University of
CINCINNATI
CANCER CENTER

University of Cincinnati • UC Health • Cincinnati Children's

2022 REPORT TO THE COMMUNITY

From the lab to the bedside, impacting cancer care around the world

In January 2020, the University of Cincinnati, UC Health and Cincinnati Children's came together to form the University of Cincinnati Cancer Center. While the founding entities remain focused on providing patient care and educating the next generation of oncologists, the University of Cincinnati Cancer Center unifies cancer research at the three entities under one umbrella. This provides us the opportunity to collectively focus our resources and research in specific areas where we can best achieve high-impact discoveries that contribute to our national cancer effort.

Over the past two years, we have made tremendous progress by:

- Refocusing our mission, vision and values, which will distinguish our institution and define how we serve patients
- Identifying core focus areas in three research programs across the three organizations
- Designating specific types of cancer where we will invest to become destination centers to provide care to patients from across the United States
- Recruiting nationally recognized leaders in areas of focus
- Developing 10 disease-based centers that integrate cutting-edge research, clinical trials and patient care

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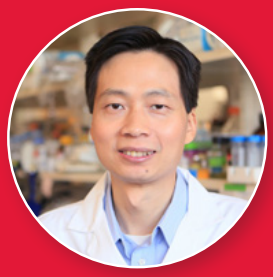
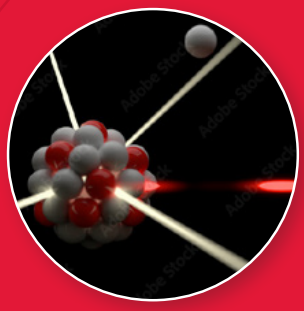
REPORT HIGHLIGHTS





PHOTOS COURTESY OF UNIVERSITY OF CINCINNATI FOUNDATION

CONNECTING to Conquer Cancer

To our community and readers of this report,

At the University of Cincinnati Cancer Center, our overwhelming priority is reducing the suffering and mortality associated with cancer in our community and beyond. We'll do this by making Cincinnati the smartest city in the world when it comes to cancer. That's a lofty statement but provides an inspirational vision when measured in outcomes. Being the smartest city means that we must understand how cancer develops and find ways to reduce occurrences to the lowest rate possible. And for those who develop cancer, we must continue to build the knowledge and means to treat it effectively so that those impacted can live long and healthy lives.

Achieving our vision requires a three-pronged approach: We must attack cancer at the molecular level in our laboratories, the individual level through patient care in our clinics and hospitals, and the community level with education, prevention and reduction initiatives.

The Cancer Center, which includes the resources and labs at the University of Cincinnati, UC Health, and Cincinnati Children's, supports research at each of these levels. In 2021, we designated specific areas we would pursue that take advantage of our unique strengths:

- **Basic Science Research: Cancer cell signaling and metabolism**
- **Clinical/Translational Research: Emerging therapies**
- **Population Science Research: Relationship between environmental exposures and cancer**

Each of these areas is critical to our goal of conquering cancer, and no one area can be overlooked or diminished. Just as importantly, we have to connect the talent and expertise in all three areas so that knowledge can flow from our researchers in the lab to our clinicians on the front line of care to our outreach and survivorship teams in the community and back again.

Little did we know when we announced the formation of the Cancer Center at the end of 2019 that the world was hurtling into a global pandemic, around-the-world lockdowns, and more than 1 million U.S. deaths over the next two years. Not the most auspicious time to launch such a major and complex project.

In hindsight, however, it was perhaps the most critical time to assemble and organize cancer research across our institutions. During the past two years, UC Health and Cincinnati Children's have remained focused on delivering patient care despite COVID-19 surges and lockdowns, while UC has innovated to continue providing world-class medical education in a virtual environment. Given these justifiable priorities, cancer research could have easily fallen by the wayside. Instead, the formation of the University of Cincinnati Cancer Center provided the structure to support sustained and targeted movement forward. You can see these connections at work in the stories throughout this report.

The coming years are going to be particularly fascinating in the field and will be significant in the trajectory of our cancer program. We are excited about the coming advancements in cancer understanding and management on the molecular level and are proud to be at the forefront.

Sincerely,

Syed A. Ahmad, MD
Co-Director, University of Cincinnati Cancer Center
The Hayden Family Endowed Chair for Cancer Research
Professor of Surgery
Chief, Division of Surgical Oncology

William L. Barrett, MD
Co-Director, University of Cincinnati Cancer Center
Professor and Chair, Radiation Oncology
Medical Director, Barrett Center for Cancer Prevention, Treatment and Research

PHOTOS COURTESY OF UC HEALTH

PHOTO COURTESY OF UNIVERSITY OF CINCINNATI

UNIVERSITY OF CINCINNATI CANCER CENTER IS CINCINNATI'S #1 PREFERRED CANCER CARE PROVIDER*

PHOTOS—LEFT: ©ADOBESTOCK.COM/NO-TE; RIGHT: COURTESY OF CINCINNATI CHILDREN'S

*NRC Health, Market Insights, Cincinnati-Middletown, FY20

PHOTOS—LEFT: COURTESY OF UC HEALTH; RIGHT: COURTESY OF UNIVERSITY OF CINCINNATI FOUNDATION

ROLE REVERSAL

UC breast cancer surgeon is also a breast cancer survivor

Beth Shaughnessy, MD, PhD, is a University of Cincinnati professor of surgery, UC Health breast cancer surgeon and co-director of the University of Cincinnati Cancer Center's Breast Cancer Disease Center. She is also a breast cancer survivor.

In January 2019, Dr. Shaughnessy felt a suspicious lump during a breast self-exam on Martin Luther King Jr. Day. She was alarmed but not surprised.

"I'd just turned 60 two weeks before," she says. "I told everyone my warranty had expired." She immediately texted her nurse, who scheduled her screening mammogram for the following week and ordered a diagnostic workup.

"The next day, I was back to work but going between patients and getting my own imaging," Dr. Shaughnessy says. "The mammogram showed nothing — it can happen with dense tissue — so I had an ultrasound. There they were: three additional suspicious masses, besides the one I felt."

She had a biopsy and diagnosis by the end of the day and scheduled her surgery for the following week. Being "in the business," Dr. Shaughnessy knows the who's who in breast cancer around the country, and she didn't hesitate moving forward at her home institution.

Surgery revealed more problems, including larger-than-expected tumors. Several of her lymph nodes also tested positive for cancer, and her tumors were found to have different "biologies," meaning they required different treatments. The team prepared for a full double mastectomy and after surgery, Dr. Shaughnessy had chemotherapy, proton therapy and reconstruction surgery.

Throughout it all, she didn't quit working, catching up on paperwork and submitting studies to scholarly journals. She just took lots of naps in between.

> *"The work doesn't stop," she says. "Deadlines don't care if you have cancer. It kept my mind off of everything."*

That go-getter attitude is nothing new for Dr. Shaughnessy. In addition to being a researcher, surgeon, wife, mom and general caregiver, she's involved in Susan G. Komen for the Cure; the Breast Cancer Registry of Greater Cincinnati; and national organizations like the Association of Women Surgeons, for which she currently serves as president.

Yet, she still takes the time to hold each patient's hand as they drift off to sleep before surgery. "I don't want them to be anxious or scared," she says. "With my patients, I always tried to prepare them that the steps in their care plan might change," she says. "Now, I totally understand what they were going through when that did happen. Since I always figured this would happen to me, I'd already created my own algorithm to treatment; but I had so many surprises along the way."

Beth Shaughnessy, MD, PhD

PHOTO COURTESY OF UNIVERSITY OF CINCINNATI

ADVANCING CANCER CARE

University of Cincinnati Cancer Center BY THE NUMBERS

UNIVERSITY OF CINCINNATI CANCER CENTER

Data provided by:

- University of Cincinnati
- UC Health
- Cincinnati Children's

10 Multidisciplinary Disease Centers

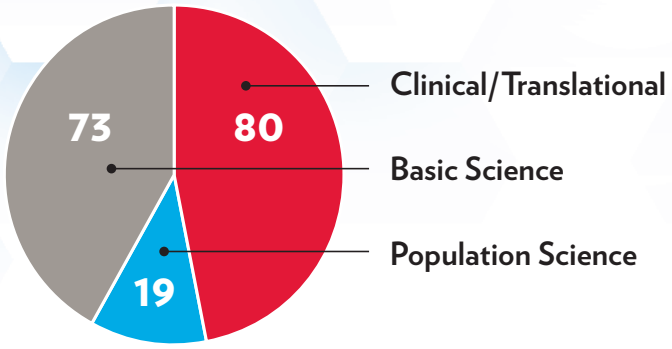
1. Blood & Bone Marrow Transplant
2. Brain & Nervous System
3. Breast
4. Gastrointestinal
5. Genitourinary
6. Gynecologic
7. Head & Neck
8. Lung
9. Ocular
10. Skin Cancer & Sarcoma

16 Cincinnati Children's Centers & Programs

- Advanced Cancer Therapies
- Brain Tumor
- Cancer Survivorship
- Cardio-Oncology
- Comprehensive Fertility Care & Preservation
- Hereditary Cancer
- Kidney Tumor
- Leukemia & Lymphoma
- Liver Tumor
- Neuroblastoma Advanced Therapies
- Neurofibromatosis
- Pediatric Cancer Rehabilitation
- Proton Therapy
- Retinoblastoma
- Sarcoma
- Young Adult Cancer

Cancer Center Members

172 members representing 7 UC Colleges and Cincinnati Children's:



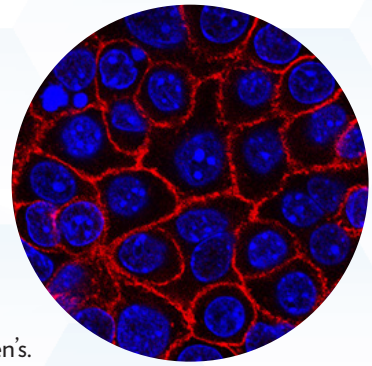
2019 PATIENT CARE

3,888
Analytic cases (patients)

34
Types of cancer treated

TOP 10 Most Common Cancer Sites

1. Breast	454	6. Melanoma, Skin	169
2. Lung	393	7. Thyroid	153
3. Prostate	382	8. Colon	149
4. Lip, Oral Cavity & Pharynx	267	9. Liver	130
5. Brain & Nervous System*	177	10. Pancreas	128



*Cancer of the brain and nervous system was the No. 1 type of cancer for patients at Cincinnati Children's.

