



**Embargoed for Release:**  
12:30 p.m. CT, Dec. 11, 2009  
*Unless noted below*

**Media Contact:**  
Jeremy Moore  
(267) 646-0557  
[jeremy.moore@aacr.org](mailto:jeremy.moore@aacr.org)  
**In San Antonio, Dec. 9-13:**  
(210) 582-7031

## **New Treatment Paradigms for Breast Cancer: Managing the Flow of New Data**

SAN ANTONIO – As scientists and clinicians continue to uncover new information about breast cancer, the landscape of acceptable treatment and management continues to shift.

Leading researchers will present new data on existing therapies that have been tested in unique ways at the CTRC-AACR San Antonio Breast Cancer Symposium, now in its 32nd year.

A press conference on some of the most impactful studies will be moderated by Edith Perez, M.D., director of the Breast Cancer Program at the Mayo Clinic in Jacksonville, Fla. The press conference will take place on Friday, Dec. 11, 2009, at 12:30 p.m. CT, in the Henry B. Gonzales Convention Center. Reporters who cannot attend in person can call in using the following information:

- U.S. & Canada: (888) 282-7404
- International: (706) 679-5207
- Access Code: 39119275
- Topic: AACR

The following abstracts will be presented during this press conference:

### **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**

Two targeted therapies — lapatinib plus trastuzumab — are better than one in the fight against HER2-positive metastatic breast cancer, according to study results presented at the CTRC-AACR Annual San Antonio Breast Cancer Symposium, held Dec. 9-13, 2009.

“These two targeted therapies against HER2, sort of a ‘one-two punch,’ conveyed a more than four month significant improvement in survival when compared to lapatinib alone,” said Kimberly L. Blackwell, M.D., associate professor of medicine and director of the Clinical Trials Program in Breast Cancer at Duke University Medical Center.

What makes these results stand out from previous studies, according to Blackwell, is that this study demonstrated an improvement in survival without the incorporation of endocrine therapy or chemotherapy.

“We demonstrated the effectiveness of combined targeted therapy; no other study has examined this combination in a phase III, randomized design,” she said.

The researchers randomized 296 metastatic breast cancer patients to receive lapatinib 1,500 mg once a day or lapatinib 1,000 mg once a day in combination with trastuzumab 2 mg/kg every week. Patients’ tumors had progressed on a number of trastuzumab-chemotherapy combination treatments, and patients were faced with limited treatment options.

Lapatinib is an orally active small molecule inhibitor against HER2 and epidermal growth factor receptor for use against solid tumors, and for combination therapy for metastatic breast cancer patients. Trastuzumab is a monoclonal antibody that binds selectively to the HER2 protein, and has demonstrated benefits when combined with chemotherapy in early stage and metastatic breast cancer patients.

Overall survival significantly improved among the patients who used combination therapy, compared with those who were treated with the lapatinib monotherapy, they found. Even after adjusting for prognostic factors, the survival benefit was maintained.

Further, Blackwell and colleagues noted a trend toward a 25 percent reduction in risk of death.

The same combination of lapatinib and trastuzumab from this study is now being compared to either drug alone in the prevention of breast cancer recurrence in patients faced with HER2-positive, early stage breast cancer.

“In the treatment of HER2-positive breast cancer, we have highly effective treatments and when we combine them, we can make a significant difference in survival,” she said. “This represents a step forward toward a day when we don’t have to give chemotherapy for breast cancer at all.”

#### **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**

RIBBON-2 results demonstrated that adding bevacizumab to chemotherapy as a second-line treatment for metastatic breast cancer significantly improved progression-free survival.

“Potentially, we have another biologic agent that can improve the survival or at least the progression-free survival of women with metastatic breast cancer,” said Adam Brufsky, M.D., Ph.D., associate professor of medicine, associate chief of hematology-oncology and associate director of clinical investigation, University of Pittsburgh Cancer Institute. “Clearly, this may be an indication to use bevacizumab in this setting, but we really have to consider the results of this trial in terms of how best to use these drugs in metastatic breast cancer.”

