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Risk for Developing New Cancer in Other Breast Increased for Survivors With *BRCA* Mutation

- Survivors with a *BRCA1* or *BRCA2* mutation had a more than 10 percent greater risk for developing cancer in their other breast.
- Age at diagnosis and triple-negative or estrogen receptor status of first cancer further affected risk.
- Guidelines should be amended to consider these factors when counseling women with the mutation.

SAN ANTONIO — Breast cancer survivors who carry the *BRCA1* or *BRCA2* genetic mutation are at high risk for developing contralateral breast cancer — a new primary tumor in the other breast — and certain women within this group of carriers are at an even greater risk based on age at diagnosis and first tumor status, according to data presented at the 2011 CTRC-AACR San Antonio Breast Cancer Symposium, held Dec. 6-10, 2011.

“Our studies show that certain subgroups of women [with this mutation] who have already had cancers are also at risk for developing a second new cancer in their other breast, much more so than survivors who do not carry the mutation,” said Alexandra J. van den Broek, M.Sc., a doctoral candidate at the Netherlands Cancer Institute. “Our study is, as far as we know, the first study showing that within certain carriers of *BRCA* mutations, subgroups with an increased or decreased risk for contralateral breast cancer (CBC) can be made.”

Researchers surveyed 5,061 women diagnosed with unilateral, invasive breast cancer at 10 hospitals in the Netherlands. Two hundred eleven women (4.2 percent) were carriers of the *BRCA1* or *BRCA2* mutation. Overall, at a median of 8.4 years of follow-up, 8.6 percent of participants developed CBC.

Van den Broek and colleagues found that the overall 10-year risk for developing CBC in noncarriers was 6.0 percent, while risk for carriers was 17.9 percent.

For carriers diagnosed with their first breast cancer when aged younger than 40 years, the 10-year risk for CBC jumped to 26.0 percent. For carriers between the ages of 40 and 50 years at first diagnosis, the risk was 11.6 percent. In addition, mutation carriers with a triple-negative first tumor had a 10-year cumulative CBC risk of 18.9 percent compared with 11.2 percent among carriers with a non-triple-negative first tumor.

Although these numbers can be overwhelming to carriers who have already survived breast cancer, van den Broek said it is crucial to know who is most at risk and by how much.

“Guidelines for prophylactic measures and screening in the follow-up of patients with breast cancer carrying the *BRCA1* or *BRCA2* mutation are important to provide patients with the best information and counseling,” she said. “If these results are confirmed, [it will be] possible to personalize the guidelines for these specific subgroups.”

The next step will be to confirm the results in larger studies and to look at other factors that define subgroups of patients with an increased or decreased risk for CBC.

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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: Alexandra J. van den Broek, M.Sc.

Abstract Number: S4-2

Title: The Risk of Contralateral Breast Cancer in BRCA1/2 Carriers Compared to Non-BRCA1/2 Carriers in an Unselected Cohort.

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Background: Women who survived their first breast cancer have a higher risk to develop a new primary tumor in the contralateral breast than the risk of women in the general population to develop a first breast cancer. Especially women who carry a germline mutation in either the *BRCA1* or the *BRCA2* gene face a high lifetime risk of developing a synchronous or metachronous bilateral breast cancer. It is important to provide precise risk estimates of contralateral breast cancer and identify factors which predict the risk of CBC in this group of high risk women. To answer these questions, we looked at the effect of BRCA1/2-carriership and its interaction with other factors on the risk to develop a CBC in an unselected cohort of breast cancer patients.

Materials and Methods: We collected clinico-pathological, treatment and follow-up data for 4856 patients with unilateral, invasive breast cancer, diagnosed under the age of 50, between 1970 and 2003, in ten different hospitals throughout The Netherlands. Germline DNA was isolated from formalin-fixed paraffin-embedded tissue and patients were tested for the most prevalent pathogenic BRCA1 and BRCA2 mutations in The Netherlands. DNA and clinical data were coded before the analyses. All second primary breast tumors in the contralateral breast diagnosed more than 3 months after the diagnosis of the first breast cancer were considered as events. Preliminary results from life-table analysis and Cox Proportional Hazard models adjusted for age at diagnosis are shown here. Further statistical analyses will include competing risk analysis.

Results: In 4856 patients genotyped for BRCA1/2 mutations, 206 (4.2%) carriers were identified. During a median follow-up of 9.8 years (range 0-38), 9% of the patients developed a CBC, resulting in a cumulative 15-year risk for CBC of 10.4% (95% CI = 9.25-11.7) for non-carriers and 35.4% (95% CI = 25.9-46.9) for carriers of a BRCA1 or BRCA2 mutation (HR = 4.04 (95% CI = 2.88-5.68)). Patients carrying a BRCA1/2 mutation who were diagnosed under the age of 40 with their first breast cancer experienced a cumulative 15-year risk for CBC of 52.4 % (95% CI = 36.4-70.3) versus 21.3 % (95% CI = 12.0-36.0) in those over the age of 40 (HR = 0.30 (95% CI = 0.14-0.65)). Furthermore, BRCA1/2 mutation carriers with a triple negative first tumor had a cumulative risk for CBC of 43.6 (95% CI = 25.1-67.7), in contrast, BRCA1/2 mutation carriers with a non-triple negative first tumor had a cumulative risk for CBC of 13.4 % (95% CI = 4.21-38.4) (HR = 0.24 (95% CI = 0.07-0.86)). Age at diagnosis and triple negative status were not found to be predictors of the risk of CBC in non-carriers (HR = 0.81 (95% CI = 0.53-1.24) and HR = 1.49 (95% CI = 0.91-2.41) respectively).

Discussion: In this study we identified subgroups of patients with a high risk to develop a CBC after their first breast cancer. Guidelines about treatment decisions and screening for follow-up should take into account these high risk subgroups to provide even better information and counseling for BRCA1/2 mutation carriers.

On behalf of more than 20 involved authors of the BOSOM study from 10 different hospitals and institutions throughout The Netherlands.