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DAN HAYES WITNESSED CANCER HISTORY, NOW HE IS DOCUMENTING IT IN A PODCAST

Daniel Hayes is racing to record the stories of oncology's greats.

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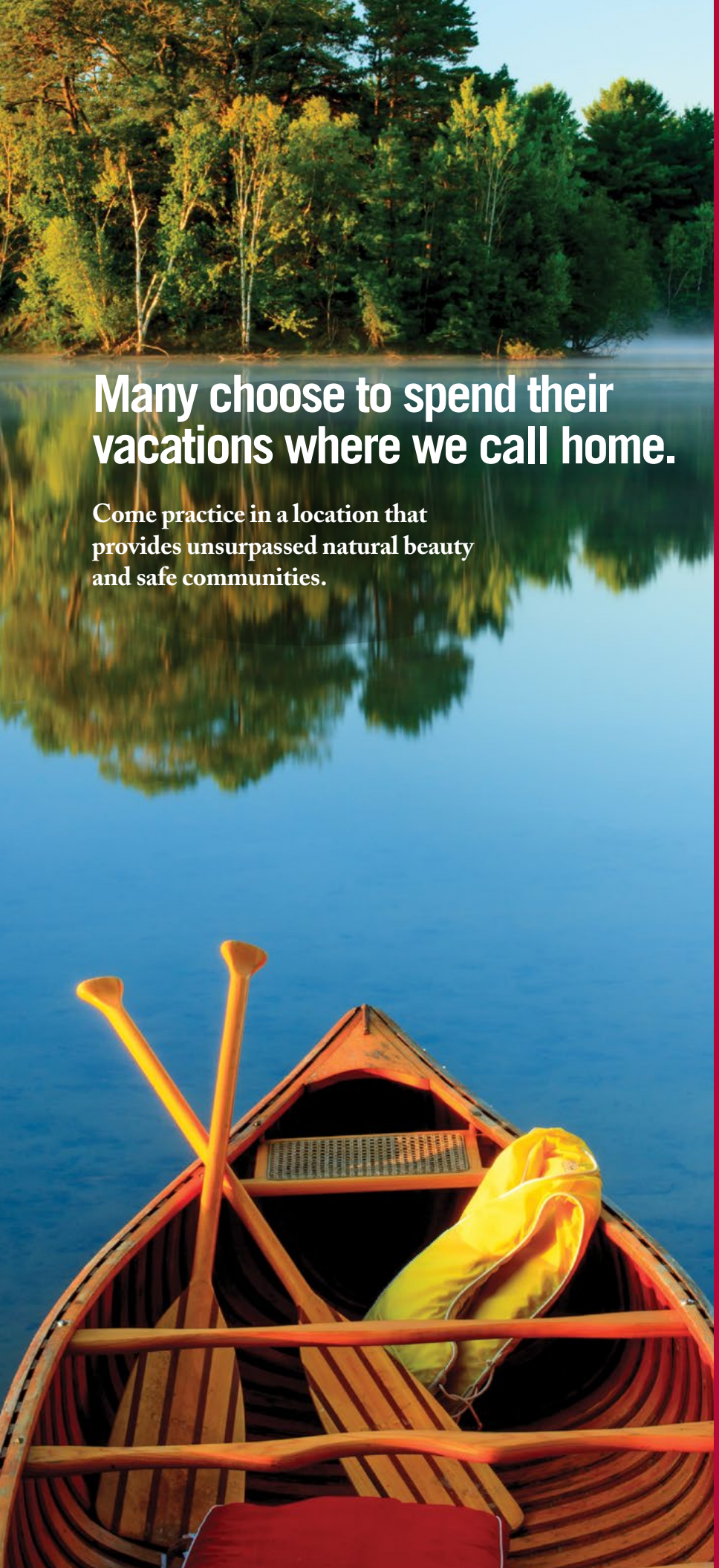

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In this issue

DAN HAYES WITNESSED CANCER HISTORY, NOW HE IS DOCUMENTING IT IN A PODCAST

Daniel F. Hayes, MD
The Stuart B. Padnos Professor of Breast Cancer Research, Professor of internal medicine, University Michigan Rogel Cancer Center

Q & A

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

CONVERSATION WITH THE CANCER LETTER

CANCER HISTORY PROJECT

Daniel Hayes is racing to record the stories of oncology's greats.

In May 2018, Hayes, the Stuart B. Padnos Professor of Breast Cancer Research and professor of internal medicine at University Michigan Rogel Cancer Center, started to conduct interviews with friends, mentors, and colleagues.

The podcasts are published in the *Journal of Clinical Oncology*'s *Cancer Stories*.

"I try to make it—if you could be in a cab for 20 minutes with one of your heroes, like we do if you like sports, or medicine, or literature, or music, and just say—'How did you do this? What made you think you could even do this sort of thing?'" Hayes said to *The Cancer Letter.*

Hayes's podcast, a program of the American Society of Clinical Oncology, is a part of a larger effort to commemorate the history of the cancer field in 2021.

Hayes is a member of the editorial board of the Cancer History Project, a collaborative historical resource created by *The Cancer Letter* that places—in perpetuity—a vast collection of archives and historical analysis within easy reach of researchers, medical professionals, students, policy-makers, and survivors. ASCO is a contributor to the Cancer History project, as well as a platinum sponsor.

Cancer centers, advocacy groups, professional societies, pharmaceutical companies, and key players in oncology are invited to join our growing list of contributors. To inquire, contact admin@cancerhistoryproject.com.

NCI, too, is commemorating the National Cancer Act in an effort to build a coalition of support for cancer research, including raising the payline to 15% by 2025. NCI's tagline for the campaign—"Nothing will stop us"—is available to cancer centers, professional societies, and others. NCI is also a contributor to the Cancer History Project, with over 50 published articles—all primary sources.

The Cancer History Project is highlighting oral histories of cancer research, including a selection of National Cancer Act oral histories and numerous videos. A growing list of books is also available.

In his podcasts, Hayes tries to avoid the minutiae.

"I try to tease out of them, 'What were the things that made you believe you could do this? What were the obstacles? How did you get around them?'" Hayes said.

Hayes has collected an unabridged history of sorts—in one instance, the late Emil J Freireich, a pioneer in the treatment of chemotherapy and professor in the Department of Leukemia, Division of Cancer Medicine at MD Anderson Cancer Center, divulged that he stole and sold hubcaps to help pay for medical school.

MD Anderson is also a contributor to the Cancer History Project.

"He told me that story. I said, 'I can't believe this. The father of my field was a juvenile delinquent.'"

Hayes' biggest obstacle is time. He was fortunate to have interviewed Clara Bloomfield, Distinguished University Professor at The Ohio State University, former director and longtime senior adviser to The Ohio State University Comprehensive Cancer Center – James, just before she died.

"Clara reluctantly agreed at some point, and said 'Why do you care about me?' and I said, 'Because, you're famous. That's why.' We had an interview that was, if you listen to it—at times it was contentious," Hayes said. "And then, sadly, about a week or two weeks be-

> "I think it's important for, especially our young doctors, to know that what they're doing didn't just suddenly appear. It took a lot of work and courage. I think that becomes inspirational."

fore we got it edited—and about two or three weeks before we got it posted, she fell and had died. That was really too bad, because I think she would've enjoyed hearing it."

Bloomfield died in March 2020.

There are many people Hayes didn't get to in time—"I wanted to get Jimmie Holland, but unfortunately, she and Jim [Holland] both died before I had a chance to do that."

Bernard Fisher, who revolutionized the field of breast cancer, died podcastless in October 2019.

"Unfortunately, Bernie Fisher was still alive, but was unable to be interviewed, because of his age (he was 99 years old when the podcast program started)," Hayes said. "To think about what Bernie Fisher did to get surgeons to run randomized trials, which they'd never heard of—specifically to challenge their dogma, and to challenge what Halsted said."

Hayes likes the storytelling format of a podcast.

"It's important for, especially our young doctors, to know that what they're doing didn't just suddenly appear. It took a lot of work and courage. I think that becomes inspirational," Hayes said. "The fellows don't have time to learn history—this is a good problem. There's so much about oncology to know now. Whereas, when I trained, basically there were five or six diseases that we could actually treat. Now, there's all kinds of stuff. It takes a lot to learn all that."

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

Alexandria Carolan: Let's jump into it then. I spoke with you a while back, actually, when I was at ASCO. We ran a story in *ASCO Connection*, super brief, just about the podcast. I remember the reason why you got the idea for it and got started was super interesting. Could you talk about that?

Dan Hayes: I, just by happenstance, am an oncologist. I had little or no interest in being an oncologist. I was going to be an endocrinologist. In my third year as a medical student, I was assigned to the oncology ward at University Hospital at Indiana University—which is where I was a medical student. I recall thinking, "This is going to be a terrible month." In fact, I went to the chief resident and said, "Can I do anything else besides oncology?" I told him I'd do GI, which in my opinion is the absolute worst. He said, "Shut up. You're a med student, go do what you're told." The attending physician that month was Dr. Larry Einhorn. This was 1977, and he was busy proving he could cure testicular cancer with cisplatin. It was just an unbelievable month.

These young men were coming in, and their X-rays looked like that wall—and then they'd come in a month later, and look like that window. We didn't have CT scans in those days, but we had chest X-rays. It was really exciting, and I was hooked: I would be an oncologist.

By-the-way, Dr. Einhorn's first cure, is a social friend of mine. John Cleland. And, he's gone on to be married, and have several children, and had a great career as a high school teacher, and a track and field coach, and it's really a great story. The reason I'm telling you all of this. I got them on one of the podcasts.

Fantastic.

DH: Of course, they've remained very close through the years, and Dr. Einhorn and I have remained close, and John and I remain close. So, the three of us triangulate. I just sort of threw some raw meat on the table with a couple of questions, and let them talk to each other. And it's just incredible. What is it, 40 years later now? He was cured in 1973. So, almost 50 years later.

And they were talking about what it was like then, and some of the stories. I think that's a really great underlining of this whole story.

After medical school, I did my residency at UT Southwestern in Dallas, and subsequently I got into what was then the Sidney Farber Cancer Institute for my fellowship. At the time, Emil "Tom" Frei was the physician chief, and remained so for 12 of my 14 years there. As you probably know, he and Emil J. Freireich, and the late Jim Holland were all together at the NCI, and put together the first clinical trial combination therapy for childhood ALL, which led to going from a 0% cure rate, when people were just getting one drug, and a patient would progress, and they'd try another one, and a patient progressed, to a 10% cure rate. Now, it's 95% , or close to it.

