TCL
THE CANCER LETTER

Inside information on cancer research and drug development

Vol. 48 No. 29

JULY 22, 2022

www.cancerletter.com

MONICA BERTAGNOLLI, FIRST WOMAN AND FIRST CLINICAL TRIALS GROUP CHAIR TO DIRECT THE NATIONAL CANCER INSTITUTE

Monica M. Bertagnolli, a professor of surgery at Harvard Medical School, stands poised to become the first woman and the first chair of a clinical trials cooperative group to be named director of the National Cancer Institute.

→ PAGE 4

WITH $100M GIFT, SLOAN KETTERING INSTITUTE ESTABLISHES KRAVIS CANCER ECOSYSTEMS PROJECT TO STUDY TUMOR ENVIRONMENT

→ PAGE 8

UNDERSTANDING GENES ISN'T ENOUGH TO STOP CANCER—IT'S TIME TO USE A SYSTEMS APPROACH TO TARGET METASTASIS

→ PAGE 12

JEROME CARL LANDRY, RADIATION ONCOLOGIST AT EMORY AND GRADY, DIES AT 66

→ PAGE 14

CLINICAL ROUNDUP

YALE CANCER CENTER STUDY: FOR MEDICAID-COVERED PATIENTS WITH CANCER, INSURANCE DOES NOT ALWAYS MEAN ACCESS

→ PAGE 25

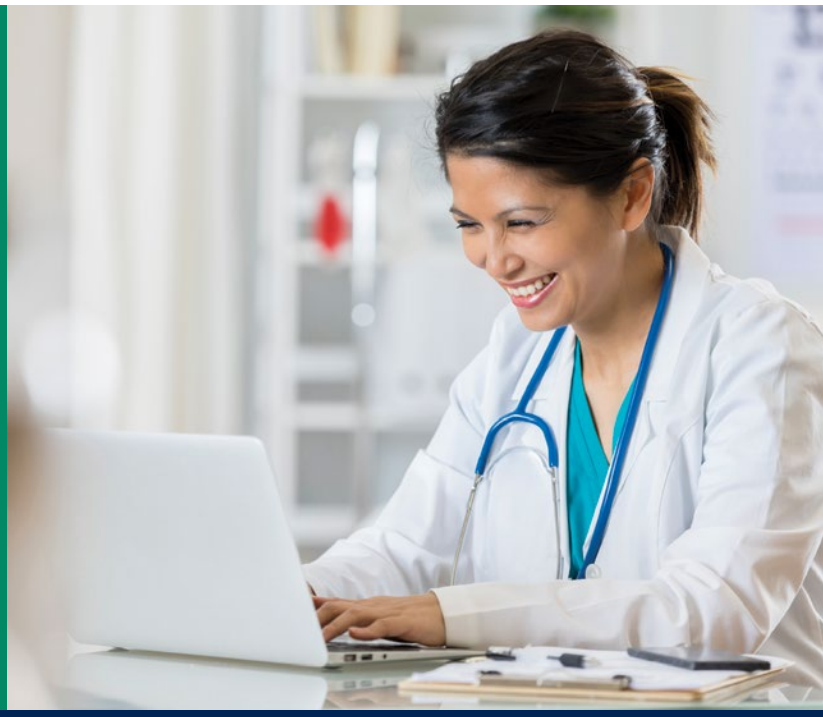
ASCO® Plenary Series

Today's Science Can't Wait

Call for Abstracts

Online
plenaryseries.asco.org/abstracts

#ASCOPlenarySeries



Your research could be the next headline

Each program will feature up to two **practice-changing** and **clinically relevant** abstracts on the latest advances in cancer care. The abstract presentation will be accompanied by a discussant presentation and followed by a live question-and-answer session.

The ASCO Plenary Series will take place through April and will resume after the ASCO Annual Meeting. Featured abstracts will be released the day prior to presentation.

Mark your calendar for the following dates:

AUGUST PLENARY SESSION
Abstract Submission Deadline: July 5
Abstract Presentation: August 16

SEPTEMBER PLENARY SESSION
Abstract Submission Deadline: August 2
Abstract Presentation: September 14

OCTOBER PLENARY SESSION
Abstract Submission Deadline: September 6
Abstract Presentation: October 18

NOVEMBER PLENARY SESSION
Abstract Submission Deadline: October 4
Abstract Presentation: November 15

DECEMBER PLENARY SESSION
Abstract Submission Deadline: November 8
Abstract Presentation: December 20

Visit **plenaryseries.asco.org/abstracts** for broadcast details and additional dates in 2022.

ASCO® AMERICAN SOCIETY OF CLINICAL ONCOLOGY
KNOWLEDGE CONQUERS CANCER

Editor & Publisher
Paul Goldberg

Associate Editor
Matthew Bin Han Ong

Reporter
Alexandria Carolan

Director of Operations, Illustrator
Katie Goldberg

Marketing & Account Manager
Mona Mirmortazavi

Designer
Jacqueline Ong

IT Manager
David Koh

Editorial, Subscriptions and Customer Service
PO Box 9905 -
Washington, DC 20016

T 202-362-1809
F 202-379-1787
W www.cancerletter.com

Individual subscriptions $555 per year worldwide. Group subscriptions required for institutional distribution. To subscribe, click here.

ISSN 0096-3917. Published 46 times a year by The Cancer Letter Inc. Founded Dec. 21, 1973, by Jerry D. Boyd.

In this issue

WHITE HOUSE

Monica Bertagnolli, first woman and first clinical trials group chair to direct the National Cancer Institute

By Paul Goldberg and Matthew Bin Han Ong

Monica M. Bertagnolli, a professor of surgery at Harvard Medical School, stands poised to become the first woman and the first chair of a clinical trials cooperative group to be named director of the National Cancer Institute.

President Joe Biden is expected to name Bertagnolli, who is now chief of the Division of Surgical Oncology at Brigham and Women's Hospital and Dana-Farber Cancer Institute, to the position of institute director.

The rollout of Bertagnolli's appointment didn't go smoothly, as news leaked out on Twitter and in the press, first appearing in STAT, in the morning of July 21, shortly after the White House announced that the president had contracted COVID-19.

Bertagnolli, 63, will be the 16th NCI director since the institute's founding in 1937 and the tenth since the National Cancer Act elevated the job to the status of a presidential appointment. The NCI director is presidentially appointed but is not subject to approval by the Senate.

Bertagnolli, a past president of the American Society of Clinical Oncology, has decades of clinical expertise and executive leadership in oncology and cancer policy. Her expertise in clinical trials, along with her presidential theme at ASCO in 2018-2019—"Caring for every patient, learning from every patient"—can be taken as clues that her agenda for NCI will include an emphasis on translational science, observers say.

Bertagnolli serves as chair of Alliance for Clinical Trials in Oncology, a clinical trials cooperative group funded through NCI's National Clinical Trials Network.

At NCI, Bertagnolli replaces Ned Sharpless, who stepped down April 29 (*The Cancer Letter*, April 9, 2022).

"I believe Monica is a terrific choice to lead the super-charged Cancer Moonshot and be director of the National Cancer Institute," Sharpless said to *The Cancer Letter*. "She is an outstanding researcher in surgical oncology, and will understand the challenges of basic scientists, health services researchers, and clinical trialists.

"She has a long-standing commitment to excellence in patient care, training, and addressing health care disparities; all key issues for the NCI today."

Karen E. Knudsen, CEO of the American Cancer Society, said Bertagnolli is an exceptional choice for leading NCI.

"Her strong track record as a surgical oncologist, scientist, innovator, and leader provide an unparalleled foundation for guiding the next phase of the NCI," Knudsen said to *The Cancer Letter*. "At the American Cancer Society, wherein Dr. Bertagnolli serves on the board of directors, we have benefitted from her wisdom, creativity, and dedication to our goal of improving the lives of cancer patients and their families.

"We look forward to continuing to work closely with the NCI to end cancer as we know it—and with Dr. Bertagnolli in this new role."

Clifford A. Hudis, CEO of the American Society of Clinical Oncology, described Bertagnolli as "an accomplished cancer surgeon and researcher with deep expertise in community-based cancer research."

Said Hudis:

> During her presidential year, she continually highlighted the need for oncologists to learn from every single patient with cancer, including through clinical research and the application of real-world data and real-world evidence, so that we can accelerate progress and every patient can have the best possible outcome for their disease.
>
> She also spearheaded efforts to increase access to equitable cancer care in rural areas, challenging the status quo and working to remove barriers to patient participation in clinical research, like geographic distance and lack of coverage for routine care costs associated with participating in trials.
>
> Additionally, as group chair of the Alliance for Clinical Trials in Oncology, Dr. Bertagnolli has a strong understanding of the NCI's mission and how it works to improve the lives of cancer patients. This expertise will be critically important as the NCI continues to address priorities like improving overall access, eligibility, and diversity in clinical trials, increasing investigator-initiated research funding, and advancing the Cancer Moonshot to improve outcomes for patients with cancer.

Margaret Foti, CEO of the American Association for Cancer Research, said Bertagnolli's expertise as a translational scientist makes her an excellent choice for NCI.

"Dr. Bertagnolli brings impressive qualifications to this vital position, including her background as a top-tier physician-scientist and much admired professor," Foti said. "Her appreciation for the value and importance of basic research to advancing translational discoveries, as well as her commitment to ensuring that such treatment innovations reach patients in all populations across the United States, will ensure that the NCI continues to lead the way in programs aimed at improving health, preventing cancer, and reducing the incidence and mortality from this devastating disease."

Bertagnolli is a member of the AACR's Tumor Microenvironment Working Group and Women in Cancer Research membership group.

