TCL
THE CANCER LETTER

Inside information on cancer research and drug development

Vol. 47 No. 35

SEPTEMBER 24, 2021

www.cancerletter.com

NIH TELLS CONGRESS IT LACKED AUTHORITY TO INVESTIGATE WHISTLEBLOWER COMPLAINTS ABOUT AXEL GROTHEY'S SEXUAL MISCONDUCT

Women who report sexual misconduct to NIH may find that their complaints have a limited shelf life—these complaints may become null, or at least ineligible for "even a cursory review" once perpetrators cut ties with NIH.

→ PAGE 4

Editor & Publisher
Paul Goldberg

Associate Editor
Matthew Bin Han Ong

Reporter
Alexandria Carolan

Reporter
Alice Tracey

Director of Operations, Illustrator
Katie Goldberg

Marketing & Account Manager
Mona Mirmortazavi

Designer
Jacqueline Ong

IT Manager
David Koh

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

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

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

ISSN 0096-3917. Published 46 times a year by The Cancer Letter Inc. Other than "fair use" as specified by U.S. copyright law, none of the content of this publication may be reproduced, stored in a retrieval system, or transmitted in any form (electronic, photocopying, or facsimile) without prior written permission of the publisher. Violators risk criminal penalties and damages. Founded Dec. 21, 1973, by Jerry D. Boyd.

In this issue

CLINICAL ROUNDUP

DRUGS & TARGETS

CAPITOL HILL

NIH TELLS CONGRESS IT LACKED AUTHORITY TO INVESTIGATE WHISTLEBLOWER COMPLAINTS ABOUT AXEL GROTHEY'S SEXUAL MISCONDUCT

By Matthew Bin Han Ong

Women who report sexual misconduct to NIH may find that their complaints have a limited shelf life—these complaints may become null, or at least ineligible for "even a cursory review" once perpetrators cut ties with NIH.

Axel Grothey, MD
Former co-chair of NCI's National Clinical Trials Network GI Steering Committee

Rep. Cathy McMorris Rodgers (R-WA)
Republican leader of the House Committee on Energy & Commerce

Lawrence Tabak, DDS, PhD
Principal deputy director, NIH

NIH may be "constrained" from investigating sexual misconduct at NIH-funded institutions once alleged perpetrators are no longer affiliated with grantee institutions, according to NIH Principal Deputy Director Lawrence Tabak, writing in a letter to members of Congress.

Tabak's letter, dated Sept. 17, is NIH's response to an Aug. 9 congressional letter asking NIH to describe the procedures employed for rooting out sexual misconduct committed by advisors (*The Cancer Letter*, Aug. 10, 2021).

The congressional letter, addressed to NIH Director Francis Collins, also asks for an explanation of policies used in investigating sexual harassment complaints from whistleblowers.

The initial letter was signed by Rep. Cathy McMorris Rodgers (R-WA), ranking member of the House Committee on Energy and Commerce, and Rep. H. Morgan Griffith (R-VA), ranking member of the House E&C Subcommittee on Oversight and Investigations. Their Democratic counterparts didn't sign the letter.

> "NIH leadership is still not fully protecting women and other victims of sexual harassment from achieving their rightful place in science."
>
> *– Rep. Cathy McMorris Rodgers (R-WA)*

The congressional inquiry is based on *The Cancer Letter*'s investigative story of the case of Axel Grothey, an oncologist who was able to retain an influential advisory position at NCI even after being disciplined by three states for inappropriate sexual behavior that involved a mentee (*The Cancer Letter*, May 28, 2021).

In the Grothey case, two women reported Grothey's misdeeds to NIH and NCI in April and May 2019, with no results. The NIH Office of Extramural Research sent an automated response to one of the women and never followed up.

Tabak said NIH was unable to conduct an inquiry into allegations of sexual misconduct because Grothey had left Mayo Clinic—an NIH-funded institution—in May 2018, a year before the complaints were filed with NIH, and was no longer "key personnel" on NIH grants.

"Dr. Grothey was not employed by an NIH grantee institution in 2019," Tabak wrote in the Sept. 17 letter. "Dr. Grothey was not then and is not now key personnel on any NIH award. Nor was he at the time or is he at the present employed by an institution that receives NIH funding. This greatly constrained NIH's authority to make inquiries or conduct even a cursory review of the allegations made."

NIH didn't respond to questions from *The Cancer Letter* for this story.

"NIH leadership is still not fully protecting women and other victims of sexual harassment from achieving their rightful place in science," Rodgers, the Energy and Commerce Republican leader, said to *The Cancer Letter*. "There are still

two critical questions Dr. Collins has yet to answer for Congress:

"Where are NIH plans to foster a safer environment for junior faculty? Why isn't NIH uniformly implementing across all institutes and centers the new policies to properly vet candidates for NIH leadership positions so a case like Dr. Grothey's never happens again?"

Reportage by *The Cancer Letter* prompted NCI Director Ned Sharpless to remove Grothey from the NCI National Clinical Trials Network's Gastrointestinal Steering Committee, which he co-chaired. More than 10 cancer organizations and institutions have censured or barred Grothey (*The Cancer Letter,* June 4, 2021).

In his letter, Tabak did not describe NIH's rationale for allowing Grothey to remain on the NCI steering committee until May 27, 2021—two years after the two women filed complaints with NIH, and a year after medical boards in Minnesota, Tennessee and Arizona issued reprimands against Grothey.

"The NIH Office of the Director worked with and strongly supported Dr. Sharpless in his removal of Dr. Grothey from an NCI steering committee," Tabak wrote.

Rep. Frank Pallone (D-NJ), chairman of the E&C Committee, and Rep. Diana DeGette (D-CO), chair of the E&C Subcommittee on Oversight and Investigations, are cc-ed in Tabak's letter.

Karyn Goodman, the remaining co-chair of the GI Steering Committee following Grothey's termination, said NIH could have initiated an investigation earlier.

"I believe that the response from Lawrence A. Tabak, D.D.S., Ph.D. did not fully address the NIH's lack of any response to the email notifications in 2019 from two women who had filed complaints of sexual misconduct at Mayo Clinic, leading to an investigation and his departure from Mayo Clinic in 2018, and filed grievances to the Minnesota Board of Medical Practice, which ultimately led to a reprimand and fine for engaging in 'unethical or improper conduct' in March 2020," Goodman said to *The Cancer Letter.*

"The NIH could have investigated the womens' complaints earlier given the leadership position Dr. Grothey held as the NCI GI Steering Committee co-chair where he played an influential role in the decision-making about study concepts that were proposed, oftentimes by junior faculty," Goodman said.

"Unfortunately, these situations have for too long been brushed under the rug, and it took media coverage by *The Cancer Letter* to initiate any action."

Advocates: Poor excuses for multiple failures by NIH leadership

Does NIH's authority to ask questions peter out the moment an alleged perpetrator leaves an NIH-funded institution?

Do NIH leaders owe the women an explanation for why Grothey was allowed to remain on the NCI steering committee?

The Cancer Letter asked two experts on professional misconduct to review Tabak's response:

- Pringl Miller, founder and president of Physician Just Equity, a nonprofit that provides peer support for physicians who experience harassment, discrimination, and retaliation; and

- Shea Holman, director of law and policy at the Purple Campaign, a nonprofit focused on ending sexual harassment in the workplace.

Miller and Holman have no involvement in the Grothey case. Their full remarks appear on page 12.

NIH's apparent inaction on the Grothey case is unjustifiable, Miller said to *The Cancer Letter*

"In the interest of adhering to their no-tolerance policy and being a stakeholder in the scientific and academic community, I would think that ethically, [NIH] would be obligated to pursue the proper course of action," Miller said. "They may not have legal standing if the perpetrator is not receiving NIH funds and/or working at an NIH-funded site.

"I think the fact that Dr. Grothey had during the events, but not at the time of recognition, is a poor excuse for their inaction," Miller said. "[NIH leadership] should have taken action when the complaints were brought to their attention."

NIH is facing bipartisan pressure to formulate rules on sexual harassment for institutions receiving NIH funds through grants or cooperative agreements. A disclosure provision, contained in the FY2022 House appropriations committee bill, would give NIH the authority to "issue regulations" that would delineate reporting requirements for institutions (*The Cancer Letter,* July 23, 2021).

Many individuals who experience sexual harassment remain silent because they assume that their institutions will not take corrective action—and NIH exemplifies that problem in the Grothey case, Holman said to *The Cancer Letter.*

"We advocate for fair and thorough investigations and steps demonstrating accountability, neither of which have fully occurred here," Holman said. "Although NIH has stated it is unable to legally require reporting of sexual misconduct by outside entities, NIH failed to conduct even the most basic follow-up

that it promises to internal employees and employees at awardee institutions.

"The organization did not follow up with these women, did not reach out to senior leadership to ask about a timeline to investigate or restrictions placed on Grothey, or inquire whether corrective action was being taken," Holman said.

"Not only did NIH fail to reach out to the awardee institution, but it failed to maintain any transparency with the reporting parties on whether an investigation would occur or what corrective action would take place."

NIH's support for Sharpless's decision to fire Grothey from the NCI steering committee is "only one element of accountability, ' Holman said.

"Grothey maintained his position at NCI as a co-chair of the National Clinical Trials Network GI Steering Committee and NIH has failed to explain why Grothey wasn't removed from the committee at the time the complaints were made," Holman said.

NIH should be held accountable for their inaction, particularly in light of their Feb. 28, 2019, update on Efforts to Address Sexual Harassment in Science, Miller said.

"'Demonstrate accountability and transparency'—how did they do that in Dr. Grothey's case?" Miller said. "'Provide clear channels of communication'—they didn't do that, because the complaints went unaddressed as far as I can tell until *The Cancer Letter* contacted NCI in May 2021. Did the NIH 'incorporate the survivors' perspectives into future actions'?"

"A need-to-know basis"

In the Aug. 9 congressional letter, lawmakers sought clarification on NIH's policies on confidentiality:

"It is unclear why the NIH cannot provide confidentiality to such whistleblowers but is able to maintain confidentiality of other personnel or intellectual property information," the congressional letter states. "We … want to ensure that the NIH is holding its committee leaders to the highest standards of conduct and to promote a safe work environment for junior researchers, particularly those in mentor relationships that are vulnerable to abuse of authority."

NIH doesn't inform individuals who report sexual harassment of the outcome of investigations at NIH-funded institutions, said Holly Atkinson, a clinical professor at the City University of New York, a member of Physician Just Equity, and past president of Physicians for Human Rights, a nonprofit that investigates and documents human rights violations.

"The NIH says 'it is on a need-to-know basis' … they wouldn't even provide us with a definition when asked for further clarification of what they mean by 'need to know basis,'" Atkinson said to *The Cancer Letter*. "We, as survivors, of course, need to know.

"[It's] so easy for an institution to say, 'We investigated their complaint, there is no problem—doesn't rise to level of sexual harassment.' NIH then just goes away? Not enough transparency on the NIH investigation part. Reporters risk coming forward to NIH and get little in return."

NIH perpetuates "ongoing trauma to survivors" through a system that places all risk on the individuals who report, said Anu Anandaraja, a pediatrician, a member of Physician Just Equity, a public health educator, and founding director of Women Together Global Inc.

"Reporters are not guaranteed confidentiality and are also told not to expect any information on progress or outcome of investigation, thereby placing the reporter at risk of further retaliation but with no means to prove it," Anandaraja said to *The Cancer Letter*. "How is this a safe, effective or survivor-friendly system? We know that this process deters reporting and will grossly underestimate the incidence of sexual harassment among grantees and grantee institutions."

In his letter, NIH's Tabak noted that a "large proportion" of over 300 individuals who were being investigated for misconduct were "removed from peer review committees" while NIH investigated allegations.

"In June 2021, NIH provided the [Advisory Committee to the Director] with an update of its approaches to addressing sexual harassment, along with results to date," Tabak wrote. "At that time, the Office of Extramural Research had handled extramural harassment (sexual and other) allegations involving over 300 individuals since 2018. A large proportion of these individuals were removed from peer review committees, at least temporarily, while allegations were being assessed. The update was well-received by the ACD."

However, NIH has failed to follow its own procedures for enforcing accountability in the Grothey case, Holman points out.

"NIH has policies which state the organization will follow up with the relevant applicant/grantee institution to request information such as timeline to investigate and restrictions on persons designated on an award," Holman said. "Yet, NIH allowed Grothey to maintain his position at NCI as a co-chair of the National Clinical Trials Network GI Steering Committee and allowed him to retire with his reputation intact.

"As a result, NIH leadership should explain why it failed to follow its own policies in this case."

Tabak's Sept. 17 letter in response to the congressional inquiry follows:

September 17, 2021

The Honorable Cathy McMorris Rodgers
Ranking Member
Committee on Energy and Commerce
U.S. House of Representatives
Washington, DC 20515

Dear Representative McMorris Rodgers:

Thank you for your August 9 letter to National Institutes of Health (NIH) Director Dr. Francis Collins. As the Principal Deputy Director of NIH, I am pleased to reply.

Sexual harassment is morally indefensible, it's unacceptable, and it presents a major obstacle that is keeping women and other victims of sexual harassment from achieving their rightful place in science. NIH takes sexual harassment seriously and has made clear that it does not tolerate sexual harassment. In 2015, NIH issued Guide Notice NOT-OD-15-152 to make stakeholders aware that existing civil rights regulations apply to activities supported by NIH and protect individuals from unlawful sexual harassment, sexual violence, and sexual assault. From late 2018 through 2020, recognizing that more needed to be done, NIH developed a series of policies and approaches to address sexual harassment in both internal and external environments.