That was really the first great step forward. Dr. Frei was one of my mentors in many ways for most of the time I was there. He and my laboratory mentor, Don Kufe, introduced me to Dr. Holland. I got to know Dr. Holland very well through the years, and his wife Jimmie C. Holland, who had started the field of psycho-oncology. A real power couple. My brother's a psychiatrist, and he happened to work with Jimmie quite a bit. So, again then, I fell into another situation in which I was associated with pioneers in our field.

At DFCI, the division chief was George P. Canellos, who was part of the so-called "gang of five" at the NCI that put together MOPP and CHOP. Dr. Canellos also developed CMF for breast cancer, all which had a huge impact on the field. They showed you could cure Hodgkin's Disease with MOPP, and that you could cure non-Hodgkin's lymphoma with CHOP, and CMF was one of the first combination treatments for breast cancer. Subsequently, Dr. Gianni Bonadonna took CMF back to Italy and proved that it was effective in the adjuvant setting.

Also at Dana Farber, the fellowship director for 25 years was Dr. Robert J. Mayer, and you look at the people he trained during that time—they are now cancer center directors, division chiefs, Nobel Prize winners (2019: William G. Kaelin). It's really remarkable. And I was just sort of in the middle of all this maelstrom that was going on.

Fast forward 35 years, when I became president of ASCO, two things occurred to me.

One: that I've been in the middle of a lot of really great people through the years, just being in the right place at the right time.

Two: that these are the people that started our field. There aren't many fields that are sufficiently young enough that people who started the field are still alive.

Also, just as I was elected president, I lost my hearing in my left ear. I ended up getting a cochlear implant towards the end of my presidency. I'm not looking for sympathy. I'm very open to sympathy—it's worked out great. But this is directly related to the podcast program.

My physical therapy for my cochlear implant was listening to podcasts. I'd never heard of a podcast, I guess because I'm a little over 65. I began to listen to all podcasts I could get my hands on, including several ASCO podcasts. I initially listened to ASCO podcasts about clinical issues, and about government policy issues. For example, our CEO Cliff Hudis just did a couple of really great ones. And then I listened to the Cancer Stories podcast series that Lidia Schapira has done such a great job in establishing.

Further, I began listening to all the NPR podcasts, and finally I said, "Gee, if Terry Gross can do this, so can I." And so I got ASCO, and Lidia, to agree to allow me to serve as a host, and I gave them a list of people I want to interview—and ASCO also provides the services of a really talented staff person, Ashley Ketelhut, who has been the key to making the podcasts happen.

There are around 400 ASCO staff, so when I was president I tried but I didn't get to meet everybody. I didn't know Ashley, but I do now. She's been just terrific. I keep thinking she's going to complain, because it's been a lot of work for her. But, she hasn't. She puts us together, and she records them.

Basically, I try to make it—if you could be in a cab for 20 minutes with one of your heroes, like we do if you like sports, or medicine, or literature, or music, and just say, "How did you do this? What made you think you could even do this sort of thing?" sort of thing.

People can listen on their way to work—20 minutes. Principally, I ask the same questions, but I do some homework beforehand, and Google people and figure out what they are and what they've done, who they are. More than I knew about them before. And then try to tease out of them, not just kind of dry... "Well, we saw a 14% difference in overall survival in the P-value," well, I don't care about that. I try to tease out of them, "What were the things that made you believe you could do this? What were the obstacles? How did you get around them?"

I think I told you that probably my favorite story is from Dr. Freireich. He got into medical school when he was 16. He had grown up basically in a ghetto in Chicago, living in a ghetto with his mother. His mother was ironing clothes to support him and his family. And he needed money, so he started stealing hubcaps, selling hubcaps so he could go to medical school.

He told me that story. I said, "I can't believe this. The father of my field was a juvenile delinquent."

One of the other stories I really enjoyed was told by Dr. Saul Rosenberg. He trained in radiation oncology at Memorial Sloan Kettering, back in the '50s, maybe early '60s. Then he went to Stanford to work with Dr. Henry Kaplan. Dr. Kaplan had demonstrated that you could cure Hodgkin's Disease with radiation oncology, and he wrote the book on Hodgkin's disease that's just incredible. Sadly, he passed away many years ago.

But anyway, Dr. Rosenberg went out to California to work with Dr. Kaplan, but before he did he heard there was this guy named Karnofsky, who was giving chemotherapy at MSK—and I think you're aware of this, but of course ASCO's most prestigious award is named after Dr. Karnofsky.

Dr. Rosenberg went to him and said, "I want to learn how to give chemotherapy." And in those days it didn't take long to learn how to give chemotherapy, because there wasn't much chemotherapy to learn about. And then he went to Stanford, and he went to Dr. Kaplan and said, "I know you are curing people with radiation, but we need to start giving chemotherapy too. Because, I was just on the East Coast, and they're curing people who have metastasis beyond the field you can treat with radiation."

And to his credit, Dr. Kaplan apparently really embraced this, said, "I'm actually

in favor of it. Do what you need to do." Well, he went to the chair of medicine, who said, "This chemotherapy is crazy. It makes people sick, doesn't help anybody, and you're not even an internist. You're a radiation oncologist, and forget it. We're not going to do this."

But he got a hematologist to give a room in the hematology clinic, and so, he set up a clinic room. He told me that he would see patients in the room, and if he thought they needed chemotherapy, he had a chair in the hallway outside their room with an IV pole. He'd mix up the chemotherapy himself, because there were no oncologic nurses.

He'd mix up the chemotherapy himself. Then he would put the patient in the chair, start the IV himself, and drip the chemotherapy in while he saw the next patient in the room.

I said, "You know, that's a little different than what the fellows learned about these days." This is exactly the kind of story I want.

I really enjoyed doing this. I've got some great stories. I tried to branch out from just the people who started giving chemotherapy to some of the other issues, like anti-estrogen therapy for breast cancer. Dr. Trevor Powles in Great Britain was really great on that one. The other thing is, the people that started the fields of translational research, for example, Drs. Clara Bloomfield, John Minna, and Marc Lippman.

Right, we ran her obituary last year (*The Cancer Letter*, March 6, 2020).

DH: Clara and I worked together in CALGB. Because, I started doing translational science stuff in breast cancer, and since she was doing it for leukemia and lymphoma, and kind of let me squeeze in.

Clara was a really tough cookie. I loved her, but she was tough. She and I had several knock down-drag outs, where then we'd go out and get a drink. So I emailed her and said, "Clara, I want to interview you for this." She said—"well, what do you want to do that for?" "Well, because you started the field of translational science, arguably—in oncology, in leukemia and lymphoma—and you're one of the few women who was at the forefront who's still with us."

For example, two of the really courageous pioneers in our field have both passed away long before I started the podcast series: Dr. Jane Cooke Wright was one of the founding members of ASCO, but she passed away in 2013. [A collection of archives about women in oncology is available here.]

Dr. Janet Rowley, at University of Chicago, started the field of cancer genetics, but she died several years ago. And as I said, I very much wanted to interview Jimmie Holland, but unfortunately, she and her husband Jim both died before I had a chance to do that.

Clara reluctantly agreed at some point, and said "Why do you care about me?" and I said, "Because, you're famous. That's why." We had an interview that was, if you listen to it—at times it was contentious. I would say, "Well, what made you decide that?" "Oh, I don't know. I can't remember."

I said, "Yes you can. Come on." It was actually a pretty good interview. I have to say.

That's amazing.

DH: And then, sadly, about a week or two weeks before we got it edited—and about two or three weeks before we got it posted, she fell and had died. That was really too bad, because I think she would've enjoyed hearing it.

So, I got to interview her. I've also interviewed Marc Lippman, who was one of the first translational scientists in solid tumors with breast cancer. He and the late William L. McGuire really changed the field, showing that observations in the laboratory (in their cases, the importance of estrogen receptor in breast cancer culture) could have profound effects in the clinic.. John D. Minna did the same thing in lung cancer. There are many others. I think I have, actually I was just going to count them when I came online here.

As I noted, I haven't just interviewed medical oncologists. Given his incredible contributions to the field, I really wanted to interview Dr. Bernie Fisher. Unfortunately, Bernie Fisher was still alive, but was unable to be interviewed, because of his age (he was 99 years old when the podcast program started). To think about what Bernie Fisher did to get surgeons to run randomized trials, which they'd never heard of—specifically to challenge their dogma, and to challenge what Halsted said.

So, I got hold of Norman Wolmark, who was his mentee and now runs the NSABP (now the NRG) and he basically took Dr. Fisher's position when he stepped down as director of the group.

I called Norm and said, "This is insulting. Because, you in your own right should be interviewed. But, I really want you to talk about Dr. Fisher. Is that okay?" And he went, "Oh, of course," and he was great. That's a really good interview too. Because, he talks a lot about the early days of the NSABP, and how he got all these surgeons to agree to challenge dogma. I don't think these young doctors realize how courageous that was, what Bernie Fisher did (*The Cancer Letter*, Oct. 25, Nov. 1, 2019). Norman's interview is just terrific—so much history and he tells it so well.

I've also interviewed radiation oncologists other than Dr. Rosenberg, in-

cluding Drs. Samuel Hellman and Allen Lichter. Dr. Lichter gave me a great interview, mostly about the history of radiation oncology. Not so much about ASCO. I'm going to circle back with him and do one specifically about ASCO, since he was the CEO for a decade.

The other one that I just did was with Patricia Ganz. Dr. Ganz is about my age or just a little older—so she's not one of the early, early pioneers, but she started the field of survivorship—and she and Jimmie Holland really initiated the field of non-oncologic therapy; in other words, treating the patient and not just the cancer. All of us have learned a lot from Patty Ganz, and I hope the listeners enjoy her interview as much as I did.

So, you've been doing this for about two years now?

DH: Actually, I was just thinking, "How long have I been doing this?" You know what? The first one I did was Dr. Hellman. Let me just see what date that is. About two and a half years. It was May of 2018.

And how often is the podcast posted?

DH: Not on any kind of specific timeline. About every two months or so.