"I offer my heartfelt congratulations to Dr. Bertagnolli on her appointment as the next NCI Director," said AACR President Lisa M. Coussens. "The AACR looks forward to collaborating with her in

support of the NCI's many initiatives, including increasing diversity in cancer research, furthering education and training of the cancer research workforce, improving funding across the cancer continuum, and working together with NCI-designated cancer centers to solve the biggest problems in cancer."

"They don't get any more expert than Dr. Bertagnolli"

Chairs of clinical trials groups were delighted to see their peer appointed to lead the institute.

Charles D. Blanke, chair of SWOG Cancer Research Network and Professor of Medicine at Oregon Health and Science University's Knight Cancer Institute, said Bertagnolli's expertise will allow NCI to rapidly test emerging scientific leads.

"This is the perfect time, given the amazing recent breakthroughs achieved in translational oncology research, to have a National Clinical Trials Network expert head up the NCI. And they don't get any more expert than Dr. Bertagnolli," Blanke said to *The Cancer Letter*. "SWOG could not be happier with this choice. It's wonderful news for the country and for everyone involved in cancer research."

"Dr. Bertagnolli is a high-profile leader in cancer research and an early and visionary proponent of collaborative interactions across basic and clinical research," Peter J. O'Dwyer, group co-chair of the ECOG-ACRIN Cancer Research Group and professor of medicine at the Hospital of the University of Pennsylvania and the Presbyterian Medical Center of Philadelphia, said to *The Cancer Letter*.

"She brings the insights of her highly successful leadership of the Alliance for Clinical Trials in Oncology to the potential for clinical trials to be amplified through engagement of diverse populations, so as to bring advances in cancer care to all."

"I am happy to see a giant in cancer care and clinical research appointed as the next director of the NCI," said Mitchell D. Schnall, group co-chair ECOG-ACRIN and the Eugene P. Pendergrass of Radiology, and the Chair of the Radiology Department at the Perelman School of Medicine at UPenn, said to *The Cancer Letter*.

> "She has a long-standing commitment to excellence in patient care, training, and addressing health care disparities; all key issues for the NCI today."
>
> – *Ned Sharpless*

"Dr. Bertagnolli brings many strengths to this national leadership role, especially an innovative approach to collaboration, advancement of women to leadership positions, and her understanding of cancer as a practitioner. I look forward to seeing what she will bring to the future of the institute's programs," Schnall said.

"The right person at the right time"

"I am thrilled. This is fantastic news for cancer, cancer patients, and cancer science," Ellen V. Sigal, founder and chair of Friends of Cancer Research, said to *The Cancer Letter*. "It's a fantastic choice. She is the right person at the right time. I am thrilled that she is a woman leader and that she is a physician treating patients. The fact that she has clinical trials experience is incredible."

Otis W. Brawley, the Bloomberg Distinguished Professor of Oncology and Epidemiology at Johns Hopkins University, said the depth of Bertagnolli's understanding of clinical trials and health equity makes her an excellent choice.

"I have known Monica for three decades. She is a wonderful human being. She is the consummate physician scientist and a superb clinical trialist," Brawley said to *The Cancer Letter*. "She understands all the issues, she appreciates the need to focus on prevention/risk reduction as well as equity in care, efficiency of treatment and survivorship."

Bertagnolli's emphasis on health disparities and the need for strengthening clinical research shaped her ASCO presidency.

Many cancer patients are not realizing the benefits of progress against cancer "either because we lack acceptable treatments for their cancer or because of the widening gaps in socio-economic status across the United States that put available treatments out of reach for some," Bertagnolli wrote in a guest editorial in this publication (*The Cancer Letter*, Jan. 18, 2019).

As ASCO president, she held a series of meetings with patients and care providers.

Wrote Bertagnolli:

> These visits are heart-warming and heart-breaking. At every meeting is a story of dedication, resourcefulness, and community support to meet the needs of cancer patients. This illustrates a central dilemma that we face: how to structure our healthcare system so that each

unique community has what it needs to support the patients and providers of cancer care.

We cannot solve complex problems without understanding them, and understanding requires information: data from the clinical setting. It is time to give every patient the opportunity to participate in research and contribute to progress. ASCO is working toward this mission in a number of areas, including expanding eligibility criteria for clinical trials and removing financial barriers to broaden clinical trial participation.

I once heard someone say the only participants in cancer clinical trials are marathon runners who have cancer and happen to live in cities with large cancer centers. Notwithstanding the hyperbole, the fact remains that clinical trial participants differ significantly from the greater population of cancer patients, especially as it relates to race, ethnicity, and age.

This potentially makes the results of our research less applicable to treating more diverse patient populations seen in clinical practice. We know from many studies involving cancer patients that the greatest determinant of whether a patient participates in a clinical trial is whether their physician discusses participation. While there are many reasons that trial participation by both clinicians and patients is low, we need to do what we can to encourage clinicians to enroll patients and make it easier to participate in research.

A major barrier to clinical trials access is stringent eligibility criteria, leading to fewer patients qualifying to participate. Cancer researchers and sponsors have a responsibility to broaden eligibility criteria for clinical trials participation in order to rectify this issue. ASCO, Friends of Cancer Research, FDA, NCI, the NCI Cooperative Groups, and many other stakeholders are working to increase the diversity of clinical trial participants by broadening eligibility criteria…

Considerable work remains to give every patient the opportunity to participate in, and benefit from, cancer clinical trials, but it is a task that all oncologists must embrace. We owe it to our patients and our field to give everyone a chance to contribute to research that increases our understanding of and leads to better treatments for cancer.

As president of ASCO, Bertagnolli set out to create a lingua franca for electronic health records and deployed an initiative, dubbed mCODE, to introduce common standards for cancer data elements (*The Cancer Letter*, June 7, 2019).

"Through her work as chair of the mCODE Executive Committee, Dr. Bertagnolli successfully spearheaded development of mCODE—short for Minimal Common Oncology Data Elements—a health data standard now approved by Health Level Seven International (HL7) designed to facilitate digital cancer data interoperability and improve patient care and research," ASCO's Hudis said to *The Cancer Letter.*

Bertagnolli's research is focused on the APC (Adenomatous Polyposis Coli) gene, an important factor in colorectal carcinogenesis and in the development of desmoid tumors, according to the Dana-Farber/Harvard Cancer Center research consortium.

Using animal tumor models of the human disease, Familial Adenomatous Polyposis, Bertagnolli's laboratory investigates the mechanisms of tumor transformation initiated by APC mutation or loss. Her laboratory also studies modulation of APC gene activity and tumor formation by chemopreventive drugs. This work includes animal model studies, and also human clinical trials in colorectal adenoma prevention and risk assessment.

Bertagnolli credits her grit as a physician and surgeon to her formative years on her family's cattle ranch in Wyoming. "Back then surgery was a fairly hostile environment for women: the hours were brutally demanding, and it took many years to finish," Bertagnolli said in 2018 to The ASCO Post. "I came from a ranching background, so I wasn't about to let a male culture intimidate me.

"When I was a kid, we raised sheep, but it later became a working cattle ranch and remains one to this day. It was a wonderful way to grow up; the state itself is simply gorgeous," Bertagnolli said. "We were 60 miles away from the nearest town, so we had to be independent and resourceful. If something broke you needed to fix it yourself, and when it came time to make dinner, you had to make do with whatever was available. I have two brothers and a sister, and we're all pretty good at preparing and planning ahead, largely due to growing up on an isolated ranch."

Bertagnolli attended Princeton University as an undergraduate, received her medical degree from the University of Utah College of Medicine, and completed her residency at Brigham and Women's Hospital. She was elected to the National Academy of Medicine in October 2021.

Douglas Lowy will continue to serve as the NCI acting director while Bertagnolli's appointment is finalized.

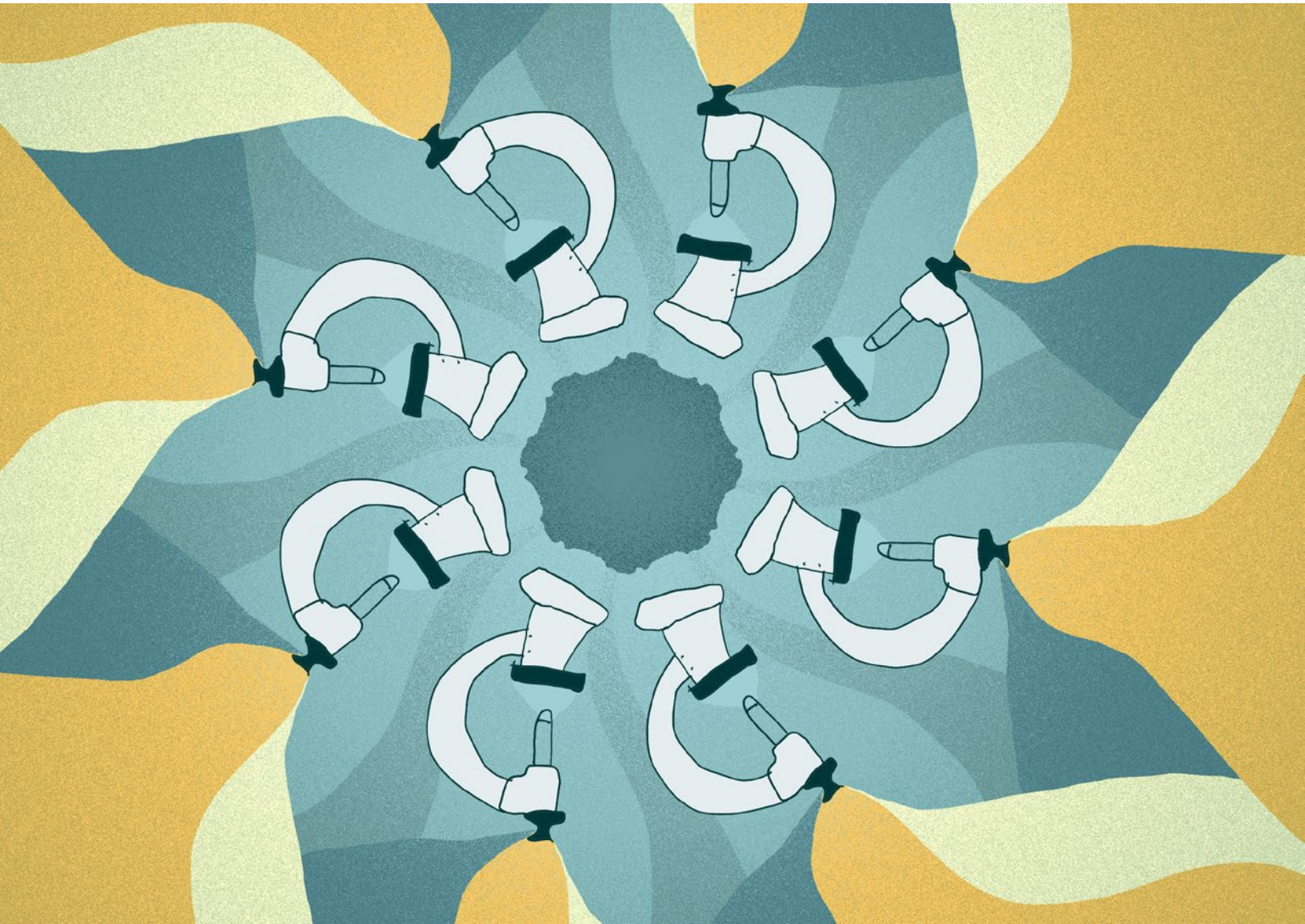
Lowy has stepped up in the acting director role three times in recent years: following Harold Varmus's departure in 2015, during Sharpless's stint at the helm of FDA, and following Sharpless's resignation.

