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-- PRESS BRIEFING SUNDAY, JUNE 6, 10 AM (CDT) --

STUDIES REPORT PROGRESS AGAINST BREAST CANCER

Chicago – Studies describing new advances against breast cancer were released today at a press briefing at the 46th Annual Meeting of the American Society of Clinical Oncology (ASCO).

“The studies presented today provide us with new insight into the treatment and behavior of breast cancer, especially for difficult-to-treat metastatic disease,” said Eric P. Winer, MD, professor of medicine at Harvard Medical School, and moderator of the briefing. “We’re also learning the best ways to detect cancer spread in the lymph nodes, finding that in many cases, women can be spared from extensive, often painful, lymph node removal.”

Studies highlighted in the press briefing include:

- *New Agent, Eribulin, Derived from a Marine Sponge, Increases Survival Among Women with Metastatic Breast Cancer:* A Phase III randomized trial finds that a new chemotherapy agent, eribulin mesylate, extends median overall survival by 2.5 months among women with locally recurrent or metastatic breast cancer who had already been heavily treated with conventional therapies.
- *Breast Cancers that Spread to the Liver May Change Biology, Impacting Treatment Effectiveness:* A retrospective study of women with metastatic breast cancer showed that the biological characteristics of their primary tumors – including estrogen, progesterone, and HER2 status – often changes when the cancer spread to the liver, requiring a change in therapy for many women.
- *Removing Axillary Lymph Nodes Based on Metastases in the Sentinel Node Does Not Improve Survival in Early Breast Cancer:* Removing additional axillary (underarm) lymph nodes to look for breast cancer in women with limited disease spread in the sentinel node does not improve survival, according to results from a Phase III study. These findings are important because many physicians routinely remove multiple axillary nodes in women with micrometastases in the sentinel lymph node, which increases the risk of side effects, such as pain and swelling.

2318 Mill Road, Suite 800
Alexandria, VA 22314
T: 571-483-1300
F: 571-366-9530
www.asco.org

Making a world of difference in cancer care

- *Using Immunohistochemistry Testing to Identify Breast Cancer Micrometastases in the Sentinel Node and Bone Marrow Does Not Help Predict Survival:* A large observational trial of women with early-stage breast cancer who had breast-sparing surgery (lumpectomy) showed that using immunohistochemistry (IHC) to detect micrometastases in sentinel lymph nodes and the bone marrow does not predict overall survival and should not be used to guide treatment decisions. Micrometastases are smaller, hidden pockets of metastatic disease that may be missed by standard pathology.

For consumer-oriented information on these studies and more than 120 cancer types, please refer your readers to ASCO's patient website, www.Cancer.Net.

**Oral Abstract Session: Breast Cancer-Metastatic
Tuesday, June 8, 2010 9:30 – 9:45 AM, CDT
E Hall D1**

**Lead author: Christopher Twelves, MD
Leeds Institute of Molecular Medicine
and St. James's Institute of Oncology
Leeds, UK**

New Agent, Eribulin, Derived from Marine Sponge, Increases Survival Among Women with Metastatic Breast Cancer *

A Phase III randomized trial finds that a new chemotherapy agent, eribulin mesylate, extends median overall survival by about 2.5 months among women with locally recurrent or metastatic breast cancer who had already been heavily treated with conventional therapies.

“Until now, there hasn’t been a standard treatment for women with such advanced breast cancer. For those who have already received all of the recognized treatments, these are promising results,” said lead author Christopher Twelves, MD, professor of clinical cancer pharmacology and oncology, and Head of the Clinical Cancer Research Groups at the Leeds Institute of Molecular Medicine and St. James’s Institute of Oncology in Leeds, U.K. “These findings may establish eribulin as a new, effective option for women with heavily pre-treated metastatic breast cancer.”

