



Evidence-Based Series 4-13 Version 3

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

Adjuvant Care for Stage I Ovarian Cancer

Members of the Gynecology Cancer Disease Site Group

An assessment conducted in November 2023 deferred the review of Evidence-based Series (EBS) 4-13 Version 3. 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](#))

EBS 4-13 Version 3 is comprised of 3 sections. You can access the summary and full report here:

<https://www.cancercareontario.ca/en/guidelines-advice/types-of-cancer/646>

Section 1: Clinical Practice Guideline (ENDORSED)
Section 2: Systematic Review
Section 3: Document Assessment and Review

March 15, 2022

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Guideline Report History

GUIDELINE VERSION	SYSTEMATIC REVIEW		PUBLICATIONS	NOTES and KEY CHANGES
	Search Dates	Data		
Original 2004	1965 to May 2003	Full Report	Peer review publication. Web publication.	N.A.
Version 2 May 2016	2003 to December 1 2015	New data found in Section 3: Document Summary and Review Tool (APPENDIX A)	Updated web publication	2004 Recommendations are ENDORSED
Current Version 3 March 2022	2015 to December 31 2021	No new data was found. See Section 3 Document Assessment and Review	Updated web publication	2004 Recommendations are ENDORSED

**A Quality Initiative of the Program in Evidence-based Care (PEBC),
Cancer Care Ontario (CCO)
Developed by the Gynecology Cancer Disease Site Group**

**Adjuvant Care for Stage I Ovarian Cancer:
Guideline Recommendations**

*L. Elit, A. Fyles, A. Chambers, M. Fung Kee Fung, A. Covens, M. Carey, and members of the
Gynecology Cancer Disease Site Group.*

**These guideline recommendations have been ENDORSED, which means that the recommendations are still current and relevant for decision making.
Please see Section 3: Document Assessment and Review for a summary of updated evidence published between 2003 and 2022, and for details on how this Clinical Practice Guideline was ENDORSED**

Report Date: March 15, 2022

Guideline Questions

1. What is the role of adjuvant care in women with completely surgically staged stage I ovarian cancer?
2. What is the role of adjuvant care in women who receive incomplete or no surgical staging of ovarian cancer?
3. What is the optimal strategy for adjuvant care in women with ovarian cancer?

Target Population

These recommendations apply to women with newly diagnosed stage I ovarian cancer.

Recommendations

- The stage of ovarian cancer is an important prognostic factor that influences survival and the choice of therapy. The quality of the surgical staging is a key determinant of treatment recommendations (*Draft Evidence Summary “#4-15 Management of an Ovarian Mass” will further describe optimal surgical staging*).
- Women who have undergone optimal surgical staging, including pelvic and para-aortic lymph node sampling, and have stage I disease may or may not benefit from adjuvant platinum-based chemotherapy (see Qualifying Statements section below).
- Women who have not undergone optimal surgical staging can be offered two options. The first option is that they undergo re-operation to optimally define the tumour stage and then be offered adjuvant therapy based on the findings. The other option is that they be offered platinum-based chemotherapy to decrease the risk of recurrence and improve survival.

- There is insufficient evidence to make a recommendation on the role of adjuvant pelvic radiation, whole abdominal-pelvic radiotherapy, or intraperitoneal radioactive chromic phosphate.

Qualifying Statements

- Accurate staging and tumour histology information is essential for developing recommendations on the management of ovarian cancer. A tumour pathology causing doubt should be reviewed by an expert.
- The standard of care for stage IA and IB grade I ovarian cancer in Ontario has been surgical resection with optimal staging and no adjuvant therapy. This standard is based on the work by Young et al¹ involving non-optimally staged, stage I cancer and the prognostic studies by Vergote et al² that reported an extremely low probability of recurrence in this population.
- The results of the largest trial comparing adjuvant chemotherapy to no chemotherapy in women with early stage ovarian cancer (International Collaborative Ovarian Neoplasm Study/Adjuvant ChemoTherapy In Ovarian Neoplasm [ICON/ACTION] Trial) are controversial because:
 - A subgroup analysis of the ACTION Trial showed no benefit from adjuvant chemotherapy in women who underwent optimal surgical staging, but that analysis was underpowered.
 - The entry criteria for the ICON Trial were vague and did not reflect the standard of surgical care offered in Canadian centres.
 - The meta-analysis included in this practice guideline demonstrates that stage I patients have an improved outcome with adjuvant chemotherapy. However, an estimated 90% of women undergoing surgical resection for ovarian cancer do not undergo optimal surgical staging. If the restaging of a sub-optimally staged patient reveals a more advanced disease, chemotherapy is the preferred treatment option. If reoperation confirms stage I disease, there is insufficient evidence for or against adjuvant chemotherapy. The treatment decision must be based on a discussion with the patient about potential benefits and risks.

