Genomic-guided therapy leads to better outcomes for cancer patients, according to IU study

July 15, 2016

INDIANAPOLIS – Cancer patients with advanced disease fared better when they received genomic-guided therapy, according to a study by Indiana University School of Medicine researchers.

Lead and senior authors Milan Radovich, Ph.D., assistant professor of surgery, Patrick Kiel, Pharm.D., adjunct assistant professor of medicine, and Bryan Schneider, M.D., associate professor of medicine and the Vera Bradley Investigator in Oncology, and colleagues found that patients with metastatic cancer (cancer that had spread) that had not responded to other treatments had improved outcomes when they received therapy guided by genomics compared to those who did not.

The study was published online July 15 in Oncotarget.

The researchers found that 43.2 percent of those patients who received genomic-guided therapy had improved duration of response when compared to their own prior therapy compared to only 5.3 percent of those who did not receive such treatment.

"We found patients who had genomic sequencing had better outcomes," Dr. Schneider, also a researcher at the Indiana University Melvin and Bren Simon Cancer Center, said. "What we already know across cancer types is that for each subsequent line of therapy, a patient can expect a shorter amount of time to experience benefit from the therapy. We looked at the percentage of patients who actually beat their prior line of therapy in terms of success. This allowed us to really use each patient as his or her own benchmark."

Dr. Schneider added: "While there has been incredible enthusiasm for use of genomics to help guide patients to personalized therapy, there still needs to be additional evidence that this approach helps patients.

"This study gives us evidence in a real clinical world with patients with a variety of tumors who are getting a variety of therapies – both on and off clinical protocol – that they do indeed gain a benefit."

The research team studied 101 patients from the Indiana University Health precision genomics program with metastatic solid tumors who had progressed on at least one line of therapy. The patients' tumor samples were submitted for DNA and RNA next-generation sequencing. The majority of patients had a diagnosis of soft tissue sarcoma, breast cancer, pancreatic cancer, or colorectal cancer, although multiple others were included.

"An important aspect of our program is the deliberation of genomic results by a multi-disciplinary advisory board composed of more than 20 IU faculty and IU Health staff encompassing medical oncologists, genomic scientists, pharmacists, pathologists, nursing, and bioethicists," Dr. Radovich, also a researcher at the IU Simon Cancer Center, said. "As the landscape of precision medicine evolves, both technologically and clinically, having access to broad-based academic expertise will be critical to ensure that every facet of potential treatment avenues is explored."

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Dr. Schneider said genomic-guided therapy can help patients by matching the acquired genetic mistake seen in the tumor with a drug that is designed to target that genetic vulnerability.

"Each of us carries an amazing blueprint in our DNA, which is our genome," Dr. Schneider said. "The genome is made up of about three billion letters. Think of it as an instruction manual or blueprint. We can get mistakes or changes in that blueprint that can make it difficult for the cell to read the instruction manual. When that happens, the cell misbehaves and becomes cancerous.

"The goal behind using the genome in cancer therapy is not to only understand why these mistakes might make the cancer occur but also to learn that these mistakes might lead to an understanding of the tumor's vulnerability. For those vulnerabilities where we have drugs either in trials or already approved that are known to attack the vulnerability, we can match that vulnerability with that drug."

Because of the emerging body of evidence that shows better outcomes with genomic-guided therapy, the authors wrote that it should be considered with appropriate patients to help guide patients to clinical trials or optimal therapies.

Other authors from Indiana University included Bert O'Neil, Safi Shahda, Paul Helft, Todd Skaar, J. Thomas Callaghan, Nasser Hanna, Roberto Pili, Patrick Loehrer, Daniel Rushing, Darrell Davidson, Mehdi Nassiri, Liang Cheng, Lawrence Einhorn, Natraj Ammakkanavan, and Guanglong Jiang, and Meagan Ferguson, Megan Parsley, Erin Niland, and Stacy Nance of the IU Health precision genomics program.

The study was made possible in part by a grant from the Walther Cancer Foundation.

IUSCC news

June 2014

IU study: Increased number of moles may indicate higher breast cancer risk for women

An Indiana University cancer researcher and colleagues have found that the number of moles on a woman's body might predict her risk of developing breast cancer.