Eribulin mesylate is a new type of “microtubule dynamics inhibitor” that affects cell division; the drug is derived from a marine sponge. The international, multicenter trial, called EMBRACE, is the first to compare eribulin mesylate to “treatment of physician’s choice” in women with locally recurrent or metastatic breast cancer who had already received an average of four prior chemotherapy drugs, such as anthracyclines or taxanes. Because no single chemotherapy regimen is standard for these women, physicians chose which treatment to give patients in this study’s control arm, to reflect real-life choices.

Dr. Twelves and his colleagues compared overall survival among 762 patients with metastatic breast cancer who were randomized to receive either eribulin (508 women) or their physician’s choice of therapy (254 women), which was almost always another chemotherapy. The median survival for the eribulin group was significantly longer: 13.1 months versus 10.7 months. The study’s secondary endpoints (progression-free survival and objective response rate) also favored eribulin, which was generally well tolerated.

Abstract CRA 1004

A phase III study (EMBRACE) of eribulin mesylate versus treatment of physician’s choice in patients with locally recurrent or metastatic breast cancer previously treated with an anthracycline and a taxane.

C. Twelves, D. Loesch, J. L. Blum, L. T. Vahdat, K. Petrakova, P. J. Chollet, C. E. Akerle, S. Seegobin, J. Wanders, J. Cortes, on behalf of the Study 305 investigators

Background: Eribulin mesylate (E7389; E) is a nontaxane microtubule dynamics inhibitor with a novel mode of action. This study is the first to compare overall survival (OS) with this new chemotherapeutic (CT) agent to real-life choices in heavily pretreated patients (pts) with metastatic breast cancer (MBC).

Methods: Women with locally recurrent or MBC were enrolled in this phase III open-label, randomized, multicenter study. Pts had received 2-5 prior CT (≥ 2 for advanced disease), including an anthracycline and a taxane, unless contraindicated. Pts were randomized 2:1 to E 1.4 mg/m² 2-5 min IV bolus on days 1 and 8 of a 21-day cycle or treatment of physician’s choice (TPC). TPC was any monotherapy (cytotoxic, hormonal, biologic) or supportive care only. The primary endpoint was OS; secondary endpoints were objective response rate (ORR), and progression-free survival (PFS) by independent review, and duration of response (DOR). Safety and tolerability were assessed. Data are from the final analysis after 422 deaths.

Results: 762 pts were treated (508 E, 254 TPC). Median age was 55.2 (range 27-85), 16% were HER2-positive, 19% triple-negative, 73% received prior capecitabine, median no. of prior CT was 4. Median OS was 13.1 months (mo) for E vs. 10.7 mo for TPC, $p=0.04$ (primary analysis, stratified log rank test; HR 0.81; 95% CI 0.66, 0.99). Median PFS was 3.7 mo for E and 2.3 mo for TPC $p=0.09$ (HR 0.85; 95% CI 0.70, 1.03). ORR was 12% (0.4% complete response [CR], 11.5% partial response [PR]) for E and 5% (0 CR; 5% PR) for TPC, $p=0.005$. Median DOR was 4.1 mo for E (56 responders) vs. 6.7 mo for TPC (11 responders). Grade [G] 3/4 treatment-related adverse events (AEs) of interest for E were asthenia/fatigue (7.6%), neutropenia (44%), peripheral neuropathy (8.4%). 10% of pts experienced treatment-related serious AEs (12% E, 7% TPC).

Conclusions: The study met its primary endpoint with a significant improvement in OS by a median of 2.5 mo with E vs. TPC. E demonstrated a manageable tolerability profile, acceptable for a CT agent used as monotherapy in this late-line setting.

Disclosures: Christopher Twelves, Consultant or Advisory Role, Eisai, Expert Testimony, Eisai; Joanne Blum, Consultant or Advisory Role, Eisai; Linda Vahdat, Consultant or Advisory Role, BMSO, Eisai, Research Funding, BMSO, Eisai, Research Funding, ImClone Systems; Corina Akerele, Employment/Leadership Position, Eisai; Seth Seegobin, Employment/Leadership Position, Eisai; Jantien Wanders, Employment/Leadership Position, Eisai; Javier Cortes, Consultant or Advisory Role, Eisai.

