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RACIAL, ETHNIC MINORITIES ARE SYSTEMICALLY UNDERREPRESENTED IN LEADERSHIP TEAMS ACROSS NCI CANCER CENTERS

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→ PAGE 6

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Fifty years after Congress passed the National Cancer Act of 1971, establishing the effort to tackle cancer as a national priority, Cancer History Project co-editor Otis Brawley sits down with the directors of America's first three comprehensive cancer centers to discuss the history, achievements, goals, and future directions of NCI-designated Comprehensive Cancer Centers.

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Otis Brawley, MD is a globally-recognized expert in cancer prevention and control. He has worked to reduce overscreening of medical conditions, which has revolutionized patient treatment by increasing quality of life and reducing health disparities. Dr. Brawley currently leads a broad interdisciplinary research effort on cancer health disparities at the Bloomberg School of Public Health and the Johns Hopkins Kimmel Cancer Center, striving to close racial, economic, and social disparities in the prevention, detection, and treatment of cancer in the United States and worldwide. He also directs community outreach programs for underserved populations throughout Maryland. Dr. Brawley joined Johns Hopkins University as a Bloomberg Distinguished Professor in 2019 from the American Cancer Society and Emory University.

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President and CEO, Roswell Park Comprehensive Cancer Center

Candace S. Johnson, PhD, was named president and CEO of Roswell Park Comprehensive Cancer Center in 2015 after more than a decade as deputy director and chair of pharmacology and therapeutics at the Buffalo, NY-based cancer center. Dr. Johnson, who also holds the M&T Bank Presidential Chair in Leadership, joined Roswell Park in 2002 from the University of Pittsburgh Cancer Institute. She holds a doctorate in immunology from The Ohio State University, and completed fellowships in immunology and cell biology at the Michigan Cancer Foundation. A pioneer in translational research on vitamin D-mediated anticancer effects and other pharmacological interventions, she is a member of both the National Institutes of Health Reviewers Reserve and the Frederick National Laboratory Advisory Committee, and is a two-term past member of the National Cancer Institute Review Group's Subcommittee A–Cancer Centers.

Peter WT Pisters, MD, MHCM
President, MD Anderson Cancer Center

Peter WT Pisters, MD, MHCM, has served as president of The University of Texas MD Anderson Cancer Center in Houston, Texas since December 2017. A renowned cancer surgeon, researcher, professor and administrator, Dr. Pisters established his career at MD Anderson, serving over 20 years in faculty and senior leadership positions. He left MD Anderson to serve as president and CEO of the University Health Network in Toronto, Canada's largest research hospital, before returning to MD Anderson. Dr. Pisters earned his medical degree at Schulich School of Medicine and Dentistry at the University of Western Ontario in Canada before completing his postgraduate work at Memorial Sloan Kettering Cancer Center in New York. In 2014, he received a master's degree in health care administration at the Harvard T.H. Chan School of Public Health in Boston. He earned designation as a Certified Physician Executive in 2014 and was named a fellow of both the American College of Healthcare Executives and the American College of Surgeons.

Craig B. Thompson, MD
President and CEO, Memorial Sloan Kettering Cancer Center

Craig B. Thompson, MD, is the president and CEO of Memorial Sloan Kettering Cancer Center (MSK). Dr. Thompson received his BS from Dartmouth and MD from the University of Pennsylvania, followed by clinical training in internal medicine at Harvard Medical School and in medical oncology at the Fred Hutchinson Cancer Research Institute. Dr. Thompson has extensive research experience in cancer, immunology, and translational medicine. His current research focuses on the regulation of cellular metabolism during cell growth/differentiation and on the role that metabolic changes play in the origin and progression of cancer. Dr. Thompson is a member of the Institute of Medicine, the National Academy of Sciences, and the American Academy of Arts and Sciences. He is also a fellow of the AACR Academy.

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In this issue

THE CLINICAL CANCER LETTER

CLINICAL ROUNDUP

DRUGS & TARGETS

RACIAL, ETHNIC MINORITIES ARE SYSTEMICALLY UNDERREPRESENTED IN LEADERSHIP TEAMS ACROSS NCI CANCER CENTERS

By Matthew Bin Han Ong

Racial and ethnic minorities that are underrepresented in medicine have even lower representation in leadership of NCI-designated cancer centers, a study by Memorial Sloan Kettering Cancer Center researchers found.

In an analysis of the diversity in leadership across all 63 NCI-designated cancer centers, the researchers identified 856 members in leadership teams, finding that 82.2% of cancer center leaders—or 688 individuals— were non-Hispanic white.

The study, published June 7 in JAMA Network Open, noted that non-Hispanic white individuals make up 60.6% of the U.S. population and 56.2% of active physicians.

"Our findings are similar to a recent director survey from the Association of American Cancer Institutes and *The Cancer Letter*, which found a high percentage of White men in director roles," study authors wrote (*The Cancer Letter*, Oct. 9, 2020).

Twenty-three institutions—more than a third of NCI-designated cancer centers—"did not have a single Black or Hispanic member" on their leadership teams, and eight cancer centers had all non-Hispanic white leadership teams, the MSK study found.

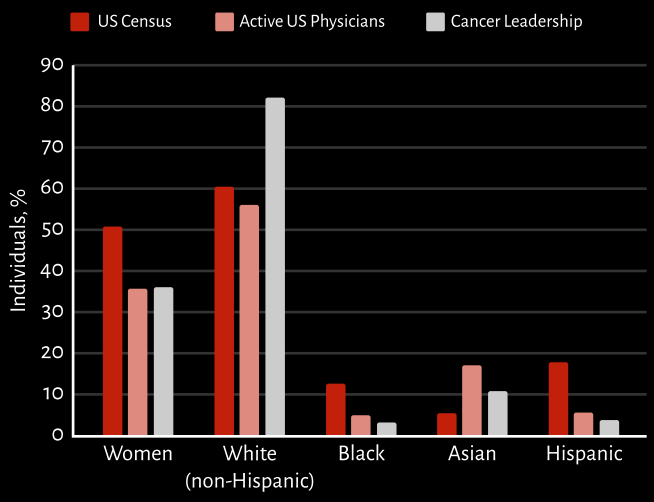
These results (Figure 1) demonstrate that workforce diversity, equity, and inclusion is critical for improving health care equity in oncology, senior author Fumiko Chino said to *The Cancer Letter*.

"In terms of actual patient care, we know that patients are more likely to trust providers that look like them," said Chino, a radiation oncologist at MSK, who specializes in the treatment of gynecological and breast cancers. "I think dive-bombing into a community outside of your own and to try to say, 'Well, this is what you should do to fix this problem,' is probably one of the most harmful things that we can do within clinical research."

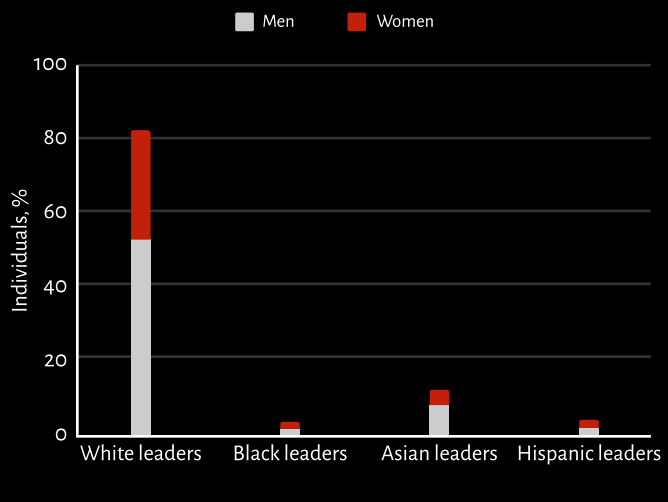
The authors of the study—a diverse team that includes student researchers from Arkansas—also found:

- Leadership teams with more women and institutions in the South were more likely to have at least one Black or Hispanic leader;
- A weak to moderate correlation between city Hispanic population and Hispanic representation on leadership teams, but no significant association between Black population and Black leadership was found;

FIGURE 1. GENDER, RACE, AND ETHNICITY IN CANCER LEADERSHIP



Cancer leadership by gender and race/ethnicity



Gender representation in leadership by race/ethnicity

Population data from the US Census and accessed on Nov 12,2020 at: https://www.census.gov/data.html
Active physician data from the Association of American Medical Colleges and accessed on Nov 12, 2020 at:
https://www.aamc.org/data-reports/workforce/report/diversity-medicine-facts-and-figures-2019

Source: Fumiko Chino, Memorial Sloan Kettering Cancer Center

- Both Black and Hispanic physicians were underrepresented (Black: 12.7% of US population, 5.0% of active physicians; Hispanic: 18.1% of U.S. population, 5.8% of active physicians); however, they were even more scarce in leadership positions (Black leaders, 3.5%; Hispanic leaders, 3.8%);
- Asian physicians were overrepresented, compared with their census population (17.1% of active physicians, 5.6% of U.S. population); however, Asian individuals were underrepresented in leadership positions (11.0%) when compared with their percentage of active physicians.

"We already know that, for example, within medical school, Black students are more likely to be scored poorly when performing at the same level," Chino said. "They're more likely to be judged based on physical appearances ... that element of systemic racism is downgrading them.

"'Professional,' it's almost like a code word at this point for, 'They were too different. They didn't go to the same school that I did. They don't meet my expectations of what a leader looks like.' This goes beyond even looks.

"There's this *sharp* decrease when we think about [Asians] in leadership. And so again, Asians are allowed to be physicians, but somehow no one trusts us to be leaders," Chino said. "This is backed up by other research, again, showing that it's okay to think of Asians as a physician, but you don't want an Asian American president or you don't want an Asian American CEO of a company.

"And in that, itself, again, another manifestation of systemic racism."

The study's findings mirror many trends and demographic patterns identified via a leadership pipeline survey conducted by this reporter and AACI last year.

"When *The Cancer Letter* published your survey data, which is remarkably similar to the study that was just published, there was some consternation, but there wasn't as much focus," said Christopher Lathan, chief clinical access and access officer at Dana-Farber Cancer Institute, faculty director for cancer care equity, and assistant professor of medicine at Harvard Medical School.

"The focus on structural inequity throughout our system has really made the medical leadership rethink their approach," Lathan, who wasn't involved in Chino's study, said to *The Cancer Letter*. "What I want to see, though—what I really want to see—is in three, four, or five years, do they remain as committed? And where are they when some of these initiatives start off a little rocky and they don't necessarily give fruit early?"

This begs the question: What, then, are academic cancer centers doing, right now, to improve health care equity?

"I think one of the easiest ways—this is something that can only come from leadership—is to just say, 'Hey, this is a priority of our cancer center,'" Chino said. "And it's amazing how much things can happen if leadership has said X is a priority.

"In terms of even getting people into the pipeline, we're kind of at a standstill. We're not making improvements over what we have historically, if anything, we're backsliding. Providing more logistical support—for example, fee waivers, MCAT preparation classes—more mentorship, I feel is just so essential."

To answer that question, *The Cancer Letter* asked executive leaders at several cancer centers across the United States to describe their hiring processes, pipeline programs, and initiatives aimed at mitigating disparities in access and cancer outcomes; and to comment on the state of diversity in oncology:

- "This sort of thing takes time and effort and commitment. And the trap is, *if* these physicians are not in the position to succeed, then leadership gets to say, 'Oh, we're going to go back to what we're doing,'" Dana-Farber's Lathan said.
- "One of the best practices that we have in our cancer center is to ensure that our research faculty and research team members reflect our diverse patient population," said Karriem Watson, associate director of community outreach and engagement at University of Illinois Cancer Center.
- "We have designed a portfolio of training programs emphasizing opportunities for diverse students to develop careers as cancer investigators and physicians that begin at the high school level through the junior faculty level," said Ruben Mesa, executive director of Mays Cancer Center at UT Health San Antonio MD Anderson.

The responses from Lathan, Watson, and Mesa appear on page 17.

Sustained, committed efforts to improve equity and access, for instance, in clinical trials, have proven to be effective. Over a five-year period, researchers at the Abramson Cancer Center at the University of Pennsylvania doubled clinical trial enrollment of Black patients with cancer from 12% to 24%, according to data presented at the most recent annual meeting of the American Society for Clinical Oncology.

This is also possible on a national scale. NCI, too, has made progress, albeit over 20 years. Last year, NCI announced that it has nearly doubled the proportion of racial and ethnic minority patients in institute-funded trials over two decades—from 14% in 1999 to 25% in 2019 (*The Cancer Letter*, June 26, 2020).

Q & A

Chino spoke with Matthew Ong, associate editor of The Cancer Letter.

CONVERSATION WITH THE CANCER LETTER

"The onus is on us as members of these leading cancer centers to really think about, how do we work from within to make this a priority, to make meaningful change not just for our patients, but also for our fellow providers, for our staff members—so that we can really, again, lead the charge to a better and more equitable future," Chino said.

Chino spoke with Matthew Ong, associate editor of *The Cancer Letter.*

Matthew Ong: I'm so glad we're able to discuss your study, now published in JAMA Network Open. What's the most important takeaway?

Fumiko Chino: I think what this study shows is that there's a real pipeline issue within cancer leadership.

> "Dive-bombing into a community outside of your own and to try to say, 'Well, this is what you should do to fix this problem,' is probably one of the most harmful things that we can do within clinical research."

Fumiko L. Chino, MD
Radiation oncologist,
Memorial Sloan Kettering Cancer Center

We know that as the population in the United States gets distilled down to those attending medical school, we lose a lot of passionate and qualified Black or Hispanic potential leaders that don't even make it into medical school.

Then, once you're an active physician, and you progress through your career, we lose more and more underrepresented in medicine Black and Hispanic physicians that don't make it into a leadership position.

And ultimately, this leads to a leadership group which is not reflective of the population of the United States, the population of cancer patients who are receiving care, and I think it really highlights that we could be serving our patients better.

I can't help but notice that your findings and conclusions are very similar to the leadership pipeline survey that we administered last year with the Association of American Cancer Institutes (*The Cancer Letter*, Oct. 9, 2020).

How should hiring and recruitment committees use these findings to inform their processes?

FC: Thankfully there's a number of different potential diversity inclusion efforts out there. I think that a dedicated effort to have broad search criteria—highlighting how different voices can really bring important perspectives into a leadership team—having things like blinded searches, and having specific bias training before you even start the process can really help improve the leadership hiring process.

Thinking about how to eliminate the obstacles that some potential leaders have on their way to success is also important, so thinking about how to improve and support mentorship opportunities that may not come as easily to certain populations.

Along the process from undergraduate to medical school to residency to first faculty position to becoming chair of your department, there are certain things that can give you a lift, and there are certain weights that can pull you down. We need to be working to remove weights from some of our faculty so that they can achieve their leadership potential.

I think what the study highlights is that we are potentially not elevating the full range of our potential leaders to the top, and that there really is this overrepresentation of non-Hispanic white men in leadership, which is not indicative of their ratio as part of the United States and is an overrepresentation of their population, even as active physicians.

Speaking of pipeline issues, a common response to underrepresentation often sounds like "it's not us, it's them"—characterizing those populations as not "making it" into the pipeline to begin with, thereby contributing to a limited pool of diverse "qualified candidates" for leadership. How do you frame that conversation?

FC: I think that we could be doing better in terms of giving people the support they need and encouraging them to become leaders.

And it's not just imposter syndrome, which is real, but I think imposter syndrome exists because there are so few, for me, women of color in leadership positions. So—even without someone saying a word—I know that my place at a leadership table may be limited.

If we want to improve the diversity of the leaders, we have to start thinking: how do we provide opportunities for our junior faculty, and how do we pay back time spent on mentoring, committees, and diversity-related activities? Dr. Theresa Williamson wrote an excellent piece recently on how to "pay back" the taxes placed on minority faculty members.

