

Highlights from the 32nd Annual San Antonio Breast Cancer Symposium

December 9–13, 2009
San Antonio, Texas

Breast Cancer In Focus

Complete abstracts are available in *Cancer Research*. 2009;69(No 24):413s-900s (Supplement to *Cancer Research*)

22 A Comparison of Denosumab Versus Zoledronic Acid for the Prevention of Skeletal-Related Events in Breast Cancer Patients with Bone Metastases

A Stopeck, R de Boer, Y Fujiwara, et al

In this randomized study of denosumab versus zoledronic acid in patients with breast cancer and bone metastases, 2,046 patients who had no previous exposure to intravenous (IV) bisphosphonates were randomized to receive either subcutaneous denosumab (120 mg) and placebo or subcutaneous placebo and IV zoledronic acid 4 mg every 4 weeks. The primary endpoint was time to first on-study skeletal-related event (SRE), and secondary endpoints included time to first radiation of bone, time to first on-study SRE or hypercalcemia of malignancy, skeletal morbidity rate (SMR), and proportion of patients with at least 1 on-study SRE. Study findings showed that denosumab was superior to zoledronic acid in delaying the time to first SRE (HR, 0.82; 95% CI, 0.71–0.95) and time to first and successive SRE (95% CI, 0.66–0.89; $P=$.001). Denosumab also demonstrated a significant delay in time to first radiation and time to first SRE or hypercalcemia of malignancy compared to zoledronic acid. The SMR was lower with denosumab (0.45 vs 0.58). There were 491 and 623 SREs reported for denosumab and zoledronic acid, respectively. Overall, adverse events were similar to those reported in previous studies.

42 RIBBON-2: A Randomized, Double-Blind, Placebo-Controlled, Phase III Trial Evaluating the Efficacy and Safety of Bevacizumab In Combination with Chemotherapy for Second-Line Treatment of HER2-Negative Metastatic Breast Cancer

A Brufsky, IN Bondarenko, V Smirnov, et al

Since the clinical benefit of adding bevacizumab to chemotherapy as first-line treatment of metastatic breast cancer (MBC) has been established by previous studies, this trial sought to examine the efficacy and safety of

the addition of bevacizumab to various chemotherapy agents as second-line treatment for MBC. Patients were randomized to receive chemotherapy (paclitaxel, nab-paclitaxel, docetaxel, gemcitabine, capecitabine, or vinorelbine) plus bevacizumab or chemotherapy plus placebo. Patients enrolled in the study had previously received 1 cytotoxic treatment for MBC, had an ECOG performance status of 0–1, and were HER2-negative or of unknown status. The primary endpoint was investigator-assessed progression-free survival (PFS) calculated across all chemotherapy cohorts. The secondary endpoints included overall survival (OS), PFS within individual chemotherapy cohorts, overall response rate (ORR), and safety. A total of 684 patients at 211 sites in 19 countries were randomized. Study findings demonstrated a significantly improved PFS in patients receiving chemotherapy plus bevacizumab (7.2 vs 5.1 months). The ORR was also improved when bevacizumab was added to chemotherapy (39.5% vs 29.6%). At the interim analysis, the median OS was 16.4 months in the placebo group and 18.0 months in the bevacizumab group. Serious adverse events were reported more frequently with the addition of bevacizumab (17.6% vs 24.5%), though the incidence of bevacizumab-related toxicities was consistent with previous studies.

61 Updated Survival Analysis of a Randomized Study of Lapatinib Alone or in Combination with Trastuzumab in Women with HER2-Positive Metastatic Breast Cancer Progressing on Trastuzumab Therapy

KL Blackwell, HJ Burstein, GW Sledge, et al

In this study (EGF104900), lapatinib plus trastuzumab was compared to lapatinib alone in women with HER2-positive MBC that had progressed on multiple lines of trastuzumab-based therapy. Preliminary data showed that combination therapy was superior in terms of PFS compared to lapatinib alone. Women were randomized to receive either lapatinib 1,500 mg/day (n=148) or lapatinib 1,000 mg/day plus trastuzumab

2 mg/kg (n=148). Enrolled patients had a median of 3 prior trastuzumab-containing regimens. Of the women who were randomized to receive lapatinib alone, 52% crossed over to the combination arm. Median OS in the combination arm was significantly longer than in the lapatinib alone arm (60.7 vs 41.4 weeks). Survival benefit was maintained after adjusting for baseline prognostic factors (95% CI, 0.54–0.93; $P=.012$). A clinically significant reduction in risk of death was also observed after adjusting for patients who crossed over to combination therapy. The investigators concluded that the combination of lapatinib and trastuzumab was superior to lapatinib alone in terms of OS, and they suggested that the survival benefit of the combined therapy may have been underestimated because of the high rate of crossover.

