

CGC UPDATE

Newsletter for the Cancer Genetic Counseling Program at Yale

FALL 2007

PATIENT NEWSLETTER

Yale Cancer Genetic Counseling Program • 55 Church Street, Suite 402 • New Haven, CT 06510 • (203) 764-8400 • fax (203) 764-8401 • www.yalecancercenter.org/genetics

Fall 2007

We hope that you enjoyed a safe and healthy summer. This newsletter edition will conclude our series focused on hormones and hormonal therapy use by BRCA mutation carriers. Also in this issue are exciting updates regarding our Hope Chest Endowment Fund and important information regarding local and national actions directed in response to a direct-to-consumer marketing campaign for genetic testing. As always, we are looking for comments and suggestions for future newsletters and are interested in hearing from you.

Sincerely,

Karina L. Brierley, MS

Rachel E. Barnett, MS

Danielle Campfield, MS

Ellen T. Matloff, MS

In this issue

- ▶ Tamoxifen Use 1, 3
- ▶ Genetic Testing Risk 2
- ▶ Resources 3
- ▶ Research Updates 4-5
- ▶ Hope Chest Event 5
- ▶ CGC Clinics 5

Yale CANCER CENTER

A Comprehensive Cancer Center Designated
by the National Cancer Institute

Hormone Use in *BRCA1* and *BRCA2* Mutation Carriers - Part 2

This section is a continuation of our last newsletter's review of exogenous (produced outside of the body) hormone use and hormonal therapy in *BRCA1* and *BRCA2* mutation carriers. (Please see the "fact sheets" section of our website at www.yalecancercenter.org/genetics.) This summary will focus on the use of Tamoxifen to reduce breast cancer risks.

Tamoxifen and BRCA Mutation Carriers

Some types of breast cancer grow more rapidly in the presence of estrogen. These cancers are called "estrogen receptor positive (ER+) tumors". The majority of *BRCA2*-related breast cancers are ER+, while the majority of *BRCA1*-related breast cancers are estrogen receptor negative (ER-). Chemopreventative medications, such as Tamoxifen, reduce the development of ER+ breast cancers. However, Tamoxifen is associated with a small, but increased risk of uterine cancer (<1%) (not ovarian cancer) amongst other side effects.

It is well-known that Tamoxifen can reduce the risk of breast cancer in women at increased risk for the disease due to age, family history, or high-risk findings on breast biopsy. Several studies have examined whether Tamoxifen also decreases the risk for breast cancer in BRCA mutation carriers, although this area needs to be thoroughly examined via other study designs (e.g. a controlled study).

In one study of 491 BRCA mutation carriers who were diagnosed with stage I or stage II breast cancer, Tamoxifen reduced the risk of future breast cancers within the same breast of the original diagnosis (ipsilateral) and also cancers in the other breast (contralateral).¹

Another study compared 209 female BRCA mutation carriers with bilateral breast cancer to 384 female BRCA mutation carriers with unilateral breast cancer. This study demonstrated that the risk of a contralateral breast cancer was 50% lower in *BRCA1* mutation carriers who used Tamoxifen as treatment for their initial breast cancer.¹

(continued on page 3)

The Lesser-Known Risk of Genetic Testing

The greatest fear cited by patients considering genetic testing is whether their health insurance company will discriminate against them based on their test results. We now have laws, both state and federal, that help protect patients against genetic discrimination. Luckily, we have not seen the discrimination we feared when this technology began.

Surprisingly, we have found that one of the greatest risks of genetic testing is more subtle--it is the risk that your test results will be misinterpreted. In fact, we have now seen several patients who have either had prophylactic surgery or considered it, based on result misinterpretation. Why? One of the main issues is that genetic testing companies are aggressively targeting provider offices and encouraging them to order their own genetic testing. In fact, many testing companies offer their employees financial incentives for the *number of test kits sold*, and the *number of kits ordered* by new providers. These employees have been known to discourage ordering physicians from referring their patients to graduate-trained cancer genetic specialists (even in areas like Connecticut, where these services are widely available), and encourage them to order the testing themselves after little or no training in genetics. The conflict of interest here is clear.

One genetic testing company is planning to launch a direct-to-consumer campaign via television and magazine ads that is slated to hit Connecticut, Massachusetts and New York City this fall. Unlike ads for prescription medications, these ads are currently not regulated by the federal government.¹⁻⁵ As a result, they include no information about the risk factors for hereditary cancer. Furthermore, they have been described in several publications as inaccurate, misleading, and utilizing scare tactics.^{2,3,6} These ads end by encouraging consumers to contact the company directly, where company employees will provide phone counseling and refer them to providers they recommend--these providers are not required to have graduate training in genetics, and some may receive hefty monetary incentives from the company.