*Abstract presented or published pursuant to an exception to the ASCO Conflict of Interest Policy.

**Oral Abstract Session: Breast Cancer-Metastatic
Tuesday, June 8, 2010 11:45 AM-12:00 PM CDT
E Hall D1**

**Author: Giuseppe Curigliano, MD, PhD
European Institute of Oncology
Milan, Italy**

Breast Cancers that Spread to the Liver May Change Biology, Impacting Treatment Effectiveness
[Note: This summary contains updated data not in the abstract]

A retrospective study of women with metastatic breast cancer shows that the biological characteristics of their primary tumors – including estrogen, progesterone, and HER2 status – often changes when cancer spread to the liver, requiring a change in therapy in more than 12 percent of patients.

“These results indicate that tumor biology often changes between primary and metastatic lesions, and suggest that biopsies of these secondary tumors should be performed whenever feasible,” said co-author Giuseppe Curigliano, MD, PhD, senior deputy director in the division of medical oncology at the European Institute of Oncology in Milan, Italy. “Traditionally, we start therapy according to the biological features of the primary tumor, and these results can influence treatment choices as many as 10 years later. Retesting secondary tumors will help us ensure that patients get the most effective therapy possible, which can have a dramatic impact on their overall outcome.”

The choice of therapy for women with breast cancer is based on the status of key biological markers, such as estrogen and progesterone receptors and HER2. For example, trastuzumab (Herceptin) is only effective in women whose tumors overproduce HER2, while tamoxifen or aromatase inhibitors only work in breast cancer patients with estrogen receptor-positive tumors. But doctors don't routinely biopsy metastases, relying on the results of the primary tumor biopsy to guide treatment -- sometimes for many years.

In this study, researchers examined biopsy data from primary breast tumors and liver metastases in 255 women with metastatic breast cancer to determine the status of estrogen and progesterone receptors and HER2. They found changes in estrogen receptor status in the secondary tumor in 14.5 percent of women, progesterone status in 48.6 percent and HER2 status in 13.9 percent. This led to changes in therapy in 12.1 percent of the patients.

Abstract: CRA 1008

Should liver metastases of breast cancer be biopsied to improve treatment choice?

M. A. Locatelli, G. Curigliano, L. Fumagalli, V. Bagnardi, G. Aurilio, P. Della Vigna, L. Monfardini, S. Giudici, G. Viale, A. Goldhirsch

Background: Decision making on systemic treatment of women with metastatic breast cancer is based on features like estrogen receptor (ER), progesterone receptor (PgR), and HER2 status assessed on the primary tumor. We evaluated the concordance of receptor status between primary tumor and liver metastases (mts) and its impact on treatment choice.

Methods: We retrospectively analyzed a database including ultrasound guided liver biopsies performed from 1995 to 2008. All tissue samples, both from primary tumor and liver mts, were analyzed for ER, PgR and HER2 status. Clinical and biological data were obtained from medical charts. Differences between proportions were evaluated using the Pearson chi-square test.

Results: We identified 255 consecutive patients (pts) with matched primary and liver tissue samples. Median time from primary diagnosis to liver biopsy was 3.4 years (range 0-18.3 years). Changes in ER status were observed in 41/255 pts (16.0%). 16/58 pts (27.6%) changed from ER-negative to ER-positive and 25/197 pts (12.7%) changed from ER-positive to ER-negative ($p=0.0066$). Changes in PgR status were observed in 76/255 pts (29.8%). 18/91 pts (19.8%) changed from PgR-negative to -positive and 58/164 pts (64.6%) from PgR-positive to PgR-negative ($p<0.0001$). 12/52 pts (23.1%) changed from ER- and PgR-negative to ER- or PgR-positive (group A) and 27/203 pts (13.3%) changed from ER- or PgR-positive to ER- and PgR-negative (group B) ($p=0.087$). In the group A the treatment of 4/12 pts (33.3%) was changed after biopsy: 2/4 started endocrine treatment (HT) and 2/4 stopped it. In group B the treatment of 18/27 pts (66.6%) was changed after biopsy: 17/18 stopped HT. Changes in HER2 status were observed in 22/167 pts (13.1%): 6/116 pts (5.1%) changed from HER2-negative to HER2-positive and 16/51 pts (31.4%) changed from HER2-positive to negative ($p<0.0001$). In this group pts started and/or stopped a trastuzumab containing treatment after biopsy.

