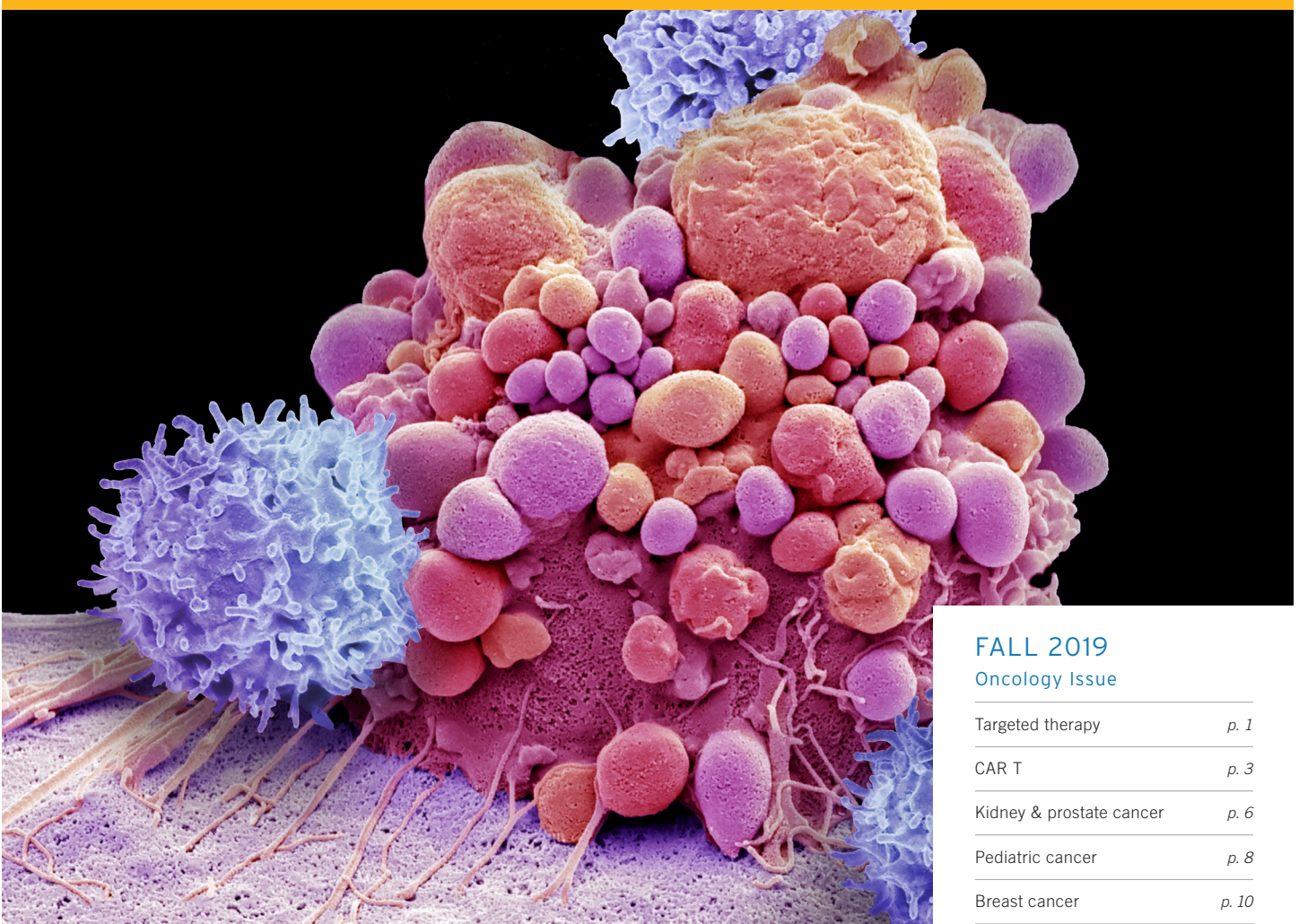


Physicians Update



FALL 2019
Oncology Issue

Targeted therapy	p. 1
CAR T	p. 3
Kidney & prostate cancer	p. 6
Pediatric cancer	p. 8
Breast cancer	p. 10



Herceptin has saved countless women's lives and earned UCLA's Dr. Dennis Slamon the Lasker Award

Not only has development of the drug Herceptin saved the lives of an untold number of women with a particularly aggressive form of breast cancer, it also opened new avenues of research that have led to multiple other targeted therapies that attack the disease at its genetic roots. For his pioneering contribution to the creation

of Herceptin, UCLA's Dennis Slamon, MD, PhD, has been awarded the 2019 Lasker-DeBakey Clinical Medical Research Award, widely regarded as America's top biomedical research honor.

Dr. Slamon, professor and chief of hematology/oncology at the David Geffen

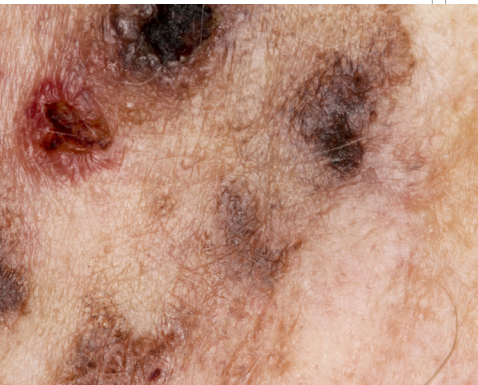
continued on p. 4

Three-drug combination helps curb the growth of a deadly type of skin cancer

STORY HIGHLIGHTS

Clinical trials demonstrated that the three-drug combination did not cause the debilitating side effects that have occurred by a combination of one targeted drug and an immunotherapy drug.

Participants in the Phase II study who received the three-drug combination had progression-free survival for an average of 16 months.



Darkly pigmented nodules and lesions, arising from a patch of irregularly pigmented flat brown patches on the cheek of an elderly woman with lentigo maligna melanoma.