- In September 2018, NIH issued a Federal Register Notice on a new policy manual chapter on addressing and preventing harassment, inappropriate conduct, and inappropriate relationships in the NIH workplace. NIH used the opportunity to state that the agency "expects that organizations receiving NIH funds have in place similarly rigorous policies and related procedures for their employees, contractors, trainees, and fellows who engage in agency-funded activities."

- In February 2019, the NIH Director issued a detailed statement, which described steps the agency had already begun, at the suggestion of both an internal Anti-Harassment Steering Committee and the newly formed Advisory Committee to the Director (ACD) Working Group on Changing the Culture to End Sexual Harassment. These steps included clarifying expectations of organizations to ensure a safe workplace and inform the agency of investigator or key personnel changes and to provide clear channels of communication to NIH whereby anyone can report concerns. At that time, NIH established a dedicated mailbox granteeharassment@nih.gov to receive notifications of possible violations of NIH policy or rules.

- In March 2019, the Director of the NIH Center for Scientific Review (CSR) issued a statement that, out of an abundance of caution, CSR would exclude some reviewers from committees until concerns had been resolved.

- In December 2019, the NIH ACD endorsed recommendations issued by the Working Group, and the NIH Director accepted those recommendations. The recommendations included steps NIH should take to address sexual harassment as seriously as it takes other types of misconduct.

- In June 2020, NIH issued a detailed description of its processes for handling sexual harassment allegations. The processes are centralized (mainly in the NIH Office of Extramural Research, which sits in the NIH Office of the Director) and include the ability to remove individuals from NIH committees (usually peer review committees that may be located in CSR or in Institutes or Centers). In addition, NIH issued a Guide Notice NOT-OD-20-124 which stated that organizations should inform the agency of concerns about safe working conditions (including concerns about sexual harassment) when they seek prior approval for changes in principal investigators or key personnel named in the Notice of Award.

- In September 2020, NIH and the Department of Health and Human Services (HHS) Office for Civil Rights signed a memorandum of understanding whereby the two entities would share information and work with each other on addressing specific allegations.

- In June 2021, NIH provided the ACD with an update of its approaches to addressing sexual harassment, along with results to date. At that time, the Office of Extramural Research had handled extramural harassment (sexual and other) allegations involving over 300 individuals since 2018. A large proportion of these individuals were removed from peer review committees, at least temporarily, while allegations were being assessed. The update was well-received by the ACD.

In the case of Dr. Grothey, NIH was concerned about the complaints when they were received and worked to determine how it might be able to address them. However, two factors affected NIH's ability to respond more fully to the complaints we received in 2019. First, in many of the oversight processes that NIH conducts, it is the institution's acceptance of federal funding that gives NIH the authority to gather information from the institution about employee conduct. When NIH received the complaints detailed in your letter, OER conducted a thorough search of Dr. Grothey's involvement in NIH activities. Dr. Grothey was not then and is not now key personnel on any NIH award. Nor was he at the time or is he at the present employed by an institution that receives NIH funding. This greatly constrained NIH's authority to make inquiries or conduct even a cursory review of the allegations made.

Second, the complaints were made at a critical time in NIH's deliberations about how to change our policies to address sexual harassment. As noted above, NIH established mechanisms for notifying NIH about concerns related to harassment at NIH-funded institutions in February 2019. When establishing those notification channels, NIH indicated that they would follow up with the relevant applicant/grantee institution on all concerns related to NIH-funded research. As previously stated, Dr. Grothey was not employed by an NIH grantee institution in 2019. Further, the NIH notice recommended that affected individuals could make formal reports to the HHS Office for Civil Rights, providing another avenue for someone to report sexual harassment at an institution that receives financial support from HHS, even if they are not NIH-funded. Since 2019, NIH has made great strides to address harassment in research. We deeply regret that these women endured harassment during their training. Harassment has no place in science, and NIH remains committed to developing an improved culture in which any type of harassment is not tolerated.

NIH's efforts in addressing harassment have led to substantive change, with certain individuals removed from NIH-funded activities, including from NIH committees. The NIH Office of the Director worked with and strongly supported Dr. Sharpless in his removal of Dr. Grothey from an NCI steering committee.

This case exemplifies the need for other entities to play a role in reducing harassment in science. While NIH plays a very crucial role in reducing harassment in biomedical science, the biomedical research space is much larger than NIH-funded research alone. NIH needs partners from other organizations, including licensing boards, scientific societies, and research institutions, to successfully minimize harassment in science.

We hope you find this information helpful and would be happy to offer a briefing on NIH's anti-sexual harassment efforts.

I have also provided this response to Representative H. Morgan Griffith who co-signed your letter.

Sincerely,
Lawrence A. Tabak, D.D.S., Ph.D.
Principal Deputy Director

cc:
The Honorable Frank Pallone, Jr.
The Honorable Diana DeGette

> [It's] so easy for an institution to say, 'We investigated their complaint, there is no problem—doesn't rise to level of sexual harassment.' NIH then just goes away? Not enough transparency on the NIH investigation part.
>
> *– Holly Atkinson*

Chief Patient Officer

The American Cancer Society invites applications and nominations for the position of Chief Patient Officer.

The American Cancer Society (ACS) is the foremost voluntary cancer organization in the world with a renewed and innovative focus on its research and cancer control mission. Under the new leadership of CEO, Dr. Karen E. Knudsen, the ACS is re-shaping its business model and structure to accelerate improving the lives of cancer patients and their families through a four-pillar structure (Advocacy, Discovery, Patient Support, and Development), complemented by 6 regional home offices, >40 local offices, and a network over 1.5 million volunteers who play vital roles in execution of the ACS mission. A key goal, consonant with its original mission, is to serve as a critical resource to all those confronting the reality of cancer, whether it is prevention, early diagnosis, therapy, or palliative care and survivorship, ACS will offer a helping presence. Advancing that goal will require new leadership, focus, and resources and the first step will be the filling a new senior leadership position, the Chief Patient Officer.

The Chief Patient Officer (CPO) leads the Patient Support pillar, serves on the enterprise Executive team, reports directly to the CEO, and maintains broad systemwide authority over all aspects of programs that directly assist cancer patients, survivors, caregivers, and those trying to prevent a diagnosis. The CPO uses evidence-based analysis to identify gaps in the cancer prevention, cancer care, and survivorship continuum that are uniquely suited to be addressed by ACS and develops programs of differentiation that measurably improve the lives of cancer patients and their families. Identifying and implementing new technologies as well as other forms of innovation will be a key component of success. The CPO has oversight and is accountable for all aspects of patient support execution, from setting enterprise strategy to regional execution, and leverages the strength of both field employees and volunteers to achieve pillar goals.

The CPO, who is widely viewed as the patient voice of the ACS, will be a skilled physician and/or nurse and recognized in the field with a strong track record of impactful contributions towards patient care. They must be a respected leader who is operationally savvy and a visionary in the new age of cancer science. As part of the senior leadership team, the CPO participates in the development of the Society's national/global priorities, strategies, and initiatives. The CPO guides the efforts to enhance and focus the Society's patient program, advises the Society's advocacy positions, and concentrates community cancer control efforts in areas where they will be most effective. They will lead the ACS' programmatic efforts and advance the ACS' agenda with donors/investors and all appropriate external organizations. In addition, the CPO will serve as the ACS national spokesperson to advocate for policies and programs related to patient support and advance the reputation of ACS as a key thought leader in the field.

Korn Ferry is assisting the American Cancer Society with this important search. Please forward, as soon as possible, applications or nominations of appropriate candidates, in confidence, to:

c/o Alana Aisthorpe
Korn Ferry
1201 West Peachtree Street, NW Suite 2500, Atlanta, Georgia 30309
Email: **alana.aisthorpe@kornferry.com**

Q & A

Miller and Holman spoke with Matthew Ong, associate editor of The Cancer Letter.

THE CANCER LETTER | SEPTEMBER 24, 2021 | VOL 47 | ISSUE 35

In Grothey case, NIH gets failing grades on follow-up, transparency, internal compliance

CONVERSATION WITH THE CANCER LETTER

Miller, Holman discuss NIH's response to congressional inquiry on sexual misconduct

Pringl Miller, MD
Founder and president, Physician Just Equity

Shea Holman, JD
Director of law & policy, The Purple Campaign

NIH may be "constrained" in investigating sexual misconduct at NIH-funded institutions once alleged perpetrators are no longer affiliated with these institutions, NIH officials implied in their response to a congressional inquiry on sexual misconduct (*The Cancer Letter*, Sept. 24, 2021).

The congressional inquiry is based on *The Cancer Letter*'s investigative story of the case of Axel Grothey, an oncologist who was able to retain an influential advisory position at NCI even after being disciplined by three states for inappropriate sexual behavior that involved a mentee (*The Cancer Letter*, May 28, 2021).

In the Grothey case, two women reported Grothey's misconduct to NIH and NCI in April and May 2019, with no results. The NIH Office of Extramural Research sent an automated response to one of the women and never followed up.

> "NIH failed to conduct even the most basic follow-up that it promises to internal employees and employees at awardee institutions."
>
> *– Shea Holman*

Does NIH's authority to ask questions end the moment an alleged perpetrator leaves an NIH-funded institution? Should NIH leaders explain why they allowed Grothey to remain on the NCI steering committee for two years after complaints were filed?

To understand the limits of NIH's authority and best practices for investigating allegations of sexual misconduct, *The Cancer Letter* asked two experts on professional misconduct to review NIH's response to the House Committee on Energy & Commerce inquiry:

- Pringl Miller, founder and president of Physician Just Equity, a nonprofit that provides peer support for physicians who experience harassment, discrimination, and retaliation; and
- Shea Holman, director of law and policy at the Purple Campaign, a nonprofit focused on ending sexual harassment in the workplace.

Miller and Holman spoke with Matthew Ong, associate editor of *The Cancer Letter*.

Matthew Ong: What are your initial reactions to—and takeaways from—NIH's response to the congressional letter?

Pringl Miller, Physician Just Equity: I'm not convinced safe reporting exists, even though there's a process. I don't trust institutions to report, due to inherent conflicts of interest.

The NIH needs to establish a direct and safe line of communication with all key personnel regularly, so that victims/survivors can report with the confidence that the NIH will actually do something about it—bringing in the institution is fraught with further harassing, discriminatory, and retaliatory repercussions.

Perpetrators should be exposed publicly for their actions. To date, the consequences for gender discrimination and sexual harassment have not significantly deterred people from acting out those behaviors.

The NIH, as a federal agency, must be an exemplar by identifying perpetrators and eliminating sexual harassment. The NIH should follow the law and their Anti-Sexual Harassment statement and the 2018 NASEM consensus study report on sexual harassment recommendations to a "t," so that other institutions follow their example.

Shea Holman, The Purple Campaign: Firstly, in NIH's response letter, the principal deputy director discussed that the agency "expects that organizations receiving NIH funds have in place similar policies and related procedures for their employees, contractors, trainees, and fellows who engage in agency-funded activities."

It also included clarifying expectations of organizations to ensure a safe workplace and inform the agency of investigator or key personnel changes.

This requirement that NIH-funded organizations have rigorous policies and procedures regarding sexual harassment put in place is a positive step toward addressing the issue.

We know that transparency helps prevent workplace harassment by creating shared norms and expectations, building trust, and demonstrating accountability. In particular, establishing clear written policies and communicating them effectively to employees and third-parties can deter problematic behavior from occurring in the first place.

We've seen that companies in the private sector, for example, are increasingly sharing their written policies externally with third-parties, including members of the public, in order to create shared

norms around acceptable and unacceptable behaviors in the workplace.

Many organizations are also sharing information about their *response* to policy violations, both internally to employees and externally to the public.

While NIH has stated in the past that it expects organizations receiving NIH funds to have similarly rigorous policies and related procedures in place for employees, NIH needs to make it clear that any organization receiving NIH funding should take allegations of discrimination seriously, will investigate allegations in a timely manner, and will hold accountable any perpetrator of acts of discrimination.

Secondly, the NIH response letter noted that NIH provides clear channels of communication, whereby anyone can report concerns. NIH established a dedicated mailbox "granteeharassment@nih.gov" to receive notifications of possible violations of NIH policy or rules.

Given the significant barriers that exist to reporting internally, establishing multiple channels for reporting can break down those barriers and build trust within the workforce. Reporting is a central component of addressing workplace harassment and, as a result, many organizations now provide employees with options to report anonymously, online, via phone, or to one of several individuals within the organization.

The NIH is taking an important step—and one we'd like to see other federal workplaces mimic—by providing an *external* channel for people to report misconduct in the sciences. This gives people an option of reporting to an entity other than their employer. They can instead go around and report to NIH as the grantor.

While the NIH's establishment of an email account is a necessary first step in providing varied channels for reporting, this addition can only be successful if NIH also follows-up on all reports of harassment received through those channels.

NIH Director Francis Collins has testified in the Senate that, without statutory conveyance of authority, NIH is unable to require reporting of sexual misconduct at grantee institutions. Does this mean that NIH cannot make an inquiry or conduct a "cursory review of the allegations made," even if grantee institutions aren't legally required to respond or provide information?

Miller, PJE: It's not enough for the NIH to require institutions receiving NIH funding to report a change in key personnel removed from their position for harassment. Institutions by and large will not do that, because there is a conflict of interest, and survivors do not report.

I'm impressed with the accounting of persons temporarily removed until full investigations were conducted and or removed when found guilty of sexual harassment or other illegal/unethical behavior.

Holman, TPC: NIH has made it clear that individuals who have concerns that an NIH-funded project has been affected by sexual harassment may notify NIH through a web form, by phone, or by email.

