶ **For 2 years + bevacizumab***

- Tumour assessment scans Q24W or Q12W if evidence of CA-125 progression
- CA-125 levels assessed Q12W

Definitions of CA-125 progression

CA-125 progression	CA-125 ≥2X nadir level† or ULN‡ on two occasions ≥1 week apart
CA-125 progression *BEFORE* RECIST progression	CA-125 progression >7 days before RECIST progression
Concomitant CA-125 and RECIST progression	CA-125 progression ≤7 days before or after RECIST progression

*Bevacizumab 15 mg/kg Q3W for a total of 15 months, including when administered with chemotherapy.
†Nadir value: patients with abnormal pretreatment CA-125 levels. ‡ULN: patients with normal pretreatment/normalized CA-125 levels.
BID, twice daily; BRCA, breast cancer gene; CA-125, cancer antigen-125; CR, complete response; m, mutation; NED, no evidence of disease; PR, partial response; Pt, platinum; Q3W, every three weeks; RECIST, Response Evaluation Criteria In Solid Tumours; ULN, upper limit of normal.
Hietanen S, et al. Presented at the SGO 2021 Virtual Annual Meeting on Women's Cancer, 19–25 March 2021.

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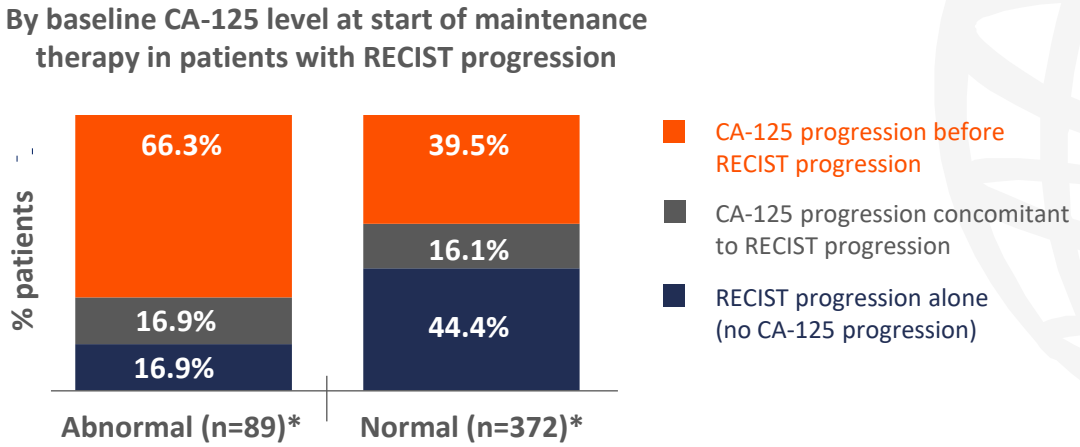
PAOLA-1: RECIST/CA-125 progression by baseline CA-125

Hietanen S, et al.

Baseline CA-125 levels at the beginning of maintenance therapy with olaparib plus bevacizumab may guide subsequent follow-up methods



*P<0.001 for CA-125 status by RECIST progression alone vs CA-125 progression concomitant with or before RECIST progression.
CA-125, cancer antigen-125; RECIST, Response Evaluation Criteria In Solid Tumours.
Hietanen S, et al. Presented at the SGO 2021 Virtual Annual Meeting on Women's Cancer, 19–25 March 2021.

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Summary

- Three PARP inhibitor options available for newly diagnosed stage III/IV HGOC, but indications vary
- Benefit in first line for both **HIGH** and **LOW** risk *BRCA*m^{+} population in SOLO-1; bevacizumab alone had greatest benefit in high-risk/bulky-disease patients[1,2]
- In PRIMA, slightly greater benefit with PARP inhibitor maintenance in high-risk patients with visible residual disease
- Monitoring for relapse with first-line PARP inhibitor maintenance:
  - If CA-125 normal at maintenance initiation, approximately 40% of patients progress radiologically without an increase in CA-125 (PAOLA-1)
- Second trial demonstrating feasibility of niraparib and bevacizumab
  - 27% grade ≥3 hypertension (OVARIO)

BRCA, breast cancer gene; CA-125, cancer antigen-125; HGOC, high-grade ovarian cancer; m, mutation; PARP, poly (adenosine diphosphate-ribose) polymerase.