Image: Medical Images

A three-drug combination researched by an international team of UCLA-led scientists could prove to be an effective new therapy for people with a specific type of advanced melanoma. The approach shows promise for extending the lives of people with a type of melanoma that contains a potent gene mutation, BRAF V600E. In clinical trials, it appeared not to cause the debilitating side effects that are caused by a combination of one targeted drug and an immunotherapy drug.

The researchers found that people with the melanoma survived longer without the cancer progressing or growing when they received a combination of two targeted inhibitors that block the BRAF mutation — dabrafenib and trametinib — and an immune checkpoint inhibitor drug — pembrolizumab — as the initial treatment for their disease.

“Utilizing the three drugs together sensitized the patient’s own immune system to bolster the power of immunotherapy and block the growth of two genes — BRAF and MEK — that cause cancer cells to reproduce and grow out of control,” says Antoni Ribas, MD, PhD, professor of medicine at the David Geffen School of Medicine at UCLA and director of the UCLA Jonsson Comprehensive Cancer Center’s Tumor Immunology Program.

Half of the 120 participants in the Phase II study received the three-drug combination and had progression-free survival — meaning that the disease did not worsen or progress — for an average of 16 months. The participants who received trametinib, dabrafenib and a placebo lived for an average of 10.3 months without the disease progressing.

Previous studies have found that using one of the three drugs alone can dramatically shrink tumors in a small percentage of people with melanoma. A majority of people on the treatment, however, do not see any benefit or end up experiencing a relapse. Two-drug combinations also have been tested, but they,

too, have had limited success. “Earlier attempts to combine a targeted agent with an immune checkpoint inhibitor as a double-combination therapy had debilitating side effects for patients, and it was just too toxic to continue testing, so we went back to the drawing board,” says Dr. Ribas, who also is director of the Parker Institute for Cancer Immunotherapy Center at UCLA and a member of the Eli and Edythe Broad Center of Regenerative Medicine and Stem Cell Research. “We found that by using two targeted inhibitors, instead of just one, in combination with a checkpoint inhibitor, we could safely and effectively treat the cancer.”

The results of the triple therapy, Dr. Ribas says, are so much more encouraging than double-therapy combinations with these drug agents. “With this triple combination, we are doing two things at once: using the two inhibitors to block the cancer from spreading and stimulating the immune system. An immune response has the ability to remember foreign invaders and help protect the body from similar infections in the future, so enlisting an immune response to the cancer is aimed at having more durable responses to the therapy.”



For more information about melanoma programs, research and clinical trials at UCLA, go to:

cancer.ucla.edu/patient-care/understanding-cancer/cancer-types-101/skin-cancer

CAR T clinical trial aims at extending the lives of people with most common types of lymphoma and leukemia

As the field of immunotherapy continues to revolutionize the way people with incurable cancers are treated, there still are many people who do not benefit from treatment or who have a relapse of their cancer. In an effort to further improve therapy to help more people, UCLA Health researchers have begun a pioneering chimeric antigen receptor (CAR) T cell immunotherapy trial that will attack cancer cells on two fronts. By launching a simultaneous bilateral assault against two targets — CD19 and CD20 — that are expressed on B-cell lymphoma and leukemia instead of using the conventional single-target approach, researchers are hoping to minimize resistance and increase the life expectancy for people diagnosed with these cancers.

“One of the reasons CAR T-cell therapy can stop working in patients is because the cancer cells escape from therapy by losing the antigen CD19, which is what the CAR T cells are engineered to target,” says Sarah Larson, MD, a UCLA hematologist-oncologist and the principle investigator on the trial, which is being offered exclusively at UCLA. In fact, up to two-thirds of the patients who experience relapse after being treated with the FDA-approved CD19 CAR T-cell therapy develop tumors that have lost CD19 expression.

“One way to keep the CAR T cells working is to have more than one antigen to target,” says Dr. Larson, a member of UCLA’s Jonsson Comprehensive Cancer Center. “By using both CD19 and CD20, the thought is that it will be more effective and prevent the loss of the antigen, which is known as antigen escape, one of the common mechanisms of resistance.”

In preclinical studies led by Yvonne Chen, PhD, associate professor of microbiology, immunology and molecular genetics and codirector of the UCLA Jonsson Comprehensive Cancer Center

Tumor Immunology Program, the team was able to show that by simultaneously attacking two targets, the engineered T cells developed in her lab could achieve a much more robust defense compared to conventional, single-target CAR T cells against tumors in mice.

Dr. Chen’s team designed the CARs based on the molecular understanding of the CAR’s architecture, the antigen structure and the CAR/antigen binding interaction to achieve optimal T-cell function. This design helps the T cells have dual-antigen recognition to help prevent antigen escape. “Based on these results, we’re quite optimistic that the bispecific CAR can achieve therapeutic improvement over the single-input CD19 CAR that’s currently available,” Dr. Chen says.

This first-in-humans study will evaluate the therapy in patients with non-Hodgkin’s B-cell lymphoma or chronic lymphocytic leukemia that has come back or has not responded to treatment. The goal is to determine a safe therapeutic dose.

Patients enrolled in the trial will have their white blood cells (T cells) collected intravenously then reengineered in the laboratory so the T cells can produce tumor-specific receptors, which allow the T cells to recognize and attack the CD19 and CD20 proteins on the surface of tumor cells. The new “smarter and stronger” T cells are then infused back into the patient and primed to recognize and kill cancer cells.



For more information about this clinical trial, go to:
tinyurl.com/car-t-clinical-trial



To refer a patient for possible enrollment in the clinical trial, email:
BHabtemariam@mednet.ucla.edu



For more information about CAR T-cell therapy at UCLA, go to:
uclahealth.org/car-t-cell-therapy

Promise of CAR T-cell therapy may extend beyond current uses

UCLA Health is among a select group of health systems in the country certified by the U.S. Food and Drug Administration to administer CAR T-cell therapy outside of clinical trials. Currently, UCLA is approved to treat certain types of lymphoma and leukemia in adults, pediatric and young-adult patients who have not benefited from two standard treatments.