The organization has also made it clear that shortly after filing a report, the person who notified NIH of the concern will receive a response from the NIH Office of Extramural Research (OER) letting them know that OER is reaching out to senior leadership at the awardee institution, and that NIH will follow up with the relevant institution to request information such as the timeline to investigate and restrictions on persons designated on an award.

NIH policies also state that OER will expect awardee institutions to provide a written response within 30 days of being notified.

In this case, however, two women reported Grothey's misdeeds to NIH and NCI, with no results. The NIH OER sent an automated response to one of the women and never followed up.

Although NIH has stated it is unable to legally require reporting of sexual misconduct by outside entities, NIH failed to conduct even the most basic follow-up that it promises to internal employees and employees at awardee institutions.

The organization did not follow up with these women, did not reach out to senior leadership to ask about a timeline to investigate or restrictions placed on Grothey, or inquire whether corrective action was being taken.

We know that one reason many individuals fail to report harassment is because they assume their organization will not take any corrective action. Over half (53%) of employees say that their company has "talked the talk since #Metoo" but they do not see it "walking the walk."

Not only did NIH fail to reach out to the awardee institution, but it failed to maintain any transparency with the reporting parties on whether an investigation would occur or what corrective action would take place.

When NIH received complaints about Axel Grothey in April and May 2019, he had already resigned from his position at Mayo Clinic—which is noted in NIH's response to the congressional inquiry. Does Grothey's departure from Mayo Clinic, an NIH-funded institution, absolve NIH from *all* responsibility to initiate an inquiry or conduct a cursory review at Mayo Clinic? (I.e. if NIH is notified that an alleged perpetrator has left, does it mean NIH can't/doesn't have to take further measures?) What would've been the appropriate course of action?

Miller, PJE: In the interest of adhering to their no-tolerance policy and being a stakeholder in the scientific and academic community I would think that ethically they would be obligated to pursue the proper course of action.

They may not have legal standing if the perpetrator is not receiving NIH funds and/or working at an NIH-funded site.

I think the fact that Dr. Grothey had, during the events, but not at the time of recognition, is a poor excuse for their inaction.

Holman, TPC: We advocate for fair and thorough investigations and steps demonstrating accountability, neither of which have fully occurred here.

Half of employees say that consequences for workplace harassment are still inadequate and three out of 10 employees think that high performers are never or rarely held accountable when they harass someone.

While the NIH Office of the Director worked with and strongly supported Dr. Sharpless in his removal of Dr. Grothey from an NCI steering committee, this is only one element of accountability.

Grothey maintained his position at NCI as a co-chair of the National Clinical Trials Network GI Steering Committee and NIH has failed to explain why Grothey wasn't removed from the committee at the time the complaints were made.

As the EEOC has stated: "Because organizational culture is manifested by what behaviors are formally and informally rewarded, it all comes down to accountability—and accountability must be demonstrated."

The two women who contacted NIH in early 2019 did so because Grothey had maintained his position at NCI as a co-chair of the National Clinical Trials Network GI Steering Committee—a fact that was presented in their 2019 complaints to NIH. In response to the congressional letter, NIH does not explain why Grothey wasn't removed from the committee at the time the complaints were made, and doesn't describe any review or investigation in 2019-2020 (before *The Cancer Letter* contacted NCI in May 2021). Should NIH have taken action sooner on this matter, which is arguably well within their authority to respond to? And should NIH leadership provide an explanation for why no action was taken at the time?

Miller, PJE: Yes, they should have taken action when the complaints were brought to their attention.

Yes, the NIH should be held accountable for their inaction especially in light of their 2/28/19 update on Efforts to Address Sexual Harassment in Science: "Demonstrate accountability and transparency"—how did they do that in Dr. Grothey's case?

"Provide clear channels of communication"—they didn't do that, because the complaints went unaddressed as far as I can tell until TCL contacted NCI in May 2021; correct? Did the NIH "incorporate the survivors' perspectives into future actions"?

Holman, TPC: Women and men both say organizations need to do more to create a safe and respectful work environment. Forty percent say disrespectful behavior toward women is often quickly addressed and just 32% think their organization swiftly acts on claims of sexual harassment.

It is important for organizations like NIH to investigate sexual harassment complaints promptly. At the Purple Campaign, we advocate for timely, fair, thorough, and impartial investigation procedures to respond effectively when individuals report instances of workplace sexual harassment.

It is also important for organizations to take appropriate interim steps to prevent harassment and retaliation during the investigation process. NIH has policies which state the organization will follow up with the relevant applicant/grantee institution to request information such as timeline to investigate and restrictions on persons designated on an award.

Yet, NIH allowed Grothey to maintain his position at NCI as a co-chair of the National Clinical Trials Network GI Steering Committee and allowed him to retire with his reputation intact.

As a result, NIH leadership should explain why it failed to follow its own policies in this case.

THE CANCER LETTER | SEPTEMBER 24, 2021 | VOL 47 | ISSUE 35

Biden administration blocks Trump's last-minute appointees from getting on NCAB

By Alice Tracey and Paul Goldberg

On Dec. 8, 2020, a month after losing the election, then-president Donald Trump announced his intent to name 26 people to advisory boards across the federal government.

Among them were three would-be members of the National Cancer Advisory Board, and in the months following, these three appointments—which have been blocked and ultimately terminated by the Biden administration—have plunged NCI into unfamiliar political terrain.

Before we get to the facts, let's review the civics:

- Technically, lame duck presidents can make appointments until a chopper spirits them away from the White House lawn.

- Stuffing advisory boards with loyalists as administrations change is a venerable tradition in American politics. Since the laws on firing presidentially appointed board members are murky, last-minute appointees are usually allowed to serve out their terms, frustrating the administration upon which they have been inflicted.

- Under the National Cancer Act of 1971, NCI has the only presidentially appointed boards at NIH: the NCAB and the President's Cancer Panel. For example, members of the NIH Advisory Committee to the Director aren't appointed by the president.

- Usually, NCI has been spared blatant politicization. Even NCI directors—presidential appointees—are usually left alone as parties change at the White House (*The Cancer Letter*, Jan. 22, 2021).

Trump's last-minute appointees included his former counselor, Kellyanne Conway, who was embedded on the Board of Visitors to the U.S. Air Force Academy.

The NCAB appointees on the list included a Florida nursing home entrepreneur with a history of advocating for right-to-try laws, a Washington D.C.-based energy and raw materials supplier and consultant, and a retired oncologist.

Reached by *The Cancer Letter*, these appointees said that they had been waiting for invitations to take part in the NCAB meetings, all of which have been virtual. The invitations never came, and on Sept. 15, the trio received emails directing them to step down or face termination by the end of that day.

A copy of the letter obtained by *The Cancer Letter* appears on page 17.

Meanwhile, President Joe Biden appointed seven clincians and scientists to the NCAB last week, including John D. Carpten as chair. He is the first African American chair of the advisory board.

THE WHITE HOUSE
WASHINGTON

September 15, 2021

Chang Oh Turkmani
National Cancer Advisory Board
9609 Medical Center Drive
7th Floor, West Tower, Room 7W-412, MSC 9750
Bethesda, MD 20892-9750

Dear Ms. Turkmani,

On behalf of President Biden, I am writing to request your resignation as a Member of the National Cancer Advisory Board. Please submit your resignation to me by the close of business today. Should we not receive your resignation, your position with the Board will be terminated effective 6:00 pm tonight. Thank you.

Sincerely,

Catherine M. Russell
Assistant to the President
Director, White House Office of Presidential Personnel

"A senile old creep"

The three Trump appointees to NCAB were Elizabeth Fago, Chang Oh Turkmani, and Jack Evjy—all of whom chose not to resign. Their memberships were terminated.

Evjy, Turkmani, and Fago said they were asked to join the NCAB in December 2020 and officially appointed to the board in early January 2021, but were never contacted about meetings. The NCAB has met four times so far this year.

Both Evjy and Fago said they contacted the Biden White House when they didn't receive any information related to the NCAB onboarding process. Fago said someone at the White House told her she could listen in to a virtual meeting, but that she'd have to be muted.

Two of the three would-be NCAB members said they aren't pleased with Biden's decision to terminate their memberships.

"It's very annoying when you have someone [who is] a senile old creep," the nursing home operator Elizabeth Fago said to *The Cancer Letter*. "I want to see him drop."

Elizabeth Fago

Fago said she is qualified for the position because of her business experience, her personal experiences with cancer, her political advocacy for right-to-try laws, and because she had served on the Harvard Medical School Systems Biology Board.

Fago is the founder of Home Quality Management, a company that acquired underperforming nursing homes and assisted living facilities. She is also a co-founder and partner of Palm Health Partners, a long-term care provider. Through this company, Fago launched two post-acute care and rehabilitation facilities in 2011 under the name NuVista Care.

According to press reports, the NuVista facilities have since been renamed and placed under new management. Another senior care project, the Institute for Healthy Living, based in Jupiter, FL, never came to fruition after the Scripps Research Institute and Jupiter Medical Center cut ties with Palm Health Partners, *The Palm Beach Post* reported. In 2018, the IRS filed liens against Fago and her son, Paul Walczak. At the time, they owed more than $8 million in unpaid payroll taxes, *The Palm Beach Post* reported. Fago didn't respond to *The*

Cancer Letter's questions about the status of her tax liability.

According to Open Secrets, the has been a consistent donor to Republican causes and candidates, including Trump.

Fago said Biden's move was clearly political.

"This is an advisory board. We don't get paid, we're there to help. I'm a big philanthropist. I do more, I save more lives than you'll ever know," Fago said to *The Cancer Letter.*

"I'm being discriminated against because I'm a white woman and I'm elderly—just awful."

Chang Oh Turkmani

Chang Oh Turkmani, the D.C.-based businesswoman who was born in South Korea, raised the issue of racial imbalance.

"I don't see Asians or minority groups represented on this board," Turkmani said to *The Cancer Letter.*

Turkmani is the managing director and principal at The Mega Company of Washington, which she co-owns with her husband, Salah Turkmani.

She is also the principal of American Construction Technologies; managing director of Crest Energy; and managing director and principal of CDM Global—all in Romania. She is the principal and president of Blackwater Power Co., Korea Hydro and Nuclear Power Co. Ltd (*The Cancer Letter,* Dec. 11, 2020).

The donations made by Mega Company include $77,400.00 to the Republican National Committee in 2020, according to Open Secrets.

"I'm not some crazy MAGA person," Turkmani said to *The Cancer Letter.* "I don't espouse any particular political theory that is so dividing the country at this point. I was extremely shocked, actually, with this approach that the White House has taken, because I remember as a candidate, Biden was talking about reaching out to the other side of the aisle."

Turkmani said she's interested in diagnostics and treatments for ovarian cancer, particularly from the perspective of industry, and was looking forward to joining the NCAB.

"To take something so serious as this cancer disease and politicizing [it], I think it's shameful," Turkmani said.

Jack Evjy

The third Trump appointee to NCAB, Jack Evjy, is a retired oncologist who received his medical degree from the Boston University School of Medicine. He is a former member of the Massachusetts Delegation to the American Medical Association and the former president of the Massachusetts Medical Society.

Evjy said he, too, is disappointed—he is still energetic despite having recently turned 87. He saw a stint on NCAB as an opportunity to serve, but said that the previous and current boards "have done a marvelous job in guiding cancer control efforts for this great country."

No information is available about his political donations.

Murky law

Last June, the U.S. Supreme Court decided a case that gave Biden the right to replace the director of the Federal Housing Finance Agency, expanding the presidential power to remove officials appointed by previous administrations before the end of their terms.

The case, *Collins vs. Yellen*, was decided June 23, 2021. Relying on this ruling, Biden has been ousting Trump loyalists from federal positions, particularly in the Department of Defense. Those removed included Conway and Sean Spicer, former White House press secretary. Spicer and two others are suing.

In a press conference on Sept. 8, White House Press Secretary Jen Psaki denied accusations that these decisions were driven by partisan ties.

"I will let others evaluate whether they think Kellyanne Conway and Sean Spicer and others were qualified or not political to serve on these boards, but the president's qualification requirements are not your party registration," Psaki said. "They are whether you're qualified to serve and whether you are aligned with the values of this administration."

Unique authorities

Presidential appointment of the 18 members of the National Cancer Advisory Board is one of the unique authorities of the National Cancer Act of 1971. The president also selects one of these members to act as chair.

> The president's qualification requirements are not your party registration. They are whether you're qualified to serve and whether you are aligned with the values of this administration.
>
> – *Jen Psaki*

"It is appropriate to think of the NCAB as the 'board of directors' of the National Cancer Program," Richard A. Rettig wrote in *Cancer Crusade*, an authoritative history of the NCA. The book was republished by the Cancer History Project last August.

NCAB reflects the government's intent 50 years ago to make cancer control a national priority. No other NIH entity has an equivalent presidentially appointed board.

Similarly, the NCI director is the only director of an NIH institute to be appointed by the president. No other institute has an equivalent of the President's Cancer Panel or the authority to present the Bypass Budget, which reflects the NCI director's professional judgment of opportunities in cancer control.

In addition to these presidentially appointed members, NCAB has 12 ex-officio, non-voting, members representing federal agencies that have an impact on cancer.

According to the board's charter as it now stands, NCAB must have the following composition:

- Up to 12 of the appointed members must be chosen "from among the leading representatives of the health and scientific disciplines." No fewer than two scientist members must be "leaders in the fields of public health and the behavioral or social sciences relevant to the activities of NCI."
- Up to six appointed members must be "representatives from the general public, including leaders in fields of public policy, law, health policy, economics and management.
- No fewer than five of the appointed members must be "individuals knowledgeable in environmental carcinogenesis (including carcinogenesis involving occupational and dietary factors)."
- All non-federal employees will serve as Special Government Employees.