2021 CLINICAL TRIALS

362 interventional clinical trials open to accrual

814 patients participated in a clinical trial

4.9% estimated accrual rate to interventional clinic trials

20.2% estimated overall clinical trial accrual rate

PHOTO COURTESY OF UNIVERSITY OF CINCINNATI FOUNDATION

2021 FUNDING

81
Active research grants

$18.2M
Research funding

2021 Research Grants (Direct Costs)

Basic Science	Clinical/Translational*	Population Science
52 awards	17 awards	8 awards
$10.6 million	$5.3 million	$1.5 million

*Figures above do not include clinical trial grants. An additional 4 training grants for $0.09M are not listed.

COMMUNITY SUPPORT

$12.63M Donated

OVERCOMING RESISTANCE

Researchers identify gene that helps thwart breast cancer therapy

As researchers continue to develop new cancer treatments, cancer cells continue to find their way around them. A particularly aggressive subset of breast cancer express a protein called HER2, which accounts for about 20% of all breast cancer cases, and is especially adept at finding new pathways to survive.

University of Cincinnati Cancer Center researchers have discovered one reason why.

Using a specialized mouse model they developed, the researchers found that overexpression of the MED1 gene promotes tumor growth, stem cell formation, metastasis and resistance to anti-HER2 therapy in HER2+ breast cancer.

"What we show is not only is MED1 there with HER2, but it's doing something very important together in the tumor development process," says Xiaoting Zhang, PhD, professor and Thomas Boat Endowed Chair in UC's Department of Cancer Biology, director of the Breast Cancer Research Program and a member of the Cancer Center. The research was conducted in Dr. Zhang's lab and published in the March 9, 2021, online edition of *Cell Reports*.

MED1 is located within the same chromosomal region where HER2 and a few other genes are frequently multiplied in breast cancer. Earlier studies by Dr. Zhang's lab showed a correlation between MED1 and HER2 overexpression in breast cancer as well; however, it was unclear what role MED1 played.

"It wasn't known whether it was simply a passenger gene, and let HER2 do the driving, or if it actually collaborated with the HER2 gene to play a significant role in the growth, spread, and treatment resistance of this type of breast cancer," Dr. Zhang says.

Gene collaboration

To investigate whether HER2 and MED1 were working together, the team created an animal model with an overproduction of both genes. They discovered that MED1 overexpression promotes epithelial-to-mesenchymal transition (EMT), cancer stem cell (CSC) formation and resistance to anti-HER2 therapy of HER2+ tumors. In addition to HER2+ breast cancer, MED1 also has previously been found to play a role in treatment resistance in estrogen receptor-positive breast cancer.

The work also culminated in the creation of a more clinically relevant HER2+/MED1+ tumor model that has important implications in both basic and translational research.

"This new animal model we created has a wide range of future applications and will allow us to continue to study basic molecular mechanisms of this type of breast cancer and to further find and test new therapies," says Yongguang Yang, PhD, first author on the study and a research associate in Dr. Zhang's lab.

Targeting MED1

Dr. Zhang and his team have developed a recently patented RNA nanotherapy targeting MED1 and have observed highly desirable outcomes in preclinical studies. "Our findings suggest that targeting MED1, alone and in combination with current therapies, could be a safer and more effective treatment strategy for nearly 90% of breast cancer patients," Dr. Zhang says.

Supported by the Cancer Center's focus on developing technologies and tools to enhance patient outcomes, Dr. Zhang works closely with colleagues providing care to patients.

"I am very fortunate to be able to work with Dr. Elyse Lower and other colleagues who provide the clinical point of view with firsthand knowledge of the unmet needs of patients," he says. "When we can combine lab research focus with clinical interests, our research could make an even bigger impact and the treatment we developed will be especially clinically relevant."

PHOTO COURTESY OF UNIVERSITY OF CINCINNATI

Playing to Your STRENGTHS

National collaboration fuels discoveries into lipidomics

Cancer cells require a lot of energy to reproduce quickly. To do so, they rely on lipids, fats in the body, to supply that energy.

Researchers at the University of Cincinnati Cancer Center are collaborating with investigators at other cancer centers across the country to study this complex process, leading to two major discoveries in the past two years. The first study uncovered a novel target involved in the role of lipid metabolism in glioblastoma. The second project, now in Phase 2 clinical trials, resulted in the development of a novel therapy to stop KRAS-positive lung cancer cells from producing protective lipids.

This work is being led by Pier Paolo Scaglioni, MD, professor and Herbert F. Koch Endowed Chair in the Division of Hematology Oncology in the UC College of Medicine, associate director for translational research in the Cancer Center and a UC Health oncologist; and Caterina Bartolacci, PhD, and Cristina Andreani, PhD, research scientists in the UC College of Medicine.

Trading expertise to treat glioblastoma

Working with researchers at the University of Texas MD Anderson Cancer Center and the University of Michigan, the University of Cincinnati Cancer Center team studied the role of lipid metabolism in glioblastoma (GBM). Using the center's mass spectrometry — one of only three labs in the U.S. with this technology — the researchers uncovered a novel target for drug development. The study was published in the journal *Cancer Discovery*.

The researchers identified that GBM is highly dependent on medium-chain acyl-CoA dehydrogenase (MCAD) to prevent medium-chain fatty acids (MCFAs) from accumulating, which poisons the cancer cells. While blocking MCAD appears to be detrimental to GBM cells, normal brain cells were not affected by loss of the enzyme, suggesting that targeting MCAD could be an effective therapy.

Pier Paolo Scaglioni, MD, speaking with Bryan Hambley, MD, MPH, and Tahir Latif, MBBS, MBA

PHOTO COURTESY OF UC HEALTH

Blocking lipid creation leads to lung cancer cell death

In a separate initiative, the University of Cincinnati Cancer Center team and researchers from University of Texas Southwestern (UTSW) are studying the role of lipids in lung cancer.

They found that KRAS-positive lung cancer cells prefer to make their own fats rather than importing them from the nearby environment. Working in mouse models, the team used a novel drug to block the protein responsible for fatty acid synthesis. As predicted, when the cells couldn't make fats, growth was hampered and the cancer cells died.

The researchers are now conducting a Phase 2 clinical trial of the drug.

"Collaborating with UT Southwestern researchers, who are worldwide experts in the field of lipidomics, gave us more technical expertise and new perspectives," Dr. Bartolacci says.

"We can run the mass spectrometry-based studies on lipids, so that opens up collaborations with other investigators that can provide other types of expertise," Dr. Scaglioni says. "It elevates your game, and other people want to play with you."

A University of Cincinnati Cancer Center-led study identified the first nonenergetic role of fatty acid metabolism in cancer.

GUT CHECK

Bacteria in the gut microbiome could be key to reducing C. difficile infections in chemotherapy patients

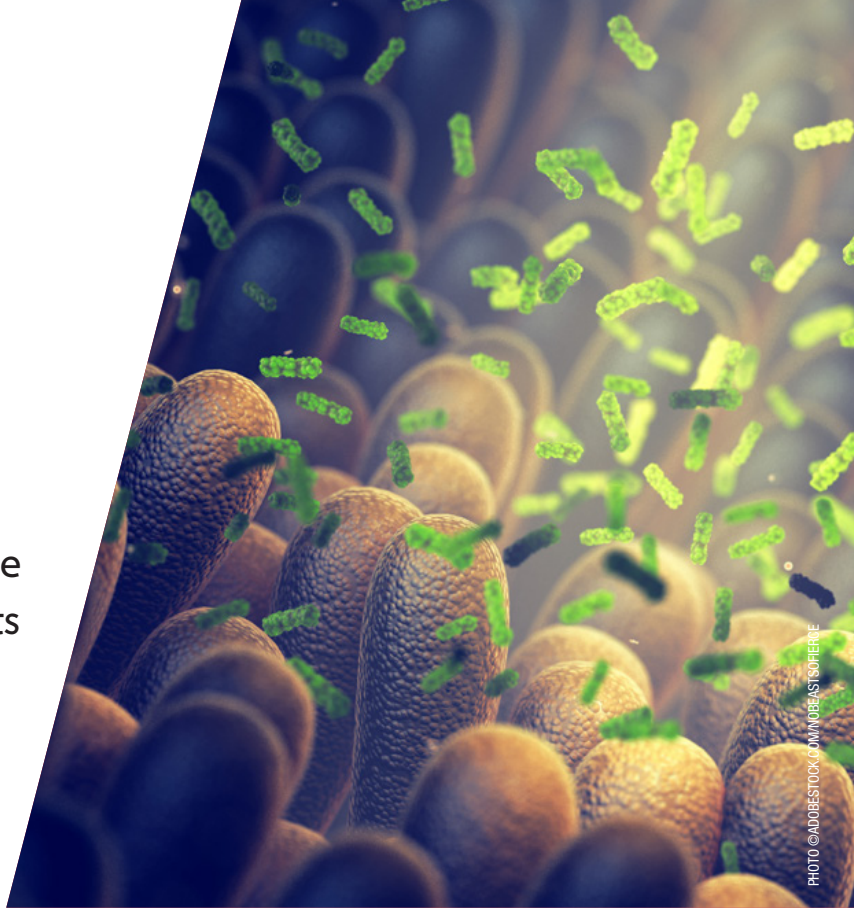


PHOTO ©ADOBESTOCK.COM/DEBASTSOHERBE

More than 20% of U.S. adults receiving chemotherapy every year will contract a C. difficile infection, making them significantly more likely to die. Senu Apewokin, MD, an associate professor in the UC College of Medicine and a UC Health infectious diseases specialist, believes the problem — and the solution — may lie in the gut microbiome.

