

SPECIAL ARTICLE

ESMO Clinical Practice Guideline Express Update on the management of epithelial ovarian cancer

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INTRODUCTION

This Express Update provides new recommendations for the following ESMO Clinical Practice Guideline (CPG): Newly diagnosed and relapsed epithelial ovarian cancer: ESMO Clinical Practice Guideline for diagnosis, treatment and follow-up.¹

View the original CPG here: <https://www.esmo.org/guidelines/esmo-clinical-practice-guideline-epithelial-ovarian-cancer>.

MANAGEMENT OF ADVANCED EPITHELIAL OVARIAN CANCER (INTERNATIONAL FEDERATION OF GYNECOLOGY AND OBSTETRICS STAGE III-IV)

Systemic therapy

Poly (ADP-ribose) polymerase inhibitor maintenance treatment. Maintenance treatment with poly (ADP-ribose) polymerase inhibitors (PARPis) has shown efficacy in delaying disease recurrence or progression for patients with epithelial ovarian cancer (EOC; also known as tubo-ovarian carcinoma) who have achieved no evidence of disease (NED), complete response (CR) or partial response (PR) to first-line chemotherapy (ChT). Previously, olaparib, olaparib—bevacizumab or niraparib were recommended as first-line maintenance for patients with *BRCA1/2* mutations (mut). Similarly, niraparib or olaparib—bevacizumab were recommended for *BRCA1/2*-wild type (wt)/homologous recombination deficiency (HRD)-positive tumours. In addition, niraparib could be considered an alternative to bevacizumab for HRD-negative tumours, if maintenance were to be given.

The phase III, double-blind, multicentre ATHENA-MONO (GOG-3020/ENGOT-ov45) trial evaluated rucaparib monotherapy as first-line maintenance in a broad population of patients with newly diagnosed advanced ovarian cancer, providing additional evidence on the role of PARPi maintenance therapy in this setting.² Rucaparib demonstrated a significant improvement in investigator-assessed progression-free survival (PFS) compared with placebo.

In the HRD-positive population [*BRCA*-mut or *BRCA*-wt/genomic loss of heterozygosity (LOH)-high], the median PFS was 28.7 months [95% confidence interval (CI) 23.0 months-not reached] with rucaparib versus 11.3 months (95% CI 9.1-22.1 months) with placebo [log-rank $P = 0.0004$; hazard ratio (HR) 0.47, 95% CI 0.31-0.72].²

In the intention-to-treat population, the median PFS was 20.2 months (95% CI 15.2-24.7 months) with rucaparib versus 9.2 months (95% CI 8.3-12.2 months) with placebo (log-rank $P < 0.0001$; HR 0.52, 95% CI 0.40-0.68).²

A PFS benefit was also observed in the HRD-negative subgroup (*BRCA*-wt/LOH-low), with a median PFS of 12.1 months (95% CI 11.1-17.7 months) with rucaparib versus 9.1 months (95% CI 4.0-12.2 months) with placebo (HR 0.65, 95% CI 0.45-0.95). Overall survival (OS) data were immature at the time of data cut-off.²

The safety profile of rucaparib in ATHENA-MONO was consistent with previous findings for rucaparib in other settings and other PARPis in the first-line maintenance setting. The most common grade ≥ 3 treatment-emergent adverse events (TEAEs) were anaemia (28.7%) and neutropenia (14.6%). TEAEs led to discontinuation in 11.8% of patients treated with rucaparib. Myelodysplastic syndrome and acute myeloid leukaemia were reported in two patients (0.5%) in the rucaparib group and no patients in the placebo group.² An updated algorithm for the management of advanced EOC is shown in Figure 1.