“The degree to which some patients benefit is remarkable,” says Josh Sasine, MD, PhD, director of UCLA’s CAR T-cell program and a member of the UCLA Jonsson Comprehensive Cancer Center. “Most successful therapies for advanced cancers increase overall survival by a few months but almost never cause long-term remissions. With CAR T cells, we’re seeing durations of benefit that are very long lasting — many years of cancer-free periods. About one-third to half of the patients who receive this therapy are having durable remissions.”

He cautions, however, that “the treatment is so new that we don’t yet know who has experienced a true cure.”

Dr. Sasine is hopeful that one day, CAR T-cell therapy can be extended to other forms of cancer. “It is significant that this treatment platform is very different from what we have done in oncology in the past, and, in principle, it is broadly applicable,” he says. “Until ongoing and future clinical trials are complete, we won’t know whether or not we can make CAR T cells recognize other forms of cancer. If we can, this could benefit many more patients.”

Testing for other cancers already is underway. “It is one thing to have success in the lab, but the fact that we are seeing so much success with CAR T cells validates the idea that we can genetically engineer the immune system to fight cancer,” Dr. Sasine says. “This is likely to encourage investigators to examine other strategies to genetically engineer immune cells for cancer therapy. It opens up an exciting new direction. I have not seen any other approach demonstrate this much success so quickly.”

COVER STORY

Herceptin has saved countless women's lives and earned UCLA's Dr. Dennis Slamon the Lasker Award

(continued from cover)

School of Medicine at UCLA, shares the award with H. Michael Shepard, an American cancer researcher honored for work he completed at biotechnology company Genentech, and Axel Ullrich, a German cancer researcher from the Max Planck Institute of Biochemistry. The three scientists showed that the monoclonal antibody Herceptin binds to, and destroys, abnormal cells without harming nearby healthy tissue, much like a laser-guided missile hitting a select target. This was a major departure from then-common chemotherapies that Dr. Slamon refers to as the “hand grenade” approach, indiscriminately killing healthy as well as diseased cells.

Proving that antibodies that bind to cancerous cells are an effective method for treating solid tumors transformed cancer care at a time, in the 1980s, when most cancer therapies were focused on excising tumors and developing better chemotherapies. Between 2.7 million and 3 million women have been treated with Herceptin, and women with HER2-positive breast cancer now have among the highest survival rates compared with all women with breast cancer.

“There were a lot of preconceived notions that this approach couldn't work because prior antibody therapies in cancer had failed,” says Dr. Slamon, who also is director of clinical and translational research at the UCLA Jonsson Comprehensive Cancer Center. “However, we had clear data to back us up, and we really stuck to pursuing it. I grew up being told that I was only limited by my own ability. That always stayed with me. You have to be very careful and critical of your data, but if it looks correct, believe it and chase it despite what others may think.”

The Lasker Awards were established in 1942 by Albert and Mary Lasker to recognize researchers, clinical scientists and public servants who have made major advances in the understanding, diagnosis, treatment, cure or prevention of disease, and to raise awareness of the ever-present need for research funding.

The first human clinical trial led by Dr. Slamon was performed at UCLA in 1990. Twenty women — whom he credits as being the real heroes in the story of Herceptin — participated.

“Those women who entered the Phase I trials are not research subjects or patients, they're colleagues,” Dr. Slamon says. “They're every bit as much of the story as any of us because they participated in a trial knowing that we might be giving them something that would hurt them. And because it was a safety test, we had to start at levels that were not likely to even help them. But they all agreed and volunteered with the attitude that while it may not directly help them, it might help the next person behind them.”

The Lasker Awards were established in 1942 by Albert and Mary Lasker to recognize researchers, clinical scientists and public