Dr. Apewokin and his team are investigating how cancer treatment response is impacted by a person's unique gut flora, microorganisms such as bacteria that live in the digestive tract and act as another organ crucial to health.

"The fact that I'm an infectious disease physician, but funding for my lab comes from the National Cancer Institute, to me is a testament of how those connections have been recognized," says Dr. Apewokin, a University of Cincinnati Cancer Center member.

The difficult problem of C. difficile

In patients undergoing intense chemotherapy, complications often occur in the gut and respiratory system because both are lined with cells that divide rapidly like cancer cells. Most cancer drugs affect these cells, creating an inflammatory response. Dr. Apewokin's findings could help determine if some C. difficile infections in patients undergoing chemotherapy are chemotherapy-induced and thus require unique considerations.

Senu Apewokin, MD

"A lot of the complications that people receiving chemotherapy experience are infection-related," he says. "If we can treat these infections or complications, it probably would move the needle in terms of better outcomes and better mortality numbers."

Measuring the microbiome

Dr. Apewokin's lab is also exploring how the gut microbiome impacts chemotherapy drug metabolism. Microorganisms in the gut control enzymes that metabolize these drugs, either speeding up or slowing down the process. The rate of metabolism can dramatically change the amount of exposure one person gets to a drug, compared to a person getting the same dose. Being able to analyze a person's unique gut microbiome would allow physicians to manipulate it to make cancer treatments more effective, Dr. Apewokin explains.

Dr. Apewokin's lab has developed a simple test to measure a person's microbiome that is similar to a pulse oximeter. "Changes in pulse ox can affect lung health," he says. "We don't have the equivalent in the gut yet, but my lab has pioneered technology that is promising and we're working on trying to get an equivalent to that measurement tool."

PHOTO COURTESY OF UNIVERSITY OF CINCINNATI

LOOKING FORWARD

Renowned leukemia researcher named University of Cincinnati Gordon and Helen Hughes Taylor Endowed Chair and professor of internal medicine

When John C. Byrd, MD, joined the University of Cincinnati in mid-2021, he recognized the strengths of the University of Cincinnati Cancer Center and the role he would assume. But what really spurred his decision was the vision of what is to come.

At The Ohio State University, Dr. Byrd was the D. Warren Brown Chair of Leukemia Research, director of the Clara Bloomfield Center for Prognosis in Myeloid Leukemia, and senior advisor for cancer experimental therapeutics at the Arthur G. James Cancer Hospital and Richard J. Solove Research Institute.

"Coming here was 150% a 'go,'" says Dr. Byrd, the Gordon and Helen Hughes Taylor Endowed Chair and professor in the Department of Internal Medicine in the UC College of Medicine, and a UC Health oncologist. "I was able to see what phenomenal cancer leadership is able to accomplish." What excites Dr. Byrd is a unified vision across the university, UC Health, Cincinnati Children's and community leadership to build a comprehensive cancer program.

What really made the appointment a triumph was Dr. Byrd's renowned scientific research background and his exceptional clinical care. Dr. Byrd draws patients from across the country who are seeking expertise and excellence in the treatment of chronic lymphocytic leukemia (CLL) and acute myeloid leukemia (AML). He is a recognized biomedical researcher focused on developing novel targeted therapies and has been honored with multiple national awards recognizing the impact of his work. Dr. Byrd has been continuously funded by the National Institutes of Health (NIH) for more than 20 years and has published more than 550 scientific peer-reviewed papers. He is one of the most cited people in the world of biomedical sciences. The Leukemia & Lymphoma Society calls him a world-renowned scientist. His clinical care is recognized as exceptional, resulting in his election to Best Doctors in America® from 2005-2021.

Building a leukemia center of excellence

As the University of Cincinnati Cancer Center continues to grow, it has committed to becoming a leukemia destination program that will draw patients from around the country. Several of the critical components already exist, including the Hoxworth Blood Center; an internationally recognized leader in transfusion and cellular therapy medicine led by Jose Cancelas, MD, PhD; a strong pediatric basic, translational and clinical program at Cincinnati Children's; and a dedicated team that specializes in treating blood cancers in the UC Division of Hematology-Oncology.

"There is a very, very big commitment to growing the cancer program here," Dr. Byrd says. "Our hope over the next five years is to build something very special for patients in Cincinnati and beyond."

As part of its plan to build an exceptional leukemia and blood cancer program, the University of Cincinnati is renovating a new space that will support a dedicated Phase I clinical trial unit, a dedicated blood cancer clinic, an inpatient unit for blood cancer and cellular therapy, and a 24/7 infusion center to facilitate effective inpatient-outpatient management. Additional areas will be designated for translational and fundamental blood cancer research and integrative medicine. Finally, there are hotel-type rooms located within the building that will be available for outpatients who require close observation but not inpatient care. The integration of inpatient-outpatient care is truly revolutionary and was a major attraction to Dr. Byrd joining the University of Cincinnati Cancer Center team.

"Our goal is to increase the number of first-in-human clinical trials with new targeted drugs to provide access very early to patients," Dr. Byrd says. "This type of unit attracts the pharmaceutical companies with the best drugs that ultimately lead to therapies that really impact patients' lives."

Dr. Byrd has focused his research on translational immune and molecular pharmacology in treating chronic lymphocytic leukemia and acute myeloid leukemia. His work with ibrutinib (Imbruvica®) was transformative in eliminating the use of chemotherapy in most patients with CLL. Dr. Byrd is currently working to identify genomic-specific targeted therapies for AML as one of the national leaders of a multicenter precision medicine trial with the Leukemia & Lymphoma Society (Beat AML). Participation in this trial will help provide new therapies to patients with leukemia in Cincinnati. (See "Beating Acute Myeloid Leukemia" on page 17.)

John C. Byrd, MD, and Ola Elgamal, PhD

PHOTO COURTESY OF UNIVERSITY OF CINCINNATI FOUNDATION

Dr. Byrd is an active, elected member of several honorary societies, including:

- Association of American Physicians
- American Society for Clinical Investigation
- Henry Kunkel Society
- Fellow, American Association for the Advancement of Science
- Fellow, American College of Physicians

Dr. Byrd has received multiple national awards for the impact of his work:

- Rai-Binet Lifetime Achievement Award from the International Workshop for CLL
- Leukemia & Lymphoma Society Return of the Child Award
- American Association for Cancer Research Joseph H. Burchenal Memorial Award for Outstanding Achievement in Clinical Cancer Research
- American Society of Hematology William Dameshek Award
- American Society of Hematology Emil J. Freireich Award
- William Crosby Research Award from the United States Army

Small Incisions, BIG BENEFITS

Robotic surgery could reduce risk of cancer recurrence

Robotic surgery was first introduced as a minimally invasive technique for treating prostate cancer just over 15 years ago. Today, University of Cincinnati Cancer Center oncologic surgeons are using robotic surgery for even the most complex procedures, including cystectomies, Whipples, liver resections and esophagectomies.

Abhinav Sidana, MD, MPH

Our urological surgeons now perform nine out of 10 cancer surgeries robotically, says Abhinav Sidana, MD, MPH, associate professor of surgery and director of urologic oncology. That includes radical cystectomy, an open procedure for bladder cancer with high complication risks. Performing the procedure robotically leads to less blood loss, lower risk of complications, shorter hospital stays and a quicker recovery.

The benefits of robotic surgery may extend further. Researchers are studying the implications of robotic surgery for inflammatory markers, says Greg Wilson, MD, assistant professor of clinical surgery at the UC College of Medicine and a surgical oncologist at UC Health. "There's so much less stress to the body with some of these minimally invasive approaches," he says. "That may be beneficial not only to the patient's recovery, but also for potential cancer recurrences."

Robotic surgery for urological cancers

UC urology surgeons now perform more than 200 robotic surgeries annually. "With our robotics skill set, technology and technique, we are doing more than 90% of our oncology cases robotically; and I think that number will keep getting better and better," Dr. Sidana says.

In addition to cystectomies, University of Cincinnati Cancer Center surgeons can perform robotic removal of complex kidney tumors, including cases where the kidney cancer has moved into big blood vessels going toward the heart, Dr. Sidana says. Surgeons are also using a new technique called enucleation, where they "scoop" out the tumor versus cutting it out.

Dr. Sidana predicts that single-port robotic surgery, performed through one incision versus up to seven, will become more common as the surgeons continue to evolve the technique. Many robotic surgeries in the near future also might be performed

PHOTO COURTESY OF UNIVERSITY OF CINCINNATI

University of Cincinnati Cancer Center performs 90% of urological oncology surgeries with minimally invasive techniques and offers the region's only robotic GI procedures, including the Whipple procedure for pancreatic cancer.

Greg Wilson, MD, the region's only fellowship trained robotic GI surgeon, meets with a patient.

as outpatient surgery rather than requiring an overnight stay, he says.

Expanding the use of robotic surgery

A similar evolution is happening for gastrointestinal (GI) cancers. As the region's only fellowship-trained robotic GI surgeon, Dr. Wilson is unique in performing the robotic Whipple procedure used to treat pancreatic cancer.

"It's probably one of the more complex abdominal operations a person can undergo," he says. "There's a lot of fine sewing, small needles, difficult angles. It initially was very challenging to do minimally invasively. But as the robotic approach matured, we can now do the surgery the exact same way it would be done in a traditional open approach."

In addition to the Whipple procedure, Dr. Wilson is performing robotic esophagectomy, gastrectomy, liver resections, and complex bile duct resections and reconstructions.

PHOTO COURTESY OF UC HEALTH

Throughout her treatment, including participating in a clinical trial, Ginny Wiltse continued her work obtaining grants to aid development in Madagascar. Shown here (right) with Dr. Wise-Draper.

PHOTO COURTESY OF UC HEALTH

Stunning Recovery

Unexpected outcome spurs clinical trial for rare cancer

For most people, a diagnosis of an incurable cancer would seem frightening and hopeless. But for Ginny Wiltse, it was an opportunity to give hope to others in the process.