> I began listening to all the NPR podcasts, and finally I said, 'Gee, if Terry Gross can do this, so can I.'

It sounds like it does really well. It's great to focus on cancer history at the moment because NCI is doing its commemoration of the National Cancer Act. Now is a good time to talk about it.

DH: Yeah, possibly one of my favorite interviews was with Vince DeVita, who really led the "gang of 5" at the NCI that I mentioned earlier, along with Drs. George Canellos, Bob Young, Bruce Chabner, and Philip Schein., In the interview with Dr. DeVita, we talked about the battles to get the National Cancer Act signed, since he was the NCI director when President Nixon signed it.

He's got lots of good stories. He just wrote a book, so many are in it, but one of the stories that he told me was about Mary Lasker.

The Lasker Award, named after her and her husband, is the so-called America's Nobel Prize. Indeed, several Americans who have won the Nobel Prize for Medicine and Physiology have won the Lasker Award prior to that. Her husband was an industrialist and they were quite wealthy, and they lived in Boston. They were very supportive of Dr. Farber as he was putting together the Sidney Farber Cancer Institute. And they were also very big donors to the Republican party.

So, there are two stories here.

One, it's not in my podcast, but she got Dr. Farber, and they went down and suggested to President Nixon that he better sign the National Cancer Act. And President Nixon, being a good Republican, said, "No. That's going to cost money. We're not going to do that." And she apparently said, "That's a shame. Because, all of my friends are giving money to your re-election campaign, and I just don't think they're going to be able to now." And so he signed it.

She called Dr. DeVita one morning when he was the Director of the NCI and said, "My chauffeur's going to pick you up at 10, and we're going to have lunch with Mrs. so-and-so here in DC," and Vince said, "Well, I'm kind of busy. I've got a full schedule, I'm director of the cancer center," and on and on."

She said, "No, this is going to be really important to the Cancer Act," and so, he agreed. He went to lunch, and there was a nicely dressed, older man who was there, and they had a nice lunch together, and he asked really good questions. Vince answered them to the best of his ability, and then the gentleman excused himself and left.

Dr. Devita assumed this must be a senator, or a U.S. representative. He didn't know who he was. He said, "Who was that?" and she said, "Well, that was Representative so-and-so's chauffeur." And he said, "I dropped everything and came over to have lunch with a chauffeur?" And she said, "Yup. He is the chauffeur's Representative so-and-so's wife all over DC—wherever she wants to go, and he's head of the committee that the bill is going through now. We need to get that committee. And I'm certain that she will tell him he has to sign it, and we'll get that out of committee so the president can sign it."

Those are the kind of stories I wanted to get on this. It's been a lot of fun.

Why is it important to document this history? What can we learn?

DH: George Santayana once said that, "Those who do not remember the past are doomed to repeat it." Besides, I like history anyway, and I like good stories.

I love to listen to the Moth on NPR. I like this kind of stuff. I think it's important for, especially our young doctors, to know that what they're doing didn't

just suddenly appear. It took a lot of work and courage. I think that becomes inspirational.

To think about what Bernie Fisher did to get surgeons to run randomized trials, which they'd never heard of—specifically to challenge their dogma, and to challenge what Halsted said: "This is how you have to do it." 75 years later, Fisher said, "I don't think so." And got a bunch of surgeons to do randomized trials. Plus, not only did he randomize trials to challenge their dogma, it challenged what they got paid to do.

I think that young doctors need to hear how all of this got started. The stories of giving combination chemotherapy. When I first started, I told some surgeon I wanted to be a medical oncologist, and that the adjuvant therapy for breast cancer was just thrilling. He just recoiled at this—that we would be giving women chemotherapy, make their hair fall out, make them throw up, kill some of them, when he was curing all these people with surgery by itself.

That was sort of the dogma. Now, the surgeons love us—please, make the tumor shrink. I think these kinds of things really need to be there in the minds of the young people. I don't think we teach history very well. Part of the problem is that there's so much to learn now.

The fellows don't have time to learn history—this is a good problem. There's so much about oncology to know now. Whereas, when I trained, basically there were five or six diseases that we could actually treat. Now, there's all kinds of stuff. It takes a lot to learn all that.

Is there anything else you'd like to add to this story?

DH: Well, there are two things. One is I hope more people will go listen, and I hope they enjoy it as much as I am. It doesn't take too long to listen to any of these, and you can listen to them on your way to work, or having morning coffee, whatever, since these days nobody drives to work anymore.

The other is, I'm open to suggestions. If people have suggestions they'd like to hear have interviewed, I can't guarantee I can do them, but I'm very open. I pretty much interviewed almost everybody on my original list.

I mean, you've done 20 interviews over two and a half years. That's really something.

DH: But again, a lot of these are my friends. Well, I knew Saul Rosenberg, but not very well. I only knew him because he always goes to the business meetings at ASCO. The only people at our annual business meetings are the ASCO board members, the staff, and a few scattered people who probably wandered in and realized it was a free lunch.

That sounds right.

DH: Saul Rosenberg is there every year. The only other interviewee I didn't really know well was Dr. Freireich. I had met Dr. Freireich a couple times, because he and Dr. Frei were really close friends, and Dr. Frei used to bring him up to the Dana Farber every once in a while to give a talk. Before the interview, I thought, "Boy, I hope I can get him to even talk." I wasn't sure if that was going to be a good one. I couldn't get him to shut up. He went on for an hour—and was just terrifically entertaining!

That's probably your biggest problem.

DH: Yeah, it was great. Just like me and you.

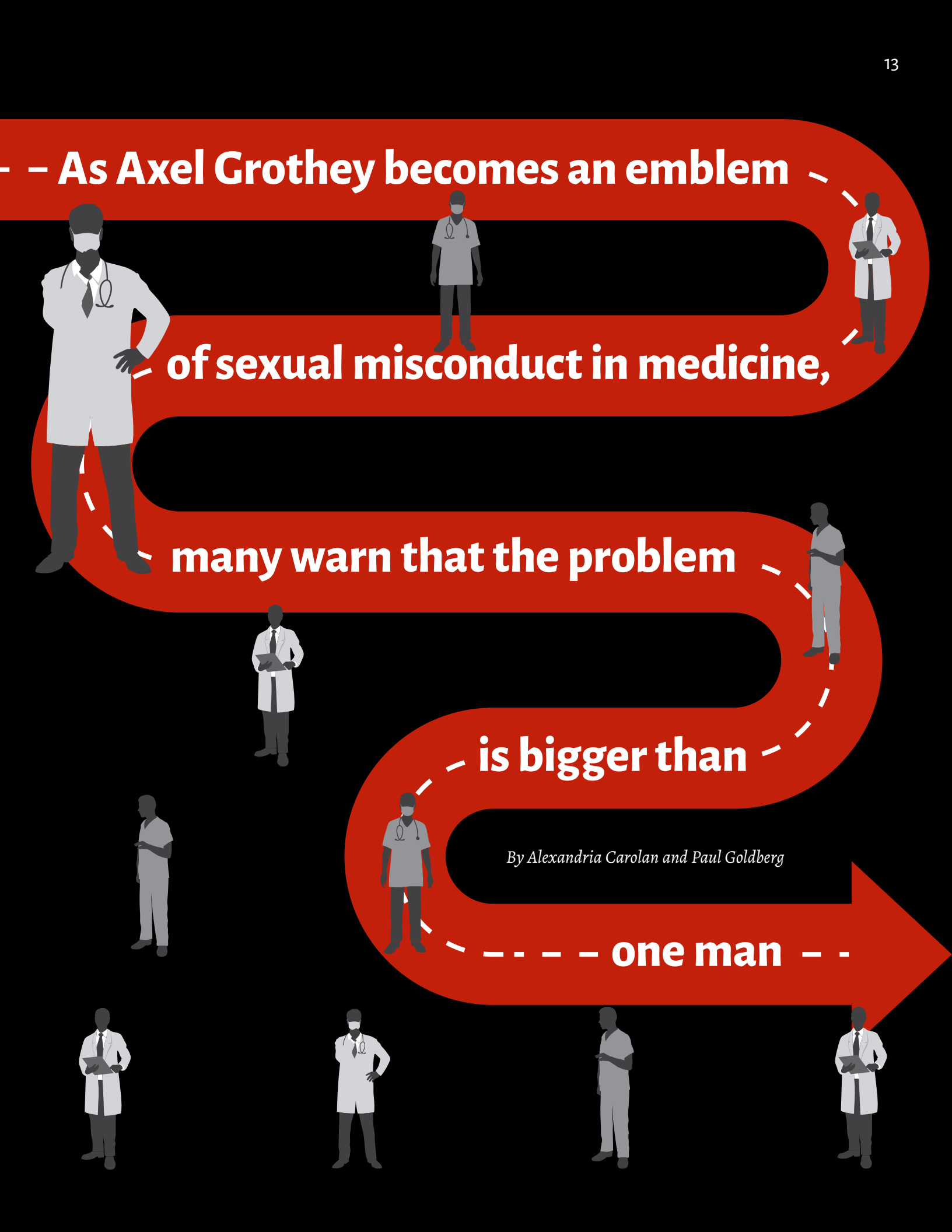
I hope that people enjoy it, and I'd love to do some others if they get good names of people. I mean, I'm not looking for people who are considered so-called giants now. I'm interested in folks who've really challenged dogma, and a generation above me, basically. Even two. I mean, Dr. Frei is two generations above me.

This was very helpful, and I think your podcast sounds really interesting. Thank you for sharing.

“I don't think we teach history very well. Part of the problem is that there's so much to learn now. The fellows don't have time to learn history—this is a good problem. There's so much about oncology to know now.”

As Axel Grothey becomes an emblem of sexual misconduct in medicine, many warn that the problem is bigger than one man

By Alexandria Carolan and Paul Goldberg



Inappropriate sexual relationships of the sort Axel Grothey engaged in at Mayo Clinic may be all too common.

The Grothey case is unique, because it has slipped out from under the cloak of confidentiality, making Grothey into a symbol of sexual misconduct, including abuse of power in the relationship between mentor and mentee.

The Cancer Letter's story about Grothey's misconduct has sparked a brush fire on social media. Hundreds of people spoke openly and loudly about a problem that is usually whispered about.

