the
INHERITED CANCER REGISTRY®
at the Moffitt Cancer Center
JANUARY 2013

What's Inside?

ICARE Recruitment and Participation Update

Participation in the ICARE initiative continues to expand through referrals, events and active outreach efforts. We have enrolled more than 1100 participants, including over 750 individuals from families with *BRCA* mutations. Participants in ICARE represent 45 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. We would like to especially thank those who have returned their ICARE questionnaires and copies of their genetic test result and family tree. The information you provide to the registry is critical to answer important questions about issues faced by those at risk for inherited cancer predisposition. ICARE participants now have the option to complete each study questionnaire online. If you have not completed your initial or follow-up questionnaire and would like to complete it online, 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 fourth update of the ICARE initiative, since it was launched in Summer 2010. We have continued to experience tremendous growth, and now have over 1100 registry participants. We continue to use the information you have shared with us through contributing it to research efforts focused on furthering our understanding about issues relevant to those with inherited cancer predisposition.[1] We have also experienced changes in staff, and are lucky to have welcomed our two new coordinators, Emily Robinson and Lucia Camperlengo.

Another successful opportunity to grow ICARE was during the 7th Annual Joining FORCEs Against Hereditary Cancer Conference, from October 18-20, 2012 in Orlando, Florida at the Hyatt Regency Grand Cypress, which marked the third year the ICARE study team has attended this event. This conference represents the largest patient-focused conference for those impacted by *BRCA* mutations. It continues to bring together researchers, healthcare providers and members of the high-risk community from all over the world together to discuss advances relevant to those affected by *BRCA* mutations. 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. McLaughlin JR, et al. J Natl Cancer Inst. 2012 Dec 20.

Plug-in to ICARE

We encourage you to visit our website, www.Moffitt.org/ICARE, to learn more about the purpose of the registry, find out about other research opportunities that may be of interest to you, and meet the ICARE study team. You can now "*Like*" ICARE on Facebook--visit www.facebook.com/ICAREatMoffitt to stay up to date on registry news!

The selection of chemotherapy in BRCA patients with pancreatic cancer

Some evidence suggests that individuals with *BRCA* mutations who develop pancreatic cancer may benefit from specific chemotherapy regimens. In a recent review of this topic, Kim et al reported on a study of 5 patients with *BRCA* mutations (4 *BRCA2* and 1 *BRCA1*) who were treated with a platinum-based chemotherapy regimen.[1] Of these patients, 3 had advanced disease and all had some response to platinum; an additional 2 patients had resectable and locally advanced disease, both of whom were downstaged after receiving platinum as part of their treatment and eventually underwent resection of their tumor. Another study was conducted based on 15 *BRCA* carriers with pancreatic cancer.[2] Of these patients, 4 received a PARP inhibitor alone or in combination with chemotherapy, of which 3 demonstrated an initial radiographic response and one patient had stable disease for 6 months. Six patients received platinum-based chemotherapy as first line treatment for metastatic disease, of whom five had a radiographic partial response.

"These studies … suggest that therapeutic agents that target DNA repair may potentially offer a significant benefit in treating BRCA-associated pancreatic cancers."

These studies add to the limited literature to suggest that therapeutic agents that target DNA repair (e.g., PARP inhibitors, Platinum-based agents) may offer benefit when treating *BRCA*-associated pancreatic cancers, even in advanced stages. However, the numbers reported remain very small and it is critical to perform prospective studies in individuals with *BRCA*-associated pancreatic cancers to truly determine the efficacy of targeted therapies.

1. Kim R, et al. JOP. 2012 Mar 10;13(2):180-1.
2. Lowery MA, et al. Oncologist. 2011;16(10):1397-402.

In the Media…Decoding Annie Parker

A new movie to be released in March 2013 tells the true story of one woman, Annie Parker (played by Samantha Morton), whose life is forever changed by cancer, and Dr. Mary-Claire King (played by Helen Hunt) whose conviction of a hereditary basis for some breast cancer led to the discovery of the location of the *BRCA1* cancer gene.

Points to consider regarding bilateral salpingectomy as a risk reduction procedure for ovarian cancer

Over the last few years, there has been evidence to suggest that a substantial proportion of ovarian cancer may start in the fallopian tubes, although some cancer clearly arises in the ovary. As a result, removal of both fallopian tubes (called 'bilateral salpingectomy') has been suggested as an interim procedure to reduce risk in *BRCA* mutation carriers.[1,2] But it is still very important to remember that there are no data available to tell us how effective this procedure is at reducing the future risk of ovarian cancer.

"…until bilateral salpingectomy is more fully assessed, this procedure does not eliminate cancer risks as completely as a bilateral salpingo-oophorectomy."

In essence, bilateral salpingectomy preserves ovarian function, thus it does not put premenopausal patients into premature menopause. The procedure can be done through a minimally invasive approach, and may allow patients to defer removing their ovaries until they are closer to menopause. In fact, a small study of 14 young *BRCA* mutation carriers documented the procedure as feasible.[3] However, this study could not assess how effective the procedure was in reducing future ovarian cancer risk, nor was it able to assess whether the procedure had an effect on ovarian function. Ultimately, until the usefulness of bilateral salpingectomy is more fully assessed, patients need to remember that this procedure does not eliminate their cancer risks as completely as if they had undergone a bilateral salpingo-oophorectomy (i.e. removal of both ovaries as well as the fallopian tubes). As much as salpingectomy may become an important ovarian cancer risk reduction measure, it is exceedingly important to further study the validity of the procedure as a risk-reducing intervention in the context of research efforts.