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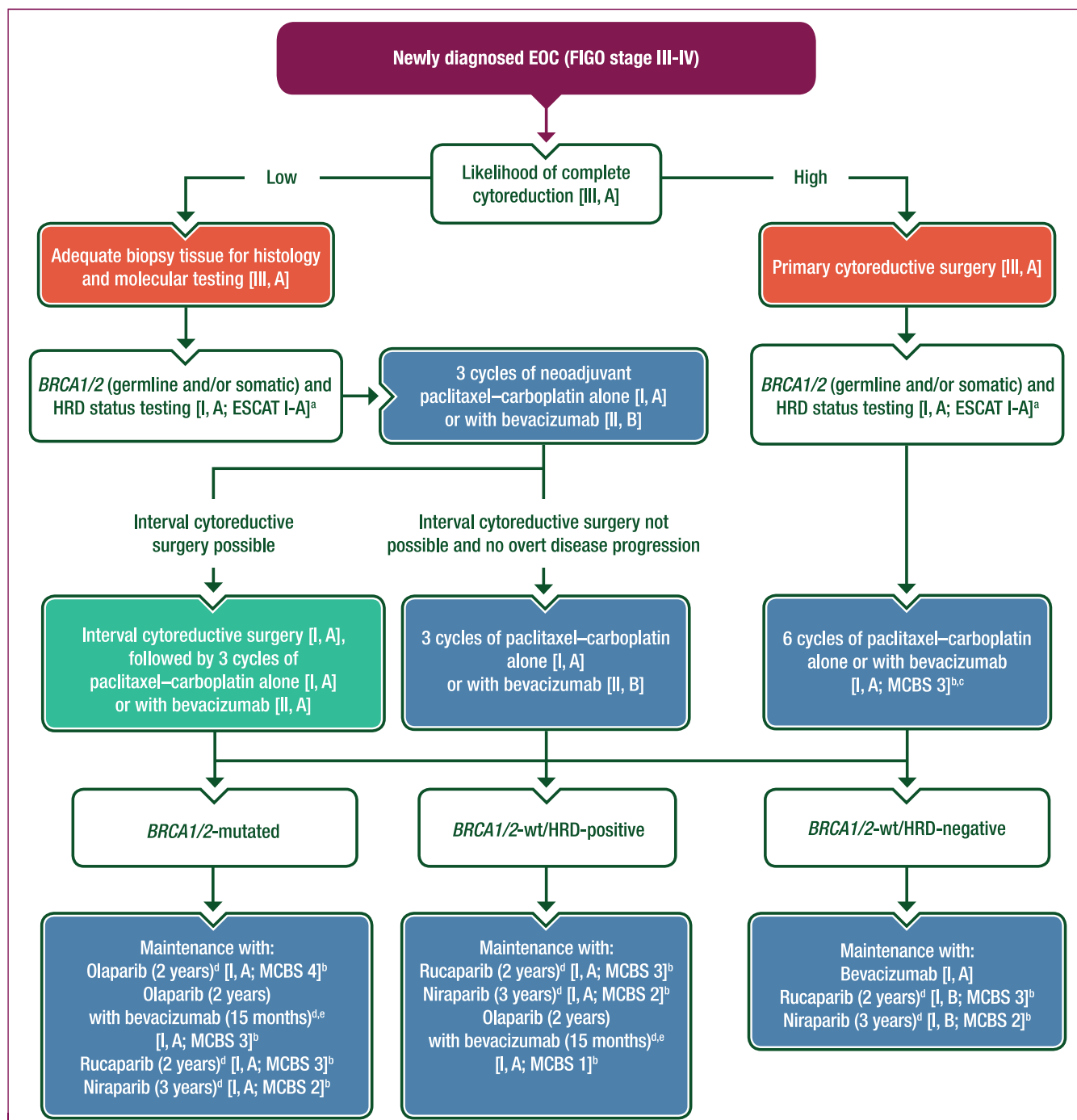


Figure 1. Management of advanced EOC (FIGO stage III-IV).

Purple: algorithm title; orange: surgery; blue: systemic anticancer therapy or their combination; turquoise: nonsystemic anticancer therapies or combination of treatment modalities; white: other aspects of management and non-treatment aspects.

AUC, area under the curve; ChT, chemotherapy; EMA, European Medicines Agency; EOC, epithelial ovarian cancer; ESCAT, ESMO Scale for Clinical Actionability of molecular Targets; FDA, Food and Drug Administration; FIGO, International Federation of Gynecology and Obstetrics; HRD, homologous recombination deficiency; MCBS, ESMO-Magnitude of Clinical Benefit Scale; PARPi, poly (ADP-ribose) polymerase inhibitor; wt, wild type.

^aESCAT scores apply to alterations from genomic-driven analyses only. These scores have been defined by the guideline authors, assisted if needed by the ESMO Precision Medicine Working Group.⁷

^bESMO-MCBS v2.0³ was used to calculate scores for new therapies/indications approved by the EMA or FDA. The scores have been calculated by the ESMO-MCBS Working Group and validated by the ESMO Guidelines Committee (<https://www.esmo.org/guidelines/esmo-mcbs/esmo-mcbs-evaluation-forms>).

^cWeekly ChT with paclitaxel (60 mg/m²)—carboplatin (AUC 2) can be an alternative in frail patients [I, B].