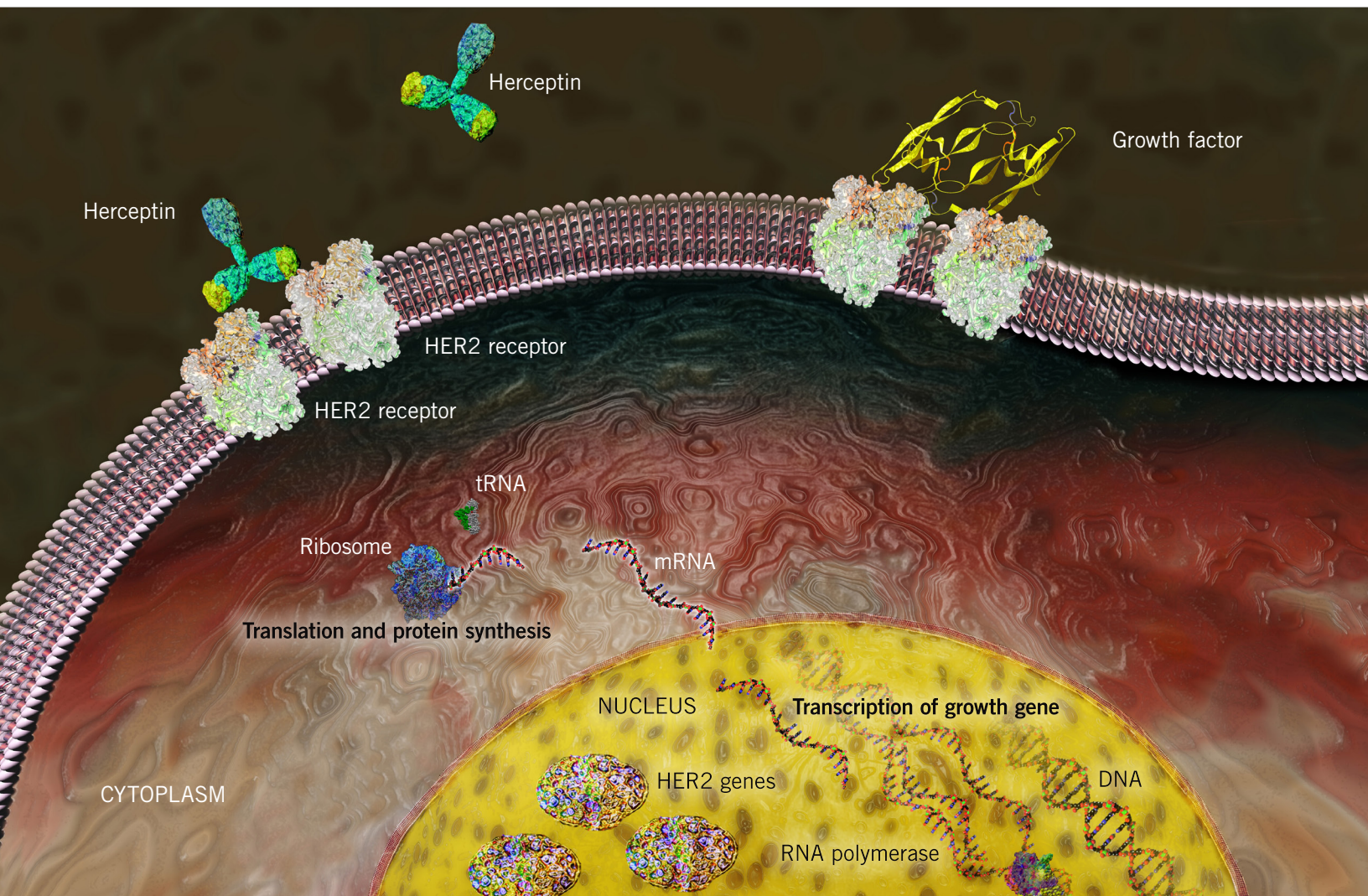


Photo: UCLA Health

STORY HIGHLIGHTS

The development of Herceptin opened new avenues of research that have led to multiple other targeted therapies that attack cancer at its genetic roots.

The monoclonal antibody binds to, and destroys, abnormal cells without harming nearby healthy tissue, much like a laser-guided missile hitting a select target.



servants who have made major advances in the understanding, diagnosis, treatment, cure or prevention of disease, and to raise awareness of the ever-present need for research funding. They are known as the “American Nobel” — eighty-eight Lasker winners have gone on to be awarded Nobels. Dr. Slamon is the second David Geffen School of Medicine scientist to win the award in the past two years; Michael Grunstein, PhD, Distinguished professor Emeritus of biological chemistry, received the Albert Lasker Basic Medical Research Award in 2018 for his groundbreaking research on gene expression.

“Over the course of his 40-year tenure at UCLA, Dr. Slamon has persevered in his research, leading to improved outcomes for patients,” says Johnese Spisso, president of UCLA Health and CEO of the UCLA Hospital System. “His efforts resulted in a new way of understanding breast cancer, and we are grateful for the

tremendous impact his work has had on the lives of millions of women worldwide.”

Dr. Slamon and colleagues opened an entirely new area of research. In turn, targeted therapies for cancer, including Erbitux, Sprycel, Nerlynx and Avastin, have emerged, thanks to research by other scientists.

Dr. Slamon continues to lead the development of groundbreaking new treatments, such as palbociclib (Ibrance), which was approved by the Food and Drug Administration in February 2015 for women with advanced estrogen receptor-positive, HER-2-negative breast cancer.



For more information about breast cancer services and research at the UCLA Jonsson Comprehensive Cancer Center, go to:

cancer.ucla.edu/breastcancer



For information about the UCLA Breast Program, go to:

cancer.ucla.edu/breasthealth

Close-up illustration showing a cancerous breast cell producing too many HER genes, which in turn produce an excessive number of HER2 receptors. The receptors attract growth factors, which stimulate the growth of more cells. Herceptin and other antibodies inhibit HER2 receptors and VEGF growth factors.

Image: Medical Images

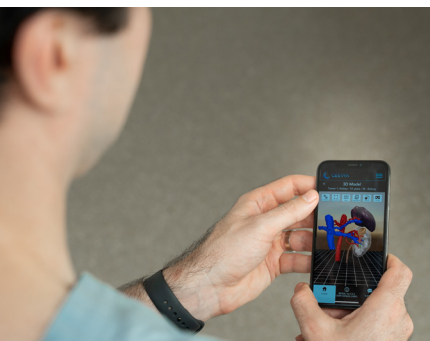


Image: UCLA Health

3D modeling to prepare for cancer surgeries should become new standard

UCLA physicians studying the efficacy of using three-dimensional virtual reality models to prepare for cancer surgeries say the technology “is no longer something we should be considering for the future — it is something we should be doing now.”

“Surgeons have long theorized that using 3D models would result in a better understanding of the patient anatomy, which would improve patient outcomes,” says urologic oncology surgeon Joseph Shirk, MD, who is a clinical instructor in urology at the David Geffen School of Medicine at UCLA and at the UCLA Jonsson Comprehensive Cancer Center. “But actually seeing evidence of this magnitude, generated by

very experienced surgeons from leading medical centers, is an entirely different matter.”

The study led by Dr. Shirk demonstrated that using 3D models to prepare for kidney tumor surgeries resulted in substantial improvements, including shorter operating times, less blood loss during surgery and a shorter stay in the hospital afterward. Previous studies involving 3D models have largely asked qualitative questions, such as whether the models gave the surgeons more confidence heading into the operations. This is the first randomized study to quantitatively assess whether the technology improves patient outcomes.

STORY HIGHLIGHTS

Study demonstrates that using 3D models to prepare for kidney tumor surgeries resulted in substantial improvements, including shorter operating times, less blood loss during surgery and a shorter stay in the hospital.

