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Practice Guidelines

Neoadjuvant chemotherapy for newly diagnosed, advanced ovarian cancer: Society of Gynecologic Oncology and American Society of Clinical Oncology Clinical Practice Guideline☆

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HIGHLIGHTS

- Women with high perioperative risks or low likelihood of achieving cytoreduction <1 cm (ideally no visible disease) should receive NACT.
- NACT is non-inferior to PCS for progression-free and overall survival and has lower peri- and postoperative morbidity and mortality.
- However, primary cytoreductive surgery may offer superior survival in selected patients.

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ABSTRACT

Purpose. To provide guidance to clinicians regarding the use of neoadjuvant chemotherapy and interval cytoreduction among women with stage IIIC or IV epithelial ovarian cancer.

Methods. The Society of Gynecologic Oncology and the American Society of Clinical Oncology convened an Expert Panel and conducted a systematic review of the literature.

Results. Four phase III clinical trials form the primary evidence base for the recommendations. The published studies suggest that for selected women with stage IIIC or IV epithelial ovarian cancer, neoadjuvant chemotherapy and interval cytoreduction are non-inferior to primary cytoreduction and adjuvant

☆ *Editor's note*: This joint American Society of Clinical Oncology (ASCO) and Society of Gynecologic Oncology (SGO) Clinical Practice Guideline provides recommendations with comprehensive review and analyses of the relevant literature for each recommendation. The guideline is being published simultaneously in *Journal of Clinical Oncology* and *Gynecologic Oncology*. Additional information, including a Data Supplement with additional evidence tables, a Methodology Supplement, slide sets, clinical tools and resources, and links to patient information at www.cancer.net, is available at www.asco.org/NACT-ovarian-guideline and www.asco.org/guidelineswiki. Authors' disclosures of potential conflicts of interest and author contributions are found at the end of this article.

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chemotherapy with respect to overall and progression-free survival and are associated with less perioperative morbidity and mortality.

Recommendations. All women with suspected stage IIIC or IV invasive epithelial ovarian cancer should be evaluated by a gynecologic oncologist prior to initiation of therapy. The primary clinical evaluation should include a CT of the abdomen and pelvis, and chest imaging (CT preferred). Women with a high perioperative risk profile or a low likelihood of achieving cytoreduction to <1 cm of residual disease (ideally to no visible disease) should receive neoadjuvant chemotherapy. Women who are fit for primary cytoreductive surgery, and with potentially resectable disease, may receive either neoadjuvant chemotherapy or primary cytoreductive surgery. However, primary cytoreductive surgery is preferred if there is a high likelihood of achieving cytoreduction to <1 cm (ideally to no visible disease) with acceptable morbidity. Before neoadjuvant chemotherapy is delivered, all patients should have confirmation of an invasive ovarian, fallopian tube, or peritoneal cancer.

Additional information is available at www.asco.org/NACT-ovarian-guideline and www.asco.org/guidelineswiki.

1. Introduction

Nearly 75% of women with ovarian cancer are diagnosed with advanced stage disease (International Federation of Gynecology and Obstetrics [FIGO] IIIC or IV) at presentation. Treatment with primary cytoreductive surgery (PCS) followed by chemotherapy has been the standard of care for these women. Recently, however, two randomized clinical trials (RCTs) compared PCS and chemotherapy to neoadjuvant chemotherapy (NACT) followed by interval cytoreductive surgery (ICS) and adjuvant chemotherapy for women with advanced ovarian cancer [1,2]. These trials demonstrated that NACT was non-inferior to PCS with respect to progression-free and overall survival and resulted in a lower incidence of treatment-related morbidity and mortality. However, both trials have been criticized because the median overall survival, mean operative time, and rates of optimal cytoreduction were lower than expected [3]. The choice between PCS and NACT remains controversial. The purpose of this guideline is to provide clinicians with information regarding the use of NACT and interval cytoreduction versus primary cytoreduction and chemotherapy among women with stage IIIC or IV epithelial ovarian cancer.

2. Guideline questions

This clinical practice guideline addresses the following clinical questions: (1) what clinical evaluations should be performed in all women with suspected or newly diagnosed stage IIIC or IV epithelial ovarian cancer? (2) Which patient and disease factors should be utilized as criteria for identifying patients who are not suitable for PCS? (3) How do NACT and PCS compare with respect to progression-free survival, overall survival, and perioperative morbidity and mortality in women with newly diagnosed stage IIIC or IV epithelial cancer who are fit for primary cytoreduction and have potentially resectable disease, and how should this information be used to select initial treatment? (4) What additional clinical evaluations should be performed in all women with suspected or newly diagnosed stage IIIC or IV epithelial ovarian cancer before NACT is delivered? (5) What is the preferred chemotherapy regimen for women with stage IIIC or IV epithelial ovarian cancer who will receive NACT? (6) Among women treated with NACT, does the timing of interval cytoreduction or the number of chemotherapy cycles after interval cytoreduction affect the safety or efficacy of treatment? (7) What are the treatment options for patients with progressive disease on NACT?

The bottom line

Neoadjuvant chemotherapy for newly diagnosed, advanced ovarian cancer: Society of Gynecologic Oncology and American Society of Clinical Oncology Clinical Practice Guideline

Guideline question

To provide guidance to clinicians and patients regarding the use of neoadjuvant chemotherapy (NACT) and interval cytoreduction among women with advanced epithelial ovarian cancer.

Target population

Women with newly diagnosed or suspected stage IIIC or IV epithelial ovarian cancer, fallopian tube cancer, or primary peritoneal cancer.

Target audience

Gynecologic and medical oncologists and women with advanced ovarian cancer.

Methods

An Expert Panel was convened to develop clinical practice guideline recommendations based on a systematic review of the medical literature.

Key points

Recommendation 1.1. All women with suspected stage IIIC or IV invasive epithelial ovarian cancer should be evaluated by a gynecologic oncologist prior to initiation of therapy to determine whether they are candidates for primary cytoreductive surgery (PCS). (Type: evidence based; benefits outweigh harms; Evidence quality: intermediate; Strength of recommendation: strong)

Recommendation 1.2. A primary clinical evaluation should include a computed tomography (CT) scan of the abdomen and pelvis with oral and intravenous contrast and chest imaging (CT preferred) to evaluate the extent of disease and the feasibility of surgical resection. The use of other tools to refine this assessment may include laparoscopic evaluation or additional radiographic imaging (e.g., [^{18}F]fluorodeoxyglucose positron-emission tomography [FDG-PET] scan or diffusion-weighted magnetic resonance imaging [MRI]). (Type: informal consensus; benefits outweigh harms; Evidence quality: intermediate; Strength of recommendation: moderate)

Recommendation 2.1. Women who have a high perioperative risk profile or a low likelihood of achieving cytoreduction to <1 cm (ideally to no visible disease) should receive NACT. (Type: evidence based; benefits outweigh harms; Evidence quality: intermediate; Strength of recommendation: moderate)