Highlights From the 2012 ASCO Breast Cancer Symposium

September 13–15, 2012
San Francisco, California

Complete abstracts are available at http://breastcasymposium.org

98 Primary Results From EMILIA, a Phase III Study of Trastuzumab Emtansine (T-DM1) Versus Capecitabine (X) and Lapatinib (L) in HER2-Positive Locally Advanced or Metastatic Breast Cancer (MBC) Previously Treated With Trastuzumab (T) and a Taxane

MD Pegram, K Blackwell, D Miles, GV Bianchi, IE Krop, M Welslau, J Baselga, D-Y Oh, V Dieras, E Guardino, SR Olsen, L Fang, M Lu, S Verma

Pegram and associates presented data from the first planned interim analysis of the randomized, open-label, phase III EMILIA (An Open-Label Study of Trastuzumab Emtansine [T-DM1] vs Capecitabine Plus Lapatinib in Patients With HER2-Positive Locally Advanced or Metastatic Breast Cancer) trial. The study compared monotherapy with T-DM1 to combination therapy with capecitabine (Xeloda, Hoffman La Roche)/lapatinib (Tykerb, Smith-Kline Beecham) in 991 patients with human epidermal growth factor receptor 2 (HER2)-positive locally advanced or metastatic breast cancer who had previously been treated with trastuzumab (Herceptin, Genentech) and taxane-based chemotherapy. Patients were randomized to receive either T-DM1 monotherapy (3.6 mg/kg) every 3 weeks (n=495) or capecitabine (1,000 mg/m^2) twice daily for 14 days plus daily lapatinib (1,250 mg) during a 3-week cycle (n=496). Patients in the T-DM1 and capecitabine/lapatinib groups were followed for a median of 12.9 and 12.4 months, respectively. A co–primary endpoint of the study was progression-free survival (PFS), which was determined by independent review. The median PFS among patients treated with T-DM1 was 9.6 months, compared with 6.4 months for patients treated with capecitabine/lapatinib (stratified hazard ratio [HR], 0.650; *P*<.0001). Overall survival (OS) at 1 year was 84.7% in the T-DM1 treatment arm versus 77% in the capecitabine/lapatinib arm, and OS at 2 years was 65.4% versus 47.5%, respectively. The objective response rate was 43.6% for T-DM1 versus 30.8% for capecitabine/lapatinib (*P*=.0002). Among patients with an objective response, T-DM1 produced a 6.1-month absolute improvement in the median duration of response (12.6 months vs 6.5 months). When data were collected for this planned first interim analysis, there was a trend in favor of T-DM1 for improved OS (stratified HR, 0.621; *P*=.0005), but the difference between treatment groups did not technically achieve statistical significance. However, recent updates to the OS analysis do show statistical confidence, and will be presented in October at the 2012 European Society for Medical Oncology Congress in Vienna, Austria. In addition to improved efficacy, T-DM1 also demonstrated a better safety profile than capecitabine/lapatinib. Adverse events of grade 3 or higher were reported among 40.8% of patients receiving T-DM1 compared with 57% of patients receiving capecitabine/lapatinib. The most common grade 3/4 adverse events observed with T-DM1 included thrombocytopenia (12.9%), liver enzyme elevations (2.9% vs 4.3%), and anemia (2.7%). Cardiac toxicity was not increased with T-DM1. The median dose intensity received by patients was 99.9% with T-DM1, 93.4% with lapatinib, and 77.2% with capecitabine. Dose reductions due to toxicity were only required in 16.3% of patients in the T-DM1 arm, whereas the doses of lapatinib and capecitabine had to be reduced for 27.3% and 53.4% of patients, respectively.

99 Everolimus For Postmenopausal Women With Advanced Breast Cancer: Updated Results of the BOLERO-2 Phase III Trial

FP Arena, S Noguchi, KI Pritchard, HA Burris III, HS Rugo, M Gnant, GN Hortobagyi, L Latini, DA Yardley, B Melichar, K Petrakova, W Harb, W Feng, A Cahana, T Taran, M Campone, J Baselga, T Sahmoud, DE Lebwohl, MJ Piccart-Gebhart

In an updated 18-month analysis of the phase III BOLERO-2 (Breast Cancer Trials of Oral Everolimus) trial reported by Rugo and colleagues, the addition of everolimus (Afinitor, Novartis) to exemestane (Aromasin, Pfizer) prolonged PFS by 4.6 months over exemestane alone (median PFS, 7.8 months vs 3.2 months, respectively) in postmenopausal women with advanced estrogen receptor–positive breast cancer who recurred or progressed while on or following previous treatment with letrozole (Femara, Novartis) or anastrozole (Arimidex, AstraZeneca). For patients receiving combination treatment with everolimus plus exemestane, the objective response rate was 12.6%, compared with 1.7% for patients treated with exemestane plus placebo (control group). The

percentage change in OS increased with each follow-up analysis; however, OS has yet to meet the endpoint for statistical significance. Adding everolimus to exemestane significantly reduced the risk of cancer progression by 55% versus exemestane alone (HR, 0.45; *P*<.001).

