



Guideline 4-3 Version 4

A Quality Initiative of the
Program in Evidence-Based Care (PEBC), Cancer Care Ontario
(CCO)

Systemic Therapy for Recurrent Epithelial Ovarian Cancer

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An assessment conducted in November 2023 deferred the review of Guideline 4-3 Version 4. This means that the document remains current until it is assessed again next year. The PEBC has a formal and standardized process to ensure the currency of each document ([PEBC Assessment & Review Protocol](#))

Guideline 4-3 Version 4 is comprised of 5 sections. You can access the summary and full report here:

<https://www.cancercareontario.ca/en/guidelines-advice/types-of-cancer/37871>

Section 1:	Guideline Recommendations
Section 2:	Recommendations and Key Evidence
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PUBLICATIONS RELATED TO THIS REPORT

Fung Kee Fung M, Kennedy E, Francis J, Mackay H, and members of the Gynecologic Cancer Disease Site Group. Optimal chemotherapy for recurrent ovarian cancer. Toronto (ON): Cancer Care Ontario; 2011 Nov 21. Program in Evidence-based Care Evidence-Based Series No.: 4-3.

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Systemic Therapy for Recurrent Epithelial Ovarian Cancer

Recommendations

This is a quick reference guide and provides the guideline recommendations only. For key evidence associated with each recommendation, the systematic review, and the guideline development process, see the [Full Report](#).

GUIDELINE OBJECTIVES

To recommend systemic therapy options for women with recurrent epithelial ovarian cancer including fallopian tube and primary peritoneal cancers.

TARGET POPULATION

The target population comprises women with recurrent epithelial ovarian cancer who have previously received platinum-based chemotherapy. Specific subgroups of interest are identified based on response to therapy.

INTENDED USERS

The intended users of this guideline are gynecologic oncologists or medical oncologists in the province of Ontario.

BACKGROUND INFORMATION

This guideline was based on an updated systematic review of the 2011 evidence base [1]. New evidence has led to new recommendations in some areas.

RECOMMENDATIONS

Recommendations 1, 2, and 3 are endorsements of those found in the 2011 version of this guideline; the original recommendations continue to be valid and have not changed.

Recommendations 4 and 5 are new in this current version of the guideline.

Recommendation 1

Systemic therapy for recurrent ovarian cancer is not curative. As such, it is recognized that, to determine the optimal therapy, each patient needs to be assessed individually in terms of recurrence, sensitivity to platinum, toxicity, ease of administration, and patient preference.

Recommendation 2

All patients should be offered the opportunity to participate in clinical trials, if appropriate.

Recommendation 3

Chemotherapy for patients with platinum-sensitive recurrent ovarian cancer:

- If the option to participate in a clinical trial is not available, combination platinum-based chemotherapy should be considered, providing that there are no contraindications. The decision regarding which combination to use should be based on toxicity experienced with primary therapy, patient preference, and other factors. Recommended combinations are:
 - carboplatin and paclitaxel
 - carboplatin and gemcitabine
 - carboplatin and pegylated liposomal doxorubicin
- If combination platinum-based chemotherapy is contraindicated, then a single

platinum agent should be considered. Carboplatin has demonstrated efficacy across trials and has a manageable toxicity profile.

- If a single platinum agent is not being considered (e.g., because of toxicity or allergy), then monotherapy with paclitaxel, topotecan, or pegylated liposomal doxorubicin is a reasonable treatment option.

Recommendation 4

For patients with platinum-sensitive recurrent ovarian cancer:

- Women with platinum-sensitive recurrent ovarian cancer should be offered chemotherapy with biologics after a discussion concerning the safety profile

Targeted agents:

- Bevacizumab combined with combination chemotherapy and as maintenance therapy can be considered.
- Cediranib administered during the chemotherapy and maintenance therapy can be considered.
- PolyADP-ribose polymerase (PARP) inhibitors are recommended for patients with known *BRCA* 1 or 2 mutation (somatic and germline) as maintenance treatment post platinum-based chemotherapy for recurrent disease.
- Niraparib can be considered for patients who are *BRCA* wild-type as maintenance post-platinum-based chemotherapy for recurrent disease.

Qualifying Statements for Recommendation 4

- With the increase in evidence supporting the use of PARP inhibitors in patients with homologous recombination deficiency mutations, consideration should be given to testing the *BRCA* status of all women with ovarian cancer at initial diagnosis.
- PARP inhibitors have demonstrated an increase in progression-free survival in patients with *BRCA* mutations without a significant improvement in overall survival
- Women with wild-type *BRCA* also showed a minor improvement in progression-free survival

Recommendation 5

For patients with platinum-refractory or platinum-resistant recurrent ovarian cancer:

- Lower levels of response to treatment are expected for this group; therefore, the goals of treatment should be to improve patient's quality of life by extending the symptom-free interval, reducing symptom intensity, increasing progression-free interval, or if possible, prolonging life.
- Monotherapy with a non-platinum agent should be considered since there does not appear to be an advantage in the use of non-platinum-containing combination chemotherapy in this group of patients. Single-agent paclitaxel, topotecan, pegylated liposomal doxorubicin, and gemcitabine have demonstrated activity in this patient population and are reasonable treatment options.
- There is no evidence to support or refute the use of more than one line of chemotherapy in patients with platinum-refractory or platinum-resistant recurrences. There are many treatment options that have shown modest response rates but their benefit over best supportive care has not been studied in clinical trials.
- Bevacizumab combined with chemotherapy (pegylated liposomal doxorubicin, weekly paclitaxel, or topotecan) can be considered for women who meet the eligibility

criteria of the Avastin Use in Platinum-Resistant Ovarian Cancer (AURELIA) phase III randomized controlled trial: confirmed epithelial ovarian, fallopian tube, or primary peritoneal cancer that had progressed within six months of completing ≥ 4 cycles of platinum-based therapy, age ≥ 18 years, Eastern Cooperative Oncology Group performance status ≤ 2 , and adequate liver, renal, and bone marrow function. Ineligible patients include those who have received > 2 prior anticancer regimens or who had refractory disease, patients with a history of bowel obstruction (including subocclusive disease) related to underlying disease, a history of abdominal fistula, gastrointestinal perforation, or intra-abdominal abscess, or evidence of rectosigmoid involvement by pelvic examination, bowel involvement on computed tomography, or clinical symptoms of bowel obstruction.

Qualifying Statements for Recommendation 5

- At the time of the writing of this guideline there are numerous targeted agents in addition to vascular endothelial growth factor inhibitors, programmed death-1 and programmed death ligand-1 inhibitors, as well as other immunotherapies that are under investigation and that show promise in early trials. It is likely that one or some of these will become part of the lexicon of treatment protocols in the near future, either independently or in combination with conventional chemotherapy.