Results of three phase III studies — E2100, AVADO and RIBBON-1 — have shown the clinical benefit of adding bevacizumab to chemotherapy as a first-line metastatic breast cancer treatment. Brufsky and colleagues designed RIBBON-2 to evaluate the efficacy and safety of adding bevacizumab to chemotherapy as a second-line treatment of metastatic breast cancer.

The study included 684 patients in 19 countries at 211 sites. Patients were eligible if they met the following criteria: one prior cytotoxic treatment for metastatic breast cancer, Eastern Cooperative Oncology Group performance status of 0 to 1, HER2 negative disease and no central nervous system metastases.

The primary endpoint was progression-free survival; secondary endpoints included overall survival, overall response rate, duration of response and safety. Researchers randomly assigned patients to chemotherapy plus bevacizumab or chemotherapy plus placebo.

The results were predictable, Brufsky said. Adding bevacizumab to various chemotherapy regimens as a second-line metastatic breast cancer treatment significantly improved progression-free survival.

“The fact that bevacizumab has a benefit in first- and second-line treatment really begs the question: Should we be giving this drug to someone through the entire course of metastatic disease?” he said.

To address this question, Brufsky and colleagues are considering conducting a long-term clinical trial that to compare bevacizumab or no bevacizumab treatment in women with metastatic breast cancer.

**41. Final overall Survival (OS) Results from the Randomised, Double-Blind, Placebo-Controlled, Phase III AVADO Study of Bevacizumab (BV) Plus Docetaxel (D) Compared with Placebo (PL) Plus D for the First-Line Treatment of Locally Recurrent (LR) or Metastatic Breast Cancer (mBC)**

Results of the AVADO study showed that adding bevacizumab to docetaxel treatment significantly improved progression-free survival for patients with metastatic breast cancer.

“The AVADO study confirms that the use of bevacizumab in combination with a taxane, in this case docetaxel, increases the chance of reducing tumor burden and prolongs the time for which disease is controlled,” said David W. Miles, M.D., consultant medical oncologist, Mount Vernon Hospital, Northwood, Middlesex, United Kingdom. “The greater ability to control metastatic breast cancer, particularly in patients with immediately life-threatening disease, is reflected in the significant improvement in one-year survival.”

Miles presented final overall survival results from the AVADO trial, which included 736 patients in 24 countries at 106 sites, here at the CTRC-AACR San Antonio Breast Cancer Symposium.

In this double-blind, placebo-controlled phase III trial, researchers randomly assigned patients with HER2-negative, locally recurrent or metastatic breast cancer, and no central nervous system metastases, to first-line treatment with either docetaxel 100 mg/m<sup>2</sup> plus placebo (n=241), docetaxel plus bevacizumab 7.5 mg/kg (n=248) or docetaxel plus bevacizumab 15 mg/kg (n=247). The researchers administered docetaxel once every three weeks for up to nine cycles. They administered bevacizumab or placebo once every three weeks until disease progression or unacceptable toxicity.

The primary endpoint was progression-free survival; secondary endpoints included overall survival, time to treatment failure, overall response rate, duration of response and safety.

Primary analysis results about after 10 months of follow-up showed that adding bevacizumab to docetaxel significantly improved progression-free survival without affecting toxicity.

“Bevacizumab does not exacerbate the toxicity of chemotherapy but increases its effect in terms of response rate and progression-free survival,” Miles said. “We must make efforts to identify those most likely to benefit based on conventional characteristics or molecular markers, though the latter remain somewhat elusive.”

Final overall survival results showed that despite the improved response and progression-free survival results, there was no difference in median survival, Miles said.

**11. Five Years of Exemestane as Initial Therapy Compared to 5 Years of Tamoxifen Followed by Exemestane: The TEAM Trial, a Prospective, Randomized, Phase III Trial in Postmenopausal Women with Hormone-Sensitive Early Breast Cancer**  
*Embargoed until 9:15 a.m. CT, Dec. 10, 2009*

Researchers presented late breaking five-year data from the TEAM (Tamoxifen Exemestane Adjuvant Multinational) trial, a prospective, randomized trial comparing initial therapy with the steroidal aromatase inhibitor exemestane vs. a switch from initial therapy of tamoxifen to exemestane after a few years, at the CTRC-AACR San Antonio Breast Cancer Symposium.