We have joined with other professionals across the country to counter this campaign and others like it. **You can help.** Go to: **www.responsiblegeneticstesting.org** to learn more and to sign a petition asking for federal oversight before this campaign can launch. **Please spread the word.**

References:

1. *JCO* 2003; 21(17):3191-3193.
2. *New Genetics and Society* 2006; 25(1):89-107.
3. *JAMA* 2002; 288(14):1762-1767.
4. *Issues in Science and Technology* 2006; 22(3):59-66.
5. *Science* 2006; 313:1853.
6. *Hastings Center Report* 2001; 31(3):33-35.

Additional references:

Williams S and Javitt G. (7/25/2006, update 6/15/2007). Direct-to-consumer genetic testing: Empowering or endangering the public? In *Policy and Public Opinion: Issue Briefs*. Retrieved May 22, 2007, from <http://www.dnapolicy.org/policy.issue.php> .

Greendale K and Pyeritz RE. Empowering primary care health professionals in medical genetics: How soon? How fast? How far? *Am J Med Genet* 2001;106:223-232.

Resources

Some women having a mastectomy with reconstruction find it helpful to talk to other women who have had this surgery and to view pictures of the completed reconstruction process ahead of time. Every woman's reconstructive process is different and no two women look alike; however, seeing similar examples can be helpful for some people. Here we review two websites that provide information and photographs of the reconstruction process.

www.myselftogetheragain.org/process.htm

The *Myself: Together Again* project was started as a resource for young women diagnosed with breast cancer who have chosen to have breast reconstruction after mastectomy. This website includes black and white photographs taken by a professional photographer which documents one woman's decision to have breast reconstruction using implants and provides a photo-narrative of the reconstruction process.

www.breastcenter.com

This is a website for the Center for Restorative Breast Surgery in New Orleans, Louisiana. This site features a photo album of actual patients who have agreed to allow their 'before' and 'after' photographs to be used as a resource for other women contemplating breast reconstruction. Various methods of breast reconstruction are featured on this site. These images are graphic and may not be suitable for everyone

Hormone Use in *BRCA1* and *BRCA2* Mutation Carriers - Part 2

(continued from page 1)

A recent follow-up to this study, which included a larger sample size, found Tamoxifen equally effective in reducing the risk of a future breast cancer in both *BRCA1* and *BRCA2* positive breast cancer survivors who were pre-menopausal or had reached natural menopause.²

It is unclear whether Tamoxifen further reduces the risk of breast cancer in women who have had their ovaries and fallopian tubes removed pre-menopausally. Further studies are needed in this area.^{1,2,3}

There are little data regarding preventive Tamoxifen use in *BRCA1* and *BRCA2* mutation carriers who have never been diagnosed with breast cancer. The National Surgical Adjuvant Breast and Bowel Project (NSABP-P1) is a well-known study which analyzed the effect of Tamoxifen on breast cancer incidence in women never diagnosed with breast cancer; however, this trial did not examine the *BRCA* status of all of its participants, making conclusions difficult.

Therefore, women who carry either a *BRCA1* or *BRCA2* mutation and have been diagnosed with an ER+ breast cancer may consider taking Tamoxifen or another such medication to reduce their risk of a future breast cancer. *BRCA2* and possibly *BRCA1* mutation carriers who have never had a diagnosis of breast cancer may consider using Tamoxifen (or Raloxifene, a similar medication) prophylactically and should discuss the pros and cons of this medication further with their doctors.

References:

1. Metcalfe et al. *J Clin Oncol* 2004; 22(12): 2328-35.
2. Gronwald J et al. *Int J Cancer* 2006; 118: 2281-84.
3. Narod et al. *Lancet* 2000; 356: 1876-81.

Research Updates

Updates in Breast Screening using MRI

CA Cancer J Clin 2007;57(2):75-89. and *NEJM* 2007;356(13):1295-303.

These two studies summarize important new information about breast magnetic resonance imaging (MRI). The first study reviews the findings of an expert panel convened by the American Cancer Society that has developed new recommendations for the use of MRI in women at increased risk for breast cancer. The panel recommends annual breast MRI screening in addition to annual mammography for women who:

- carry a *BRCA1* or *BRCA2* mutation;
- have a first-degree relative with a *BRCA1* or *BRCA2* mutation *and are untested*;
- have an increased lifetime risk of breast cancer due to their family history;
- have another known genetic susceptibility to breast cancer, or;
- have received radiation treatment to the chest, such as treatment for Hodgkin's Disease.

