Looking for Links: Inherited Genetic Mutations in Breast Cancer Patients

Rates of inherited mutations in genes other than BRCA1/2 are twice as high in breast cancer patients who have had a second primary cancer – including, in some cases, different types of breast cancer – compared to patients who have only had a single breast cancer. But the rates of these mutations were still found to be low overall, meaning it’s difficult to assess whether and how these individual mutations may drive the development of cancer. The study from the Basser Center for BRCA at the Abramson Cancer Center of the University of Pennsylvania also investigated the use of polygenic risk scores – which have recently been added to some commercial clinical multiplex genetic testing panels. Kara N. Maxwell, MD, PhD, an instructor of Hematology-Oncology and the study’s lead author, presented the findings at the 2018 American Society of Clinical Oncology Annual Meeting in Chicago earlier this month (Abstract #1503).

Genetic testing can help identify patients with a genetic predisposition that puts them at risk for developing cancer. Recently, new therapies called PARP inhibitors have been FDA approved to specifically target cancers caused by certain mutations – such as BRCA1/2, which carry a lifetime breast cancer risk of as much as 85 percent and 50 percent for ovarian cancer, as well as higher risks of pancreatic, prostate and other cancers.

“We need to gain a better understanding of why patients who have multiple cancers may be susceptible to them, and that work needs to go beyond the common genes we’re already been looking at,” Maxwell said.

The team – led by Susan M. Domchek, MD, executive director of the Basser Center for BRCA, and member of the ACC’s Breast Cancer Research Program, and Katherine L. Nathanson, MD, deputy director of the Abramson Cancer Center, specifically looked at patients who did not have a BRCA1/2 mutation and tested them for a panel of 15 different genetic mutations. They evaluated 891 patients who had a second primary cancer – breast or otherwise – after initial breast cancer and compared them to 1,928 who only had a single breast cancer. About eight percent of patients who had second primary cancers had mutations, compared to just four percent of patients from the single cancer cohort. The current threshold for whether or not genetic testing is recommended is five percent.

(Continued on page 2)

Using Telemedicine to Bring Genetic Counseling to Community Cancer Care

Genetic counseling for cancer patients has become standard of care at academic medical centers, but patients cared for at community-based medical practices across the United States may not have access to these resources. Video and phone sessions can close that gap and bring genetic counseling to patients who would not otherwise have the chance to receive it, according to a new study from the Basser Center for BRCA at the University of Pennsylvania’s Abramson Cancer Center.

Researchers conducted a randomized, controlled trial to determine whether patients at community practices would undergo genetic testing after a remote phone or video counseling session and found 77 percent of patients chose to do so, compared to just six percent in the group of patients that were offered usual care options for genetic testing, such as driving to a center with genetic counselor or having genetic testing with their doctor and without the assistance of a genetics professional. The study’s lead author, Angela R. Bradbury, MD, an assistant professor of Hematology-Oncology and member of the ACC’s Breast Cancer Research Program, presented the findings at the 2018 American Society of Clinical Oncology Annual Meeting in Chicago earlier this month (Abstract #6506).

Germline genetic testing helps doctors identify patients at increased risk for cancer who may benefit from additional or early screening or other cancer prevention interventions. This testing in-
Inherited Genetic Mutations in Breast Cancer Patients

“Our data show that patients who have had multiple primary cancers should undergo genetic testing, and likely this holds true for a number of other types of second cancer,” Maxwell said. “However, the overall numbers are still low, which shows the level of uncertainty that still exists and highlights the need for further research.”

The research also evaluated polygenic risk scores, a somewhat controversial metric recently added to some commercial clinical multiplex genetic testing panels. Polygenic risk scores are determined by how many single nucleotide polymorphisms (SNPs) a person has. SNPs are common variants with smaller effect sizes, and if a patient has multiple of certain SNPs, they may be at a similar increased for cancer as patients with a single rare mutation.

“Our study does not provide strong evidence of higher polygenic risk scores in patients with more than one breast cancer,” but many more patients will need to be studied to confirm this,” Maxwell said.

Source: Penn Medicine Communications


Telemedicine for Community Cancer Care

Bradbury and her team randomly assigned 115 patients who were candidates for genetic testing into two groups – one that received a phone or video counseling session and one that were provided information on how they can get genetic testing. All participants were patients at primary care practices throughout Pennsylvania, New Jersey, Delaware, and Maryland.