In June 2014, Ginny was diagnosed with an aggressive squamous cell carcinoma of the tongue. The cancer would eventually spread to her neck even after radiation therapy.

"Ginny always remained positive, no matter the news I had to deliver, and was always willing to try something new," says Trisha Wise-Draper, MD, PhD, a UC Health head and neck cancer subspecialist who cared for Ginny. After her cancer failed to respond to an immunotherapy drug, Dr. Wise-Draper started Ginny on cetuximab, an EGFR monoclonal antibody drug that normally has a 10-14% response rate. That didn't show much promise either and was leading to some side effects, so Dr. Wise-Draper switched her back to the immunotherapy drug. Then, all of a sudden, her tumor started disappearing.

"When you use antibody drugs, they don't get out of your system quickly," Dr. Wise-Draper explains. "So when you switch to another type of drug, you're actually using both at the same time."

For Ginny, that combination resulted in a stunning recovery. For the University of Cincinnati Cancer Center, it led to testing the treatment protocol to see if it can help other patients.

"Her unprecedented response to two therapies used in close succession resulted in what some would call a miracle," Dr. Wise-Draper says. "Her outcome led to the development of an investigator-initiated clinical trial that is now open to patients with her type of cancer so others may benefit. Ginny's positive outlook allowed us to make such a discovery."

COVID-19 and Cancer

Nearly two years into the pandemic, researchers across the globe are still trying to comprehend COVID-19 and how the virus affects all kinds of people — including those who are immunocompromised. In 2020, the University of Cincinnati Cancer Center joined a consortium of more than 100 cancer centers and other organizations looking for connections between cancer and COVID-19. What they found is that patients with COVID-19 had different outcomes to different types of cancer treatments.

Patients on certain therapies, including chemotherapy and especially B-cell depleting antibody therapies, had up to 50% mortality if they contracted COVID-19, says Trisha Wise-Draper, MD, PhD, medical director of the Cancer Center's Clinical Trials Office, who oversaw the local arm of the study. "In addition to not being able to fight COVID-19, they also were not able to develop an antibody response to the vaccination, so those patients were uniquely susceptible both to infection as well as not being protected by vaccination."

University of Cincinnati Cancer Center researchers also examined how checkpoint inhibitor immunotherapies might affect the immune cells of patients with both COVID-19 and cancer. They found that patients receiving the immunotherapy alone did not have bad outcomes. However, COVID-19-positive cancer patients receiving the immunotherapy in combination with immune-depleting drugs had worse outcomes in hospitalization, ICU admittances and increased mortality rate.

The study "helps us understand if certain types of therapy prevent infection or, if on the other hand, therapy should be postponed in cancer patients already infected with COVID-19 to prevent complications," says Dr. Wise-Draper, who is also an associate professor in the UC College of Medicine, a UC Health physician and co-leader of the Head and Neck multidisciplinary disease center.

Progress despite the pandemic

In addition to understanding what treatments were the safest, she says UC staff also faced the challenge of simply treating patients. "Early in the pandemic, there were definitely patients not coming to get things checked out when they should have because they were so fearful of the virus," she says. "As a result, we were having a lot of later diagnoses and some surgeries were pushed off because of hospital volume."

The pandemic also affected the Cancer Center's research capabilities. "Clinical trials were stop-and-go, and keeping staff healthy and engaged was challenging," she says, but added that the struggles also forced the team to be innovative to keep clinical trials moving forward. Staff, for instance, used remote options to take care of regulatory processing and quality control, and monitoring of studies was set up through secure remote access to electronic medical records (EMRs).

Trisha Wise-Draper, MD, PhD; Rowena Schwartz, pharmacist; and Alie Match, dietitian

PHOTO COURTESY OF UC HEALTH

BEATING Acute Myeloid Leukemia

Acute myeloid leukemia (AML) is called acute because it's a cancer that progresses very rapidly. It's also very lethal. Only about one in four patients who develop AML survive five years after diagnosis, according to the Leukemia & Lymphoma Society. But that outlook is growing brighter with the development of drugs that precisely target the genetic mutations that cause AML to thrive.

The University of Cincinnati Cancer Center is one of 16 institutions nationally working to discover which of these drugs is most effective. The center is part of the Leukemia & Lymphoma Society's Beat AML® master clinical trial, the first collaborative precision medicine clinical trial in a blood cancer. John C. Byrd, MD, chair of the Department of Internal Medicine at the UC College of Medicine, is the national chief medical officer for the trial and oversees the program across all sites.

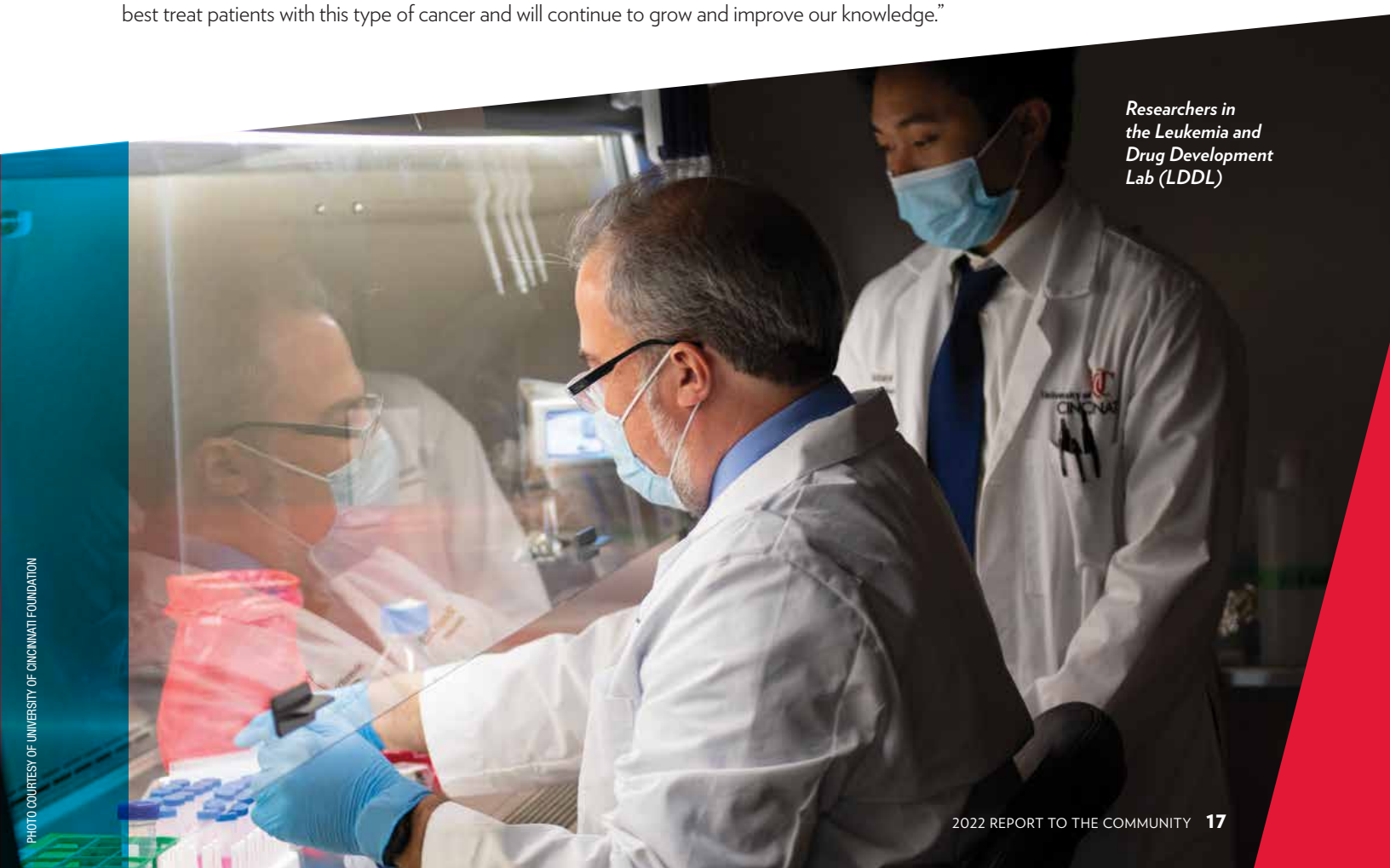
In the trial, researchers are using advanced genomic technology to identify patients' cancer-driving genetic mutations within seven days of initial diagnosis, and then match the patients to the most promising targeted treatment. Unlike many clinical trials that are open only to patients with advanced cancer, the Beat AML trial enrolls patients who are newly diagnosed to try to stop the cancer before it advances.

"This is not a one-size-fits-all approach to treatment, and it's not really one single trial; we are testing multiple therapies in multiple study arms at the same time to determine what does and does not work for patients," says Emily Curran, MD, an assistant professor in the UC College of Medicine and a UC Health oncologist who leads the trial locally. "The beauty of this method is that we are constantly learning how to best treat patients with this type of cancer and will continue to grow and improve our knowledge."

John C. Byrd, MD

Emily Curran, MD

BYRD PHOTO COURTESY OF UNIVERSITY OF CINCINNATI FOUNDATION
CURRAN PHOTO COURTESY OF UC HEALTH



Researchers in the Leukemia and Drug Development Lab (LDDL)

PHOTO COURTESY OF UNIVERSITY OF CINCINNATI FOUNDATION

TARGETING a Killer

Cancer center researcher leads national trial to stop the nation's most deadly and elusive cancer

Pancreatic cancer is the world's deadliest cancer, killing 80% of its victims in the first year and 94% within six years. Davendra Sohal, MD, MPH, an associate professor in the UC College of Medicine, associate director of clinical/translational research at the University of Cincinnati Cancer Center and experimental therapeutics and clinic medical director at UC Health, is intent on taming this killer.

"Pancreatic cancer is one of the deadliest cancers, and we have taken it on. We will keep going until we find cures," says Dr. Sohal.

