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-- PRESSCAST TUESDAY, OCTOBER 6, 12:00 PM EDT –

STUDIES ADVANCE EARLY DETECTION, EVALUATION AND TREATMENT OF BREAST CANCER

SAN FRANCISCO – New studies on the early detection, evaluation and treatment of breast cancer were released today in advance of the 2009 Breast Cancer Symposium. The symposium is being held October 8-10, 2009, at the San Francisco Marriott.

Four major studies were highlighted today in a presscast (press briefing via live webcast):

- *Majority of breast cancer deaths occur among women who don't receive regular mammography:* A large, retrospective study shows that nearly three-quarters of breast cancer deaths occur among the minority of women who do not undergo regular screening mammograms.

- *Women under age 44 with DCIS have a higher risk of recurrence:* A study reports that women with ductal carcinoma in situ (a pre-invasive form of breast cancer) age 44 and younger have almost double the risk of recurrence following breast conservation surgery and radiation therapy than women age 45 to 50, suggesting that more aggressive treatment should be studied in this population.

- *Adding low-cost ultrasound prior to surgery can reduce need for second breast cancer surgery:* An analysis demonstrates that the addition of axillary ultrasound prior to initial breast-conserving surgery spared nearly one-third of women with early-stage breast cancer who had underarm (axillary) lymph node metastases from a second breast cancer surgery to remove additional axillary nodes.

- *New technique identifies breast cancer subtypes and predicts response to adjuvant paclitaxel (Taxol) chemotherapy:* A study validates a novel method of tissue analysis, called tissue microarrays, for determining the "intrinsic subtype" of a breast tumor, and accurately uses breast cancer sub-typing to predict response to a specific anticancer drug. These findings will improve physicians' ability to personalize treatment to maximize benefits and spare patients from unnecessary side effects.

"The studies presented today remind us that mammography is one of the most powerful tools we have for improving breast cancer survival rates," said Lori Pierce, MD, professor of radiation oncology at the University of Michigan School of Medicine, who moderated the presscast. "They will also allow physicians to better tailor therapy, make treatment more tolerable and effective, and improve outcomes for patients."

Breast cancer is diagnosed in approximately 194,000 people in the United States every year. This year's symposium will focus on a range of issues in breast cancer, including advances in targeted therapies, translational science, new diagnostic technology, and management of high-risk patients.

The third annual Breast Cancer Symposium is co-sponsored by the American Society of Breast Disease, The American Society of Breast Surgeons, the American Society of Clinical Oncology, the American Society for Radiation Oncology, the National Consortium of Breast Centers and The Society of Surgical Oncology. *Susan G. Komen for the Cure®*, the world's largest grassroots network of breast cancer survivors and advocates, is the primary supporter of the symposium.

Information for Media: www.asco.org/BCSpresskit09

Relevant Links on ASCO's Cancer.Net:

- Cancer.Net Guide to Breast Cancer
- Cancer.Net Feature: Breast Cancer: Questions to Ask Your Doctor
- Cancer.Net Feature: Frequently Asked Questions About Radiation Therapy
- ASCO Expert Corner: Race and Breast Cancer
- ASCO Expert Corner: Health Disparities in Cancer
- What to Know: ASCO's Guideline on HER2 Testing for Breast Cancer
- Cancer.Net Feature: Mammography – What to Expect
- Expert Perspective from ASCO on MRI Breast Cancer Screening

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Oral Abstract Presentation A
Thursday, October 8, 2009
2:30- 2:45 PM PST

Lead Author: Blake Cady, MD
Cambridge Hospital Breast Center
Cambridge, MA

Majority of Breast Cancer Deaths Occur in Women Not Receiving Regular Mammograms

A large, retrospective population-based study has found that nearly three-quarters of breast cancer deaths occur among the minority of women who do not undergo regular screening mammograms.

The study suggests that having a regular screening mammogram can help to reduce the risk of dying from breast cancer, according to lead author Blake Cady, MD, professor of surgery (emeritus) at Harvard Medical School and Brown University Medical School. "Breast cancer mortality reductions have been seen in every country after widespread population screening with mammography was introduced. These reductions are more closely associated with the use of screening than with the use of treatment," said Dr. Cady.

Prior randomized studies have demonstrated breast cancer mortality reductions of 25 to 40 percent among women offered screening mammography compared to women not offered screening, because mammography helps detect breast cancers at earlier, more curable stages. Another study of women who actually received mammography indicated that breast cancer mortality was reduced by more than 50 percent. But the impact of this screening test on population-wide breast cancer mortality has been unclear.