For example, I have three undergraduate/early medical school mentees this summer that I am trying to help design and implement research projects. This takes time away from my research and what I would be doing normally, so that's sort of a tax on me.

Please do not mistake, I'm honored to play this role, and Memorial Sloan Kettering has so many amazing programs, including the SCORE program and the NIH-funded Medical Student Summer Fellowship program to help introduce cancer research early to young minds from diverse backgrounds.

But I feel that if we actually compensated people for the time that they spend helping lift up those behind them and then supported junior faculty mentoring programs to help advance new faculty, I feel it could create a chain reaction.

A rising tide lifts all boats in terms of acknowledging that the education that I put in helps the next generation, but it also weirdly punishes me by taking time away from writing grants to fund comprehensive investigator-led research.

Although, [*laughs*] actually, I guess this study itself is sort of the negative example of that, because this was with an Memorial Sloan Kettering Summer Pipeline student Austin Morgan that I worked with last year and it's in a JAMA journal, so I think we've done well with it.

The Pipeline program was specifically designed to foster the next oncology leaders in those students who are un-

der-represented in medicine (*The Cancer Letter*, Oct. 23, 2020).

Right; quite the juxtaposition. This is probably DEI 101, but could you briefly provide examples for how a diverse workforce in oncology can improve patient outcomes, specifically on three points—basic research, translational research, and clinical care?

FC: I think that a diverse workforce can really improve basic research in that we're talking about different perspectives and a different approach to potentially complex problems within the communities that are the least served by basic science.

And so, when we're thinking about healthcare disparities and poor cancer outcomes, it really is patients who are in certain groups—for example Black patients—that have some of the worst outcomes.

When we're thinking about how to fundamentally improve their care, investigators coming from within those groups are likely to have the best, most intuitive ideas in terms of providing even the research questions that should be asked.

For example, think about disparities in triple-negative breast cancer. We know that Black women have some of the worst oncological outcomes, they also have some of the highest rates of triple-negative breast cancer at diagnosis, and so if there's a genetic component that's driving some of the worse prognosis, someone within the community, within that background could maybe ask the better question of how to address that unique biology.

I think within clinical research, again, the access concerns that patients have receiving cancer screening, cancer diagnosis, cancer treatment, and then survivorship care—we are losing patients all along the cancer cascade, in terms of patients not being able to get a mammogram or not being able to get in the door to actually start their cancer treatment or having delays to care.

And again, active, engaged physicians within those communities are most likely the ones who will have the most insight in terms of overcoming those obstacles.

Using a different example, thinking about Asian American patients who have significant cultural barriers to receiving mental health care.

Given all of the potential downstream effects of a cancer diagnosis, including anxiety, depression—again, the providers within those communities are most likely going to have unique insights which can help really tap into potential engaged solutions, and they're also more likely to have connections within those communities to do the best type of research.

I think dive-bombing into a community outside of your own and to try to say, "Well, this is what you should do to fix this problem," is probably one of the most harmful things that we can do within clinical research.

Right; that breaks trust.

FC: And then in terms of actual patient care, we know that patients are more likely to trust providers that look like them. They're more likely to have better communication. They're more likely to adhere to therapies from providers that look like them.

And I think, again, it's a cycle of, if someone has never had a Black physician and they walk in the door and they see that their physician is Black, they realize that they may have more trust in their counsel —even though historically and presently, Black patients are really underserved by the medical community.

It may foster more of a trust connection there, and they may be more likely to trust their diagnosis, come in for their cancer treatment, take their medications as planned, and potentially avoid some downstream effects that could ultimately affect the fidelity of their cancer treatment.

I like your description of the cancer care pathway as a cascade. You've done a lot of work on patient access, or rather, lack of access to health care. Would you say that's the primary barrier in this country to better outcomes?

FC: It's so hard, because I think what I consider difficulties in access for many of our patients is really just a manifestation of the social determinants of health and, for some, structural racism.

For example, I'm a radiation doctor, and I can design the very best radiation plan for someone who may even have access to see me in consult, but ultimately is not able to actually receive that radiation treatment, because they're not able to take the time off work because they work an hourly job and they're too afraid of losing their work, or they may not be able to arrange child care for their kids and so, they no-show to their actual treatment appointments.

So, it is such an interwoven mixture of access and structure in terms of the tangled web of the U.S. healthcare system.

And not to mention the coverage options that are available—or more often than desired, not available—to these patients as well; right?

FC: Exactly. At Memorial Sloan Kettering, we have a lot of resources including copay assistance, quality of life funds, financial navigation through the patient financial services team, but even here we sometimes struggle to get the right resources into the right people's hands. It can be almost like a missed connection.

The challenge continues to be: how do we provide not just the best quality of care, but actually allow someone who could be cured of their cancer to be cured of their cancer each and every time, instead of being sidelined and delayed because some of the barriers are outside of the cancer center—their parking or their potential time off work, or sick leave.

Take parking for example. In July 2020, I published research in *JAMA Oncology* where we found that some cancer patients pay $1,680 over the course of treatment.

These parking fees can be a huge barrier when it comes to financial toxicity in cancer treatment. At Memorial Sloan Kettering, patients can apply for aid to cover parking costs, but this aid is only helpful if patients know about it and are encouraged to apply.

In what ways can a diverse leadership improve access, however kaleidoscopically, to historically underserved and underrepresented communities?

FC: I think one of the easiest ways—this is something that can only come from leadership—is to just say, "Hey, this is a priority of our cancer center." And it's amazing how much things can happen if leadership has said X is a priority.

I know, again, speaking from my own experience at Memorial Sloan Kettering, within strategy and innovation, it has become a priority for us to usher some people in the door who have been historically excluded, and so, specifically trying to do targeted outreach to certain populations.

For example, New York has an incredible, huge immigrant population. So, how do we provide the resources for non-English speaking patients to come in the door to get over those barriers, and so, many of our educational materials are available in multiple, multiple languages. Last time I checked, we had over 4,000 educational resources in Spanish, for example.

But that's not something that happened organically.

It had to be made a priority to invest in translating the educational resources to other languages. How do we make it a priority for our staff to have cultural competency and implicit bias training? Because I think there is a lot of lip service to this idea of like, "Oh, we have equal care."

But ultimately, you still need to have training. There are very few individual people who are wholly racist, but many more who have implicit bias and therefore have racist or biased actions. Part of improving the standard of care—the quality of care for diverse populations—is acknowledging our own biases.

It goes beyond just being required to do a module. But even within the institution level, within each department, how do we engage at every aspect of the healthcare system from the front desk person to the person who does the lab draws, all the way—physicians, nurses, techs—to think about really the whole person as opposed to just their diagnosis and what they look like.

I think that the leadership team really has a lot of power in terms of pushing the entire institution. Again, just to use an example from my own institution, we have now a stated research priority of trying to actively engage certain underrepresented populations in clinical trials.

So, we are designing programs around the idea of: How do we provide navigation for certain patients to try to get them to the clinical trials that they would potentially qualify for but they were not getting offered now?

There are many, many ways that we can improve access from patient facing to provider facing interventions. I think, again, there's a ground up and then there's a top down, and I think we can do both those.

Another really important thing in your study: you found no link between cities with large Black populations and representation in leadership at corresponding cancer centers.

You only saw a relationship that has to do with regional factors—in the South; and at a low magnitude for Hispanic populations. What do you think is going on here?

FC: There are just so few Black leaders, and I think there are so many potential obstacles to rise to a position of leadership for Black physicians.

I would have loved to have seen diverse cities have more diverse leadership in that respect, but I just think that there are so many, even maybe potential additional barriers than some other racial or ethnic groups with our Black physicians.

In terms of even getting people into the pipeline, we're kind of at a standstill. We're not making improvements over what we have historically, if anything, we're backsliding. Providing more logistical support—for example, fee waiv-

ers, MCAT preparation classes—more mentorship, I feel is just so essential.

And of course, I've seen it manifest from the other side for some friends: If you are a Black physician, students and trainees and junior faculty approach you constantly like, "Mentor me. Mentor me."

You're one of the few. And that can be itself also very overwhelming to be one of the few people who, again, feels the onus of the obligation to provide mentorship for the next generation while you're also just trying to do your own work.

I'm recalling your study on cancer mortality and Medicaid expansion and how, for many Black communities, the baseline was just so much worse, which is why Medicaid expansion doesn't close the mortality gap (*The Cancer Letter*, June 5, 2020).

So, how does systemic racism and worse baselines—i.e. for Black communities—contribute to these numbers? And perhaps, not just for Black Americans, but also other minorities that we're seeing in your study?

FC: I think that there's so many potential ways that the pipeline is leaking all the way from education within certain neighborhoods, to potential restrictions in terms of what universities people can even afford to go to, to then again barriers to even getting into medical school and so on.

We already know that, for example, within medical school, Black students are more likely to be scored poorly when performing at the same level. They're more likely to be judged based on physical appearances.

> "In terms of even getting people into the pipeline, we're kind of at a standstill. We're not making improvements over what we have historically, if anything, we're backsliding."

There was a really great study evaluating how women were judged by their hairstyle—and so, things that were essentially superficial or not related to their performance as a physician or their potential as a future leader. But that element of systemic racism is downgrading them.

When you get to the point in which you are saying, "Well, who are the qualified candidates for a leadership position," you're seeing a discrete lack of certain types of individuals, because along the way, their path has been stymied. And again, I don't think that anyone within the hiring committees is specifically saying, "Well, I don't want a Black physician."

But this idea of, for example, "This person didn't have as many achievements." or "Well, this person wasn't professional." "Professional," it's almost like a code word at this point for, "They were too different. They didn't go to the same school that I did. They don't meet my expectations of what a leader looks like." This goes beyond even looks.

Even for me, if I see this physician went to Duke, I'm going to give them a leg up, because, hey, they went to my alma mater; whereas this person went to Morehouse, and I don't know anyone who went to an HBCU [Historically Black Colleges and Universities].

I'm reminded of Dr. Narjust Duma's recent talk at ASCO, in which she described how she'd received comments like, "You're so Latina." Whatever that means; right?

And feeling a sort of ethnocentric, perhaps Puritannical peer pressure to tone down on colors and culture-rich demeanor (*The Cancer Letter*, June 11, 2021).

FC: Absolutely. You get downgraded all the time.

Our unconscious bias is to elevate people who are like us. It is a forward feeding problem with, for example, an overrepresentation of non-Hispanic white men in leadership positions in that it reinforces the next generation, the next wave of non-Hispanic white men.

And I think even if we get to the point of diversifying the search committee, that itself will help. And then of course ironically being in the search committee is a lot of work and it's, you're behind the scenes elevating, but you are yourself still doing a lot of unpaid labor.

And so, ironically, by getting a more diverse search committee, we're adding to the burdens of our limited faculty

who are already overburdened, and so, even the solution has its own potential problems.

This brings me back to discussions I participated in during AAPI Heritage Month, in which many community members talked about the emotional labor of being visible as an individual of minority status—how does one manage that burden?

How much of that equates to a duty and obligation to educate, be an antiracist advocate, and change culture? How can minority leaders do that without overextending, to preserve bandwidth?

FC: I just wanted to highlight one thing that we found which I think hearkens back to something I think you had mentioned, again, last year, which is that there's a real problem in terms of seeing Asian physicians as leaders.

I think outside of the discrete finding that those who are underrepresented in medicine are *even less* represented in leadership, we also found that although Asians are way overrepresented as physicians, according to our percentage in the population, there's this *sharp* decrease when we think about them in leadership.

And so, again, Asians are allowed to be physicians, but somehow no one trusts us to be leaders.

This is backed up by other research, again, showing that it's okay to think of Asians as a physician, but you don't want an Asian American president, or you don't want an Asian American CEO of a company. And in that, itself, again, another manifestation of systemic racism.

And that's a whole other conversation as well—the unique challenges for each community. For Asian Americans, it's "Well, what's the bamboo ceiling?"

FC: Yes. We finally have representation, we have Crazy Rich Asians, "Okay, we had a Hollywood blockbuster movie, so we can move forward."

But, I think again, there was a racial reawakening last year with both Black Lives Matter and the increased percentage of violence against the AAPI community.

I think, in that respect, I'm glad that this study comes out now, because I think it really highlights the fact that each population has its burdens.

So, we were talking about gender equity or parity as another major focal point, and we've been doing a lot of work on gender bias and sexual harassment (*The Cancer Letter*, May 28, June 4, 2021; Oct. 2, 2020; Dec. 13, 2019; June 15, 2018).

But beyond that, what are women also dealing with when it comes to opportunities for leadership at NCI-designated cancer centers?

FC: According to our study, in terms of percentages of women who are active physicians, and percentages in leadership, we're doing okay.

I think this may be a manifestation of some discrete efforts, in terms of trying to think about gender equity within medicine.

But ultimately, we know that women are still paid less than men, even in medicine, for the same position.

We know that women are more likely to have other taxes of their time, so for example, child care or home duties. Specifically during COVID, we know that we were more likely to sacrifice our time.

So, we had less time for research due to, for example, having to monitor children doing homeschooling online classes.

And so, there's a lot of additional potential burdens that women in medicine face.

My mother raised seven kids and was an active physician, so I have a 1000% respect for her, because I really did see how much she did have to sacrifice in order to have a successful career and to have a family. And I think again, it's baby steps, sometimes literally.

But I was at least encouraged to see that we're doing okay in terms of leadership.

Got it. Did we miss anything?

FC: This is the baseline, and then, what's next is really the most important, because I think a lot of large corporations last year, again, during the Black Lives Matter protests, announced all of these.

They had plans to make donations, support equity efforts, and I think a lot of people—appropriately—are calling them out now for not following through.

Same timely conversation, now that it's Pride Month; right? One could almost hear our LGBTQ+ friends lamenting, "Look at all these rainbow versions of the apps popping up on our phones now! Here comes the rainbow tornado, but where's the money?"

FC: Exactly. This idea of "rainbow capitalism," which is, you stick a rainbow on it and suddenly you're like, "I'm gay-friendly or I'm an ally."

And so, the onus is on us as members of these leading cancer centers to really think about, how do we work from within to make this a priority, to make meaningful change not just for our patients, but also for our fellow providers, for our staff members—so that we can really, again, lead the charge to a better and more equitable future.

I will say it's important to think about the next generation. And so, for example, when I was picking a student to work with me through the Summer Pipeline Program, I specifically picked someone from the University of Arkansas, because I thought the likelihood that he would have a similar opportunity would be small.

That is another way to think about outreach and to try to actually get new and engaged people into our field. So, a Black man from a state medical school in Arkansas—that is exactly the person that I want to try to work with. And we really developed this project together, and I couldn't be prouder of the incredible work he put into it.

Thanks for speaking with me, and for your work on this study.

FC: Thank you.

> "Asians are allowed to be physicians, but somehow no one trusts us to be leaders. But, I think again, there was a racial reawakening last year with both Black Lives Matter and the increased percentage of violence against the AAPI community."

This story is part of a reporting fellowship on health care performance sponsored by the Association of Health Care Journalists and supported by The Commonwealth Fund.

Will cancer centers remain committed to improving equity in the long term?

By Matthew Bin Han Ong

Cancer center leaders discuss their hiring and diversity pipeline efforts

This is the first installment of conversations about diversity, equity, and inclusion in recruitment and mentorship at academic cancer centers.

These conversations, which will continue in upcoming issues, are intended to help disseminate best practices employed to diversify the oncology workforce of the future.