Lay members of NCAB have included key leaders in cancer research, starting with Mary Lasker, the socialite whose campaign led to passage of the National Cancer Act. Since the appointment is political, there were also a few questionable choices, notably the Hon. Jim McGreevey, a Clinton appointee who would rise to—and fall from—the governorship of New Jersey.

In 1980, President Carter appointed the nationally syndicated advice columnist Ann Landers to serve on NCAB. This was a solid choice, considering that Landers, who had millions of readers, had galvanized support for the National Cancer Act and was consistently campaigning against smoking.

The Landers appointment gave *The Cancer Letter* founder Jerry Boyd an opportunity to write a news story that opened with a parody of a request for practical advice, similar to what one would find in a Landers column:

Dear Cancer Letter:

I have just been appointed to the National Cancer Advisory Board. Here is my problem: How should I know if a grant in molecular biology with a priority score of 217 should be funded while a program project in virology with a score of 210 is not? Also, do they really expect us to read 10,000 pages of grant applications the night before the meeting?

—Concerned in Chicago

Dear Concerned:

The fact that you recognize you have a problem means you are halfway to the solution. You need professional help. You may even need a psychiatrist before you complete your term on the Board. Hang in there, dear, and let us know how it works out.

Don't be intimidated by the science and scientists. Don't be afraid to ask questions; if you don't understand what the hell they are talking about, chances are that most of the rest of us don't either.

Most important, dear Ann Landers, when the time is right, use your column to drum up support for the Cancer Program, as you did in 1971 when mountains of mail from your readers helped convince Congress to pass the National Cancer Act.

THE CANCER LETTER | SEPTEMBER 24, 2021 | VOL 47 | ISSUE 35

GUEST EDITORIAL

How the pandemic elevated cancer telehealth and changed care delivery

By George Yoo, MD
Head and neck surgical oncologist,
Chief medical officer and director of clinical affairs,
Karmanos Cancer Institute in Detroit, a part of McLaren Health Care;
Professor, Departments of Otolaryngology-Head and Neck Surgery and Oncology,
Wayne State University School of Medicine

In early 2020, telehealth was a hot new trend in patient care, but with utilization sporadic and episodic at best, providers were generally skeptical as to whether this virtual technique of delivering care was a viable option for advanced clinical services, especially in oncology.

Our attitude quickly changed as governments initiated COVID lockdowns across the country. Even though essential patient visits were allowed, including for cancer treatment, many patients became hesitant to travel outside the home—especially to a hospital.

Since cancer doesn't wait, we were suddenly forced to incorporate telehealth into cancer care wherever possible to mitigate the risk of COVID transmission to patients. This new way of delivering care was adopted, utilized and valued—among patients and providers—within a few short weeks.

Ramping up

During the initial stages of the pandemic, everything was in crisis. As we were seeing a spike in consultation requests and the need for cancer surveillance, we knew initiating and implementing a new process was going to be a challenge.

While a virtual consultation is not difficult, we had to add tools to our video communication capabilities. We also had to modify our electronic medical record system to schedule appointments and prepare administratively to deliver records and obtain prior authorization via telehealth.

We recognized some of our patients might be technologically challenged so we had to be adaptable and provide the resources to help them easily navigate this new process.

Occasionally, if video-based virtual care was simply not an option, we conducted telehealth visits by telephone. Our dedicated team of patient navigators led these efforts.

Since this was such a departure from how we typically managed patient consults and visits, we provided our oncologists with extensive support.

We scheduled regular internal meetings, sometimes more than once a week when needed, to provide our clinicians with information about the regulations, the variety of platforms they were allowed to use, and how to schedule telehealth appointments.

In the beginning, it took about a week of massive planning to make these options available. We soon began using a standardized, proprietary technology—McLaren Now—so we were all operating on the same platform.

That standardization will help us prepare for more restrictive regulations as temporarily relaxed rules on telehealth and pandemic funding eventually change.

A lockdown necessity

Before the pandemic, we offered telehealth at Karmanos, but it was used sparingly by both physicians and patients.

To better protect our cancer patients, who are often immunocompromised, we have expanded our telehealth offerings and are encouraging patients to use this alternative to traditional care delivery.

We originally viewed telehealth largely as a temporary emergency measure and expected a short-term spike in telehealth appointments.

To our surprise, as lockdowns eased in late 2020, we didn't immediately see a corresponding decline in telehealth utilization. This was partially because of emergency regulations that improved reimbursement for telehealth during the pandemic, but even after the lockdowns, patients often chose it for convenience and safety as many live far from our flagship Detroit hospital.

“To our surprise, as lockdowns eased in late 2020, we didn't immediately see a corresponding decline in telehealth utilization.”

For example, I have a patient from Petoskey, which is 300 miles away from Detroit, who had a diagnosis that required surgery. We were able to conduct most of her initial evaluation virtually and we used telehealth for her follow-up visit, saving her several 600-mile round trips. We scheduled all her imaging and lab work near her home, and those results were sent to us here electronically.

As an NCI-designated Comprehensive Cancer Center, Karmanos attracts many patients from out of state for initial care or second opinions.

A patient from North Carolina, who presented with advanced cancer, wanted a second opinion. After a telehealth consult, we agreed with her doctors on her diagnosis and treatment, but after her initial treatment unfortunately failed, she contacted us for help and is now participating in a clinical trial at Karmanos. The expanded clinical opportunities through telehealth introduced her to our cancer center and a potentially life-saving treatment option.

The efficacy and convenience telehealth offers to both patients and physicians—even with something as medically complex as cancer care—has been a clinical game-changer.

Overcoming challenges

The initial skepticism from providers was not a resistance to new technology, but a fear that the clinical impact of the in-person patient interaction would be compromised, potentially impacting patient care.

To help alleviate that concern and to standardize our patient interactions through telehealth, we implemented a five-step communications protocol to train physicians and other clinicians who use the technology on how to interact and establish a rapport with patients remotely.

Although we are still accumulating data to study the impact of the communication protocol on patient satisfaction in telehealth, anecdotally we've heard from many patients who loved the experience, and received few complaints.

As we ramped up this program, our physicians and patients relied heavily on our staff of patient navigators, an irreplaceable and critical resource.

Without their commitment to making cancer telehealth work by serving as de facto tech support for patients or their patience helping both sides communicate better, this initiative would never have worked.

Despite the skillful assistance of our patient navigators, we recognize technology will always be a barrier for some patients.

Older patients sometimes are not comfortable with technology, and those without smartphones, computers, or other devices as well as patients who live in areas where high speed internet is not available or affordable can be alienated by telehealth.

Where we can, we are assisting patients in bridging these technology gaps. The future of cancer telehealth depends in part on expanding options to help patients achieve better connectivity and implement remote measurement tools.

We've already worked with a company that can send a customized box of tools directly to the patient's home, from devices they can use for video chats to ancillary devices that can offer real-time vital sign measurements.

Do patients like it?

Several factors will determine the future of telehealth in cancer care, but patient feedback is at the top of the list. If our patients are a good indicator of how people feel in general, providing more telehealth options where it makes sense is definitely the preference.

Of course, future reimbursement will also play a pivotal role in how telehealth continues to advance, but we think patients will fight for the option.

We surveyed our patients on their clinical preferences and telehealth options performed very favorably.

As patients discover an in-person visit for cancer treatment isn't always necessary, we think the number of people who prefer telehealth will increase, especially when it comes to second opinions, because pathology slides and radiological studies can be easily reviewed by an oncologist remotely.

Additionally, as part of our multidisciplinary approach to treating cancer at Karmanos, the patient's case is presented at our regular tumor conferences, allowing multiple cancer experts to provide input on treatment options, without having to see the patient in person.

> "The future of cancer telehealth depends in part on expanding options to help patients achieve better connectivity and implement remote measurement tools."

Treatment recommendations can be delivered to the patient virtually and we can work with local providers who can administer treatment if one of our 15 Karmanos locations isn't nearby.

As for physician satisfaction, we're still gathering data and feedback, but anecdotally we're hearing a preference for face-to-face initial exams, which are difficult virtually. Most are open to using telehealth more frequently for other types of visits and consults.

As cameras, vital sign monitoring, and other technologies become more advanced, and as broadband access continues to improve across rural areas, I predict physicians will become more receptive to virtual care.

The future of cancer telehealth

With positive patient feedback and growing acceptance of telehealth among our providers, we plan to expand telehealth moving forward by working with technology partners who can provide better ancillary equipment for home vital sign monitoring, including more powerful cameras.

In the future, we envision certain types of appointments moving almost exclusively to telehealth, such as second opinions, screenings for clinical trials, and routine follow-ups.

We've already discovered that some cancer specialties, like genetic counseling, can be provided almost 100% via telehealth.

With enhanced IT platforms and equipment on the way, telehealth visits will be improved even further, but long term, the key to further telehealth adoption in cancer care is out of our control because reimbursement will ultimately drive its fate.

Certainty about reimbursement and regulation drives adoption, and if insurance companies and government cut offs greatly reduce reimbursement, telehealth may continue to be an option, but on a very limited basis.

Telehealth holds promise for offering the right care at the right time, and, critically, at the right place, for patients.

As we move away from the pandemic, insurers and governments must recognize cancer telehealth as more than an emergency solution. It's a vital tool in improving care and comfort for our most vulnerable patients.

Q & A

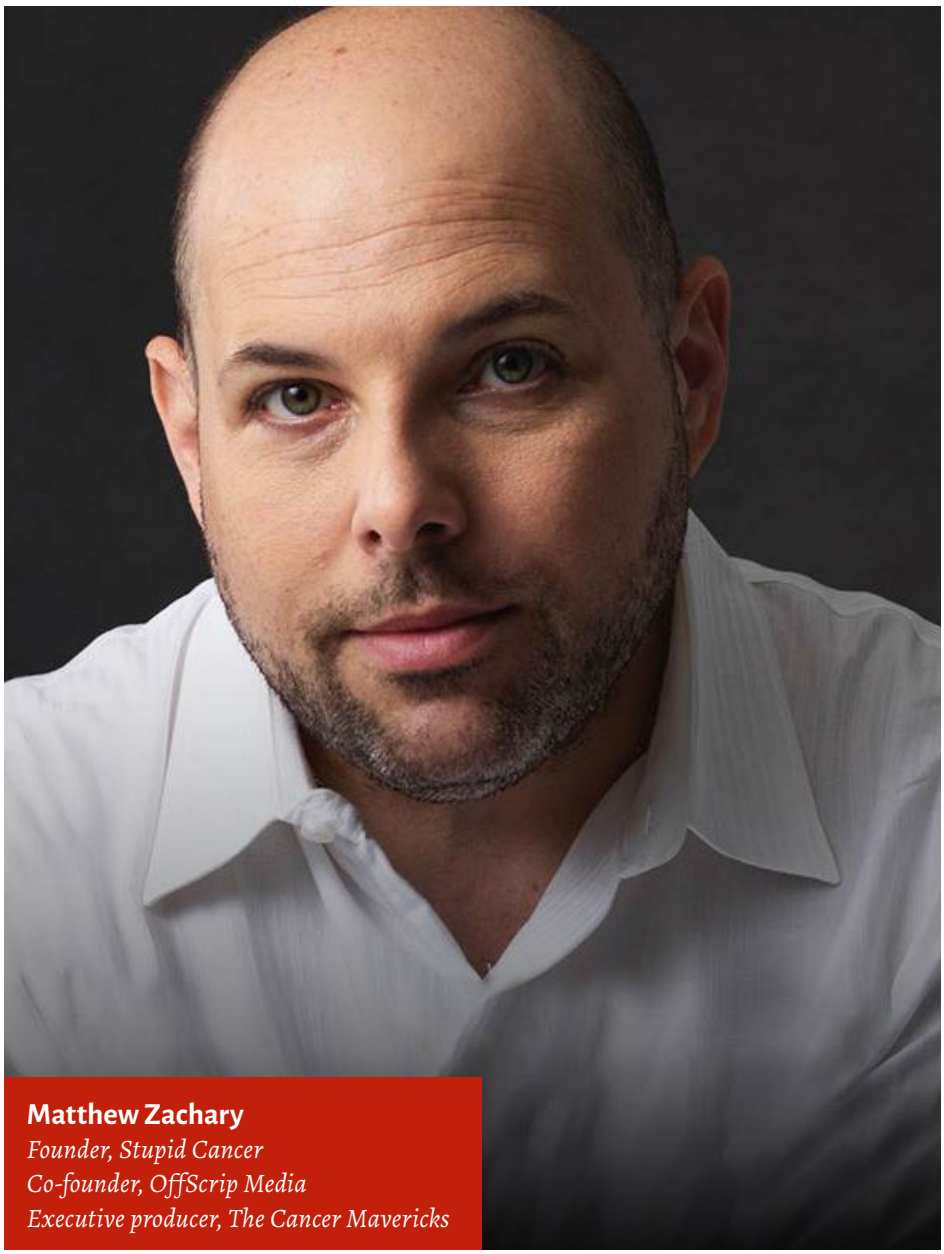
Zachary spoke with Alexandria Carolan, a reporter with The Cancer Letter.

THE CANCER LETTER | SEPTEMBER 24, 2021 | VOL 47 | ISSUE 35

CONVERSATION WITH THE CANCER LETTER

CANCER HISTORY PROJECT

Cancer Mavericks docu-series explores a history of cancer survivorship



Matthew Zachary
Founder, Stupid Cancer
Co-founder, OffScrip Media
Executive producer, The Cancer Mavericks

> “Shouldn’t someone be protecting the American citizen who happens to enter the ‘shit happens store’ of cancer, or rare and chronic disease? Who’s making sure that you get to live your best life?”

