Pregnancy Doesn't Alter Breast Cancer Outcomes

BY JANE SALODOF MACNEIL
Southwest Bureau

ATLANTA — Young women who became pregnant after breast cancer treatment were significantly less likely to have a recurrence or to die of the disease than were those who did not become pregnant, according to a French retrospective study presented at the annual meeting of the American Society of Clinical Oncology.

Dr. Rémy Largillier reported that 5-year overall survival was 97% for 118 women who became pregnant after breast cancer, but only 80% for 762 women who did not. The hazard ratio in favor of pregnancy was 0.23.

"Perhaps it is not a counterindication to have a pregnancy," Dr. Largillier, of the Centre Antoine Lacassagne in Nice, and his coinvestigators concluded.

In a discussion of the poster, Dr. Robert W Carlson, professor of medicine at the cancer center of Stanford (Calif.) University, described the study as important, but cautioned that it was not cause to encourage breast cancer survivors to become pregnant. The positive outcome "may be nothing but a healthy mother effect," he said. "They become pregnant because they feel physiologically able to."

The take-home message, Dr. Carlson said, is that "pregnancy subsequent to breast cancer does not have a negative impact on breast cancer outcome, and a pregnancy recent to a diagnosis of breast cancer does not independently predict for a poor outcome."

In conducting the study, the investigators cited the lack of data supporting the decision of many women to wait at least 2 years after breast cancer treatment before they become pregnant. Although some studies have suggested that pregnancy might be protective, Dr. Largillier's group acknowledged that these may have been biased by the "healthy mother" effect, in which only women who feel healthy and disease-free choose to become pregnant.

Results may be biased by the 'healthy mother' effect in which women become pregnant because they feel healthy.

DR. LARGILLIER

The study reviewed 908 patients younger than age 35 years who were treated for nonmetastatic and unilateral invasive breast carcinoma at eight French hospitals between 1990 and 1999. The women's average age was 31.4 years, and the median follow-up was 87 months.

Included in the analysis were 105 women who gave birth during the year before their diagnosis. The investigators found that these women were significantly more likely to have a positive axillary node (48.6% vs. 35.5% of those who did not give birth before diagnosis), a tumor staged as T2 or greater (75% vs. 55.8%), and a cancer classified as estrogen-receptor negative (54.2% vs. 42.5%).

Pregnancy in the year before diagnosis increased the risk of death and risk of local recurrence in univariate analysis. Only the relationship to local recurrence persisted in multivariate analysis, however. The hazard ratio was 1.75.

Women who became pregnant after treatment were significantly younger than the rest of the population and less likely to have a family history of breast cancer. More than half (52.5%) were younger than 30 years of age, compared with 28% of those who did not become pregnant as breast cancer survivors.

The posttreatment mothers also were more likely to have positive axillary nodes (38.1% vs. 28.8% of women who did not become pregnant after diagnosis), but their tumor size and estrogen-receptor status were similar to the rest of the population.

Women with good prognoses after completing breast cancer treatment had a low annual risk of distant recurrence that remained constant over time, according to the investigators. This was not the case for the women with poor prognoses: They had a high annual risk of distant recurrence that did not level off for 80 months. After that point, their risk was no greater than the risk for the women with good prognoses.

"In this large study population, pregnancy was not associated with poorer survival," the investigators concluded, but they advised that for women with poor prognoses after breast cancer treatment, "it is very important to wait 5 years before a pregnancy." ■

HER2+ Breast Ca Mortality Is Lowered With Trastuzumab

BY JANE SALODOF MACNEIL
Southwest Bureau

ATLANTA — New results from the international Herceptin Adjuvant (HERA) trial show that taking trastuzumab for 12 months after standard chemotherapy significantly reduced the risk of death for early-stage HER2-positive breast cancer patients.

At a median follow-up of 2 years, 1,703 patients treated with trastuzumab (Herceptin), a monoclonal antibody, also continued to have better disease-free survival, compared with 1,698 patients in the observation arm of the study.

Risk of cardiotoxicity remained low in the updated data presented by Dr. Ian Edward Smith at the annual meeting of the American Society of Clinical Oncology.

The researchers for the phase III trial, conducted by the Swiss-based Roche pharmaceutical company and the Breast International Group (BIG), previously reported a disease-free survival benefit based on 1-year data (N. Engl. J. Med. 2005;353:1659-72). They have yet to report on a third arm of the study that randomized 1,694 women to 24 months of adjuvant therapy with trastuzumab.

The monoclonal antibody was effective whether the women were lymph node negative or positive and whether they had neoadjuvant therapy or not.