If you'd like to take part, reach out to Matthew Ong (matthew@cancerletter), associate editor of *The Cancer Letter.*

Christopher S. Lathan, MD, MS, MPH

Chief clinical access and access officer; Dana-Farber Cancer Institute;
Medical director;
DFCI at St. Elizabeth's Medical Center;
Associate medical director, DFCI Network;
Faculty director for cancer care equity;
Assistant professor of medicine, Harvard Medical School

Matthew Ong: What best practices in hiring and recruitment—or in pipeline programs—do you use at your institution to elevate potential diverse leaders? How effective are these strategies?

CL: I think, first, as I answer that question, I want to put it in context, because I think that this conversation is quantitatively different from a conversation that could have been had a couple of years ago.

So, when *The Cancer Letter* published your survey data, which is remarkably similar to the study that was just published, there was some consternation, but there wasn't as much focus. The focus on structural inequity throughout our system has really made the medical leadership rethink their approach. There's always been good intentions, there's always been good thoughts, but I think that some of this was not seen as the priority.

To answer your question now, I would say our institution has always focused on some of the standard efforts that you've seen. We have focused on the usual approaches in the past. Pipeline issues, trying to support underrepresented leaders on multiple levels.

So, one new approach is supporting young aspiring leaders with continuous mentorship, especially folks who are coming from underrepresented-in-medicine backgrounds. In addition to that, creating relationships with, whether it's medical schools and community leaders, where you can try to build those new diverse leaders. So, I think the first part is your pipeline.

The second part is prospectively thinking about support group situations. So, if you have underrepresented minority faculty, then, again, putting folks in groups and efforts to try to give them support through. I think those have kind of been the standard approaches. And I would say our institution has utilized those.

What I would say is that those approaches work somewhat. I think one of the things that we haven't seen until fairly recently is really putting leadership in the executive suite, because that's where the difference comes in.

I would also say there isn't enough time yet to see. For example, my position is relatively new just within the last few months. And I think there's a lot of folks in the country who are in a similar situation.

So, let's see, I think these efforts will pay off, but I think the pipeline and the fermenting of young dynamic leaders and reaching out to try and pull established leaders from other institutions is another thing that, I think, institutions have tried to utilize, and my institution has done that as well—kind of thinking outside the box and maybe really thinking about leadership tracks and looking at folks who don't fit the same mold, I think, and maybe having people really broaden what they think a leader can do as well as what a leader looks like would be really helpful.

In your experience as a member of your center's executive leadership, how has increased diversity among your faculty improved patient outcomes, as well as your ability to reach and engage underserved communities in your catchment area? Could you provide a few examples?

CL: I would say the short answer to your question is, again, in the executive suite, looking at representation there, it's relatively recent at our institution. So, we're going to have to see those outcomes; we'll look at that going forward.

I would say we have seen other institutions, though, where this has paid off. At ASCO this year, Dr. [Carmen] Guerrera and Dr. [Robert] Vonderheide [from Penn's Abramson Cancer Center] actually presented some data that showed how their intervention—it was an in-

tervention, but it was really supported by the cancer center director—to really diversify their patient population and have it match up with Philadelphia's catchment area .

And they showed, *how* these kinds of initiatives are actually supported from the top throughout the institute—integrating the whole institute's mechanism to really think about clinical trials and improving clinical trials for marginalized populations, African Americans for the most part—really made a huge difference in recruitment of folks to clinical trials, *and* greater representation of the marginalized catchment area.

I think that that is a good example of how Dr. Guerrera's work where she is, in a leadership-level job, with the support of the cancer center director, has shown that if you put people who are interested in outreach, who are dedicated to outreach, and I think looking for leaders who are from different and diverse backgrounds, gives you folks who might have slightly different emphasis in their career. If you give them the support, they will build the initiatives and put the folks together and really make things work.

I do think that there are other examples out there. Derek Raghavan's efforts at the Levine Cancer Center, and what they've been doing, I think, is another example of how you find the people who want to do this kind of work. You support that from the cancer center leadership on down.

You pick executives who want to do this work, medical leaders who want to do this work, and you can make incredible gains and get the outcomes that you're looking for.

The trap for me in the question that you asked is, "Hey, so you're going to do this. You're going to diversify your leadership. Well, where's the money? When are we going to see the outcomes that we want?"

This sort of thing takes time and effort and commitment. And the trap is, *if* these physicians are not in the position to succeed, then leadership gets to say, "Oh, we're going to go back to what we're doing."

That's the one thing about having it so black and white, you've got to have a longer term view and plant the seeds so that the leaders can grow strong and can integrate their ideas throughout your institution.

Right; my question is a response to a dated and very loaded "colorblind" approach to science that I often run into in my work on DEI issues, i.e. "Good science is good science, regardless of race. How is a good doctor from Baltimore different from a good doctor from Idaho? It's patronizing to racial minorities to tokenize them."

But I hear what you're saying here; you can't ask for outcomes on deadline as if it's an engineering project.

CL: Right. That's exactly right.

What programs have you led or are leading that are directly contributing to greater equity i.e. a reduction in disparity of outcomes or disparity of access in your catchment area? What is the nature of those disparities and what have you learned?

CL: We've been fortunate. Even though my particular role is relatively new, there have been some efforts that we've been working on at our institution for some time that we have some data on.

I'll talk about two things, and they're related. One is one of the efforts I've been involved in for about 10 years. It's our Cancer Care Equity Program where we've actually set up outreach clinics in Federally Qualified Health Centers. And the idea is that we would help the primary care docs with any cancer-related questions.

So, we do expedited workups, survivorship, lung cancer screening visits, all in their health center under their license. For people who actually need to get biopsies or other things, they come into the cancer center. And that's a navigated process. It's built around a nurse navigator.

We put that program together about 2011. And so, over the nearly 10 years, we've collected data that shows that, not only do we help people, we decrease the time to evaluation for cancer-related questions, and we've got a manuscript that we'll be sending out, but there's some other published work that we've done.

Also, we found that the folks who did get diagnosed with cancer who were sent to our program were more likely to go on clinical trials. And this is a majority diverse population, about 40% of the patients speak Spanish and 70% identify as African American.

So, I think we have some preliminary data that shows that this kind of prolonged, determined, navigation, clinical access program not only helps the patient, but it also gives what we're looking for in the long term, which is more access and higher representation in clinical trials.

Now, the actual total N is small, because this is a small pilot program, but we're expanding this program and we're trying to make a bigger impact.

The other thing is our Community Benefits Office and our research programs have long been working hand in hand to really innovate and try to come up with different types of interventions that can have impact.

So, besides some of the work that we've been doing, there's some work on prostate cancer, there's work on liver cancer, where they're really trying to integrate the research process much more in addition to the clinical process.

And in our breast cancer group, there is a Boston-wide navigation program where all the different institutions, different academic institutions are coming together.

And the data isn't quite published yet, but that's another, probably seven or eight year program that we have some good data showing the impact of navigation for breast cancer patients, specifically, for comparing what happens to folks who are coming from underserved neighborhoods from marginalized communities.

So, these programs have been going on for a while. I think it's just we need to ramp them up a little bit more.

Speaking of next steps, are you working on any new initiatives or new priorities, on a very high level, at your institution?

CL: We are working on, like many institutions, rethinking the integration of our approach to clinical access throughout the institution.

One specific example is integrating navigation into the disease center in a much more prospective way for vulnerable and underserved patient populations.

So, as opposed to having a navigator that's supported by a philanthropic program, we're talking about in the center, integrating the navigator, the community-focused navigator, to really assist all the way through their process on a disease center level throughout the cancer center.

That's something that I really haven't seen often, even in programs that have navigators in clinical operation systems. So, we've started that program where we're going to integrate, we're going to look at some metrics, and we're going to try to demonstrate that approach over time.

And in addition to that, I think really building up some of our outreach programs, some of the interventions from the ground up, removing structural barriers and actually focusing on some socioeconomic and other barriers it takes for folks to get on clinical trials.

Lastly, our institution has been able to renegotiate some of the insurance contracts. So, before there was a big gap. Many patients who were in Boston who had a specific managed Medicaid product that *excluded* our institution, or the health insurance program at our institution was too expensive.

They renegotiated that, so that these patients can, just like everybody else, come into the institution and get a second opinion or get their transplant or specialty care, if need be.

And I think that's also going to allow us to have a positive impact on the patients.

Did we miss anything?

CL: I will say that I'm happy that there's a majority of institutions that are thinking about this in a prospective way.

What I want to see though—what I really want to see—is in three, four, or five years, do they remain as committed?

And where are they when some of these initiatives start off a little rocky and they don't necessarily give fruit early? Where is their commitment and how strong is their will for change?

That is where I think we will really see where we're going with this and whether this is representation that is weaved in, or if this is a reflexive response to the moment, because many of us who've been doing this work for 15, 20 years have been pushing these things.

Go back and look at the guidelines that ASCO's done, that any of the groups have talked about, and you'll see the same thing.

Even NCI, when they changed the core grant, the CCSG grants include more about community engagement. People have been trying to push this for a while.

So, these aren't new concepts. What we want to see, in all of this, is as we go forward, is it going to be sustained? And that's, to me, where we're going to see the difference in communities, and communities will know the difference then, too.

Right; a friend described it very succinctly to me in a conversation about equity initiatives now popping up everywhere: "Y'all, we've been seeing it for a long time before COVID and before BLM, but thank you, better late than never."

CL: Exactly. That's very true. I think that's very true. So, I think, good, if you're late to the party and you want to help, that's great, but let's see what it's going to look like going forward.

Karriem S. Watson, DHSc, MS, MPH
Associate director, Community Outreach and Engagement, University of Illinois Cancer Center; Research assistant professor, UIC School of Public Health Community Health Sciences; Associate executive director, UI Health Mile Square Health Center

Matthew Ong: What best practices in hiring and recruitment—or in pipeline programs—do you use at your institution to elevate potential diverse leaders? How effective are these strategies?

Karriem Watson: One of the best practices that we have in our cancer center is to ensure that our research faculty and research team members reflect our diverse patient population.

This is clearly seen in our office of Community Engagement and Health Equity (CEHE) of the UI Cancer Center, which is affiliated with the Community Outreach and Engagement (COE) and health equity program of the UI Cancer Center—where the majority of the leadership and team members of CEHE and the COE program are from diverse racial/ethnic backgrounds that reflects the UI Cancer Center catchment area.

One of the strategies that we deploy is ensuring that new researchers and public health professionals are recruited from our UIC School of Public Health.

In your experience as members of your center's executive leadership, how has increased diversity among your faculty improved patient outcomes, as well as your ability to reach and engage underserved communities in your catchment area? Could you provide a few examples?

KW: It is well documented in the literature, as well as in my professional experience as associate director of Community Outreach and Engagement of the UI Cancer Center, that having research faculty and staff that reflect a cancer center's catchment area improves the ability of cancer centers to reach and engage with communities in which they share similar lived experiences.

One example of this is how the UI Cancer Center has been able to increase its workforce diversity by creating intentional pipelines from health equity research and engagement efforts such as the NCI funded U54 Chicago Cancer Health Equity Collaborative (Chicago CHEC). Chicago CHEC has served as a major asset in advancing the careers of early stage investigators from underrepresented groups as well as creating workforce opportunities for students who matriculate in the Chicago CHEC fellows research program.

I currently lead a R01-level research project supported by Chicago CHEC engaging African American men in lung cancer screening and two members of our research team are former students from the Chicago CHEC program including the lead study coordinator for the project.

What programs have you led that are directly contributing to greater equity i.e. a reduction in disparity of outcomes or disparity of access in your catchment area? What is the nature of those disparities and what have you learned?

KW: In addition to the NCI funded U54 Chicago CHEC program, the director of CEHE, Dr. Vida Henderson and I have led a community-engaged research and service project to improve colorectal and cervical cancer outcomes among underserved populations in the UI Cancer Center catchment area.

The project is funded by the Bristol Myer Squibb Foundation (BMSF) and engages barbers, beauticians and safety net hospitals in the UI cancer Center catchment area. Data from our catchment area showed colorectal cancer disparities on Chicago's Southside were greater than many state and national averages.

The catchment area data also showed inequities in access and screening uptake for cervical cancer among African American and Latina/Hispanic women on Chicago's west side area.

We have learned from this project that it is both feasible and effective to implement community based colorectal cancer screening within community settings including barbershops, beauty salons and Federally Qualified health centers.

We also learned that embedded patient navigators in safety net hospitals in collaboration with cancer centers is an effective way to increase cervical cancer screening and identify system level barriers that can prevent timely cervical cancer screening.

What are your next steps?

KW: Our next steps are to continue to leverage NCI funded centers for health equity like Chicago CHEC to support early stage investigators and to grow the pipeline of students from underrepresented groups engaged in health disparities research.

We will also work with the seven health science colleges at UIC to ensure opportunities for research and student and faculty engagement to support researchers from underrepresented groups.

We are also actively seeking funding that can examine the impact of systemic racism on both cancer screening and uptake as well as its impact on the cancer research workforce.

Ruben Mesa, MD

Executive director,
Mays Cancer Center at UT Health San Antonio MD Anderson;
Mays Family Foundation Distinguished University Presidential Chair;
Professor of medicine

Amelie G. Ramirez, DrPH

Chair, Department of Population Health Sciences;
Director, Institute for Health Promotion Research;
Associate director, Community Outreach and Engagement, Mays Cancer Center;
Dielmann Chair in Health Disparities Research & Community Outreach;
Max and Minnie Tomerlin Voelcker Endowed Chair in Cancer Health Care Disparities;
Professor of Epidemiology & Biostatistics, Institute for Health Promotion Research

Matthew Ong: What best practices in hiring and recruitment—or in pipeline programs—do you use at your institution to elevate potential diverse leaders? How effective are these strategies?

Ruben Mesa: The Mays Cancer Center at UT Health San Antonio is based in a catchment area of San Antonio and South Texas, a 38-county region of 4.9 million people of which 69% are Latino, so a diverse team and leadership team is crucial.

Working closely with our wonderful vice dean for diversity—Dr. Chiquita Collins of the Long School of Medicine—the Mays Cancer Center is dedicated to first developing diverse faculty.

We have designed a portfolio of training programs emphasizing opportunities for diverse students to develop careers as cancer investigators and physicians that begin at the high school level through the junior faculty level.

We deeply value diversity in new faculty hires, and work to have a diverse pool of candidates before offers are extended. We actively focus on retention, looking at mentorship, career development, and competitive hiring and retention efforts.

Our university, Long School of Medicine, and Mays Cancer Center have a robust leadership development program, which enriches the career development of potential diverse leaders.

New leadership searches begin with a discussion on diversity, intentional efforts to reach out to diverse candidates and seek their recruitment. We have a very diverse faculty, staff, and leadership structure.

In your experience as members of your center's executive leadership, how has increased diversity among your faculty improved patient outcomes, as well as your ability to reach and engage underserved communities in your catchment area? Could you provide a few examples?

RM: We have a diverse faculty who is focused on conducting research in our very diverse catchment area. South Texas is diverse with both rural and urban areas, with 4.9 million people, mostly Latinos (69%). Nearly half speak Spanish as their primary language, and many face barriers like poverty and low educational attainment.

Amelie Ramirez: Many people in our community fear getting cancer. Cancer has become the leading cause of death for Latinos. I have lost a family member to cancer, and it is not something we want anyone to have to go through.

This is why I am leading studies that are focused on Latinos, engaging them in research and delivering interventions and communications to help them.

And this is why every researcher, clinician, education specialist, and health care worker at the Mays Cancer Center is working hard to make a difference in preventing, reducing, and eliminating cancer for all people.

What programs have you led that are directly contributing to greater equity i.e. a reduction in disparity of outcomes or disparity of access in your catchment area? What is the nature of those disparities and what have you learned?

RM: We know Latinos are getting vaccinated for COVID-19 at much lower rates than their peers. Dr. Ramirez and her *Salud America!* program created the "*Juntos*, We Can Stop COVID-19" bilingual digital communication campaign to inform and urge Latino families to take action to slow the spread of coronavirus, including getting the vaccine when it's available.