Matthew Zachary, a 25-year cancer survivor and founder of Stupid Cancer, didn't always know what it meant to be a cancer advocate, or the complex and rich history behind the term.

He's hoping to shine a light on the robust history of the survivorship movement through a docu-series podcast, "The Cancer Mavericks: A History of Survivorship," which explores cancer activism from the 1930s onward.

"This is all being done in the lens of a pseudo semi-autobiographical way, where I'm kind of reacting to history, and observing history, and forecasting the future," Zachary, who narrates the podcast, said to *The Cancer Letter*. "What advocacy meant in the sixties is very different from what it means today, and will be very different from what it will mean 10 years from now."

Zachary focuses on the Bernie Fishers of the world, doctors who changed the face of medicine despite putting their reputations at risk and facing backlash.

"I think it just takes a specific kind of person, who either has the gumption out of the gate, or is pissed off just enough to realize that they can do something so radical, so counterintuitive, as to believe it's possible to change something that is just seemingly immovable in that space," he said. "Whether it is one doctor saying 'I'm changing medicine, I don't want to do this anymore, we need to reinvent the way we think about oncology writ large for the next hundred years,' and end up chastised and reputationally lambasted for their radical thinking that people should be treated like people."

Episodes will be released monthly through the end of December 2021 to commemorate the 50th anniversary of the signing of the National Cancer Act of 1971.

Zachary spoke with Alexandria Carolan, a reporter with *The Cancer Letter*.

Alexandria Carolan: How did you get started with "The Cancer Mavericks: A History of Survivorship?"

Matthew Zachary: I'm a 25 year cancer survivor and was given six months to live when I was 21 in 1995, wandering the earth, not knowing what the hell was going to happen to me.

I happened to find a peer in the middle of nowhere, who was another young adult brain cancer guy who happened to be on the board of the National Coalition for Cancer Survivorship—and I got thrown into the deep end of the pool pretty quickly in 2002—only to be asked, would you like to be a cancer advocate? To which I responded, what even is a cancer advocate?

He said, "That's what I said when I was asked if I wanted to be a cancer advocate."

Then I got into the nonprofit game, I quit my career in advertising and marketing, and spent 14 years running Stupid Cancer that I created from scratch because I was really pissed, and I met so many people along the way.

I learned all this rich history. These people have been doing this since the eighties and the nineties. I think, when I left the organization, I was like "well, how did we get to then? Surely things happened before the eighties to get to where we are."

I looked at *Emperor of All Maladies* by Siddhartha Mukherjee, and it was great, but it's jargony and it's sciency, and it's nerdy and it's academic. No offense to sid, it's a great piece. But it flew over the heads of anyone. And I was like, why has no one told the story of these unsung people that even—I didn't know—who the hell they were—let alone people I thought knew who they were, who didn't know who they were.

In my spare time, I realized that Offscrip Media had the capability of producing its first long form audio series, a history series. What the hell happened between 1971, when the National Cancer Act passed, to now 50 years later. Does anyone have any idea the shit that people had to go through to get us from then to now, and how much easier it is today than it used to be by comparison, even though we think shit's really hard today.

That's where it all started from. I was really upset that no one told this story. I thought, well, if no one is going to tell it, I am. And there you go. That's where a spark was lit to begin the quest of storyboarding and figuring out how the hell me, a non-documentary person, produces a documentary.

What year does your docu-series begin?

MZ: It's an eight part series, so it's sort of chronological for the first couple of episodes. You really do have to go back to the thirties and the forties and the fifties, and really get some context on what that word cancer even meant to society and culture—let alone medicine, for years and years.

We kind of pick up in the mid-to-late sixties, when people just started to realize this is not okay. The sixties were turbulent enough as is, let alone this massive uprising of society, on how—you'll have to listen to the episodes to get all the data that our production team put together, and the clips they pulled on how media, radio, television, for that matter, talked about cancer. It was insane to know that this was actually a little narrative in America in that decade.

They had, as we say, the chutzpah, the moxie, the wherewithal, the balls people had to question the government, to question medicine. These were just civilians, regular voting American citizens that got really pissed, along with everyone else that decade. Episode one picks up where a small group of committed citizens decided to change the world. They got the national cancer act passed in '71. That's how we start the series.

You mentioned that when you first learned about being a cancer advocate, you had no idea what it meant. How does your podcast explore this, and how has cancer advocacy changed over time?

MZ: This is all being done in the lens of a pseudo semi-autobiographical way, where I'm kind of reacting to history, and observing history, and forecasting the future. What advocacy meant in the sixties is very different from what it means today, and will be very different from what it will mean 10 years from now.

What we had to fight for in the sixties, what our parents and our grandparents had to fight for, was just the right to live. Just to be acknowledged that this is not OK. How about some government money? How about the National Cancer Institute? How about there being all these systems that should just exist in the first place?

That's what advocacy meant in the sixties. In the seventies, it was like, can we just stop dying, please? I'm glad there are some kinds of systems that are thinking about this, but we'd really like to stop dying. The eighties were like: Can we possibly live? And if we do, what the hell does that mean? Who should we be? Where do we go? What do we do? The nineties were like, fuck all of that. We're equally pissed more than ever before.

We need more money, we need more funding, we're going to march on the government, we're going to demand things.

We're doing die-ins and sit-ins at pharma conferences. We lost our shit, like a network, mad as hell. In the 2000s we were like: Are we living now? Is this a thing? What does that mean? And diversity started to matter.

It became this more diverse approach to citizenship and liberties, which moved us towards the genomic age, where it's not about getting napalm, your genes determine whether you live or die, which is also contingent on whether you are rich or poor. It really is an extraordinary arc across these eight episodes that are debuting Q3, Q4, 2021.

What do you typically cover in one episode? What sort of research goes into this?

MZ: I want to qualify, there's an army of people behind me. We hired award-winning producers from NPR, and PBS, and CBS, and *Slate*, and they did all of this extraordinary reconnaissance—going through archives, listening to news clips, pulling information from TV and radio from 30, 40, 50 years ago.

I can't really get into the granularity of your question—you have to listen to the series. All of that is articulated in the episode descriptions that you can find on Apple Podcasts and Spotify. When I first presented the team with the storyboard, there were 300 or 400 people that I storyboarded. We had to whittle down this Sequoia tree into a toothpick. Essentially, what does it mean to be a Cancer Maverick?

What qualifies? What does that stand for? Who's the listener? What do we want that person to hear and do and think across eight episodes? Whether it's the doctor who invented cancer navigation, the people who took a risk and drove to Albuquerque in the middle of nowhere in 1986 to start this national movement of survivorship and invent the word survivor, or women who fought to fundamentally change the role toxic masculinity played in breast surgery.

Whether it was people who just rose up and said, you call me a victim again, I'm going to punch a kitten. You have to look at the specific ways in which unique heroes just pick their poison and jump into the lake to swim and change everything.

What have you learned about being a cancer maverick? You have your own experiences, but I'm sure this podcast has taught you a lot.

MZ: The series has shown me what I think we already know to be true, especially in this highly tumultuous society we live in today, that the loudest people get the most attention. But when you're willing to do it for good, it matters more.

I think it just takes a specific kind of person, who either has the gumption out of the gate, or is pissed off just enough to realize that they can do something so radical, so counterintuitive, as to believe it's possible to change something that is just seemingly immovable in that space. Whether it is one doctor saying "I'm changing medicine, I don't want to do this anymore, we need to reinvent the way we think about oncology writ large for the next hundred years," and end up chastised and reputationally lambasted for their radical thinking that people should be treated like people.

What a concept for women to rise up and say "Screw you, men; women will determine what's best for us in breast cancer." And they made that change. Or the black Panthers, who took an active

role in breast cancer screenings. Who knew this? That's maverick, that's crazy shit, that's just saying, I'm sick and tired of this crap. I'm going to rise up like anyone else who's done that in the past and currently, to demand social justice.

It seems like cancer advocacy has gone hand in hand with social justice.

MZ: Yes it has. I would say the boat wake of the efforts of these, again, unsung American heroes you've never heard of, makes so much sense because this all came down to human rights.

I've found that it was such an unexpected communing of all races, Indian Americans, Native Americans, African Americans, Hispanic Americans, Caucasian Americans, they all got together just to demand that we have the right to live. We have the right to not die from cancer and the government should do something.

Fast forward to the 2000s and these breakthrough drugs and these medications that make you not throw up and have better white cells and take care of your quality of life—we wound up living better with cancer, increasing survival rates, reducing mortality, creating better screenings to detect them earlier.

That's a good problem to have, because now we can worry about your mental health, and your fertility, and your employment issues, and your financial issues, and your survivorship late effect issues. We didn't even know those things would be a glimmer of something to worry about when we were just dying of cancer.

Here we are in the 2020s with precision medicine and genomics and biomarkers, where it's not even about where in your body that cancer is, it's what your genes are. We're again in this health equity conversation of rich versus poor, where the haves have, and the have nots have not. Who has access to a genetic test, or a screening, or some kind of diagnostic, where you don't have to have cancer, you can detect it earlier and it's cheaper and it's easier and you live. What if you're poor? You die.

Here we are, 50 years later, and the institutional racism of this country rears its ugly head in medicine even more now that people aren't dying as much. On top of the pandemic and on top of all the other absolutely necessary uprisings in the chaos of modern day justice.

It seems like you've learned a lot about how the role of cancer advocacy has functioned and continues to function. What about cancer advocacy and survivorship has stood out to you most in these episodes?

MZ: Not everyone knows what advocacy means, but everyone knows what justice should mean. In any context, it's not a competition. And the only thing that's ever changed anything is the American citizen willing to stand up to bullshit.

How can we use this history that you're delving into to inform how we view cancer and survivorship today?

MZ: History is a teacher, and this is a story that's never been told before. As word spreads, as people listen to the series, as people learn from these predecessors we never even knew we had, the future has yet to be written about what society is going to do by gaining this basic understanding of how far we've come with perspective to the issues we have today.

I would like to believe that the 2020s will begin a brand new era of advocate. Now that everything is genomic, this is not about cancer. This is about disease. This is about just living your life with the dignity you're entitled to. You shouldn't go broke from this shit, and you have the civil liberty to pursuit of happiness.

Shouldn't someone be protecting the American citizen who happens to enter the "shit happens store" of cancer, or rare and chronic disease? Who's making sure that you get to live your best life? Odds are we're going to be living better lives—but now how do we build the equity up?

Not just the equality, but the equity, where everyone is entitled to the choices that they didn't even know they had, to make decisions that are best for them, to live the life they need, want, and deserve.

Is there anything else you'd like to add?

MZ: No one's ever been able to say "know your history" for cancer. You can go back to Emperor of All Maladies, there've been many books about the biology of cancer, the medical advancements in terms of gene codes and mammograms and whatnot.

These are about people. Stories matter, and these stories have never been told. Hearing that there were people who got this done is so important to gain that perspective.

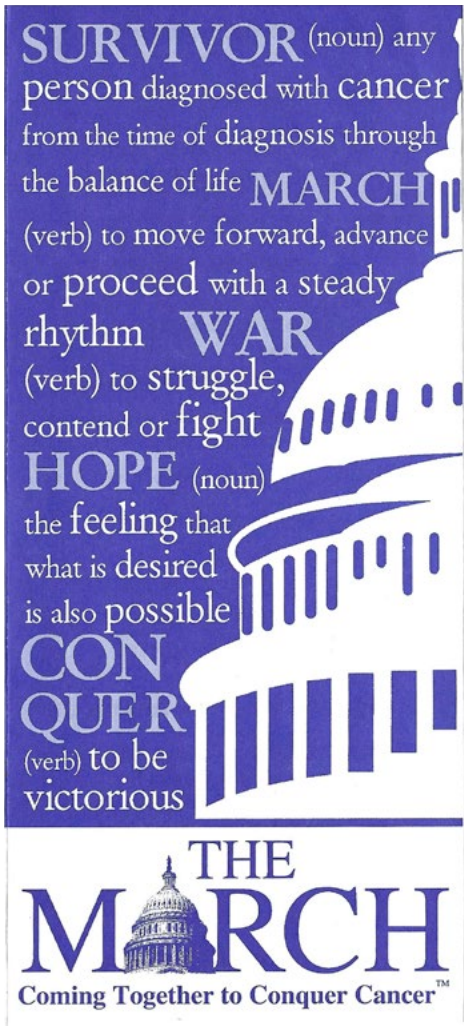
I'm really hoping that we start to see an upsurge of the next generation of health advocates, patient advocates, and consumer health warriors who are going to equally demand better of a system that typically doesn't give a shit about you, because all they care about is profit.

Until such time, as it's profitable to guarantee this to patients, we have to fight.

IN THE ARCHIVES

CANCER HISTORY PROJECT

Sept. 26, 1998: The March



As we approach the 23rd anniversary of The March, *The Cancer Letter* archives offer a unique way to reflect on the leadup to—and events of—the day. In October, 1997, *The Cancer Letter* dedicated the entirety of what was then an 8-page publication to a lengthy analysis of the vision for The March. Then, one year later, those same 8 pages were trained on the event—the speeches, the attendance, the music, and more.

Here is our real-time coverage:

1997: The plan

Ellen Stovall and Donna Doneski at The March

- To Wage New War On Cancer, Advocates Plan A Campaign Inspired By Earth Day
  By *The Cancer Letter* | Oct. 31, 1997

Consider a vision:

Cancer survivors, researchers, and clinicians agree to advance a common agenda. That agenda is endorsed by trade unions, industries and advocates for the environment, children and the elderly.

Then, one day in September 1998, hundreds of thousands of marchers come to Washington to demand that the government launch a new War on Cancer. Millions more take part in rallies, sit-ins and teach-ins nationwide.

