Maximizing the potential of PARP inhibitors as first-line maintenance therapy in ovarian cancer: Improving patient identification and treatment selection

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The rationale for PARP inhibitors in the first-line maintenance setting

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PARP inhibitor 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]
HRD+ (incl. *BRCA*m+) Total cohort: HR 0.43 / HR 0.62	Total cohort (all *BRCA*m+): HR 0.30	HRD+: *BRCA*m+ HR 0.33; *BRCA*m- HR 0.43

HR for disease progression or death

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

Disease recurrence and poor survival rates remain challenging

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

Median PFS (months)

Long-term follow-up data on survival benefit with PARP inhibitor 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; gBRCAm, germline BRCA mutation; OS, overall survival; PARP, poly(adenosine phosphate-ribose) polymerase; PFS, 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.

Identifying patients who may benefit from a PARP inhibitor in the first-line maintenance setting

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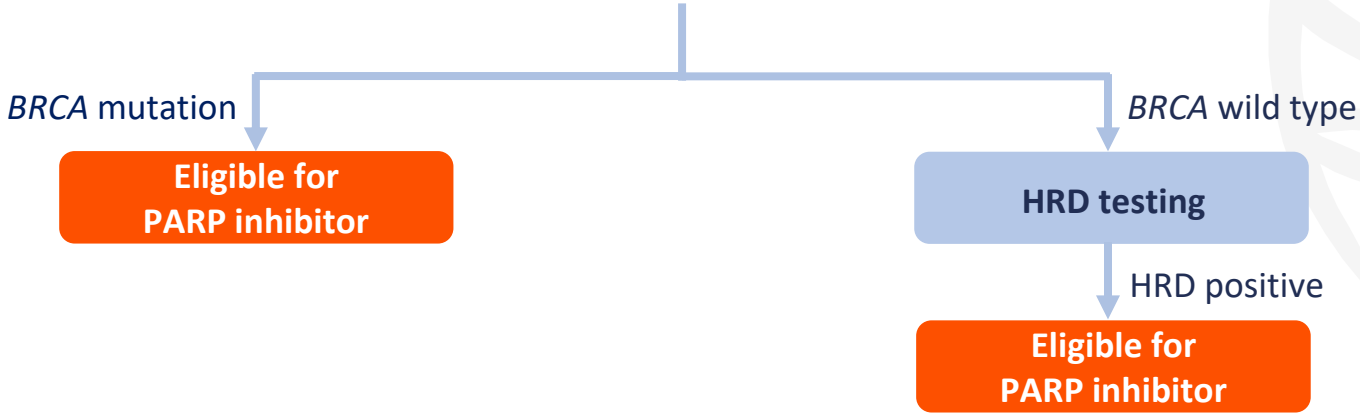
Updated ESMO recommendations for PARP inhibitor 1LM therapy in AOC

1. Test for somatic and germline *BRCA1/2* mutation at diagnosis
2. Observe partial or complete response to first-line platinum-based chemotherapy



1LM, first-line maintenance; AOC, advanced ovarian cancer; ESMO, European Society for Medical Oncology; HRD, homologous recombination deficiency; PARP, poly(adenosine phosphate-ribose) polymerase.

Colombo N, Ledermann JA; ESMO Guidelines Committee. *Ann Oncol.* 2021;32:1300–3.

Selecting a maintenance treatment regimen for individual patients

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Factors informing selection of maintenance therapy

Maintenance therapy aims to delay disease progression and prolong time between recurrences[1]

Clinical history and patient status[2–4]

- Comorbidities
- FIGO staging
- Prior treatment
- Recurrence
- Other options

Treatment-related factors[2–4]

- Safety profile
- Convenience
- Patient choice
- Other options
- Trial eligibility

Molecular pathology and genomics[2–4]

- HRD status
- *BRCA* status
- Genomic reversions

Financial considerations[2–4]

- Approval status
- Indications
- Reimbursement

FIGO, International Federation of Gynecology and Obstetrics; HRD, homologous repair deficiency.

1. Lorusso D, et al. *Cancer Treatment Rev*. 2020;91:102111; 2. Nero C, et al. *Cancers (Basel).* 2021;13:1298; 3. Mirza MR, et al. *Ann Oncol*. 2020;31:1148–59; 4. Madariaga A, et al. *Int J Gynecol Cancer*. 2020;30:903–15.

Dosing schedules for EMA-approved PARP inhibitors in the 1LM setting

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

Olaparib

- 300 mg taken twice daily
- Up to 2 years if there is no radiological evidence of disease
- More than 2 years if potential further benefit

Niraparib

- Weight ≥77 kg + baseline platelet count ≥150,000/µL, the starting dose is 300 mg once daily
- Otherwise, 200 mg taken once daily

Olaparib + bevacizumab

- 300 mg olaparib taken twice daily + 15 mg/kg bevacizumab once every 3 weeks

1LM, first-line maintenance; EMA, European Medicines Agency.

EMA SmPC for olaparib and niraparib. Available at: www.ema.europa.eu/ (accessed 30 May 2022).

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