Dr. Sohal is leading a national trial investigating whether a drug used for other types of cancer might work to stop metastatic pancreatic cancer. In fall 2020, Dr. Sohal received a $1.9 million Food and Drug Administration orphan drug grant to study a therapy that targets a small molecule in cancer known as AKT, which has been found to play a role in helping cancer cells survive and form tumors. The drug has shown promise in treating lung and uterine cancer — and Dr. Sohal believes it could have similar benefits for pancreatic cancer.

Putting UC research on the map

The clinical trial, led by the University of Cincinnati Cancer Center, is currently being conducted in collaboration with Massachusetts General Hospital and the University of Kansas. It is open to patients with Stage 4 metastatic pancreatic cancer.

"This was one of the first clinical research grants from the federal government for a clinical trial at UC," Dr. Sohal says. "That puts us on the national map for pancreatic cancer research. It's also a collaboration with a European pharmaceutical company, which puts us on the international map for pancreas cancer research."

Connections and collaborations expand research reach

Dr. Sohal's multidisciplinary collaboration with UC surgeons, oncologists and laboratory research partners is considered translational, or research that goes from the lab to the bedside and back again. Samples from patients in the trial are sent to multiple UC labs. "They do extensive cutting-edge research on those samples to try to understand why the cancer is or is not responding to treatment," he says.

Partnering with other research institutions is also advancing the cause, Dr. Sohal says. "It allows us to expand our reach so we can get more patients on these trials quicker and get an answer quicker. We also gain knowledge from the way others do things."

Davendra Sohal, MD, MPH

PHOTOS COURTESY OF UC HEALTH

6

After evaluation by more than 90 rare disease and clinical trial experts on scientific and technical merit, the University of Cincinnati Cancer Center-led national clinical trial was one of just six grants awarded by the FDA.

Davendra Sohal, MD, MPH; Sandra L. Starnes, MD; and Milton T. Smith, MD

10 Years of Supporting Pancreatic Cancer Research

Experiencing personal losses due to pancreatic cancer bonded the founders of two Cincinnati organizations and led to a partnership that has provided more than $1 million to help advance pancreatic cancer research at the University of Cincinnati Cancer Center. In 2021, GIVEHOPE and BSI Engineering celebrated 10 years of giving to this cause.

"What GIVEHOPE and BSI have accomplished is truly unique," says Syed Ahmad, MD, co-director of the University of Cincinnati Cancer Center. Their support was essential in "virtually building our pancreatic cancer research operation from the ground up. It's an incredible partnership that we have with GIVEHOPE and BSI, and we're extremely grateful for their vision."

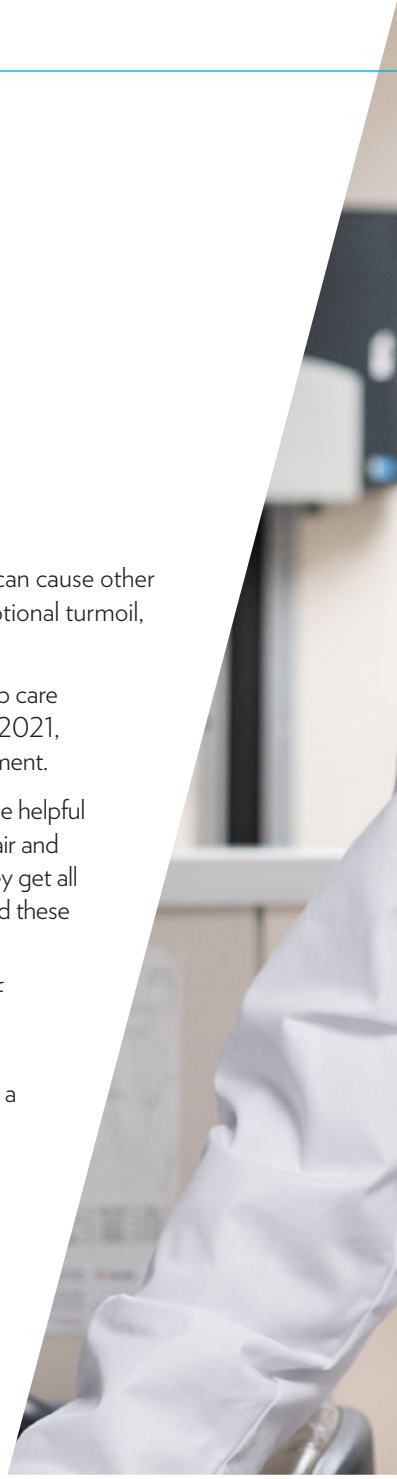
GIVEHOPE and BSI funding has supported multiple pilot research projects at the Cancer Center. The funds are awarded to investigators studying the causes, disease path and treatment for pancreatic cancer, and are a key pipeline for early stage research that can lead to national funding and clinical trials.

PHOTO COURTESY OF UNIVERSITY OF CINCINNATI FOUNDATION

Syed Ahmad, MD; Jenny Phillips, vice president of GIVEHOPE; Nick Long, principal and project manager at BSI Engineering and secretary of GIVEHOPE; Susan Henry, GIVEHOPE board member

COMBINING FORCES

New wellness clinic integrates multiple disciplines to provide whole person care



Like every war, the battle against cancer doesn't affect only the enemy. The disease and its treatment can cause other immediate and long-term fallout. People diagnosed with cancer can suffer treatment side effects, emotional turmoil, increased risk of treatment-related health risks, and an increased risk of secondary cancers.

The University of Cincinnati Cancer Center has united the forces of integrative medicine and survivorship care to address the consequences of treatment side effects. The Cancer Wellness Clinic, opened in February 2021, combines the two disciplines to help manage these issues for patients, both during and after cancer treatment.

"Our job as an academic health center is to bring forward every therapy and treatment that we know can be helpful to cancer patients," says Sian Cotton, PhD, research professor and Turner Farm Foundation Endowed Chair and director of the UC Center for Integrative Health and Wellness. "They should have a place to go where they get all of the conventional treatments and all of the supportive services they need at the same point of care — and these teams should work together."

The Cancer Wellness Clinic is co-led by Mladen Golubic, MD, PhD, a professor in the UC College of Medicine, medical director of the UC Center for Integrative Health and Wellness at UC Health and a UC Health physician; and Melissa Erickson, MD, an adjunct assistant professor in the UC College of Medicine, medical director of the Cancer Center's Survivorship and Supportive Services program and a UC Health physician. Providers in three disciplines coordinate services to manage patient issues:

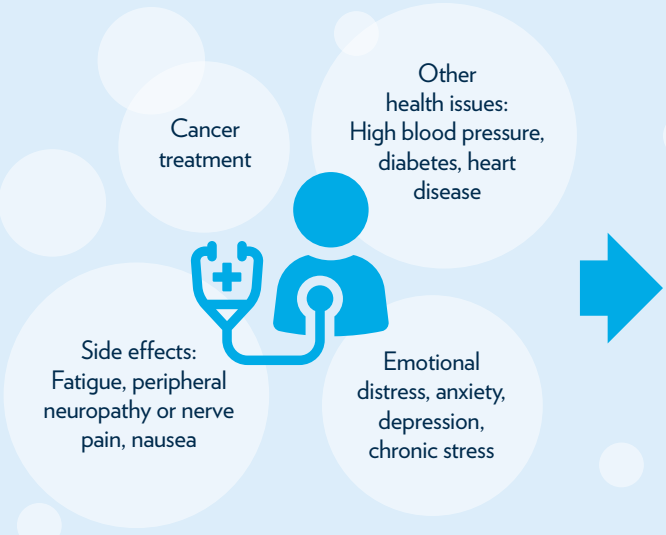
- **Primary care** to address coexisting or new noncancer conditions, such as high blood pressure or diabetes
- **Integrative therapies**, such as acupuncture, yoga, music therapy and meditation to improve overall health and wellness
- **Survivorship care** to manage side effects during treatment and long-term effects after treatment

The care provided is integrated into the patient's cancer treatments, Dr. Erickson says. "Having all of these services available at the same time and in the same location not only makes things

Continued on page 22 >

WHOLE PERSON HEALTH MODEL

When a patient is treated for cancer, it is not in isolation. The patient may have coexisting health conditions; treatment may cause health issues; and the patient's emotional well-being is impacted. In recognition of this complexity, the University of Cincinnati Cancer Center created its Wellness Clinic to unite primary care, survivorship care, and integrative medicine to address a patient's entire well-being during and after cancer treatment.



Mladen Golubic, MD, PhD, and Melissa Erickson, MD

PHOTO COURTESY OF UC HEALTH

ONCOLOGY PRIMARY CARE

Identify and treat coexisting non-cancer health conditions; minimize impact on cancer treatment.

SURVIVORSHIP CARE

Manage cancer treatment side effects, long-term effects of treatment and cancer recurrence.

INTEGRATIVE THERAPIES

Support overall health and wellness with acupuncture, massage, mindfulness, yoga, Tai Chi and music therapy.

Whole person care available from time of diagnosis throughout life span

COMBINING FORCES | CONTINUED

logistically easier for patients, it also allows for improved, coordinated care by our multidisciplinary team, leading to better outcomes for our cancer patients."

Survivorship starts at diagnosis

Providing survivorship care during and after cancer treatment is recognition that surviving cancer starts the day a patient is diagnosed and continues throughout life. The goal is to see the patient as a whole person and address any issues that stem from the cancer itself or as a result of the treatments they receive, Dr. Erickson says. Common concerns include fatigue, peripheral neuropathy or nerve pain, and nausea, as well as emotional distress, anxiety, and depression.

"A common thing I hear from some of my survivors is, 'I should just be grateful that I'm alive, and suck it up.' But our goal is to say, 'No, we're glad you're alive, but we're here to help you thrive. There are things we can do to improve your quality of life.'"

The clinic also provides evaluation and planning for patients after they have completed treatment. This includes evaluating long-term health effects of treatment; screenings for cancer recurrence or development of secondary cancers; and promotion of overall wellness with an emphasis on healthy diet, exercise, smoking cessation, and stress-relief practices such as meditation and/or yoga.