The #JuntosStopCovid campaign features Latino culturally relevant fact sheets, infographics, and video role model stories in English and Spanish. Dr. Ramirez and her *Salud America!* program also created the Latino COVID-19 Vaccine "Change of Heart" Bilingual Storytelling Campaign to move Latinos from vaccine hesitancy to vaccine confidence.

The campaign uplifts the stories of real Latinos from South Texas and beyond who overcame misinformation, got the vaccine, reconnected with family, and are helping end the pandemic. We want our families to be able to get back together. We want to visit our sisters and brothers, parents, and abuelos and abuelas.

And we want to be able to do our jobs and go to school safely. The best way to achieve what we want is to get the vaccine right when it is available. Vaccines help our bodies become immune to a virus without becoming ill from it.

AR: We are continuing to build the pipeline for a diverse healthcare and cancer research workforce. My NCI-funded program, *Éxito!* Latino Cancer Research Leadership Training, annually recruits 25 Latino students and health professionals annually for a culturally tailored curriculum to promote pursuit of a doctoral degree and cancer research career.

The program also offers internships and ongoing support. Of 101 program participants from 2011-2015, 43% applied to a doctoral program and 29.7% were currently enrolled.

We proved that *Éxito!* is a strong model pipeline program that equips Latinos for applying to and thriving in doctoral programs, with added potential to boost the pool of cancer health disparities researchers.

What are your next steps?

RM: We are working to engage more Latinos in clinical trials. Latinos represent 18.5% of the U.S. population, but are less than 10% of those in federal cancer and drug studies.

Dr. Ramirez has received a three-year, $650,000 grant from Genentech, a member of the Roche Group, to create Latino-focused recruitment strategies and systems for clinical trials in cancer treatment and Alzheimer's disease.

The new funding, part of Genentech and The Genentech Foundation's $16 million initiative to promote health equity and diversity in STEM, will help her team expand its work into inclusive clinical trial promotion and recruitment.

This includes using culturally relevant digital health communications, advocacy networks, and clinical partnerships to promote health equity and advance clinical trials for cancer treatment and Alzheimer's disease among Latinos.

AR: Ever-changing technologies motivate us to find new, culturally relevant ways to reach our Latino population with cancer prevention and healthy lifestyle messages.

My team helped create Quitxt, a quit-smoking coach that utilizes text messages or Facebook Messenger to help young adult Latinos kick the habit in South Texas. Quitxt is being expanded to include messaging to quit vaping, too.

My team also is pioneering a culturally tailored app to help Latinas with breast cancer adhere to their endocrine hormonal therapy.

There are fewer and fewer limits on technology, creating an opportunity for health communicators to innovatively help people increase their healthy behaviors.

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GUEST EDITORIAL

Fly the pride flag—and free the LGBTQ+ community from the oppression of smoking

Phoenix A. Matthews, PhD
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Pride month is upon us, and the rainbow flag is flying high. At levels that would have been unimaginable a few decades ago, corporate sponsors acknowledge and celebrate the right of LGBTQ+ individuals to live free of violence, discrimination, and oppression.

Whether their actions reflect changing societal norms, the assertion of an equity mission, or engagement in "performative activism," corporations as diverse as Google, MasterCard, and Legos are changing corporate logos to include the rainbow colors synonymous with the gay pride movement.

These visible signs of corporate support are vitally important and have contributed to the growing acceptance of LGBTQ+ individuals in sports, education, business, and entertainment. But, unfortunately, these more affirming corporate supporters arrived late to the "Pride Parade."

Thirty years ago, in pursuit of new customers, the tobacco industry set its sights upon an untapped market characterized as "alternative lifestyles."

In 1995, the R.J. Reynolds Tobacco Company established Project SCUM, an outreach strategy to sell cigarettes to gay men and people experiencing homelessness in the Castro and Tenderloin districts of San Francisco. The acronym "SCUM" officially stood for subculture urban marketing and reflected most corporate stances toward the LGBTQ+ communities.

During that same period, several other tobacco companies began active outreach to LGBTQ+ communities with targeted advertisements, event sponsorship, including pride festivals, and financial support for non-profit organizations struggling to provide services at the height of the AIDS epidemic. This early corporate attention garnered appreciation and even loyalty to those companies that frequented gay bars with free products and were ever-present at fund-raising galas and pride parades.

Perversely, this early "investment" in the LGBTQ+ communities by the tobacco industry has paid off. Although cigarette use among adults in the U.S. is at a 50-year low, tobacco use among LGBTQ+ youths and adults remains elevated. Indeed, many studies suggest that smoking rates among LGB adults are approximately 50% higher than heterosexual individuals.

Additionally, data indicate that LGB individuals are at elevated risk for lung health inequalities due to earlier age of initiation, use of highly addictive mentholated cigarettes, and a longer duration of high-frequency smoking. Data on tobacco use among transgender populations is more limited compared to sexual minorities.

However, over the past five years, several nationally representative studies have documented rates of tobacco use as more prevalent among transgender adults. With few exceptions, transgender male respondents had the highest

use patterns across all the products (cigars, cigarettes, e-cigarettes) compared to cisgender males and females and transgender female respondents.

The current data on smoking underscore the need for attention and investment in the LGBTQ+ communities by tobacco prevention and control organizations. Effective tobacco prevention and control efforts consist of multi-pronged strategies, including outreach and awareness campaigns, targeted resources for minority populations, access to smoking cessation interventions, and public health policies.

Despite consistent tobacco-use disparities, gender and sexual minorities are not systematically included in most tobacco prevention and control efforts, and funded research to promote smoking cessation research among LGBTQ+ populations is limited. Specifically, there is scant information on evidence-based interventions for LGBTQ+ smokers.

The available research suggests that evidence-based treatments (e.g., individual counseling, pharmacotherapy) recommended in the U.S. Public Health Service's *Clinical Practice Guideline: 2008 Update* (Fiore et al., 2008) are as effective for sexual minorities—if they are used. However, intervention research for transgender smokers is limited, and awareness and uptake of evidence-based treatments remain low among LGBTQ+ smokers.

Further, the LGBTQ+ community has been highly underserved by the medical community, including recommendations and assistance with smoking cessation. The barriers to accessing appropriate health care services are linked to bias among providers and system-level factors (e.g., inability to indicate gender identity, preferred name, and pronouns in the EHR) that create a hostile environment for sexual and gender minority patients.

The elimination of smoking inequalities among sexual and gender minority populations will require an investment in systematic and rigorous research. Many of the existing frameworks for understanding individual-level predictors of health risk behaviors among adult smokers can also be applied to research on LGBT populations (i.e., Transtheoretical Model of Behavioral Change).

In addition to individual-level factors, social factors including education, racial segregation, and poverty account for over a third of the total deaths in the U.S. each year. In response, health disparity researchers are moving beyond the exclusive focus on individual-level predictors of risk to evaluate the influence of social determinants on health inequalities.

Similarly, recent calls for the systematic study of the effect of social determinants (economic stability, neighborhood and physical environment, education, community, and social context, and the health care system) on LGBTQ+ health inequalities. LGBTQ+ individuals have been the target of systemic violence, oppression, and social exclusion. These factors influence life opportunities and influence health outcomes via the social determinants of health and should be examined and ultimately eliminated.

Finally, research is needed to understand the health implications of smoking among LGBTQ+ populations. A higher prevalence of smoking across the lifespan exposes LGBTQ+ people to elevated risk for lung cancer and other smoking-related morbidities. However, research on lung cancer risk among LGBTQ+ individuals is limited except for research among HIV-positive individuals.

A significant barrier for evaluating rates of smoking-related diseases in LGBTQ+ patients is that cancer registries do not collect information on sexual orientation or gender identity; thus, limiting examination of the influence of smoking on cancer-related incidence and mortality.

Two recent studies reported on the eligibility of LGB older adults for low-dose computed tomography (LDCT) lung cancer screening (a proxy for chronic high-frequency smoking and an indicator of elevated risk for lung cancer).

In the first study, my colleagues and I, using population-based data sets, examined the overall prevalence of eligibility for low-dose computed tomography (LDCT) lung cancer screening among older adults based on sexual orientation. Overall, 11.2% of older U.S. adults met eligibility criteria for LDCT lung cancer screening. Eligibility for LDCT lung screening was associated with sexual orientation; the highest eligibility rates were observed among bisexual women and men (26.9 and 24.5%, respectively).

A separate study using data from the Behavioral Risk Factors Survey Study (BRFSS) found that LGB respondents were more likely to meet guidelines for screening than heterosexuals but less likely to have received a screening test for lung cancer.

Together, these two studies demonstrate the need to increase awareness and develop lung cancer screening interventions for LGBTQ+ smokers. Appropriate interventions should be developed in collaboration with community partners and housed within LGBTQ+ serving health care facilities around the country.

As we continue to celebrate the tremendous strides achieved in the movements toward LGBTQ+ liberation, we cannot lose sight of the work that remains for LGBTQ+ health equity. During Pride month and throughout the rest of the year, freedom from oppression also includes freedom from smoking.

To achieve equity in lung health risk factors and outcomes, the tobacco prevention and control communities will need to take a page out of the corporate playbook and fly that pride flag high.

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GUEST EDITORIAL

Let's stop passing the buck on sexual harassment in academic medicine

Shikha Jain, MD
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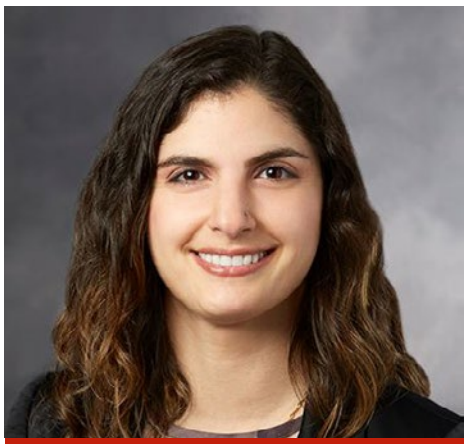

Arghavan Salles, MD
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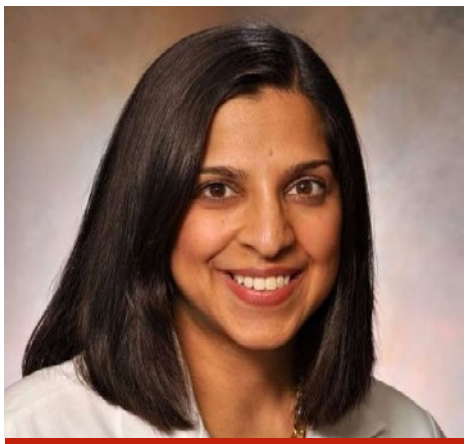


Vineet Arora, MD, MAPP
Herbert T. Abelson Professor of Medicine, Board-certified academic hospitalist, Associate chief medical officer for clinical learning environment, University of Chicago Medicine; Member, National Academy of Medicine

We've all heard this story before, just with a different set of names and places. Man harasses woman after woman, eventually someone (usually a woman) is brave enough to report him, a quiet investigation confirms the reports, and he quietly and seamlessly gets hired elsewhere with no one the wiser.

The story is familiar, albeit with different names, institutions and specialties each time. Though the gender identities of those involved may vary, the most common situation is a man harassing a woman, which is the framework we will use henceforth.

The most recent public case centers around an oncologist who was employed at one of the most respected medical institutions in the world, the Mayo Clinic, and sexually harassed at least two women he mentored, one of whom was in training.

A clear timeline of the account, painstakingly put together by the investigative team at *The Cancer Letter,* depicts how those who misbehave often face little consequence and are passed along from one institution to another, able to perpetuate abuse ad infinitum (*The Cancer Letter,* May 28, 2021).

As three women physicians who study gender equity, we were struck by how clearly this story highlighted the painful

truth: organizations value silence rather than workplace safety.

Men who behave inappropriately, regardless of the type of sexual harassment (categorized by the National Academies of Science, Engineering, and Medicine as gender harassment, unwanted sexual attention, or sexual coercion) they engage in, simply "fail up" while their victims often face negative personal and professional repercussions and may leave academic medicine or medicine altogether.

New data confirms how prevalent sexual harassment is in oncology. At the American Society of Clinical Oncology annual meeting June 4, Dr. Ishwaria Subbiah and colleagues presented data showing that sexual harassment by peers/superiors and patients is prevalent among oncologists and especially among women (*The Cancer Letter*, June 11, 2021).

> It is no longer acceptable for all of us to stand idly by, watching women's careers be damaged or ruined by harassers.

Moreover, the consequences of sexual harassment are significant and translate into decreased mental health, lower perceptions of workplace safety and increased intention to leave.

The Mayo case highlights two root causes that perpetuate the vicious cycle of sexual harassment in academic medicine. First, the traditional master-apprentice training model of medicine creates a power imbalance that enables harassment to occur.

Furthermore, trainees and junior faculty in small specialties are often isolated, depending on one senior faculty member for professional advancement. This dependence often silences survivors due to fear of repercussions and can also contribute to "Stockholm syndrome" with the victim feeling sympathetic to their abuser due to a pathologic dependency.

Passing the trash

The second issue is often dubbed "pass the trash" or "pass the harasser" and refers to the phenomenon of men who sexually harass others being supported in climbing the leadership ladder by simply changing institutions.

In their wake, the survivors struggle with the aftermath of their own damaged reputations, derailment of their professional careers, and a lack of support from their institutions.

While documenting the prevalence of sexual harassment, as Dr. Subbiah's study did, is important, we must focus on implementing solutions. For example, to address the pass the harasser problem, the University of Wisconsin has enabled the sharing of standard personnel files, including information about sexual harassment, between its campuses and state agencies, to be used during hiring decisions.

The university also explicitly asks whether any potential hire has a history of sexual harassment. The state of Washington codified these ideas into the first state law to end "pass the harasser" by requiring personnel files be shared among all Washington's colleges and universities. Such policies could make sure that people who sexually harass others will need to, at the very least, pursue remediation prior to re-entering the workforce.

One way to minimize the harm caused by powerful individuals who engage in misconduct such as sexual harassment is to redistribute power in mentoring relationships. For example, having teams of mentors facilitates having more eyes on mentors and creates potential allies for mentees.

Frequent assessment of mentors' performance based on experiences of past mentees coupled with regular check-ins with current mentees by program leaders can also create accountability. It is also vital to ensure greater diversity in senior faculty to diversify the mentor pool and ensure the promotions process has accounted for any setbacks that women, and especially women of color, may have faced, including due to bias and harassment.

Lastly, it is no longer acceptable for all of us to stand idly by, watching women's careers be damaged or ruined by harassers. We must break the well-described "network silence" that surrounds survivors and step up as allies to hold others accountable.

This support is even more important for Black, Indigenous, and people of color individuals and those who are nonbinary and therefore at greater risk of being marginalized, attacked and harassed in hostile learning environments.

This will not be easy. We are entrenched in a tradition of steep hierarchy and culture of silence that cannot be changed without the support of those at the top. We must all, regardless of our position, summon the courage to lead efforts to make change.

Solutions from the business world and the National Academy of Science Engineering and Medicine's Action Collaborative to End Sexual Harassment can guide our efforts.

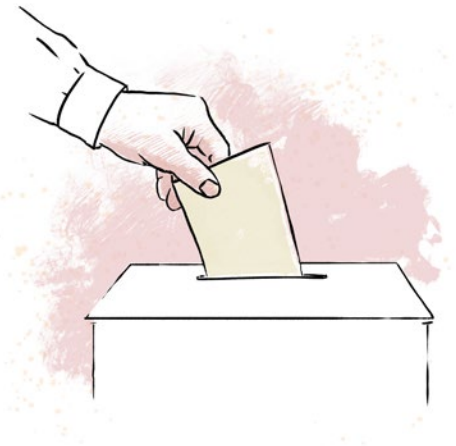
Whatever changes we make, we must hold each other and our institutions accountable both when harassment occurs and when the harasser is being passed along to another, unsuspecting institution.