^dOnly when patients have complete or partial response to platinum or no evidence of disease. For patients without response to platinum, a PARPi is not indicated; these patients can be managed with bevacizumab maintenance if appropriate (mainly stable disease), or with second-line therapy if they have progressive disease (see Figure 3 in the original Clinical Practice Guideline¹).

^eOption for patients for whom bevacizumab was added to paclitaxel—carboplatin.

Updated recommendations incorporate ESMO-Magnitude of Clinical Benefit Scale (MCBS) v2.0³; the magnitude of clinical benefit scores were adjusted due to revised toxicity evaluation. See [Supplementary Table S1](https://doi.org/10.1016/j.esmoop.2025.106032), available at <https://doi.org/10.1016/j.esmoop.2025.106032>, for the relevant ESMO-MCBS scorecard links.

Recommendations

- Maintenance treatment with PARPis, with or without bevacizumab, is recommended for patients with *BRCA1/2*-mut or *BRCA1/2*-wt/HRD-positive tumours with NED at the end of ChT or with CR or PR to platinum–paclitaxel first-line ChT [I, A].
 - Options for *BRCA1/2*-mut [ESMO Scale for Clinical Actionability of molecular Targets (ESCAT) score: I-A]:
 - Olaparib for 2 years [ESMO-MCBS v2.0 score: 4]
 - Olaparib for 2 years combined with bevacizumab for 15 months [ESMO-MCBS v2.0 score: 3]
 - Rucaparib for 2 years [ESMO-MCBS v2.0 score: 3]
 - Niraparib for 3 years [ESMO-MCBS v2.0 score: 2]
 - Options for *BRCA1/2*-wt/HRD-positive [ESCAT score: I-A]
 - Rucaparib for 2 years [ESMO-MCBS v2.0 score: 3]
 - Niraparib for 3 years [ESMO-MCBS v2.0 score: 2]
 - Olaparib for 2 years combined with bevacizumab for 15 months [ESMO-MCBS v2.0 score: 1].
- Maintenance treatment with bevacizumab for 15 months [I, A], rucaparib for 2 years [I, B; ESMO-MCBS v2.0 score: 3] or niraparib for 3 years [I, B; ESMO-MCBS v2.0 score: 2] can be recommended for HRD-negative tumours (the PARPis in patients with NED, CR or PR to platinum–paclitaxel first-line ChT). The choice of treatment should be based on the distribution of disease, response to ChT and the clinical characteristics of the patient.

MANAGEMENT OF RECURRENT EOC

Treatment decisions are guided by the likelihood of response to platinum-based therapy. The probability of response and its duration are related to the platinum-free interval (PFI). Response and PFS are generally lower when the preceding PFI is <6 months. For patients progressing on platinum-based therapy or with clinical progression shortly after completing treatment, further platinum is not considered an option, and non-platinum-based treatment is recommended.

Systemic therapy when platinum is not an option

For patients with recurrent EOC where re-exposure to platinum is not considered clinically appropriate (e.g. due to proven resistance, expected resistance, platinum intolerance or patient choice/quality-of-life issues), alternative systemic treatments are available. These primarily consist

of non-platinum-based ChT [e.g. weekly paclitaxel, pegylated liposomal doxorubicin (PLD) or topotecan] with low objective response rates (ORR; <15% with a non-weekly paclitaxel agent and 30%–35% with weekly paclitaxel) and no substantial OS benefit.^{4,5} While bevacizumab combined with non-platinum-based ChT has improved PFS and ORR in platinum-resistant disease, it has not shown an OS benefit. There is a clear need for new effective and targeted therapeutic options for this difficult-to-treat population.

Antibody–drug conjugates. Mirvetuximab soravtansine-gynx (MIRV) is a first-in-class antibody–drug conjugate that targets folate receptor α (FR α), commonly overexpressed in ovarian carcinomas.

The pivotal phase III, open-label, randomised, controlled trial, MIRASOL (GOG-3045/ENGOT-Ov55), compared MIRV with investigator's choice ChT (paclitaxel, PLD or topotecan) in 453 patients with platinum-resistant (defined here as PFI <6 months), high-grade serous ovarian cancer.⁴ Participants had received one to three previous lines of therapy and had high FR α tumour expression ($\geq 75\%$ of cells with $\geq 2+$ staining intensity as determined by immunohistochemistry). Median PFS (primary endpoint) was 5.62 months (95% CI 4.34–5.95 months) with MIRV versus 3.98 months (95% CI 2.86–4.47 months) with ChT ($P < 0.001$).⁴ Key secondary endpoints included ORR, which was 42.3% in the MIRV group versus 15.9% in the ChT group (odds ratio 3.81, 95% CI 2.44–5.94, $P < 0.001$) and OS, with a median of 16.46 months (95% CI 14.46–24.57 months) versus 12.75 months (95% CI 10.91–14.36 months) with ChT (HR for death 0.67, 95% CI 0.50–0.89, $P = 0.005$).