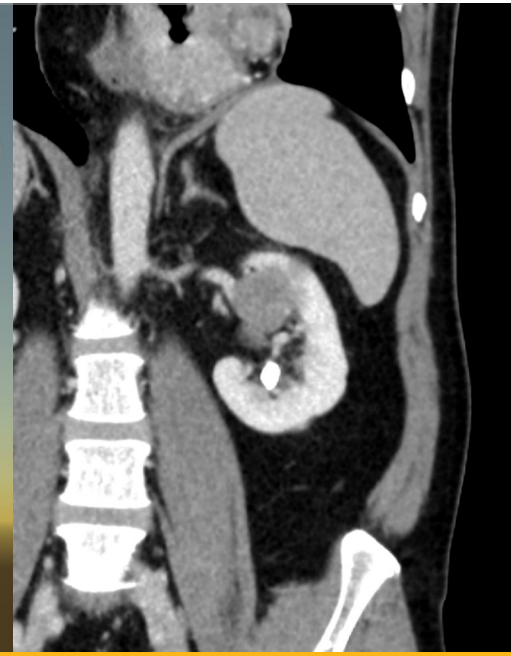
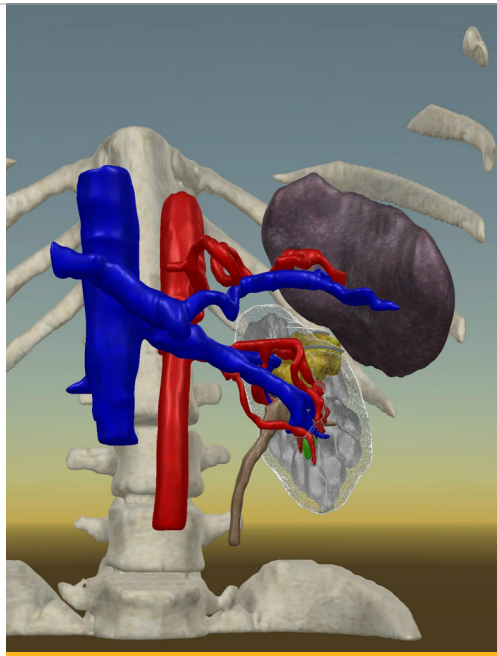
Another urologic cancer study shows that men with low- or intermediate-risk prostate cancer can safely undergo higher doses of radiation over a significantly shorter period of time and still have the same, successful outcomes as from longer courses of treatment.

Shorter course of radiation therapy effective in treating men with prostate cancer

UCLA researchers have found that men with low- or intermediate-risk prostate cancer can safely undergo higher doses of radiation over a significantly shorter period of time and still have the same, successful outcomes as from a much longer course of treatment. This type of radiation, known as stereotactic body radiotherapy, is a form of external beam radiation therapy and reduces the duration of treatment from 45 days to four to five days. The approach has been in use since 2000, but has not yet been widely adopted because of concerns over how safe and effective this approach would be in the long term.

“Most men with low- or intermediate-risk prostate cancer undergo conventional radiation, which requires them to come in daily for treatment and takes an average of nine weeks to complete,” says radiation oncologist Amar Kishan, MD. “That can be very burdensome on a patient and be a huge interruption in their life. With the improvements being made to modern technology, we’ve found that using stereotactic body radiotherapy, which has a higher dose of radiation, can safely and effectively be done in a much shorter time frame without additional toxicity or compromising any chance of a cure.”

The 3D-model technology, which is FDA approved, provides surgeons with a better visualization of a person's anatomy, allowing them to see the depth and contour of the structure, as opposed to viewing a two-dimensional picture. In the study, 92 people with kidney tumors at six large teaching hospitals were randomly placed into two groups. Forty-eight were in the control group and 44 were in the intervention group. For those in the control group, the surgeon prepared for surgery by reviewing the patient's CT or MRI scan only. For those in the intervention group, the surgeon prepared for surgery by reviewing both the CT or MRI scan and the 3D virtual reality model. The 3D models were reviewed by the surgeons from their mobile phones and through a virtual reality headset.



“Visualizing the patient's anatomy in a multicolor 3D format, and particularly in virtual reality, gives the surgeon a much better understanding of key structures and their relationships to each other,” Dr. Shirk says. “This study was for kidney cancer, but the benefits of using 3D models for surgical

planning will translate to many other types of cancer operations, such as prostate, lung, liver and pancreas.”



To view a video of a 3D model, click on the link to this article at: uclahealth.org/physiciansupdate

The 3D model (left) provides surgeons with a better visualization of a person's anatomy, allowing them to see the depth and contour of the structure, as opposed to viewing a two-dimensional picture (right).

Images: UCLA Health

The UCLA research team analyzed data from 2,142 men with low- or intermediate-risk prostate cancer across multiple institutions who were treated with stereotactic body radiotherapy for prostate cancer between 2000 and 2012. The men were followed for a median of 6.9 years. Just over half of the men had low-risk disease (53 percent), 32 percent had less aggressive intermediate-risk disease, and 12 percent had a more aggressive form of intermediate-risk disease.

The recurrence rate for men with low-risk disease was 4.5 percent, the recurrence rate for the less aggressive intermediate risk was 8.6 percent, and the recurrence rate for the more aggressive intermediate-risk group was 14.9 percent. Overall, the recurrence rate for intermediate-risk disease was 10.2 percent. These are essentially identical to rates following more conventional forms of radiation, which are about 4 percent to 5 percent for low-risk disease and 10 percent to 15 percent for intermediate-risk disease.

The research team at the UCLA Jonsson Comprehensive Cancer Center had previously found that stereotactic body radiation therapy was more cost effective because of the fewer treatments involved. Other research has also suggested psychological benefits, such as less regret about undergoing treatment. The current study now provides long-term data regarding the safety and clinical efficacy of this approach.

