

From the 28th Annual San Antonio Breast Cancer Symposium

Advances in breast cancer treatment

Several studies presented at the 28th Annual San Antonio Breast Cancer Symposium highlight the many important advances in the diagnosis, prevention, and treatment of breast cancer. Of primary interest were new data on the addition of trastuzumab (Herceptin) to chemotherapeutic regimens for patients with early breast cancer.

Trastuzumab improves disease-free survival

Dennis J. Slamon, MD, Jonsson Cancer Center, Los Angeles, CA, presented the first interim results of the breast cancer division of the Breast Cancer International Research Group (BCIRG) 006 study. In this trial, 3,222 women with HER2-positive and early breast cancer were randomly assigned to receive chemotherapy alone (Adriamycin [doxorubicin] and cyclophosphamide followed by Taxol [paclitaxel]) (AC-T; $n = 1,073$) or a regimen that combined trastuzumab (Herceptin) with either the same anthracycline-based regimen of AC-TH ($n = 1,074$) or a nonanthracycline regimen of Taxotere (docetaxel)/carboplatin (Paraplatin) with 1 year of trastuzumab (Herceptin; TCH; $n = 1,075$).

At a median follow-up of 23 months, disease-free survival (DFS) was significantly improved in both trastuzumab arms compared with chemotherapy alone, with a hazard ratio (HR) of 0.49 with AC-TH versus AC-T ($P < 0.0001$) and 0.61 with TCH ($P = 0.0002$). No significant difference in DFS was found between the two trastuzumab arms.

Cardiac events, however, were significantly increased in patients treated with AC-TH compared with AC-T (2.62% vs 0.86%; $P = 0.0024$); no difference was seen between TCH and AC-T (1.04% vs 0.86%; $P = 0.82$). An

unexpected finding of this study was the significant and persistent cardiotoxicity found with the combination of trastuzumab and the anthracycline-based regimen. Despite these findings, the addition of trastuzumab, regardless of the chemotherapeutic regimen, is still associated with a significant DFS benefit in these patients.

In another presentation, Richard D. Gelber, PhD, Dana-Farber Cancer Institute, Boston, MA, reported 1-year results of the Herceptin Adjuvant (HERA) trial, a multicenter, three-arm trial that randomized women with HER2-positive early breast cancer to undergo either 1 or 2 years of trastuzumab treatment or observation. All patients had completed their adjuvant chemotherapy and radiation therapy (if given), and all had a baseline left ventricular ejection fraction $> 55\%$ following chemotherapy prior to enrollment.

An interim analysis based on 475 events and presented last year at the American Society of Clinical Oncology annual meeting showed a significant improvement in DFS in patients treated with 1 year of trastuzumab compared with observation (HR, 0.54; $P < 0.0001$). Data presented in San Antonio also showed a significant improvement in time to recurrence (HR, 0.51; $P < 0.0001$) and time to distant recurrence (HR, 0.49; $P < 0.0001$) with 1 year of trastuzumab compared with observation. No difference was found in overall survival (HR, 0.76; $P = 0.26$). Trastuzumab was associated with a significant increase in severe congestive heart failure (0.5% vs 0% in the observation arm), but overall cardiac events were manageable and reversible, the authors concluded.

Anastrozole reduces the risk of disease recurrence

Other studies looked at the ongoing

question of optimal adjuvant endocrine therapy for early breast cancer. In an update of the Austrian Breast Cancer Study Group 8 trial, Raimund Jakesz, MD, of the Vienna Medical School, Austria, reported on outcomes of postmenopausal women with estrogen- and/or progesterone-positive disease. The women were treated with 2 years of tamoxifen and then switched to either 3 more years of tamoxifen or anastrozole (Arimidex). Of the 2,529 evaluable patients, those who switched to anastrozole had a 38% reduction in the risk of disease recurrence compared with those who stayed on tamoxifen for the full 5 years (HR, 0.62; $P = 0.01$) at a median follow-up of 31.1 months. Furthermore, when events from the initial tamoxifen treatment period were included, the event rate was reduced by 24% ($P = 0.07$) in patients sequenced to anastrozole. According to the authors, this reduction is similar to that found in the Arimidex or Tamoxifen Alone or in Combination and Breast International Group 1-98 trials.

Longer tamoxifen use, better disease-free survival for node-positive women

The optimal duration of tamoxifen in postmenopausal women with early breast cancer has also been evaluated. In this study, women received 2–3 years of tamoxifen after primary therapy and then were randomized to continue on tamoxifen (long; $n = 1,890$) or receive no further tamoxifen (short; $n = 1,863$). As reported by Thierry Delozier, MD, Centre Francois Baclesse, Caen, France, longer tamoxifen use was associated with a significant increase in DFS in all patients ($P = 0.001$) as well as in estrogen receptor-positive women ($P = 0.02$) and women with node-positive disease ($P = 0.0009$). No significant difference was found in patients with node-negative disease. The reduction in recurrence decreased over time, however, leading the authors to conclude that the optimal duration of tamoxifen is 5–6 years in this setting.