

**The practicalities of PARP:
Optimizing the use of PARP inhibitors for
first-line maintenance treatment in
ovarian cancer**

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Expert panel



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Agenda

Welcome and introduction

Case 1: Lucia
BRCAM+ patient

Case 2: Francesca
HRD *BRCAt* patient

Case 3: Teresa
HRP patient

Conclusions

Why do we need PARP inhibitors as a first-line maintenance treatment option in ovarian cancer?

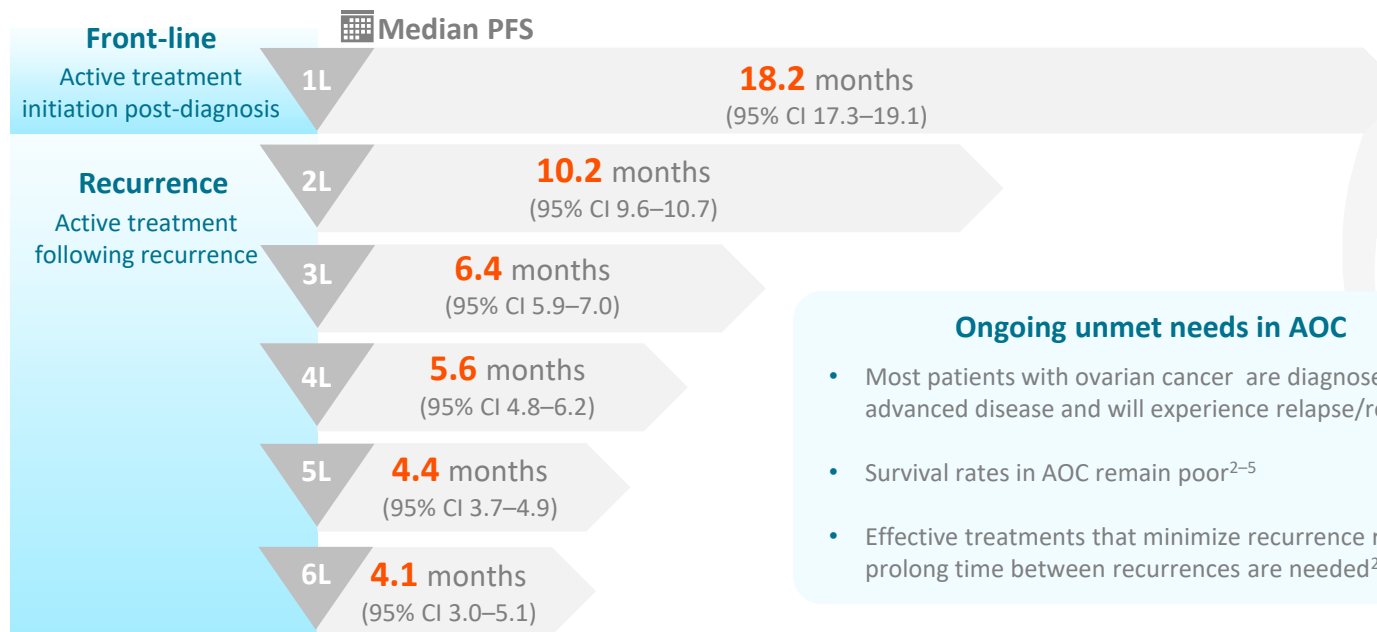
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Advanced ovarian cancer: A disease with multiple relapses