There is simply too much at stake.

THE CANCER LETTER | JUNE 25, 2021 | VOL 47 | ISSUE 25

Pazdur expresses "profound concerns" about single-arm studies of PD-1/PD-L1 drugs; ODAC nixes retifanlimab for anal cancer

By Paul Goldberg



The FDA Oncologic Drugs Advisory Committee, in an 13-4 vote, recommended against approval of retifanlimab, a PD-1 inhibitor, for the treatment of squamous carcinoma of the anal canal.

The agent's sponsor, Incyte Corp., was seeking an accelerated approval based on an ongoing, open-label, single-arm trial that accrued 94 patients with locally advanced or metastatic SCAC. The committee recommended deferring the decision until completion of a randomized trial, which is expected in 2025.

At the June 24 ODAC, the company was seeking an accelerated approval "for the treatment of patients with locally advanced or metastatic squamous carcinoma of the anal canal who have progressed on or are intolerant of platinum-based chemotherapy."

If approved, Incyte's retifanlimab would become the seventh PD-1/PD-L1 drug on the market.

FDA has been taking a hard look at "dangling" indications of this class of drugs. The term, coined by the agency's cancer czar Richard Pazdur, refers to "accelerated approval indications where a required trial did not confirm benefit—hence, this indication is 'dangling' between an accelerated approval status and market withdrawal."

In April, at a three-day meeting, ODAC reviewed five such indications (*The Cancer Letter*, April 30, 2021). Over preceding months, FDA convinced four drug companies in as many months to voluntarily withdraw four dangling indications. Press releases announcing the withdrawals said the indications were being pulled "in consultation with the agency" (*The Cancer Letter*, March 12, March 5, 2021).

The prevalence of dangling indications was thus reduced by 40%. The remaining 60%, presumably those that weren't quite so open-and-shut, went to ODAC. (A date with ODAC had to be the or-else in the agency's behind-the-scenes persuasion tour.)

By taking Incyte's retifanlimab before ODAC, the agency was asking for a discussion of settings where single-arm trials are appropriate as well as about the value of demonstrating a small improvement in a response rate in such a trial.

"After three days of lengthy discussions, it appears that low response rate, even when some of these responses are durable, do not always translate into clinical benefit when larger numbers of

patients are studied in clinical trials," May Tun Saung, a clinical reviewer, said at the ODAC meeting June 24.

In Incyte's trial, called POD1UM-202, 13 of the 94 patients in the trial had demonstrated objective response per Independent Central Review.

The FDA staff pointed out that it's unclear whether this 14% response rate can be held as reasonably likely to predict clinical benefit. The ORR per ICR is 14% (95% confidence interval [CI]: 8, 22); median estimated duration of response (DoR) is 9.5 months (95% CI: 4.4, not estimable).

Making things worse, about half of the patients who demonstrated improved ORR in the study had limited follow-up for durability of response, meeting documents show. ORR hasn't been shown to be a predictor of either overall survivors or progression-free survivors for immune checkpoint inhibitors.

The agency threw the application to ODAC to get advice on whether the request for accelerated approval should be deferred pending the results of a randomized, which is ongoing. The results are expected in about four years, the company said.

Also, the sponsor was presenting the results of a small study of patients who were not representative of the SCAC population, FDA said. Few of the POD1UM-202 patients were HIV-positive or were members of racial minority groups. About 8.1% of SCAC patients have HIV.

Incyte has filed an application despite words of caution it received at a pre-BLA meeting last September. The meeting, summarized by the agency, didn't seem encouraging:

- ORR magnitude was modest in POD1UM-202 and less than the target ORR of 25% that was proposed by Incyte in POD1UM-202; thus, it was unclear if the ORR was reasonably likely to predict clinical benefit,
- DoR data was limited - only 7 of the 13 responders had DoR >6 months,
- The BLA would be a stronger application if it were supported by positive results from the POD1UM-303/InterAACT 2 clinical trial, and
- If the BLA is submitted with results only from the POD1UM-202 clinical trial, FDA might elect to discuss the application in an ODAC.

"Although FDA cannot discuss the follow-up with respect to the [April] advisory committee meetings held in April, an important lesson is that when voting can maintain an indication, members of the advisory committee considered if alternative confirmatory trials were being conducted and the timing of when these trial results are expected," Saung said at the ODAC meeting. "The FDA would like to highlight that in today's meeting, we will discuss an application with a single confirmatory trial that has enrolled only 28 patients as of May 25, 2021, which is only 9% of the plan trial population."

Though Incyte inferred delay in disease progression from the data, FDA said single-arm trials cannot produce such data.

"The problem with single-arm trials is you don't get a great risk/benefit assessment, because you don't have a control arm," said Steven Lemery, acting director of the Division of Oncology 3 at the Office of Oncologic Diseases. "So, we have to carefully think about when single-arm trials shouldn't use in, perhaps when they shouldn't."

Pazdur, director of the Oncology Center of Excellence and acting director of the Office of Oncologic Diseases, said the agency has "profound concerns" about continued reliance on single-arm studies as a basis for accelerated approval of PD-1/PD-L1 drugs.

Pazdur continued:

> There's an adage: "Those who don't learn from history are destined to repeat it." And I think we had a very painful discourse over the past ODAC, with many trials that had relatively low response rates not demonstrating clinical benefit. And we really have to reassessed this.
>
> And that's why we're bringing this to this ODAC meeting, and we'd like some discussion on this. There is no reason why people cannot do randomized studies to get their drugs approved. And the single-arm trial is not the only way that a drug can be approved.
>
> We've advocated this multiple times to companies. This data was known many years ago, of the activity of this drug, and a randomized trial could have been initiated earlier,

> There is no reason why people cannot do randomized studies to get their drugs approved. And the single-arm trial is not the only way that a drug can be approved. We've advocated this multiple times to companies.
>
> – *Richard Pazdur*

perhaps even in an earlier disease setting in anal canal cancer.

So, there are profound concerns here of whether continuing this practice for this class of drugs—and I want to make it quite clear—is a reasonable registration strategy. Here. again, there are areas where single-arm trials make sense.

These may include where there's very high response rates for some of the targeted therapies, and we've given actually full approval on the basis of response rates, but there's no reason why we only have to do single-arm trial for many of these diseases and then look at randomized trials.

One of the options that we would have had here is to do a randomized trial and take a look in interim analysis for response rates, and have a continuation of the trial to demonstrate clinical benefit. And we would actually have had a randomized trial going on here.

I'd also like to point out for the committee, since many of you may not be familiar. When we take a look at single-arm trials, we are only taking a look at response rates.

We cannot make any inferences regarding stable disease, because it may reflect the natural history of the patients that were enrolled in the studies, nor can we make any claims regarding time to progression, or overall survival.

So, although that was presented in the sponsor's presentation, from a regulatory point of view, we would not be taking a look at these endpoints of disease stabilization, or time to progression, or overall survival. These need to be demonstrated in a randomized setting.

Mark Cornfeld, Incyte's vice president for immune-oncology drug development, disagreed with Pazdur:

We actually agree with FDA that that's not all trials will be confirmed and should not be considered by way, but it's the biology that's the key here.

And if you take a look at those, the list of the trials, where there have been concerns, and if I did not participate in the April ODAC, but we certainly followed it with interest and all of these trials were in indications other than a squamous tumor, and specifically none of them were in HPV-driven disease.

And if you look at the trials specifically in HPV-driven malignancy, which is a very unique biology, and remember biology is key here, the results are consistently predictive of survival.

If we limit our discussion to the HPV-driven cancer biology, which is unique, and which is what we're talking about here today, since all of anal cancer is an HPV-driven cancer, these very low response rates have consistently predicted for survival benefit.

There are no approved second-line treatments for SCAC, but other PD-1/PD-L1 agents are being used off-label for this rare cancer.

NCI BSA approves four new concepts, concurs with 31 reissue PARs

By Alexandria Carolan

The NCI Board of Scientific Advisors approved four new concepts, which includes Requests for Applications, Cooperative Agreements, and Program Announcements.

The board additionally voted to concur with 31 reissue PARs. The NCI receives a large volume of PAR reissues annually, and so, the board has agreed to review these as a group.

The projects, presented at the June 15 meeting of the BSA and National Cancer Advisory Board, are available here.

Implementation Science for Cancer Control in People Living with HIV in Low-and Middle-Income Countries (RFA/Coop. Agr.)

The goal of this RFA/Coop. Agr. is to support the development, adaptation, and testing of implementation strategies to deliver evidence-based inter-

ventions, tools, and technologies for cancer control among people living with HIV (PLWH) in low-and middle-income countries (LMICs).

This RFA seeks to support projects tailored to the diverse cancer control needs of PLWH while leveraging existing capacity for HIV care delivery in LMICs.

The project, presented by the Office of the Director, has an estimated total budget of $25 million. Year One (2022) has set aside funds of $5 million, and application budgets are limited to $500,000 in direct costs per year.

The project antitipcates funding through six to eight U01 awards (clinical trial optional).

Opportunities for cancer control in LMICs include:

- Leveraging and building on community infrastructure for HIV treatment and prevention to promote the uptake of evidence-based cancer control interventions.
- Integrating or bundling evidence-based cancer control interventions into HIV treatment and prevention programs that engage remote and vulnerable communities.
- Develop or adapt innovations in telemedicine and mobile health to improve the uptake and reach of evidence-based cancer control interventions in PLWH.

Example research topics are:

- Studies to design, develop, and test theory-informed implementation strategies to improve uptake and integration of evidence-based cancer control interventions for PLWH.
- Studies evaluating the comparative effectiveness and cost-effectiveness of different implementation strategies.
- Studies of policies and other contextual factors that influence the success of dissemination and/or implementation efforts.
- Studies that explore strategies to support the integration of telehealth/telemedicine interventions to deliver evidence-based cancer control.
- Studies to understand how and why implementation efforts are successful (or unsuccessful) in HIV positive populations in LMICs.

Reviewers for this RFA will also be asked to consider the following changes:

- Does the project adequately account for characteristics of the local health systems, and is the proposed implementation approach appropriate for the problem and population proposed?
- Are the research methods relevant, rigorous, and practical in the context of the LMIC setting?
- Does the proposal demonstrate relevant community engagement in the research project including equitable partnership opportunities for the LMIC clinical research community?
- Does the proposal clearly describe potential for scalability and sustainability of the project or intervention within the local LMIC context?
- Does the proposal include an adequate training and dissemination plan involving LMIC investigators, institutions, and stakeholders?

A Multi-Level Approach to Connecting Underrepresented Populations to Clinical Trials (CUSP2CT) (RFA)

The purpose of this RFA (CUSP2CT) is to implement and evaluate multi-level and culturally tailored outreach and education interventions with the primary goal to increase referral of racial/ethnic minority populations to NCI-supported clinical trials.

The project, submitted by the Office of the Director, has an estimated total cost of $18.28 million (over five years).

Up to four U01 grantee sites will be awarded. The project period is for five years, with $450,000 in direct costs ($765,000 total costs) for each award per year. The budget will encompass Fiscal Years 2022-2026.

One U24 grant will be awarded. The project period is for five years, with $350,000 in direct costs ($595,000 in total costs) per year. The estimated total costs per year are $3.67 million.

The CUSP2CT Network is composed of a Data, Evaluation, and Coordinating Center, which connects and coordinates the grantee sites (U01).

Objectives of the project:

- Educate racial and ethnic minorities about NCI-supported clinical trials utilizing community health educators and lay health advisors in the integrated team.
- Engage primary care and referring providers to increase clinical trial awareness to refer racial/ethnic minority populations to NCI-supported clinical trials utilizing community

health educators and lay health advisors in the integrated team.

- Enhance referral of racial/ethnic minority populations to NCI-supported clinical trials at the site, provider, and patient levels utilizing community health educators and lay health advisors, in the integrated team.
- Address barriers and facilitators that impede and support pathways by which racial/ethnic minority populations access NCI-supported clinical trials at the site, provider, and patient levels. Identify and disseminate best practices.

Areas of research interest:

- Test the effectiveness of interventions designed to educate racial and ethnic minority communities about clinical trials generally and the importance of inclusion into clinical trials.
- Encourage and facilitate referral of racial and ethnic minorities who are eligible for a specific clinical trial.
- Address implicit bias and strengthen communication skills of primary care and referral providers.
- Develop referral pathways to clinical trials that would require minimal resource investment on the part of healthcare organizations.
- Test the effectiveness of using virtual/technology-driven interventions, initiated during the COVID-19 pandemic, to increase referral, recruitment, and consent of racial and ethnic minority patients to NCI-supported clinical trials.

Components of a competitive application:

- Cancer type and target population,
- Integrated site team,
- Community intervention,
- Provider intervention,
- Referral system; and
- Identification of best practices.

The coordinating center will:

- Receive, store, and analyze data from the U01 grantee sites.
- Identify and/or develop common metrics and measures to be collected by all U01 grantee sites to facilitate a CUSP2CT program evaluation.
- Assist sites in evaluating their specific interventions and making changes as appropriate at the patient, provider, and site levels.
- Develop an overall program evaluation plan and conduct an evaluation of the CUSP2CT network.
- Disseminate results for all implemented interventions within and outside of the CUSP2CT network, with sufficient detail to allow non-grantee sites to replicate the evaluated interventions.
- Encourage the replication and scale up of effective interventions and best practices.

Mechanisms that Impact Cancer Risk after Bariatric Surgery (PAR)

The purpose of this PAR, submitted by the Division of Cancer Prevention, is to promote studies examining the mechanism(s) through which bariatric surgery impacts cancer risk.

The project, which anticipates funding through the R21 and R01 mechanisms, aims to attract talented scientists who understand the dynamic changes caused by bariatric surgery.

The R21 mechanism will allow for early stage or resource development projects (clinical trial not allowed); and the R01 mechanism will accommodate broader scoped or in-depth mechanistic studies (clinical trial optional).

There was no associated budget with this concept.

Currently, very little has been published on the is the mechanistic link between bariatric surgery and cancer risk reduction, either in animal models or in humans.

The focus thus far has been on benefits seen more quickly after surgery, which includes reduction in body weight, reduction in type II diabetes mellitus, reduction in metabolic syndrome, and reduction in cardiovascular risk.

Questions to address:

- Do alterations in risk biomarkers occur before weight loss? If so, in what organ, tissue, or cell type do they originate?
- Is maximum weight loss or long term weight loss more important for cancer risk reduction? If so, how do the two differ at a cellular and/or biochemical level?
- What mechanism(s) explain the evidence that bariatric surgery is more beneficial in cancer risk reduction in women than men?
- Does bariatric surgery increase or decrease the risk of colorectal cancer, and if so, what are the mechanism(s)?
- Which cancers are favorably impacted by bariatric surgery, and what are the mechanism(s) that explain the effect?

Does the specific bariatric surgery procedure influence cancer impact? If so,

what are the mechanism(s) driving the difference in impact?

Cancer Prevention and Control Clinical Trial Planning Grant Program (PAR)

The purpose of this PAR, submitted by the Division of Cancer Prevention, is to yield information that is both scientifically necessary and also sufficient to permit final decisions about the design or conduct of the large phase II or beyond clinical trial.

It aims to save time and cost by ensuring future trial success.

There is no set aside budget for a PAR, but the direct costs are expected to be $225,000 per year, which totals $450,000 over the two year project period. If the project includes a feasibility trial, the budget can be up to 600,000 direct costs over three years.