Dr. Kishan says the data show that the majority of the men followed are free of prostate cancer seven years after treatment. He added that there was no evidence that this therapy caused worse toxicity in the long term. “In fact,” Dr. Kishan says, “we not only confirm that this method is both safe and effective, but we provide significant evidence that this could be a viable treatment option for men with low and intermediate risk of prostate cancer.”



For more information about kidney cancer programs at UCLA, go to: urology.ucla.edu/kidney-cancer-program

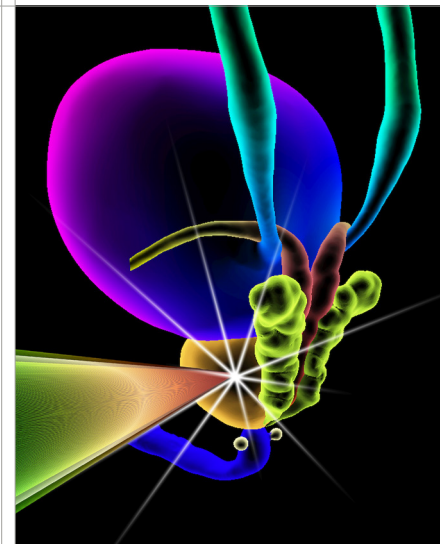


Illustration of radiotherapy for treatment of prostate cancer using an external beam. Radiotherapy focuses on the tumor site to disrupt and kill the cancer cells.

Image: Science Photo Library

Center works to identify children with genetic predisposition to cancer

STORY HIGHLIGHTS

A pioneering clinic at UCLA Mattel Children's Hospital is making a significant impact on the lives of children and their families with rare genetic conditions that predispose them to cancer.

The UCLA Pediatric Cancer Predisposition Clinic brings together oncologists, geneticists, genetic counselors and social workers to provide diagnostic genetic testing and counseling, as well as personalized screening protocols as needed.

A pioneering clinic at UCLA Mattel Children's Hospital is making a significant impact on the lives of children and their families with rare genetic conditions that predispose them to cancer, as well as those diagnosed with pediatric cancers that are potentially related to a rare genetic syndrome.

The UCLA Pediatric Cancer Predisposition Clinic was established in 2012, at a time when powerful new genetic testing technologies were first being implemented clinically at UCLA. This so-called next-generation DNA sequencing enabled, for the first time, comprehensive testing of all of the protein-coding regions of the genome to diagnose rare conditions and identify genetic predispositions.

"At the time, little was known about the utility of genetic testing in children with genetic syndromes that could predispose them to early cancers," says Julian A. Martinez, MD, PhD, a clinical geneticist and the center's codirector. "We believed it had potential value in that it would enable surveillance of patients with these predispositions to detect and treat the tumors early, as well as facilitating targeted treatments in patients already diagnosed with cancer based on the genetic cause identified."

That initial vision has borne out, Dr. Martinez notes, and the clinic's approach to patients

with cancer-predisposing genetic conditions or cancers resulting from genetic syndromes has become the international standard for how such patients should be evaluated and managed. The clinic's value has only grown with the continued advances in DNA sequencing technologies and the development of new treatments that target the specific genetic mutations underlying an individual patient's cancer.

The UCLA Pediatric Cancer Predisposition Clinic remains one of the few multidisciplinary efforts of its kind, notes Vivian Y. Chang, MD, MS, a pediatric hematologist-oncologist and codirector of the clinic. The clinic brings together oncologists, geneticists, genetic counselors and social workers to provide diagnostic genetic testing and counseling, as well as personalized screening protocols as needed. All cases are discussed at a weekly genomic board meeting that includes bioinformatics specialists and pathologists, as well as clinicians.

Most of the clinic's patients fall into one of two categories. The first are those who have already been diagnosed with a genetic syndrome associated with a high risk for developing a cancer. "My role as the oncologist is to educate these patients about their cancer risk and develop personalized cancer screening plans," Dr. Chang explains. "We know that if we catch these cancers early, it offers the best prognosis and the best treatment options. We can now utilize targeted treatment for patients who are identified to have specific genetic mutations, whereas in the past, we had no specific treatments or we used broad-stroke chemotherapy and/or radiation to kill cancer cells. This is how we envision personalized medicine in the future for everyone."

Dr. Chang has been a leader in developing surveillance guidelines for patients with underlying genetic syndromes that predispose to cancer risk, as part of an expert panel convened by

"With our state-of-the-art genetic testing, we can put an end to the diagnostic journey so that these families are no longer making their way through the medical system, trying to find answers. We are able to provide a medical home for these patients and a roadmap for what to expect, in addition to better-informed treatment."



Image: Science Photo Library

underlying genetic syndromes that predispose to cancer risk, as part of an expert panel convened by the American Association for Cancer Research. “With these genetic diagnoses that are this rare, it’s important to share data across centers,” she notes. “By doing so, we have developed evidence-based guidelines so that these patients can be treated in a standardized way.”

The second major population of patients seen at the clinic are children — and in some cases, adults — who have already been diagnosed with a cancer, but certain features of their presentation or family history suggest an underlying genetic cause. Often, Dr. Martinez notes, these patients have gone through what is commonly referred to as a diagnostic journey, presenting with multiple medical conditions that have eluded a unifying diagnosis. “With our state-of-the-art genetic testing, we can put an end to the diagnostic journey so that these families are no longer making their way through the medical system, trying to find answers,” Dr. Martinez says. “We are able to provide a medical home for these patients and a roadmap for what to expect, in addition to better-informed treatment.”

Ending the diagnostic journey brings multiple benefits, Dr. Martinez notes. For families, there is great psychological benefit to finding closure after a long, emotionally trying odyssey in search of an explanation for their child’s symptoms. That journey can include expensive and ultimately fruitless testing, at significant cost to both the families and the health care system. In some cases, the definitive diagnosis points to a condition that could affect other family members, who can then benefit from being tested and, if they test positive, being treated or more frequently screened, as appropriate.