Without maintenance treatment, PFS shortens with each recurrence¹



Ongoing unmet needs in AOC

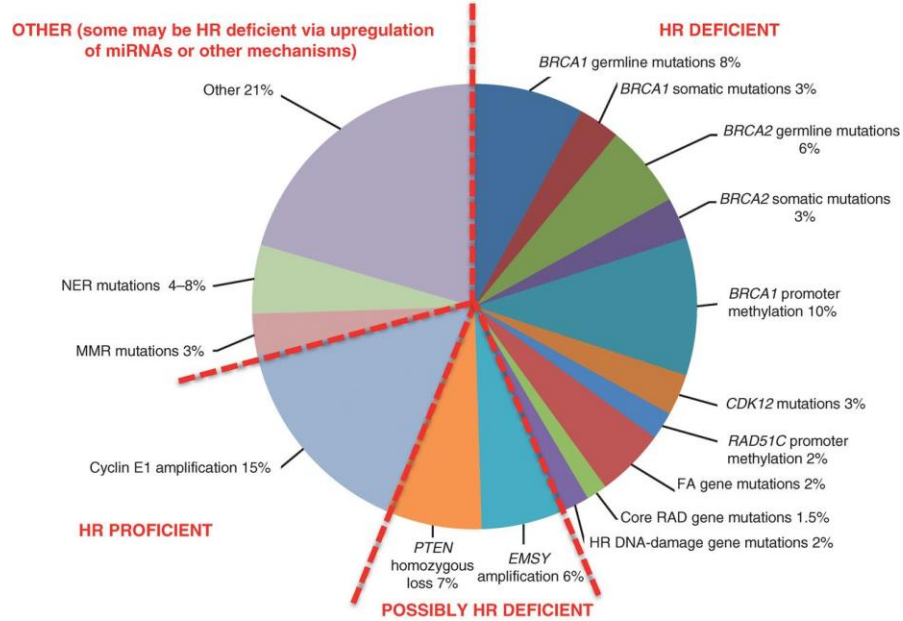
- Most patients with ovarian cancer are diagnosed with advanced disease and will experience relapse/recurrence^{2–5}
- Survival rates in AOC remain poor^{2–5}
- Effective treatments that minimize recurrence risk and prolong time between recurrences are needed^{2–4}

AOC, advanced ovarian cancer; CI, confidence interval; PARP, poly (adenosine diphosphate-ribose) polymerase; PFS, progression-free survival.

1. Hanks LC, et al. *Ann Oncol.* 2012;23:2605–12; 2. Pignata S, et al. *Ann Oncol.* 2017;28(Suppl. 8):viii51–6; 3. Colombo N, et al. *Int J Gynecol Cancer.* 2017;27:1134–40; 4. Jiang X, et al. *Cancer Manag Res.* 2019;11:4371–90; 5. Colombo N, et al. *Crit Rev Oncol Hematol.* 2006;60:159–79.

Targeting HRR defects in AOC with PARP inhibitors

PARP inhibitors exploit genetic defects in HRR pathways in AOC molecular subtypes¹⁻³



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AOC, advanced ovarian cancer; BRCA, breast cancer gene; CDK, cyclin-dependent kinase; EMSY, EMSY transcriptional repressor, BRCA2 interacting; FA, Fanconi anaemia; HGS, high-grade serous; HR, homologous recombination; HRD, homologous recombination repair deficient; HRP, homologous recombination repair proficient; HRR, homologous recombination repair; miRNA, micro-RNA; MMR, mismatch repair; NER, nucleotide excision repair; PARP, poly (adenosine diphosphate-ribose) polymerase; PTEN, phosphatase and tensin homolog.

1. Hollis RL, Gourley C. *Cancer Biol Med*. 2016;13:236-47; 2. Hollis RL, Gourley C. *Cancer Biol Med*. 2017;14:196-201; 3. Konstantinopoulos PA, et al. *Cancer Discov*. 2015;5:1137-54.



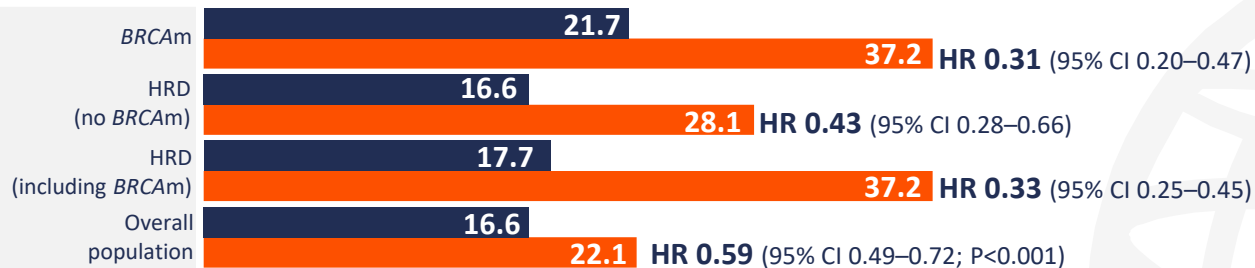
PARP inhibitors in the first-line maintenance setting