THE CANCER LETTER | JULY 22, 2022 | VOL 48 | ISSUE 29

With $100M gift, Sloan Kettering Institute establishes Kravis Cancer Ecosystems Project to study tumor environment

By Matthew Bin Han Ong

Two years ago, as next-generation sequencing and checkpoint inhibitors became the standard of care in many cancers, Joan Massagué started hearing questions from philanthropists about the "next big thing" in cancer research.



There wasn't an immediately obvious answer—the heyday for molecular characterization of cancers was already underway—but Massagué, director of Sloan Kettering Institute, realized that more investment was needed further upstream of the clinic, beyond oncogenes.

"Now is high time to go get concrete answers beyond what genes rendered cells more aggressive than their companions," said Massagué, who has led SKI, the basic and translational research arm of Memorial Sloan Kettering Cancer Center, since 2014.

"It's a great watershed moment for physicians and scientists to come together and go get it," he said to *The Cancer Letter.*

That goal of driving novel cancer science through preclinical research became a guiding principle for The Marie-Josée and Henry R. Kravis Cancer Ecosystems Project, SKI's flagship initiative within MSK's latest strategic plan for preclinical research.

The project, which is funded by a $100 million gift from the Marie-Josée and Henry R. Kravis Foundation, seeks to solve the mysteries of tumor metastases and the biological relationships between cancers and their environments.

CAR T-cell therapy and the advent of checkpoint immunotherapy, for example, stemmed from tumor immunobiology and the investigation of several immune cells and a few molecules, said Massagué, who serves as the chief strategist for the Kravis Cancer Ecosystems Project.

"There is much more where this came from to go get," Massagué said. "That is how we came about, that we need the means and inspiration to mobilize people to go out of their routine high-end project, to come together and attack these questions."

A guest editorial by Massagué and Marie-Josée Kravis, vice chair of the board of trustees at MSK, appears on page 12.

The Kravis Foundation was established in 1985 by Henry R. Kravis, a business financier and investor who is a co-founder of Kohlberg Kravis Roberts & Co., an asset manager specializing in private equity, fixed income and capital markets. The foundation primarily provides support for education, arts and culture, and social services.

Why was SKI chosen for a cancer ecosystems program?

"We are not unique in being a cancer center that has great cancer research, translational and basic research on cancer," Massagué said. "There are others. They are great, and they are all needed.

"But we are more unique in being a center that, in addition to that, has a very robust and very confident investment in basic science that is relevant to cancer, even though it is not yet at cancer."

Mission: Double the pace of preclinical research

With a budget of $10 million per year over 10 years, the SKI project will be focused on *de novo*, meritorious research that would be directed from within MSK, with invitations for experts with actionable concepts to collaborate and submit ideas—regardless of institutional affiliation or country of origin.

"We know each other. We know everybody. We know who is good at what," Massagué said. "It's going to be very concrete, very ready. For example, taking three groups now by coming together, they just get done in three years what would take otherwise six, with twice as many people and funds.

"But that is going to be not by a request for applications," Massagué said. "It will be connoisseurs identifying people out there who they know have the goods or the talents needed to make the strongest possible case."

A primary goal of the Kravis project is to empower current expertise and technologies to focus on a select set of grand challenges related to cancer progression, and to accomplish within 10 years what would otherwise require 20. Researchers would also look at how progressing cancers respond to—or fail to respond—to therapy, and how failure, i.e., metastases, could be prevented.

While the project isn't designed for conduct of clinical trials, its scope isn't limited solely to preclinical research, either.

"Biology, immunology, metabolism, a microbiome relationship of stress or age or whatever. It's a long list. We are going to source from within this list," Massagué said. "We'll be very happy to solve, say, three big hits per year. Over 10 years, that's 30 big hits that were accelerated."

Other recent philanthropic initiatives in oncology with parallel "grand challenge" missions include:

- Break Through Cancer, a research alliance of five top-tier academic cancer centers that was announced with a challenge pledge of $250 million from William H. Goodwin, Jr., Alice T. Goodwin, and their family, and the estate of William Hunter Goodwin III (*The Cancer Letter,* Feb. 25, 2021).
- Cancer Research UK's Grand Challenge, which supports multidisciplinary teams across the globe, has invested £200 million since its launch in 2015. In 2020, NCI and CRUK partnered to create the Cancer Grand Challenges (*The Cancer Letter,* July 21, 2017; June 17, 2022).
- Parker Institute for Cancer Immunotherapy, established in 2016 with $250 million from Sean Parker, brings together immunologists from premier academic institutions with industry and government (*The Cancer Letter,* April 15, 2016).

"We are excited for our colleagues at Memorial Sloan Kettering Cancer Center to be receiving this transformative gift from the Kravis family," said Tyler Jacks, president of Break Through Cancer, and the David H. Koch Professor of Biology and director of the Koch Institute for Integrative Cancer Research at MIT.

"The approach of deeply investigating the genetic, epigenetic and environmental regulators of disease initiation and progression is important and timely," Jacks said to *The Cancer Letter*. "We at Break Through Cancer look forward to interfacing with the investigators funded through the Kravis Cancer Ecosystems Project in collaborative efforts in the years ahead."

MSK is a founding member of Break Through Cancer, and is a participant in the Cancer Grand Challenges as well as at Parker Institute. "It is interesting that different parties arrive at the same sense, that is, asking for task forces to self-identify themselves with a clear mission to conquer that hill," Massagué said.

The SKI project will use a "systems-level approach" to study the tumor environment—separate from the discipline of systems biology—because cancer is a systemic disease that isn't just about cells with certain constellations of mutations that determine progression and metastasis.

"Our bodies have defenses of all kinds to prevent this from happening almost every minute of the day or every day. This happens in the context of a whole body system," Massagué said. "So, our term 'systems' has to do with the fact that the questions that we're going to concentrate on are, for example, why do immune cells that are rallying to invasive tumors become exhausted and become subjugated by that tumor?

"What biology in the immune cells is the tumor exploiting to muffle them and how could that be reversed?"

Following that, there is an abundance of hypothesis-generating questions for the SKI project to interrogate. For instance:

- How are metabolic conditions of the whole organ impacting a cancer's ability to evade the immune system and dampen natural regulatory processes?
- How is the microbiome directly impacting a tumor resistance mechanism that has been linked to the microbiome? What is the biology?
- Based on existing literature on the biology of disseminated disease, what is known or unknown about residual disease after a tumor or a metastasis responds well to therapy?
- What aspects of the biology of dormant disseminated cells, prior to a first relapse, is recaptured by a disseminated population after significant, but not fully successful, elimination of a tumor mass by combinations of targeted therapy and immunotherapy?
- What are the vulnerabilities of residual disease, knowing the biology of resistance in residual cancer cells?

"These are all cases in which the whole-body system can impact the answer," Massagué said. "There could be systemic immunity. There could be clonality phenomena, explaining how the answer may differ depending on the age of the individual.

"The imagination is the limit about what it could be."

Massagué: Let's invite great partners and solve mighty problems

The SKI-Kravis model for accelerating research and sourcing expert partners is innovative, as well as reminiscent of the Biden administration's push to create "transformative" progress in cancer research through the Advanced Research Projects Agency for Health, or ARPA-H, using unconventional collaborations across a broad spectrum of stakeholders (*The Cancer Letter*, April 9, June 18, 2021).

Like ARPA-H—which sparked discussion about what the agency can do to complement NCI's basic and translational science portfolio—the SKI project can be expected to inhabit the gray area between solving engineering problems in oncology and addressing scientific questions that aren't ready to be solved through engineering (*The Cancer Letter*, April 23, 2021; May 6, 2022).

"It will not be wide open, curiosity-driven research. We have that, too; we have support for that as well—very generous support," Massagué said. "But this is going to be very problem-directed. Problems that within three years of activity ought to be solved.

"What shape this will take, time will tell. It's biology. Biology is very soft around the edges," Massagué said. "The intention here is just to contribute as an institution through our resources and through these additional wonderful resources to help the field make the biggest possible difference. That's what we're all about."