Conclusions: There was a discordance in receptor status between primary tumor and liver mts, which led to change in therapy for 48/255 of pts (18.8%). Biopsy of metastases for reassessment of biological features should be considered in all pts when safe and easy to perform, since it is likely to impact treatment choice.

**Oral Abstract Session: Local,
Regional and Adjuvant Therapy
Monday, June 7, 2010, 10:00-10:15 AM CDT
N Hall B1**

**Lead Author: Armando Giuliano, MD
John Wayne Cancer Institute
Santa Monica, CA**

**Removing Axillary Lymph Nodes Based on Metastases in the Sentinel Node Does Not Improve
Survival in Early Breast Cancer**

[Note: This summary contains updated data not in the abstract]

Removing additional axillary (underarm) lymph nodes to look for more breast cancer cells in women with limited disease spread in the sentinel node does not improve survival, according to results from a Phase III study. These findings are important because many physicians routinely opt for axillary node dissection in women with metastases in the sentinel lymph node.

“Axillary lymph node removal has been the standard approach for women with micro- and macro-metastases in the sentinel node,” said lead author Armando E. Giuliano, MD, director of the John Wayne Cancer Institute Breast Center in Santa Monica, Calif. “Our findings suggest that there may not be a benefit to removing more lymph nodes than the sentinel node only, and that women can avoid the risk of additional side effects that come with more extensive lymph node removal. Axillary lymph node dissection will still be needed in some cases, but these findings show it may be necessary for far fewer women.”

When cancer is detected in the sentinel lymph node (the first node cancer cells would spread to from a tumor), the usual practice is to surgically remove more lymph nodes under the arm to look for additional cancer cells. While this procedure, axillary lymph node dissection (ALND), has been shown to help control the disease locally, its effect on survival has been controversial. ALND can also cause significant side effects, including pain, discomfort and swelling (lymphedema) of the affected arm.

In the largest Phase III study of axillary node dissection for sentinel node-positive women to date, 991 women who had lumpectomy, radiation therapy and a positive sentinel node were randomly assigned to no ALND (446 women) or ALND with removal of 10 or more additional axillary lymph nodes (445 patients). All were followed for local/regional recurrence and overall survival.

After a median follow-up of nearly six years, the researchers found no survival advantage to having more lymph nodes removed, despite the fact that some of these lymph nodes had cancer in them. The five-year overall survival in patients undergoing ALND was 91.9 percent compared to 92.5 percent for those who had sentinel node biopsy alone. The ALND group had a disease-free survival of 82.2 percent, versus 83.8 percent for those who did not have ALND. The rate of local/regional recurrence was 4.3 percent among women who had ALND and 3.4 percent among those who had only sentinel node biopsy. None of these differences was statistically significant.

Abstract: CRA 506

ACOSOG Z0011: A randomized trial of axillary node dissection in women with clinical T1-2 N0 M0 breast cancer who have a positive sentinel node.

A. E. Giuliano, L. M. McCall, P. D. Beitsch, P. W. Whitworth, M. Morrow, P. W. Blumencranz, A. M. Leitch, S. Saha, K. Hunt, K. V. Ballman
Background: Sentinel node biopsy (SNB) eliminates the need for axillary dissection (ALND) in patients whose sentinel node (SN) is tumor-free. However, completion ALND remains the gold standard for patients with a tumor-involved sentinel node. ALND achieves regional control, but its effect on survival remains controversial. The main objective of ACOSOG Z0011 was to compare outcomes of patients with hematoxylin and eosin (H&E) detected metastasis in SN managed with or without ALND and no axillary irradiation.