After the crowds are gone, a grassroots network remains. This network is able to mobilize enough votes–and enough dollars–to swing elections. Within months, politicians declared to be weak on cancer are driven out of Washington, state capitols, and city halls.

"If the average voter understood how much can be done about cancer and how little is being done, a national movement would materialize," said Ellen Stovall, executive director of the National Coalition for Cancer Survivorship, who has pulled together a loose coalition of advocacy groups and financial supporters for The March…Coming Together to Conquer Cancer. The march is scheduled for next September.

Sept. 26, 1998

Ellen Stovall speaking at The March

- The March Attracts Thousands To Rally For Research Funding, Access To Care
  By *The Cancer Letter* | Oct. 2, 1998

Organizers of The March: Coming Together to Conquer Cancer estimated that at least 150,000 people attended a noon rally on Sept. 26 in Washington, DC, the main event in a two–day extravaganza designed to draw national attention to the need for greater funding for cancer research and wider access to quality cancer care.

That the event even took place at all, considering the disparate organizations that had to set aside their

differences and work together over the past year, was an achievement worth noting. That The March came off with hardly a glitch and attracted as many people as can be seated at the Rose Bowl and Oriole Park at Camden Yards combined, astounded many activists.

- It's "High Noon" For Cancer, Vice President Says
  By *The Cancer Letter* | Oct. 2, 1998

Vice President Al Gore has called for increased funding for cancer research and urged Congress to approve measures to widen access to clinical trials and protect patients' rights.

Speaking to The March: Coming Together to Conquer Cancer on Sept. 26 in Washington, also challenged NCI to complete the following tasks:

- Finalize procedures to include patient advocates on peer review committees.
- Speed the process of enrolling patients on clinical trials.
- Develop new techniques for early detection.

The three initiatives have been in development at the Institute for the past year. NCI Director Richard Klausner said the Institute would have procedures for integrating patient advocates into peer review committees by Gore's deadline of next spring.

- In Radio Address, Clinton Outlines Administration Priorities
  By *The Cancer Letter* | Oct. 2, 1998

President Bill Clinton's radio address on Sept. 26 repeated some of the same themes of Vice President Al Gore's speech at The March rally the same day.

In the address, Clinton discusses NCI initiatives to include cancer patient advocates on study sections and advisory groups and to develop informatics systems that will streamline patient enrollment on clinical trials. He also issues a "challenge" to scientists to develop new cancer diagnostic techniques—a reference to the new NCI Unconventional Innovations Program.

Below is an excerpt from his speech:

"This morning I want to talk to you about our overall vision of cancer care and research as we approach the 21st century. This is a time of striking progress, stunning breakthroughs. With unyielding speed, scientists are mapping the very blueprint of human life, and expectations of the Human Genome Project are being exceeded by the day. We are closing in on the genetic causes of breast cancer, colon cancer and prostate cancer. New tools for screening and diagnosis are returning to many patients the promise of a long and healthy life. It is no wonder scientists say we are turning the corner in the fight against cancer."

- "We Will Move Forward With Bold Expectations," NCI Director Says
  By *The Cancer Letter* | Oct. 2, 1998

An excerpt from NCI Director Richard Klausner's speech at The March rally Sept. 26:

"I'm pleased to speak today on behalf of the discoverers, the scientists, the clinicians, and the patients who together are going to make the discoveries, are going to make the advances, that will move us forward.

"We have with this march a new and powerful metaphor for our struggle against cancer. Together we will move forward, inexorably, driven not by promises, but by real purpose.

"This is not a sprint and we'll not tire. The scientists are just as frustrated, just as impatient, as the survivors and all who form this community together. It doesn't matter how long this march takes, we will be motivated by the suffering we all feel, motivated by the sure conviction that ignorance and inaction means defeat, and knowledge and its application are our only certain road to victories."

Quote of the week

> We had the march that will make the change. Now we need to implement it. That's going to take our energy for a long time.
>
> *– Ellen Stovall*

Ellen Stovall at The March

Recent contributions

- The National Cancer Act's Impact on Cancer Survivorship
  By ASCO | Sept. 23, 2021

- ASCO Remembers Patient Advocate Karen Durham
  By ASCO | Sept. 23, 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

Massey, Hollings, City of Hope receive SPORE focused on racial inequities in lung cancer

Virginia Commonwealth University Massey Cancer Center, Medical University of South Carolina Hollings Cancer Center, and City of Hope Comprehensive Cancer Center were awarded a SPORE grant from NCI that aims to address lung cancer racial disparities through precision medicine, targeted smoking cessation programs, and community outreach.

The approximately $3 million grant will establish the Translational Research Center in Lung Cancer Disparities, or TRACER, based at VCU Massey, in partnership with MUSC Hollings and City of Hope.

TRACER, will engage a host of community groups, including local health departments, community health centers, marginalized populations, civic activists, educational institutions, faith-based groups, and cancer survivors.

"It's important that the community has a seat at the table," said TRACER principal investigator Robert Winn, director and Lipman Chair in Oncology at VCU Massey, senior associate dean for cancer innovation and professor of pulmonary disease and critical care medicine at the VCU School of Medicine. "We're optimistic that this dream team of researchers and community stakeholders will translate our basic science into clinical impact in reducing lung cancer disparities."

Although the racial gap in lung cancer cases appears to be closing, likely due to the success of anti-smoking campaigns, Black men still have a higher risk of developing lung cancer compared to white men, even though they tend to smoke less—an effect referred to as the "Black smoking paradox." Black patients are also more likely than white patients to be diagnosed at later stages and to receive no treatment at all for their cancer.

To better understand the Black smoking paradox, TRACER will investigate how stress and smoking interact with gene expression to raise lung cancer risk for Black men. Preliminary data show that Black men tend to express the PRMT6 gene—which drives lung tumor development—at higher levels than white men, and smoking further stimulates PRMT6 expression. This project will ask how stress plays in and create early detection tools suitable for use in the Black population.

Winn will co-lead the project with S. Patrick Nana-Sinkam, a member of Massey's Cancer Prevention and Control research program and the Linda Grandis Blatt Endowed Chair in Cancer Research.

The next project, led by Chanita Hughes-Halbert, will investigate how cortisol—the body's main stress hormone—relates to racial differences in smoking behaviors and overall lung cancer risk. These findings could lead to more tailored approaches to smoking cessation as well as medications that reduce the lung cancer burden on the Black community by counteracting stress.

Both projects will use human tissue and fluid samples collected across Massey, Hollings, and City of Hope to ensure genetic and geographic diversity of research participants.

Victoria Seewaldt, City of Hope's Ruth Ziegler Chair in Population Sciences, will lead TRACER's Developmental Research Program, which will identify and fund new lung cancer disparities research projects, beyond those explicitly outlined in this grant. For instance, projects may investigate how pollution contributes to lung cancer burden in Black communities.

After the three-year funding period of this initial award, which is considered a P20 exploratory grant, the infrastructure will be in place to apply for a larger, five-year P50 SPORE award that will establish a more permanent research program devoted to ending racial inequities in lung cancer.

ACS and four historically Black colleges and universities establish Diversity in Cancer Research Program

The American Cancer Society, along with four historically black medical schools including Charles Drew Medical School, Howard University, Meharry Medical College, and Morehouse School of Medicine, launched the Diversity in Cancer Research Program, which aims to improve diversity, equity, and inclusion in cancer research.

One of the first initiatives of this program is the distribution of DICR Institutional Development Grants, which are designed to enhance the competitiveness of faculty at minority-serving institutions when applying for nationally competitive grant support and aid in faculty development and retention.

ACS has committed to a $12 million investment to support the four HBCU medical schools with grants in a pilot program for 2021-2022. DICR seeks to launch or sustain the careers of 104 individuals by 2025.

"There are many reasons the Black community continues to experience disparities in cancer care outcomes," said Wayne A. I . Frederick, president of Howard University. "But one of the most critical factors behind the imbalance, and one of the most promising paths to closing the gap, is diversity in cancer care research. We must improve diversity and representation in our laboratories if we expect different outcomes in our hospitals."

Data show that African Americans and Black people, Hispanics and Latinos, indigenous people, and native Hawaiians and other Pacific Islanders are underrepresented in grant funding. Fewer than 2% of applicants for the National Institute of Health's principal grant program come from Black/African Americans, and fewer than 4% from Hispanic/Latino populations.

Huda Salman selected to lead IU's Brown Center for Immunotherapy

Huda Salman was named the first executive director of the Indiana University School of Medicine's Brown Center for Immunotherapy, effective Nov. 1.

Salman will hold the titles of Don Brown Chair in Immunotherapy and professor of medicine in the department of medicine, division of hematology and oncology.

Salman is joining IU School of Medicine from Stony Brook University and Stony Brook Cancer Center, where she is associate professor, section chief of hematological malignancies, and director of the CAR T-cell program.

Salman founded the hematological malignancies section as well as the Cancer Center Adolescence and Young Adult Program at Stony Brook. A leukemia survivor, Salman's clinical expertise is focused on hematological malignancies and bone marrow transplantation and cellular therapy, particularly for acute and aggressive lymphomas.

Established in 2016, the Brown center studies new ways to deploy immune-based therapies to treat cancer and pioneer use of technology in other diseases. The Brown Center focuses on multiple myeloma and triple negative breast cancer; researchers will also investigate potential opportunities to prevent and treat Alzheimer's disease and other neurodegenerative disorders with immunotherapies.

Velda González-Mercado receives grant to study cancer-related fatigue

Velda González-Mercado, assistant professor at NYU Meyers, has received a grant from the National Institute of Nursing Research, supporting her research on the biologic underpinnings of cancer-related fatigue in men undergoing radiation therapy for prostate cancer, through a translational, bedside-to-bench omics approach.

The three-year grant is a K23 Mentored Patient-Oriented Career Development Award and amounts to more than $500,000.

While researchers still do not fully understand why and how radiation causes fatigue, mTOR has emerged as a focus of fatigue-related research. Previous research by González-Mercado illustrates how mTOR pathway dysregulation may lead to debilitating fatigue during radiation treatment.

González-Mercado's new NINR-funded study will explore the network of interactions among the biomolecules present in mTOR signaling pathways at the systems level. The research will aim to identify and investigate mTOR pathway and activity-related genes, regulation of the genes, and changes in mTOR signaling pathway and activity-related proteins as they relate to changes in fatigue before and after radiation therapy in men with prostate cancer.

"Exploring the relationship of changes in mTOR signaling pathway at the levels of gene expression, epigenetic regulation, and protein expression will give us initial information about potential mechanisms behind the development of cancer-related fatigue, and may provide molecular targets for individualized treatments, leading to more effective management of fatigue in this patient population," González-Mercado said.

MSK establishes Stuart Center for Adolescent and Young Adult Cancers

Memorial Sloan Kettering Cancer Center has established the Lisa and Scott Stuart Center for Adolescent and Young Adult Cancers, which will unite experts across pediatric and adult specialties to improve cancer treatment for MSK patients aged 15 to 39.

This builds on the work of MSK's Adolescent and Young Adult Program, which is tailored to meet the treatment and psychosocial needs of patients in this age group.

The Stuart Center is made possible through a donation from Scott Stuart, chair of MSK's Boards of Trustees and Governing Trustees, and his wife, Lisa.

The survival rate for children with cancer has improved greatly in the past three decades, but for adolescents and young adults, there hasn't been as much progress. This population faces challenges such as delayed diagnoses and underrepresentation in clinical trials, which could lead to worse outcomes.

The Stuart Center will be led by William Tap, chief of the Sarcoma Medical Oncology Service, and Julia Glade Bender, vice chair for pediatric clinical research. Services offered will include expanded access to clinical trials for adolescents and young adults; family planning and fertility specialists; personalized medicine; and the use of apps and social media.

The Stuart Center will be one of the first to run digital clinical trials for adolescents and young adults. Patients will work with a team of specialists to create a holistic care plan beyond medical treatment, with counseling, nutrition, exercise, and family planning through the use of apps, social media, and more. In addition, the Lounge at MSK App will offer individuals the opportunity to connect with other young adults in treatment and beyond, ask questions to peers and MSK clinicians, and find resources and events.

Graham A. Colditz Honored with AACR Distinguished Lectureship on the Science of Cancer Health Disparities

Graham A. Colditz was awarded the 2021 American Association for Cancer Research Distinguished Lectureship on the Science of Cancer Health Disparities.

Colditz will present his award lecture, titled "Making progress, together: An inclusive, broad-based approach to reducing excess burden of breast cancer among African American women in St. Louis—with lessons for national implementation," during the opening session of the virtual 14th AACR Conference on the Science of Cancer Health Disparities in Racial/Ethnic Minorities and the Medically Underserved on Wednesday, Oct. 6, 2021.

This AACR lectureship recognizes an investigator whose work has impacted on the etiology, detection, diagnosis, treatment, or prevention of cancer health disparities.

Colditz is the Niess-Gain Professor of Surgery, professor of medicine, and associate director of prevention and control for the Alvin J. Siteman Cancer Center and deputy director for the Institute for Public Health at Washington University School of Medicine and Barnes-Jewish Hospital. He is also the chief of the Division of Public Health Sciences, department of surgery at Washington University School of Medicine.

Colditz is receiving the AACR lectureship for his contributions to translating epidemiological studies to reduce cancer health disparities. He is also being recognized for facilitating significant reductions in late-stage breast cancer diagnoses in Black women by pursuing the identification of genetic drivers that contribute to aggressive breast cancer subtypes in this population.