1. Perren TJ, et al. *N Engl J Med.* 2011;365:2484–96; 2. Burger RA, et al. *N Engl J Med.* 2011;365:2473–83.

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Emerging real-world outcomes with PARP inhibitors

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

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Known safety of PARP inhibitors as maintenance therapy

	SOLO-1[1] N=391		PRIMA[2] N=733		PAOLA-1[3] N=806	
	Olaparib (n=260)	Placebo (n=130)	Niraparib (n=484)	Placebo (n=244)	Olaparib + bevacizumab (n=535)	Placebo + bevacizumab (n=267)
Any grade AE, %	98	92	98.8	91.8	99	96
Grade ≥3 AE, %	39	18	70.5	18.9	57	51
Treatment discontinuation due to AE,* %	12	2	12.0	2.5	20	6
Dose reduction due to AE,* %	28	3	70.9	8.2	41	7
Selected grade ≥3 AEs, %						
Fatigue/asthenia	4	2	1.9	0.4	5	1
Nausea	1	0	1.2	0.8	2	1
Anaemia	22	2	31.0	1.6	17	<1
Thrombocytopenia	1	2	28.7	0.4	2	<1
Neutropenia	9	5	12.8	1.2	6	3

*Treatment discontinuation or dose reduction due to any grade AE.
AE, adverse event; ; PARP, poly (adenosine diphosphate-ribose) polymerase.
1. Moore K, et al. *N Engl J Med.* 2018;379:2495–505; 2. Gonzalez-Martin A, et al. *N Engl J Med.* 2019;381:2391–402; 3. Ray-Coquard I, et al. *N Engl J Med.* 2019;381:2416–28.

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Real-world survival: PARP inhibitor use across indications

Wield A, et al.

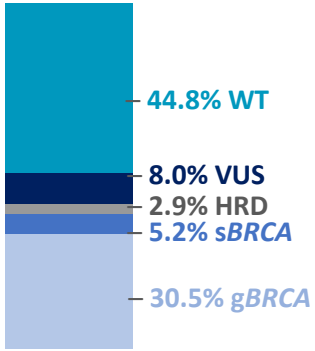
Explore real-world use, effectiveness and safety of PARP inhibitors, including impact on subsequent lines

N=174

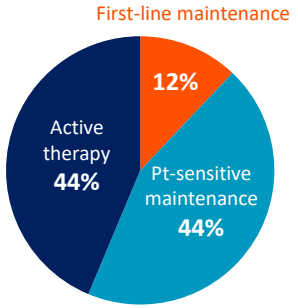
- IRB-approved single-institution retrospective review of patients with EOC that received PARP inhibitor therapy between March 2014 and March 2020

Cohort characteristics (% patients)

Tumour mutation status



PARP inhibitor indication



Clinical trial – **9.2%**
Non-FDA indication – **27.0%**
PARPi after PARPi – **5.7%**

n=132 Patients with PARP inhibitor progression receiving next-line therapy

		Disease control rate
101	Any next-line therapy	**44.6%**
87	Cytotoxic chemotherapy	**50.6%**
10	PARPi after PARPi	**40.0%**

ORR to next-line cytotoxic chemotherapy after PARP inhibitor progression

First-line maintenance	Pt-sensitive maintenance	Active therapy
22% (n=2/9)	34% (n=14/41)	24% (n=9/37)

BRCA, breast cancer gene; CR, complete response; EOC, epithelial ovarian cancer; FDA, US Food and Drug Administration; gBRCA, germline BRCA mutation; HRD, homologous recombination deficient; IRB, Institutional Review Board; ORR, objective response rate; PARP, poly (adenosine diphosphate-ribose) polymerase; PARPi, PARP inhibitor; PD, progressive disease; PR, partial response; Pt, platinum; sBRCA, somatic BRCA mutation; SD, stable disease; VUS, variant of uncertain significance; WT, wild-type.