Melissa Erickson, MD

PHOTO COURTESY OF UC HEALTH

Whole person wellness approach

While Dr. Erickson's team works to identify short- and long-term health conditions, Dr. Golubic and the integrative medicine team work on strategies to help manage them. "There is an abundance of evidence that chronic pain, fatigue, anxiety, insomnia, nausea, vomiting, cold flashes, chronic stress — all of these things affect patients and their caregivers," he says. "We can use integrative modalities like acupuncture, massage, mindfulness, yoga, Tai Chi, music therapy, and lifestyle medicine's self-care practices to improve quality of life."

Integrative medicine combines traditional medical treatment with evidence-based complementary therapies to address areas such as stress, nutrition, movement, sleep and environment. The plan is included in the patient's electronic health record, so all providers — including the patient's oncology team — are alerted to the treatments being provided.

The survivorship and integrative medicine model "is a wonderful way to practice medicine, especially when you involve those experts who normally are not considered," Dr. Golubic says. "Now, food is medicine, movement is medicine, meditation is medicine."

HELPING Childhood Cancer Survivors Thrive

At some point in every teen's life, they must transition from a pediatrician to an adult primary care provider. For young adults who have had a cancer diagnosis, that transition can be an especially fraught time. Cincinnati Children's Cancer Survivorship Center was established in 1987 to address this problem.

Although many pediatric hospitals are unable to continue to follow their survivors much past early adulthood, Cincinnati Children's provides specialized medical care and psychosocial support for childhood cancer survivors through adulthood.

Rajaram Nagarajan, MD, MS

Without this type of program, "a childhood cancer survivor who is now an 'adult' may get a sheet of paper saying that you need to have XYZ screenings," says Rajaram Nagarajan, MD, MS, a professor in the UC College of Medicine and co-clinical director of the Cancer Survivorship Center at Cincinnati Children's. "I think that's sometimes hard to navigate when you're a young adult."

Family practice and internal medicine/pediatric physicians trained in survivorship provide care for patients. The team develops a risk-based evaluation for each patient that looks at factors such as surgery and the types and amounts of radiation therapy or chemotherapy received. That information helps inform the provider as well as the patient of treatment-related health risks, symptoms to be aware of and appropriate cancer screening schedules. Childhood cancer survivors — like adult cancer survivors — can face an increased risk of heart, lung and kidney disease; fertility issues; and secondary cancers, Dr. Nagarajan says. One of the most important components of the survivorship program is helping patients understand the lifelong impact of their cancer and their treatments so that they can advocate for themselves — no matter where they are treated, he says.

The center provides access to genetic counselors, social workers, nutritionists, as well as rehabilitation services. Specialized services, including cardio-oncology clinics and fertility preservation, also are available.

Cincinnati Children's is one of just a few centers nationwide that provides ongoing survivorship care to patients throughout their lives.

PHOTO COURTESY OF CINCINNATI CHILDREN'S

Transforming Cancer Survivorship

A transformational gift is having a dramatic impact on cancer survivorship across the region. The Robert and Adele Schiff Family Foundation made a $10 million gift to the University of Cincinnati Cancer Center Survivorship Program. Funds from this gift are now enhancing clinical offerings, expanding avenues for research and growing training for the next generation of cancer survivorship specialists.

One example of the gift's impact is the expansion of survivorship care services. Now open for two years, the UC Health Oncology Primary Care Clinic treats patients with a history of cancer. Clinic physicians monitor patients for treatment-related effects, manage comorbid conditions and continue risk-based screenings specific to cancer survivors.

Future plans for the gift include supporting faculty recruitment, research and education initiatives, including an endowed chair in cancer survivorship research and cancer survivorship programming in the UC College of Medicine and future residency and fellowships.

Dr. Erickson coordinates primary care with cancer care in the moment.

Bobby Rogers

LIFE BEYOND CANCER

Bobby Rogers is a two-time cancer survivor. He was diagnosed with colon cancer in January 2019 and a year later learned he had prostate cancer. Both were treated successfully at UC Health.

When he started experiencing gastrointestinal symptoms, he worried they were a sign of something serious — maybe even a third round of cancer. But he wasn't sure which provider he should contact — he had a urologist, a GI physician and oncologists. But like many cancer patients, he did not have a primary care physician.

Then Bobby met Melissa Erickson, MD, clinical director of the region's first hospital-based Oncology Primary Care Clinic at University of Cincinnati Cancer Center. Dr. Erickson noted Bobby's history of high blood pressure and seizures, and she moved his scheduled scans earlier to rule out cancer. She also referred Bobby to a dietitian to help address his GI issues. "I coordinated with all of his specialists, so everyone was on the same page, nothing was happening in isolation."

"I've never had a PCP before meeting Dr. Erickson, and she's been wonderful," Bobby says. "She keeps me up to date on what's going on with my body."

And now when he has an ache here or a pain there, Bobby doesn't waste time worrying because he has a professional who can find the answer.

PHOTOS COURTESY OF UC HEALTH

Connecting CARE

Region's first Oncology Primary Care Clinic provides care in context of cancer

Caring for hundreds of cancer survivors as the clinical director of the University of Cincinnati Cancer Center Survivorship Program, Melissa Erickson, MD, discovered a problem she wasn't looking for — many patients didn't have a primary care provider (PCP).

"These were patients who had other conditions in addition to their cancer, like high blood pressure, diabetes — chronic illnesses that needed to be treated," she says. "Sometimes they may have put their everyday wellness on the back burner, and these conditions were going unmanaged."

In some cases, uncontrolled chronic conditions were hampering a patient's ability to get some essential cancer treatments. That was the impetus for the opening of the Oncology Primary Care Clinic in late 2019. As the only clinic of its kind in the region, the clinic is attracting patients from across the region who are interested in this unique coordinated care model.

Dr. Erickson works alongside UC Health oncologists, oncology social workers and oncology pharmacologists to make treatment decisions. For example, some treatments may elevate blood pressure significantly — to the point where a patient may not be able to get the treatment. "Instead of saying, 'Go see your primary care doctor,' the oncologist just walks over to me and we can discuss a plan in real time," she says. "Having that synergy prevents delays in care and ultimately, provides better outcomes."

The Oncology Primary Care Clinic views the patient's long-term health through the lens of being a cancer survivor. "If you've had chest radiation therapy, for example, we know that is going to increase your risk of premature heart disease. So, we're going to be more aggressive about getting your blood pressure and your cholesterol under control ," Dr. Erickson explains.

The clinic's other main focus is preventing second primary cancers. People who have had one type of cancer often have overlapping risk factors — obesity, smoking, genetic factors — for other types of cancer. In addition, some cancer treatments can increase the risk of developing a second primary cancer. Dr. Erickson's team educates patients about their risks and navigates them toward the appropriate services to help prevent those second cancers — or find them at earlier stages with customized screening schedules.

Leading philanthropic investments in whole person care are furthering the work of the University of Cincinnati Cancer Center faculty. In 2019, a $2 million gift by John and Carrie Hayden created the Carrie K. Hayden Endowed Chair of Integrative Oncology Research, to work in tandem with clinicians and study the best models of care for cancer survivors.

In December 2021, Bernard Osher and The Bernard Osher Foundation made a $5.5 million gift to support and expand the work of the UC Center for Integrative Health and Wellness — which includes integrative therapies such as acupuncture and massage offered to patients of the Cancer Center.

OUTREACH That's Relatable

Building relationships that break down barriers

Community outreach involves more than just *meeting* the needs of the community. It involves actually *meeting* the communities.

"We can't assess and understand needs without engagement," says Melinda Butsch Kovacic, MPH, PhD, professor and associate director for community outreach & engagement at the Cancer Center. "And to do that, you have to build trusting relationships within the community."

These relationships help ensure the outreach is based not just on statistics such as community risk factors, but also on factors such as access to care and effective communication. It also means making sure that what the Cancer Center thinks is good for the community is something the community thinks is good.

Dr. Butsch Kovacic has had a long-standing relationship with Seven Hills Neighborhood Houses in Cincinnati's West End, where she co-creates health promotion materials in collaboration with the West End Community Research Advisory Board. At their urging, she and her 15-plus member interdisciplinary We Engage 4 Health team created an advocacy program aimed at helping communities become "research ready."

"The idea behind this program is to have representatives of local communities host discussions with friends and family and help them to learn the three Ps" of participating in research, she explains.

- **Purpose:** Why studies are being conducted and what participants will be asked to do
- **Protection:** How research participants are protected from harm while participating
- **Participation:** Why diverse representation helps make the outcomes relevant for all people

Much of the University of Cincinnati Cancer Center's outreach work is within the African American community, which accounts for 42% of Cincinnati's population. Although African Americans in Cincinnati experience some of the area's highest cancer death rates, African American representation in cancer research is low. Often that's due to a failure in communicating why diversity is needed in research, she says.

"If we want to have more diverse treatment plans that are really going to minimize health disparities, then we need diverse populations to be a part of our research studies," Dr. Butsch Kovacic explains.

Clockwise from left:

Melinda Butsch Kovacic, MPH, PhD, with West End Community Research Advisory Board members Sheila Nared and Vonnie Tawwab at a neighborhood event.

Melinda Butsch Kovacic, MPH, PhD, with We Engage 4 Health volunteers and Dana Boll, founder of Keep Norwood Cool at a parade to raise awareness of the impact of heat islands on the community's health.

Kelly Hummel, Herschel Chalk, and William Barrett, MD, at Black Family Reunion.

The Next GENERATION

While some cancer centers have ambitions to be the largest, the most well-funded or the institution with the most scientific breakthroughs, the University of Cincinnati Cancer Center defines success in terms of its community.

"One of our goals is for Cincinnati to be the smartest city in the world when it comes to cancer," says William Barrett, MD, co-director of the Cancer Center.

William Barrett, MD (center), with students at DePaul Cristo Rey High School

Accomplishing that will require a new generation of cancer researchers and clinicians — many of whom are currently too young to drive but could change the face of cancer care in Cincinnati and the world.

It's one of the reasons that the Cancer Center goes into local schools to educate young people about cancer prevention, diagnosis, and treatment, to stimulate their interest in health care careers, particularly cancer treatment. Students can form a Bearcats Against Cancer Club in their school and invite Cancer Center clinicians and researchers to speak or arrange cancer screening days where they can encourage their parents to get their cancer screenings.