Median PFS (months) by BRCA and HRD status


PAOLA-1¹

 N=806

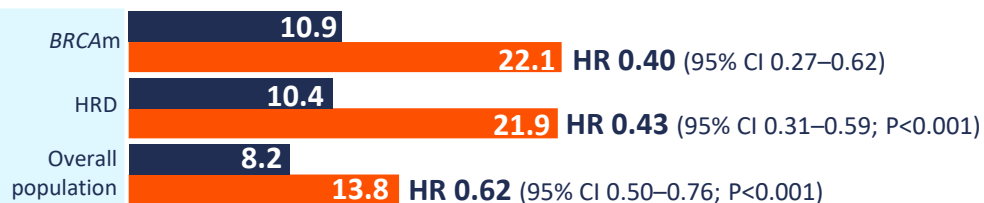
OLAP+BEV vs PBO+BEV



PRIMA²

 N=733

NIR vs PBO



SOLO-1³

 N=391

OLAP vs PBO



BEV, bevacizumab; BRCA, breast cancer gene; CI, confidence interval; HR, hazard ratio; HRD, homologous recombination deficient; m, mutation; OLAP, olaparib; NIR, niraparib; PBO, placebo; PFS, progression-free survival; PARP, poly (adenosine diphosphate-ribose) polymerase.

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

Factors informing selection of maintenance therapy

Maintenance therapy aims to delay disease progression and prolong time between recurrences¹

Clinical history and patient status²⁻⁴

- Comorbidities (e.g. hypertension, thromboembolism)
- FIGO staging
- Prior therapies and surgical outcome(s)
- Timing and site of recurrence
- Other treatment options (e.g. surgery, NACT)

Molecular pathology and genomics²⁻⁴

- HRR pathway status (HRD versus HRP)
- *BRCA1/BRCA2* mutation status
- Genomic reversions

Treatment-related factors²⁻⁴

- Safety profile and risk of AEs
- Convenience (e.g. dosing, route of administration)
- Patient preference
- Other treatment options (e.g. surgery, NACT)
- Clinical trial eligibility for new investigational agent(s)

Financial considerations²⁻⁴

- Regulatory approval status
- Indication(s) for use
- Reimbursement and payor decisions

AE, adverse event; *BRCA*, breast cancer gene; FIGO, International Federation of Gynecology and Obstetrics; HRD, homologous recombination repair deficient; HRP, homologous recombination repair proficient; HRR, homologous recombination repair; NACT, neoadjuvant chemotherapy; PARP, poly (adenosine diphosphate-ribose) polymerase.
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.



Case-based panel discussion



Case 1: Lucia



- 44 years of age
- History of uncontrolled hypertension
- No other underlying comorbidities or systemic disease



Immediate family history of cancer:

- Mother: breast cancer



- Histology: FIGO stage IIIC HGS OC
- Molecular pathology: germline *BRCA1* mutation positive



Treatment to date:

- Primary debulking surgery (RT=0)
- Adjuvant platinum-paclitaxel chemotherapy

Case 2: Francesca



- 55 years of age
- Hypertension (well controlled)



Family history of cancer:

- None



- Histology: FIGO stage IIIB HGS OC
- Molecular pathology: *BRCA* wild-type
- Myriad MyChoice[®] score: >42
- Foundation CDx LOH score: >16



Treatment to date:

- Primary debulking surgery (RT=1 cm)
- Adjuvant platinum-paclitaxel chemotherapy

Case 3: Teresa



- 65 years of age
- Inflammatory bowel disease (Crohn's disease)



Family history of cancer:

- None



- Histology: FIGO stage IIIC HGS OC
- Molecular pathology: *BRCA* wild-type
- Myriad MyChoice[®] score: <42



Treatment to date:

- Primary debulking surgery (RT=0.5 cm)
- Adjuvant platinum-paclitaxel chemotherapy