Massagué anticipates that SKI will be working with other institutions, including the NCI, to eliminate potential redundancies and ensure that the project is funding research that fills a knowledge gap.

"If we become aware that the NCI or other bodies have great activity in that area, we will want to coordinate that, to do it as economically and frugally as possible, in as coordinated a manner as possible," Massagué said.

MSK and the Kravis Foundation have done this before.

The cancer center's Marie-Josée and Henry R. Kravis Center for Molecular Oncology—which is now "self-propelled" to expedite and streamline cancer genomics research and guide cancer treatment—was established in 2014 with a similar $100-million-over-10-years gift from the Kravis Foundation.

Another noteworthy investment at MSK is the $50 million Alan and Sandra Gerry Metastasis and Tumor Ecosystems Center, designed to support research initiatives that specifically focus on metastasis.

"All of these have given us a sense of what is possible with philanthropic support," Massagué said. "We are emerging enriched by the knowledge and insights that cancer genome science has put on the table and all the additional ancillary technologies, single cell analytics, and so forth.

"It is now high time that we address the questions that affect the patient in the clinic—the fear of relapse, the fear of metastasis, the fear that there are behaviors in diet, in exercise, that may affect positively or negatively the course of their disease, or what they perceive to be the possibility of disease, latent disease, dormant disease.

"While we will not be able to provide all these answers quickly, these are the kind of answers that is now the time to go after."

Peer review for research funded by the SKI initiative will be conducted on an ad hoc basis and tailored to the projects under review. Panels will include teams composed of external reviewers and one or two internal reviewers.

"The leadership of the whole endeavor will be aware of those projects [and] who is coming together," Massagué said. "But we will not let that impression dominate or bias the awarding.

"We are going to call in experts to say whether this has a good chance of cracking open a problem," Massagué said. "Those external colleagues would be procured from the worldwide community."

An argument for robust investment in basic cancer science

SKI has a mission to fund "any and all" science that is relevant to cancer, including projects that, at a singular point in time, may have no direct link to cancer.

"We believe that this will end up impacting cancer in a way that very directly benefits the patient," Massagué said. "We believe that not just as an act of faith, but, by now, one after another, examples from history where that happened."

Massagué said his initiative stands on the shoulders of giants at SKI:

- In 1984, physician-scientists Malcolm Moore and Karl Welte isolate granulocyte colony-stimulating factor from human cells that stimulates new blood cell growth and could be used to boost the ailing bone marrow stem cells of patients undergoing cytotoxic therapies. G-CSF forms the basis of filgrastim (Neupogen), one of the most impactful cancer drugs to be developed.

- Physician-scientist John Mendelsohn, who co-led the SKI Molecular Pharmacology Program from 1985 to 1990, developed the concept of using antibodies to block the epidermal growth factor receptor as a way to treat cancer—spurring the development of the EGFR-blocking drug cetuximab (Erbitux) and opening a path for other growth factor receptor-targeting drugs, including trastuzumab (Herceptin).

- In 2002, Michel Sadelain, Renier Brentjens, and Isabelle Rivière developed genetically engineered T cells with a chimeric antigen receptor, which at the time involved assessing the ability of these T cells to recognize cancer cells in a Petri dish. FDA approved the first CAR T therapies, Kymriah and Yescarta, in 2017 (*The Cancer Letter*, July 14, Oct. 20, 2017).

Not too long ago, basic research was siloed within basic science-directed programs, including structural biology, cell biology, and molecular biology.

"Not anymore," Massagué said. "We have basic research projects in most labs at SKI, and we have cancer-directed, including translationally-intended projects in most labs, or in many labs at SKI, regardless of whether these labs are in a program that, overall, is more basic-oriented or more translation-oriented.

"There is full amalgamation, as it should be, because this is what cancer demands of us as scientists. We cannot be self-contained in discipline-oriented means," Massagué said. "But we are called upon to solve problems or acquire the knowledge, basic knowledge, to solve these problems, whatever it takes."

History has proven that special emphasis on basic science is a "great secret component of the sauce" for patient benefit and progress in cancer medicine, Massagué said.

"That also distinguishes us from other institutions, which are restricting themselves more to cancer research that has a clear, certain path to translation," Massagué said.

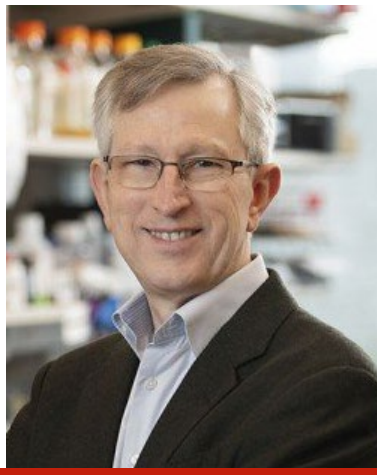
"That's the vision, and the reality, and how we cultivate SKI going forward."

THE CANCER LETTER | JULY 22, 2022 | VOL 48 | ISSUE 29

GUEST EDITORIAL

Understanding genes isn't enough to stop cancer—it's time to use a systems approach to target metastasis

The past two decades have been a golden age of discovery in genetics and cancer research. Using fast, affordable DNA sequencing, scientists have identified scores of gene mutations associated with cancer and developed highly effective drugs to target them.



Joan Massagué, PhD
Director, Sloan Kettering Institute;
First incumbent of the Marie-Josée and Henry R. Kravis Foundation Chair

Marie-Josée Kravis
Vice chair of the Board,
Memorial Sloan Kettering Cancer Center;
Chair of the Board, Sloan Kettering Institute;
Chair, Joint Science Committee

As tumor sequencing has become a routine part of cancer diagnosis, we have stopped treating cancer based on its location in the body and focused instead on the genes that drive its growth in each individual patient.

This revolutionary approach, called precision oncology, has saved countless lives. Yet too many people are still dying from cancer, and we now know that addressing genetics alone cannot save most of them.

Up to 90% of the 600,000 Americans who will die from cancer this year will die from metastasis, when cells from a primary tumor spread and grow in other parts of the body. Precision oncology cannot treat metastatic cancer because, to our knowledge, there are no metastasis genes.

We have certainly searched for metastasis genes—researchers at Memorial Sloan Kettering Cancer Center (MSK), for example, have analyzed tumors from more than 25,000 patients whose cancer had spread, finding no mutations that specifically drive metastasis.

This prompts one of the largest questions in the field: What spurs the spread of cancer if not genes alone? To answer it, and to save even more lives in the next decade, we need to look at cancer through a different lens.

The next treatment revolution will come from understanding cancer as a systemic, rather than a predominantly genetic, disease—one that begins in a single location, but relies on conditions throughout the body in order to spread. Just as invasive species of plants or fish can only thrive in a nurturing environment, there is ample evidence that cancer, too, requires the right conditions to flourish in the body's complex ecosystem.

The idea that metastasis depends on cooperation between tumor cells and the organs they invade stretches back more than a century, and we have long observed that some tissues, notably those of the lung, liver, brain, and bone, foster metastatic cells better than others. We don't know why—but we have never been in a better position to find out.

“Advanced imaging and computational techniques that didn't exist a decade ago allow us to observe and understand this disease as never before—and to pursue answers to some of our most challenging questions.”

Recognizing the importance and urgency of this quest, MSK recently launched The Marie-Josée and Henry R. Kravis Cancer Ecosystems Project, an ambitious effort to understand metastasis and develop new cancer treatments that target factors beyond genetics.

We already know that treatments that target the environment surrounding cancer cells can be powerfully effective. For example, immunotherapy—which was conceptualized in the 1890s and came to fruition in our labs 100 years later—does not kill cancer cells directly, as traditional chemotherapy does.

Instead, it mobilizes the body's own defenses to fight cancer, turning a once-welcoming ecosystem into a hostile one. And while the immune system plays a major role in cancer progression, we know that other factors do as well. Studies show that the nervous and endocrine systems, obesity and inflammation, and even the gut microbiome, may tip the balance in ways we are just beginning to understand.

Partnerships between philanthropists and scientists are vital accelerators of medical research, having prompted major breakthroughs in HIV, malaria, and more recently, promising COVID-19 vaccines and treatments. It is no less true for cancer.

Nearly 10 years ago, we partnered to jump-start research in cancer genomics, recognizing that neither government nor the scientific community would advance this work as quickly as people diagnosed with cancer deserve.

Our collaboration and others yielded extraordinary results in precision oncology, including a technology that can identify more than 500 cancer-associated mutations in tissue samples and a liquid biopsy test that pinpoints fragments of tumor DNA in blood. Dozens of new drugs that target gene mutations have been approved, bringing more treatment options to patients than at any other time in cancer history.

This latest endeavor will accelerate progress in cancer research once again. Advanced imaging and computational techniques that didn't exist a decade ago allow us to observe and understand this disease as never before—and to pursue answers to some of our most challenging questions.

We invite other scientists and philanthropists to join this effort.

This is a time of extraordinary potential for cancer research. We cannot predict the outcome of the work ahead, but our vision is clear: By tackling the leading cause of cancer death, we aim to help the next generation face every cancer diagnosis with hope and confidence.

THE CANCER LETTER | JULY 22, 2022 | VOL 48 | ISSUE 29

OBITUARY

Jerome Carl Landry, radiation oncologist at Emory and Grady, dies at 66

By Winship Cancer Institute of Emory University news staff

Jerome Carl Landry, MD, MBA, a radiation oncologist at Winship Cancer Institute of Emory University, a professor at Emory University School of Medicine, and former medical director of Grady Memorial Hospital, died recently.

Landry was born and raised in Louisiana. After overcoming neurologic complications of polio at a young age, he graduated magna cum laude from Xavier University in New Orleans and then earned his medical degree from Harvard Medical School.