He currently leads the Program for the Elimination of Cancer Disparities at the Alvin J. Siteman Cancer Center. Through outreach, education, screening support, and the monitoring of underrepresented minority enrollment in clinical trials, the program has resulted in the significant reduction of late-stage breast cancer diagnoses among Black women in St. Louis, from more than 30% in 1999 to 14% today. This rate is similar to the percentage of late-stage diagnoses among white women in St. Louis. Colditz has since expanded this program to other underserved areas, while adapting the breast cancer program to address other cancer types.

Colditz has also led numerous scientific investigations to understand the underlying basis for increased breast cancer risk in young Black women. His research has found that, compared to white women, Black women are at an increased risk of developing hormone receptor-negative and other aggressive subtypes of breast cancer following initial detection of benign lesions. He has also reported that although treatment approaches to ductal carcinoma in situ are equally accessed by Black and white patients in Missouri, Black women present with significantly higher rates of invasive breast cancer in the 10 years following a DCIS diagnosis.

Colditz was elected as a fellow of the American Association for the Advancement of Science in 2018 and as a member of the National Academy of Medicine in 2006. He serves on the Board of Scientific Advisors of NCI and the National Institutes of Health Council of Councils.

John Byrd receives Binet-Rai Medal Award for contributions to CLL research

John Byrd has received the Binet-Rai Medal Award for his research findings, which led to the use of Bruton tyrosine kinase inhibitors in almost every phase of chronic lymphocytic leukemia therapy.

The award was presented during the XIX International Workshop on Chronic Lymphocytic Leukemia.

Byrd is the Gordon and Helen Taylor professor of medicine and chair of the department of internal medicine at the University of Cincinnati. He joined the UC College of Medicine faculty in July from Ohio State University, where he was the D. Warren Brown Chair of Leukemia Research and Distinguished University Professor, in addition to director of the Clara Bloomfield Center for Prognosis in Myeloid Leukemia, senior advisor for cancer experimental therapeutics, and co-leader of the Leukemia Research Program.

Byrd also serves as the national chief medical officer for Beat AML, a multisite precision medicine study that provides access to novel treatments for Acute Myeloid Leukemia.

In 2013 and 2014, Byrd and his colleagues published two papers in *The New England Journal of Medicine* that demonstrated the efficacy of BTK inhibitors in treating relapsed and refractory CLL. Subsequent publications have proved that this class of agents also are effective in the treatment-naïve CLL setting, leading to their wide usage throughout the phases of CLL treatment today.

THE CLINICAL CANCER LETTER

CLINICAL ROUNDUP

Libtayo + chemo significantly improve OS in advanced NSCLC

Results from a phase III trial demonstrated the clinical benefit of using PD-1 inhibitor Libtayo (cemiplimab), in combination with a physician's choice of platinum-doublet chemotherapy, in the treatment of patients with locally advanced or metastatic non-small cell lung cancer, irrespective of histology and across all PD-L1 expression levels.

The trial compared this combination treatment to chemotherapy alone. Results from the study were presented at the European Society for Medical Oncology Congress 2021.

Libtayo is sponsored by Regeneron Pharmaceuticals and Sanofi.

These results were achieved in a patient population with varied baseline characteristics and will form the basis of regulatory submissions, including in the U.S. and European Union.

In the overall population, patients treated with the Libtayo combination (n=312) experienced significant improvements compared to those receiving chemotherapy alone (n=154), including a:

- 22-month median overall survival compared to 13 months for chemotherapy, representing a 29% relative reduction in the risk of death (HR: 0.71; 95% CI: 0.53-0.93; p=0.014). The 12-month probability of survival was 66% for the Libtayo combination and 56% for chemotherapy.

- 8-month median progression-free survival compared to 5 months for chemotherapy, representing a 46% relative reduction in the risk of disease progression (HR: 0.56; 95% CI: 0.44-0.70; p<0.0001). The 12-month probability of PFS was 38% for the Libtayo combination and 16% for chemotherapy.

- 43% objective response rate compared to 23% for chemotherapy.

- 16-month median duration of response compared to 7 months for chemotherapy.

Favorable patient-reported outcomes were also observed. Specifically, the Libtayo combination delayed deterioration in pain symptoms (HR: 0.39; 95% CI: 0.26-0.60; nominal p<0.0001) and showed a trend towards delayed deterioration in global health status/quality of life (HR: 0.78; 95% CI: 0.51-1.19; nominal p=0.248), compared to chemotherapy. The Libtayo combination also improved pain symptoms, compared to chemotherapy (-4.98 difference in baseline changes between treatment groups; 95% CI: -8.36 to -1.60; nominal p=0.004).

HER2-targeting antibody-drug improves PFS in deadly form of advanced breast cancer

UCLA Jonsson Comprehensive Cancer Center researchers found that treating women with HER2 positive metastatic breast cancer with the HER2-targeting antibody-drug conjugate trastuzumab deruxtecan (T-DXd) significantly mitigates disease progression, compared to the current standard of care, trastuzumab emtansine (T-DM1).

The results from the clinical trial were featured in the Presidential Symposium at the European Society for Medical Oncology Congress. This is the first phase III trial to report a comparison in the safety and efficacy of T-Dxd versus a standard therapy in metastatic breast cancer.

T-DXd delivers high concentrations of chemotherapy directly to cancer cells that have HER2 on their surfaces. Patients who received the drug had a 72% improvement in progression-free survival compared to T-DM1.

When compared at the 12-month mark, 76% of patients who were treated with T-DXd had not yet experienced disease progression. For those treated with T-DM1, only 34% of patients did not see their disease progress after 12 months.

T-DXd received accelerated FDA approval in 2019 for patients with unresectable or metastatic HER2-positive breast cancer who have received two or more prior anti-HER2-based regimens in the metastatic setting. This approval was based on a smaller, non-comparative trial, DESTINY-Breast01, that demonstrated very promising efficacy in patients whose disease had progressed after T-DM1.

The results from the newly reported clinical trial, called DESTINY-Breast03, shows that T-DXd, is significantly better than T-DM1 when used after a patient's disease has progressed on trastuzumab and chemotherapy.

The DESTINY-Breast03 trial included 524 patients who were randomized to either the T-DXd arm or the comparator T-DM1 arm. Median age of participants was 54 and ranged from 20-83. All were previously treated with trastuzumab and chemotherapy before starting the clinical trial.

Along with a longer progression-free survival, almost 80% of patients in the T-DXd arm saw their tumors shrink compared to only 34% treated with T-DM1. And 16% of T-DXd treated patients had their diseases completely disappear.

The safety profile was consistent with other reported data regarding T-DXd.

The next step is to study T-DXd in the front-line metastatic setting and in early stage disease. At the UCLA JCCC, DESTINY-Breast03 senior author Sara Hurvitz is investigating how well T-DXd works alone or in combination with anti-estrogen therapy, in treating patients with HER2-low, hormone receptor positive breast cancer.

Keytruda + chemo reduces risk of death by one-third vs. chemo as first-line treatment for persistent, recurrent, or metastatic cervical cancer

Results from the phase III KEYNOTE-826 trial demonstrate that Keytruda (pembrolizumab) plus chemotherapy with or without bevacizumab improved disease outcomes when compared to chemotherapy with or without bevacizumab as a first-line treatment of persistent, recurrent, or metastatic cervical cancer.

Keytruda is an anti-PD-1 therapy sponsored by Merck.

Keytruda plus chemotherapy (paclitaxel plus cisplatin or paclitaxel plus carboplatin) with or without bevacizumab reduced the risk of death by one-third, or 33% (HR=0.67 [95% CI, 0.54-0.84]; p<0.001), versus chemotherapy with or without bevacizumab. Median overall survival for Keytruda plus chemo ± bev was 24.4 months (95% CI, 19.2-not reached) compared to 16.5 months (95% CI, 14.5-19.4) for chemo ± bev.

Median progression-free survival (HR=0.65 [95% CI, 0.53-0.79]; p<0.001) was 10.4 months (95% CI, 9.1-12.1) in those treated with Keytruda plus chemo ± bev and 8.2 months (95% CI, 6.4-8.4) among those treated with chemo ± bev.

In the trial, Keytruda plus chemo ± bev showed an overall response rate of 65.9% (95% CI, 60.3-71.2), and chemo ± bev showed an ORR of 50.8% (95% CI, 45.1-56.5). Median duration of response was 18.0 months (range, 1.3+ to 24.2+) in the Keytruda plus chemo ± bev arm and 10.4 months (range, 1.5+ to 22.0+) in the chemo ± bev arm.

The results were consistent with or without bevacizumab use.

Sugemalimab is a potential treatment option in a broad range of NSCLC patients, stage 3 and 4 studies suggest

The phase III GEMSTONE-301 study demonstrated the efficacy and safety of the anti-PD-L1 antibody sugemalimab as consolidation therapy in patients with locally advanced/unresectable stage 3 non-small cell lung cancer without disease progression after concurrent or sequential chemoradiotherapy.

These results were presented at the European Society for Medical Oncology Congress 2021. GEMSTONE-301 is the first positive phase III trial of a PD-(L)1 agent in this broad stage 3 NSCLC patient population setting.

Sugemalimab, as a consolidation therapy, demonstrated statistically significant and clinically meaningful improvement in progression-free survival vs. placebo as assessed by blinded independent central review.

- Median progression-free survival was 9.0 months vs. 5.8 months (HR=0.64, p=0.0026).
- Clinical benefits were observed in patients who received either concurrent or sequential chemoradiotherapy prior to sugemalimab.

- For patients who received prior concurrent chemoradiotherapy, median PFS was 10.5 months vs. 6.4 months (HR=0.66).
- For patients who received prior sequential chemoradiotherapy, median PFS was 8.1 months vs. 4.1 months (HR=0.59).
- Overall survival data were immature, but an encouraging trend for a survival benefit with sugemalimab vs. placebo was observed with follow-up of patients ongoing.
- Median OS was not reached for sugemalimab vs. 24.1 months for placebo (HR=0.44).
- Sugemalimab had a well-tolerated safety profile and no new safety signals were observed.

These results build upon recently updated data from the GEMSTONE-302 study in stage 4 NSCLC, positioning sugemalimab as a potential treatment option for both stage 3 and 4 NSCLC.

Tecentriq shows promise in treating early-stage lung cancer

The phase III IMpower010 trial reinforced the significant disease-free survival benefit offered by Tecentriq (atezolizumab) for people with stage II-IIIA non-small cell lung cancer whose tumors express PD-L1≥1%.

Tecentriq is sponsored by Genentech.

These results were presented at the European Society for Medical Oncology Congress 2021 Presidential Symposium and published in *The Lancet*.

In IMpower010, treatment with the adjuvant Tecentriq, following surgery and chemotherapy, reduced the risk of disease recurrence or death by 34% (HR=0.66, 95% CI: 0.50-0.88) in people with stage II-IIIA NSCLC whose tumors express PD-L1≥1%, compared with best supportive care.

Tecentriq offers a DFS benefit in the stage II-IIIA patient population irrespective of the stage of disease and across the main prior therapies. Specifically, time to relapse appeared to be improved with Tecentriq, compared with BSC, among people with stage II-IIIA NSCLC whose tumors express PD-L1 TC ≥1%, for both locoregional and distant sites.

There was no clear difference in patterns of relapse. An extended analysis of PD-L1 subgroups in the stage II-IIIA population shows there is a higher magnitude of benefit from adjuvant Tecentriq in people with PD-L1 expression ≥50%, compared with those with 1-49% PD-L1 expression. The exploratory nature of the analysis in patients with 1-49% PD-L1 expression prevents any firm conclusions, and these data will be further analyzed and shared at a future medical congress.

Additional IMpower010 data, recently presented at the International Association for the Study of Lung Cancer 2021 World Conference on Lung Cancer Presidential Symposium, showed that treatment with Tecentriq improved DFS in the PD-L1≥1% stage II-IIIA NSCLC population, compared with BSC, regardless of most surgery types and adjuvant chemotherapy regimens.

Safety data for Tecentriq were consistent with its known safety profile and no new safety signals were identified.

Based on the IMpower010 data, the FDA recently granted Priority Review to Tecentriq as an adjuvant treatment for certain people with early NSCLC and is reviewing the application under the Real-Time Oncology Review pilot program. The FDA is expected to make a decision on approval by December 1, 2021.

MIT study finds global cancer risk from burning organic matter comes from unregulated chemicals

MIT researchers found that benzo(a)pyrene plays a small part—about 11%—in the global risk of developing polycyclic aromatic hydrocarbons (PAHs)-associated cancer.

PAHs are a class of pollutants that are known to cause lung cancer. Although most of the regulatory science and standards for PAHs are based on benzo(a)pyrene levels, 89% of that cancer risk comes from other PAH compounds, many of which are not directly regulated.

The study was published in *GeoHealth*.

About 17% of PAH-associated cancer risk comes from "degradation products"—chemicals that are formed when emitted PAHs react in the atmosphere. Many of these degradation products can in fact be more toxic than the emitted PAH from which they formed.

The team hopes the results will encourage scientists and regulators to look beyond benzo(a)pyrene, to consider a broader class of PAHs when assessing a community's cancer risk.

MIT co-authors include Noelle Selin, Jesse Kroll, Amy Hrdina, Ishwar Kohale, Forest White, and Bevin Engelward, and Jamie Kelly (now at University Col-

lege London). Peter Ivatt and Mathew Evans at the University of York are also co-authors.

When the researchers compared calculated PAH-associated cancer risks around the world, they found significant differences depending on whether that risk calculation was based solely on concentrations of benzo(a) pyrene or on a region's broader mix of PAH compounds.

"If you use the old method, you would find the lifetime cancer risk is 3.5 times higher in Hong Kong versus southern India, but taking into account the differences in PAH mixtures, you get a difference of 12 times," lead author Kelly said in a statement. "So, there's a big difference in the relative cancer risk between the two places. And we think it's important to expand the group of compounds that regulators are thinking about, beyond just a single chemical."

