Weekly Paclitaxel Best for Breast Cancer Survival

BY LAUREN SCOTT ZOELLER
Contributing Writer

A weekly dose of paclitaxel prolongs overall survival of breast cancer patients more effectively than weekly docetaxel or the standard 3-week schedule for either taxane, according to investigators of a randomized trial comparing these adjuvant regimens in nearly 5,000 women.

Weekly paclitaxel (Taxol) and docetaxel (Taxotere) every 3 weeks were associated with better 5-year disease-free survival than was the standard paclitaxel regimen, with odds ratios of 1.27 (P = .0006) and 1.23 (P = .02), respectively, the investigators reported (N. Engl. J. Med. 2008:358;1663-71).

The study found that administering paclitaxel on a weekly basis over 12 consecutive weeks was the most effective way to use it.

Only weekly paclitaxel produced significantly longer overall survival (OR 1.32, P = .01), however. The 32% reduction in the hazard ratio for death, the authors noted, is comparable to that seen with anthracycline-based chemotherapy in the absence of adjuvant cytotoxic therapy.

"The take-home message is that paclitaxel is effective for tumors that are hormone receptor positive and HER2 negative, which accounts for about two-thirds of all breast cancer," lead investigator Dr. Joseph A. Sparano of Montefiore Medical Center, New York, said in an interview.

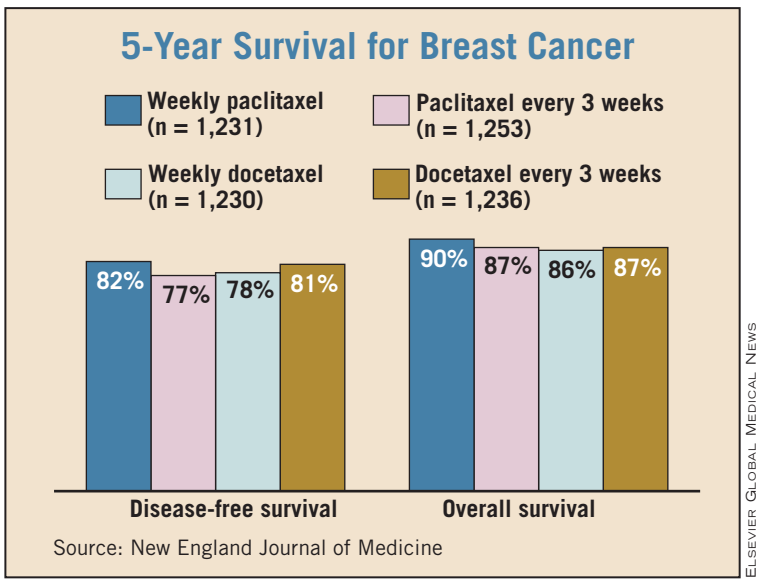
These types of tumors were present in 70% and 19% of the women in the trial, respectively. "This is important," Dr. Sparano said, "because a recent study suggested that those patients may not benefit from paclitaxel therapy."

The finding that "the most effective way to administer paclitaxel was on a weekly basis over 12 consecutive weeks" was also clinically significant. This allows treatment to be completed in a shorter period, which is an advantage.

"What was somewhat surprising was that we didn't see a similar benefit for weekly docetaxel," Dr. Sparano said. This may be attributable to higher toxicity and poorer patient compliance with this regimen.

Moderate to severe neuropathy was observed in 27% of the patients receiving weekly paclitaxel vs. 20% of women given paclitaxel every 3 weeks and 16% of women on either docetaxel regimen. Otherwise, overall grade 3/4 adverse events with weekly paclitaxel were comparable to those with standard dosing and lower than with either docetaxel schedule.

Four cooperative research groups collaborated on the trial, which was led by investigators from the Eastern Cooperative Oncology Group. The study followed 4,950 women who had lymph node–positive or high-risk lymph node–negative breast cancer for a median of 63.8 months.



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The standard of care for these patients was completion of chemotherapy followed by a taxane given every 3 weeks. The most effective taxane and dosing schedule had not been established, however.

All women in the trial received doxorubicin (60 mg/m^2) and cyclophosphamide (600 mg/m^2) every 3 weeks for four cycles. They were then randomized to receive treatment with paclitaxel (175 mg/m^2) or docetaxel (100 mg/m^2) every 3 weeks for four cycles or weekly paclitaxel (80 mg/m^2) or weekly docetaxel (35 mg/m^2) for 12 weeks.

According to Dr. Sparano, an ongoing trial (SO221) is addressing the next logical question, comparing weekly and every-2-week paclitaxel schedules in women with hormone receptor–positive and HER2–negative breast cancer. ■

VRT May Preserve Fertility in Younger Cervical Ca Patients

BY SHARON WORCESTER
Southeast Bureau

Tampa — Vaginal radical trachelectomy is a safe and effective option for preserving fertility in young women with early-stage cervical cancer, according to a review of outcomes in 113 patients.