Serious AEs of any grade were less frequent with MIRV (23.9%) than with ChT (32.9%).⁴ Discontinuations due to AEs occurred in 9.2% of MIRV patients compared with 15.9% of ChT patients. The most common AEs reported in the MIRV group included blurred vision (40.8%), keratopathy (32.1%), abdominal pain (30.3%) and fatigue (30.3%). Ocular AEs occurred in 56.0% of MIRV-treated patients, but they were predominantly low-grade and reversible, with established management strategies.

Only 1.8% of participants discontinued MIRV due to ocular AEs.⁴ Proactive management of ocular events, including lubricating artificial tears, along with regular ocular examinations, is crucial for patient safety and treatment adherence.⁶

An updated algorithm for the management of recurrent EOC is shown in [Figure 2](#). As the treatment landscape evolves, MIRV emerges as an option for patients in whom platinum-based therapy is not considered optimal according to the algorithm, and for those with a PFI <6 months, where the expected clinical benefit from platinum-based therapy is likely to be limited.

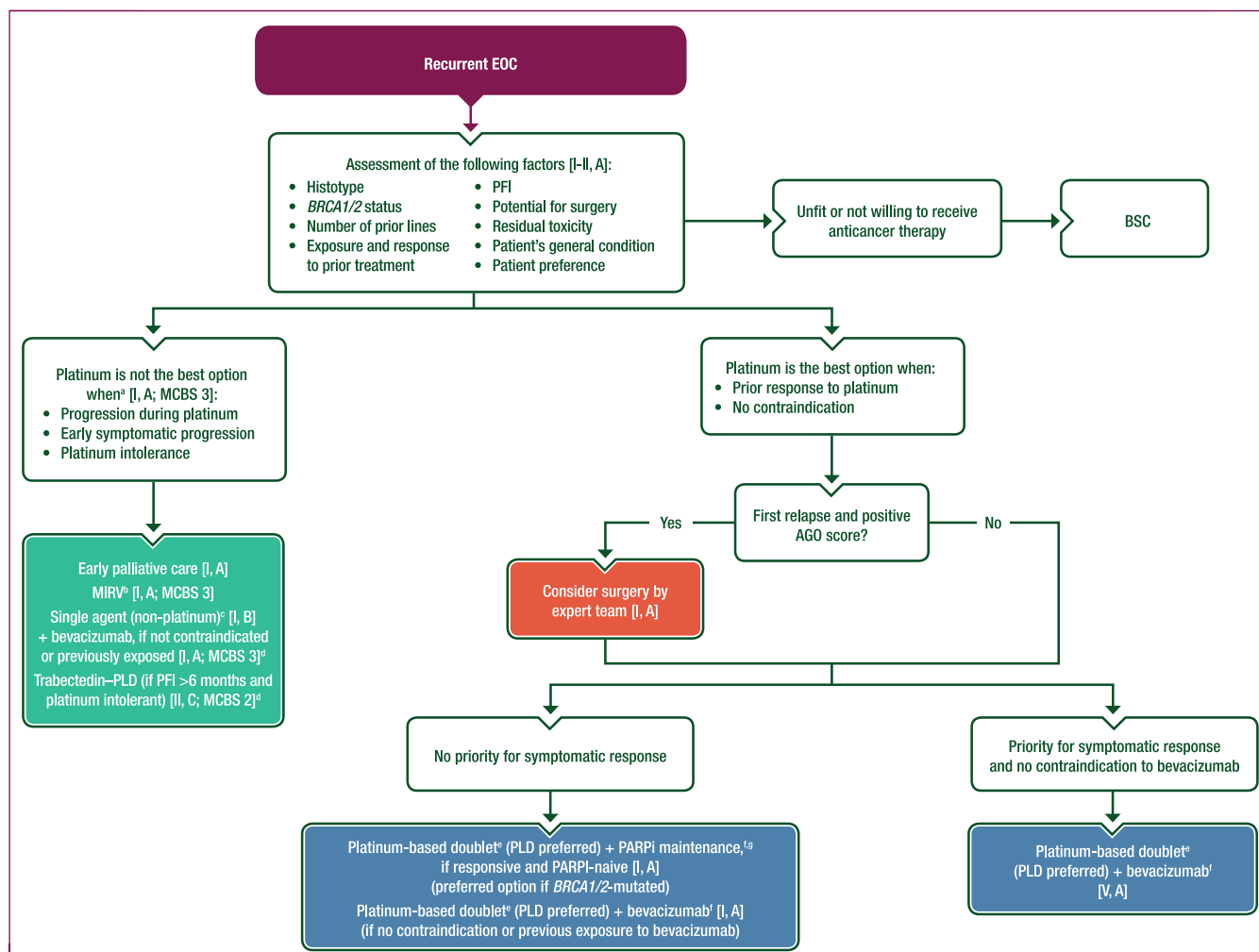


Figure 2. Management of recurrent EOC.

Purple: algorithm title; orange: surgery; blue: systemic anticancer therapy or their combination; turquoise: nonsystemic anticancer therapies or combination of treatment modalities; white: other aspects of management and non-treatment aspects.

AGO, Arbeitsgemeinschaft Gynaekologische Onkologie; BSC, best supportive care; EMA, European Medicines Agency; EOC, epithelial ovarian cancer; FDA, Food and Drug Administration; FR α , folate receptor α ; MCBS, ESMO-Magnitude of Clinical Benefit Scale; mut, mutation; MIRV, mirvetuximab soravtansine-gynx; PARPi, poly (ADP-ribose) polymerase inhibitor; PFI, platinum-free interval; PLD, pegylated liposomal doxorubicin.

*Patient choice and quality-of-life issues may also suggest that platinum is not the best option.

^bFor patients with high-grade serous EOC, a PFI <6 months and high FR α expression [defined as $\geq 75\%$ of viable tumour cells with moderate (2+) or strong (3+) staining intensity using a validated assay], who have received one to three prior lines of systemic therapy.

^cWeekly paclitaxel, PLD, topotecan or gemcitabine.

^dESMO-MCBS v2.0³ was used to calculate scores for new therapies/indications approved by the EMA or FDA. The scores have been calculated by the ESMO-MCBS Working Group and validated by the ESMO Guidelines Committee (<https://www.esmo.org/guidelines/esmo-mcbs/esmo-mcbs-evaluation-forms>).