Methods

Entries to MEDLINE (1965 through May 2003), CANCELIT (1975 through October 2002), and Cochrane Library (2003, Issue 1) databases and abstracts published in the proceedings of the annual meetings of the American Society of Clinical Oncology (1997 to 2003) were systematically searched for evidence relevant to this practice guideline report.

Evidence was selected and reviewed by three members of the Practice Guidelines Initiative's Gynecology Cancer Disease Site Group and methodologists. This practice guideline report has been reviewed and approved by the Gynecology Cancer Disease Site Group, which is comprised of medical oncologists, radiation oncologists, a pathologist, an oncology nurse, and patient representatives.

External review by Ontario practitioners is obtained for all practice guidelines through a mailed survey. Final approval of the guideline report is obtained from the Practice Guidelines Coordinating Committee.

The Practice Guidelines Initiative has a formal standardized process to ensure the currency of each guideline report. This process consists of the periodic review and evaluation of the scientific literature and, where appropriate, integration of this literature with the original guideline information.

Key Evidence

- Twenty-five randomized controlled trials were identified that compare treatments for stage I ovarian cancer. Eight of the studies reported results for stage I patients only.
- The randomized trials compared a variety of adjuvant therapies (chemotherapy, radiotherapy, and surgery), making it difficult to form recommendations on the optimal adjuvant therapy.
- Eleven randomized controlled trials reported at least minimal surgical staging.
- The majority of patients in the five randomized controlled trials comparing adjuvant chemotherapy to no chemotherapy did not receive lymphadenectomy as part of their surgical staging. The pooled results for stage I patients indicated a survival benefit with the addition of chemotherapy (relative risk, 0.71; 95% confidence interval, 0.56 to 0.90; $p=0.005$), and there was a benefit in terms of reduced recurrence favouring adjuvant chemotherapy (relative risk, 0.62; 95% confidence interval, 0.47 to 0.80; $p=0.0003$).
- A subgroup analysis of one randomized controlled trial demonstrated that if lymph node sampling is not conducted as part of the staging surgery then adjuvant chemotherapy is favoured in terms of overall survival (relative risk, 0.71; 95% confidence interval, 0.54 to 0.92).
- The largest trial to date randomized 925 women with stage I ovarian cancer to receive either adjuvant chemotherapy or no adjuvant chemotherapy. Platinum-based adjuvant chemotherapy was reported to improve overall five-year survival (absolute survival difference, 8%; 95% confidence interval, 2% to 12%; hazard ratio, 0.67; 95% confidence interval 0.50 to 0.90; $p=0.008$).
- The most frequently reported adverse effects associated with chemotherapy were grade 3 or 4 vomiting/nausea and grade 3 or 4 leukopenia.

Future Research

Future research needs to evaluate the implementation of surgical staging as a means of avoiding the use of chemotherapy in women who may not require toxic therapy. The role of adjuvant therapy in women with poor prognostic factors who are optimally staged needs to be assessed. The optimal chemotherapy regimen in terms of agents, dose, and duration has yet to be defined.

Related Guidelines

1. Practice Guidelines Initiative Practice Guideline Report #4-1-2: *First-line Chemotherapy for Postoperative Patients with Stage II, III or IV Epithelial Ovarian Cancer, Fallopian Tube Cancer, or Primary Peritoneal Cancer.*
2. Practice Guidelines Initiative Evidence Summary Report #4-3: *Chemotherapy for Recurrent Epithelial Ovarian Cancer Previously Treated with Platinum.*
3. Practice Guidelines Initiative Draft Evidence Summary Report #4-15: *Management of an ovarian mass (in progress).*

References

1. Young RC, Walton LA, Ellenberg SS, Homesley HD, Wilbanks GD, Decker DG, et al. Adjuvant therapy in stage I and stage II epithelial ovarian cancer. Results of two prospective randomized trials. *N Engl J Med* 1990;322:1021-7. [31]
2. Vergote I, Vergote-De Vos LN, Abeler VM, Aas M, Lindegaard MW, Kjorstad KE, et al. Randomized trial comparing cisplatin with radioactive phosphorus or whole-abdomen irradiation as adjuvant treatment of ovarian cancer. *Cancer* 1992;69:741-9. [43]

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*The Practice Guidelines Initiative is sponsored by:
Cancer Care Ontario & the Ontario Ministry of Health and Long-term Care.
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