Wield A, et al. Presented at the SGO 2021 Virtual Annual Meeting on Women's Cancer, 19–25 March 2021.

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Survival outcomes and toxicities with PARP inhibitor use across indications

Wield A, et al.

PFS and OS were significantly associated with PARP inhibitor indication

PARPi indication	Median PFS, months	Median OS, months
First-line maintenance	17.1	Not met
Pt-sensitive maintenance	15.4	158.7
Active therapy	5.7	77.9
	p<0.001	**p=0.0001**

Response to next-line Pt-therapy if progression during PARP inhibitor use

PARPi indication	Median PFS, months	Disease control rate, %
First-line maintenance	3.6	50
Pt-sensitive maintenance	5.4	75
Active therapy	4.9	60

Real-world toxicities reflected clinical trial safety profiles

Toxicity rate (% patients)

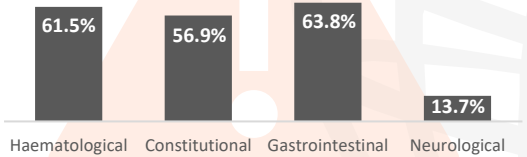
n=174

92.5% any

28.2% grade 3/4

16.1% prompted discontinuation

Type of AE (% patients)



In patients receiving next-line cytotoxic chemotherapy

n=87

23.0% grade 3/4 toxicity

77.0% haematological toxicity

AE, adverse event; OS, overall survival; PARP, poly (adenosine diphosphate-ribose) polymerase; PFS, progression-free survival; Pt, platinum.

Wield A, et al. Presented at the SGO 2021 Virtual Annual Meeting on Women's Cancer, 19–25 March 2021.

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Ovarian cancer survivors' experiences with PARP inhibitors

Morrison M, et al.

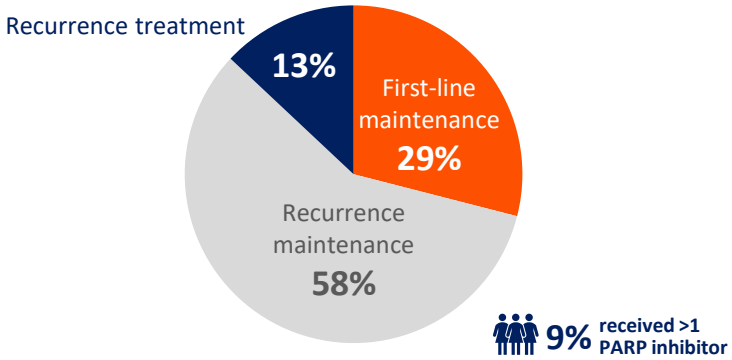
Explore self-reported experiences with PARP inhibitors amongst ovarian cancer survivors

N=160

- A 26-question survey shared via survivor networks and social media with women:
  - with a current, or prior, diagnosis of ovarian cancer *and*
  - received PARP inhibitor therapy (Dec 2019–Feb 2020)

Respondent profile (% respondents)

First PARP inhibitor treatment setting



9% received >1 PARP inhibitor

During first treatment with a PARP inhibitor, women reported a median of 2 side effects (range 0–9)

Most commonly reported side effects

Fatigue	53%
Nausea	45%
Neutropenia	22%
Aches/pains	14%
Thrombocytopenia	13%
Stomach pain	13%
Bowel changes	13%

Advice from respondents

Prepare for all side effects

Get help as soon as possible for all side effects

Be patient

PARP, poly (adenosine diphosphate-ribose) polymerase.