Methods: Clinically node-negative patients who underwent SN biopsy and had 1 or 2 SN with metastases detected by H&E were randomized to ALND or no further axillary specific treatment. All patients were treated with lumpectomy and opposing tangential field irradiation. Adjuvant systemic therapy was at the discretion of their physicians. Overall survival (OS), disease-free survival (DFS), and locoregional control were evaluated.

Results: 446 patients were randomized to SNB alone and 445 to SNB plus ALND. Patients treated with SNB alone were similar to those treated with SNB + ALND with respect to age, tumor size, Bloom-Richardson score, estrogen receptor status, adjuvant systemic therapy, tumor type, and T stage. Patients randomized to SNB alone had a median of two lymph nodes removed whereas patients randomized to ALND had a median of 17 lymph nodes removed. 17.6% of ALND patients had 3 or more involved nodes compared to 5.0% of SNB patients ($p < 0.001$). Median follow-up is 6.2 years. 5-year in-breast recurrence after ALND was 3.7% compared to 2.1% for SNB ($p = 0.16$) while 5-year nodal recurrence was 0.6% compared to 1.3% ($p = 0.44$) respectively. The five-year OS for patients undergoing SNB + ALND is 91.9% compared to 92.5% for SNB alone ($p = 0.24$), and DFS is 82.2% compared to 83.8% respectively ($p = 0.13$).

Conclusions: Despite the widely held belief that ALND improves survival, no significant difference was recognized by this study of SN node-positive women. Although the study closed early because of low accrual/event rate, it is the largest phase III study of ALND for node-positive women, and it demonstrates no trend toward clinical benefit of ALND for patients with limited nodal disease.

Disclosures: Peter Blumencranz, Honoraria, ACOSOG, Research Funding, ACOSOG; A. Leitch, Research Funding, ACOSOG, NSABP; Sukamal Saha, Employment/Leadership Position, Audit Committee.

**Oral Abstract Session: Breast Cancer –
Local-Regional and Adjuvant Therapy
Monday, June 7, 9:30 – 9:45 AM CDT
N Hall B1**

**Study Author: A. Marilyn Leitch, MD
University of Texas Southwestern
Medical Center
Dallas, Texas**

Using Immunohistochemistry Testing to Identify Breast Cancer Micrometastases in the Sentinel Node and Bone Marrow Does Not Help Predict Survival

A large observational trial of more than 5,500 women with early-stage breast cancer who had breast-sparing surgery (lumpectomy) showed that using immunohistochemistry (IHC) to detect occult micrometastases in sentinel lymph nodes and bone marrow does not predict overall survival and should not be used to guide treatment decisions. Micrometastases are smaller, hidden pockets of metastatic disease that may be missed by standard pathology testing, called histology. IHC assesses antigen-antibody interactions and is a more sensitive test that frequently finds undetected disease.

“We were hoping to find out that immunohistochemistry not only could give us a more detailed picture of the cancer and survival, but that we could use bone marrow and sentinel node micrometastases to identify patients at risk for recurrence and determine who would need systemic chemotherapy, perhaps personalizing therapy,” said study co-author A. Marilyn Leitch, MD, professor of surgery at the University of Texas Southwestern Medical Center at Dallas. “These results, for now, tell us otherwise.”

Dr. Leitch and her colleagues examined the potential clinical significance of metastases in the sentinel node and bone marrow that were identified by IHC testing. Studies had suggested a role for bone marrow micrometastases in predicting survival for early-stage breast cancer, but the effect of micrometastases in the sentinel node was unclear.

This prospective, multicenter trial included 5,539 women with early-stage, clinically node-negative (without palpable lymph nodes under the arm) breast cancer who had undergone lumpectomy. These women underwent sentinel node biopsies and bone marrow aspiration to determine if micrometastases were present. Those women who were histologically node-negative for cancer were tested by IHC to look for hidden disease, and they also had IHC testing of the bone marrow.