1. Greene MH, et al. Am J Obstet Gynecol. 2011 Jan;204(1):19.e1-6.
2. Dietl J, et al. Hum Reprod. 2011 Nov;26(11):2918-24.
3. Leblanc E, et al. Gynecol Oncol. 2011 Jun 1;121(3):472-6.

Clinical and Research Updates

Is Lynch Syndrome associated with breast cancer?

The cancer spectrum typically seen in individuals with Lynch Syndrome includes cancers of the colon, endometrium, ovary, stomach, and other cancers (including cancer of the renal pelvis, ureter, small bowel and pancreas). The issue of whether breast cancer risk is elevated in those with Lynch syndrome has been controversial, with conflicting results between various studies. However, the largest prospective study recently reported an almost 4-fold increased risk for breast cancer.[1] This same group subsequently looked at the risk for breast cancer in those with a prior diagnosis of colorectal cancer. Their results showed an almost 2-fold elevated risk.[2] However, further studies are needed to determine absolute risks and age distribution before breast surveillance guidelines can be developed for those with Lynch Syndrome. At this time, it is recommended that women with Lynch Syndrome continue to follow the general population breast cancer screening guidelines.

1. Win AK, et al. J Clin Oncol. 2012 Mar 20;30(9):958-64.
2. Win AK, et al. J Natl Cancer Inst. 2012 Sep 19;104(18):1363-72.

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 question was addressed by Dr. Lora Thompson, a Clinical Psychologist at the Moffitt Cancer Center:

Q. How do I talk to family members about my genetic test results?

A. The ability to share risk information with family members is a common reason why many individuals undergo genetic testing. Family members may feel appreciative of the information so they can have the opportunity to learn about their personal risk of cancer and to consider cancer prevention and surveillance strategies. However, when others disagree with your decision to undergo testing, being the "gatekeeper" of genetic information can be a burden. Research on genetic test result disclosure has found that less open communication was associated with higher levels of distress in individuals undergoing genetic testing, even when their results were negative.[1]

Below are some tips for communicating results:[2,3]

- Before receiving your result, begin thinking about how, when, and with whom you will share the information.
- Be sure that you have a good understanding of what your result means. This may be especially important if you receive a positive or uninformative result.
- Ask your genetic counselor to help you prepare a letter or information sheet that you can provide family members.
- Practice what you plan to say and anticipate what questions you might receive.
- Have a trusted individual available for support.

Some families may still experience tension during the sharing process even when the tested individual practices good communication skills. In this case, consider seeking additional help from a professional with expertise in working with families, such as a psychologist, social worker, or licensed counselor. Remember that your responsibility after receiving your genetic test result is to pass on information. It is up to each family member to decide how to react emotionally and whether to pursue genetic counseling and testing.

1. van Oostrom, I, et al. Clin Genet 71, 35-42 (2007).
2. DeMarco, TA, et al. Breast Disease 27, 127-136 (2007).
3. Seymour, KC, et al. J Genet Counsel 19(4), 330-342 (2010).

Messages from ICARE Participants at the FORCE 2012 Conference

"Research is crucial to unlock the BRCA mutations and the "unknowns" around them."
- Ohio

"I want to help give 'hope' to future generations of people with BRCA mutations."
- Wisconsin

"It's important—we have something only we can share—we're obligated to share it."
- Florida

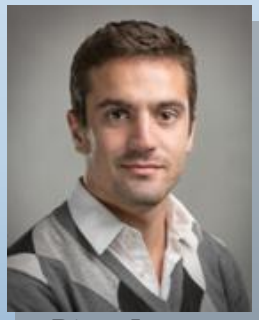
"Shared information gives increased knowledge which furthers the advancement of cures."
- Arizona

"I care for my family and their future."
- Tennessee

Introducing New Study Team Members

Emily Robinson, MPH
Research Coordinator

Lucia Camperlengo, MPH
Research Coordinator



Diego Lozano
Research Intern

Other Research Opportunities
PARP Inhibitor Clinical Trials

1. Moffitt Cancer Center- A phase II clinical trial open to both men and women with *BRCA1/2* mutations and metastatic breast cancer to evaluate a PARP inhibitor (Veliparib) in combination with other agents, as well as a Platinum-based agent.

2. University of Miami- A phase II clinical trial open to patients with triple negative breast cancer (ER-/PR-/HER2-) and *BRCA 1/2* mutations to evaluate a PARP inhibitor (Rucaparib) in combination with cisplatin.

3. Florida Hospital- A phase II clinical trial open to patients with recurrent epithelial ovarian, fallopian tube, or primary peritoneal cancer with *BRCA 1/2* mutations to evaluate a PARP inhibitor (Veliparib).

4. Holy Cross Hospital, Ft. Lauderdale- A phase II clinical trial open to men and women with *BRCA 1/2* mutations and metastatic breast cancer to evaluate a PARP inhibitor (Veliparib) in combination with both Platinum and non-Platinum based chemotherapeutic agents.

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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