Morrison M, et al. Presented at the SGO 2021 Virtual Annual Meeting on Women's Cancer, 19–25 March 2021.

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Summary

- Real-world experience with PARP inhibitors is primarily in relapsed setting (first indications)
- Toxicities reported reflect trial safety profiles
- Some concerns that PARP inhibitors may compromise subsequent chemotherapy efficacy, which is in line with data from SOLO-2 presented at ESMO 2020[1]

ESMO, European Society for Medical Oncology; PARP, poly (adenosine diphosphate-ribose) polymerase

1. Frenel J, et al. *Ann Oncol.* 2020;31(Suppl. 4):S551-89.

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Factors guiding treatment decisions surrounding PARP inhibitors as first-line maintenance therapy: Who should ***not*** receive a PARP inhibitor?

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

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Response to first-line maintenance treatment according to molecular characteristics

	*BRCA*m	HRD-positive	HRD-positive, no *BRCA*m	HRP/HRD-negative
SOLO-1 (olaparib)[1] HR for PFS (95% CI)	0.33 (0.25–0.43)	-	-	-
PRIMA (niraparib)[2] HR for disease progression or death (95% CI)	0.40 (0.27–0.62)	0.43 (0.31–0.59)	0.50 (0.31–0.83)	0.68 (0.49–0.94)
PAOLA-1 (olaparib + bevacizumab)[3] HR for disease progression or death (95% CI)	0.31 (0.20–0.47)	0.33 (0.25–0.45)	0.43 (0.28–0.66)	1.00 (0.75–1.35)
	Standard of care for all *BRCA*m patients?	**Significant benefit in patients with HRD$^+$ disease**		**Niraparib can be considered for patients with HRD$^-$ disease**

BRCA, breast cancer gene; CI, confidence interval; HR, hazard ratio; HRD, homologous recombination deficiency; HRP, homologous recombination proficiency; m, mutation; PFS, progression-free survival.

1. Banerjee S, et al. *Ann Oncol.* 2020;31 (Suppl. 4):S551–89; 2. Gonzalez-Martin A, et al. *N Engl J Med.* 2019;381:2391–402; 3. Ray-Coquard I, et al. *N Engl J Med.* 2019;381:2416–28.

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PAOLA-1: Non-*BRCA* HRRm gene panels as a predictive biomarker of maintenance with olaparib plus bevacizumab

Pujade-Lauraine E, et al.

Explore mutations in HRR genes beyond *BRCAm* as a predictive biomarker in PAOLA-1

- PAOLA-1 investigated olaparib plus bevacizumab versus placebo plus bevacizumab as a first-line maintenance treatment

Gene panel	Non-*BRCA* HRRm prevalence n (%)	
Exploratory gene panels		
Pre-defined (13 genes)	54 (6.7)	
Expanded (18 genes)	72 (8.9)	
Restricted (5 genes)	30 (3.7)	Smallest panel
Published gene panels		
Used in Study 19 (26 genes)	79 (9.8)	Largest panel
Used in ARIEL3 (19 genes)	61 (7.6)	
Used in NOVA (11 genes)	44 (5.5)	

BRCA, breast cancer gene; HRR, homologous recombination repair; m, mutation.

Pujade-Lauraine E, et al. Presented at the SGO 2021 Virtual Annual Meeting on Women's Cancer, 19–25 March 2021.