In this study, Dr. Cady and colleagues examined 6,997 women who did and did not undergo regular screening mammography, were diagnosed with invasive breast cancer in Massachusetts between 1990 and 1999 and were followed through 2007. Regular screening was defined as two or more screening mammograms at intervals of two years or less in women with no breast cancer symptoms. Surveys in 1995 indicated that about 80 percent of Massachusetts women had received mammographic screening at least every two years.

After a median of 12.5 years of follow-up, there were 461 deaths from breast cancer: 345 (74.8 percent) occurred in women who did not receive regular screening mammograms and 116 (25.2 percent) occurred in the 80 percent of women who were regularly screened. According to the researchers, extrapolating these results to the more than 192,000 women estimated to be diagnosed with breast cancer in the United States in 2009, less than 5 percent of women regularly screened with mammography would be expected to die within 13 years, compared with 56 percent of those not regularly screened – a rate similar to 1970, before the advent of mammography.

Death from Breast Cancer Occurs Predominantly in Women Not Participating in Mammographic Screening
B. Cady, M. Webb, M. Webb, J. Michaelson, b. l. smith

Background: Randomized population mammographic screening trials demonstrated statistically significant mortality reduction in screened women. However, in large general populations, it is unclear how screening impacts death from breast cancer. In a previous report, 75% of breast cancer deaths occurred in the small proportion of unscreened women. That conclusion needs confirmation.
Methods: 6,997 invasive breast cancer diagnoses occurred in a large hospital consortium between 1990 and 1999. Among all subsequent deaths through 2007, breast cancer deaths in Massachusetts women were documented by actual review of hospital and out-patient records. Regular screening was defined as two or more screening mammograms at intervals of two years or less in asymptomatic women. 1995 Behavioral Risk Factor Surveillance System (BRFSS) mammography rates in Massachusetts were obtained.
Results: After 12.5 (8-17) years median follow-up, 461 deaths from breast cancer were confirmed. 72 deaths (15.6%) resulted from non-palpable screen detected cancers; 44 deaths (9.6%) resulted from palpable interval cancers, for a total of 116 deaths (25.2%) in regularly screened women. 322 deaths (69.9%) occurred in women who never had screening mammography, and 23 deaths (5%) occurred after one or more previous mammograms, none within two years of diagnosis. Thus 345 breast cancer deaths (74.8%)

occurred in women not regularly screened. The 1995 BRFSS determined that 79.3% of Massachusetts women over 40 had mammography within the previous two years. Therefore, 75% of breast cancer deaths occurred in the 20% of women not regularly screened, while 25% of deaths occurred in the 80% regularly screened. If the 13 year mortality rate is 15% in the 192,740 women diagnosed with breast cancer in 2009, regularly screened women will have a 13 year breast cancer mortality rate of 5%, while unscreened women will have 56% mortality rate, similar to years prior to introduction of mammography.
Conclusion: The most effective method of avoiding death from breast cancer is for women to participate in regular screening mammography.
Disclosures: Nothing to disclose

Oral Abstract Presentation B
Friday, October, 9, 2009
3:00-3:15 PM PST

Lead Author: Iwa Kong, MD, FRCPC
Sunnybrook Health Sciences Centre
Toronto, ON

Younger Women with DCIS Have a Higher Rate of Breast Cancer Recurrence

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

A large population-based study of younger women with ductal carcinoma in situ (DCIS) – a pre-invasive form of early-stage breast cancer – has found that women age 44 and younger have almost double the risk of recurrence following breast conservation surgery and radiation therapy than women age 45 to 50, whose rates were similar to known rates of women over 50.

"We don't yet know why younger women with DCIS have a higher rate of recurrence compared with older women," said lead author Iwa Kong, MD, a breast oncology research fellow in the Department of Radiation Oncology at the Sunnybrook Health Sciences Centre and University of Toronto. "Further research is necessary to determine the causes of this difference and to determine the best treatment for younger women with DCIS. It is important to add that these findings do not imply that all young women with DCIS need to undergo more aggressive surgery, such as a mastectomy, to reduce recurrence risk." The researcher added that the roles of tamoxifen or higher doses of radiation also need to be evaluated.