A groundswell of indignation and calls for accountability put pressure on the organizations that kept Grothey in leadership roles:

- Reacting to the story, NCI has removed Grothey from his position as co-chair of the NCI National Clinical Trials Network Gastrointestinal Steering Committee.
- The American Society of Clinical Oncology has disallowed Grothey from presenting at its 2021 virtual annual meeting June 4-8 and initiated formal disciplinary procedures.
- OneOncology, where Grothey was medical director of OneOncology Research Network, has removed him from that role.
- West Cancer Center, where Grothey is director of GI cancer research, said the oncology practice initiated an investigation.
- The University of Tennessee has started an investigation. Grothey has no formal affiliation with the university, but medical students have in the past rotated to West Cancer Center, where some may have been informally mentored by Grothey, officials said.

The list of groups that have censured or barred Grothey includes the COVID-19 and Cancer Consortium, Alliance for Clinical Trials in Oncology, ECOG-ACRIN Cancer Research Group, Fight Colorectal Cancer, and OncoAlert.

The message from the oncology community is clear: those who engage in sexual misconduct face penalties that include getting kicked off NCI advisory boards, thrown out of cooperative groups and editorial boards, fired, and barred from presenting at meetings of professional societies.

But none of this will matter much if the issue is limited to the misdeeds of one man rather than focusing on a pervasive problem in the culture of medicine, women in oncology warn.

The Hematology/Oncology women's Facebook group, also nicknamed The Wolfpack, has been rattled with heated discussions of gender equity in the aftermath of the Grothey story, which group members regard as just one example of how sexual misconduct and gender bias against women is systemic throughout oncology (*The Cancer Letter*, Oct. 2, 2020).

The Cancer Letter has compiled a Twitter Moment highlighting some of the discussions, feedback, and policy suggestions that have emerged in the wake of the Grothey story.

Selected tweets from #OncTwitter conversations follow:

- "I was shocked to read the @TheCancerLetter piece today. Heard from many colleagues that this behavior was known in the field and went on for years. Years." - @CharuAggarwalMD
- "Everyone knows someone. But nobody does anything. The onus is on those who have the most to lose (the junior faculty, the resident/fellow) to report when often they are desperate to move on from trauma. How can we support our most vulnerable to make themselves more vulnerable?" - @fumikochino
- "I'm an oncologist with access to the most powerful anti-nausea drugs in the world but this

paragraph has been making my stomach turn since I first read it in @TheCancerLetter last night. Lechery has no place in medicine or the academy." - @marklewismd

- "Maybe *this* is a new role of professional societies: If a faculty member is released after internal review process finds them wanting—it's reported to professional societies to create institutional memory nationally &confidentially. Then a tipping point is identified." - @DrSGraff
- "Alright - I'm about done with the 'I'm shocked' phase of this story and ready to move into what WE (the individuals who can collectively impart change) do. I think we need this. It's our profession, our mentees and our collective future." - @TGeorgeMD
- "UCSF HemOnc Fellows: For Roundtable this Friday, let's start this conversation locally. What are our program and institutional policies? What are their strengths and deficiencies in supporting victims and bringing about accountability? How do we achieve zero tolerance?" - @HemoncUcsf

One of the leaders of the Wolf Pack said that many women oncologists in the closed Facebook group were asking for what amounts to legal advice, seeking to understand the range of possible repercussions individuals could face as a consequence of reporting sexual misconduct by colleagues and mentors.

Mayo explains policy

In a paper published in *Mayo Clinic Proceedings* last year, the institution summarized the handling of sexual harassment claims on its campuses in Rochester, Arizona, and Florida.

Of the 88 substantiated allegations reported from 2017 to 2019, 31 individuals—including nine physician-scientists—received formal coaching; 22—including three physician-scientists—received warnings; and 35—including 10 physician-scientists—were terminated from employment or resigned before termination.

The paper didn't separate those who were terminated from employment from those who were allowed to resign under threat of termination.

Documents obtained by *The Cancer Letter* show that an internal investigation at Mayo had recommended that Grothey be dismissed, which prompted him to resign.

Mayo Clinic's Charanjit S. Rihal, chair of the Personnel Committee and corresponding author of the paper, said that all instances of sexual harassment that result in the end of employment are reported to the Minnesota Board of Medical Practice, regardless of whether the individual resigns or is fired.

Said Rihal:

> Respect for patients and colleagues is a core value of Mayo Clinic, and our organization takes sexual and other forms of harassment in the workplace seriously.
>
> Staff members have many resources available to them and are encouraged to speak up if they see or experience behaviors inconsistent with the values of our organization.
>
> When any physician is recommended for termination, the organization has made a determination that the person has engaged in serious misconduct which is in violation of its core policies and values to such a degree that an employment relationship can no longer exist.
>
> The fact that someone may quit before the ultimate conclusion is reached does not negate the organization's stance or impact post-separation action.

All instances of sexual harassment are reported to the board of medical practice, regardless of whether a resignation or termination occurs. Mayo Clinic fully cooperates with board investigations of reported sexually harassing behavior and complies with subpoenas that are issued by state boards.

Mayo Clinic also provides truthful information about corrective action taken when references are requested and credentialing inquiries occur, and encourages all organizations to perform thorough background and reference checks on all prospective hires.

Rihal said the paper didn't distinguish between termination and resignation under threat of termination because these categories are equivalent.

Mayo Clinic's article focused on our institutional approach to addressing sexual harassment, and not on the broader issue of how other entities can coordinate efforts to eliminate harassing behavior across healthcare.

Our article did not distinguish between termination and resignation because they are the substantially equivalent, as both occur after Mayo Clinic has made a recommendation for termination.

As previously stated, even when a resignation occurs prior to completion of the termination process, Mayo Clinic takes necessary actions, which include board reporting and cooperation with subpoenas issued by state boards.

Mayo Clinic also provides truthful information in connection with reference requests and credentialing inquiries. Mayo Clinic does not enter into severance or confidentiality agreements when a determination has been made that sexually harassing behavior has occurred.

If this statement is correct, licensure boards in other states as well as prospective employers would have been able to obtain accurate information about the circumstances of Grothey's departure from Mayo.

The Tennessee Department of Health, which in 2019 granted Grothey a license to practice medicine in the state, declined to comment on the matter. In three questionnaires submitted to state authorities, Grothey said he had not been disciplined or been forced to resign from any institution. On two occasions, Grothey responded "NO" to the following question:

- "Within the previous ten (10) years, have you ever been asked to or allowed to resign from or had any medical staff privileges restricted or not renewed by any hospital in lieu of or in settlement of a pending disciplinary action related to competence or character?"

Statements by organizations that condemned Grothey's sexual misconduct follow:

ASCO

Dr. Axel Grothey acknowledged a pattern of sexual misconduct, was reprimanded by state licensure boards and resigned from his employment rather than face termination for unethical sexual conduct.

Upon becoming aware of this abuse of power, ASCO initiated formal member discipline procedures and invoked its Event Conduct Policy to disallow Dr. Grothey from presenting at the 2021 ASCO Annual Meeting. Dr. Grothey is not an ASCO volunteer and is not eligible to be a volunteer while member discipline proceedings are pending.

ASCO policies and actions reflect an expectation that members of the Society will exercise professionalism, consideration, and respect in their speech and actions with zero tolerance for harassment or abuse of power.

ASCO also tweeted:

@ASCO: Our policy is that we have zero tolerance for sexual harassment in the workplace, at ASCO events, and by our members/volunteers/faculty https://fal.cn/3fNT2

In light of Dr. Grothey's admission of sexual misconduct & discipline by state medical boards, we have initiated formal member discipline procedures as well as invoked our Event Conduct Policy to disallow Dr. Grothey from presenting at #ASCO21

Thru our programs we're committed to promoting a culture of respect, equity, safety & accountability in the workplace & onc community. Join us Fri 6/4 at #ASCO21 for sessions on Moving Toward Equity & Dismantling Gender Disparities https://fal.cn/3fOys

We plan to continue this important conversation & invite women in oncology to join us for a prof dev webinar & discussion on gender bias & harassment in the workplace on 6/21 at 4 PM ET. Register surveymonkey.com/r/29WNXL6

OneOncology

We strongly condemn inappropriate workplace conduct of any

nature, and as a result we are removing Dr. Grothey as medical director of OneR.

While Dr. Grothey is not a One-Oncology employee, what we've recently learned regarding his actions at the Mayo Clinic does not align with our values and the Code of Conduct to which we hold our employees and contractors.

West Cancer Center

To uphold our commitment to workplace integrity and transparency, we've launched an internal investigation into Dr. Grothey.

Per company policy, we will not discuss ongoing personnel matters of current or past employees.

The University of Tennessee

The University of Tennessee does not have a relationship with Dr. Grothey. He is not on our faculty. He is not an employee of the University of Tennessee, neither in a volunteer nor in any sort of a paid position.

We do have a fellowship program in medical oncology, and so, as part of that program, early on, some of our fellows could rotate with him—but it was on an informal basis, because he did not have a faculty appointment.

Once an allegation comes to the surface, our primary goal is to make sure that all of our learners—and by that I include any learner, has an educational experience that is free of any sort of sexual overtone, sexual harassment, etc.

We are deeply committed to that as part of our overall learning environment. If we ever become aware of anything that could impact any of our trainees, we're going to look into that.

This has no place in a mentor-mentee environment, and just simply can't exist in academic medicine.

Scott E. Strome, MD
Robert Kaplan Executive Dean
Vice Chancellor for Clinical Affairs
University of Tennessee Health Science Center College of Medicine

Alliance

Last Friday, the oncology community became aware of allegations of improper conduct by a former Alliance member, Dr. Axel Grothey, following the publication of a *Cancer Letter* article detailing this issue.

The article raises many troubling issues for our community. It is absolutely clear that abusive or bullying behavior of any form cannot be tolerated, and it is particularly egregious if an individual in a position of authority or power uses these tactics to coerce more vulnerable colleagues.

None of us, no matter what our relative status, can abdicate responsibility for maintaining a professional environment that is respectful and supportive of all our members.

When difficult situations arise, each of us can be a force for positive change. This current event reminds us all how important it is to care, to listen, and to support our colleagues in the best way we know how.

Monica Bertagnolli, MD
Group chair

ECOG-ACRIN

The publication last week in *The Cancer Letter* documents allegations of misconduct by a colleague in the GI cancer community. ECOG-ACRIN unequivocally stands against sexual harassment in any form.