Using standard histological testing, the researchers found cancer in 23.9 percent (1,239) of patients' sentinel nodes. IHC detected cancer cells in an additional 10.5 percent (350) of patients' sentinel nodes.

Despite the fact that IHC found more cancer, the team found that overall survival was statistically similar between the two groups. Using IHC, they found that 95.1 percent of women with cancer-positive lymph nodes lived at least five years, compared to 92.8 percent for women with positive lymph nodes as detected by standard pathology.

Bone marrow metastases were identified in 3 percent (105) of 3,491 women who agreed to bone marrow testing and were evaluated by IHC. The median five-year survival of women with IHC-positive bone marrow was 90.2 percent compared to 95.1 percent for women with IHC-negative bone marrow – a difference that was statistically significant. While not predictive of overall survival in multivariate analysis, the detection of bone marrow metastases by immunohistochemistry identified patients with an increased risk for death, supporting findings of earlier studies.

Abstract CRA 504

ACOSOG Z0010: A multicenter prognostic study of sentinel node (SN) and bone marrow (BM) micrometastases in women with clinical T1/T2 N0 M0 breast cancer.

R. Cote, A. E. Giuliano, D. Hawes, K. V. Ballman, P. W. Whitworth, P. W. Blumencranz, D. S. Reintgen, M. Morrow, A. M. Leitch, K. Hunt

Background: SN biopsy (SNB) with immunohistochemistry (IHC) of histologically negative SN identifies metastases (mets) not seen by standard histology. The impact of IHC-detected BM mets has been reported in several large single-institution studies. 5,539 patients (pts) were entered into this prospective multicenter observational study to determine the clinical significance of SN and BM mets.

Methods: Patients underwent lumpectomy and SNB with bilateral iliac crest BM aspiration. BM and histologically negative SN were evaluated with IHC in a central laboratory (results not clinically reported). Overall survival (OS), disease-free survival, and locoregional recurrence were determined. Results with OS (the primary endpoint) are reported here.

Results: SN were successfully identified in 5,184 of 5,485 pts (94.5%). Histologic SN mets were found in 1,239 pts (23.9%). IHC detected an additional 350 pts (10.5%) with SN mets. BM mets were identified by IHC in 105 of 3491 examined (3.0%). 5-yr overall survival is shown in the Table. BM IHC positivity significantly predicted decreased OS (p=0.015). A multivariable analysis that included SN and BM status, ER, PR, grade, size, and age showed that neither IHC detected mets in SN (p=0.66) or BM (p=0.08) were independent predictors of OS, although BM status showed a strong trend.

Conclusions: The detection of BM mets by IHC in pts with clinical T1/2 N0M0 breast cancer identifies those pts at significantly increased risk for death; the impact of BM mets on outcome supports and confirms prior studies. In this study, SN IHC-detected mets appear to have no significant impact on OS. The routine examination of SN by IHC is not supported in this patient population by this study.

5-year OS by SN and BM status

Group	% alive at 5 years (95% CI)	p value
SN histology status		
Positive	92.8 (91.3 to 94.3)	
Negative	95.6 (95.0 to 96.3)	0.0002
SN IHC status		
Positive	95.1 (92.7 to 97.5)	
Negative	95.8 (95.0 to 96.5)	0.53
BM IHC status		
Positive	90.2 (84.6 to 96.2)	
Negative	95.1 (94.3 to 95.8)	0.015

Disclosures: Peter Blumencranz, Honoraria, ACOSOG, Research Funding, ACOSOG; A. Leitch, Res

Moderator Dr. Winer reported the following disclosures: Employment or Leadership Position: Susan G. Komen for the Cure, Consultant or Advisory Role: Esai (uncompensated), Pfizer, Roche/Genentech (uncompensated), Research Funding: Genentech, Stand Up to Cancer, Susan G. Komen for the Cure.

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