He joined Emory University in 1983 as a resident in internal medicine, prior to returning to Harvard for his residency training in radiation therapy at Massachusetts General Hospital, where he was chief resident in his final year. He later received an MBA degree from Kennesaw State University in Kennesaw, Georgia.

In 1987, he returned to Emory to join a small group of medical and surgical oncologists that formed what is now known as the Winship Cancer Institute.

Additionally, he was tasked with developing radiation oncology services at Grady Memorial hospital, and was medical director there until 2016.

An expert and pioneer in the field of radiation oncology and treatment of gastrointestinal tumors, Landry was the first to use and develop image-guided and advanced therapeutic techniques that now define modern radiation treatments and continue to improve patient outcomes.

He published extensively on intensity modulated radiation therapy for gastrointestinal tumors and soft tissue sarcomas, providing on-site IMRT training in more than 40 radiation oncology centers in the United States and abroad. His work has been highlighted at medical and academic conferences.

"Dr. Landry's ground-breaking research in developing new techniques in radiation therapy has helped to improve cancer care for patients with cancer

in Georgia and beyond," said Jeffrey Bradley, James W. Keller Distinguished Professor in Radiation and interim chair for the Emory Department of Radiation Oncology. "His transformative work established Winship of Emory as a leader in IMRT."

"Landry was a leader in the field of GI oncology and led national clinical trials," said Suresh Ramalingam, executive director of Winship Cancer Institute. "He leaves a long-lasting legacy in the field and at Winship."

During his time at Winship, Landry won numerous awards and was recognized by his peers as one of the best doctors in America by several publications, including *Atlanta Magazine*.

"Jerome was a foundational figure in our department, a passionate advocate for patient care at Grady, and beyond his academic accomplishments, he was a genuinely kind person who provided joy to those who knew him," said Joseph Shelton, associate professor of radiation oncology and medical director of the Loughlin Radiation Oncology Center at Grady Memorial Hospital. "He was a valued mentor and friend to me throughout my career."

After three decades, Landry left Emory in 2016 for health-related issues, but remained an engaged and valuable resource to those at Emory. In 2018, an endowed professorship was established in his name—and is held by David S. Yu, the inaugural Jerome Landry, MD, Chair of Cancer Biology and associate professor of radiation oncology.

"He was a force in our department, mentoring and training countless faculty and students," Yu said.

Landry is survived by his long-time partner, Dwillete Johnson.

In lieu of flowers and to honor Landry's passionate service to this institution, the family requests donations be made to Emory University to support the endowed professorship named in his honor and to host an annual invited lecture at Winship Cancer Institute on topics related to his passions: representation of racial minorities in medicine, oncologic and health care delivery in underserved populations, and evolving paradigms in radiation and cancer care.

> "Jerome was a foundational figure in our department, a passionate advocate for patient care at Grady, and beyond his academic accomplishments, he was a genuinely kind person who provided joy to those who knew him."
>
> *– Joseph Shelton*

Contributions can be made to the Winship Cancer Institute of Emory University, Office of Gift Records, Emory University, 1762 Clifton Rd. NE, Suite 1400, Atlanta, GA 30322.

IN THE ARCHIVES

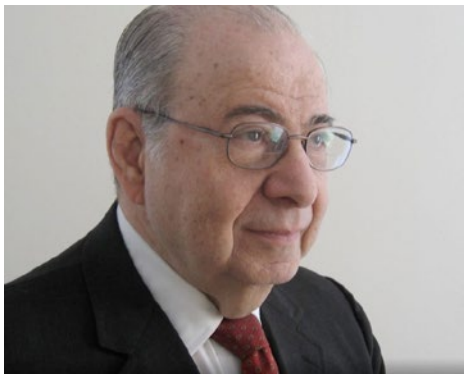
CANCER HISTORY PROJECT

Joe Bertino, Yale Cancer Center's founding director

In July, The Cancer History Project is focusing on the founders of cancer centers. Joseph R. Bertino was the founding director of Yale Cancer Center, who served in that role from 1973 to 1975 and remained at Yale through 1986.

Bertino's pioneering work at that time focused on the role of methotrexate in cancer treatment. He died Oct. 10, 2021.

Founding the Yale Cancer Center



- **Book:** The Clinical Cancer Program at Yale
  By Yale Cancer Center | Dec. 2, 2021

The following is an excerpt of *The Clinical Cancer Program at Yale*, written by David S. Fischer, clinical professor of medicine (oncology) at Yale School of Medicine, attending physician, Smilow Cancer Hospital at Yale:

Bertino testified before the Senate-House Finance Committee in Washington on March 14, 1974 about the construction grant application and a core program grant application to establish a State Comprehensive Cancer Center at Yale. The total construction cost of the Cancer Center would be $6.2 million.

Yale would offer a match, or $2.4 million, which is a proportion consistent with that offered by other institutions. The State of Connecticut would contribute $1.2 million and Yale University would contribute $1.2 million.

This would be a one-time-only request and no future building was now planned, but it was assumed that in future years, the budget would increase and additional construction would be necessary.

There would also be a request for $6.2 million for a "core" program for 3 years and this annual budget would increase and did not require matching funds. The proposed comprehensive cancer center at Yale would be an important statewide resource. It would serve as a model for top quality cancer care and research and would be an invaluable resource to the individual cancer patient, the community physicians and other health care organizations and facilities.

Yale was officially established as a NCI comprehensive cancer center in May 1974 and Bertino became the first director of the YCCC.

Advances in chemotherapy

- **Podcast:** Conversation between Ed Chu and Vince DeVita
  By Yale Cancer Center | July 22, 2022

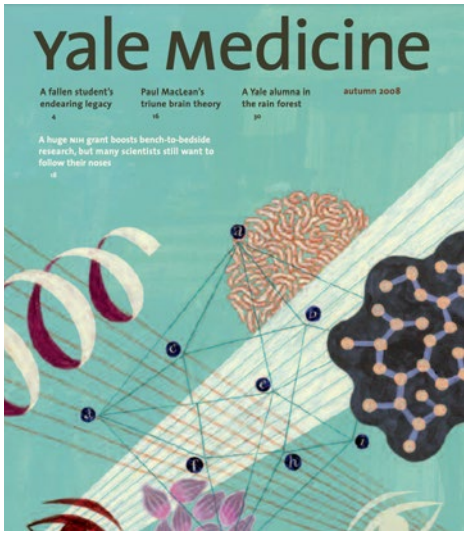
In a recording of Cancer Answers: The History of Chemotherapy, from July 6, 2008, Ed Chu interviews Vince DeVita about the history of chemotherapy.

In this conversation, DeVita overviews Bertino's impact on the field.

"As a matter of fact, later in 1955, because of the interest in nitrogen mustard another drug was developed called methotrexate, which was also worked on here at Yale by Joe Bertino and people like you in the lab.

"The Cancer Chemotherapy National Service Center was started in 1955, which was a national program to begin to screen chemicals for cancer in a major way so that the birth of chemotherapy here lead to development of a national screening program."

The full podcast and transcript are available here.



- A gene to protect bone marrow from chemotherapy
  By Yale Cancer Center | July 22, 2022

The following is an excerpt from an autumn 2008 edition of *Yale Medicine*.

In a new approach to cancer treatment, researchers are studying a form of gene therapy that may make bone marrow more resistant to chemotherapy, allowing for higher doses and better outcomes.

"We are turning the tables," said Joseph R. Bertino, MD, interim director and chief scientific officer of the Cancer Institute of New Jersey, at Yale Cancer Center grand rounds in May. "This therapy will allow for safer use of drugs and an increase in dosage. If we do this we can protect patients from a wide variety of chemotherapy drugs."

Bertino, who was director of the Yale Comprehensive Cancer Center from 1973 to 1975, said this approach calls for introducing a drug-resistant gene into hematopoietic progenitor cells.

That could limit the drugs' toxicity and preserve the marrow's ability to produce infection fighting white blood cells.

Oncologists would then be able to prescribe higher doses of chemotherapy, potentially leading to improved outcomes. Bertino said two clinical trials—one for lymphoma and another for pancreatic and breast cancer—are in the planning stages.

The Legacy of Joe Bertino

- Joseph R. Bertino: 50 Years of Cancer Research, A "Golden" Opportunity
  By Rutgers Cancer Institute of New Jersey | April 21, 2021

For some 60 years, Joseph R. Bertino, MD, researcher and former interim director and chief scientific officer at Rutgers Cancer Institute of New Jersey, has devoted his life to improving therapies for cancer and hematologic disorders and has contributed his expertise toward establishing the foundation of modern cancer research.

In 2018, he was recognized by the American Association for Cancer Research with a Lifetime Achievement Award for his significant fundamental contributions to cancer research, either through a single scientific discovery or a collective body of work. Recognizing a half century in the field at the time, Bertino was the subject of an interview that appeared in the spring 2013 edition of The Cancer Institute of New Jersey's *Oncolyte* newsletter.

While having taken care of thousands of patients with lymphoma and other blood cancers, it is also at the laboratory bench where Joseph R. Bertino leaves an indelible impression.

Motivated by the passing of a young nephew from leukemia and the patients he first cared for as a resident, Bertino has devoted most of his life to improving therapies for cancer and hematologic disorders. For more than 50 years he has contributed his expertise toward establishing the foundation of modern cancer research.

How far has cancer research come in the past half century?

To put things in perspective, a form of nitrogen mustard, developed initially for military use, was considered "advanced" for its time in the 1940s. It was used to treat lymphoma and became one of the first modern chemotherapy drugs.

Methotrexate, used in the treatment of both solid and non-solid tumors, was another early chemotherapy drug that led to successful treatment outcomes and would serve as a focal point in later years for Bertino's work.

Over the past few decades, safer and more effective chemotherapy agents have been developed, but this form of treatment was still in its infancy when Bertino first started his career.

