



This issue of our newsletter focuses on breast cancer research and clinical trials at the Chao Family Comprehensive Cancer Center.



Study aims to improve wisdom about breast cancer screening protocol

The American Cancer Society says one thing about when women should start getting regular mammograms and how often they should get them. The U.S. Preventive Services Task Force says another. And when in doubt, women are advised to discuss their particular circumstances with their doctors, which is of limited use to physicians who have been left with no clear protocol to follow.

“We don’t have a protocol anymore,” said Dr. Hoda Anton-Culver, professor and chair of epidemiology at the UC Irvine School of Medicine. “What the experts are saying is that we’re not going to give you a definite recommendation; you figure it out with your doctor. The problem is we are dealing with women as a whole bunch of people without personalizing the way we look at one woman.”

Anton-Culver is the UC Irvine principal investigator for the Wisdom Study, a California-wide research project that aims to determine better answers for optimizing screening based not on universal recommendations — “annual mammograms for women over age X” — but on women’s personal risk of breast cancer, including breast density, family history and genetics.

UC Irvine will recruit and track 10,000 of the 100,000 women participating in the study, a collaboration among all the University of California medical centers. Signing up to participate is simple via the wisdomstudy.org website, and participation is open to all women 40 to 74 years old who have never had breast cancer and who get their healthcare in California. They do not need to be patients at UC medical centers.

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The participants can choose to be randomly assigned to receive either annual screening or risk-based screening; for scientific reasons, random assignment is ideal. However, women who prefer to participate in one group or the other have that option as well. Those in the risk-based group will receive a risk assessment, which includes genetic analysis of a saliva sample, and their screening schedule will be based on that assessment.

The study, funded by the Patient-Centered Outcomes Research Institute, the Robert Wood Johnson Foundation and private donations, might determine, for example, that women at low risk would benefit from fewer screenings. At the other end of the scale, the study will help identify women at very high risk, who would be advised to get alternating mammography and MRI scans every 6 months, and perhaps consider taking chemoprevention, or medication that could reduce their risk by 50 percent.

“Our main aim is to determine how safe risk-based screening is as compared with annual screening,” said Hannah Lui Park, UCI assistant professor of epidemiology, and site director

for the study. “While we want to minimize the number of false-positives, we still need to be able to detect breast cancers early enough so that patients can be treated effectively, with no increase in morbidity or mortality.

“Our main aim is to determine how safe risk-based screening is compared with annual screening.”

“I’m glad to see the Task Force recommendations say that you should have a conversation with your healthcare provider,” she added, “but how can you figure out what you’re comfortable with if you don’t know your risk?”

To participate in the Wisdom Study, visit wisdomstudy.org

Breast cancer clinical trial evaluates less-toxic chemotherapy

A Phase 2 study underway at the Chao Family Comprehensive Cancer Center examines whether women with HER2-positive breast cancer can be treated effectively with a safer regimen of chemotherapy.

The research by Dr. Rita Mehta, a health sciences professor of medicine with the UCI School of Medicine, seeks to determine whether a weekly regimen of carboplatin plus paclitaxel with pertuzumab plus trastuzumab provides similar response to the commonly used combination of cyclophosphamide and anthracyclines followed by paclitaxel with trastuzumab plus or minus pertuzumab.

“Anthracyclines have been known to cause heart disease or heart failure, and known to cause leukemia,” Mehta said. “Now we are hoping we can dial back on anthracyclines.

“Pertuzumab is one of the main drugs of the four,” she said. “If the new pertuzumab-based combination can achieve a high rate of complete response, women can avoid anthracyclines.”

A high rate of remission has previously been reported with anthracycline followed by paclitaxel, followed by trastuzumab, in up to 70 percent of women with HER2-positive breast cancer, Mehta said. With the new regimen, she hopes to achieve similar rates. Then, only women who do not achieve pathologic response will need to receive anthracyclines. If successful, the change would lead to a steep overall reduction in toxicity for the vast majority of women undergoing chemotherapy for this type of breast cancer.

Previous research by Mehta played an important role in changing the treatment of breast cancer when her study showed remarkable results in women with advanced disease through the use of chemotherapy plus trastuzumab before surgery.

Mehta’s current study has openings for about 90 more participants. In order to be eligible, women must have HER2-positive breast cancer at stages I to III, including women with inflammatory breast cancer. The cancer, or its loco-regional recurrence, must have been recently diagnosed and not yet treated. However, women whose primary cancer was treated with chemotherapy before the current recurrence are eligible.

There also are openings for participants in two other breast cancer studies by Mehta.

“We have similar trials for patients with triple-negative breast cancer and hormone-receptor-positive breast cancers,” she said. Those also center on the possibility of reducing or eliminating the use of anthracyclines.