“This is the only aromatase inhibitor study that has used exemestane as initial endocrine therapy compared to tamoxifen followed by exemestane,” said study author Daniel Rea, M.D., senior lecturer in medical oncology at the University of Birmingham, United Kingdom. “This is also the only study with sufficient power to reliably determine if an aromatase inhibitor as initial therapy is superior to a sequential approach starting with tamoxifen.”

In the TEAM trial, researchers randomly assigned 9,775 postmenopausal women with hormone receptor-positive early breast cancer to exemestane 25 mg per day or tamoxifen 20 mg per day. The trial began in 2001, and in 2004 the researchers reassigned all women who were initially receiving tamoxifen to switch to exemestane after 2.5 to three years. All women had undergone surgery with curative intent for invasive breast cancer. All tumors were hormone receptor positive, 50 percent were node negative and 36 percent had received chemotherapy.

The trial’s two primary endpoints were disease-free survival for tamoxifen vs. exemestane at 2.75 years — data that were presented at the 2008 CTRC-AACR San Antonio Breast Cancer Symposium — and disease-free survival at five years for women initially receiving exemestane vs. those who switched from tamoxifen to exemestane.

“Our hypothesis under examination in this presentation is that exemestane taken as initial endocrine therapy will improve relapse-free survival compared with starting tamoxifen,” Rea said.

He also explained that the TEAM trial is large enough for researchers to potentially identify subgroups that might benefit from different treatment approaches.

“In addition to analysis by traditional prognostic features, we may be able to identify subgroups defined by relatively simple biomarkers which can be used or combined with standard prognostic variables to rationally select optimal treatment strategies,” Rea said.

Late breaking data will be presented at the CTRC-AACR San Antonio Breast Cancer Symposium.

###

The mission of the CTRC-AACR San Antonio Breast Cancer Symposium is to produce a unique and comprehensive scientific meeting that encompasses the full spectrum of breast cancer research, facilitating the rapid translation of new knowledge into better care for breast cancer patients. The Cancer Therapy & Research Center (CTRC) at The University of Texas Health Science Center at San Antonio, the American Association for Cancer Research (AACR) and

Baylor College of Medicine are joint sponsors of the San Antonio Breast Cancer Symposium. This collaboration utilizes the clinical strengths of the CTSC and Baylor, and the AACR's scientific prestige in basic, translational and clinical cancer research to expedite the delivery of the latest scientific advances to the clinic. The 32nd annual symposium is expected to draw more than 8,500 participants from more than 90 countries.

**Presenter Name:** Kimberly L. Blackwell, M.D.

**Institution** Duke University Medical Center

**Abstract Number:** 61

**Abstract Title:** 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

**Abstract Body:**

**Background:** The synergistic interaction of lapatinib combined with trastuzumab was established in HER2-positive preclinical models, hence providing the rationale to evaluate this combination in a clinical setting. Progression-free survival (PFS) from study EGF104900 revealed the combination of lapatinib plus trastuzumab was superior to lapatinib alone in women with HER2-positive metastatic breast cancer (MBC) that progressed on multiple lines of trastuzumab-based therapy. Preliminary data showed a trend in overall survival (OS) favoring the combination therapy; however, data were not mature. Updated OS analyses are reported.

**Methods:** Women with HER2-positive MBC progressing on prior trastuzumab-containing regimens were randomized to receive either lapatinib 1500 mg once daily or lapatinib 1000 mg once daily in combination with trastuzumab 2 mg/kg (after a 4-mg/kg loading dose). If objective disease progression occurred on or after 4 weeks of lapatinib alone, crossover to the combination arm was permitted. OS was summarized using Kaplan-Meier curves and compared between treatment arms using stratified log-rank tests. Analyses adjusting for baseline prognostic factors and crossover were also performed.

