Giving intraperitoneal (IP) chemotherapy along with intravenous (IV) chemotherapy can improve survival of women with Stage III ovarian cancer by more than a year, according to a recent study. The results, which appeared in the *New England Journal of Medicine* (*2005;354*:34–43), prompted the National Cancer Institute (NCI) to issue a clinical announcement encouraging use of this approach for appropriate patients.

“IP chemotherapy allows higher doses and more frequent administration of drugs, and it appears to be more effective at killing cancer cells in the peritoneal cavity, where ovarian cancer is likely to spread or recur first,” the NCI said in a statement preceding the clinical announcement.

Although IP chemotherapy has been around for decades, it has not been widely used, said the lead author of the *NEJM* study, Deborah Armstrong, MD.

“There has been a prejudice against IP therapy in ovarian cancer because it’s an old idea, it requires skill and experience for the surgery and for the chemotherapy, and it’s more complicated than IV chemotherapy,” said Armstrong, who is a medical oncologist and associate professor at the Johns Hopkins Kimmel Cancer Center in Baltimore. “But now we have firm data showing that we should use a combination of IP and IV chemotherapy in most women with advanced ovarian cancer who have had successful surgery to remove the bulk of their tumor.”

Armstrong’s study included 210 women assigned to six cycles of standard IV chemotherapy with cisplatin and paclitaxel, and 205 women assigned to six cycles of both IV and IP chemotherapy with cisplatin and paclitaxel. The women all had Stage III ovarian cancer that had been optimally debulked, with no residual masses larger than 1 cm.

Women in the IP group had longer progression-free survival (about 23 months versus 18 months for IV chemotherapy, \(P = 0.05\)) and lived longer overall. Women who had only IV chemotherapy survived a median of 49.7 months, whereas those who got IP and IV chemotherapy had a median survival of 65.6 months \(P = 0.03\).
That improvement is “one of the largest benefits ever observed for a new therapy in gynecologic oncology,” according to Stephen A. Cannistra, MD, who wrote an editorial published with the study. Cannistra is Professor at Harvard Medical School and Director of the Division of Gynecologic Medical Oncology at Beth Israel Deaconess Medical Center in Boston.

However, the IP treatment was much harder on the patients. Although the number of treatment-related deaths was similar in both groups (five in the IV-IP group versus four in the IV-only group), women who got IP treatment had many more Grade 3 or 4 side effects, including leukopenia, infection, fatigue, and pain. Many of these side effects were related to the abdominal catheters. These problems were so serious that only 42% of the women assigned to receive IP chemotherapy completed all six planned treatment cycles. That makes the survival improvement seen in this trial that much more remarkable, Cannistra wrote.

Women who got IP therapy reported significantly worse quality of life during and just after treatment, but both groups reported similar quality of life 1 year after completion of treatment.

Although the side effects were serious, the National Cancer Institute said the results of this study, combined with those of previous research, are enough to warrant recommending IP chemotherapy to eligible women.

Other experts agree with NCI’s action. “I think NCI has wisely brought this treatment approach, which has been limited in use, to everyone’s attention by recommending it be used to treat late-stage ovarian cancer,” said Carolyn Runowicz, MD, National Volunteer President of the American Cancer Society (ACS) and Professor of Obstetrics and Gynecology, Division of Gynecologic Oncology, at the University of Connecticut School of Medicine.

But Armstrong’s study also raises many questions about IP chemotherapy that can only be answered by conducting further clinical trials, added Runowicz, who is also Director of the Carole and Ray Neag Comprehensive Cancer Center at the University of Connecticut Health Center in Farmington.

We still must learn which drugs work best with IP chemotherapy, how many IP treatments and what schedule are needed to be effective, and whether women with earlier stage cancer also would benefit from IP therapy. It is also important to look for ways to reduce the side effects the treatment causes without compromising its effectiveness. Finding the optimal catheter design to use with IP chemotherapy will be key.

Runowicz said women who want IP treatment for ovarian cancer should either enroll in a clinical trial or get one of the regimens that have been proven to increase survival, like the one described in this study.

“I think we’re making marked advances in the understanding of cancer that will translate into better therapies, so if you can stay alive longer, you have a better chance of getting one of these new treatments in the pipeline,” she said. “If it were me, I’d choose IP therapy as the initial therapy, since this study showed such a marked improvement in survival.”