Of the 71 patients in the group offered remote genetic counseling services, 55 of them (77 percent) went on to complete the counseling. Just two of 36 patients (six percent) in the usual care group completed genetic counseling. In addition, 55 percent of patients in the remote services arm proceeded to actual genetic testing, leading to the identification of four genetic carriers. Only 17 percent of patients in the usual care arm underwent testing, and no carriers were identified.

“The data definitively show the impact of remote genetic services, and it’s clear from this study that this telemedicine approach improves on what community practices can do on their own,” Bradbury said. “That said, it’s noteworthy that just 56 percent of patients who underwent remote counseling went on to undergo genetic testing. It shows we still have work to do to help equip patients with this information, which can be life-saving in some cases.”

Bradbury also noted another important area to address: the discrepancy between patients in the usual care arm who underwent counseling and those who underwent testing.

“The data confirm that some people in community practices are getting testing without going through counseling first, and previous studies have shown that patients have lower levels of knowledge and lower satisfaction when that happens,” Bradbury said.

The study also compared the effectiveness of the two telemedicine options and preliminary findings suggest that videoconference leads to a greater increase in knowledge and a greater decrease in depression when compared to baseline than phone sessions. The authors note this finding is preliminary and points to a need for further research.

Susan M. Domchek, MD, executive director of the Basser Center for BRCA, and member of the ACC’s Breast Cancer Research Program, was a co-investigator on the study, which was supported by the Basser Center for BRCA.

Source: Penn Medicine Communications

Abstract: “Uptake of genetic testing and outcomes in a randomized study of remote genetic services as compared to usual care in community practices without genetic providers.” Abstract #6506 presented 6/1/2018, 2018 ASCO Annual Meeting
Seminars and So Forth

Monday 6/18/18  12:00 pm
Distinguished Seminar Series/CDB Seminar
“Modulating and rewiring cell division.” Iain Cheeseman, Member, Whitehead Institute; Professor of Biology, MIT
BRB II/III Glen Gaulton Auditorium

Monday 6/18/18  12:00 pm
Path & Lab Medicine Grand Rounds
“Genetics of the Hypoxia Inducible Factor Pathway.”
Frank S. Lee, MD, PhD, Associate Professor of Pathology and Laboratory Medicine, PSOM
CRB Austrian Auditorium

Wednesday 6/20/18  8:00 am
ACC Grand Rounds
“Know Thy Cells (and Antibodies): Improving Biomedical Research Reproducibility.” Leonard P. Freedman, PhD, Founding President & Chief Scientific Officer, Global Biological Standards Institute
SCTR 8-146AB

Thursday 6/21/18  9:00 am
CECB Seminar Series
“Breast Cancer Epidemiology in Diverse Populations: Etiology and Beyond.” Dezheng Huo, PhD, Associate Professor of Public Health Sciences, University of Chicago
JMB Class of ’62 Auditorium

Thursday 6/21/18  5:30 – 8:45 pm
2018 New Advances in Lung Cancer:
Stretching the Envelope (CME Course)
Sessions will feature information on surgery, radiation and systemic therapies with case presentations and question/answer sessions with the multidisciplinary team. Register online at PennMedicine.org/Abramson/LungCME
210 W Rittenhouse Square, Philadelphia, PA

Tuesday 6/26/18  9:00 am – 4:30 pm
Wistar Institute Melanoma Symposium
“Noreen O’Neill Melanoma Research Symposium – Host Response in Melanoma.” Details and registration (required) at https://wistar.org/melanoma2018
The Wistar Institute, 3601 Spruce St.

Wednesday 6/27/18  12:00 pm
CT3N Seminar Series
“Polymeric Nanomaterials for Therapeutic Delivery and Regenerative Engineering.” Hai-Quan Mao, PhD, Professor, Materials Science and Engineering, Johns Hopkins University
SCTR 10-146AB

Thursday 6/28/18  12:00 pm
Penn Radiation Oncology Invited Speaker
“Abemaciclib, a Selective CDK4/6 Inhibitor Enhances the Radiosensitivity of Non-Small Cell Lung Cancer in vitro and in vivo.” James B. Mitchell, PhD, FAS-TRO, Branch Chief, Radiation Biology, NCI
SCTR 8-146AB