The incidence of DCIS has risen with the widespread use of mammography. While treatment with surgery and radiation has resulted in substantial reductions in recurrence, there has been concern that younger women may be at greater risk of recurrence.

In this retrospective study, investigators examined the rate of breast cancer recurrence among women age 50 and younger diagnosed with DCIS in Ontario, Canada, between 1994 and 2003 who had standard breast conservation surgery (lumpectomy) and radiation therapy. After a median follow-up time of 8.5 years, the rate of recurrence among women age 44 and younger was significantly higher than those age 45 to 50 (20 percent for those age 40 and younger, 19 percent for those age 40 to 44, and 12 percent for those age 45 to 50). By comparison, the rate of recurrence among women over age 50 is typically 10 to 15 percent ten years after diagnosis.

Outcomes of young women with DCIS treated with breast-conserving surgery and radiotherapy: A Population- based analysis

I. Kong, E. Rakovitch, C. Taylor, S. Nofech-Moses, W. Hannah, L. Paszat

Background: Ductal carcinoma *in situ* (DCIS) is a non-invasive form of breast cancer predominantly diagnosed by mammographic screening of postmenopausal women. Most women will be managed by breast-conserving surgery (BCS) followed by radiation (XRT), proven in randomized trials to lead to low local recurrence rates. However, past studies include relatively few women ≤ 50 years of age and there is increasing concern that younger women have a significantly greater risk of recurrence, although the high risk age group remains uncertain. The objective of this study is to evaluate the outcomes of a population-based cohort of young (≤ 50 years) women diagnosed with DCIS treated with BCS+XRT.

Methods: We identified all women diagnosed with DCIS in Ontario from 1994-2003, aged ≤ 50 years at diagnosis. We performed linkage of administrative databases to identify treatment (type of breast surgery, radiation) and outcomes with validation of data through primary chart abstraction. Survival analyses were used to evaluate the outcomes of women treated with BCS + XRT. The median follow-up period was 8.5 years.

Results: From 1994-2003, 8203 women were diagnosed with DCIS in Ontario, 1015 women were ≤ 50 years at diagnosis and 583 received BCS+XRT (≤ 40 years, N=60; 40- 44 years, N=184; 45-50 years, N=339). Most women received 50 Gy in 25 fractions and 121 (21%) women received a boost. 99 (17%) women developed a local recurrence corresponding to 5- and 10- year actuarial local-recurrence free survival rates (LRFS) of 88% and 81% respectively. 38 (6.5%) women developed invasive local recurrence, for 5- and 10-year actuarial invasive LRFS rates of 95% and 93% respectively. Women aged ≤ 44 years had significantly higher recurrence rates compared to women aged 45-50 years (23% for ≤ 40 yrs; 21% for 40-44 yrs; 14% 45-50 yrs) (unadjusted HR = 1.68 (1.13, 2.49) p = 0.01; 10-year actuarial LFRS 75% v 85% (p=0.005)

Conclusions: Younger women have a higher rate of local recurrence following BCS + XRT for DCIS. Multivariable analyses of factors associated with recurrence will be presented.

Disclosures: Nothing to disclose

General Session VI
Friday, October 9, 2009
10:30 AM-12:00 PM PST

Lead Author: Bedanta P. Baruah
Cardiff University
Cardiff, UK

Axillary Ultrasound Can Prevent Second Surgeries for Some Women with Early-Stage Breast Cancer

Researchers in the United Kingdom have shown that the addition of axillary ultrasound prior to initial breast-conserving surgery spared nearly one-third of women with early-stage breast cancer who had underarm (axillary) lymph node metastases from a second breast cancer surgery to remove additional axillary nodes. The study found that AUS can be useful for detecting large deposits of cancer cells ("macrometastases") in axillary lymph nodes, which can be removed at the same time as initial breast cancer surgery.

"Axillary ultrasound combined with needle biopsy for suspicious nodes is a low-cost, accurate and minimally invasive procedure that should be performed routinely before surgery in women with breast cancer, even those with early-stage disease," said lead author Bedanta Baruah, MD, surgical research fellow in breast cancer at the Cardiff University School of Medicine. "Routine use of this approach will give oncologists and surgeons an earlier picture of cancer spread to underarm lymph nodes, and help some women avoid the trauma, costs and anxiety associated with a second surgery."