University of Cincinnati Cancer Center also hosts several programs to give students hands-on experience in cancer research:

CANCER RETREAT: In 2017, the Cancer Center facilitated a cancer retreat for 24 middle and high school students nominated by their principals and science teachers. During the retreat, 12 eighth graders and 12 high school seniors collaborated with premed college students, medical school or PhD graduate students, residents, fellows, UC physicians and scientists to come up with ideas on how to make Cincinnati the smartest city in the world when it comes to cancer.

SUMMER RESEARCH PROGRAM: For more than 20 years, high school students from throughout the region participate in summer programs where they assist with basic science research or clinical research to get early exposure to a variety of science and clinical issues related to cancer.

HOPE on the HORIZON

Targeted therapies are providing answers for people with acute myeloid leukemia

All cancers are bad but when you ask oncologists about the really bad cancers, acute myeloid leukemia (AML) usually makes the short list because of the lack of effective treatment options. In the past few years, however, researchers believe they are making inroads by discovering therapies that are based on the biology of the disease.

Daniel Starczynowski, PhD, the newly appointed associate director of basic science at the University of Cincinnati Cancer Center, says several encouraging drugs are on the horizon. "These therapies are based on genetic markers and on understanding the complex, unique biology of myeloid malignancies, which are extremely heterogeneous," says Dr. Starczynowski, who is also a member of the Division of Experimental Hematology and Cancer Biology at Cincinnati Children's. "Because of that, personalized approaches really could be transformative for patients who have the appropriate biomarkers."

Three of the most exciting therapeutic developments are:

1. **A group of three inhibitors that target mutations** in an oncogenic driver receptor called FLT3, a specific mutation found in 30-40% of AML patients
2. **Inhibitors that target IDH1 and IDH2 mutations**, which account for approximately 7% and 11% of AML cases respectively
3. **A therapy targeting the survival pathways of leukemia** by inhibiting the Bcl-2 oncoprotein, which is present in more than 87% of AML cases at onset

In December 2021, the FDA issued fast track designation to CYNK-001, a nongenetically modified allogeneic natural killer (NK) cell therapy for adults with relapsed or refractory AML.

"Even though these therapies have been approved, we're still learning a lot about mechanisms of resistance, mechanisms of response, and how to further refine these targeted therapies to improve on them," Dr. Starczynowski says.

Investigating the inner wiring of AML

Before these therapies ever progressed to the clinical trial phase, Dr. Starczynowski's lab was trying to understand the cellular, molecular and genetic basis of hematologic malignancies, with a particular emphasis on myelodysplastic syndromes and AML. "If we have a better understanding of the blueprint of these leukemic cells, the inner wiring if you will, it will perhaps allow us to pursue novel therapeutic approaches and identify unique vulnerabilities," he says.

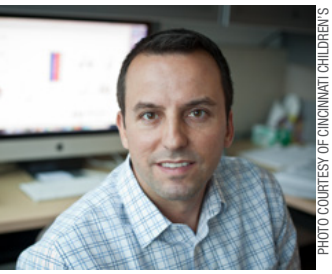


PHOTO COURTESY OF CINCINNATI CHILDREN'S

Daniel Starczynowski, PhD

Currently, Dr. Starczynowski is working to discover how evolutionary conserved pathways that typically sense and respond to foreign pathogens have been "rewired" or hijacked by the cancer cells to help the cells propagate the disease and resist therapy.

"We're involved in the iterative process of informing clinical trials based on our research, learning about the positive — and maybe disappointing — news that might come from early stage clinical trials; then going back to the laboratory to learn more about those processes to further develop and improve on those strategies."

He's taking a similar approach in his new role at the Cancer Center, where his goals are to identify areas of strengths and opportunities for growth where investigators who don't normally work together can collaborate. "This is going to help me crystallize our priorities as a cancer center for the research being done and the path forward," he says.

Researchers at Cincinnati Children's played a significant role in the FDA's 2021 approval of Vyxeos, a targeted anti-leukemia nanoparticle drug that is shown to be effective and safe for AML. Cincinnati Children's researchers are continuing to study Vyxeos in hopes of making it more effective. This work has led to a new clinical trial — the first of its kind in the U.S. and only available at Cincinnati Children's — that combines Vyxeos with a drug called venetoclax, which targets a mechanism that leukemia cells use to escape being killed.

Small Start Leads to BIG RESULTS

Cincinnati Children's discovers targeted therapy for rare but debilitating disease

One of the biggest advances in the treatment of children with neurofibromatosis type 1 (NF1) and inoperable plexiform neurofibromas started at Cincinnati Children's with something small: a mouse.

The MEK inhibitor selumetinib is a new therapy approved by the FDA in April 2020. It's the first of its kind for children with this debilitating, rare disease — and its development began back in 2008 with a mouse model in the Cincinnati Children's lab of Nancy Ratner, PhD, a professor in the UC College of Medicine and a Cancer Center member. The mouse model was the first to mimic the disease that occurs in humans and the first to predict drug efficacy in the clinical setting.

In 2013, Dr. Ratner and her colleagues published a Phase 1 preclinical study showing that blocking the MEK protein in the NF1 molecular process could shrink plexiform neurofibromas by more than 70%. As many as half of patients born with NF1 develop one or more plexiform neurofibromas (PNs). Without treatment, PN tumors can continue to grow, causing pain, numbness, weakness and mobility issues.

From mouse to clinical trials

Excited about the potential for MEK inhibitors to shrink plexiform neurofibromas in patients, Dr. Ratner teamed up with Brian Weiss, MD, a professor in the UC College of Medicine and pediatric oncologist at Cincinnati Children's. Dr. Weiss helped establish the Neurofibromatosis Clinical Trials Consortium (NCTC), of which Cincinnati Children's was a founding member.

In 2016, Drs. Weiss and Ratner and researchers from three other pediatric institutions published a Phase 1 clinical study showing that the MEK inhibitor selumetinib could shrink plexiform neurofibromas in pediatric patients.

PHOTO COURTESY OF CINCINNATI CHILDREN'S

"NF1 researchers at Cincinnati Children's have been a major contributor to advancements for neurofibromatosis through clinical trials, primarily through the consortium," says Dr. Weiss.

The selumetinib trial that led to FDA approval was sponsored by the National Cancer Institute, which chose Cincinnati Children's and Children's Hospital of Philadelphia to participate. The Phase 2 study showed that shrinking the tumors led to clinical benefits such as reduced pain and reduced motor impairment.

Although the drug approval has made a significant difference in treating children with NF1, the researchers are focused on a higher goal: curing NF1.

"MEK inhibitor therapy provides a remarkable tumor response, but eventually the patient becomes resistant," Dr. Weiss explains. "We are looking for something more durable, where the tumors disappear after taking a short course of a drug."

John Breneman, MD

PHOTO COURTESY OF UC HEALTH

Cincinnati Proton Therapy Center was the first in the world to treat a patient with FLASH radiotherapy.

In the Blink of an Eye

In late 2020, University of Cincinnati Cancer Center researchers treated the first patient in the world with FLASH radiotherapy. Just 14 months later, they were eagerly awaiting verification that the ultra-high dose rate radiotherapy successfully treats metastatic cancer in the bone while sparing healthy tissue.

FLASH radiotherapy (FLASH-RT) is defined as a single ultra-high dose rate (≥ 40 Gy/s) of ionizing radiation to control or kill cancer cells. FLASH-RT is 400-fold more rapid than conventional irradiation. In layman's terms, FLASH-RT does in less than a second what is equal to treatments with standard radiotherapy for days at a time.

Cincinnati Children's and UC Health opened the Cincinnati Proton Therapy Center in 2016 and delivered the world's first FLASH-RT to a lung lesion phantom target in 2020. By November of that year, the center had opened the Feasibility Study of FLASH Radiotherapy for the Treatment of Symptomatic Bone Metastases, also known as FAST-01.

"The prior three years of preparation by the researchers, engineers, clinical and physics teams culminated in a treatment that was completed in literally a blink of the eye, and the patient was discharged," says John Breneman, MD, professor of radiation oncology and neurosurgery in the UC College of Medicine and medical director of the Cincinnati Proton Therapy Center.

Oxygen may be the key

Using high enough levels of traditional radiotherapy to completely destroy tumors near organs is constrained by the damage it inflicts on healthy tissue. It is believed that FLASH-RT can safely deliver a dose high enough to treat the cancer without causing as much damage to healthy tissue. While researchers haven't yet identified the mechanism for this benefit, they believe it is tied to oxygenation levels in healthy cells, Dr. Breneman says.

For radiation to work, it requires oxygen in the cells, Dr. Breneman explains. "Cancer cells are often oxygen-starved, which makes them more resistant to radiation, while healthy cells that have high oxygen levels are more susceptible. With FLASH, it's believed that oxygen levels in normal tissue are depleted so quickly that they become hypoxic and resist the radiation."

If the FAST-01 study is successful, researchers and radiation oncologists hope to use FLASH-RT to treat other tumors located close to vital organs, such as the heart and lungs, more aggressively.

"FLASH is potentially a transformational advance for cancer treatment for many patients," says John Perentesis, MD, director of the Division of Oncology and Cancer Programs at Cincinnati Children's. "If the side effects of radiation on the normal tissues surrounding a tumor can be significantly reduced, the dose of radiation to treat a cancer can be greatly increased. This would raise hope to cure malignancies that respond to radiation but aren't completely cured at the current dose."

SELECTED RESEARCH GRANTS

The University of Cincinnati Cancer Center researchers were funded by more than 80 active grants totaling more than $18 million in 2021. Following are some highlights of those grants.