The attention brought to this matter is critical for all concerned, and for our broader cancer research community. It speaks to the care and respect we must exercise in our professional environments, each doing our part to eliminate inequality and inequity, and to support vulnerable persons. We must cultivate an environment in which we all can thrive.

In ECOG-ACRIN we are committed to gender equity, equity in sexual orientation, and we have espoused a specifically anti-racist stance. This process—which has been and will be a long-term commitment on our part—will be accelerated by a specific committee charged to focus on issues related to gender representation and equality.

Peter J. O'Dwyer, MD
Group co-chair

Mitchell D. Schnall, MD, PhD
Group co-chair

The COVID-19 and Cancer Consortium

By now, most of you who are regularly on social media or are regular readers of *The Cancer Letter* will have seen the piece on Dr. Axel Grothey, one of the first members of the COVID-19 and Cancer Consortium. While every story has (at least) two sides, the accusations appear credible and substantiated, and

the National Cancer Institute has already taken the step of removing Dr. Grothey from the National Clinical Trials Network's Gastrointestinal Steering Committee.

Just as the SARS-CoV-2 pandemic was a moment of crisis that brought us together, we must use these difficult moments to catalyze change. CCC19 takes a stand for fairness, transparency, and ethical rigor, and so it is that the Steering Committee voted to remove Dr. Grothey from CCC19, effective immediately. Rest assured that these decisions are not made lightly, but we must have zero tolerance for such violations of the CCC19 Code of Conduct, whether they occurred before the existence of CCC19, or not.

We invite you to review the Code of Conduct, which is available in the shared Box folder. We also want to state plainly that we strongly support equality and diversity in our field, and will not hesitate to take such action again, if needed. We sincerely hope that it will not, but if you have concerns that you would like to share privately with the Steering Committee, we can assure you that such communications will remain confidential.

The CCC19 Steering Committee

AACR

The American Association for Cancer Research is committed to a work environment in which all individuals are treated with respect and dignity. Each individual has the right to work in a professional atmosphere that promotes equal employment opportunities and prohibits discriminatory practices, including harassment.

The AACR enforces a Code of Conduct that "prohibits intimidating, threatening, or harassing conduct of any kind. This applies to all conference participants—attendees, presenters, exhibitors, staff, vendors, etc."

Further, "The AACR is committed to a safe, hospitable, and productive environment for all conference participants, regardless of age, disability, ethnicity, gender, religion, or sexual orientation."

OncoAlert

@OncoAlert: Due to the events recently published at "The Cancer Letter" & after verifying this with colleagues. We have removed Axel Grothey from the OncoAlert Network.

The OncoAlert network makes it perfectly clear that we have ZERO tolerance for abuse & harassment of ANY KIND & stand by our values.

Fight Colorectal Cancer

@AnjeeDavis: TY to the @TheCancerLetter for reporting predatory behavior exploiting women in the scientific community. Effective immediately Axel Grothey is removed from @FightCRC Medical Advisory Board.

Yale Cancer Outcomes, Public Policy, and Effectiveness Research Center

@YaleCOPPER: Horrible example of serial harassment. One of many. Misogyny in academia has to stop. As we struggle against #cancer in our clinical care, research, the oncology community must acknowledge that sexism is also a #cancer in our midst. #ListentoWomen #BelieveWomen #HeForShe

Cancer Center at Brown University

@BrownUCancer: It is long overdue to have a culture that supports and celebrates individuals without harassment, abuse, or racism. Certain behaviors as described are unacceptable period. Those affected must be empowered to speak up to make those in leadership aware so swift action can be taken.

NRG Oncology

@NRGonc: In wake of @TheCancerLetter reporting of women exploited yet again in the scientific community, we are deeply saddened it affected the mentor-mentee relationship, critical to our future. Together, we must change this while continuing to support those & other victims. #HeForShe

NIH

We are reviewing our processes for responding to people who submit to NIH allegations of sexual harassment by individuals affiliated with NIH.

We want to ensure we are being responsive and that our policies and procedures are clearly articu-

lated to the person submitting the allegation so they know what to expect next.

The Grothey scandal broke at a time when NIH is facing congressional scrutiny over its policing of sexual harassment.

In the past, NIH has insisted that it's up to institutions to regulate ethics of their faculty members. NIH doesn't have specific rules or policies for handling matters of moral turpitude on the part of grantees.

However, NCI Director Ned Sharpless acted decisively on May 27, firing Grothey from an influential role as co-chair of the NCI NCTN GI Steering Committee (*The Cancer Letter*, May 28, 2021).

The day before the Grothey story was published, NIH Director Francis Collins faced sharp criticism from Sen. Patty Murray (D-WA), chair of the Senate appropriations subcommittee on Labor, Health and Human Services, Education, and Related Agencies.

A video appears here, and a transcript of the exchange follows:

Murray: In 2018, the National Academies, as you know, released a report that found that nearly 60% of women in academia have experienced—60%—have experienced sexual harassment on the job, and recommended that federal research agencies require institutions to notify them when individuals on grants have violated harassment policies, or are put on administrative leave due to harassment allegations.

Other science agencies like National Science Foundation have implemented these changes. Tell me, what is NIH doing to require its research institutes to do the same?

Collins: Senator, I share the sense that this is an extremely important issue.

The National Academy report that you mentioned, I think really got everybody to recognize how pervasive sexual harassment is and what a significant negative it has been for far too long for women in our scientific workforce.

We conducted our own working group, the Advisory Committee to the Director, that reported to me in December of 2019, and made a series of very significant recommendations about how we might change our approach to this.

We have been working through those, and have already implemented a significant fraction of them. There are some that still require some additional legal authority that is hard for us to be able to do at the present time.

In terms of what you're particularly pointing to, we have had now more than 300 allegations that have been brought to us about sexual harassment in our grantee institutions, others within our own intramural program.

Of those 300, about 30% of them have been turned out to be actually entirely validated. That has resulted in 100 different changes in grants—particularly, removal of principal investigators and replacement of those with other individuals. 125 individuals have been taken out of our pool of peer reviewers because of this kind of concern about the bias that they bring to that experience.

And we have made it very clear to our institutions that we expect them to report any—

Murray: Expecting them doesn't require them to.

Collins: Senator, you and I are in an interesting discussion here [...]. I wish we were able to simply require—at the present time, legally, we are told we don't have that authority. We would have to go through a two-year rulemaking effort, or we would need statutory assistance.

Murray: OK. This is really important, and whatever we need to do. I know you've worked on it, I know you've focused on it, but I know of women who have left our scientific research institutes because of this.

We can't afford to have that happen for a thousand reasons. Whatever it is we need to do here, we need to know what it is so we can do it.

Collins: I am so with you [...] I will say, that what we've said in terms of expecting response from our institutions, has gotten their attention in a pretty remarkable way, even without requiring it. We are seeing reporting coming through.

Murray: Well, to every one of them that's listening, I'm not done with this.

Collins: OK.

Matthew Bin Han Ong and Katie Goldberg contributed to this story.

WHITE HOUSE

Senate leaders show bipartisan support for Biden's FY22 request to increase NIH budget by $9B, including $6.5B for ARPA-H

By Matthew Bin Han Ong

President Joe Biden is requesting $52 billion in FY2022 for NIH—$9 billion above the enacted FY21 level—of which $6.5 billion is slated for the proposed Advanced Research Projects Agency for Health.

While the $9 billion investment, if approved by Congress, would amount to the largest raise in the history of NIH, $2.5 billion of that increase would be appropriated for regular NIH operations, according to NIH's Office of Budget. $9 billion is about 21% of NIH's current budget, whereas $2.5 billion is equivalent to about 6%.

When program-level funds are included, the FY 2021 funding level for NIH is $42.9 billion, and $6.56 billion for NCI. Oncology groups welcome Biden's proposed FY22 increases, urging Congress to work with President Biden to generously fund cancer research and support innovation in cancer research (*The Cancer Letter*, April 9, May 28, 2021).

Biden's FY22 budget proposal for NCI states: "[$6,364,852,000] $6,539,302,000, of which up to $30,000,000 may be used for facilities repairs and improvements at [NCI's Frederick National Laboratory for Cancer Research]."

Sources say Biden is requesting $6.735 billion for NCI, a $175 million increase—or 2.67% increase—over the institute's FY21 funding level of $6.56 billion. This proposed NCI funding level includes $194 million for the Cancer Moonshot Program, as well as $50 million for the Childhood Cancer Data Initiative (*The Cancer Letter*, Dec. 4, 2020).

Biden's full budget request, released May 28, states that ARPA-H would have an "initial focus on cancer and other diseases such as diabetes and Alzheimer's ... this major investment in Federal R&D would drive transformational innovation in health research and speed application and implementation of health breakthroughs."

Senate leadership appears to be in agreement with Biden on the necessity of a DARPA-like agency to accelerate biomedical research and innovation, including for cancer.

"Like the defense initiative it is inspired by, ARPA-H is envisioned as breaking the mold for how cutting-edge research is conducted, speeding up the development of medical treatments by funding innovative projects," Sen. Patty Murray (D-WA), chair of the Senate appropriations subcommittee on Labor, Health and Human Services, Education and Related Agencies, said at a May 26 hearing with NIH officials.

ARPA-H would be one of two proposed DARPA-like initiatives—Biden's request also calls on Congress to provide $500 million for ARPA-Climate, and an unspecified budget for an ARPA at the Department of Transportation "to accelerate technology that improves infrastructure performance."

> "Dr. Collins, I look forward to working with you and Chair Murray and the administration in making ARPA-H a reality. I think there's a moment, it's ready for that. I think because of what's happened in the last two years, NIH is ready for that."
>
> *– Sen. Roy Blunt (D-MO)*

Murray's Republican counterpart on the subcommittee, Ranking Member Sen. Roy Blunt (R-MO), said NIH is ready for ARPA-H, too.

"I want to work with the administration to support the ARPA-H initiative," Blunt said at the May 26 hearing. "They'll have the flexibility and tools necessary to both nimbly and innovatively respond to both the next pandemic and also some of the big health issues we face today."

NIH Director Francis Collins said ARPA-H could halve the amount of time needed to bring innovative ideas to fruition.

"The president believes that with your help, we can learn from the lessons of the pandemic and transfer this scientific momentum into big improvements in the health of all Americans. I do, too," Collins said at the hearing.