**Results:** 296 women were randomized (148 per arm). The median number of prior trastuzumab-containing regimens for MBC treatment was 3. Of the women randomized to lapatinib alone, 52% (77/148) crossed over to the combination arm. At data cut-off for updated OS, 218 deaths (74%) had occurred. Median OS following treatment with lapatinib plus trastuzumab was 60.7 weeks compared with 41.4 weeks for lapatinib alone. A significant improvement in OS was demonstrated with combination therapy compared with lapatinib monotherapy (HR: 0.74; 95% CI: 0.57, 0.97; P=.026). The survival benefit was maintained after adjusting for baseline prognostic factors (HR: 0.71; 95% CI: 0.54, 0.93; P=.012). A trend toward a clinically relevant 25% reduction in risk of death (P=.080) was also observed after adjusting for crossover.

**Conclusion:** A statistically significant OS benefit was observed in women with heavily pretreated, HER2-positive MBC treated with lapatinib in combination with trastuzumab compared with those treated with lapatinib alone. The actual survival benefit of the combination therapy may be underestimated due to the high frequency of crossover.

**Presenter Name:** Adam Brufsky, M.D., Ph.D.

**Institution:** University of Pittsburgh Cancer Center

**Abstract Number:** 42

**Abstract Title:** 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

**Abstract Body:**

**Background:** Three prior Phase III trials (E2100, AVADO, and RIBBON-1) have established the clinical benefit of adding bevacizumab (B) to various chemotherapies as first-line treatment for metastatic breast cancer (MBC). A previous Phase III study in patients with heavily pre-treated MBC, in which B was added to capecitabine (Cape) resulted in a significant increase in objective response rate (ORR), but did not meet the primary endpoint of progression-free survival (PFS). The current study, RIBBON-2, was designed to evaluate the efficacy and safety of the addition of B to chemotherapies used as second-line treatment for MBC.

**Methods:** Patients were randomized in a 2:1 ratio to chemotherapy+B or chemotherapy+placebo. Prior to randomization, investigators chose one of the following chemotherapy agents: taxane (T; paclitaxel 90 mg/m<sup>2</sup>/wk for 3 of the 4 weeks; paclitaxel 175 mg/m<sup>2</sup>, nab-paclitaxel 260 mg/m<sup>2</sup>, docetaxel 75–100 mg/m<sup>2</sup>, all given q3wk), gemcitabine (G; 1250 mg/m<sup>2</sup> on Days 1 and 8 q3wk), Cape (2000 mg/m<sup>2</sup> Days 1–14 q3wk), or vinorelbine (V; 30 mg/m<sup>2</sup>/wk). B or placebo was administered to patients at 10 mg/kg q2wk or 15 mg/kg q3wk. The study was powered at 80% to detect a hazard ratio of 0.75 between the two arms (chemotherapy+B vs. chemotherapy+placebo) for PFS. The primary analysis for PFS will occur after 500 PFS events have been observed. Key eligibility criteria included one prior cytotoxic treatment for MBC, ECOG performance status of 0 to 1, HER2-negative disease, and no CNS metastases. The primary endpoint was investigator-assessed PFS and secondary endpoints included overall survival, ORR, duration of response, and safety.

**Results:** Study enrollment has been completed: 684 patients (T=303, G=162, Cape=143, and V=76) in 19 countries at 211 sites were randomized between February 2006 and June 2008. Results on the final analysis of primary endpoint, PFS, and secondary endpoints, including OS, ORR, duration of response, and safety, will be presented.

**Conclusions:** The detailed results will be presented.

**Presenter Name:** David W. Miles, M.D.

**Institution:** Mount Vernon Hospital

**Abstract Number:** 41

**Abstract Title:** Final overall Survival (OS) Results from the Randomised, Double-Blind, Placebo-Controlled, Phase III AVADO Study of Bevacizumab (BV) Plus Docetaxel (D) Compared with Placebo (PL) Plus D for the First-Line Treatment of Locally Recurrent (LR) or Metastatic Breast Cancer (mBC)

**Abstract Body:**

**Background:** BV, an anti-VEGF monoclonal antibody, significantly improves efficacy in the treatment of multiple solid tumour types, with limited impact on toxicity. The E2100 and AVADO phase III studies demonstrated that addition of BV to taxanes significantly improved progression-free survival (PFS) and overall response rates (ORR) in the first-line treatment of mBC. The phase III RIBBON 1 study of BV in combination with taxanes, anthracyclines or capecitabine in this setting has also met its primary endpoint of PFS.