Han

Jiali Han, PhD, the Rachel Cecile Efroymson Professor in Cancer Research at the Indiana University Melvin and Bren Simon Cancer Center and professor and inaugural chair of the Department of Epidemiology at the Fairbanks School of Public Health, and colleagues found that women with 15 or more cutaneous nevi, or moles, were 35 percent more likely to be diagnosed with breast cancer than women with no nevi.

The findings were published online June 10 in *PLOS Medicine*.

Dr. Han is an epidemiologist and a melanoma (skin cancer) expert. The more moles a person has is a known risk factor for developing melanoma, but this new research indicates a high count of moles may also be a factor in a woman's risk of developing breast cancer.

"We found that a higher count of moles also indicates higher levels of sex hormones," Dr. Han said. "Higher levels of hormones have been attributed to increased risk of developing breast cancer. Therefore, it's possible that the number of moles might be used as a marker for breast cancer risk."

The researchers used data from 74,523 white, female nurses who participated in the Nurses' Health Study. Dr. Han used data from the women who had reported the number of nevi less than 3 millimeters in diameter on their left arms from 1986 to 2010.

Dr. Han cautioned that additional studies need to be conducted to study the relationship between cutaneous nevi and breast cancer risk, especially in other populations, as this study focused only on white women.

"There is much yet that we need to investigate to gain a better understanding of this relationship," Dr. Han said. "We are seeking research funding to support our work because we next want to examine whether the mole count

can improve the current breast cancer risk prediction model."

Other authors of the study included Mingfeng Zhang, Xuehong Zhang and A. Heather Eliassen of Brigham and Women's Hospital and Harvard Medical School; Abrar A. Qureshi of Brown University; and Susan E. Hankinson of the University of Massachusetts.

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VA and Regenstrief researchers working to identify risk factors for colon cancer under 50

July 21, 2016

INDIANAPOLIS -- While the incidence of colon cancer has been declining in individuals 50 years old and older in the United States, it is steadily rising in those under age 50. With funding from the U.S. Department of Veterans Affairs, Thomas F. Imperiale, M.D., a VA and Regenstrief Institute clinician-researcher, is developing and validating a model to predict risk for colon cancer in those under 50 with no family history of the disease.

"We should be moving from an age-based system of screening for colon cancer to one that is risk-based because age is only one factor that contributes to risk," said Dr. Imperiale. "In our study we are identifying demographic, physical, and clinical factors that are different in people younger than 50 with colon cancer compared to those without colon cancer. These factors make them more comparable to those 50 and over.

"There have been calls to lower the age for routine colon cancer screening below age 50, but doing that doesn't make sense at this point. It would simply be a reactive response that would likely result in net harm because we would be screening so many people unnecessarily and placing those with small adenomas into surveillance programs younger so they would have more lifetime colonoscopies – nearly all of them unnecessary. At this point, lowering the screening age would be time consuming and expensive and not necessarily good medicine."

Building upon his previous work, Dr. Imperiale's new retrospective study uses de-identified information from the electronic medical records of veterans from across the country age 35 to 49 with colon cancer and contrasting them with the medical records of two disease-free control groups of individuals under 50 with no family history of the disease. One of these control groups is comprised of veterans who have undergone colonoscopy and the other group of those who have not. All individuals whose records are being reviewed received health care from the VA between 2008 and 2014.

Age and sex are among the demographic factors being evaluated. Potential clinical risk factors under investigation are body mass index, cholesterol and triglyceride levels, blood pressure readings, as well as medical history. Lifestyle factors being studied include details on smoking and alcohol use, exercise, and occupation.

The researchers will determine which factors differ between cases with colon cancer and controls without colon cancer. According to Dr. Imperiale, who also holds appointments with the Indiana University Melvin and Bren Simon Cancer Center and the IU School of Medicine, this has not been previously studied in people under 50.

"The VA is one of very few healthcare systems where this work could be done," he said. "The VA's electronic medical record systems are so broad and deep we should able to discover candidate factors that will allow us to identify a subgroup of people under age 50 whose risk is comparable to older adults. For this group we

Thomas Imperiale

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could recommend some type of "early" screening -- not necessarily colonoscopy -- but perhaps blood stool test or another less invasive test before age 50."