The late John Mendelsohn, Joseph R. Bertino, and Steven Averbuch at the AACR annual meeting in 2008. Bertino was the recipient of the Burchenal Award. *Photo credit: ©2008 AACR/Todd Buchanan*

- Joseph R. Bertino made fundamental discoveries in oncology, was president of ASCO, AACR
  By *The Cancer Letter* | Oct. 15, 2021

Joseph R. Bertino, a physician who made fundamental discoveries in cancer biology, defined curative cancer treatment regimens, trained generations of influential cancer researchers, ran productive laboratories, and served as the inaugural director of Yale Cancer Center, died on Oct. 10. He was 91.

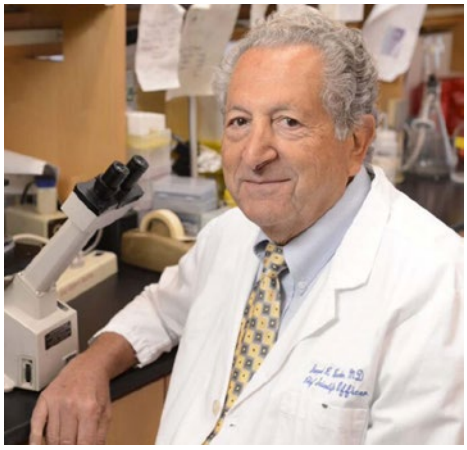
After Bertino was awarded the 2007 Pinedo Prize at the VU Cancer Center in Amsterdam, his friend and former fellow Bruce A. Chabner wrote in *The Oncologist*, a journal he edits:

"Dr. Bertino began his remarkable career in research in Seattle in the late 1950s, where he worked with one of the great biochemists of that generation, Frank Huenneikens.

"[Bertino] discovered that methotrexate exposure led to a rapid increase in the intracellular level of its target, probably an effect on dihydrofolate reductase (DHFR) transcription, and later, with Bob Schimke at Stanford, he reported the quite remarkable observation of gene amplification of DHFR, opening a whole new era in drug resistance research and unveiling an unexpected aspect of the plasticity of the tumor genome.

"Many other important observations followed, both in the laboratory and in the clinic, including the evolution of high-dose methotrexate therapy and other aspects of methotrexate pharmacology.

"Largely as a result of his work, this drug has become the stalking horse for understanding how cancer drugs work and why they fail."



- Remembering Joseph Bertino, MD, a Leader in Drug-Resistance Research
  By Memorial Sloan Kettering Cancer Center | Oct. 22, 2021

Joseph Bertino, MD, who served as Chair of Memorial Sloan Kettering Cancer Center's Molecular Pharmacology and Therapeutics Program from 1987 to 2002, passed away October 11, 2021, at the age of 91.

He was a true giant in the field of cancer biology who helped usher in a new era in drug-resistance research, and a dedicated physician who treated thousands of patients with lymphoma and other blood cancers.

He was also an exceptionally kind, beloved mentor and colleague who helped launch the careers of many physicians and scientists who went on to become prominent leaders in cancer care and research.

Dr. Bertino served as past president of AACR and ASCO and was the founding editor of the Journal of Clinical Oncology, now the premier oncology journal. He also received numerous honors and awards during his 60-year career, including the 2018 AACR Award for Lifetime Achievement in Cancer Research.

Among Dr. Bertino's most notable scientific accomplishments were his pioneering studies of the drug methotrexate, which led to greater understanding of why some cancer drugs work and others fail.

His work revealed that use of methotrexate leads to an increase in a protein called dihydrofolate reductase that causes cells to block the drug from attacking the cancer. This observation of "gene amplification" at work paved the way for a multitude of therapeutic advances and helped Dr. Bertino earn an international reputation for his role in finding treatments for leukemia and lymphoma.

In 1961, he joined the faculty at Yale in Pharmacology/Medicine where he held several positions, including

the first Director of Yale Cancer Center in 1973.

He stepped down from this position when he was awarded an American Cancer Society Research Professorship in 1975.

- AACR Remembers Past President and Fellow Joseph R. Bertino
  By AACR | Oct. 21, 2021

Joseph R. Bertino, MD, a past president of the AACR and a Fellow of the AACR Academy whose research on drug resistance led to lifesaving new treatments for leukemia and lymphoma, died October 11, 2021, at the age of 91.

Born in Port Chester, New York, on August 16, 1930, Bertino earned his medical degree from the State University of New York Downstate Medical School in Brooklyn in 1954. After a fellowship at the University of Washington, he joined the faculty of Yale University School of Medicine in 1961 and served there until 1987.

His tenure included serving from 1973 to 1975 as director of the Yale Cancer Center. He then joined Memorial Sloan Kettering Cancer Center and worked there until he joined the Rutgers Cancer Institute of New Jersey in 2002. At Rutgers, he was senior adviser to the director of the cancer institute and University Professor of Medicine and Pharmacology at Robert Wood Johnson Medical School.

From the early days of his career, Bertino's research focused on drug resistance, particularly as it pertained to methotrexate, a chemotherapeutic agent for blood cancers and various other malignancies.

Bertino and colleagues reported that dihydrofolate reductase (DHFR) gene amplification was an important driver of methotrexate resistance. These seminal findings helped explain why some cancer drugs work, while others fail, and paved the way for new cancer treatment regimens to be introduced into the clinic.

Bertino's research dedicated to hematologic malignancies led to his becoming closely involved with the Lymphoma Research Foundation, where he served as founding chair of the organization's Scientific Advisory Board.

In recent years, his research was dedicated to novel drug development for solid tumors and drug target identification for rare lymphomas.

Joseph R. Bertino, MD, FASCO, speaking to trainees during Giants in the Field of Oncology session in the Trainee & Early Career Oncologist Member Lounge at the American Society of Clinical Oncology (ASCO) 2017 Annual Meeting

- ASCO Mourns Cancer Drug Development Pioneer, Past President Dr. Joseph R. Bertino
  By ASCO | October 21, 2021

ASCO is saddened by the passing of Joseph R. Bertino, MD, FASCO, who played a pivotal role in the organization's history. He served as the Society's president from 1975-1976 before becoming the founding editor-in-chief of the Journal of Clinical Oncology.

In an editorial printed in the premiere issue, published in January 1983, Dr. Bertino wrote, "The aim of the Journal of Clinical Oncology is to be a focus for communication for research pertaining to the clinical disciplines of oncology." Today, the journal is ASCO's flagship publication, serving readers as the most credible, authoritative, peer-reviewed resource for oncology research.

"Dr. Bertino did it all—major scientific discoveries, organization and professional leadership, teaching, and clinical care—with a rare grace and dignity. He made everyone feel respected and motivated everyone to contribute their best," ASCO CEO Clifford A. Hudis, MD, FACP, FASCO, said.

In the wider field, Dr. Bertino's best known contribution was his discovery—together with Robert N. Schimke, MD, Rodney E. Kellems, PhD, and Frederick W. Alt, PhD—that gene amplification was a mechanism of methotrexate resistance; specifically, the DHFR-gene was found to be a mechanism for overproduction of dihydrofolate reductase.

Later, while at Memorial Sloan Kettering Cancer Center, Dr. Bertino's continued research of methotrexate yielded the discovery that defective uptake of methotrexate and low-level amplification of DHFRcaused resistance to the drug in

patients with leukemia and soft-tissue sarcomas.

This and other discoveries eventually led to new analogues and treatments for these patients.

- Remembering Joe Bertino
  By Bruce Chabner | Oct. 15, 2021

My dear friend and mentor, Joseph R. Bertino, MD, died Sunday, Oct. 10, 2021, in New Brunswick, NJ, after an extended illness.

He remained active in his laboratory until the last days of his struggle, as one would expect, knowing his passionate commitment to research. Joe was a unique man, one of the early physician scientists comfortable in a basic laboratory, active in the clinic throughout his career, and "translational" in his work to better the treatment of cancer.

Joe's career and impact have been described in detail in a recent interview in the Cancer History Project. He grew up in Port Chester, NY, one of three brothers, all of whom excelled in school and sports.

Joe attended the Cornell as a 6'2" basketball player, a big guy in those days, found his love for science as an undergraduate, and attended medical school SUNY Downstate Medical School after his junior year in college. Following his medical residency at the University of Washington Hospitals, he discovered his true calling in the laboratory of Frank Huennikens, a brilliant biochemist who loved basketball and folic acid.

Joe and Frank described the induction of dihydrofolate reductase by methotrexate in 1959. How that induction occurred was not clear, only later to be resolved when in 1977 Joe, on sabbatical from Yale, partnered with Schimke, Rod Kellems, and Fred Alt in the discovery of gene amplification.

This research represented a major breakthrough in understanding how tumors become resistant to targeted agents such as methotrexate, 5-fluoro-uracil, and even more contemporary targeted drugs.

This column features the latest posts to the Cancer History Project by our growing list of contributors.

The Cancer History Project is a free, web-based, collaborative resource intended to mark the 50th anniversary of the National Cancer Act and designed to continue in perpetuity. The objective is to assemble a robust collection of historical documents and make them freely available.

Access to the Cancer History Project is open to the public at CancerHistoryProject.com. You can also follow us on Twitter at @CancerHistProj, or follow our podcast.

Is your institution a contributor to the Cancer History Project? Eligible institutions include cancer centers, advocacy groups, professional societies, pharmaceutical companies, and key organizations in oncology.

To apply to become a contributor, please contact admin@cancerhistoryproject.com.

IN BRIEF

NRG Oncology appoints committee chairs, vice chairs

NRG Oncology has appointed the following committee chairs and vice chairs:

Vinai Gondi will lead the NRG Early Career New Investigators (ECNI) Committee alongside Angeles Alvarez-Secord and Priya Rastogi. Gondi is the director of research and education at the Northwestern Medicine Chicago Proton Center and the co-director of the Brian and Spine Tumor Center at the Northwestern Medicine Cancer Center, Warrenville. He also was the Brain Tumor Committee Disease Site liaison for the NRG ENCI Committee.

