Family History Tied to Triple-Negative Breast Ca

BY PATRICE WENDLING

Having a family history of breast cancer was associated with a significant 2.2-fold increased risk of triple-negative breast cancer in Hispanic women, but not in black women, according to preliminary data from a study of 466 patients.

Moreover, Hispanic women were six times more likely to develop this aggressive form of cancer before age 50 years (odds ratio 6.1) when compared with black women (OR 1.5), Betsy C. Wertheim reported at the American Association for Cancer Research conference on the science of health disparities. The mean age at breast cancer diagnosis was 49 years for Hispanics and 52 years for blacks.

Subset analyses suggest that the increased risk for triple-negative breast cancer is confined to Hispanics who were born in Mexico and not in the United States.

Because the breast cancer tumors of affected women are negative for three important targets of available treatment regimens—estrogen receptors (ER), progesterone receptors (PR), and/or human epidermal growth factor receptor 2 (HER2)—their response to some treatments may be poor.

The association between family history of breast cancer and triple-negative breast cancer was increased nearly fivefold (OR 4.9) among Hispanic women living in Arizona, of whom 17% were American born. In contrast, there was no significant association among Hispanics living in Texas (OR 1.4), of whom 58% were American born.

"We aren't sure whether this association is due to environmental exposure or if it has to do with the ancestry of these women from Arizona versus Texas," Ms. Wertheim, an assistant scientific investigator at the Arizona Cancer Center, University of Arizona, Tucson, told reporters at a press briefing.

The findings were based on 260 Hispanic women participating in the ongoing ELLA Binational Breast Cancer study and 206 black women studied with the same protocol at University of Texas M.D. Anderson Cancer Center, Houston. They ranged in age from 22 to 80 years. Family history was defined as self-reported history of breast or ovarian cancer in a relative before age 50 years.

Tumor marker data taken from medical records were used to determine if tumors were negative for ER, PR, and HER2/neu.

One genetic factor that may help explain the strong association ... is a higher burden of BRCA1 mutation carriers in the Mexican American cases.

One genetic factor that may help explain the strong association between family history and triple-negative breast cancers is a higher burden of BRCA1 mutation carriers in the Mexican American cases, principal investigator Maria Elena Martinez, Ph.D., said in an interview.

This observation is supported by a recent study, led by Dr. Jeffrey N. Weitzel, that identified and characterized a novel large BRCA1 deletion in five unrelated high-risk families—four of Mexican ancestry (Cancer Epidemiol. Biomarkers Prev. 2007;16:1615-20). The families had a personal or family history of breast or ovarian cancer, but not necessarily triple-negative breast cancer.

Still, the findings suggest that the presence of these BRCA mutations may account for a higher proportion of breast cancer cases in young Mexican American women, similar to that of women of Ashkenazi ancestry, when compared with women who are black or non-Hispanic white.

"We're putting the pieces together," Dr. Martinez said. "We believe there is possibly a BRCA1 mutation in these women based on his findings and extending those to our findings. Young onset, triple negative, and family history: It's crying out, as Dr. Weitzel would say, that there is a BRCA mutation in these women."

The next logical step is to assess the rate of BRCA1 mutations in the current cohort and to confirm the findings of Dr. Weitzel, chief of the division of clinical cancer genetics at the City of Hope in Duarte, Calif.

Prior to the current study, very little was known about the rate of triple-negative breast cancer in Hispanic women, said Dr. Martinez, an epidemiology professor also with the university's Arizona Cancer Center.

If future research confirms a higher rate of BRCA1 mutations among Mexican American women, genetic counseling and advice regarding prophylactic mastectomy or oophorectomy is advisable. This must be done, however, in a culturally and language-sensitive environment, Dr. Martinez stressed.

The investigators reported no conflicts of interest. The ELLA study is supported by funding from the Avon Foundation and the National Cancer Institute. ■

OncoVue Genetic Test Beats Gail Model In Identifying High Breast Cancer Risk

BY BRUCE JANCIN

SAN ANTONIO — The investigational OncoVue breast cancer risk test provided a 2.4-fold improvement over the Gail model in accurately identifying women at elevated risk of breast cancer in a blinded validation study.