	Lead PI	Title	Sponsor*
CINCINNATI CHILDREN'S	H. Leighton Grimes, PhD; Stephani Halene, MD, PhD (Yale School of Medicine)	Modeling myelodysplasia	NCI
	Yutaka Maeda, DVM, PhD; Eric L. Snyder, MD, PhD (University of Utah Huntsman Cancer Institute)	Patho-Genetic Analysis of Invasive Mucinous Adenocarcinoma of the Lung	NCI
	Nathan G. Salomonis, PhD	Unbiased identification of spliceosome vulnerabilities across cancer	NCI
	Daniel Starczynowski, PhD	Targeting IRAK1/4 in Myelodysplastic Syndromes	NIDDK
	E. Melinda Mahabee-Gittens, MD, MS, Georg E. Matt, PhD (San Diego State University)	Contribution of Thirdhand Smoke to Overall Tobacco Smoke Exposure in Pediatric Patients	NIEHS
	Parinda A. Mehta, MD	IND: 113343 Quercetin Chemoprevention for Squamous Cell Carcinoma in Patients with Fanconi Anemia	FDA
	Meghan Eileen McGrady, PhD	Patient Preferences and Adherence in Adolescents and Young Adults with Cancer	NCI
UNIVERSITY OF CINCINNATI	Jun-Lin Guan, PhD	Mechanisms of FIP200 regulation of breast cancer through its autophagy and non-autophagy functions	NCI
	T. Douglas Mast, PhD	Monitoring and control of human liver cancer ablation using real-time, 3D echo decorrelation imaging	NCI
	Timothy N. Phoenix, PhD	Regulation of Angpt1 and DIPG blood-brain barrier integrity by H3K27M mutations	NINDS
	Teresa M. Reyes, PhD	Identification of causal factors underlying cognitive deficits in a mouse model of childhood leukemia survival	NINR
	Atsuo Sasaki, PhD	Therapeutic resistance and aggressive malignancy in glioblastomas: the contribution of GTP metabolism through regulation by IMPDH2	NCI
	Pier Paolo Scaglioni, MD	Fatty acid metabolism regulates ferroptosis in mutant KRAS lung cancer	NCI
	Susan E. Waltz, PhD; Susanne I. Wells, PhD (Cincinnati Children's)	Defining genetic and metabolic requirements of aggressive breast cancer	NCI
	Yuhang Zhang, PhD	Reprogramming of the stromal microenvironment in melanoma progression and therapeutic escape	NCI
	John C. Byrd, MD	Targeted Therapy for Leukemia	NCI
	John C. Byrd, MD	ITSC for Leukemia: Novel Molecular strategies for NCTN "Individualized" Therapies	NCI
	Shuchi Gulati, MD	Combining PD1 Inhibition and Cesium-131 Brachytherapy with Salvage Surgery to Enhance Immunogenicity and Improve Local Control in Head and Neck Cancer	CCF
	Davendra Sohal, MD, MPH	Phase I/II clinical evaluation of ABTL0812, a novel PI3K/Akt/mTOR inhibitor, with a unique mechanism of action in pancreatic cancer	FDA
	Trisha Wise-Draper, MD, PhD	Harnessing the Natural Killer Cytotoxic Response in Head and Neck Cancer	ACS
	Melinda Butsch Kovacic, MPH, PhD	The Cancer Research Scholars Program (CRSP): Exploring Research Across the Cancer Continuum and into Underserved Communities	NCI
	Scott M. Langevin, PhD, MHA	Oral Rinse Methylation for Follow-Up Surveillance of Oral/ Pharyngeal Cancer	ACS
	Senu Apewokin, MD	Harnessing Induced Human Intestinal Organoids (iHIOs) and Metagenomics to Unravel Host Immune-microbiota Interactions During Cancer Chemotherapy-associated Clostridium difficile Infections	NCI
	Susan E. Waltz, PhD. Carolyn Price, PhD	Pathways to Cancer Therapeutics	NCI

* Sponsors (in order listed): National Cancer Institute (NCI); National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK); National Institute of Environmental Health Sciences (NIEHS); U.S. Food & Drug Administration (FDA); National Institute of Neurological Disorders and Stroke (NINDS); National Institute of Nursing Research (NINR); Conquer Cancer Foundation (CCF); American Cancer Society (ACS)

SELECTED CLINICAL TRIALS

In 2021, the University of Cincinnati Cancer Center had 362 interventional clinical trials open to accrual (patient enrollment). Following is a sampling of those studies.

The Use of Active vs. Receptive Music Listening to Reduce Symptoms of Chemobrain in Breast Cancer Survivors (PI: Soma Sengupta, MD, PhD)

Prospective Comparison of Treatment of Dyspareunia With Fractional CO2 Laser Therapy Versus 4% Topical Lidocaine Gel in the Setting of Breast Cancer Survivors (PI: James Whiteside, MD, MA, MHA)

Prospective Evaluation of Carvedilol in Prevention of Cardiac Toxicity in Patients With Metastatic HER2+ Breast Cancer, Phase III (PI: Elyse Lower, MD)

Duloxetine to Prevent Oxaliplatin-Induced Chemotherapy-Induced Peripheral Neuropathy: A Randomized, Double-Blind, Placebo-Controlled Phase II to Phase III Study (PI: Jordan Kharofa, MD)

Using Novel Objective Bio-data to Improve Quality of Life Assessment in Patients Undergoing Cytotoxic Chemotherapy: An Interventional Pilot Study (PI: Thomas Herzog, MD)

A Phase 2b/3, multicenter, randomized, double-blind, placebo-controlled study comparing the efficacy and safety of clonidine mucoadhesive buccal tablet to placebo to prevent chemoradiotherapy-induced severe oral mucositis in patients with oropharyngeal cancer (PI: Vinita Takiar, MD, PhD)

How to decrease Morbidity of Neck Dissections in Head and Neck Cancer Patients (PI: Yash Patil, MD)

A Randomized Trial of the Altering Intake, Managing Symptoms Intervention for Bowel Dysfunction in Rectal Cancer Survivors Compared to a Healthy Living Education Control: A Feasibility and Preliminary Efficacy Study (AIMS-RC) (PI: Jordan Kharofa, MD)

Evaluation of Complicated Living Grief in Head and Neck Cancer Patients and Survivors (PI: Chad Zender, MD)

Self-management Behaviors and Quality of Life in Adults Post Hematopoietic Stem Cell Transplant (SAGE HSCT) (PI: Caroline Morrison, PhD, MSN)

Factors Contributing to Symptoms of Survivors of Adult Blood and Marrow Transplant (SOS-A BMT) (PI: Caroline Morrison, PhD, MSN)

1-2 PUNCH: Palliative UNConventional Hypofractionation Trial for Metastatic Bone Disease. (PI: Timothy Struve, MD)

Adaptive Approach to Neoadjuvant Therapy to Maximize Resection Rates for Pancreatic Adenocarcinoma. (PI: Davendra Sohal, MD, MPH)

Brandi Turner, RN

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Neoadjuvant Therapy in Biliary Adenocarcinoma. (PI: Jordan Kharofa, MD)

Durvalumab (MEDI4736) and Tremelimumab for Hepatocellular Carcinoma in Patients Listed for a Liver Transplant. (PI: Davendra Sohal, MD, MPH)

Combining Pembrolizumab and Metformin in Metastatic Head and Neck Cancer Patients (PI: Trisha Wise-Draper, MD, PhD)

Study Evaluating the Efficacy of Niraparib and Dostarlimab (TSR-042) in Recurrent/Metastatic HNSCC (PI: Trisha Wise-Draper, MD, PhD)

Study of Biomarker-Based Treatment of Acute Myeloid Leukemia (PI: John Byrd, MD)

Trial Combining Pembrolizumab and Cesium 131 Brachytherapy With Salvage Surgery in HNSCC (PI: Chad Zender, MD)

Digital Tomosynthesis Mammography and Digital Mammography in Screening Patients for Breast Cancer (PI: Lawrence Sobel, MD)

ABTL0812 in Combination With FOLFIRINOX for First-line Treatment of Metastatic Pancreatic Study (PanC-ASAP) (PI: Davendra Sohal, MD, MPH)

SELECTED PUBLICATIONS

In 2021, University of Cincinnati Cancer Center researchers published numerous studies in peer-reviewed journals.

Allmen, Douglas, et al. **"Modified Head and Neck Swallow Scale: Using EORTC-QLQ-H&N35 to Predict Overall Survival."** *The Laryngoscope*, 2021, https://doi.org/10.1002/lary.29559.

Andreassen, Paul R., et al. **"Understanding BRCA2 Function as a Tumor Suppressor Based on Domain-Specific Activities in DNA Damage Responses."** *Genes*, 2021, https://doi.org/10.3390/genes12071034.

Arnold, Danielle E., et al. **"Reduced-Intensity/Reduced-Toxicity Conditioning Approaches Are Tolerated in XIAP Deficiency but Patients Fare Poorly with Acute GVHD."** *Journal of Clinical Immunology*, 2021, https://doi.org/10.1007/s10875-021-01103-6.

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Desai, Janki, et al. **"EXTH-52. Systemic and Brain Pharmacokinetics of the AMP-Activated Protein Kinase Selective Inhibitor SBI-0206965 as a Potential Therapeutic Agent for the Treatment of Glioblastoma Multiforme."** *Neuro-Oncology*, 2021, https://doi.org/10.1093/neuonc/noab196.691.

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IN THE NEWS

The University of Cincinnati Cancer Center is regularly featured in regional, national and even international news stories. Here are a few prominent stories:

NHK World-Japan: Developing a new way to fight cancer

UPI: Promising pancreatic cancer treatment

US News & World Report: Immunotherapy and cancer, COVID-19

Cincinnati Business Courier: Flash therapy for cancer

Pharmacy Times: Hierarchy of breast cancer cells

WCPO: Raising colorectal cancer awareness

Local 12: Chemotherapy in recurrent ovarian cancer patients

ABC News: Impact of pandemic cancer screening pause

MSN/Columbus Dispatch: Ohio legislation aims to cover dense breast screening

Scientific American: Oncologists wrestle with COVID-19 pandemic's effect on cancer

WCPO: UC participates in international breast cancer screening trial

Local 12: New robotic technology helps diagnose lung cancer sooner

Cincinnati Enquirer: COVID-19 vaccines and patients with cancer

WCPO: RNA treatment for brain cancer

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