The project anticipates funding through the R34 and U34 grants. The PAR intends to fund four to six applications per year across DCP and DCCPS.

The application must include a summary of the future planned clinical trial. A planning grant is not a prerequisite for an R01 funding clinical trial or a large trial through a network.

Examples of research needs include but are not limited to:

- Identify the appropriate control or comparison group to use in the subsequent clinical trial.
- Standardize and evaluate feasibility of the intervention or outcome across multiple sites.
- Feasibility and plan for development of a placebo
- Validate survey instruments.
- Test effectiveness of training tools.
- Adapt and test an intervention or outcome instrument for a population that differs culturally from the population for which the instrument was originally designed.
- Modeling data to support trial assumptions in the study design.
- Statistical planning and design

Short term metrics for this PAR:

- Number of R34 or U34 projects that identified issues needing correction,
- Modifications in the subsequent trial that resulted from the knowledge gained
- Number that proceeded to a full clinical trial or definitively did not,
- Number of clinical trial applications or protocols approved from R34 or U34 awardees; and
- The publication of results, positive or negative.

Long term metrics for this PAR:

- Frequency of one or more major feasibility issues encountered in full clinical trials conducted by R34 or U34 awardees versus those conducted by non-R34 or U34 awardees.
- Frequency of no-cost extensions or cost overruns, or insufficient accrual, in full clinical trials conducted by R34 or U34 awardees versus those conducted by non-R34 or U34 awardees.

IN THE ARCHIVES

CANCER HISTORY PROJECT

Betty Ford and the press conference that changed oncology

Sept. 30, 1974: NCI hits the tabloids

Spotlight article: Breast Cancer Report To The Profession Suddenly Is a Report To The Nation; Treatment Progress Noted
The Cancer Letter | Oct. 7, 1974

An NCI press conference is rarely a tabloid affair—except on Sept. 30, 1974. What was anticipated to be a dry occasion shifted when Betty Ford, wife of President Gerald Ford, underwent a radical mastectomy Sept. 28.

The Cancer Letter was there: "Breast Cancer Report To The Profession Suddenly Is a Report To The Nation; Treatment Progress Noted," was the Oct. 7, 1974 issue's lead story.

Nathaniel Berlin, then director of NCI's Division of Biology & Diagnosis and chairman of the Breast Cancer Task Force, had been concerned the breast cancer report would receive limited public attention. Instead, he got a media circus—leading to fears of publishing the findings prematurely.

No one talked about their cancer diagnosis in the 1970s. Surprisingly, Betty Ford credits Richard Nixon—in part—for her pioneering openness about her breast cancer diagnosis:

"There had been so much cover-up during Watergate that we wanted to be sure there would be no cover-up in the Ford administration," Betty Ford told Gloria Steinem in a 1984 interview. "So rather than continue this traditional silence about breast cancer, we felt we had to be very public."

"Too many women are so afraid of breast cancer that they endanger their lives," Ford said in remarks to the American Cancer Society Nov. 7, 1975. "These fears of being 'less' of a woman are very real, and it is very important to talk about the emotional side effects honestly. They must come out into the open."

Betty Ford's openness had results: "At the time of my mastectomy, I was pleased to see the response to it," she said in 1976 at a dedication of MD Anderson facilities. "It prompted many women to get a check up."

This phenomenon became known as the "Betty Ford blip."

What was her prognosis? *The Cancer Letter*'s 1974 article notes that "historically more than 50% of breast cancer patients die with metastatic disease.... More than 75% of patients with 1 or

more positive nodes will have recurrent disease at 10yrs and most of the patients will die of their disease."

Betty Ford, who was found in 1974 to have four positive nodes, was prescribed an L-PAM regimen, and beat the odds. As a cancer survivor, she continued her advocacy and breast cancer awareness campaigns.

Concluding her 1975 ACS address, Ford said, "My illness turned out to have a very special purpose—helping save other lives, and I am grateful for what I was able to do."

Ford died in 2011 at the age of 93. A comprehensive obituary ran in *Time*.

Recent contributions

Connie Henke Yarbro: 1984 Cancer Nursing Perspective
By Oncology Nursing Society | June 24, 2021

Women in Science: Candace Johnson, PhD
By Roswell Park Comprehensive Cancer Center | June 21, 2021

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.

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

John H. Stewart named center director of LSU Health New Orleans/LCMC Health Cancer Center

John H. Stewart was named center director of the LSU Health New Orleans/LCMC Health Cancer Center.

He will also join the LSU Health New Orleans School of Medicine faculty as a professor of surgery.

Stewart will set the overall mission, vision and direction for multidisciplinary cancer care and cancer clinical research programs for LSU Health New Orleans and LCMC Health in his new leadership role.

He and his team will develop a robust cancer clinical trials program, leverage resources to build an innovative targeted cancer research enterprise and create a comprehensive community outreach and engagement program to reduce cancer risk behaviors and cancer incidence.

Initiatives will integrate disease-specific research and care delivery into a comprehensive patient-oriented approach to benefit patients of Louisiana and surrounding regions, including those currently underserved in accessing leading-edge cancer care.

Stewart, originally from Shreveport, was recruited from the University of Illinois College of Medicine in Chicago. There, he was a University of Illinois Presidential Scholar, professor of surgery in the College of Medicine, deputy director of the University of Illinois Cancer Center, and physician executive for oncology sciences at the University of Illinois Health.

Stewart's role will be effective July 1.

Julio Aguirre-Ghiso named founding director of the Cancer Dormancy and Tumor Microenvironment Institute at Albert Einstein Cancer Center

Julio Aguirre-Ghiso was named founding director of the Cancer Dormancy and Tumor Microenvironment Institute, director of the Gruss-Lipper Biophotonics Center, and co-leader of the AECC Tumor Microenvironment and Metastasis Program at Albert Einstein Cancer Center.

He will also be an endowed professor of cell biology at Einstein. He will assume these roles Oct. 1, 2021.

"His talents as a scientist make him the ideal candidate to lead this first-of-its-kind research institute focused on cancer dormancy and the tumor microenvironment," Edward Chu, director of AECC and vice-president of cancer medicine at Montefiore Medicine, which is comprised of Montefiore Health System and Albert Einstein College of Medicine, said in a statement. "His seminal research has identified the key micro-environmental and signaling mechanisms involved in the biology of dormant cancer cells, which then provides the rational basis for developing novel therapeutic approaches."

The new institute will build upon the current strengths in tumor microenvironment research at Einstein, while expanding its purview to include cancer dormancy, which also closely aligns with the biology of aging, stem cells, epigenetics, and systems biology among other disciplines strongly represented at Einstein.

The CDTMI will also focus on developing novel technologies to better detect dormant cancer and prevent and control recurrent disease. The goal of the institute is to bring together the strengths of new recruits and existing investigators to advance the field and develop novel diagnostic tools and therapies.

Aguirre-Ghiso and colleagues helped lead a major shift in cancer biology by showing that cancer is not perpetually proliferating, as had been thought. They discovered that crosstalk between cancer cells and the tumor microenvironment regulates the cells' ability to switch between dormancy and proliferation.

His lab has also provided key insights into the early spread of breast cancer and how that process contributes to dormancy and to metastatic progression. His research has also explored how adaptive pathways within cancer cells enable the cells to survive while in a state of dormancy.

Those insights led Aguirre-Ghiso to develop novel strategies for preventing cancer recurrences by targeting residual but undetectable cancer cells that have survived initial chemotherapy. To pursue those strategies, Aguirre-Ghiso has developed clinical trials supported by funding agencies and also founded a start-up company, HiberCell, that is conducting clinical trials and drug development.

His work is revealing ways to maintain residual cancer-cell dormancy, kill dormant cancer cells, and use biomarkers to determine whether disseminated cancer cells are in a dormant or active state.

Aguirre-Ghiso is an endowed Mount Sinai Professor of Cancer Biology in the Departments of Medicine, Otolaryngology, and Oncological Sciences at the Icahn School of Medicine at Mount Sinai.

He co-leads the cancer mechanisms program at The Tisch Cancer Institute and directs head and neck cancer basic research in the department of otolaryngology. He is a member of Mount Sinai's Precision Immunology Institute and the Black Family Stem Cell Institute. He is also president of the Metastasis Research Society and has served at several leadership levels at American Association for Cancer Research.

Lauren Hackett named deputy director of administration at Albert Einstein Cancer Center

Lauren Hackett was named deputy director of administration of Albert Einstein Cancer Center and associate vice president of cancer medicine at Montefiore Medicine.

Hackett, who is currently the chief operating officer at the Allen Institute, will assume these roles in August 2021.

At AECC, Hackett will have oversight and authority over the administrative team and structure, running all aspects of its operations. A key part of her role is partnering with the senior leaders at AECC, Einstein, and Montefiore to align and implement strategic priorities across its cancer enterprise.

As COO at the Allen Institute, a private, non-profit research institute, she led the institute through the COVID-19 pandemic and co-developed the institute's diversity, equity, and inclusion initiative. She also partnered with colleagues to integrate scientific strategy and planning efforts throughout administration and operations teams across the institute.

Erika Newman named Rogel Cancer Center's first associate director for diversity, equity, inclusion and justice

Erika Newman was named the first associate director for diversity, equity, inclusion and justice at University of Michigan Rogel Cancer Center.

She will lead the center's efforts to diversify the next generation of healthcare professionals and researchers, and to champion an anti-racist and just culture within the cancer center.

"This is a really important time for these efforts," Newman said in a statement. "We've had a rough year with the health disparities underscored by COVID-19 and the events that have prompted a larger racial awakening across the

country, including the killings of Ahmaud Arbery and George Floyd. So, this is an opportunity for us to take a look at ourselves, to take a look at our organization, and understand how we can contribute to positive change across clinical care, research, education and training, and service to our community."

Newman is an associate professor of pediatric surgery at Michigan Medicine.

Newman maintains a busy clinical practice with broad expertise in the care of children with solid tumors as well as a basic-science research lab that focuses on understanding tumor-specific DNA repair mechanisms as novel therapeutic options for pediatric neuroblastoma. She is surgical director of the C.S. Mott Children's Hospital's solid tumor oncology program.

Newman is a founding member of the Michigan Women's Surgical Collaborative, a diverse group of academic surgeons with the mission of implementing strategies that advance women surgeons across disciplines.

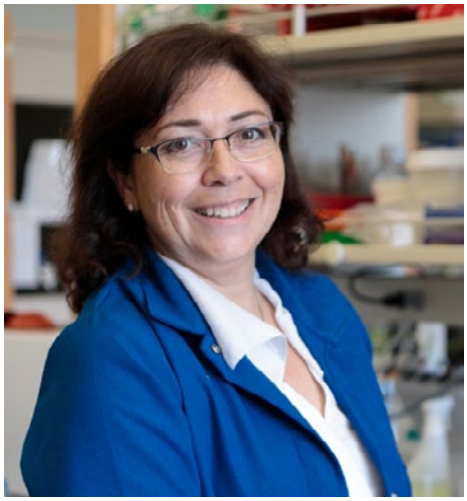
She also facilitated the development and implementation of the Michigan Promise within the Department of Surgery, a series of innovative initiatives aimed at improving faculty and resident excellence and strengthening the core culture to create a more open and inclusive environment.

Her appointment was effective June 1.

Luisa Iruela-Arispe named co-leader of the TEAM Program at Lurie Comprehensive Cancer Center

Luisa Iruela-Arispe, a vascular biologist, was named co-leader of the Tumor Environment and Metastasis Program at the Robert H. Lurie Comprehensive Cancer Center of Northwestern University.

The goal of the TEAM Program is to elucidate how interactions between tumor cells, immune cells, and components of the host stromal microenvironment impact tumor development and progression.



Iruela-Arispe is chair of the Department of Cell and Developmental Biology and the Stephen Walter Ranson Professor. Her research focuses on the signaling pathways that regulate vascular morphogenesis during development and pathological settings. Her cancer research interests include the molecular mechanisms that result in the emergence of angiosarcomas and the cross-talk between endothelial and tumor cells in the process of metastasis.

In collaboration with TEAM co-leader, Hidayatullah Munshi, she will help advance efforts to translate basic science discoveries from the TEAM Program into clinical practice.

Navneet Majhail named deputy physician-in-chief of blood cancers at Sarah Cannon

Navneet Majhail was named deputy physician-in-chief of blood cancers for the Sarah Cannon Transplant and Cellular Therapy Network (formerly the Sarah Cannon Blood Cancer Network).

In his role, Majhail will focus on the continued expansion of the Sarah Cannon Transplant and Cellular Therapy Network Centers of Excellence providing increased access for patients to cutting-edge cell and transplant therapies in the communities served by Sarah Cannon.

Majhail is director of the Cleveland Clinic's Blood and Marrow Transplant Program, professor of medicine and vice chair for the Department of Hematology and Medical Oncology at the Cleveland Clinic Lerner College of Medicine.

He is a past-president of the American Society for Transplantation and Cellular Therapy and has been recognized as a fellow for his contributions to the field of transplantation and cellular therapy.

Majhail researches the prevention and management of early and late complications of hematopoietic cell transplantation and health policy issues such as healthcare disparities, quality of care, survivorship and economic issues related to transplantation and cellular therapy.

In addition to his work at Sarah Cannon, Majhail will be program medical director for the Sarah Cannon Transplant and Cellular Therapy Program at Centennial Medical Center.

Majhail will formally begin his position in late September 2021.

RWJBarnabas Health and Rutgers Cancer Institute of New Jersey break ground on Jack & Sheryl Morris Cancer Center

RWJBarnabas Health and Rutgers Cancer Institute of New Jersey, in partnership with the New Brunswick Development Corporation, broke ground on the state's first freestanding cancer hospital.

At the ceremony, it was also announced that the 510,000-square-foot structure will be named the Jack and Sheryl Morris Cancer Center in recognition of the philanthropic leadership of Jack Morris, who has been a longtime supporter and pillar in New Brunswick development, and his wife, Sheryl.

The 12-story facility, to be located on Somerset Street, will house inpatient, outpatient and ancillary services, as well as state-of-the-art laboratories where research faculty can provide hands-on educational opportunities for students, and enable physician-scientists to translate scientific findings directly to patients.

The Jack and Sheryl Morris Cancer Center will enable ease of access for imaging and other diagnostic tests, treatment and follow-up exams all in one space. It will also have the capacity to offer wellness and education resources including offerings catered specifically to the needs of cancer survivors. The estimated project cost is $750 million.

The facility, which will be positioned adjacent to the existing Rutgers Cancer Institute building and Robert Wood Johnson University Hospital, also will house state-of-the-art research laboratories.

The project is expected to be completed in 2024.

UCSF establishes $250M initiative to develop living therapeutics

University of California, San Francisco has established a initiative to propel the development of living therapeutics and bring them quickly to patients.

The Living Therapeutics Initiative will bring together UCSF's scientific and clinical expertise to accelerate research and quickly advance promising therapies to clinical trials for patients who have few, if any, good treatment options.

As a federation of established UCSF initiatives, the LTI will allow disparate research and clinical programs to share information, tools, and platforms. In the fall, the initiative will launch a $50 million grants program, made possible by philanthropy, to fund UCSF faculty living-therapeutics projects.

Over the past few years, UCSF has raised philanthropic gifts and made institutional commitments totaling more than $250 million to support living therapeutics-related efforts across the university.

Living therapeutics have been called a "new third pillar" of medicine, following small-molecule drugs (relatively simple compounds that can be chemically manufactured) and biologics (proteins and other molecules synthesized within microorganisms or cells).

Researchers across UCSF are already building the next generation of cellular therapies to treat diseases including solid tumors, autoimmunity, neurodegeneration, diabetes, and infectious diseases. These therapies aim to be smarter, safer, and more effective than CAR T, thanks to recent breakthroughs in cell engineering and gene editing. The LTI will connect tools and expertise from across the ecosystem of UCSF initiatives and partner institutions working to advance cell-based therapeutics.