112 Prediction of 10-Year Chemotherapy Benefit and Breast Cancer-Specific Survival by the 21-Gene Recurrence Score (RS) Assay in Node-Positive, ER-Positive Breast Cancer—An Update of SWOG-8814 (TBCI 0100)

K Albain, W Barlow, S Shak, et al

In this study, tumor samples from node-positive, estrogen receptor-positive breast cancer patients who participated in the SWOG/Breast Cancer Intergroup of North America trial that examined anthracycline-based chemotherapy followed by tamoxifen versus tamoxifen alone were analyzed to observe the prognostic and predictive effects of the *Oncotype* DX RS for breast cancer specific survival (BCSS). The primary objective was to update the 5-year report with 10-year disease-free survival (DFS) analyses in the 1–3 and 4 or more positive node categories. The final sample in this analysis included 367 patients. The RS was very prognostic in patients in the tamoxifen alone group ($P=.006$); it was also found to be predictive in patients treated with chemotherapy followed by tamoxifen. The study did not find an anthracycline-based chemotherapy benefit in the low RS group over 10 years (log rank $P=.97$; HR, 1.02); although a significant improvement in DFS was observed in the high RS group (log-rank $P=.03$; HR, 0.59). Study results also demonstrated a very high 10-year BCSS rate (regardless of treatment) in the low RS group despite patients having positive nodes.

701 Do the ASCO/CAP 2007 HER2 Testing Guidelines Improve Prediction of Benefit to Adjuvant Trastuzumab? Data from North Central Cancer Treatment Group N9831 Adjuvant Trial

EA Perez, MM Reinholz, AC Dueck, et al

In 2007, new guidelines to define HER2 positivity by immunohistochemistry (3+ IHC, uniform intense

membrane staining of >30% of invasive tumor cells), or fluorescent in situ hybridization (FISH+, HER2/CEP17 ratio >2.2) were recommended by the American Society of Clinical Oncology and College of American Pathologists (ASCO/CAP). This analysis was performed to evaluate the effect of the ASCO/CAP guidelines on patient eligibility and DFS compared to the original definitions approved by the U.S. Food and Drug Administration (FDA). A total of 2,268 patients from the N9831 trial of adjuvant trastuzumab were analyzed. IHC was centrally performed and re-analyzed to determine the percent of tumor cells with 0, 1+, 2+, and 3+ staining intensities. Of all patients, 83 (3.7%) were 3+ by FDA definitions but not 3+ by ASCO/CAP guidelines. Of these patients, 64 (77%) were FISH amplified centrally by ASCO/CAP guidelines. Of all patients, 34 (1.5%) who were eligible under FDA guidelines from the N9831 trial did not meet the ASCO/CAP guidelines. Investigators concluded that the trastuzumab effect was similar for HER2-positive patients regardless of the type of guidelines.

710 A Phase II Study of Trastuzumab-DM1 (T-DM1), a Novel HER2 Antibody-Drug Conjugate, in Patients with HER2+ Metastatic Breast Cancer who were Previously Treated with an Anthracycline, a Taxane, Capecitabine, Lapatinib, and Trastuzumab

I Krop, P LoRusso, KD Miller, et al

This open-label, single-arm, multicenter, phase II study of trastuzumab-DM1 (T-DM1) in patients previously treated with lapatinib, trastuzumab, and chemotherapy was conducted to gather additional safety and efficacy data in patients with refractory HER2-positive MBC. Patients received 3.6 mg/kg T-DM1 IV every 3 weeks. The primary objectives were to evaluate ORR (by independent review board) and the safety and tolerability of this regimen; secondary objectives included assessment of duration of response, clinical benefit rate (CBR), and PFS. Therapy was administered until disease progression or unmanageable toxicity. Study findings revealed that T-DM1 shrank tumors in 32.7% of all patients (n=110), and the CBR was 44.5% (complete or partial response or stable disease ≥ 6 months). Median PFS was 7.3 months. In the 84% of patients who had HER2-positive disease, the ORR was 39.5%, and the CBR was 52.6%. The safety analysis showed that toxicities were similar to those reported in previous T-DM1 trials. Of all patients, 25 developed a serious adverse event and 46 experienced a grade 3 or higher toxicity. Investigators concluded that single-agent T-DM1 demonstrated significant anti-tumor activity in this heavily pretreated patient population and was well tolerated with no dose-limiting cardiotoxicity.