^ePaclitaxel, PLD or gemcitabine (carboplatin–gemcitabine–bevacizumab: ESMO-MCBS v2.0 score: 2).^d

^fUntil disease progression or next line of treatment is started [I, A].

^gOlaparib for BRCA1/2-mutated: ESMO-MCBS v2.0 score: 1^d; niraparib regardless of BRCA1/2-mut status: ESMO-MCBS v2.0 score: 2^d; rucaparib regardless of BRCA1/2-mut status: ESMO-MCBS v2.0 score: 2.^d

Recommendation

- For patients with high-grade serous EOC, a PFI <6 months and high FR α expression [defined as $\geq 75\%$ of viable tumour cells with moderate (2+) or strong (3+) staining intensity using a validated assay], who have received one to three prior lines of systemic therapy, MIRV is recommended [I, A; ESMO-MCBS v2.0 score: 3].

METHODOLOGY

This Express Update was developed in accordance with the ESMO standard operating procedures for Express Update

development (<https://www.esmo.org/guidelines/esmo-guidelines-methodology>). All recommendations provided are based on current scientific evidence and the authors' collective expert opinion. Where recommendations for multiple different treatment options exist, prioritisation is illustrated by ordering these options according to: level of evidence (LoE) and grade of recommendation (GoR); where equal, by ESMO-MCBS score; where equal, by alphabetical order. The relevant literature has been selected by the expert authors. ESCAT scores have been defined by the authors, assisted if needed by the ESMO Precision Medicine Working Group.⁷ ESMO-MCBS v2.0³ was used to calculate

scores for new therapies/indications approved by the European Medicines Agency (EMA) or Food and Drug Administration (FDA) (<https://www.esmo.org/guidelines/esmo-mcbs>). The scores have been calculated and validated by the ESMO-MCBS Working Group and reviewed by the authors. The FDA/EMA or other regulatory body approval status of new therapies/indications is reported at the time of writing this Express Update. LoEs and GoRs have been applied using the system shown in [Supplementary Table S2](#), available at <https://doi.org/10.1016/j.esmoop.2025.106032>.⁸ Statements without grading were considered justified standard clinical practice by the authors. For future updates to the Epithelial Ovarian Cancer Clinical Practice Guideline, including Express Updates, please see the ESMO Guidelines website: <https://www.esmo.org/guidelines/esmo-clinical-practice-guidelines-gynaecological-cancers>.

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