These initiatives and institutions include clinical services at UCSF Medical Center and UCSF Benioff Children's Hospitals; the Chan Zuckerberg Biohub; the Gladstone-UCSF Institute of Genomic Immunology; the Innovative Genomics Institute; the Parker Institute for Cancer Immunotherapy; and UCSF's Bakar Computational Health Sciences Institute, Bakar ImmunoX Initiative, Benioff Center for Microbiome Medicine, Cell Design Institute, and Eli and Edythe Broad Center of Regeneration Medicine and Stem Cell Research. Most recently, UCSF announced a partnership with Thermo Fisher Scientific for the co-development of a specialized facility for making cell-based immunotherapies and other cell-therapy products.

In addition to administering the $50 million in funding through an internal grant process, the LTI steering committee will help with coordination and strategy, such as thinking through regulatory issues, submitting applications FDA, and designing and evaluating clinical trials. Their evaluation of funding proposals will prioritize high-need, high-impact projects designed to lead to clinical trials.

COTA and UChicago collaborate to study racial disparities in cancer treatment

COTA, an oncology real-world data and analytics company, and University of Chicago Medicine have established a research collaboration agreement to investigate racial disparities of care in multiple myeloma to better understand differences in the diagnosis, treatment patterns, and outcomes of patients with this type of cancer.

Researchers at COTA and University of Chicago Medicine will use real-world data to examine potential disparities in clinical treatment pathways and outcomes.

"Black Americans are grossly underrepresented in clinical trials, and more data is needed to evaluate the best treatments for this population," Benjamin Derman, of University of Chicago Medicine, said in a statement. "It is critical that we understand optimal treatment pathways and risk prognostication in Black populations. Leveraging COTA's expertise in real-world data, we can evaluate reasons for racial disparities in multiple myeloma outcomes and improve the way we care for these patients moving forward."

COTA provides comprehensive oncology real-world data abstraction, curation, and analytics capabilities to leading healthcare provider organizations and life sciences companies that are caring and developing treatments for patients living with a wide range of cancers.
Huntsman Cancer Institute establishes $31 million proton therapy center

The Senator Orrin G. Hatch Proton Therapy Center has opened at Huntsman Cancer Institute, and is the first of its kind in the Mountain West.

The $31 million, 7,450-square-foot addition adds to radiation therapy technology and expertise available within University of Utah Health.

The center was named to honor Senator Orrin G. Hatch's commitment to improve the landscape for cancer care in Utah. Hatch was among the earliest supporters when Jon M. Huntsman Sr. announced his intent to build a major new cancer research center in Utah.

Up until now, the nearest proton therapy centers were more than 700 miles away.

The technology that delivers this treatment is housed in a three-story facility. The equipment includes a 110-ton gantry (a moveable framework that allows the equipment to rotate 190 degrees around the patient), which holds a 15-ton cyclotron. It accelerates protons to 2/3 the speed of light.

This precision technology allows the treatment to target the tumor from the best angles and avoid important structures in the body. A team of specially trained medical doctors, technologists, technicians, and others work to safely deliver this treatment to adult and pediatric patients as part of their cancer care plan. The new center also includes state-of-the-art tumor targeting, with a special combination of proton treatment delivery and CT imaging for tumor targeting.

When fully operational, the center is projected to care for approximately 200 patients a year.

Cancer centers, Genentech launch oncology clinical trial diversity alliance

A group of cancer centers is collaborating with Genentech on a clinical trial diversity, launching the Advancing Inclusive Research Site Alliance.

Founding partners are City of Hope Comprehensive Cancer Center, Mays Cancer Center, O'Neal Comprehensive Cancer Center, University of Alabama at Birmingham, and West Cancer Center.

This coalition of clinical research sites will partner with Genentech to advance the representation of diverse patient populations in the company's oncology clinical trials, test recruitment and retention approaches, and establish best practices that can be leveraged across the industry to help achieve health equity for people with cancer.

Each of the centers will focus on enabling the participation of historically underrepresented patient groups in Genentech's oncology trials, working collaboratively to share key learnings and explore innovative ways of increasing clinical trial access for every patient who might benefit.

The alliance also plans to expand to more research centers and additional disease areas in the near future, with the ultimate goal of building a robust and sustainable clinical research ecosystem that actively includes diverse patient groups.

ASCO, Friends of Cancer Research: Individuals with cancer must be included in COVID-19 vaccine trials

In a joint position statement, the American Society of Clinical Oncology and Friends of Cancer Research said

individuals with cancer or a history of cancer should be eligible for clinical trials—including COVID-19 vaccine trials—unless there is safety justification for exclusion.

To date, clinical trials for COVID-19 vaccines have almost universally excluded patients with cancer, and many have excluded those who have a history of cancer. Because these studies enrolled narrower, more homogenous patient populations, many of the most vulnerable patients, who have comorbidities and, in some cases, specific immune-compromise, do not know if the vaccines are safe or effective for them.

This raises risks for individuals and for society as a whole. Especially now that multiple vaccines have been authorized for emergency use by the U.S. Food and Drug Administration (FDA) and other national entities, ASCO and Friends say eligibility should be immediately expanded to include patients with cancer as the default.

"We've learned that patients with cancer are especially vulnerable to severe illness, hospitalization, or death due to COVID-19," ASCO President Everett E. Vokes said in a statement. "However, since clinical trials for COVID-19 vaccines have largely excluded patients with cancer, we still have a long way to go to better understand how safe and effective COVID-19 vaccines are for patients in active treatment."

"It is critically important to study adequate numbers of patients who have cancer or a history of cancer so that we can better understand the degree to which patients with cancer, various kinds of immunocompromise, or both respond to vaccines," he said.

ASCO and other professional organizations recommend patients across the cancer continuum receive vaccinations (including vaccinations for COVID-19) unless specifically contraindicated, such as evidence of potential risk to patient safety. This recommendation is currently based, however, on consensus expert opinion in the absence of clinical evidence.

There is a lack of understanding of the degree of immunity and clinical protection that COVID-19 vaccines provide in individuals with compromised immune systems. Until studies provide more specific insights about populations with cancer, patients with cancer who are vaccinated are encouraged to continue to follow all guidance on masking and physical distancing to reduce any potential exposure to SARS-CoV-2.

"We continue to emphasize that broadening eligibility criteria to clinical trials will help inform the optimal use of new medicines for more people, and the same principles apply to COVID-19 vaccines," Jeff Allen, president and CEO of Friends of Cancer Research, said in a statement. "Because people with cancer are at greater risk for severe outcomes from COVID-19, we urge manufacturers and trial sponsors to enroll patients with cancer and develop studies specifically geared towards patients with cancer to fully characterize the level of protection these important vaccines provide."

In the new joint position statement, ASCO and Friends recommend:

- Vaccine trial sponsors should design studies to be as broadly inclusive as possible. Existing and future COVID-19 vaccine trials should only exclude people with cancer (current or history of) and/or people who are immunocompromised if there is specific and credible risk of harm to them from trial participation.
- Vaccine manufacturers and trial sponsors should prioritize recruitment of patients with cancer through partnerships with oncology practices, cancer centers, and academic medical centers. COVID-19 vaccine trials should be prospectively designed and purposefully recruit sufficient numbers of individuals with cancer from diverse populations and age groups to enable valid subset analysis.
- Government agencies with oversight of vaccine development and review should encourage and incentivize vaccine manufacturers to include patients with cancer in existing and future COVID-19 vaccine trials.
- Public health agencies and other research organizations should design, collect, and analyze real world data on vaccine effectiveness in patients with cancer, in addition to clinical research data. For populations underrepresented in prior vaccine trials, this data collection would enable the most comprehensive understanding of practical clinical considerations.

This joint research statement builds on ongoing efforts between ASCO and Friends to broaden and modernize cancer research eligibility criteria, with the goal of making clinical trials more accessible to patients.

In April 2021, the two organizations issued recommendations to address five specific common eligibility criteria: treatment washout periods, concomitant medications, prior therapies, laboratory reference ranges and test intervals, and patient performance status, and in 2017, the organizations issued recommendations related to brain metastases, minimum age for enrollment, HIV status, organ dysfunction, and prior or concurrent malignancies.

THE CLINICAL CANCER LETTER

CLINICAL ROUNDUP

DFCI study: How cancers with common gene mutation develop resistance to targeted drugs

A study by Dana-Farber Cancer Institute researchers has given scientists their first look at the genomic landscape of tumors that have grown resistant to drugs targeting the abnormal KRASG12C protein.

Their work shows that, far from adopting a common route to becoming resistant, the cells take a strikingly diverse set of avenues, often several at a time.

The findings, reported in the *New England Journal of Medicine*, underscore the need for new drugs that inhibit KRAS differently than current agents do. And, because resistance can arise through many different mechanisms, effective treatment for these cancers will likely require combinations of KRAS inhibitors and other targeted drugs.

"Mutations in the KRAS gene are fairly common across cancer types," co-author Mark Awad, of Dana-Farber, said in a statement. "The particular mutation we focused on in this study, KRASG12C, is found in about 13% of non-small cell lung cancers [NSCLC], where it's often associated with tobacco use, in up to 3% of colorectal cancers, and less frequently in a range of other cancers.

"While no targeted therapy has been approved for this specific molecular subtype, two inhibitors of the KRASG12C protein – adagrasib and sotorasib – have shown promise in clinical trials, especially in patients with NSCLC," he said.

"While results from these early clinical trials are encouraging, the cancer usually becomes resistant to these drugs," Awad said. "The mechanisms of resistance – the genomic and other changes that occur that allow the cancer to begin growing again – are largely unknown. This study sought to identify them."

Shengwu Liu, of Dana-Farber, is also a first co-author of the study.

In a multi-institutional effort, researchers collected tumor samples from 38 patients with cancers carrying KRASG12C mutations – 27 with NSCLC, 10 with colorectal cancer, and one with cancer of the appendix. Analysis of the samples uncovered possible causes of resistance to adagrasib in 17 of the patients, seven of whom had multiple causes.

The resistance mechanisms fell into three categories:

- New alterations in KRAS – the development of mutations other than G12C (at amino acid positions such as G12, G13, R68, H95, and Y96) or an increased number of copies of KRASG12C itself.
- Abnormalities in an array of genes other than KRASG12C. These genes included BRAF, MET, ALK, RET, MAP2K1, and others.
- Two cases in which lung adenocarcinomas (cancers that start in secretory cells) transitioned to become squamous cell carcinomas, a different subtype of NSCLC.

The number of patients with KRAS alterations and non-KRAS genetic abnormalities was roughly equal, and many patients had both types of resistance mechanisms.

The effort to uncover KRAS mutations associated with drug resistance was also led by the study's senior author, Andrew Aguirre, of Dana-Farber, Brigham and Women's Hospital, and the Broad Institute of MIT and Harvard.

Aguirre and his colleagues created a series of cell lines, each containing the G12C mutation plus an additional mutation elsewhere in the KRAS gene. The set represented every possible second mutation in KRASG12C that would give rise to an abnormal protein. The researchers then ran tests to see which of the doubly mutated genes gave cells the ability to become resistant to sotorasib or an adagrasib-like compound. They also tested the further-mutated versions of KRASG12C that the team had identified in patients.

They found that some of the new mutations conferred resistance to both agents, whereas others provided resistance to just one.

"In addition to identifying resistance mutations that have already occurred in patients receiving adagrasib, our study also provides an atlas of all possible mutations in KRASG12C that can cause resistance to adagrasib and/or sotorasib," Aguirre said in a statement. "These results will be a valuable resource for oncologists to interpret future acquired mutations that occur in patients who become resistant to these drugs and may be used to guide the choice of which KRASG12C inhibitor is right for each patient."

The study results point to the variety of ways cancers with KRASG12C mutations can overcome the effects of adagrasib, the authors say.

"Cancers with the KRASG12C mutation constitute a large proportion of all lung cancers, and many pharmaceutical companies are developing KRASG12C inhibitors," Awad said. "The hope is that studies such as this, which uncover resistance mechanisms, will help drive future studies of combination therapies to delay or prevent resistance or overcome it when it occurs."

International study of rare childhood cancer finds genetic clues, potential for tailored therapy

In children with rhabdomyosarcoma, a rare cancer that affects the muscles and other soft tissues, the presence of mutations in several genes, including TP53, MYOD1, and CDKN2A, appears to be associated with a more aggressive form of the disease and a poorer chance of survival.

This finding is from the largest-ever international study on RMS, led by scientists at NCI's Center for Cancer Research, part of the National Institutes of Health.

The study, published in the *Journal of Clinical Oncology* June 24, provides an unprecedented look at data for a large cohort of patients with RMS, offering genetic clues that could lead to more widespread use of tumor genetic testing to predict how individual patients with this childhood cancer will respond to therapy, as well as to the development of targeted treatments for the disease.

"These discoveries change what we do with these patients and trigger a lot of really important research into developing new therapies that target these mutations," said Javed Khan, of NCI's Genetics Branch, who led the study.

"The standard therapy for RMS is almost a year of chemotherapy, radiation therapy, and surgery. These children get a lot of toxic treatments," said first author, Jack Shern, of NCI's Pediatric Oncology Branch. "If we could predict who's going to do well and who's not, then we can really start to tailor our therapies or eliminate therapies that aren't going to be effective in a particular patient. And for the children that aren't going to do well, this allows us to think about new ways to treat them."

RMS is the most common type of soft tissue sarcoma in children. In patients whose cancer has remained localized, meaning that it has not spread, combination chemotherapies have led to a five-year survival rate of 70%-80%. But in patients whose cancer has spread or come back after treatment, the five-year survival rate remains poor at less than 30%, even with aggressive treatment.

Doctors have typically used clinical features, such as the location of the tumor in the body, as well as its size and to what extent it has spread, to predict how patients will respond to treatment, but this approach is imprecise. More recently, scientists have discovered that the presence of the PAX-FOXO1 fusion gene that is found in some patients with RMS is associated with poorer survival. Patients are now being screened for this genetic risk factor to help determine how aggressive their treatment should be.

Scientists have also begun using genetic analysis to dig more deeply into the molecular workings of RMS in search of other genetic markers of poorer survival. In this new study—the largest genomic profiling effort of RMS tumors to date — scientists from NCI and the Institute for Cancer Research in the United Kingdom analyzed DNA from tumor samples from 641 children with RMS enrolled over a two-decade period in several clinical trials.

Scientists searched for genetic mutations and other aberrations in genes previously associated with RMS and linked that information with clinical outcomes. Among the patterns that emerged, patients with mutations in the tumor suppressor genes TP53, MYOD1, or CDKN2A had a poorer prognosis than patients without those mutations.

Using next-generation sequencing, researchers found a median of one mutation per tumor. Patients with two or more mutations per tumor had even poorer survival outcomes. In patients without the PAX-FOXO1 fusion gene, more than 50% had mutations in the RAS pathway genes, although RAS mutations did not appear to be associated with survival outcomes in this study.

The researchers believe that although they have identified the major mutations that may drive RMS development or provide information about prognosis, they have only scratched the surface in defining the genetics of this cancer, with many more mutations yet to be discovered.

They note that more work is needed to identify targeted drugs for those mutations, and future clinical trials could incorporate genetic markers to more accurately classify patients into treatment groups. Two NCI-sponsored Children's Oncology Group clinical trials are currently being developed using these markers, and all participants will have their tumors molecularly profiled.

The researchers hope that routine tumor genetic testing for rare cancers, such as RMS, will soon be a standard part of the treatment plan, as it is for more common cancers, such as breast cancer.