Dr. Martinez says that roughly 10 percent of the pediatric cancer patients referred to the clinic have been found to have a well-documented genetic syndrome, and his team has described new syndromes along the way. Other centers that have followed the UCLA clinic’s approach have found, similarly, that about 10 percent of their pediatric cancer patients will have a known genetic disorder that can benefit from surveillance and personalized care.



For more information about the UCLA Pediatric Cancer Predisposition Clinic, email clinic manager Marcela Serrano at: MarcelaSerrano@mednet.ucla.edu

Roughly 10 percent of the pediatric cancer patients referred to the clinic have been found to have a well-documented genetic syndrome.

Adding ribociclib to hormone therapy extends lives of women with most common breast cancer

STORY HIGHLIGHTS

Among premenopausal women who received the combination therapy, the disease did not progress for an average of 23.8 months, compared to 13 months for those who received endocrine therapy and the placebo.

Results of the study with postmenopausal women demonstrated a statistically significant improvement in survival, with a 28 percent reduction in risk of death.

Two UCLA-led studies have found that using the drug ribociclib in combination with a common hormone therapy may help both pre- and postmenopausal women with the most common type of breast cancer live longer than if they only receive the hormone therapy. The studies' authors say the combination should become the first line of therapy.

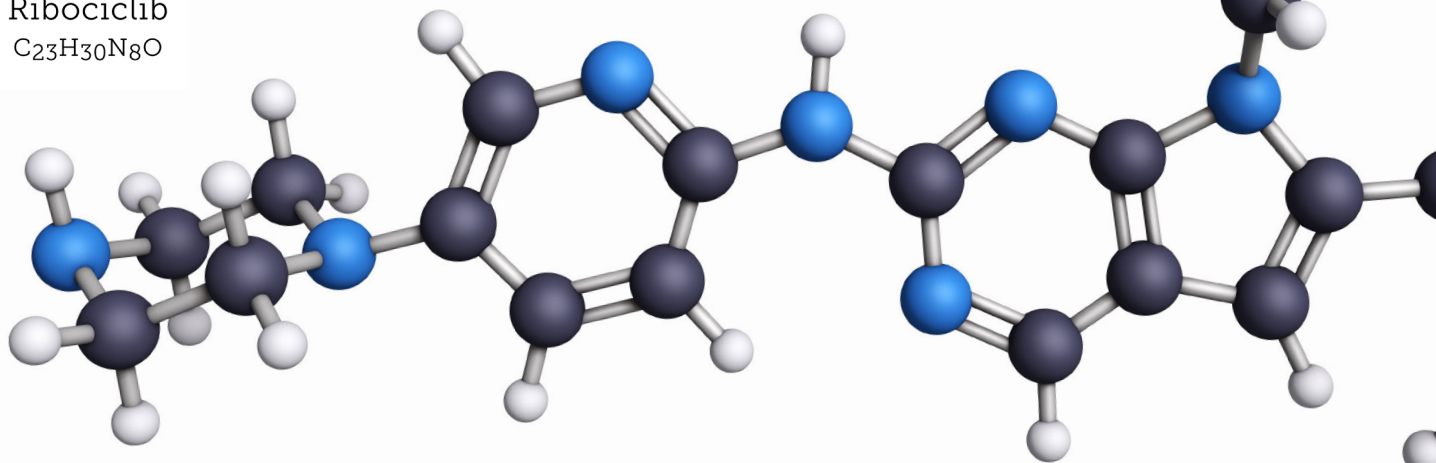
Ribociclib is a cyclin-dependent kinase inhibitor that works by blocking the activity of proteins called cyclin-dependent kinases 4 and 6 enzymes. These kinases are critical in promoting cell division and growth in both normal and cancer cells. One study involved 672 women aged 25 to 59 when the study began who had advanced hormone-receptor positive/HER2- (HR+/HER2-) breast cancer. Seventy percent of the women who took the combination therapy were alive after 42 months, compared to 46 percent of women who were treated with only the hormone therapy. The other study involved 726 postmenopausal women with advanced HR+/HER2- breast cancer, and included women who had not received prior endocrine therapy

as well as patients who were in the first-line or second-line setting. Results demonstrated a statistically significant improvement in survival with a 28 percent reduction in risk of death. At 42 months, the estimated rates of survival were 58 percent for the drug combination treatment and 46 percent for women who were treated with the hormone therapy alone.

The study of younger women who haven't gone through menopause "was unique," says Sara Hurvitz, MD, director of UCLA's Breast Cancer Clinical Research Program and medical director of the UCLA Jonsson Comprehensive Cancer Center Clinical Research Unit. "This is an important group to study since advanced breast cancer is the leading cause of cancer death in women 20 to 59, and the vast majority of breast cancer is hormone-receptor positive."

None of the women in the premenopausal study had been

Ribociclib
C₂₃H₃₀N₈O



Hormone therapy, also called endocrine therapy, is an essential part of treatment for hormone-receptor positive breast cancer, a form of the disease in which a woman's own hormones promote cancer growth.

previously treated with endocrine therapy for metastatic cancer. Half of the subjects were given hormone therapy and a placebo. The other half received hormone therapy in addition to ribociclib. In the postmenopausal study, the findings showed that the combination treatment is beneficial at the time of recurrence or after progression of disease in the second-line setting and, thus, endocrine therapy plus a cyclin-dependent kinase 4/6 (cdk-4/6) inhibitor should become the standard first- or second-line option in postmenopausal women with HR+/HER2- advanced breast cancer.

Hormone therapy, also called endocrine therapy, is an essential part of treatment for hormone-receptor positive breast cancer, a form of the disease in which a woman's own hormones promote cancer growth. Given as an oral medication, the therapy works by blocking or lowering the levels of estrogen production so cancer cells can't use them to grow and spread — but it eventually stops working in some women.