Doctors with patients who might qualify for any of these trials are encouraged to contact the Chao Family Comprehensive Cancer Center’s clinical research line at 877-UC-STUDY (877-827-8839) or by emailing ucstudy@uci.edu

Precision high-dose radiation studied for metastatic breast cancer

A Phase 2R/3 trial utilizing stereotactic body radiotherapy at the Chao Family Comprehensive Cancer Center examines whether the addition of the high-dose radiation improves outcomes for patients with oligometastatic breast cancer.

The randomized trial, led by NRG Oncology, examines how stereotactic radiosurgery combined with standard-of-care treatment — such as chemotherapy and hormonal therapy — compares with standard-of-care therapy alone for patients with limited metastatic breast cancer.

The study involves use of a “state-of-the-art radiation delivery machine that allows us to deliver high-dose radiation to a small area with very high precision.”

Chao Family Comprehensive Cancer Center is one of several centers around the country and in Canada participating in the trial, which is part of the National Clinical Trials Network program sponsored by the National Cancer Institute. There are openings for new patients to be enrolled in the trial at the Chao center.

“Usually, when patients have been newly diagnosed with metastatic disease, they will require systemic chemotherapy and/or hormonal treatment to control the disease, in addition to possible local palliative radiation to deal with any symptomatic pain,” explains Dr. Parima Daroui, a UC Irvine Health radiation oncologist specializing in breast cancer, and associate professor of radiation oncology at the UCI School of Medicine. She is the principal investigator for the study at the cancer center.

“It’s hypothesized that patients with oligometastatic disease, or only a few sites of known metastatic disease, may possibly have a lower amount of circulating cancer cells.”

One possibility, she said, is that targeting those metastatic sites early might prevent development of additional new sites of disease and provide more durable disease control, leading to improved survival.

Patients continue to receive chemotherapy during the trial, but they are also treated with stereotactic body radiotherapy (SBRT), which is high-dose radiation given in five or fewer treatments.

Part of what made the Chao Family Comprehensive Cancer Center, located at UC Irvine Medical Center, an ideal site for this national study was that the Department of Radiation Oncology had recently acquired the latest technology for delivering SBRT.

“The TrueBeam STx linear accelerator is a state-of-the-art radiation delivery machine that allows us to deliver high-dose radiation to a small area with very high precision and is a newer machine that not many facilities may have at their disposal,” Daroui said. “Because of the high accuracy needed for SBRT, we utilize a unique surface tracking system, VisionRT™ that uses optical 3D cameras to monitor the patient’s surface contours and pause radiation delivery if the patient moves out of position.”

In order to be eligible for the trial, patients must have received an initial diagnosis of metastatic breast cancer with fewer than two to four metastases visible on imaging, depending on the location of the disease.

Oncologists with patients who might qualify to participate in the trial are encouraged to contact Dr. Daroui.

Meet our breast cancer specialists



Parima Daroui, MD
pdaroui@uci.edu
Radiation oncology



Karen Lane, MD
klane@uci.edu
Surgical oncology



Erin Lin, DO
erinhl@uci.edu
Surgical oncology



Rita Mehta, MD
rsmehtha@uci.edu
Medical oncology



Ritesh Parajuli, MD
rparajul@uci.edu
Medical oncology

UC Irvine researchers to map breast cells for Human Cell Atlas

As part of a massive scientific effort to map all cell types of the human body, called the Human Cell Atlas Initiative, researchers at the Chao Family Comprehensive Cancer Center will be working on a \$500,000 pilot grant to begin the mapping process for healthy cells of the breast.

The grant, shared by UCI researchers Devon Lawson, PhD, and Kai Kessenbrock, PhD, with scientists at the MD Anderson Cancer Center in Texas, comes from the Chan Zuckerberg Initiative begun by Dr. Priscilla Chan and her husband, Facebook CEO Mark Zuckerberg, which will be a major funding source of the Human Cell Atlas. The funding was allotted through the Silicon Valley Community Foundation.

The goal is to map all of the cells' properties, including the gene signatures describing specific states of those cells, to understand how and when diseases including cancer begin, so that doctors can intervene earlier and in more targeted ways.

"Just the breast alone is a very complex organ," said Lawson, assistant professor of physiology and biophysics at UCI. "We've done some work already in this area. There are 12 to 20 different cell populations -- epithelial, endothelial, different kinds of immune cells, a lot of fat cells."