Traditionally, following the identification of a suspicious lump, women undergo a biopsy procedure such as fine-needle aspiration cytology (FNAC) or core needle biopsy to determine if the mass is malignant. Once cancer is confirmed, women are scheduled for breast-conservation surgery to remove the tumor, biopsy the "sentinel" axillary lymph node (the node to which cancer is most likely to spread), and remove other nodes for examination if the sentinel node is found to contain cancer cells. However, if post-surgical pathological examination of the sentinel node identifies cancer cells that were not found during initial surgery, a patient may have to return for a second surgery to remove additional lymph nodes.

Researchers in this study examined an alternative approach: adding AUS at the same time as breast FNAC or core needle biopsy to identify potential macrometastases in axillary lymph nodes before surgery. In 274 women with early-stage breast cancer who were scheduled for surgery, AUS and FNAC analysis of suspicious nodes detected lymph node macrometastases in 29.8 percent (17) of 57 women with nodal metastases on final pathology. These 17 women proceeded to breast cancer surgery, where the axillary lymph nodes were removed at the same time as lumpectomy, and they were spared from a second surgical procedure.

The researchers noted that preoperative AUS was not able to detect smaller "micrometastases," and was unable to detect macrometastases in many cases, suggesting that sentinel node biopsy is still indicated in patients in whom the results of preoperative AUS are normal.

Should axillary ultrasound and fine-needle aspiration cytology be performed routinely in early breast cancer patients eligible for breast conservation?

B. P. Baruah, A. Goyal, P. Young, A. G. Douglas-Jones, R. E. Mansel, on behalf of Cardiff Breast Unit

Background: The exact role of axillary ultrasound and fine-needle aspiration cytology for nodal staging in unclear. In this study, we evaluated the usefulness of axillary ultrasound (AUS) and fine-needle aspiration cytology (FNAC) in early stage breast cancer patients scheduled to undergo breast conservation surgery. In addition, we assessed whether a learning curve is seen with the use of this technique, an aspect that has not been addressed before.

Methods: Between January 2007 and December 2008, all patients scheduled to undergo breast conservation surgery in our unit underwent an AUS. Patients with suspicious nodes on AUS underwent FNAC. Cytology positive patients proceeded to axillary clearance, whilst others underwent sentinel lymph node biopsy. The primary endpoints were sensitivity, specificity, positive predictive value and negative predictive value of AUS and FNAC.

Results: 274 patients undergoing breast conservation surgery were eligible for this study. 57 patients (20.8%) had proven nodal macro-metastases on final histology. 17 of 57 (29.8%) node positive patients were accurately identified by pre-operative AUS and FNAC and, therefore, spared an unnecessary sentinel node biopsy. AUS and FNAC had a sensitivity of 29.8% (95% CI: 19.5-42.7),

specificity of 100% (95% CI: 98.3-100), positive predictive value of 100% (95% CI: 81.6 -100), negative predictive value of 84.4% (95% CI: 79.5-88.4) and an overall accuracy of 84.4% (95% CI 80.7-89.1). Pre-operative ultrasound was normal in all patients with nodal micro-metastases (n=7). No significant learning curve was seen with the use of this technique. Overall, 29.8% (17/57) of patients with sentinel node macro-metastases were spared an unnecessary sentinel node biopsy by the use of AUS and FNAC.
Conclusions: Pre-operative axillary ultrasound is a minimally-invasive outpatient procedure that can avoid unnecessary sentinel lymph node biopsy in 29.8% of node positive patients. It is highly specific with an overall accuracy of more than 80% in detection of nodal macro-metastases but is unable to detect micro-metastases. Our results suggest that AUS and FNAC should be performed routinely in early stage breast cancer patients eligible for breast conservation.
Disclosures: Nothing to disclose

Oral Abstract Presentation A
Thursday, October 8, 2009
1:45-2:00 PM PST

Lead Author: Torsten O. Nielsen, MD, PhD
University of British Columbia
Vancouver, BC

Tissue Microarrays Identify Biological Subtype of Breast Cancer and Predict Value of Adjuvant Chemotherapy

Researchers have validated a new method of tissue analysis, called tissue microarrays, to determine the "intrinsic subtype" of a breast tumor and to predict whether a patient with breast cancer that has spread to the lymph nodes will benefit from adjuvant paclitaxel (Taxol) chemotherapy. Use of breast cancer subtyping to predict response to a specific anticancer drug will improve physicians' ability to personalize treatment to maximize benefits and spare patients from unnecessary side effects.