"Potential areas of transformative research driven by ARPA-H include: the use of the mRNA vaccines to teach the immune system to recognize any of the 50 common genetic mutations that drive cancer; development of a universal vaccine that protects against the 10 most common infectious diseases in a single shot; development of wearable sensors to measure blood pressure accurately 24/7; and leveraging of artificial intelligence technology to advance care for individual patients and improve detection of early predictors of disease," Collins said in his testimony.

The director of ARPA-H would be appointed for a five-year term, with one possible renewal, Collins said. The director would have the authority to recruit 100 program managers to build "collaborative ventures."

ARPA-H would be the ideal vehicle for rapidly developing blood tests, i.e. liquid biopsies, to detect early-stage cancers, said NCI Director Ned Sharpless.

"That could have a profound effect on cancer mortality," Sharpless said at the hearing. "So, getting up a huge trial of that technology as quickly as possible is

the kind of thing that I think would be a good fit for ARPA-H."

Excerpts from the May 26 hearing follow:

Murray: You can never fully predict how the discoveries of today will prepare you for the challenges of tomorrow. That's why you have to build a robust research enterprise and recruit diverse world-class talent and make sure scientists can do their work free from political interference.

And President Biden's budget, which proposes over $40 billion for NIH and the largest increase in the agency's history will go a long ways towards making sure we can continue to prioritize this.

There's also proposed $6.5 billion for a new initiative—the Advanced Research Projects Agency for Health. Like the defense initiative it is inspired by, ARPA-H is envisioned as breaking the mold for how cutting-edge research is conducted, speeding up the development of medical treatments by funding innovative projects.

Blunt: I want to work with the administration to support the ARPA-H initiative. This will be a new institute or is proposed to be a new institute. And I think that that's what should be the case. They'll have the flexibility and tools necessary to both nimbly and innovatively respond to both the next pandemic and also some of the big health issues we face today.

This is a critical moment in a rapidly changing healthcare world, finding those things that the kind of [Operation] Warp Speed, shark-tank RADx relationship, could enhance in cancer and Alzheimer's, and every disease where there's an opportunity where we see that moment and know that this is something that doesn't necessarily call for a five-year research grant, but some sort of partnership different than that, that moves toward a real conclusion sooner than we might otherwise be able to do that.

ARPA-H should not do what the other institutes do, it should do what the other institutes can't do and a cross-cutting way that goes throughout the institutes looking for opportunities, frankly, and the other institutes where there's a breakthrough moment that we could look at differently. I think we can help fill gaps here that otherwise would not be filled and look forward to that discussion.

Now, also, as someone working with Sen. Murray for the last eight years to increase the funding and the focus in what NIH has been doing, we clearly want to be sure that this somehow doesn't take away from the solid research that proved so effective in getting this ready for what we just saw.

So, Dr. Collins, I look forward to working with you and Chair Murray and the administration in making ARPA-H a reality. I think there's a moment, it's ready for that. I think because of what's happened in the last two years, NIH is ready for that.

Collins: This new agency within NIH will catalyze novel strategies to speed transformational and innovative ideas, ideas such as simple blood tests to detect free-floating DNA or protein markers that signal a cancer is growing somewhere in the body, a micro-needle patch that delivers a vaccine to hard-to-reach communities in the mail, using an innovation funnel, to recruit, test, and scale up new technologies for ambulatory blood pressure measurement, with the potential to transform the management of hypertension.

These are just a few of the bold ideas that ARPA-H could tackle, but they are not science fiction. With standard approaches, well, they might happen in a decade or two. With ARPA-H, we believe it could take half that time. The president believes that with your help, we can learn from the lessons of the pandemic and transfer this scientific momentum into big improvements in the health of all Americans. I do, too. My colleagues and I would be pleased to answer your questions.

Murray: As you had just talked about, the president's budget includes $6.5 billion to create the ARPA-H within NIH that is modeled after DARPA. DARPA is a small, $3.5 billion agency composed mostly of program managers and empowered to push the limits of their disciplines and shape some milestone-driven breakthrough technologies in short three to five-year stints.

Given that the nature of NIH's work is different, relying on a peer review system or multi-year grants that is traditionally risk adverse, where progress is often measured in decades, how do you envision ARPA-H fitting into the NIH ecosystem?

Collins: Senator, it's a great question. I think you are right that much of what NIH does requires this kind of careful, deliberative, investigator-initiated hypothesis-driven research, and that's going to be the mainstay of what we do going forward.

That's been the success story of NIH for many decades, but there

are opportunities, as we have seen happening during COVID—such as the need to develop diagnostics in a hurry, develop vaccines in a hurry, that aren't really amenable to that approach—where you need to have program managers that are empowered to move things swiftly and have the flexibility and the resources to do so. And that is the DARPA model. We've studied that closely.

And we do think that there are projects in biomedicine now that would be greatly advantaged by that. That is not the typical peer review process that may take a year from the idea to the first award. With RADx, we made those first awards five days after Congress gave us the budget for it, and that played out really well.

So, we want to incorporate that mindset and we want to bring on perhaps 100 of these program managers, give them the opportunity to build the kind of collaborative ventures that include such organizations as small businesses that might otherwise not be likely to write an NIH grant, ride herd over these things carefully so that if they're not doing well, they get basically stopped immediately; we expect there will be failures—this is high risk—but identify the areas of greatest opportunity.

And every institute at NIH is now coming forward saying I've got at least five ideas of what I would like to do with ARPA-H that I can't do right now. So, this should not be seen as competing with the institutes. It is going to be a synergistic relationship that will allow us to do things otherwise that would take a very long time.

Murray: Well, you've said that it should be within the Office of the Director in that structure. How would decisions be made about what projects to fund?

Collins: So, we will need to hire a director for ARPA-H who will need to be a visionary person, and the idea is to bring on somebody, who's not probably going to be doing this as their long-term career, but maybe for one term, five years with one possible renewal.

That person will be very much engaged in and bringing on board these very creative program managers who have to make a pitch about what kind of projects they think are worth investing in and convince the director that that's the case. And then, they are given the flexibilities to go out and find the right partners and see what can happen.

But that's all going to be done in a way that's quite nimble. It's not going to involve our traditional peer review process.

Blunt: Dr. Collins, on the ARPA-H financial request, $6.5 billion. One part of the question would be, how do you think that number was arrived at, and is that a realistic number to commit in year one? And two, our concern would also be that we don't get in the moment.

So, we've already given NIH $6.5 billion, a sort of level fund everything else. I do like the president's $2.5 billion. I'm sure you could figure out how to spend more than that. And the other institutes, that's pretty close to the average of the last six years from our committee.

I'd certainly like to stay at at least that level, but how do you think those two numbers compete with each other? And how do you feel about actually being able to commit $6.5 billion in that first fiscal year of ARPA-H?

Collins: That's a great question, senator, and we have thought a lot about it. I am pleased the president's budget proposes that this would be three-year money, because obviously you're going to start from a standing start whenever the budget actually gets approved for FY22, we hope that'll be Sept. 30? Well, it might not be.

So, at any rate, we would then really be benefited by being able in that first year to stretch those dollars over a little bit. I do think we could, with 100 program managers readily come up with a number of projects that would fit within that envelope on an annual basis. But I hear what you're saying about a concern, cause I've heard it also, that this might in some way, compromise the interests of the institutes.

I guess I'd look at it a different way though. As I said earlier, every one of the institutes is coming forward with great ideas about how they'd like to use ARPA-H. They think of this as an augmentation of their capabilities, not a subtraction. And so they will be feeding ideas into this and have a lot to do about how those are chosen. So, even though the base number that's being proposed, $2.5 billion for the ICs, may sound like a sort of average one in terms of the science they can do, ARPA H is going to add to that.

Blunt: Thank you. Well, Dr. Sharpless, one of the things the president of course talks about in this issue in this topic is more rapidly moving toward ending cancer. Obviously, we want to do that. We also want to make the point that that's not the only thing that ARPA-H would be focused on, nor would it just be cancer or Alzheimer's.

But on that topic, how do you envision the ARPA-H role in cancer research and what might you be able to do with ARPA-H that you're not able to do in the traditional restraints of the institute?

Sharpless: Thanks for the question, Sen. Blunt. As the president has said, ending cancers as we know it is a top domestic priority for this administration where, obviously, the cancer research community is galvanized by this notion and, and is very excited.

I think, as you know, the National Cancer Institute does some things really well. We fund basic foundational science very well; we can do clinical trials quite well. But there are some areas where we're challenged, where we have struggles, and I think the scale and nimbleness and the ability to interact with industry is very appealing about ARPA-H for certain kinds of cancer projects.

I think a good example of that is this blood-based, cancer-detector technology that Dr. Collins mentioned in his opening statements, where you can find cancers at a very early stage and in otherwise asymptomatic healthy people, and that could have a profound effect on cancer mortality. So, getting up a huge trial of that technology as quickly as possible is the kind of thing that I think would be a good fit for ARPA-H.

Blunt: Thank you, Dr. Sharpless. Dr. Tromberg, let me see if I can get one more question. I think what you were part of at RADx is one of the reasons it gives me real optimism about new kinds of relationships that we might develop at ARPA-H.

Would you talk just a little bit about RADx and how that partnership continued right through the entire process of these companies that you were choosing to invest money with, going ahead and making the first home-based test and I think producing well over two million tests every day now, in addition to the tests that would have come through the regular process.

Bruce Tromberg [director, National Institute of Biomedical Imaging and Bioengineering]: Yes. Thank you so much, Sen. Blunt. And thank you for your question and for your generous support of the RADx program. The bioengineering technology community has formed partnerships all across the government—that's included working with BARDA, FDA, DOD, CDC, HHS, the White House Testing Board, where the 900 scientists are working across government, academia, and the private sector in a very unique way to make this work.

And as you've mentioned, if we fast forward to now, about one year later, we now have 33 RADx supported companies that have increased the nation's testing capacity by more than 300 million new tests, and there have been 23 new FDA authorizations. We've really changed the dialogue from laboratory testing of symptomatic folks to over-the-counter, widely available tests, point-of-care tests that are accessible to all—greater choice and greater capabilities.

And this has really happened because of all of these partnerships that we formed, the accelerated innovation. We've brought out new technologies—about 20% of our portfolio, actually not many people know about, has been based in nanoscience and nanotechnology. So, it's been a tremendous surge for innovation.

