the
INHERITED CANCER REGISTRY®
at the Moffitt Cancer Center
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What's Inside?

ICARE Recruitment and Participation Update

We have enrolled more than 900 participants, including over 500 individuals from families with a *BRCA* mutation. Participants in ICARE represent 42 U.S. states and 10 countries worldwide. We continue to foster relationships with genetics professionals throughout Florida and beyond and hope to maintain the pace at which our registry has grown over the past two years. The information you provide to the registry is critical to answer important questions about issues faced by those at risk for inherited cancer predisposition. If you have not completed your questionnaire and would like to be sent an additional paper copy or have an email sent to you containing the link to the online version, please contact the study team directly via phone (813-745-6446) or email (ICARE@moffitt.org).

Welcome Message

We are excited to provide you with the third update of the ICARE initiative, since it was initiated in Summer 2010. We have continued to experience tremendous growth, and now have over 900 registry participants. We value the information you have agreed to share with us and continue to actively use it to further our understanding about issues relevant to those with inherited cancer predisposition. To that end, data from ICARE participants has been included in a number of scientific publications. [1, 2] In addition, we are very proud of the awards recieved by members of the ICARE study team at the recent Moffitt Scientific Symposium on May 10th, 2012 (Population Sciences category: Courtney Lewis - Best Poster; Sidorela Gllava - Best Oral Presentation). Their work was based on data from the ICARE initiative, again, showing the importance of the information you have shared with us to furthering our mission.

We are also looking forward to the 7th Annual Joining FORCEs Against Hereditary Cancer Conference, which will take place from October 18-20, 2012 in Orlando, Florida at the Hyatt Regency Grand Cypress. This is a conference for anyone concerned about hereditary cancer, including cancer survivors, those with a *BRCA* mutation or family history of cancer, and healthcare providers who treat high-risk patients.

Once again, we thank you for your continued support for the ICARE initiative, and our mission to *"end the cycle of inherited cancer through research, education, and outreach."*

Sincerely,

Tuya Pal, MD, FABMG
Principal Investigator, ICARE
On behalf of the ICARE team

1. Kotsopoulos J, et al. Breast Cancer Res. 2012 Mar 9;14(2):R42.
2. Narod SA, et al. Cancer Epidemiol Biomarkers Prev. 2012 May 21.

Genetic Testing and Clinical Updates •

Emerging cancer panels for testing patients for inherited cancer predisposition

Genetic testing for inherited cancer predisposition is typically performed by testing for one condition at a time. However, with the tremendous advances in genetic testing technologies over the last few years, the cost of testing has plummeted. To put this into perspective, the first human genome cost 2-3 billion dollars to sequence and took over 10 years to complete. Based on newer technologies, the current cost of sequencing a human genome is less than $10,000 and takes 4-6 weeks to complete. As such, it has become realistic to test for multiple inherited cancer conditions at the same time through "cancer panels". These panels consist of several genes for conditions at a cost that is comparable to genetic testing for one condition.

"It has become realistic to test for multiple inherited cancer conditions at the same time through "cancer panels."

Insurance reimbursement for testing has been encouraging. An example of when to consider this test is for an individual with breast cancer in whom there is a strong family history of cancer, but the *BRCA1* and *BRCA2* testing (comprehensive BRACAnalysis® and comprehensive rearrangement testing (BART)) did not identify a mutation to be present. For more information about this testing, contact your local genetics professional.

Prostate cancer screening recommendations for men with BRCA mutations

Over the last few years, there have been several studies that suggest that men with *BRCA* mutations are at a higher risk for developing and dying from aggressive prostate cancer. It is possible that PSA testing may be of benefit in men with *BRCA* mutations. However, until the utility of PSA is determined in these men, national practice guidelines continue to recommend annual prostate cancer screening (through PSA test and digital rectal exam) starting at age 40 in men with *BRCA* mutations.

Of note, new recommendations were set forth by the U.S. Preventive Services Task Force (USPSTF) which consists of a panel of national experts. Part of their mission is to make recommendations about preventive services, such as the use of PSA screening in men. The task force revised their position on PSA screening and recently recommended against routine prostate screening for everyone. However, in May 2012, they included the following caveat: *This recommendation also does not include the use of the PSA test for surveillance after diagnosis or treatment of prostate cancer and does not consider PSA-based testing in men with known BRCA gene mutations who may be at increased risk for prostate cancer."* Thus, they now indicate that those who may be at a higher risk for prostate cancer, such as *BRCA* mutation carriers, are not part of the recommendations and therefore it is reasonable to continue screening these individuals using the PSA test.

Moffitt Cancer Center Joins the Clinical Care Centers of the Von Hippel-Lindau (VHL) Family Alliance

We are very proud to announce that the Moffitt Cancer Center has been named a clinical care center of the VHL Family Alliance enabling us to promote our multidisciplinary treatment approach to hereditary kidney cancer throughout the state of Florida. Led by Dr. Phil Spiess, Urologist/Genitourinary Oncologist, this hereditary kidney cancer clinic encompasses Moffitt physicians from over 10 medical/surgical specialties, including genetics. For more information about this multidisciplinary clinic for VHL and other hereditary kidney cancer types, contact ICARE (813-745-6446) or the Moffitt Genetic Counseling and Testing Service (813-745-3555).

