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## A life-extending advance in treatment of ovarian cancer

Surgical cytoreduction followed by intravenous plus intraperitoneal chemotherapy is likely to become the standard of care for stage III ovarian cancer

A 55-year-old woman presents with a complaint of a mild increase in abdominal girth. She reports no weight loss or other constitutional symptoms. A pelvic exam demonstrates a 4-cm nontender mobile right adnexal mass. An ultrasound shows a complex 5-cm right adnexal mass with an internal nodule that demonstrates blood flow and fluid in the cul-de-sac. CA-125 is 120 U/mL.

If she proves to have stage III ovarian cancer, what are the optimal treatment interventions?

**O**varian cancer causes more deaths than any other gynecologic malignancy. In American women, the lifetime risk of ovarian cancer is approximately 1.5%.<sup>1</sup>

### Survival after typical treatment

Stage III ovarian cancer is typically treated with surgical cytoreduction of the tumor and intravenous therapy with taxane and platinum-based chemotherapy. Using this treatment approach, stage III ovarian cancer has been associated with a median survival of approximately 37 months in women with residual tumor larger than 1 cm after cytoreductive surgery and 49 months in women with residual tumor of less than 1 cm.<sup>2</sup>

### Survival after combination treatment

Data published January 5, 2006, indicate that a combination of *optimal cytoreductive*

*surgery with both intravenous and intraperitoneal chemotherapy* significantly improves the survival of women with stage III ovarian cancer.<sup>3</sup> In this exceptionally well-designed and executed study, 415 eligible patients with stage III ovarian cancer who had undergone optimal cytoreductive surgery (defined as residual tumor nodules <1 cm in diameter) were randomized to receive 6 treatment cycles of either standard therapy with intravenous paclitaxel plus cisplatin or experimental therapy with intravenous paclitaxel *plus intraperitoneal cisplatin plus paclitaxel* for 6 treatment cycles. The median survival was 50 months in the standard therapy intravenous group compared to 66 months in the experimental intravenous plus intraperitoneal therapy group ( $P<.03$ ). In the subgroup of women who underwent a “second look” operation at the end of their chemotherapy, 41% in the intravenous chemotherapy group and 57% in the combined intravenous plus intraperitoneal chemotherapy group had a complete pathological response.

**Longest life expectancy.** The Gynecologic Oncology Group (GOG) has never previously reported a treatment of stage III ovarian cancer that had this large a beneficial effect on life expectancy. The results of this study, plus 2 previous clinical trials,<sup>4,5</sup> indicate that combined intravenous plus intraperitoneal chemotherapy will quickly become an important option for women with stage III ovarian cancer.

### FAST TRACK

**We need to identify advanced ovarian cancer preoperatively, for optimal tumor resection and intraperitoneal catheter placement in a single operation**

CONTINUED

**Side effects more serious**

Unfortunately, the marked increase in life expectancy with combined intravenous plus intraperitoneal therapy was associated with significantly more serious side effects than conventional therapy. Women treated with combined intravenous plus intraperitoneal chemotherapy had significantly more serious complications with leukopenia, thrombocytopenia, abdominal pain, and toxic events involving the gastrointestinal, metabolic, and neurological systems. The combined intravenous plus intraperitoneal therapy was so toxic that only 42% of the women in this group were able to complete the 6 cycles of the assigned chemotherapy. In contrast, 83% of the women in the standard therapy group completed 6 cycles of chemotherapy.

It is hoped that ongoing trials with new agents, such as intraperitoneal carboplatin, may find a reduction in side effects associated with intraperitoneal cisplatin. In preliminary studies, intraperitoneal carboplatin has been associated with fewer side effects, such as less abdominal pain, than cisplatin.<sup>6</sup>

**Preop detection of high risk to avert multiple operations**

The new treatment protocol requires 2 critical steps: (1) optimal cytoreduction of the ovarian cancer, and (2) placement of an intraperitoneal catheter. To minimize the number of patients with stage III ovarian cancer who need multiple surgeries to achieve these 2 critical steps, as many patients as possible need to be identified preoperatively. Preoperative identification of women at high risk of stage III ovarian cancer will allow gynecologic oncologists with expertise in both cytoreduction of ovarian cancer and intraperitoneal chemotherapy to become involved as early as possible in the patient's care.

**Modalities that may help** to identify preoperatively those patients with an adnexal mass most likely to have ovarian cancer might include measurement of CA-125 in menopausal women<sup>2</sup> and preoperative ultrasound<sup>7</sup> or CT imaging of the abdomen

and pelvis. If a patient with stage III ovarian cancer is operated on in a facility that cannot reliably provide optimal cytoreduction nor an intraperitoneal catheter, then the patient may need to undergo a second operation in order to benefit from the new treatment protocol.

It is likely that surgical cytoreduction followed by intravenous plus intraperitoneal chemotherapy will become the standard of care for stage III ovarian cancer. To best translate these research findings into practice, ObGyns will need to identify as many patients as possible preoperatively who might have advanced ovarian cancer, so that they can undergo optimal tumor resection and placement of an intraperitoneal catheter in a single operation.



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**INSTANT POLL**

**What is your opinion?**



At **OBG Management**, we value your perspective on **this question:**

To best identify the postmenopausal patients with a complex ovarian mass who are most likely to have ovarian cancer, which preoperative tests have been of the greatest clinical utility in your practice?

- History and physical examination**
- Serum CA-125 measurement**
- Pelvic sonography**
- All of the above**

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*We will publish a summary of responses in an upcoming issue.*