**URINE TEST MAY IMPROVE DETECTION OF BLADDER CANCER RECURRENTNESS**

A simple in-office urine test may help doctors find more bladder cancer recurrences than traditional urine cytology, researchers report in *JAMA* (2005;295:299–305). The test, called BladderChek, measures levels of NMP22, a protein known to be elevated in urine of people with bladder cancer. When combined with cystoscopy, the two tests detected 99% of recurrences, according to a team led by researchers from the University of Texas MD Anderson Cancer Center.

“A test like the NMP22 assay, which is accurate and easy to administer, I believe, will
help identify and treat patients earlier, when they have a better chance for a good outcome,” said lead study author H. Barton Grossman, MD, Professor and Deputy Chairperson of the MD Anderson Cancer Center Urology Department.

The study involved 668 patients with a history of bladder cancer who were being followed up for recurrences at 23 clinical sites in nine US states. Each participant gave a voided urine sample before undergoing cystoscopy. Part of the urine sample was used for traditional cytology, and some was used for the BladderChek test. The researchers compared the detection rates of each method alone and of each urine test combined with cystoscopy. The test’s manufacturer, Matritech, Inc., was involved in designing, funding, and reviewing the study.

Bladder cancer was diagnosed in 103 patients. Cystoscopy was the most accurate test, finding 94 of those cancers (sensitivity = 91%) on its own. The BladderChek test alone found only 51 cancers, but those included eight of the nine cancers missed by cystoscopy. BladderChek combined with cystoscopy found 102 of the 103 cancers (sensitivity = 99%), significantly more than cystoscopy alone ($P = 0.005$).

Urine cytology also improved the performance of cystoscopy, but not by a statistically significant amount ($P = 0.08$). It found only three of the nine cancers cystoscopy missed. Together, the two tests found 97 of 103 cancers (sensitivity = 94%). Urine cytology alone found just 12 cancers.

That’s unusually poor performance for urine cytology, especially because many of the missed lesions were high-grade, said Samuel Cohen, MD, PhD, Professor of Oncology and Chair of Pathology and Microbiology at the University of Nebraska Medical Center and a member of the panel that wrote the bladder cancer treatment guidelines for the National Comprehen-
in 78 randomized trials comparing different adjuvant treatment approaches: radiotherapy versus no radiotherapy, more versus less surgery with and without radiotherapy, and more surgery versus radiotherapy.

The analysis showed that for every four local recurrences prevented by radiation, approximately one breast cancer death could be prevented over 15 years.

“I believe what this paper does is confirm and add to the data that prevention of a local recurrence can improve your chances of surviving breast cancer,” said Christy Russell, MD, Chair of the ACS’s Breast Cancer Advisory Group and Codirector of the University of Southern California Norris Breast Center. She was not involved in the research.

Among the 7,300 women treated with breast-conserving surgery (BCS), radiotherapy reduced the 5-year local recurrence risk from 26% to 7%. The risk of 15-year breast cancer mortality decreased from 35.9% to 30.5% ($p = 0.0002$).

For the 8,500 women who had a mastectomy, radiotherapy reduced the 5-year risk of local recurrence from 23% to 6%, and reduced the 15-year risk of death from breast cancer from 60.1% to 54.7% ($p = 0.0002$).

Radiotherapy also significantly improved overall 15-year survival, regardless of which operation was performed.

The proportional reduction in local recurrence and disease-specific mortality was unaffected by tumor characteristics. However, the absolute reductions in both outcomes were greater among women with positive nodes, larger tumors, and higher-grade tumors.

Adjuvant radiation is standard treatment for most women who choose BCS, and Russell said the meta-analysis significantly confirms this approach.

“These data help strengthen the argument that there is a substantial benefit to post-BCS radiotherapy and that it should be a rare patient with a very low risk of recurrence or a very short expected life span for whom it should be eliminated,” she said. “In addition, we are all looking for the correct patient population for whom postmastectomy radiation is indicated, and this meta-analysis spells out the benefits and risks in that circumstance as well.”

Russell said medical oncologists can use the data in this new analysis to help their patients make decisions about whether to seek adjuvant radiotherapy. She cautions, though, that the large benefits seen in this analysis may be less in current patients.

“Current hormone therapies and chemotherapy regimens are better in reducing local recurrence than those that were used in the clinical trials presented,” she explained. “Both those therapies, if used, may make the benefit of radiation therapy less significant with regards to both local recurrence and breast cancer-specific survival.”

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