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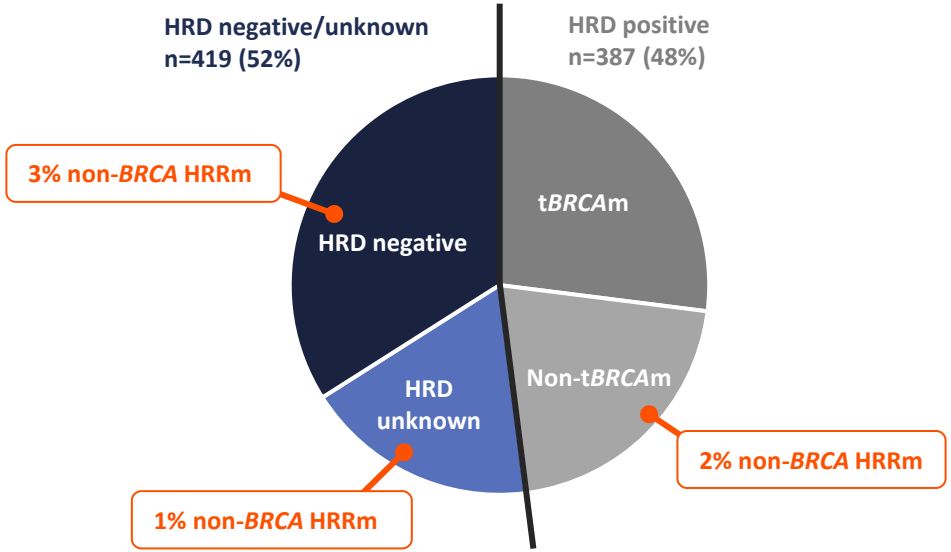
PAOLA-1: Non-*BRCA* HRRm gene panels as a predictive biomarker of maintenance with olaparib plus bevacizumab

Pujade-Lauraine E, et al.

HRD by genomic instability score and non-*BRCA* HRRm are not interchangeable



Non-*BRCA* HRRm was not predictive of improved PFS

Gene panel	HR for PFS (95% CI)
Exploratory gene panels	
Pre-defined (13 genes)	0.95 (0.49–1.94)
Expanded (18 genes)	1.01 (0.55–1.95)
Restricted (5 genes)	Not calculated (<20 events)
Published gene panels	
Used in Study 19 (26 genes)	0.92 (0.51–1.73)
Used in ARIEL3 (19 genes)	1.35 (0.65–3.14)
Used in NOVA (11 genes)	1.83 (0.76–5.43)

BRCA, breast cancer gene; CI, confidence interval; HR, hazard ratio; HRD, homologous recombination deficiency; HRR, homologous recombination repair; m, mutation; PFS, progression-free survival; t, tumour.

Pujade-Lauraine E, et al. Presented at the SGO 2021 Virtual Annual Meeting on Women's Cancer, 19–25 March 2021.

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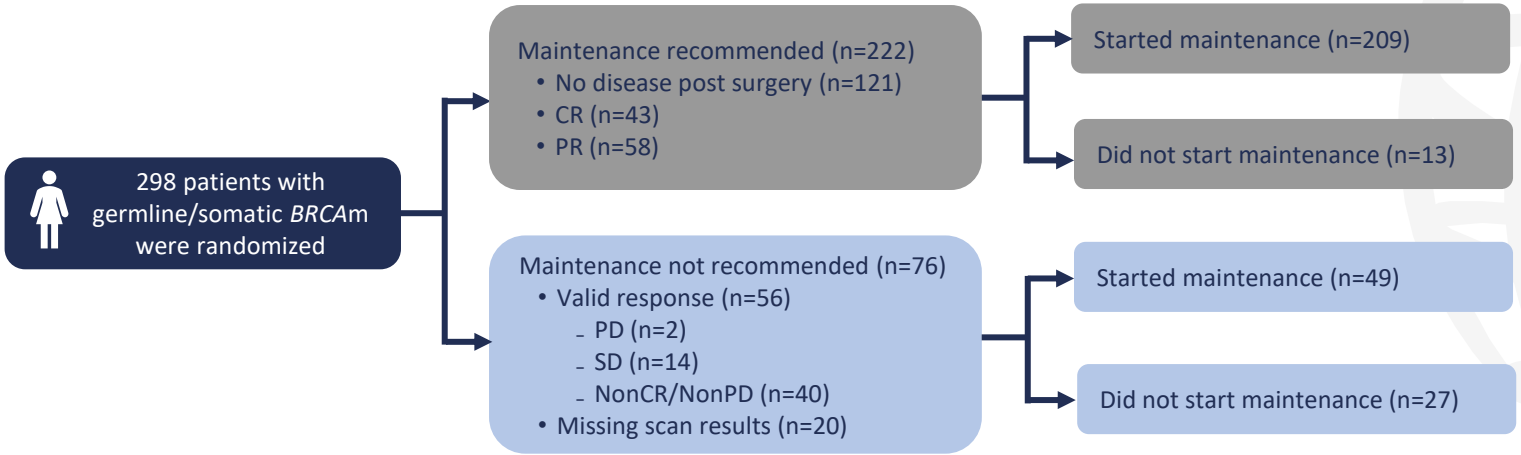
VELIA: Patients with *BRCA*m ovarian cancer who are eligible vs not eligible for PARP inhibitor maintenance therapy