Ronald Chen was named a vice chair of the NRG National Community Oncology Research Program Patient-Center Outcomes Research Committee. He is a member of the NRG Genitourinary Cancer Committee and the NRG NCORP Cancer Care Delivery Research Committee. Chen is principal investigator of the NRG-CC007CD NRG NCORP trial for increasing dose survivorship care planning in prostate cancer survivors who are receiving androgen deprivation therapy. He is the principal investigator of the NRG-GU008 "INNOVATE" phase III trial.

Stephen Y. Lai was named chair of the NRG Surgical Oncology Committee. Lai is a professor of head and neck surgery at MD Anderson Cancer Center. He is principal investigator of the NRG-HN006 study comparing sentinel lymph node biopsy with the standard of care neck dissection for early-stage oral cavity cancer in patients with negative baseline PET-CT scans.

Vered Stearns becomes vice chair of the NRG Translational Science Committee and co-chair of the NRG Breast Cancer Translational Science Working Group. Stearns is director of Women's Malignancies Disease Group and a professor of oncology at Johns Hopkins Sidney Kimmel Comprehensive Cancer Center, and medical director of the Under Armour Breast Health Innovation Center. Stearns is a member of the NRG Breast Cancer Committee and will co-chair the NRG Breast Cancer Translational Working Group.

Her main research includes utilization of biomarkers to predict response to standard regimens used to treat and prevent breast cancer and introduce new interventions.

Mothaffar F. Rimawi becomes vice chair of the NRG Breast Cancer Committee. Rimawi is the co-leader of the Breast Cancer Program, executive medical director, and associate director of clinical affairs for the Dan L. Duncan Comprehensive Cancer Center at Baylor College of Medicine.

He is a professor in the Department of Medicine, Section of Hematology and Oncology at Baylor College of Medicine. He is chief of the Oncology Service Line at St. Luke Health in Houston.

Rimawi was also chair of NSABP B-52 randomized trial evaluating pathologic complete response rates in patients with hormone receptor-positive, HER2-positive, large operable and locally advanced breast cancer treated with neoadjuvant therapy of docetaxel, carboplatin, trastuzumab, and pertuzumab with or without estrogen deprivation.

Susanna Ulahannan was named chair of the newly created NRG Immunotherapy Subcommittee. Ulahannan is an assistant professor in the Department of Hematology and Oncology at the University of Oklahoma Stephenson Cancer Center and specializes in the treatment of Gastrointestinal Cancers and phase I clinical trials.

She is associate director of the Oklahoma TSET Phase I Program, a group member of the American Society of Clinical Oncology Gastrointestinal Guideline Advisory Board, a member of Society for Immunotherapy of Cancer, a member of the Data Safety and Monitoring Committee, chair of the Molecular Tumor Board, and chair of the Early Phase Disease Site Committee at the Stephenson Cancer Center.

Ulahannan is also the institutional principal investigator of NRG Oncology for Medical Oncology.

Steven Waggoner was named chair of the NRG Ancillary Projects Committee. Waggoner is a physician in the Department of Subspecialty Care for Women's Health at Cleveland Clinic.

He is a professor in the Department of Reproductive Biology at the School of Medicine at Case Western Reserve University and a member of the Developmental Therapeutics Program at Case Comprehensive Cancer Center. Waggoner is also a member of the NRG Membership Committee.

Todd Matthew Morgan was named vice chair of the NRG Genitourinary Cancer Committee. Morgan is chief of the Division of Urologic Oncology, the Jack Lapides M.D. Research Professor, and a

professor of Urology at the University of Michigan.

He is a translational surgeon-scientist and runs an NCI-funded translational research laboratory focused on identifying biomarkers associated with treatment response, primarily through profiling of prostate cancer tumors and circulating tumor cells.

Morgan is co-chair of the NCTN Prostate Cancer Task Force and co-director of the Ronald Weiser Center for Prostate Cancer.

Fox Chase expands Division of Urology and Urologic Oncology

Fox Chase Cancer Center and Temple Health have named the following people to the Division of Urology and Urologic Oncology:

Joshua Cohn—an expert in pelvic organ prolapse, neuromodulation, urinary incontinence, bladder augmentation and urinary diversion, complex bladder pathology, and vaginal reconstruction. Before joining Fox Chase, Cohn was an attending physician in urology for the Tennessee Valley Healthcare System, Department of Veteran Affairs.

He has been both an adjunct assistant professor of urologic oncology at Fox Chase and assistant professor of urology for Einstein Healthcare Network since 2017. He was also associate fellowship director for genitourinary and reconstructive surgery for the Einstein Healthcare Network in Philadelphia. Cohn began work at Fox Chase on July 1 and will see patients at Fox Chase Cancer Center – Huntingdon Pike and Temple Health Ft. Washington.

Justin Friedlander—an expert in the treatment of kidney and ureteral stones, and performs minimally-invasive percutaneous nephrolithotomy for large and complex kidney stones.

Friedlander was previously director of endourology and the Comprehensive Kidney Stone Center for Einstein Healthcare Network in Philadelphia. There, he was associate residency program director and chair of the clinical competency committee.

He has been an adjunct associate professor of urologic oncology for Fox Chase since 2014. Friedlander began work at Fox Chase on July 1 and will see patients at Fox Chase Cancer Center – Huntingdon Pike and Temple Urology at Suburban Hospital.

Eric M. Ghiraldi—an expert in benign prostatic hyperplasia (BPH) treatment. He performs prostate enucleation, an advanced laser surgery to treat BPH.

His research interests include metabolic management for kidney stone disease and treatment options for benign prostatic hyperplasia.

Before joining Fox Chase, he served as an associate professor of urology for Einstein Healthcare Network in Philadelphia. Ghiraldi began work at Fox Chase on July 1 and will see patients at Fox Chase Cancer Center – Huntingdon Pike and Temple Health Ft. Washington.

Jay Simhan was named professor and director of reconstructive urology.

He will also be the fellowship director for the Fox Chase Reconstructive Urology fellowship.Simhan has expertise in reconstructive urology and urologic prosthetics.

He specializes in advanced perineal and abdominal reconstruction, with expertise in laparoscopic, open, and robotic surgical approaches.

He was chief resident in urologic oncology at Fox Chase from 2011 to 2012, and chief resident in urology for Temple University Hospital from 2012 to 2013.

While at Einstein, Simhan was program director for the urologic residency program, chief of urology at Einstein Montgomery, and vice chair of the Urology Department for the health system. Simhan will begin work at Fox Chase on August 15 and will see patients at Fox Chase Cancer Center – Huntingdon Pike and Temple Health Ft. Washington.

Steve Sterious—an expert in conditions including advanced benign prostatic hyperplasia (BPH), urinary tract infection, erectile dysfunction, kidney stones, and incontinence.

His specialties include minimally invasive and robotic surgery, kidney stone surgery, and erectile dysfunction and hypogonadism. Sterious completed his residency training at Temple University Hospital, where he was chief resident of urology there, as well as chief resident of urologic oncology at Fox Chase during his postgraduate training.

He went on to work as a urologist for Einstein Medical Center before joining Fox Chase.

Jordan Berlin named interim leader of Hem/Onc at VUMC

Jordan Berlin was named interim leader of the Division of Hematology and Oncology in the Department of Medicine at Vanderbilt University Medical Center.

The appointment is effective June 1.

The division's existing director, Ben Ho Park, Cornelius Abernathy Craig Professor of Medicine, became director of Vanderbilt-Ingram Cancer Center effective July 1.

Berlin, who joined Vanderbilt in 1999, is Ingram Professor of Cancer Research, professor of Medicine, and associate director for Clinical Research at VICC.

He is co-director of the administrative core for the Gastrointestinal SPORE (Specialized Program of Research Excellence) grant from the National Cancer Institute.

$10M gift from Brock family to establish Brock Family Center for Applied Innovation at VUMC

A $10 million gift from the Brock family, including John F. Brock III, his wife, Mary, and their three adult children—Rebecca Brock Dixon, John F. Brock IV and Major Brock—will establish the Brock Family Center for Applied Innovation at Vanderbilt University Medical Center.

The gift will accelerate translation of discoveries and know-how to the public domain through commercialization and industry partnerships.

John Brock III is the retired CEO of Coca-Cola European Partners PLC. Mary is a philanthropist. Rebecca, John IV and Major are on the Vanderbilt-Ingram Cancer Center Board of Overseers.

The Brock family has previously supported fellowships, cancer research, mentorship and career development for scientists at VICC and VUMC.

OneOncology establishes disease groups, appoints chairs

OneOncology has formed five OneOncology disease groups.

The disease groups and chairs are:

- **Lung:** Melissa Johnson, Tennessee Oncology
- **Breast**: Gregory Vidal, West Cancer Center & Research Institute
- **Genitourinary:** Jahan Aghalar, New York Cancer & Blood Specialists
- **Gastrointestinal:** Henry Xiong, The Center for Cancer and Blood Disorders
- **Hematologic Malignancies:** Jonathan Abbas, Tennessee Oncology

As part of the disease group portfolio, each group guides and approves OneOncology pathways that are consistent with many evidenced-based national guidelines, the company said. OneOncology has developed disease-specific pathways for cancer types including non-small cell lung cancer, renal cell, and prostate cancer.

The disease groups provide OneR direction on clinical trials to pursue, offer the Pharmacy and Therapeutics Committee expertise on newly approved therapies, oversee medical education topics, and deliver strategic direction regarding innovative care models.

Sarah Quinlan named chief program officer of Lymphoma Research Foundation

Sarah Quinlan was named chief program officer of The Lymphoma Research Foundation.

Quinlan's reports to Foundation chief executive officer Meghan Gutierrez.