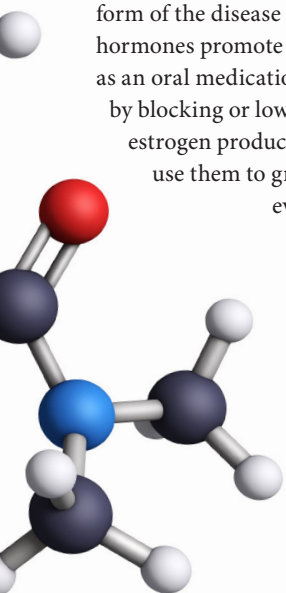


Image: Science Photo Library

Among women who received the combination therapy in the premenopausal study, the disease did not progress for an average of 23.8 months, compared to 13 months for those who received endocrine therapy and the placebo. “It’s great to see that we’re extending the length of someone’s life, not just the length of time their disease is controlled,” Dr. Hurvitz says. “Very few trials show an improvement in overall survival. That’s what is so phenomenal about the data.”

From 1976 to 2009, the incidence of advanced breast cancer among U.S. women under 40 increased an average of about 2 percent per year, a larger increase than for any other age group. In the mid-2000s, a team of Jonsson Cancer Center researchers led by Dennis Slamon, MD, PhD, director for clinical/translational research in the cancer center, were on the forefront of discovering that the cdk-4/6 inhibitors are effective in treating hormone receptor positive breast cancer. Their work ultimately helped lead to the FDA approval of ribociclib and two other related cdk-4/6 inhibitors to treat metastatic breast cancer.

“Many people had argued that the first type of treatment women with this type of metastatic cancer should receive is some other form of hormonal therapy and then wait to see if they respond to that treatment,” Dr. Slamon says. “But we found there’s a significant improvement in survival when you use the combination of ribociclib with hormone therapy as the first line of therapy. There now is absolutely no reason to wait to give women this treatment. This should be the new standard of care.”



For information about the Phase III clinical trial of ribociclib and enrollment, go to:
tinyurl.com/ribociclib



To read an abstract in the *Journal of Clinical Oncology* about the ribociclib-plus-endocrine therapy, go to:
tinyurl.com/ribociclib-abstract



To view a video about the study with Dr. Sara Hurvitz, go to:
tinyurl.com/hurvitz-video

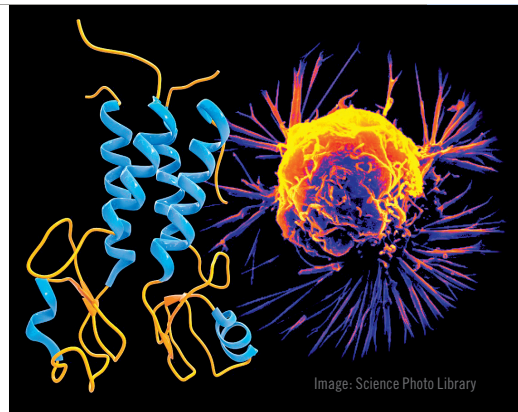


Image: Science Photo Library

BRCA initiative aims to increase access to testing

Women and men with the BRCA gene mutation have a greater risk of developing several types of cancers, including breast, ovarian and prostate, among others. It is estimated that 90 percent of carriers do not know they are at risk until someone in their family gets cancer.

“For every carrier we identify, 50 percent of that patient’s blood relatives will also be carriers,” says Beth Y. Karlan, MD, vice chair of women’s health research in the UCLA Department of Obstetrics and Gynecology and director of cancer population genetics at the Jonsson Comprehensive Cancer Center.

Dr. Karlan is principal investigator for a research initiative, BRCA Founder Outreach Study (BFOR), to develop a new model to increase access to BRCA genetic testing, at no cost to participants. Participants in the initiative, men and women, must be 25 years of age or older, have at least one grandparent of Ashkenazi Jewish heritage and should not have been previously tested. Ninety-five percent of American Jews are Ashkenazi, and Jews of Ashkenazi descent are 10 times more likely to carry the BRCA1 and BRCA2 inherited mutation than the rest of the population.

“Democratizing access to genetic testing provides knowledge that can reduce cancer risks and improve outcomes for those with a BRCA mutation,” Dr. Karlan says.



For more information or to refer a patient for enrollment, go to:
bforstudy.com

405 Hilgard Avenue
Box 956923
Los Angeles, CA 90095-6923



U.S. News & World Report's Best Hospital Survey ranks UCLA No. 1 in California and No. 6 in the nation.

David Geffen School of Medicine at UCLA ranks #6 in Research and #5 in Primary Care nationwide.



NONPROFIT
ORGANIZATION
U.S. POSTAGE

PAID

U C L A

**UCLA Health ranked
#1 in California
#6 in the Nation**
U.S. News & World Report

Physicians Update

FALL 2019

CHIEF OF COMMUNICATIONS
Rhonda Curry

CHIEF OF MARKETING
Tanya Andreadis

EDITOR
David Greenwald

CONTRIBUTOR
Dan Gordon
Denise Heady

MEDICAL EDITORS
Eve Glazier, MD
Johnese Spisso, MPA

DESIGN
Donenfeld & Associates

Putting U first keeps us first

At UCLA Health, we're proud to be ranked #1. According to *U.S. News & World Report's* annual best hospital rankings, UCLA Health is #1 in L.A. and #1 in California. We also happen to be #6 in the nation — we know this comes from putting patients first, with a culture that always strives to make health care the best it can be. With four hospitals and over 180 neighborhood locations, everything we do...begins with U.

 **SUBSCRIBE TO RECEIVE *PHYSICIANS UPDATE* ELECTRONICALLY**
uclahealth.org/physiciansupdate/subscribe

 **For more information about our UCLA physicians, go to:**
uclahealth.org/physiciandirectory



Copyright © 2019 by UCLA Health.
All rights reserved.

For inquiries about UCLA *Physicians Update*, contact UCLA Health Marketing Communications, Box 956923, Los Angeles, CA 90095-6923
uclahealth.org