"Genetic testing is going to become the standard of care," Shern said. "Instead of just the pathologists looking at these tumors, we're now going to have molecular profiling, and that's a leap forward."

This study was conducted by an international consortium comprised of scientists at NCI and the Children's Oncology Group in the United States, and the Children's Cancer and Leukaemia Group and the National Cancer Research Institute's Young Onset Soft Tissue Sarcoma Subgroup in the United Kingdom. The data are available here.

The research was supported by NCI and St. Baldrick's Foundation in Monrovia, California.

USC Study shows inherited risk of early-onset cancer is higher among Latino, African American, and Asian/Pacific Islander families

A study has demonstrated that the inherited risk of early-onset cancer is significantly higher among Latino and African American families for solid tumors, and Asian/Pacific Islander families for blood-based cancers, compared to non-Latino white families in California.

The study was published in *eLife*.

"Cancer clustering within families, meaning the devastating diagnosis of more than one early-onset cancer within the same family, usually points to a genetic cause. Interestingly, family cancer clustering has only been examined previously at the population level in white, or European origin population studies," said author Joseph Wiemels, a member of the Cancer Epidemiology Program at the USC Norris Comprehensive Cancer Center, and professor of Preventive Medicine at the Keck School of Medicine of USC. "In this study, we looked at clustering of cancer cases in young family members in California over the past 30 years within non-white populations and compared it, for the first time, to white populations. We found that family-based cancer clustering occurs more frequently among minority populations."

Researchers used California population-based health registries to evaluate the relative cancer risk among parents, siblings and children of patients diagnosed with cancer by the age of 26. Between 1989 and 2015, they identified 29,632 early-onset cancer patients and then examined cancer incidence in 62,863 healthy family members.

They found that overall, mothers and siblings of those cancer patients had a higher relative risk of early onset cancer. But when they looked at the role of race and ethnicity in genetic predisposition, they found that for patients with solid tumors, the familial cancer risk was significantly higher for Latino and non-Latino Black mothers and siblings compared to non-Latino white families. Asian/Pacific Islanders had a higher familial risk for blood-based cancers compared to non-Latino whites.

This study demonstrates the need for increased scrutiny on familial cancer clustering in minority populations. This information could help health care providers and genetic counselors offer more precision-based care and advice, particularly in the multiethnic populations that reside in Los Angeles County.

UCI-led study finds that cancer immunotherapy may self-limit its efficacy

Cancer immunotherapy involving drugs that inhibit CTLA-4 also activates an unwanted response that may self-limit its efficacy in fighting tumors, according to a new study led by Francesco Marangoni.

Marangoni is assistant professor of physiology and biophysics and member of the Institute for Immunology at the University of California, Irvine. Study results are published in *Cell*.

Some anticancer drugs of the checkpoint inhibitor family block the molecule CTLA-4 and activate both the CD8 and CD4 effector T cells, which kill cancer. Using intravital microscopy, a technique that allows imaging of cells within a living organism, researchers found that a CTLA-4 blockage also causes the expansion of T regulatory cells, decreasing the effect of immunotherapy.

"Much of our knowledge of the mechanisms by which immunotherapy works is focused on the positive aspects of the body's reaction, but that treatment targets the whole immune system. In this study, we investigated how Treg cells are activated within the tumor mass," said Marangoni, corresponding author on the study. "We discovered that Treg cells are continuously activated in cancer. In turn, they use CTLA-4 to instruct dendritic cells to become ineffi-

cient activators of the immune system. Upon CTLA-4 inhibition, dendritic cells become more active and promote the function of effector and regulatory T cells at the same time."

"This has the potential of limiting efficacy and may explain the failure of immunotherapy in some patients," he said.

Future research will focus on identifying and removing unwanted immune reactions in other forms of immunotherapy. In particular, new strategies must be developed to decrease the activation of Treg cells in a controlled manner in order to avoid "fatal autoimmunity," Marangoni said: "The indiscriminate depletion of Treg cells would cause the CD8 and CD4 effector T cells to attack our body and potentially kill us."

The research team also included physicians and scholars from Harvard Medical School and Massachusetts General Hospital in Boston, The University of Texas MD Anderson Cancer Center in Houston, and Germany's University of Cologne and University of Lübeck. This work was supported by several National Institutes of Health grants, a Melanoma Research Foundation award and a Sara Elizabeth O'Brien/Charles A. King Trust fellowship.

Study: combination treatment effective in IDH mutant cancers

A study led by Yale Cancer Center scientists revealed the combination of ATR and PARP inhibitor therapies can effectively target the enzyme isocitrate dehydrogenase-I/2 (IDH-1/2) in mutant cancer cells.

The findings could help minimize toxicities from drug treatment for patients with cancer. The research is published in the journal *NAR Cancer.*

"Mutations in IDH1/2-mutant cancers were first identified in glioma, acute myeloid leukemia (AML), and subsequently found in multiple other tumor types," said lead author Amrita Sule, a postdoctoral associate in the laboratory of Ranjit S. Bindra, professor of therapeutic radiology at Yale Cancer Center. "These findings demonstrate the efficacy of targeting these defects to help develop new treatments for patients."

Previous studies from the Bindra Lab and others have shown that cancer cells with mutations in the gene IDH-1/2 cannot repair their DNA efficiently. PARP inhibitors are effective in killing these cells due to increased unrepaired DNA. However, patients treated with PARP inhibitors often develop resistance, creating the need to develop alternate therapies.

Combined inhibition of ATR and PARP is synergistic by blocking central, but independent, DNA-repair pathways. ATR is a protein which keeps the cell cycle in check when the DNA is damaged. It ensures the cells only divide when the DNA is repaired correctly. In this study, researchers confirmed when PARP inhibitors are combined with ATR inhibitors, the cell death of IDH -1/2 cancer cells is enhanced compared to a PARP inhibitor alone.

In mechanistic studies, researchers observed that inhibiting PARP and ATR causes the IDH1-1/2 mutant cells to accumulate unrepaired DNA, leading to increased genomic instability and ultimately destruction. This combination was also tested in mice seeded with IDH-1/2 cancer cells.

The combination of PARP inhibitor (Olaparib) and ATR inhibitor (AZD6738) was well tolerated in laboratory studies and caused significant tumor shrinkage as opposed to when the mice were given the single drug. Currently, this combination is being evaluated in a clinical

trial with patients with IDH1-2 mutant solid tumors in a National Cancer Institute phase II trial.

"We continue to seek novel targets for IDH -1/2 and similar cancers and carry out pre-clinical studies, which can lay the groundwork for future clinical trials," said senior author Bindra.

Immunotherapy drug combination improves response in HER2-negative breast cancer, including a subset of estrogen receptor positive cancers

A study by researchers at Yale Cancer Center shows that combining the immunotherapy drug durvalumab and PARP-inhibitor olaparib with chemotherapy improved response to treatment for women with high-risk, HER2-negative breast cancer, including a subset of estrogen receptor positive cancers.

The findings, part of the I-SPY2 clinical trial, were published today in the journal *Cancer Cell*.

"We found a molecularly defined subgroup of ER-positive patients with breast cancer who benefited significantly from an immune oncology drug added to chemotherapy, similar to what has been seen in triple negative breast cancer," said lead author Lajos Pusztai, professor of medicine (medical oncology) and director of breast cancer translational research at Yale Cancer Center. "The results are very encouraging as they provide continued evidence for immunotherapy for women diagnosed with this potentially deadly disease."

Durvalumab is a checkpoint inhibitor immunotherapy engineered to unleash immune system T cells against tumors by inhibiting a protein on the surface of T cells called PD-1. PARP inhibitor drugs, such as olaparib help to repair DNA damage caused by chemotherapy.

Investigators studied results from a small, randomized, phase II, I-SPY2 clinical trial of stage II/III HER2-negative breast cancer. Seventy-three patients were treated with durvalumab and olaparib followed by standard neoadjuvant chemotherapy, while 299 patients received standard-of-care. The findings showed patients receiving durvalumab plus olaparib improved estimated pathological complete response rates (over control) from 20% to 37% in HER2-negative cancers, from 14% to 28% in HR-positive/HER2-negative cancers, and from 27% to 47% in Triple Negative Breast Cancer.

Funding for this study was provided by AstraZeneca.

Yale Cancer Center study reveals new pathway for brain tumor therapy

A study led by Yale Cancer Center researchers show the nucleoside transporter ENT2 may offer an unexpected path to circumventing the blood-brain barrier and enabling targeted treatment of brain tumors with a cell-penetrating anti-DNA autoantibody.

The study was published in the J*ournal of Clinical Investigation Insight*.

"These findings are very encouraging as the BBB prevents most antibodies from penetrating the central nervous system and limits conventional antibody-based approaches to brain tumors," said corresponding author James E. Hansen, associate professor of therapeutic radiology, radiation oncology chief of the Yale Gamma Knife Center at Smilow Cancer Hospital.

Deoxymab-1 (DX1) is an unusual cell-penetrating autoantibody that localizes into live cell nuclei, inhibits DNA repair, and is synthetically lethal to cancer cells with defects in the DNA damage response. Researchers have now found that the transporter ENT2 facilitates brain endothelial cell penetration and BBB transport by DX1. In efficacy studies in mice models, DX1 crossed the BBB to suppress orthotopic glioblastoma and breast cancer brain metastases.

"Our data demonstrate the ability of DX1 to cross the BBB and suppress brain tumors in multiple models, and we are particularly impressed that DX1 was able to yield these results as a single agent in these difficult to treat tumor models," said co-corresponding author Jiangbing Zhou, associate professor of neurosurgery at Yale School of Medicine.

"We believe that the ENT2-linked mechanism that transports DX1 across the BBB and into tumors has potential to contribute to multiple new strategies in brain tumor therapy," added Hansen. "In addition to establishing proof of concept for single agent use of DX1 in brain tumor models, we also now recognize the potential for DX1 to target linked cargo molecules to brain tumors or to be useful as a platform for designing additional brain tumor targeting antibodies, including DX1-based bispecific antibodies."

DRUGS & TARGETS

Libtayo approved by European Commission for first-line treatment of patients with advanced NSCLC with ≥50% PD-L1 expression

The European Commission has approved the PD-1 inhibitor Libtayo (cemiplimab) for the first-line treatment of adults with non-small cell lung cancer whose tumor cells have ≥50% PD-L1 expression and no EGFR, ALK or ROS1 aberrations.

Patients must have metastatic NSCLC or locally advanced NSCLC and not be a candidate for definitive chemoradiation.

Libtayo is sponsored by Regeneron Pharmaceuticals Inc. and Sanofi.

Libtayo is now approved for three advanced cancers in the European Union. The EC also approved Libtayo in advanced basal cell carcinoma, the first treatment to be indicated for those patients who have progressed on or are intolerant to a hedgehog pathway inhibitor. In 2019, Libtayo was approved by the EC as the first treatment for adults with metastatic or locally advanced cutaneous squamous cell carcinoma who are not candidates for curative surgery or curative radiation. Across all of its approved indications, Libtayo had a generally consistent safety profile. Immune-mediated adverse reactions, which may be severe or fatal, can occur in any organ system or tissue during or after treatment with Libtayo.

The EC approval in advanced NSCLC is based on data from a global phase III trial that enrolled 710 patients from 24 countries. The trial, which was one of the largest for a PD-1 inhibitor in advanced NSCLC, was designed to be more reflective of clinical practice by including challenging-to-treat and often underrepresented disease characteristics. Among those enrolled, 12% had pre-treated and clinically stable brain metastases, 44% had squamous cell histology and 16% had locally advanced NSCLC that was not a candidate for definitive chemoradiation. Furthermore, patients whose disease progressed in the trial were able to change their therapy: those assigned to chemotherapy could crossover to Libtayo treatment, while those assigned to Libtayo monotherapy could continue Libtayo treatment and add four cycles of chemotherapy.

In the overall study population, Libtayo significantly reduced the risk of death by 32% and extended median overall survival by eight months compared to chemotherapy, even with 74% of patients crossing over to Libtayo following disease progression on chemotherapy (hazard ratio [HR]: 0.68; 95% confidence interval [CI]: 0.53-0.87; p=0.0022). The median OS was 22 months for Libtayo (range: 18 months to not evaluable) and 14 months for chemotherapy (range: 12 to 19 months). A prespecified analysis of data from patients whose cancers had PD-L1 expression ≥50% (n=563) based on a validated assay was also conducted. As published in *The Lancet*, Libtayo reduced the risk of death by 43% for patients in this population; median OS was not reached for Libtayo (95% CI: 18 months to not evaluable) and was 14 months for chemotherapy (95% CI: 11 to 18 months).

In the phase III trial, safety was assessed in 697 patients, with a duration of exposure of 27 weeks (range: 9 days to 115 weeks) for the Libtayo group and 18 weeks (range: 18 days to 87 weeks) for the chemotherapy group.

Abecma receives positive CHMP opinion for relapsed and refractory multiple myeloma

The Committee for Medicinal Products for Human Use of the European Medicines Agency has recommended granting Conditional Marketing Authorization for Abecma (idecabtagene vicleucel; ide-cel) for the treatment of adult patients with relapsed and refractory multiple myeloma who have received at least three prior therapies, including an immunomodulatory agent, a proteasome inhibitor and an anti-CD38 antibody and have demonstrated disease progression on the last therapy.

Abecma, sponsored by Bristol Myers Squibb, is a B-cell maturation antigen (BCMA)-directed chimeric antigen receptor T cell immunotherapy. The CHMP recommendation will now be reviewed by the European Commission, which has the authority to approve medicines for the European Union.

The CHMP adopted a positive opinion based on results from the pivotal Phase 2 KarMMa study evaluating the effica-

cy and safety of Abecma in 128 patients with heavily pre-treated and highly refractory multiple myeloma.

The EC is expected to deliver its final decision within 67 days of receipt of the CHMP opinion. The decision will be applicable to all European Union member states and Iceland, Norway and Liechtenstein. The EMA previously granted Abecma access to the PRIority MEdicines (PRIME) scheme for the treatment of relapsed and refractory multiple myeloma.

Opdivo receives positive CHMP opinion as adjuvant treatment for GEJ cancer patients with residual pathologic disease following chemoradiotherapy

The Committee for Medicinal Products for Human Use of the European Medicines Agency as recommended approval of Opdivo (nivolumab) for the adjuvant treatment of adult patients with esophageal or gastroesophageal junction cancer who have residual pathologic disease following prior neoadjuvant chemoradiotherapy.

Opdivo is sponsored by Bristol Myers Squibb.

The European Commission, which has the authority to approve medicines for the European Union, will now review the CHMP recommendation.

The positive opinion is based on results from the phase III CheckMate -577 trial, which showed that treatment with Opdivo following neoadjuvant CRT and complete surgical resection doubled the primary endpoint of disease-free survival compared to placebo in the all-randomized population. The safety profile of Opdivo was consistent with previously reported studies. Results from CheckMate -577 were presented at the 2020 European Society for Medical Oncology virtual congress in September 2020 and at the American Society of Clinical Oncology annual meeting in June 2021.

Opdivo is approved in the United States for the adjuvant treatment of completely resected esophageal or GEJ cancer with residual pathologic disease in patients who have received neoadjuvant CRT.

European Commission approves Onureg for certain AML subtypes

The European Commission has approved Onureg (azacitidine tablets)as the first and only once-daily, frontline oral maintenance therapy in the EU for patients with a broad range of acute myeloid leukemia subtypes.

While many patients with AML achieve remission with induction therapy, about 50% of patients relapse within one year. In the pivotal QUAZAR AML-001 study, Onureg significantly improved overall survival and relapse-free survival in patients with AML, reinforcing its clinical benefit and role in the treatment paradigm for patients with this common acute leukemia.

Onureg is sponsored by Bristol Myers Squibb.