**Methods:** In the PL-controlled AVADO study, patients with HER2-negative LR or mBC and no CNS metastases were randomised to first-line D 100 mg/m<sup>2</sup> + PL (n=241), D + BV 7.5mg/kg (n=248) or D + BV 15mg/kg (n=247). D was administered q3w for up to 9 cycles. BV or PL were administered q3w until disease progression or unacceptable toxicity. The primary endpoint was PFS and secondary endpoints included OS, time to treatment failure, ORR, duration of response and safety.

**Results:** 736 patients in 24 countries, at 106 sites were randomised between March 2006 and April 2007. Data previously presented for the primary analysis (data cut-off October 2007; median follow-up 10.2 months) showed significant improvements in PFS and ORR for both BV containing arms compared with PL + D, with limited impact on the known safety profile of D. Safety data were comparable at each dose of BV. Updated PFS and ORR data and mature results for OS will be presented, with a later data cut-off of April 2009 (median follow-up of approximately 28 months). Data are expected by early September 2009.

**Conclusions:** AVADO demonstrated that the addition of BV to D significantly improves PFS, without impacting on toxicity. This is the first presentation of mature OS data from this study. Updated analysis of other efficacy endpoints will be presented. The effect of crossover to BV in the PL arm and continued use of BV in the experimental arms will be investigated in exploratory analyses.

**Presenter Name:** Daniel Rea, M.D.

**Institution:** The University of Birmingham

**Abstract Number:** 11

**Abstract Title:** Five Years of Exemestane as Initial Therapy Compared to 5 Years of Tamoxifen Followed by Exemestane: The TEAM Trial, a Prospective, Randomized, Phase III Trial in Postmenopausal Women with Hormone-Sensitive Early Breast Cancer

**Abstract Body:**

**Background:** Exemestane (E) is a steroidal aromatase inhibitor (AI) with an established role in early breast cancer after 2–3 years of tamoxifen (T). Additionally, AIs have shown superiority to T as initial adjuvant therapy. The Tamoxifen Exemestane Adjuvant Multinational (TEAM) study has been prospectively designed to compare the role of E as initial adjuvant therapy with a sequential approach of T followed by E (T→E).

**Methods:** Postmenopausal patients with hormone receptor–positive early breast cancer were randomized to open-label E 25 mg/d or T 20 mg/d. All patients completed surgery and chemotherapy, if indicated. Data were collected and analyzed by the Central Data Center in Leiden, The Netherlands. The trial was initiated in 2001 with the primary objective being a comparison of disease-free survival (DFS) with T vs E. In 2004, TEAM was modified in response to new data; all those initially receiving T were switched to E after 2.5–3 years. An additional 2500 patients were recruited and randomized at diagnosis to E or T→E for 5 years. The modified study design includes 2 coprimary endpoints: (1) DFS of T vs E that was previously reported at 2.75 years median follow-up (Jones S et al, abstract #15 presented at SABCS 2008); and (2) DFS at 5 years of E vs T→E that will be the focus of results presented here.

**Results:** Between 2001 and January 2006, 9775 women were randomized to TEAM. In total, 99% of patients were ER+ and/or PgR+, 50% were node-negative, 44% underwent mastectomy, 68% received radiotherapy, and 36% received chemotherapy. In September 2009, median follow-up will be 5.5 years and the protocol-specified 1285 overall DFS events (locoregional or distant recurrence, second breast cancers, or death without recurrence) will have occurred, allowing for analysis of the second coprimary endpoint. We will present a detailed analysis of the 5-year results from the TEAM trial, the only prospectively powered randomized trial to compare 5 years of an initial AI vs T→AI, 2 commonly received adjuvant therapies for women with hormone receptor–positive early breast cancer.