



Embargoed for Release:
5:30 p.m. CT, Dec. 6, 2011

Media Contact:
Jeremy Moore
(215) 446-7109
Jeremy.Moore@aacr.org
In San Antonio:
(210) 582-7021

New Test Predicts Risk for Recurrence for Patients With DCIS

- Multigene assay predicts risk for local recurrence for patients with DCIS.
- This advance combines knowledge of the genome and new molecular technologies.
- Test allows physicians to individualize treatment so that lower-risk patients avoid radiation.

SAN ANTONIO — In a significant advance for patients with ductal carcinoma *in situ*, researchers have developed and prospectively validated a multigene test to identify the risk for recurrence of breast cancer.

The method combines measuring tumor gene expression with a gene expression algorithm to decipher the genetic underpinnings of a patient's cancer and determine whether the individual patient should be treated with surgery (usually lumpectomy) or a combination of surgery and radiation.

This is the first time a multigene test has been used to differentiate lower-risk and more aggressive forms of ductal carcinoma *in situ* (DCIS) and will allow physicians to spare many patients the need to undergo radiation, according to researchers.

Lawrence J. Solin, M.D., FACR, FASTRO, chair of the department of radiation oncology at Einstein Medical Center in Philadelphia, presented the results at the 2011 CTRC-AACR San Antonio Breast Cancer Symposium (SABCS), held Dec. 6-10, 2011.

“Using a molecular-based assay, we have successfully identified patients at higher risk for recurrence and patients at lower risk,” said Solin. “This is an important advance for women with newly diagnosed DCIS. By predicting individual risk, physicians can provide a more tailored treatment program for each patient.”

The validation study of the DCIS Score was a collaboration among the Eastern Cooperative Oncology Group (ECOG), North Central Cancer Treatment Group and Genomic Health. The validation utilized patient tumor samples from E5194, an ECOG-led, multi-institutional study of patients with low-, intermediate- or high-grade DCIS who had been treated surgically but had not received radiation. E5194 was the first prospective study of local excision alone for DCIS, and its five-year results were reported at SABCS in 2006 (L. Hughes).

Researchers tested and scored tumors from 327 patients to determine their risk for recurrence. The DCIS validation study team used the Oncotype DX breast cancer assay, which has been available for invasive breast cancer since 2004, and a DCIS Score algorithm to study these tumor samples.

The test uses reverse transcriptase-polymerase chain reaction technology, which quantitates the level of RNA in the individual tumor sample to reveal its underlying biology. The level of RNA is then used by a prespecified algorithm to calculate a DCIS Score, which predicts the likelihood of local recurrence, defined as either the development of a new invasive breast cancer or the recurrence of DCIS.

Solin also reported 10-year results of E5194, in which 46 patients had an ipsilateral breast event (IBE; defined as ipsilateral local recurrence of DCIS or invasive cancer) at a median follow-up of 8.8 years. Continuous DCIS Score was significantly associated with IBE when adjusted for tamoxifen use and provided value beyond the traditional measures of tumor size, tumor grade and margin status.

Numerous studies, including the current study, have shown that routine, microscopic pathology grading is not a reliable indicator of the risk for recurrence.

“The DCIS Score will help physicians understand the underlying biology of DCIS for an individual patient and accurately gauge the risk for that person,” said Solin. “As a result, the patient and physician can decide on the appropriate course of treatment based on a more complete understanding of the risk involved.”

###

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 patients with breast cancer. 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 CTRC 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 34th annual symposium is expected to draw nearly 8,000 participants from more than 90 countries.

Presenter: Lawrence J. Solin, MD, FACR, FASTRO

Abstract Number: S4-6

Title: A Quantitative Multigene RT-PCR Assay for Predicting Recurrence Risk after Surgical Excision Alone without Irradiation for Ductal Carcinoma In Situ (DCIS): A Prospective Validation Study of the DCIS Score from ECOG E5194.