In June 2016 the U.S. Preventive Services Task Force updated its recommendation for commencement of colon cancer screening at age 50. It advised that the decision to screen adults age 76 to 85 should be an individual one, taking into account the patient's overall health and prior screening history. No guidelines were given for those under 50.

Work on the three-year nearly $900,000 study is commencing this summer.

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IUSCC news

July 2016

News briefs

Big Ten Cancer Research Consortium Summit is Sept. 9-10 in Indy

The Big Ten Cancer Research Consortium Summit, hosted by the IU Simon Cancer Center, is Sept. 9 and 10 at the JW Marriott, 10 S. West St. The summit will bring together Big Ten Cancer Research Consortium member institutions,along with colleagues from industry, to strengthen their collaboration and explore opportunities for novel therapeutic advances in clinical oncology. The summit is for senior and junior faculty and fellows involved in clinical oncology research, basic scientists involved in drug discovery and translational research, and cancer center leadership and administration. There is no registration fee. Attendees are responsible for their own travel and accommodations. Register at www.bigtencrc.org/summit.

IUSM receives $2 million gift from children of Sidney and Lois Eskenazi

The children of Indianapolis philanthropists Sidney and Lois Eskenazi have made a $2 million gift to the Indiana University School of Medicine that will be used to recruit a highly accomplished researcher focused on discovering new ways to treat, diagnose, and prevent cancer. full story>

Aug. 9 Frameworx: Innovative cancer research

From molecular biosciences to advanced clinical trials and commercialization of drug therapies, Indiana's universities are leading the charge to prevent cancer and to find a cure. Discover more at the Aug. 9 BioCrossroads' Frameworx session, "Innovative Cancer Research: A Showcase of Novel Work at Indiana's Academic Institutions." Speakers include **Milan Radovich**, PhD, of the IU Simon Cancer Center, Andrew Bullock, PhD, of the Harper Cancer Research Institute, and Timothy Ratliff, PhD, of the Purdue University Center for Cancer Research. **Patrick Loehrer**, MD, will moderate a panel discussion. Learn more and register.

BioArt image competition is now open

The Federation of American Societies for Experimental Biology (FASEB) recently launched its fifth annual BioArt competition. Images or videos produced as part of everyday research from extramural researchers are welcome. Submissions are due Aug. 30. Full details are at www.faseb.org/BioArt .

NCI seeks ideas for clinical trials

The National Cancer Institute, in partnership with White House Presidential Innovation Fellows, is looking for ways to improve how people find and understand information about NCI-supported cancer clinical trials. NCI has launched Clinical Trials Ideas, a platform to gather ideas from patients, caregivers, advocates, health professionals, and technical partners on how to make cancer clinical trials information more accessible. Deadline for idea submissions is **Tuesday, Aug. 30**.

FDA accepts ApeX Therapeuctics' IND application

The FDA has accepted ApeX Therapeutics' Investigational New Drug (IND) application for clinical testing of its lead drug candidate, APX3330, for pancreatic cancer. APX3330 has been shown in multiple in vitro and in vivo models of pancreatic cancer to be effective in reducing tumor growth and metastases as a single agent. In addition, APX3330 combined with a standard dose of gemcitabine demonstrated significant decreases in tumor volume compared to treatment by the respective drugs as single agents. **Mark Kelley**, PhD, the scientific founder of ApeX Therapeutics, said: "We are very excited to have reached this very important milestone to evaluate APX3330 in patients with pancreatic cancer. We are now poised to initiate the study in the coming months." Read news release.

Cancer center members in the news

Marino

Natascia Marino, PhD, has been named the Breast Cancer Research Foundation Investigator for Breast Cancer Research at the IU School of Medicine. Dr. Marino, also an assistant research professor of medicine, is an investigator with the Susan G. Komen Tissue Bank at the IU Simon Cancer Center. Her research focuses on the normal breast and how it relates to the development of breast cancer. The Breast Cancer Research Foundation is a nonprofit organization committed to achieving prevention and a cure for breast cancer. It provides critical funding for cancer research worldwide to fuel advances in tumor biology, genetics, prevention, treatment, metastasis and survivorship.

Brittney-Shea Herbert, PhD, and colleagues wrote "Hsp90 and PKM2 Drive the

Expression of Aromatase in Li-Fraumeni Syndrome Breast Adipose Stromal Cells," which was published in the Journal of Biological Chemistry.

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