In a discussion of the new data, Dr. Clifford A. Hudis described HERA and other studies of adjuvant trastuzumab as "amazingly consistent." The value of trastuzumab is established, but the best way to incorporate it into therapy for early-stage human epidermal growth factor receptor 2 (HER2)–positive patients still needs to be resolved, said Dr. Hudis, chief of the breast cancer service at Memorial Sloan-Kettering Cancer Center in New York.

"Approval and use in the adjuvant setting is appropriate, and we should be working on that at this time," he said.

In the 2-year data reported by Dr. Smith, head of the breast unit at Royal Marsden Hospital in London, an intent-to-treat analysis found that 92.4% of the trastuzumab arm and 89.7% of the observation group were alive at 3 years (hazard ratio 0.66). Disease-free survival was 80.6% in the trastuzumab arm and 74.3% in the observation group (hazard ratio 0.64).

Dr. Smith reported similar results in a censored analysis that did not count 861 observation arm patients who switched to trastuzumab after the first-year results were announced last year. He predicted the desire of patients to cross over to the treatment arm of a trial that reports significant benefit in its preliminary analysis will be a recurring issue in breast cancer trials.

Only intent-to-treat analysis was presented for the rest of the data. Time to distant recurrence of disease favored trastuzumab: 85.7% did not have distant disease at 3 years vs. 79.4% of the control group (hazard ratio 0.60).

There were more central nervous system events in patients treated with trastuzumab, however. Dr. Smith speculated that trastuzumab may not penetrate the CNS sufficiently or these events might be masked in the observation arm because some of these women had other distant events before brain metastases.

Subgroup analyses of the trastuzumab arm found "no evidence of substantial difference in relative treatment effect between subgroups and no evidence of any subgroup in which there is less efficacy," Dr. Smith said. He singled out nodal status and neoadjuvant therapy, emphasizing that trastuzumab was equally effective whether the women were lymph node negative or lymph node positive at entry into the trial and whether they had neoadjuvant therapy.

Conducted at 480 sites in 39 countries, the trial allowed wide latitude in the types of prior regimens the women received. Dr. Smith noted that only 26% had prior taxane therapy. About 11% had neoadjuvant therapy.

About half of the women were estrogen receptor negative, he said, proposing that it may be the largest trial ever conducted in ER-negative women. Although the arms were well balanced, he characterized the overall population as young, with a median age of 49 years. Only 16% were over the age of 60.

Not unexpectedly, serious adverse events were more frequent with trastuzumab: 9.2% of patients had at least one, compared with 6.6% of the control group. All told, 172 women (10.1%) on trastuzumab withdrew from treatment.

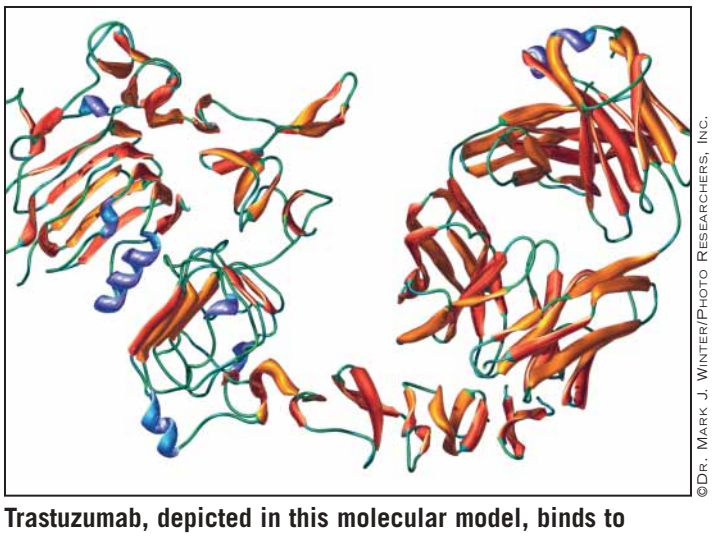
Although deaths resulting from adverse events were more common in patients on trastuzumab, Dr. Smith said none were related to the drug. The only cardiac death occurred in a patient randomized to observation.

Other measures showed that cardiac toxicity occurred in small proportions of women on trastuzumab: severe congestive heart failure in 0.6%, symptomatic congestive heart failure in 2.1%, and a confirmed significant drop in left ventricular ejection fraction in 3.0%.

"The risk of cardiac toxicity remains low," Dr. Smith said.

He promised continued safety evaluation in the ongoing long-term follow-up of these patients. Of particular interest, he said, will be data on patients who took trastuzumab for 24 months. The greatest risk of recurrence has been during the first year of the study, and investigators are hoping that longer therapy will be more protective.

Trial sponsor Roche markets trastuzumab internationally and has a majority interest in Genentech Inc., which markets the drug in the United States. ■



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Trastuzumab, depicted in this molecular model, binds to HER2 receptors and slows the spread of breast cancer.