Swisher EM, et al.

Assess predictive variables to identify patients who would benefit from PARP inhibitor maintenance according to current NCCN guidelines



- Patients in the maintenance not recommended subgroup were enriched for poorer prognosis, with higher frequency of stage IV disease and higher ECOG PS compared with the maintenance recommended group

BRCA, breast cancer gene; CR, complete response; ECOG PS, Eastern Cooperative Oncology Group Performance Status; m, mutation; NCCN, National Comprehensive Cancer Network; poly (adenosine diphosphate-ribose) polymerase; PD, progressive disease; PR, partial response; SD, stable disease.

Swisher EM, et al. Presented at the SGO 2021 Virtual Annual Meeting on Women's Cancer, 19–25 March 2021.

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VELIA: PFS in maintenance recommended vs maintenance not recommended population

Swisher EM, et al.

Treatment arm	Median PFS, months (95% CI)	HR versus control (95% CI)
Maintenance recommended population		
Control	19.7 (12.6–NR)	-
Veliparib combination only	20.0 (13.4–23.7)	1.02 (0.64–1.64)
Veliparib throughout	NR (27.3–NR)	0.29 (0.16–0.52)
Maintenance not recommended population		
Control	18.9 (9.1–NR)	-
Veliparib combination only	10.0 (5.2–16.5)	3.38 (1.22–9.36)
Veliparib throughout	16.4 (6.4–NR)	1.33 (0.52–3.44)

Among patients recommended for maintenance (in CR/PR to platinum), veliparib added upfront to chemotherapy and continued as maintenance prolonged PFS compared with chemotherapy alone.

Among patients who were not recommended for maintenance, the veliparib throughout regimen did not prolong PFS compared with chemotherapy alone.

BRCA, breast cancer gene; CI, confidence interval; CR, complete response; HR, hazard ratio; m, mutation; NR, not reached; poly (adenosine diphosphate-ribose) polymerase; PFS, progression-free survival; PR, partial response.

Swisher EM, et al. Presented at the SGO 2021 Virtual Annual Meeting on Women's Cancer, 19–25 March 2021.

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Summary

- Non-*BRCA* HRRm profiles were NOT associated with genomic instability (Myriad myChoice® HRD test) and are NOT associated with benefit from PARP inhibitor maintenance in PAOLA-1
- Patients who are NOT in PR/CR at the end of first-line Pt-based chemotherapy do NOT benefit from PARP inhibitor maintenance in VELIA

BRCA, breast cancer gene; CR, complete response; FDA, US Food and Drug Administration; HRD, homologous recombination deficient; HRR, homologous recombination repair; m, mutation; PARP, poly (adenosine diphosphate-ribose) polymerase; PR, partial response; Pt, platinum.

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Thank you for watching

SGO, Society of Gynecologic Oncology.

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