A review of consecutive patients who underwent vaginal radical trachelectomy (VRT) between October 1991 and October 2007 showed that, at 74 months, disease-free survival was greater than 95%, and 87 pregnancies had occurred in 51 of the 113 women, Dr. Marie Plante reported in a poster at the annual meeting of the Society of Gynecologic Oncologists.

Thirty-one women had one pregnancy, nine had two pregnancies, six had three pregnancies, and five had four pregnancies during the study period. There were 58 third-trimester deliveries; 17 pregnancies ended in miscarriage in the first trimester, and 3 ended in miscarriage in the second trimester. Four women had therapeutic abortions, and five women were pregnant at the time of the report, Dr. Plante said.

Of those who delivered during the third trimester, 3 delivered prior to 32 weeks' gestation, 8 delivered between 32 and 37 weeks, and 47 delivered after 37 weeks.

VRT in this study was used in patients who desired to preserve fertility and who were under the age of 45 years. However, a history of infertility and advanced maternal age are not considered absolute contraindications to the procedure, noted Dr. Plante of Laval University, Quebec City.

The patients had International Federation of Gynecology and Obstetrics stage IA1 with vascular space involvement, IA2, or IB1 disease; squamous or adenocarcinoma histology; lesion size of 2-cm diameter or less; and limited endocervical involvement.

VRT was preceded by laparoscopic sentinel node mapping and bilateral pelvic node dissection, and sentinel nodes were sent for frozen section. VRT was abandoned if the nodes were positive or if extensive endocervical involvement was found.

Neoadjuvant chemotherapy was used in three patients for locally advanced disease. Each received three cycles of chemotherapy with paclitaxel, ifosfamide, and platinum, followed by VRT, node mapping, and dissection. Of these patients, two had residual dysplasia, and all had negative lymph nodes.

One of the patients who received neoadjuvant chemotherapy delivered two term babies (1 year apart), one patient was infertile because of cervical stenosis and transient ovarian failure (but she conceived with intrauterine insemination and Clomid and delivered at 36 weeks' gestation), and one was infertile because of ovarian failure and was unable to conceive. ■

Azithromycin Matches Penicillin For Treatment of Early Syphilis

BY MICHELE G. SULLIVAN
Mid-Atlantic Bureau

Chicago — A single 2-g dose of azithromycin cures early syphilis as effectively as injected penicillin G benzathine, Dr. Edward W. Hook III said at a conference on sexually transmitted disease prevention sponsored by the Centers for Disease Control and Prevention.

However, Dr. Hook cautioned that the federally sponsored randomized controlled trial did not include any HIV-positive patients, so its results can't support the use of azithromycin in this population.

"This is the very group in which macrolide-resistant *Treponema pallidum* mutations have emerged in association with azithromycin treatment," said Dr. Hook of the University of Alabama, Birmingham. "I would certainly not recommend treating these patients with azithromycin for early syphilis."

Neither should the drug be used for syphilis in pregnant women. "In light of the history of macrolide treatment failures among pregnant women, I would caution very, very strongly against treating them with azithromycin for syphilis," Dr. Hook said.

The trial compared the efficacy and safety of 2 g of azithromycin given orally with those of 2.4 million U of penicillin G benzathine in 517 patients with early syphilis. Most of the patients (80%) were in Madagascar; the rest were seen at U.S. clinics.

The patients' mean age was 24 years; 26% had primary syphilis, 46% had secondary syphilis, and 28% had presumed early latent syphilis (a sexual partner in the past 12 months with confirmed syphilis).

Serologic cure rates at 3 months were similar in both groups in the intent-to-treat analysis (74% azithromycin vs. 76% penicillin). At 6 months, the cure rates were still not significantly different (77% azithromycin vs. 78% penicillin). Results at 3 and 6 months in the per-protocol analysis were almost identical, Dr. Hook said.

U.S. patients exhibited slightly, but not significantly, higher cure rates than did patients in Madagascar.

Serious adverse events were slightly more common in the penicillin group than they were in the azithromycin group (10 vs. 8, respectively). However, none of these was considered related to the study medication. Nonserious adverse events, especially gastrointestinal distress, were significantly more common among the patients taking azithromycin (61% vs. 46% for penicillin).

The most common adverse events were gastrointestinal, with 24% of the azithromycin group experiencing some upset, compared with 7% of the penicillin group. However, only three patients taking azithromycin vomited.

Cutaneous reactions were more common among those taking penicillin (4% vs. 1%), as were administration-related adverse events (10% vs. 5%). ■