Author Block: Lawrence J Solin¹, Robert Gray², Frederick L Baehner³, Steven Butler³, Sunil Badve⁴, Carl Yoshizawa³, Steven Shak³, Lorie Hughes⁵, George Sledge⁶, Nancy Davidson⁷, Edith A Perez⁸, James Ingle⁹, Joseph A Sparano¹⁰ and William Wood¹¹. ¹Radiation Oncology, Albert Einstein Medical Center, Philadelphia, PA; ²Eastern Cooperative Oncology Group, Boston, MA; ³Genomic Health, Inc., Redwood City, CA; ⁴Pathology, Indiana University, Indianapolis, IN; ⁵North Georgia Radiation Therapy, The Hope Center, Cartersville, GA; ⁶Medical Oncology, Indiana University, Indianapolis, IN; ⁷Medical Oncology, University of Pittsburgh, Pittsburgh, PA; ⁸Medical Oncology, Mayo Clinic Jacksonville, Jacksonville, FL; ⁹Medical Oncology, Mayo Clinic Rochester, Rochester, MN; ¹⁰Medical Oncology, Albert Einstein College of Medicine, Bronx, NY and ¹¹Surgery, Emory University, Atlanta, GA.

Background: We have previously reported the results of surgical excision without irradiation for selected patients with DCIS in ECOG E5194, where the 5-year rates of local recurrence varied with age, grade, and lesion size (Hughes et al. J Clin Oncol 27:5319, 2009). New methods are needed to provide more accurate and reproducible assessment of recurrence risk.

Methods: ECOG E5194 included 670 eligible patients with DCIS treated with surgical excision (≥ 3 mm negative margins) without irradiation, 228 of whom received tamoxifen. Patients had low or intermediate grade DCIS ≤ 2.5 cm, or high grade DCIS ≤ 1 cm. The Oncotype DXR assay was performed by quantitative RT-PCR using formalin fixed paraffin embedded tumor specimens from 327 patients (49% of the parent study). Recurrence ScoreR (RS) was calculated using the published algorithm. A new, prespecified DCIS ScoreTM was designed to predict recurrence using an optimized gene expression algorithm. The primary objective was to determine whether there was a significant association between the risk of an ipsilateral breast event (IBE) and the continuous DCIS Score in Cox models. 46 patients had an IBE (defined as ipsilateral local recurrence of DCIS [n=20] or invasive cancer [n=26]). Median follow-up was 8.8 years.

Results: The 10-year IBE rates were 15.4% for low/intermediate grade DCIS and 15.1% for high-grade DCIS (as determined by central pathology review), and for invasive IBE, 5.6% and 9.8%, respectively. Comparison between local and expert grading showed substantial disagreement. Continuous DCIS Score was significantly associated with IBE (HR 2.34 per 50 units; 95% CI 1.15, 4.59; p=0.02) when adjusted for tamoxifen use (prespecified primary analysis) and with invasive IBE (HR 3.73; CI 1.34, 9.82; p=0.01). DCIS Score was significantly associated with outcome when evaluated by the prespecified risk groups (see Table). Similar results were observed with and without adjustment for tamoxifen use or for negative margin width. Features associated with IBE in multivariate models included menopausal status (HR 0.49; 95% CI 0.27, 0.90; p=0.02), tumor size (HR 1.52 per 5 mm; 95% CI 1.11, 2.01; p=0.01), and continuous DCIS Score (HR 2.41; 95% CI 1.15, 4.89; p=0.02). The standard RS, which is calculated using thresholding of many genes unlike the DCIS Score, was not associated with IBE

or invasive IBE ($p > 0.6$).

Conclusions: We have prospectively validated a multigene assay that quantifies recurrence risk and complements traditional clinical and pathologic factors in selected patients with DCIS treated with surgical excision without irradiation. The DCIS Score provides a new clinical tool for individualized selection of treatment for patients with DCIS.

10-Year Kaplan-Meier Rate (95% CI)			
DCIS Score Risk Group	No. (%)	Ipsilateral Breast Event (Invasive or DCIS)	Invasive Ipsilateral Breast Event
Low (<39)	246 (75%)	12.0% (8.1%, 17.6%)	5.1% (2.8%, 9.5%)
Intermediate (39-54)	45 (14%)	24.5% (13.8%, 41.1%)	8.9% (2.9%, 25.8%)
High (≥ 55)	36 (11%)	27.3% (15.2%, 45.9%)	19.1% (9.0%, 37.7%)
Log rank p-value		.02	.01