"Breast cancer is an incredibly complicated, challenging disease, and the more we learn about how to customize treatment based on individual tumor biology, the more we will be able to improve outcomes for patients," said lead author Torsten Nielsen, MD, PhD, associate professor of Pathology & Laboratory Medicine at the University of British Columbia in Vancouver. "In this study we validated a new and highly efficient tissue assessment technique – tissue microarrays – that determines the molecular features of a tumor, or its intrinsic subtype, and predicts whether a patient will benefit from paclitaxel chemotherapy."

Tissue microarrays are antibody assays that can be used to detect molecular markers in tissue samples as small as 0.6 mm across and 0.004 mm thick. In this study, researchers used the antibody assays to identify the breast cancer intrinsic subtypes – such as the HER2-positive and basal subtypes – which are associated with response to paclitaxel.

Researchers in this study used tissue microarrays to perform intrinsic subtyping on breast cancer tissue obtained from 2,039 women who participated in the Cancer and Leukemia Group B study 9344. In the 1990s, this study showed that adding adjuvant paclitaxel to therapy with doxorubicin and cyclophosphamide improved survival by 5 percentage points, though not all patients experienced this benefit. Researchers in the current study compared the tissue microarray findings with data on the patients' clinical outcome. They showed that women with the intrinsic subtype Luminal A did not benefit from adding paclitaxel to their treatment. However, women with aggressive intrinsic subtypes, such as HER2-positive breast cancer or basal breast cancer, did derive significant benefit from adjuvant paclitaxel.

If confirmed by future clinical research, the biological subtyping methods developed using tissue microarrays will add to the information gained by existing biological tests (such as those for hormone receptors and HER2) to determine the optimal treatment for women diagnosed with breast cancer. The technique could also play a significant role in analyzing tissue samples from other large clinical trials.

Intrinsic subtype and response to paclitaxel in CALGB 9344 tissue microarrays
T. O. Nielsen, S. D. Jewell, A. D. Thor, D. Gao, C. M. Perou, G. Broadwater, L. N. Harris, D. F. Hayes, D. A. Berry, M. J. Ellis, Cancer and Leukemia Group B
Background: CALGB 9344 enrolled 3121 women with node positive early breast cancer, and demonstrated that adding paclitaxel to adjuvant doxorubicin-cyclophosphamide in patients receiving standard local and hormonal therapies was associated with a 5% absolute improvement in disease-free survival. Among the 42% of subjects with complete ER and HER2 information, no benefit was found in the ER+/HER2- subset. More complete and detailed subclassification into intrinsic biological subtypes is now possible using a tissue microarray approach and an immunohistochemical panel.
Methods: Using an intergroup-approved protocol, tissue microarrays were constructed from 2039 of the 3121 trial subjects, whose outcomes were representative of the trial as a whole. Immunohistochemistry for ER, HER2, Ki67, cytokeratin 5/6 and epidermal growth factor receptor was performed and interpreted by prespecified published methods, allowing categorization of each case into intrinsic subtypes. Cox proportional hazards modeling was used to determine significant prognosis of intrinsic subtype or paclitaxel treatment on relapse free survival. Correlation with outcome was performed independently by the CALGB Statistical Center.

Results: Cases were assigned as follows: 790 Luminal A, 340 Luminal B, 221 HER2-enriched, 444 core basal, and 93 ER-/HER2-/nonbasal. Tissue microarray results showed substantial agreement with previous whole section HER2 and clinical ER data. Intrinsic subtype was prognostically significant in multivariate analysis ($p<0.001$). There was no significant interaction of Ki67 with paclitaxel among ER+/HER2- patients. Core basal status predicted benefit from paclitaxel in multivariate analysis (HR 0.75, $p = 0.033$); benefit in ER-/HER2-/nonbasal cases was not significant.
Conclusions: Tissue microarrays allow biomarker assessment on large clinical trials. Intrinsic biological subtype by immunohistochemistry is independently prognostic, and predicts benefit in HER2 positive and core basal subtypes when adding paclitaxel to adjuvant AC chemotherapy. Intrinsic subtyping may permit tailoring adjuvant paclitaxel therapy in early breast cancer. Future work will assess qPCR-based biological subtyping.
Disclosures: Torsten Nielsen, Research Funding, sanofi-aventis; Charles Perou, Stock Ownership, University Genomics; Matthew Ellis, Consultant or Advisory Role, Monogram Biosciences; Matthew Ellis, Stock Ownership, University Genomics

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