NIH NATIONAL CANCER INSTITUTE

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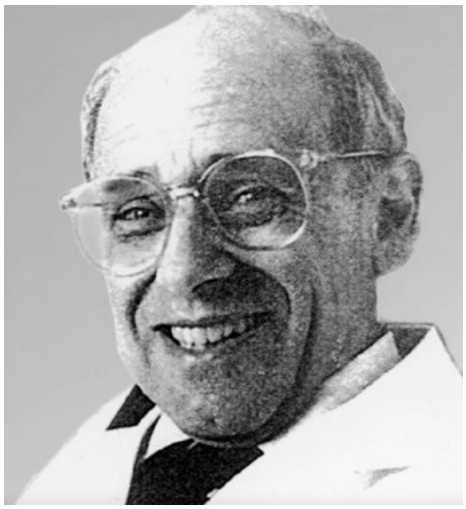
IN THE ARCHIVES

CANCER HISTORY PROJECT

Breaking new ground: Nathaniel Berlin, Paul Marks, and Val Skinner



Nathaniel Berlin on the Diagnostic Radiology Program

Nathaniel Berlin, an experimental hematologist, joined NCI in 1956 as head of the Metabolism Service in the General Medicine Branch and held that position until 1966, when he became chief of NCI's Metabolism Branch, a position he held until 1971.

This interview was conducted by History Associates Incorporated as part of the NCI Oral History Project interviews.

Nathaniel Berlin: Where did I go? What tangent did I come off of?

Gretchen Case: This was just talking about the early days of Cancer Control.

NB: Yes, right. That didn't last very long. Rauscher went out, and I think he got [John] Bailar to develop the Control Program. Bailar didn't last long at it. And Diane Fink came in. When she came in, [C. Gordon] Zubrod and I, [Frank] Rauscher-he was after Baker-we were cut out. I got what money I wanted, and I got the project started.

So that's the very early days. But that plan, I thought-you know, Carl [G. Baker] utilized the resources he had, and I think we could have moved farther if we'd been given the opportunity.

You must recognize, as I did, that there were people both within the Institute and outside of the Institute who thought that Zubrod and I and Rauscher had too much power.

GC: Really?

NB: Yes.

GC: Did you perceive it that way?

NB: I thought we were benign.

[Laughter]

NB: Sure we had power. We had money, we had power. Was it well used? I'm not going to apologize for my use either internally or externally. I made my mistakes, sure.

GC: But it sounds like you used your power wisely.

NB: Yes, we set up a Diagnosis Program. I set up a Diagnostic Radiology Program. They didn't move very far after I left. We did support the development of a Diagnosis Program, a CAT scanner for diagnosis of brain tumors. We developed the & controlled study for the diagnosis using a radiological technique. [Richard] Bolt, [Leo] Beranek, and [David] Newman did it.

And then Diane Fink took it on, and she lasted a while, and then I think Peter Greenwald got it.

GC: Peter Greenwald?

NB: And has changed its character, very much so. In large measure, in large measure scientifically. Major prevention is available today. Major preventions available today that have a base in science. Get rid of tobacco, and the Pap test. My division set up the Minnesota study to test fecal occult blood. That's all we have that's very specific.

The nutrition thing, you'll have to talk to Peter about. What's the evidence that anything nutritional has anything to do with cancer? I find it very difficult, scientifically. That's just me.

And I don't know what research we should be doing. You see, the major problem with Bailar is the data that he has on the change in mortality from breast-from cancer in total, the change in incidence, the change in mortality, I wrote up on the paper that I gave you. It was published in '95; 1 wrote it in '93 and '94. There's been not much to quarrel about in that data.

And what Bailar said in the mid-'80s when he says, "Today we've got to do prevention research,"—but the thing that Bailar doesn't tell you is what to do.

GC: He just said that something needs to be done, but not—

NB: Have you seen his interview with *The Cancer Letter*?

GC: No, I haven't seen that.

NB: Get it. It's fascinating, because when he said, "Well, we ought to put a third of our money, a half a number," and they asked him, he said, "Oh, well, that's a rubber number."

Get it. It's at home on my desk.

GC: Oh, I can get it from the NCI.

NB: Get the one with the Bailar interview. If you're writing a history. [*The Cancer Letter*, June 6, 1997]

NCI Oral History Project Interview with Nathaniel Berlin, M.D.
By NCI | March 15, 2021

Recent contributions

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Hopkins Breaks New Ground for Cancer Center, October 6, 1997
By Johns Hopkins Kimmel Cancer Center | May 24, 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.

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IN BRIEF

Amy Abernethy named president of clinical research platforms at Verily

Amy Abernethy was named president of clinical research business at Verily, an Alphabet company.

Alphabet is the parent company of Google and several former Google subsidiaries. Verily's clinical research started with the Baseline program, a suite of studies using patient-centric tools for research data collection.

The company's June 3 announcement foreshadows Verily's planned expansion into a full-scale clinical evidence generation platform supporting a broad range of clinical trials and real-world evidence studies. As president of this business unit, Abernethy will oversee this overall product vision and Verily's related clinical research portfolio.

"I have always been focused on a singular goal—taking better care of the patient sitting in front of me, smarter and faster," Abernethy said to *The Cancer Letter*. "As an oncologist, solving this problem for the cancer patient was a particular goal.

"When I was at FDA, and as the pandemic raged on, it was clear to me that we must innovate and improve the productivity of our clinical evidence generation infrastructure," Abernethy said. "New clinical trial designs, better use of data, patient-centric solutions that allow anyone to participate. Verily has already started solving this and I am excited to join and help drive the vision forward."

Abernethy was most recently principal deputy commissioner of Food and Drugs at the FDA and the agency's acting chief information officer. (*The Cancer Letter,* Jan. 4, 2019)

In over two years with FDA, Abernethy is credited with having catalyzed enduring changes in the way the FDA uses data as well as advancing FDA's work in RWE and personalized medicine.

She also spearheaded FDA's shift toward cloud-based data interoperability, thereby streamlining the agency's interaction with the health data ecosystem as outlined in the agency's technology and data modernization action plans.

"There is no one better positioned to catapult Verily's clinical research business into its next important phase than Amy, with her understanding of clinical practice, research, data science and the evolving regulatory environment," Andy Conrad, CEO and founder of Verily, said in a statement. "Amy has been at the forefront of the use of clinical data to accelerate clinical trials and enable the uptake of real-world evidence. Her focus on improving the efficiency of the development and availability of new medicines aligns with our goals to transform clinical research by making it easier and faster to run clinical studies."

Before FDA, Abernethy was chief medical officer, chief scientific officer and senior vice president of oncology at Flatiron Health, a healthcare technology and services company focused on accelerating cancer research and improving patient care that is now part of the Roche Group (*The Cancer Letter,* March 31, 2017)

Abernethy is a hematologist/oncologist and palliative medicine physician.

Before joining Flatiron, she was professor of medicine at Duke University School of Medicine and directed the Center for Learning Health Care in the Duke Clinical Research Institute and Duke Cancer Care Research Program in the Duke Cancer Institute.

John Glick to retire from Penn Medicine

John H. Glick, president of the Abramson Family Cancer Research Institute at Penn Medicine, professor of medicine, and the Madlyn & Leonard Abramson Professor of Clinical Oncology, will retire at the end of the academic year and assume emeritus status.

Glick joined the Penn faculty in 1974 as the Ann B. Young Assistant Professor, after completing fellowships at NCI and Stanford.

Glick established the medical oncology program at Penn as a young physician, and has led the Abramson Cancer Center longer than any other director, from 1985 to 2006.

Glick's clinical insight drove the development of integrated cancer clinical care at Penn Medicine, including the development of psychosocial and nutritional counseling services that led to establishment of the Patient Facilitated Services Program. He also established the Penn Medicine Academy of Master Clinicians to promote clinical excellence in all specialties across the health system.

As cancer center director, Glick made the Abramson Cancer Center a national model for a comprehensive center, drawing on resources and faculty from Penn and CHOP, according to Penn Medicine. The turning point came in 1997, with a transformative gift of $100 million from Leonard and Madlyn Abramson to establish the Abramson Family Cancer Research Institute.

In the span of less than a decade, a total of 90 new faculty were jointly recruited to multiple departments and the cancer center with AFCRI support. In recognition of their impact, the cancer center was named the Abramson Cancer Center in 2002.

In addition to his formative leadership of the ACC, Glick also played an instrumental role in the creation of the Roberts Proton Therapy Center, which was established with a naming gift from Wharton alumnus the late Ralph J. Roberts and wife Suzanne, his son Brian L. Roberts, and Brian's wife Aileen.

Glick became a driving force in philanthropy at Penn Medicine, culminating in his role as vice president and associate dean for resource development. Since 1985, he helped to raise over $600 million for Penn Medicine and the ACC, establishing many centers in partnership with patient philanthropists, including the Rena Rowan Breast Center and the Thalheimer Cardio-Oncology Center and significant funding for the Ruth and Raymond Perelman Center for Advanced Medicine.

Over the years, he has chaired the search committees for half of the current clinical department chairs at the Perelman School of Medicine.

As a clinician-scholar, Glick's research has mapped standards of care for breast cancer and lymphomas, Penn Medicine said in a statement. He pioneered the integration of adjuvant chemotherapy and definitive breast radiotherapy for early stage breast cancer and chaired

the pivotal 1985 NCI Consensus Conference on Adjuvant Chemotherapy for Breast Cancer. He subsequently chaired consecutive St. Galen International Consensus Panels for Treatment of Primary Breast Cancer (1988-2011).

In 2000, a landmark clinical study published in NEJM on the role of bone marrow transplant for advanced breast cancer transformed the standard of practice, Penn Medicine said. Glick also conducted pivotal phase III randomized trials in Hodgkin's and Non-Hodgkin's Lymphoma. His research, which was continuously funded by NIH 1974-2006, has appeared in 165 peer-reviewed publications and 28 chapters and books.

Glick has trained and mentored several generations of medical students, residents, and fellows—three of his fellows went on to become directors of NCI-designated cancer centers.

A recognition event is being planned to celebrate Glick's accomplishments and contributions to Penn Medicine.