Thursday 6/28/18  5:45 – 8:45 pm
2018 Breast Cancer Clinical Case Series:
The Year in Review (CME Course)
Clinical updates in diagnosis and local, regional, and systemic therapies. Register online at Penn-Medicine.org/Abramson/BreastCME
Sheraton Valley Forge, King of Prussia, PA

ACC Membership Updates

The Abramson Cancer Center is pleased to welcome the following Research Program members:

- Michelle Alonso-Basanta, MD, PhD, Helene Blum Assistant Professor of Radiation Oncology (Radiobiology and Imaging)
- Joshua Bauml, MD, Assistant Professor of Medicine (Cancer Therapeutics)
- M. Andrés Blanco, PhD, Assistant Professor of Biomedical Sciences, School of Veterinary Medicine (Tumor Biology)
- Lucasz J. Bugaj, PhD, Assistant Professor of Bioengineering, SEAS (Tumor Biology)
- Luca Busino, PhD, Assistant Professor, Cancer Biology (Tumor Biology)
- Brian Capell, MD, PhD, Assistant Professor, Dermatology (Tumor Biology)
- Amy Clark, MD, MSCE, Assistant Professor of Medicine (Hem-Onc) (Breast Cancer)
- Saar Gill, MD, PhD, Assistant Professor of Medicine (Hem-Onc) (Hematologic Malignancies)
- Ivan Maillard, MD, PhD, Professor of Medicine (Hem-Onc) (Hematologic Malignancies)
- Michael Mitchell, PhD, Skirkanich Assistant Professor of Innovation, Department of Bioengineering, SEAS (Cancer Therapeutics)
- Vivek Narayan, MD, Assistant Professor of Medicine (Hem-Onc) (Cancer Therapeutics)
Funding Opportunities

NCORP Community Oncology Research Program (NCORP) (UG1)

LOI Due Date: 7/31/2018
Application Due Date: 08/31/2018

NCORP is a community-based research network that:
- Designs and conducts clinical trials and other human subject studies for adults and children in cancer control, prevention, screening, and care delivery, as well as quality-of-life studies embedded within treatment trials;
- Incorporates the needs of diverse populations such as, adolescents and young adults (AYAs), and the elderly; racial and ethnic minorities; sexual and gender minorities; and rural residents into studies and takes steps to enhance participation of these groups;
- Enhances patient and provider access to treatment and imaging trials conducted under the National Clinical Trials Network (NCTN);
- Integrates cancer disparities research within the community network.

NCORP consists of three components, each with its own FOA:

NCORP Research Bases (RFA-CA-18-015) will design and conduct cancer clinical trials and care delivery research studies as well as manage and analyze the data and report the research results.

NCORP Community Sites (RFA-CA-18-016) will accrue diverse patients/participants to NCI-approved, cancer control, prevention, and care delivery research studies designed by NCI’s NCORP Research Bases as well as treatment trials within the National Clinical Trials Network Groups (NCTN).

NCORP Minority/Underserved Community Sites (RFA-CA-18-017) will accrue diverse patients/participants to NCI-approved, cancer control, prevention, and care delivery research studies designed by NCI’s NCORP Research Bases as well as treatment trials within the National Clinical Trials Network Groups (NCTN).

PA-18-821 Collaborative Activities to Promote Cancer Cachexia Research (Admin Supplement)

Application Due Date: 07/30/2018

The purpose of this FOA is to support collaborative, multidisciplinary basic and translational research that addresses an important question in cancer cachexia and to expand the cadre of investigators experienced in cancer cachexia study design, model systems and data interpretation. These supplement applications must propose a collaboration between cancer researchers and researchers with documented expertise in cachexia research. The parent grant for the supplement must have an NCI primary assignment. Overall, the long-term goal of this supplement program is to encourage a focused examination of the biology of cancer cachexia and its effect on organs and systems beyond the tumor site(s).


Astellas Oncology C3 Prize

Application Due Date: 7/25/2018

Astellas is inviting healthcare innovators to propose ideas that address specific challenges encountered in low- and middle-income countries within the following three categories: support tools, educational tools and technology. Prizes totaling $100,000 USD will be awarded to the three winners - one $50,000 USD grand prize and two $25,000 USD grants. Winners will also receive a one-year “nights and weekends” membership to MATTER, a Chicago-based healthcare innovation community, to help bring their ideas to life. More information about the awards and submission criteria can be found at www.C3Prize.com.