This is the third independent study demonstrating that the OncoVue individualized breast cancer risk estimator provides more accurate estimates than does the widely used Gail model, Dr. Kathie M. Dalessandri said at the San Antonio Breast Cancer Symposium.

OncoVue integrates genetic testing for 22 single nucleotide polymorphism variants located on 19 genes with classic Gail model personal risk factors, such as age at first menses and first live birth and the number of first-degree relatives having breast cancer. The genetic test uses DNA from a saliva sample, explained Dr. Dalessandri of the University of California, San Francisco, and the Buck Institute for Age Research in Novato, Calif.

She reported on 169 women diagnosed with breast cancer during 1997-1999, when they were a mean of 54 years old, and 177 age-matched controls. All were enrolled in the Marin County Study of Breast Cancer Adolescent Risk Factors, which was undertaken in order to determine the source of the unusually high incidence of breast cancer in county residents dating back to the early 1990s.

OncoVue proved to be 2.4-fold more accurate than the Gail model at identifying women with a 12% or greater risk of developing breast cancer between ages 30 and 69, which is 1.5 times the national average risk. The Gail model identified as high risk 37 of the 177 women who went on to develop breast cancer. OncoVue identified 56 of the women, representing a 51% improvement.

'Women are clamoring for genetic tests like this one.'

DR. DALESSANDRI

The Food and Drug Administration is developing standards for gene test–based products that are aimed at assessing breast cancer risk in the general population. It has yet to approve any such tests aside from those for BRCA1 and BRCA2, which account for only a small percentage of breast cancers. The OncoVue test, developed by InterGenetics Inc. of Oklahoma City, is available at roughly three dozen breast care centers around the country under existing FDA rules governing laboratory testing.

"Women are clamoring for genetic tests like this one," Dr. Dalessandri said.

She sees OncoVue as playing two major roles in the future: in the clinic (to help women obtain a more accurate individualized risk assessment than conventional risk factors can provide), and in large-scale breast cancer prevention trials. "You want to accurately assess risk before putting patients in a trial," she noted.

Most of the 22 single nucleotide polymorphism variants assessed in OncoVue relate to steroid hormone metabolism, DNA repair, apoptosis, growth factors, and detoxification, according to Dr. Dalessandri.

The study was supported by the California Breast Cancer Research Program and InterGenetics. Dr. Dalessandri reported having no financial conflicts of interest. ■

MammaPrint Gauges Risk in HER2-Positive Breast Cancer Patients

SAN ANTONIO — The 70-gene MammaPrint prognosis signature independently identifies a genomic low-risk subgroup of HER2-positive early breast cancer patients likely to have a good long-term clinical outcome, even without adjuvant trastuzumab and chemotherapy.

Dr. Michael Knauer of the Netherlands Cancer Institute, Amsterdam, presented a validation study of 169 women with HER2-positive unilateral breast cancer drawn from six partially published studies. All of the women had T1-3 N0-1 disease; 46% received chemotherapy and 15% got trastuzumab.

MammaPrint classified 16% of the tumors as having a "good prognosis" signature, Dr. Knauer said at the San Antonio Breast Cancer Symposium. Those 27 patients had a 10-year distant disease-free survival rate of 89%, compared with 64% in the 142 patients classified by MammaPrint as having a high genomic risk.

In a multivariate analysis adjusted for conventional prognostic factors along with adjuvant therapies, the MammaPrint signature and tumor size were the only independent predictors of 10-year distant disease-free survival. MammaPrint was the stronger predictor of the two; a "poor prognosis" MammaPrint result was associated with a 5.4-fold increased risk of distant recurrence within 10 years vs. a favorable MammaPrint signature. Among 90 patients who did not receive adjuvant trastuzumab or chemotherapy, a poor prognosis MammaPrint result conferred a 4.75-fold greater risk of distant relapse within 10 years.

Agendia Inc., which markets MammaPrint, supported the study. Dr. Knauer said he has no financial conflicts of interest regarding the study.

—Bruce Jancin