100 Final Overall Survival (OS) and Safety Analyses of RIBBON-2, a Randomized Phase III Trial of Bevacizumab (BEV) Versus Placebo (PL) Combined With Second-Line Chemotherapy (CT) for HER2-Negative BEV-Naive Metastatic Breast Cancer (MBC)

AM Brufsky, SA Hurvitz, EA Perez, H Yamamoto, V Valero, V O'Neill, HS Rugo

Brufsky and coworkers presented the final results of the double-blind, randomized, phase III RIBBON-2 (Regimens in Bevacizumab for Breast Oncology) trial, which compared the efficacy and safety of bevacizumab (Avastin, Genentech) combined with standard chemotherapy regimens versus chemotherapy alone in the second-line treatment setting for HER2-negative metastatic breast cancer. Among 684 patients, the median PFS was significantly prolonged in patients treated with chemotherapy plus bevacizumab compared to patients treated with chemotherapy alone (7.2 months vs 5.1 months; HR, 0.775; *P*=.0072), with a 10% improvement in overall response rate that was not statistically significant. Median OS was 17.8 months in the chemotherapy arm and 18.6 months in the bevacizumab-plus-chemotherapy arm (*P*=.88). The 1-year OS rates were 69% and 71%, respectively. No major differences were observed in the subanalysis of different chemotherapies, nor were there differences in response or survival among triple-negative breast cancer patients.

144 Reduced Re-Excisions While Conserving Tissue Volume Resected in DCIS Patients

BC Freedman, SK Boolbol, C Cocilovo, L Tafra

According to a large prospective study presented by Freedman and associates, intraoperative margin assessment by a device that distinguishes cancer cells from normal tissue may reduce the rate of re-excision for patients undergoing lumpectomy for breast cancer, without a significant increase in the volume of tissue excised. The study randomized 161 patients with pure ductal carcinoma in situ (DCIS) to MarginProbe (Dune Medical) or no device (control) following standard of care lumpectomy. Positive readings on MarginProbe required additional resections of the cavity. Researchers then compared the volume of tissue removed during the surgery and any extra tissue removed after the device was used to the total volume of tissue removed in initial and any repeat surgeries in the control group. The mean tissue volume removed did not differ significantly between the 2 groups (83 cc with the device vs 76 cc without). However, there was a significant decrease in candidates for re-excision with the device (13% vs 37%). For patients with DCIS and invasive carcinoma, the results were similar, with no differences in total volume excised, but a significant decrease in re-excision candidates with MarginProbe (13% vs 33%).

151 Trade-Offs Associated With Axillary Lymph Node Dissection: Implications of the Eligibility Versus Enrollment in ACOSOG Z0011

MS Krishnan, A Recht, JR Bellon, RS Punglia

Krishnan and colleagues presented a simulation study that sought to determine whether patients with early-stage breast cancer at high risk of residual nodal disease might benefit from axillary lymph node dissection (ALND). The study challenged results of the American College of Surgeons Oncology Group (ACOSOG) Z0011 trial, which concluded that ALND is not necessary for patients with only 1 or 2 positive sentinel lymph nodes. However, patients at high risk of residual nodal disease were underrepresented in that trial, making it difficult to generalize the results. In the simulation, researchers applied algorithms to trial data to approximate results for hypothetical women aged 45, 55, and 75 years with stage II breast cancer following breast-conserving surgery with positive sentinel lymph nodes. They were then treated with either ALND and whole-breast radiation (BRT) or BRT alone. Patients with a 30–60% risk of residual nodal involvement were considered high risk, while patients with a less than 30% risk were identified as low risk (similar to patients in the ACOSOG Z0011 trial). Patients in the high-risk group achieved a 20-year OS of 42% with ALND plus BRT, compared with 38% for BRT alone. The quality-adjusted life expectancy (QALE) was 14.36 years with ALND plus BRT versus 13.55 years for BRT alone. Among the low-risk group, there was virtually no difference with ALND. The 20-year OS was 47% with and without ALND, and the QALE was 15.46 years with ALDN versus 15.53 years with BRT alone.