Research Corner •

New study suggests breast cancer risk for non-carriers of family-specific BRCA mutations is not increased

Data from a population-based study was recently reported to estimate breast cancer risk among family members who tested negative for a known *BRCA1/2* family mutation (i.e., non-carriers). The study included 3047 women diagnosed with breast cancer. Results from the study indicated there was no increased risk for breast cancer in non-carriers as compared to family members of breast cancer patients who tested negative for a *BRCA* gene mutation.

"These results support clinical practice to advise patients who test negative for family-specific BRCA mutations that their breast cancer risks are not elevated"

These results support clinical practice to advise patients who test negative for family-specific *BRCA* mutations that their breast cancer risks are not elevated. Furthermore, in the absence of other strong risk factors, authors suggest that non-carriers should follow general population guidelines for breast cancer screening.

1. Kurian AW, et al. J Clin Oncol. 2011 Dec 1;29(34):4505-9.

Ask the Expert

Through each newsletter, we plan to give our participants an opportunity to have their genetics and research questions answered by experts. Please send your questions to ICARE@Moffitt.org so that we may include responses in future newsletter editions. The following questions were addressed by Drs. Pal and Lancaster at the Moffitt Cancer Center:

Q. *What are the risks of hormone replacement therapy (HRT) on breast cancer risk in women with BRCA mutations?*

A. Concern about HRT in *BRCA* carriers is its potential to raise the risk of breast cancer, as seen in the general population.[1-3] However, two studies in *BRCA* mutation carriers reported that HRT did not increase the subsequent risk of breast cancer, nor did it appear to reduce the protective effect of oophorectomy on breast cancer risk.[4,5] Recent results from the Women's Health Initiative in the general population also provide reassurance as to estrogen use for about 5 years in terms of breast cancer risk and mortality.[6]

1. Chen, C.L., et al. *JAMA.* 287, 734-41 (2002).
2. Rossouw, J.E., et al. *JAMA.* 288, 321-33 (2002).
3. Chlebowski, R.T., et al. *JAMA* 289, 3243-5 (2003).
4. Eisen, A. et al. *J Natl Cancer Inst* 100, 1361-7 (2008).
5. Rebbeck, T.R., et al. *J Clin Oncol* 23, 7804-10 (2005).
6. Anderson G.L., et al. *Lancet Oncol, 13(5), 476-86 (2012).*

Q. *What are the recommendations for screening following prophylactic surgeries?*

A. In *BRCA* mutation carriers, bilateral prophylactic mastectomy reduces the risk of breast cancer by over 90%. It essentially lowers the risk of breast cancer to below that of the general population. Similarly, in those with bilateral prophylactic salpingo-oophorectomy (BPSO), risk of ovarian cancer is reduced by 80% or more.

At the Moffitt Cancer Center, *BRCA* mutation carriers who have undergone a bilateral mastectomy are screened through clinical exams, and no imaging studies are routinely recommended. In those with BPSO, CA-125 levels (measured through a blood test) are ordered yearly, and no transvaginal ultrasounds are routinely recommended. These recommendations are based on clinical judgment of our team, and there is no data at this time to determine the necessity of this (or any) screening regimen in these individuals following prophylactic surgery.

Message from an ICARE Participant

"I recently completed a survey conducted by the Moffitt Cancer Center through the FORCE website. They contacted me and have asked if I would consider joining ICARE, an inherited cancer registry program. Seems like a no-brainer to this BRCA1-positive breast cancer survivor. If knowledge is power, combined knowledge is the greatest weapon we have in the development of tools to combat the BRCA problem.

The ICARE Inherited Cancer Registry. This is one gift of mine that will never wind up in the back of a closet, sold at a garage sale or re-gifted."

-Lee Asbell, WA

Meet a Study Team Member

My name is Courtney Lewis and I am the research coordinator for the ICARE initiative. In 2010, I began working at the Moffitt Cancer Center as an undergraduate research intern eager to gain exposure to the field of genetic counseling. Since that time, I have had the amazing opportunity to work with a dedicated team of researchers and registry participants striving to advance the scientific understanding of cancer genetics. Due to the experiences I have had while working with the ICARE initiative, I was recently accepted into the genetic counseling master's program at the University of Cincinnati. I want to thank all of our registry participants who have further inspired me to pursue my dream of becoming a genetic counselor.

Other Research Opportunities

1. *Cancer Treatment Side Effects Survey* – Online survey for *BRCA1* or *BRCA2* mutation who have received treatment for cancer
2. *Phase II PARP Inhibitor Clinical Trial* – An upcoming clinical trial will be open to both men and women with a *BRCA1* or *BRCA2* mutation and metastatic breast cancer to evaluate a PARP inhibitor (Veliparib) in combination with other agents, as well as a Platinum-based agent.

Please contact the ICARE study team by phone (813-745-6446), email (ICARE@Moffitt.org) or visit our website www.Moffitt.org/ICARE to learn more.

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