Four out of five cancer therapies tested in phase III trials do not achieve clinically-meaningful benefit in prolonging survival

A study published in the *Journal of the National Comprehensive Cancer Network* found that more than 80% of therapies tested in phase III oncology trials did not achieve meaningful clinical benefit in prolonging survival.

The researchers analyzed 362 industry-sponsored phase III randomized trials in oncology from 2008 to 2017, and found that 87% were either false-positive or true-negative for meeting overall survival goals. More than half of the initially reported positive trials were found to be false-positive (58.4%) for overall survival, while the overwhelming majority of negative results were determined to be true-negative (with only 0.9% false-negative).

"Our study highlights the need to more efficiently identify which new therapies merit phase III testing," said lead researcher Changyu Shen, PhD, associate professor at Harvard Medical School at the time this study was conducted. "In order to sustain the rate of innovation in cancer therapeutics and ensure that our patients have access to effective yet affordable therapies, the clinical trial pipeline in oncology must be efficient and accurate. Our work shows that in the past ten years, this has not been the case."

"Our study shows that reducing false positive errors by imposing a more stringent statistical threshold in Phase III trials is not likely to be practically feasible," Shen said. "A better strategy is to rethink the process that leads to the decision of moving a new therapy to phase III testing to begin with. More research is needed in this regard."

Most of the trials in this novel study focused on lung, breast, gastrointestinal, and hematologic cancers; trials with fewer than 100 participants were excluded, meaning rare cancer types were less likely to be included. The phase III trials were predominately two-arm studies of an interventional regimen compared with a control treatment.

"This paper shows that a lot of drugs with 'positive' phase III trials may have a smaller ultimate benefit than was expected, and that changing the threshold for statistical significance is not a quick fix," said Elizabeth A. Handorf, associate research professor, Fox Chase Cancer Center, who was not involved in this research. "I think it highlights the need for more efficient study designs, like adaptive trials, and clear definitions of what makes an effect clinically meaningful."

DRUGS & TARGETS

Jakafi receives FDA approval for treatment of chronic GVHD

Jakafi (ruxolitinib) has received FDA approval for treatment of chronic graft-versus-host disease after failure of one or two lines of systemic therapy in adult and pediatric patients 12 years and older.

Jakafi is sponsored by Incyte.

The FDA approval was based on the REACH3 trial, a phase III, randomized, open-label, multicenter study of Jakafi in comparison to best available therapy for treatment of steroid-refractory chronic GVHD after allogeneic stem cell transplantation. The primary endpoint of overall response rate at Week 24 (i.e., Cycle 7 Day 1) was 49.7% for Jakafi compared to 25.6% for BAT ($P<0.0001$). Furthermore, the ORR through Cycle 7 Day 1 was 70% for Jakafi compared to 57% for BAT2.

Full results from the REACH3 study were published in the *New England Journal of Medicine*.

Jakafi's supplemental New Drug Application in chronic GHVD was reviewed under the FDA's Priority Review program as well as the Project Orbis program, an initiative of the FDA Oncology Center of Excellence.

Cabometyx receives FDA approval for patients with previously treated radioactive iodine-refractory differentiated thyroid cancer

Cabometyx (cabozantinib) has received FDA approval for the treatment of adult and pediatric patients 12 years of age and older with locally advanced or metastatic differentiated thyroid cancer that has progressed following prior vascular endothelial growth factor receptor-targeted therapy and who are radioactive iodine-refractory or ineligible.

The FDA granted Cabometyx Breakthrough Therapy designation and Priority Review.

Cabometyx is sponsored by Exelixis, Inc.

The approval is based on results from COSMIC-311, a phase III pivotal trial evaluating Cabometyx versus placebo in patients with radioactive iodine-refractory DTC who progressed after up to two prior VEGFR-targeted therapies. Results were presented at the 2021 European Society of Medical Oncology Congress.

At a planned interim analysis, Cabometyx significantly reduced the risk of disease progression or death versus placebo ($p<0.0001$) in the intent-to-treat population. At a follow-up analysis with a median follow-up of 10.1 months, the median progression-free survival as assessed by blinded independent radiology committee was 11.0 months for patients treated with Cabometyx (n=170) compared with 1.9 months for patients treated with placebo (n=88); HR:0.22; 95% CI: 0.150-.31.

Cabometyx improved PFS versus placebo irrespective of prior exposure to lenvatinib and/or sorafenib.

An updated analysis for the primary endpoint of objective response rate as assessed by BIRC in the ITT population favored Cabometyx at 11%, including one complete response, versus 0% for placebo. Median overall survival, an additional endpoint, was 19.4 months for patients treated with Cabometyx and not estimable for patients treated with placebo (HR: 0.76; 95% CI: 0.45-1.31).

The safety profile was consistent with that previously observed for Cabometyx, and adverse events were managed with dose modifications.

Brukinsa receives FDA accelerated approval for marginal zone lymphoma

Brukinsa (zanubrutinib) has received FDA accelerated approval for adult patients with relapsed or refractory marginal zone lymphoma (MZL) who have received at least one anti-CD20-based regimen.

Brukinsa is sponsored by BeiGene.

Approval is based on two open-label, multicenter, single-arm trials: BGB-3111-214 (NCT03846427), which evaluated 66 patients with MZL who received at least one prior anti-CD20-based therapy, and BGB-3111-AU-003 (NCT02343120), which included 20 patients with previously treated MZL. Brukinsa was administered orally at 160 mg twice daily or 320 mg once daily.

The efficacy measures were overall response rate and duration of response, as assessed by an independent review committee using the 2014 Lugano criteria. In the first trial, the CT-based ORR was 56% (95% CI: 43%, 68%), with 20% achieving complete responses.

In the second trial, the ORR was 80% (95% CI: 56%, 94%), with a CR rate of 20%. The median DoR was not estimable; the estimated 1-year rate of DoR was 85% (95% CI: 67, 93) and 72% (95% CI: 40, 88), respectively.

Tivdak granted FDA accelerated approval for recurrent or metastatic cervical cancer

The FDA granted accelerated approval to Tivdak (tisotumab vedotin-tftv), a tissue factor-directed antibody and microtubule inhibitor conjugate, for adult patients with recurrent or metastatic cervical cancer with disease progression on or after chemotherapy.

The drug is sponsored by Seagen Inc.

Approval was based on innovaTV 204, an open-label, multicenter, single-arm clinical trial. Efficacy was evaluated in 101 patients with recurrent or metastatic cervical cancer who had received no more than two prior systemic regimens in the recurrent or metastatic setting, including at least one prior platinum-based chemotherapy regimen.

Sixty nine percent of patients had received bevacizumab as part of prior systemic therapy. Patients received Tivdak

2 mg/kg every 3 weeks until disease progression or unacceptable toxicity.

The main efficacy outcome measures were confirmed objective response rate, as assessed by an independent review committee using RECIST v1.1, and duration of response. The ORR was 24% (95% CI: 15.9-33.3%) with a median response duration of 8.3 months (95% CI: 4.2, not reached).

Cancer-detecting software Paige Prostate authorized for marketing by FDA

The FDA authorized the marketing of Paige Prostate, a software program which assists pathologists in the detection of areas that are suspicious for cancer as an adjunct to the review of digitally-scanned slide images from prostate biopsies.

Paige Prostate is the first artificial intelligence-based software designed to identify an area of interest on the prostate biopsy image, to be reviewed further by the pathologist if the area of concern was not already identified on initial review.

Paige Prostate was developed by Paige AI.

"The authorization of this AI-based software can help increase the number of identified prostate biopsy samples with cancerous tissue, which can ultimately save lives," Tim Stenzel, director of the Office of In Vitro Diagnostics and Radiological Health in the FDA's Center for Devices and Radiological Health, said in a statement.

Paige Prostate is compatible for use with slide images that have been digitized using a scanner. The digitized slide image can then be visualized using a slide image viewer.

The FDA evaluated data from a clinical study where 16 pathologists examined 527 slide images of prostate biopsies (171 cancer and 356 benign) that were digitized using a scanner. For each slide image, each pathologist completed two assessments, one without Paige Prostate's assistance and one with Paige Prostate's assistance.

While the clinical study did not evaluate the impact on final patient diagnosis, which is typically based on multiple biopsies, it found that Paige Prostate improved detection of cancer on individual slide images by an average of 7.3% when compared to pathologists' unassisted reads for whole slide images of individual biopsies, with no impact on the read of benign slide images.

Potential risks include false negative and false positive results, which is mitigated by the device's use as an adjunct (e.g., the device assists pathologists reviewing slide images) and by the professional evaluation by a qualified pathologist who takes into account patient history among other relevant clinical information, and who may perform additional laboratory studies on the samples prior to rendering a final diagnosis.

FDA grants Fast Track designation to novel immunotherapy targeting solid tumors

The FDA granted Fast Track designation to CT-0508, a human epidermal growth factor receptor 2 targeted chimeric antigen receptor macrophage for the treatment of patients with solid tumors.

CT-0508 is sponsored by Carisma Therapeutics. It was developed by Saar Gill, scientific co-founder of CARISMA Therapeutics and associate professor of hematology-oncology in the Perelman School of Medicine at the University of Pennsylvania, and Michael Klichinsky, scientific co-founder and senior vice president of discovery at CARISMA Therapeutics.

CT-0508 is currently being evaluated in a first-in-human phase I multi-center clinical trial that focuses on patients with recurrent or metastatic HER2-overexpressing solid tumors whose cancers do not have any approved HER2-targeted therapies or who do not respond to treatment.

Preclinical findings for CT-0508 published in *Nature* indicated that CAR-M therapy may have the potential to overcome challenges that T-cell therapies have encountered in the solid tumor setting.

Opdivo + chemo receives positive CHMP opinion for gastric, gastroesophageal junction, esophageal adenocarcinoma

The Committee for Medicinal Products for Human Use of the European Medicines Agency recommended approval of Opdivo (nivolumab) in combination with fluoropyrimidine and platinum-containing chemotherapy for the first-line treatment of adult patients with HER2-negative advanced or metastatic gastric, gastroesophageal junction, or esophageal adenocarcinoma whose tumors express PD-L1 with a combined positive score ≥ 5.

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

Opdivo is sponsored by Bristol Myers Squibb.

This positive opinion is based on results from the pivotal phase III CheckMate -649 trial, in which first-line treatment with Opdivo plus leucovorin, 5-fluorouracil and oxaliplatin, or capecitabine and oxaliplatin was compared to treatment with chemotherapy alone. Expanded analysis from CheckMate -649 was presented during the 2021 American Society of Clinical Oncology Annual Meeting.

Results showed a statistically significant and clinically meaningful improvement in overall survival and progression-free survival in patients with unresectable advanced or metastatic GC, GEJ cancer, or EAC whose tumors express PD-L1 with a combined positive score ≥ 5. The statistically significant OS benefit shown with Opdivo plus chemotherapy was also observed in PD-L1 positive patients with CPS ≥ 1 and in the all-randomized population.

The safety profile observed for Opdivo plus chemotherapy in the CheckMate -649 trial was consistent with the known safety profiles of the individual treatments.

Opdivo in combination with fluoropyrimidine- and platinum-containing chemotherapy is approved in the United States for the treatment of patients with advanced or metastatic gastric cancer, gastroesophageal junction cancer, and esophageal adenocarcinoma, regardless of PD-L1 expression status.

Keytruda + chemo receives positive CHMP opinion in TNBC indication

The Committee for Medicinal Products for Human Use of the European Medicines Agency recommended approval of Keytruda (pembrolizumab), an anti-PD-1 therapy, in combination with chemotherapy for the treatment of locally recurrent unresectable or metastatic triple-negative breast cancer in adults whose tumors express PD-L1 (Combined Positive Score ≥10) and who have not received prior chemotherapy for metastatic disease.

The CHMP's recommendation will now be reviewed by the European Commission for marketing authorization in the European Union.

Keytruda is sponsored by Merck.

The positive opinion is based on progression-free survival and overall survival results from the phase III KEYNOTE-355 trial, which showed that treatment with Keytruda in combination with chemotherapy (nab-paclitaxel, paclitaxel or gemcitabine/carboplatin), as compared to chemotherapy alone, significantly improved progression-free survival and overall survival in these patients.

OS data from KEYNOTE-355 were presented at the European Society for Medical Oncology Congress 2021.

Keytruda plus chemotherapy reduced the risk of death by 27% (HR=0.73 [95% CI, 0.55-0.95]; p=0.0093) in patients with mTNBC whose tumors expressed PD-L1 (CPS ≥10), as compared to chemotherapy alone. There was an increase of 6.9 months in median OS with Keytruda plus chemotherapy compared to chemotherapy alone (23.0 months [95% CI, 19.0-26.3] vs. 16.1 months [95% CI, 12.6-18.8], respectively). Although the trial was not powered to compare efficacy between treatment groups by different chemotherapy regimens, the increase in OS was observed for Keytruda plus chemotherapy across the three chemotherapy choices.

There was no statistically significant difference in OS between the treatment groups in the CPS ≥1 population; due to statistical testing hierarchy, formal testing was not performed in the intention-to-treat population. The incidence of treatment-related adverse events was similar among patients in the two treatment groups, with Grade 3-5 TRAEs occurring in 68.1% of patients in the Keytruda plus chemotherapy arm and 66.9% of patients in the chemotherapy arm.

These OS data are in line with prior analyses from KEYNOTE-355.

In the U.S., Keytruda was granted accelerated approval by the FDA in November 2020 and was subsequently granted regular approval in July 2021.