Intraperitoneal Chemotherapy

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successful surgical cytoreduction (debulking) and who were then given chemotherapy via a combined intravenous-intrapertoneal approach as opposed to the standard intravenous-only approach. The most recent of these trials showed a 16-month improvement in median overall survival in 205 women who received combined intravenous-intrapertoneal chemotherapy. According to the NCI, the treatment was study strong and free of the complexities of earlier studies.

The NCI issued the announcement “based on these combined results” and because intraperitoneal (IP) chemotherapy “has not been adopted into standard prac-tice” despite the published evidence of efficacy, according to NCI statements and a “Q&A” posted on the Internet (http://c3tp.cancer.gov/).html/hivarian.html). The “best data sources” suggest that less than 1% of women with ovarian cancer receive IP chemotherapy, NCI said.

The treatment was first proposed several decades ago because residual ovarian cancer after surgery and initial recurrences are primarily confined to the abdomen.

Many women, moreover, are not under-going optimal surgical debulking to minimal or no gross residual disease, which is the first step to improved survival and the most important determinant for chemotherapy, according to the NCI.

Dr. Edward L. Trimbble of the NCI said in a recently published editorial that the rate of optimal surgical debulking varies dramatically between centers from 20% to 80% (Gynecol. Oncol. 2006;100:3-4). And in its announcement, the NCI said that women undergoing surgery for presumed ovarian cancer “should undergo surgery by a gynecologic oncologist or a surgical team with expertise in the staging and cy-toreduction of ovarian cancer.”

Patients in the recently published trial (patients with stage III ovarian cancer or primary peritoneal carcinoma) were required to have no residual tumors greater than 1 cm in diameter. The patients were randomized to receive intravenous (IV) paclitaxel over a 24-hour period followed by either IV cisplatin on day 1 or IP cisplatin on day 2 and IV paclitaxel on day 8 (the IP group).

The regimen was administered every 3 weeks for a total of six cycles. Only 42% of the 205 patients in the IP group completed all six planned cycles of chemotherapy and 48% received three or fewer cycles—due to its toxic effects and caregiver complications.

Still, there was a significant increase in median progression-free survival and median overall survival in these patients (approximately 6 months and 16 months), compared with patients who received only IV therapy. Dr. Deborah K. Armstrong, strong of Johns Hopkins Kimmel Cancer Center in Baltimore and her coinvestiga-tors in the Gynecologic Oncology Group (N. Engl. J. Med. 2006;354:34-43).

Dr. Stephen A. Cannistra, who commented on the study in an editorial, said the increase in survival is “one of the largest benefits ever observed for a new therapy in gynecologic oncology.” The IP route, he noted, has a “considerable” pharmacologic advantage, allowing higher doses of certain drugs to be administered (N. Engl. J. Med. 2006;354:34-43).

Practice will change, he and others say, but the change will be more complex than it was following the NCI’s announcement in 1999, which encouraged a combination of chemotherapy and radiation, rather than radiation alone, for cervical cancer.

For one thing, IP chemotherapy requires familiarity with catheter placement, peritoneal administration, and management of catheter-related complications.

Also, the optimal IP regimen is unknown, and physicians will undoubtedly attempt to reduce the higher toxicity of IP thera-py by adjusting times and dosing schedules and by substituting drugs.

The NCI emphasizes that the additional toxicity of IP therapy is “generally transient” and manageable. Still, the institute is encouraging further trials, particularly to address the issue of toxicity, and is plan-ning a “broad-based dissemination and educational plan.”

The NCI considers making clinical an-nouncements when trials have “identified an intervention” that is available to the general public and that “substantially improves with reasonable certainty the survival outcome for a significant number of people.”

In 2005, an estimated 22,220 in the United States were diagnosed with ovarian cancer and another 16,210 died from the disease. More than half of women with ovarian cancer present with advanced-stage disease, and only 45% of women survive 5 years after diagnosis, according to the NCI.

Letrozole Suppresses Tamoxifen in Head-to-Head Breast Ca Trial

BY MARY ANN MOON
Contributing Writer

San Antonio — All women with atyp-ical lobular hyperplasia in a benign breast biopsy are at significantly increased risk of developing breast cancer, but the magnitude of risk is greater when the pathology involves atyp-ical lobular hyperplasia than it is with atyp-ical ductal hyperplasia, said Dr. Laura C. Collins, a pathol-ogist at Beth Israel Deaconess Medical Cen-ter and Harvard Medical School, Boston.

The adjusted odds ratio for developing breast cancer was 2.76 for women with atyp-ical ductal hyperplasia, 5.24 for those with atypical lobular hyperplasia, and 8.12 for women with both histologic abnormalities.

The risk of developing breast cancer was roughly twice as great 10 years or longer fol-lowing a benign biopsy featuring atypical ductal hyperplasia as in the first 10 years of follow-up. In con-trast, breast cancer risk in women with atypical lobular hyperplasia remained steady over time.

Atypical lobular hyperplasia also dif-fered in terms of the impact menopausal status at the time of the benign breast biopsy had on subsequent breast cancer risk. Women who were premenopausal at the time of a benign biopsy, showing atypical lobular hyperplasia had a 6.67-fold increased breast cancer risk. Women who were postmenopausal at the time of biopsy had a 3.61-fold increased risk.

In contrast, patients who were pre-menopausal when they had a benign biopsy showing atypical ductal hyperplasia had a 2.59-fold increased risk of subsequent breast cancer, whereas those whose biopsy was post-menopausal at the time of their biopsy had a 4.64-fold increased breast cancer risk, Dr. Collins noted.

This planned interim analysis compared outcomes after a median of 26 months for the 4,003 women assigned to letrozole for 3 years, 4,003 women assigned to tamoxifen for 3 years, and 4,003 women assigned to letrozole for 3 years followed by tamoxifen for 3 years.

Letrozole was associated with fewer monoe-phy by adjusting doses and dosing schedules and with fewer blood clots, headaches, and joint aches. Letrozole was associated with fewer monoe-phy by adjusting doses and dosing schedules and with fewer blood clots, headaches, and joint aches.