The second study found that breast MRI improved the detection of a second breast cancer in the contralateral (opposite) breast in women recently diagnosed with breast cancer. In this study of 969 women who were recently diagnosed with breast cancer, MRI detected 30 (3.1%) breast cancers in the opposite breast that were not detected by clinical breast exam or mammography. Therefore, women newly diagnosed with breast cancer and women at increased risk should discuss breast MRI in addition to annual mammograms with their physicians.

Hereditary Breast and Ovarian Cancer Syndrome and the Impact on Prostate Cancer Risks

JNCI 2007;99:929-35.

This study, performed in Iceland, screened 527 men diagnosed with prostate cancer for a common *BRCA2* mutation and found 30 carriers. The men carrying the *BRCA2* mutation had a younger age of diagnosis, a more advanced tumor stage, a higher tumor grade and a shorter survival time when compared with the men who did not carry this mutation. BRCA mutations are most commonly known for their association with hereditary breast and ovarian cancer; however, studies have found that male BRCA carriers may be at increased risk of prostate cancer. Therefore, males from a family with a known BRCA mutation may wish to pursue genetic counseling and testing to help determine their risks for prostate cancer and discuss early prostate screening with their physicians (including digital rectal exams and PSA blood marker screening) by age 40 if they are found to carry a mutation.

(continued on page 5)

Updated Website Coming Soon

Our website is undergoing an exciting makeover! Please check for new developments this fall at www.yalecancercenter.org/genetics

Research Updates (continued from page 4)

New Genes Linked to Increased Breast Cancer Risk

Nature 2007;447(7148):1087-93. and *Nature Genetics* 2007;39(7):865-869 and 870-874.

Reports from several teams around the world recently identified genetic changes that may increase the risk of breast cancer. Although *BRCA1* and *BRCA2* are the most commonly known genes associated with an increased lifetime risk for breast and ovarian cancer, these three studies have identified four potentially new breast cancer susceptibility genes, as well as several genetic markers, that are associated with an increased risk for breast cancer and deserve further investigation.

The first study identified variations within four genes (*FGFR2*, *TNRC9*, *MAP3K1* and *LSP1*) linked with an increased risk of breast cancer. A second study found that variations in one specific gene, *FGFR2*, were associated with a increased risk of breast cancer. The final paper found genetic variants on chromosome 2 and on chromosome 16 that increase the risk of estrogen-receptor-positive breast cancer.

It is important to note that women in these studies did not receive BRCA mutation testing and that more research is needed to better understand the association between these genes and their link to breast cancer risk. At this time, it is premature to offer genetic testing for these genes. However, these results add to our growing knowledge of breast cancer risk and may, someday, lead to clinical testing.

Hope Chest Event

The first Hope Chest event was held on May 3, 2007 at the home of Jane Savage and her husband Mark Van Allen. It was a beautiful spring evening and Jane and Mark's young sons, Will (9) and Miles (7), served as waiters for the event, at which about 30 people gathered to learn more about cancer genetics and the Hope Chest. Dr. Kevin Kelly from Yale Cancer Center spoke about the new Cancer Center building, and Jane was generous enough to share her family's story of genetic counseling and testing. Ellen Matloff, MS gave a brief overview of cancer genetics and how counseling and testing can tailor medical management and risk reduction in a family. We have since had several referrals of patients who learned about our program through this event. **Thank you Jane and Mark!**

If you are interested in making a contribution to the Hope Chest, or would like additional information, please contact Benita Palmer at (203) 436-8526.

Yale Cancer Genetic Counseling Clinics

Yale
55 Church Street, Suite 402 (203) 764-8400

Greenwich, CT
Once a month at the Bendheim Cancer Center, Greenwich Hospital (203) 764-8400

Norwalk, CT
Once a month at the Whittingham Cancer Center, Norwalk Hospital (203) 764-8400

Danbury, CT
Once a month at the Praxair Cancer Center, Danbury Hospital (203) 764-8400

This newsletter is produced by the:
Yale Cancer Genetic Counseling Program
55 Church Street, Suite 402
New Haven, CT 06510
(203) 764-8400
fax (203) 764-8401
www.yalecancercenter.org/genetics

Written by: Karina L. Brierley, MS
Rachel E. Barnett, MS
Danielle C. Campfield, MS
Ellen T. Matloff, MS
Heidi G. Edmonds

Edited by: Heidi G. Edmonds
Layout by: Karina L. Brierley, MS

Yale Cancer Genetic Counseling Program
55 Church Street, Suite 402
New Haven, CT 06510