Quinlan will oversee and provide strategic leadership for foundation education and scientific programs and develop new strategic partnerships in support of LRF programs.

Quinlan joined LRF in 2019 as the senior director of programs and strategy. Prior to this, she was director of communications at CancerCare.

Since joining the foundation, Quinlan has expanded the national patient education programs, professional education activity, and support services to serve more than 100,000 people annually. In 2020, Quinlan led the foundation's expansion of Spanish language patient resources, and the delivery of related patient and caregiver education programming.

Researchers receive $9M NCI grant for imaging tech in clinical trials

Researchers who developed a camera technology inspired by the mantis shrimp's visual system have received a $9 million P01 award from NCI.

Developed by Cancer Center at Illinois scientists Viktor Gruev and Shuming Nie, this discovery can allow clinicians to receive more information during biopsies and detection procedures, which affects intraoperative surgical procedures for cancer patients.

Researchers at the University of Pennsylvania, Purdue University, and Johnson & Johnson are also principal Investigators on the grant and are leading clinical trials with lung cancer patients at Penn Medicine.

Gruev has collaborated with Illinois colleagues to re-create the mantis shrimp's complex visual system in a single device that would provide doctors with a multi-spectral view—allowing surgeons to see exactly where the tumor is located.

This technology provides surgeons with better images during biopsy and when performing endoscopies.

This P01 award will allow Penn Medicine doctors to utilize the Illinois technology when conducting bronchoscopies on patients to detect and diagnose lung cancer.

In addition to the camera advancement, the UIUC team is researching how augmented reality can improve the information received by surgeons. Gruev's lab has created goggles that will provide 3D visualization to doctors during surgery.

The Illinois team is working with grant co-PI Timothy Fan, CCIL research program leader and Illinois professor of veterinary clinical medicine, to establish clinical trials with animal patients.

University Hospitals Cleveland Medical Center named first SpaceOAR Hydrogel Center of Excellence in the world

University Hospitals Cleveland Medical Center was designated as the first SpaceOAR Hydrogel Center of Excellence in the world, led by urologic oncologist Jonathan Shoag, and radiation oncologist Daniel Spratt.

SpaceOAR is a device manufactured by Boston Scientific that has demonstrated reduced side effects for patients receiving radiotherapy for prostate cancer. The Center of Excellence designation recognizes the commitment to prostate cancer care and the genitourinary oncology team.

The team who built the SpaceOAR program includes Daniel Spratt, Renee Roebke, Jonathan Shoag, and Christine Mack.

SpaceOAR Hydrogel is made primarily of water and polyethylene glycol that naturally leaves the body after approximately six months. A healthcare professional can implant SpaceOAR Hydrogel, a minimally invasive outpatient procedure, in an office, hospital, clinic or surgery center and, typically, patients can go back to normal activities soon after the procedure.

Clinical data has demonstrated the benefits of SpaceOAR Hydrogel, including a reduction in rectal toxicity, and a higher likelihood of maintaining urinary and sexual function.

SpaceOAR Hydrogel received 510(k) clearance from the FDA in 2015, and has been used in more than 150,000 procedures.

THE CLINICAL CANCER LETTER

CLINICAL ROUNDUP

Yale Cancer Center study: For Medicaid-covered patients with cancer, insurance does not always mean access

In a study published in *JAMA Network Open*, researchers at Yale Cancer Center assessed the acceptance of Medicaid insurance among patients diagnosed with common cancers.

"We found that Medicaid acceptance differed widely across cancer care facilities, with a substantial number of centers not offering services to patients with Medicaid insurance," Michael Leapman associate professor of urology, leader of the Clinical Program for the Prostate & Urologic Cancers Program at Yale Cancer Center and Smilow Cancer Hospital, and senior author on the study, said in a statement.

In the study led by first-author Victoria Marks, a second-year medical student at Yale, 334 Commission on Cancer-accredited facilities were sampled, of which, only 226 (67.7%) accepted new patients with Medicaid insurance for the four common cancers selected (colorectal, breast, kidney, and skin).

Acceptance varied among the facilities, with 296 (88.6%) accepting Medicaid for at least three types, 324 (97.0%) for at least two, and 331 (99.1%) for at least one type. Collectively, these findings underscore the persistent gaps that exist for patients with Medicaid in utilizing services at hospitals distinguished for high-quality cancer care.

"Having health insurance alone does not necessarily mean that patients can practically access healthcare. While major recent expansions of Medicaid have led to increases in health insurance coverage for Americans with cancer, we have to be aware and do more to ensure that insurance will actually translate to timely and high-quality care," Leapman said.

Facilitates that were more likely than others to accept patients with Medicaid included NCI-designated cancer centers, 89.7% of which offered high access to patients with Medicaid, and academic centers (86.4%). Moreover, facilities located in states that expanded Medicaid were also more likely to offer high access to Medicaid patients, 71.3% versus 59.6%.

"The results of this study do not necessarily mean that patients will not be able to access care anywhere, but may require a circuitous and impractical path, and may not be seen at centers designated for cancer care," Leapman said.

"Despite a large increase in the number of Medicaid-insured patients, most factors that limit a hospital or physician's participation in Medicaid have not changed," he said.

"These include low reimbursement, high administrative burden, and limited specialist participation in managed care organization networks. Even modest increases in reimbursement may have a positive impact, and progress in payment structures that prioritize healthcare quality are promising as well. Still, identifying these gaps in access is an important first step that can direct awareness."

Additional Yale authors include Michelle Salazar, Elizabeth Berger, and Daniel Boffa.

Merck to stop phase III LYNK-003 trial evaluating Lynparza with or without bevacizumab in metastatic colorectal cancer

Merck plans to stop the phase III LYNK-003 trial investigating Lynparza with or without bevacizumab for the treatment of patients with unresectable or metastatic colorectal cancer who have not progressed following first-line induction, citing futility.

This action follows the recommendation of an independent Data Monitoring Committee, after the DMC reviewed the data from a planned interim analysis. Lynparza is a PARP inhibitor that is being co-developed and co-commercialized with AstraZeneca.

At the pre-specified interim analysis for progression-free survival, the efficacy of Lynparza as a monotherapy and in combination with bevacizumab relative to control met the criteria for futility by

the DMC and accordingly, both experimental arms will be discontinued.

No new safety signals were observed with Lynparza in this trial, and the safety profiles of both Lynparza monotherapy and Lynparza combined with bevacizumab in this trial were generally consistent with that observed in previously reported studies. Merck will inform study investigators of the recommendation from the DMC and will advise patients in the trial to speak to their physician regarding treatment options. Data from this study will be shared in a future scientific forum.

LYNK-003 is one of several trials initiated by Merck as part of the Lynparza clinical development program. In addition to colorectal cancer, Lynparza is also being studied by Merck, in collaboration with AstraZeneca, as both monotherapy and in new combinations across DNA damage response deficient tumor types, including metastatic prostate cancer, ovarian cancer, breast cancer, and pancreatic cancer.

Multi-ethnic study uncovers unique origins of melanoma types and actionable molecular targets

Scientists from the International Agency for Research on Cancer, Barretos Cancer Hospital (Brazil), and partners have identified multi-omics markers of exposure to ultraviolet radiation that are critically involved in immune function, have the potential to drive cancer development, and could be used to predict the survival of patients with cutaneous melanoma, which occurs mainly in fair-skinned people.

The study, published in *Nature Communications*, also reveals important features of melanomas that are not associated with UV exposure; this opens a window of opportunity for new therapeutic targets for a less obvious population: patients with acral melanoma, which is the most common type of melanoma in darker-skinned people.

"We are revisiting archived clinical samples with modern technologies and computational tools to construct molecular maps of the patients' DNA that help us to uncover genes that affect survival and to trace back the origins that drive melanoma development," IARC scientist Akram Ghantous, a co-author of the study, said in a statement. "By including patients with different skin colors, we widen the resolution spectrum to various forms of melanoma and gain a better understanding of those origins, which are not necessarily triggered by UV exposure."

For cutaneous melanomas that did not occur as a result of UV exposure, the molecular landscape and clinical prognosis not only were different from those of UV-exposed melanomas but also resembled those of acral melanoma, a pathologically distinct type that develops in skin areas not often exposed to sunlight, such as the palms of the hands and the soles of the feet.

These genes–environment interactions in people of different ethnic backgrounds reveal translationally impactful mechanisms in melanomagenesis.

"The interdisciplinary findings of this work can undoubtedly help us clinicians to view and analyze melanoma tumors from various angles," Vinicius Vazquez, a physician at Barretos Cancer Hospital and a co-author of the study, said in a statement.

UV exposure is causally linked to cutaneous melanoma, but the molecular sensors of exposure have not been characterized in clinical biospecimens. In this study, the researchers used DNA sequencing technologies to infer UV exposure based on mutational signatures and integrated clinical, epigenomic (DNA methylome), genomic, and transcriptomic data of cutaneous and acral melanomas from two multi-ethnic cohorts.

DRUGS & TARGETS

FDA grants eltanexor with fast track designation; EU Commission designates eltanexor as an orphan medicinal product

FDA has granted Fast Track designation for the development program of eltanexor as monotherapy for the treatment of patients with relapsed or refractory intermediate, high-, or very high-risk myelodysplastic syndromes (MDS).

Also, the European Commission adopted the Committee for Orphan Medicinal Products opinion to designate eltanexor as an orphan medicinal product for the treatment of MDS in the European Union.

Eltanexor is a novel oral, Selective Inhibitor of Nuclear Export (SINE) investigational compound being studied for the treatment of MDS. Eltanexor is sponsored by Karyopharm.

Eltanexor also received orphan drug designation from the FDA in January 2022.

Karyopharm is investigating eltanexor in an open-label phase I/II study in patients with relapsed/refractory MDS.