Most of the necessary cells for this study come either from women who have developed cancer in one breast and decide on prophylactic mastectomy of the healthy breast as well, or from women who have breast-reduction surgery, Lawson said. That alone raises new complexities: Are the cells of a woman who has gotten breast cancer somehow different, even in the healthy breast, from those of most other women? Women who have breast reductions performed are generally large-breasted; could that mean different cellular properties as well?

For the pilot program, however, these cells are enough.

Lawson's area of research has been metastasis of breast cancer cells; almost all breast cancer deaths are caused by metastatic disease. Her partner in the atlas project is Kessenbrock, assistant professor of biological chemistry, whose research focuses on identifying biomarkers for early detection of breast cancer, perhaps before it even develops.

With the development of the cell atlas, he said, "we will now be able to understand how the tissue is composed on a cell-by-cell level, so we'll be able to detect when it deviates from normal.

"Furthermore, cancer might not develop in individual cells alone. It might involve the whole system, including cell-to-cell communications and systems-level changes. This is where our big gap on knowledge is right now."

A third UCI researcher, Jered Haun, is working on building technology that will enable better research on mapping cancer cells for future cell atlas projects.

"The thing is, tumors are tissues, not a single-cell suspension like a blood cell," said Haun, assistant professor of biomedical engineering. "How can you take tissue and create a single-cell suspension? You bathe them in enzymes. But we wanted to develop something that would be faster, more efficient, give a better yield."

He is looking at the addition of fluid forces to speed the process, and creating machinery that will carry out the process automatically. "At this point, there's a lot of manual labor involved," he said. "I'm the engineer. The goal of my lab is to develop tools."

About us: Chao Family Comprehensive Cancer Center

UC Irvine Chao Family Comprehensive Cancer Center is the only NCI-designated comprehensive cancer center in Orange County. It is a vital resource for the people of Orange County and surrounding areas for generation and dissemination of new knowledge about the causes, prevention, and treatment of cancer, training of the next generation of cancer providers and caregivers, and alleviation of the overall burden of cancer on our citizens.

Located at UC Irvine Medical Center in the heart of Orange County, the Chao Family Comprehensive Cancer Center integrates research, prevention and the most advanced diagnostics, treatment and rehabilitation programs to provide the best possible care for patients and their families.

Breast cancer services are also provided at the UC Irvine Health Pacific Breast Care Center in the Newport Coast.

Chao Family Comprehensive Cancer Center researchers form disease-oriented teams that bring together patient-centered basic, translational and clinical investigators to facilitate the movement of discoveries through the pipeline into the clinical arena.

With a world-class, multidisciplinary team of surgeons, radiation oncologists, medical oncologists, pathologists, nurses, rehabilitation therapists, pharmacists, social workers and dietitians, the Chao Family Comprehensive Cancer Center is able to address cancers of all types and degrees of severity.

University of California Cancer Consortium takes on California's \$14 billion killer

The UC Irvine Chao Family Comprehensive Cancer Center is one of University of California's five academic cancer centers, home to some of the world's leading scientists and physicians, in a consortium to better address California's most pressing cancer-related problems and opportunities, UC President Janet Napolitano and Dr. John Stobo, executive vice president of UC Health, have announced.

Despite steady declines in cancer rates over the past 20 years, cancer is soon expected to overtake heart disease as California's leading cause of death. This year alone, 176,000 state residents will be diagnosed with cancer and nearly 60,000 will die from it. The estimated cost burden of cancer in California is \$14 billion annually.

The alliance of the UC centers, each of which holds the highest designation possible from the National Institutes of Health's National Cancer Institute, reflects a new model for cancer research and treatment that calls for the best minds to work together, regardless of where they are, to tackle cancer's many problems.

"The UC Cancer Consortium represents the cancer research and treatment arm of UC Health, an academic health network with over 14 million patients under care," said Richard Van Etten, MD, PhD, director of the UCI Chao Family Comprehensive Cancer Center. "The Consortium plays a central role in alleviating the burden of cancer on the residents of California through research into the causes, prevention, and treatment of cancer, training the next generation of cancer health care providers, and providing state-of-the-art cancer care to the ethnically and socioeconomically diverse population of our state."

Among the projects the Consortium will undertake are precision medicine, clinical trials, population health science, best practices in harnessing big data to improve health, and political engagement for public benefit.

In addition to the UCI Chao Family Comprehensive Cancer Center, the centers that make up the consortium include the UC Davis Comprehensive Cancer Center, the UCLA Jonsson Comprehensive Cancer Center, the UC San Diego Moores Cancer Center and the UCSF Helen Diller Family Comprehensive Cancer Center.

Contact us

For more information about other cancer clinical trials at the Chao Family Comprehensive Cancer Center, or to determine whether we have one that might meet your patients' needs, call 877-827-8839 or email us at ucstudy@uci.edu