Andrew Aplin named deputy director of Sidney Kimmel Cancer Center – Jefferson Health

Andrew E. Aplin was named deputy director for scientific strategy of the Sidney Kimmel Cancer Center at Jefferson Health.

Aplin, who is the associate director for basic research at SKCC and the Kalbach-Newton Professor in Cancer Research, assumed the role on June 1.

As deputy director for scientific strategy, Aplin will help guide strategic research priorities to ensure SKCC is successful in its mission to deliver the most advanced, personalized care through scientific discoveries and breakthroughs in cancer detection and treatment.

One of his primary roles will be to foster collaborations among basic, translational, clinical, and population science researchers across the Jefferson enterprise and promote interdisciplinary research. He will also help lead SKCC's next NCI designation renewal. Aplin will work alongside Neal Flomenberg, SKCC's deputy director for clinical integration and chair of the Department of Medical Oncology.

Aplin's research focuses on how melanomas adapt and develop resistance to targeted therapies. He is a principal investigator of several research projects funded by the NIH and NCI, U.S. Department of Defense, Melanoma Research Alliance, and the Adelson Medical Research Foundation. He is a project leader in a funded NCI P01, which links the Sidney Kimmel Cancer Center at Jefferson with the Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins.

The Aplin lab is studying ways to alter the tumor microenvironment by inducing inflammatory forms of cell death in order to turn "cold" tumors into "hot" tumors that better respond to immune checkpoint inhibitors. Additionally, Aplin established several multi-institutional teams that study dormancy, epigenetics, and resistance to targeted inhibitors in uveal melanoma.

Aplin first joined Jefferson in 2008 as an associate professor of cancer biology. He was appointed SKCC's associate director for basic research in 2015 and was previously leader of the Cancer Cell Biology and Signaling Research Program. He also holds secondary appointments in the Department of Ophthalmology at Wills Eye Institute and the Department of Dermatology and Cutaneous Biology at Thomas Jefferson University.

Sukhmani Padda named director of Thoracic Medical Oncology at Cedars-Sinai

Sukhmani K. Padda was named director of Thoracic Medical Oncology at Cedars-Sinai Cancer.

Padda's research focuses on therapies for thoracic cancers, with a particular interest in improving treatment for genomic subsets of lung cancer, including KRAS- and EGFR-positive lung cancer, and rare thoracic tumors, such as thymic malignancies and lung neuroendocrine tumors.

She also studies questions related to tumor biomarkers to help determine the best treatments for patients.

Amy Jo Jenkins named director of clinical trials administration at UAMS Winthrop P. Rockefeller Cancer Institute

Amy Jo Jenkins was named director of the Winthrop P. Rockefeller Cancer Institute's new Office of Clinical Trials Administration and will lead early phase clinical trials at the University of Arkansas for Medical Sciences.

Jenkins will direct early phase clinical research, including operations, staffing, trial management and execution, and business development. She will also work to improve the effectiveness of executing cancer-related research contracts and filings in partnership with other institutional offices.

Her other duties include creating and managing a quality assurance and control program within the Cancer Institute's research efforts, and developing and maintaining standard operating procedures. She will also oversee the UAMS Winthrop P. Rockefeller Cancer Institute Network, which includes the UAMS Regional Campuses, the UAMS/Baptist Health joint venture and the Cancer Institute's partner practices throughout Arkansas. Jenkins will identify and use opportunities to develop and expand clinical trial participation throughout the network.

Jenkins was previously chief of staff in the office of Chancellor Cam Patterson, and CEO of UAMS Health. Prior to that, Jenkins was executive director of the Translational Research Institute from 2016 to 2020, providing oversight and leadership of the institute's daily operations. She joined TRI in 2014 as a senior project manager. She has also taught courses through the UAMS colleges of Public Health and Pharmacy as part of a program in regulatory sciences since 2012.

She first joined UAMS in 2009 as clinical research monitoring manager.

Andrew Schaefer receives $1.2M NCI grant to develop personalized approach to adaptive radiation therapy for head and neck cancers

Andrew Schaefer, the Noah Harding Chair and a professor of computational and applied mathematics and computer science at Rice's Brown School of Engineering, has received a four-year NCI grant for $1.2 million to develop a personalized approach to adaptive radiation therapy for head and neck cancers.

The goal of the study is a tool to personalize chemo- and radiation-based therapies that both reduce risks to patients and make the process more efficient for providers.

Schaefer is working with co-investigators Clifton Fuller, an associate professor in the Department of Radiation Oncology at MD Anderson Cancer Center, in addition to Rice colleagues Mallesh Pai, an associate professor of economics, and Joey Huchette, an assistant professor of computational and applied mathematics.

The grant will allow Schaefer and his team to develop a mathematical model that helps providers optimize both individual treatment strategies for patients and health care providers' policies for the implementation of new technology.

ART will take advantage of computerized tomography technology in use since the early 2000s. It allows clinicians who gather real-time images of changes in a tumor to adapt treatment. ART-based strategies vary. The simplest "fixed-interval" approach requires a midstream reconsideration of therapy, and the most sophisticated "cascade" approach involves daily evaluation of tumors and continual adjustment of chemotherapy and/or radiation in response to changes in tumor geometry.

Schaefer and colleagues plan to feed imaging data into custom Markov decision processes, mathematical models commonly used to optimize decisions over time in dynamic situations. Schaefer compared the models to maps that suggest how a driver should change course when an unexpected roadblock appears.

"The models are going to allow us to adaptively decide how we're going to adjust a treatment," he said. "It will be real-time navigation, not through a physical space but through all the treatment options."

ART, he said, replaces one-time, upfront decisions about a patient's treatment with a set of points requiring a decision to replan, thus balancing the needs of all parties.

"Replanning treatment for a patient on the fly, no matter which model is employed, realistically concerns parties with different incentives: the insurer, including Medicare, and the clinical team, including the patient," Schaefer said.

Schaefer said MD Anderson has one of the first MRI-guided linear accelerators (MR-linAc), which will enable cascade treatment plans by allowing for real-time views of tumors during therapy.

He said the team will develop the best cascade treatment plans for a variety of patients under conditions of uncertainty, and come up with the best simple policies for implementing those policies at cancer centers without MR-linAc machines. The researchers will also work to understand the insurance implications in all treatment plans.

"Just like with other drug regimes, some bodies are going to tolerate radiation very well and some not at all," Schaefer said. "With head and neck cancers, there are a lot of organs we're trying to protect because we can't deliver radiation to precisely the tumor and nothing else around it.

American Red Cross and American Cancer Society collaborate to encourage donors to Give Blood to Give Time

The American Red Cross and the American Cancer Society are collaborating to encourage people to donate blood for cancer treatment.

According to the American Cancer Society, many patient visits and procedures were forced to delay or cancel early in the pandemic to reduce the risk of exposure to COVID-19. With procedures resuming, blood donations are critical for cancer treatments.

The Red Cross is seeing fewer blood and platelet donors give as the nation begins to climb out of this pandemic. This downturn comes at a time when the Red Cross continues to see strong demand for blood products, including platelets by hospitals, causing concern for the sufficiency of the blood supply this month and throughout the summer.

The Red Cross has an emergency need for eligible donors in the Washington, D.C.and the Greater Chesapeake Region to make an appointment now to give platelets to ensure critical patient needs are met.

To schedule a blood or platelet donation appointment, visit GiveBloodToGiveTime.org. As a special thank-you, those who come to donate through June 13 will receive a limited edition Red Cross T-shirt, while supplies last.

The Red Cross is testing blood, platelet and plasma donations for COVID-19 antibodies through July 24. The test may indicate if the donor's immune system has produced antibodies to this coronavirus, regardless of whether they developed symptoms.

Testing may also identify the presence of antibodies developed after receiving a COVID-19 vaccine. The Red Cross is not testing donors to diagnose illness, referred to as a diagnostic test.

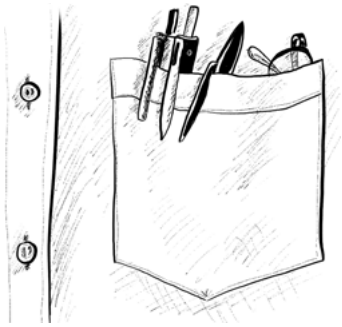
To protect the health and safety of Red Cross staff and donors, it is important that individuals who do not feel well or believe they may be ill with COVID-19 postpone donation.

The Red Cross is also screening all blood, platelet and plasma donations from self-identified African American donors for the sickle cell trait. This additional screening will provide Black donors with an additional health insight and help the Red Cross identify compatible blood types more quickly to help patients with sickle cell disease.

Blood transfusion is an essential treatment for those with sickle cell disease, and blood donations from individuals of the same race, ethnicity and blood type have a unique ability to help patients fighting sickle cell disease.

Donors can expect to receive antibody test and sickle cell trait screening results, if applicable, within one to two weeks through the Red Cross Blood Donor App and the online donor portal at RedCrossBlood.org.

THE CLINICAL CANCER LETTER

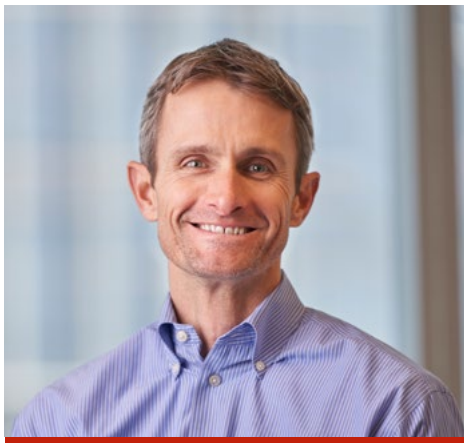


TRIALS & TRIBULATIONS

Precision oncology must evolve to address health disparities

Every person facing a cancer diagnosis deserves access to the best possible tests and treatments for their disease. It's really that simple. Even better—it's entirely feasible.

Brandon Mahal, MD
Assistant professor, radiation oncology;
Assistant director, Community Outreach & Engagement,
Sylvester Comprehensive Cancer Center,
University of Miami Miller School of Medicine



Jeffrey Venstrom, MD
Senior vice president,
Head, clinical development & medical affairs,
Foundation Medicine

Biomarker-based cancer therapies are the cornerstone of precision oncology and hold promise for expanding access to the most effective treatment options for every patient. With genomic profiling, we can find these biomarkers, and identify novel treatment and clinical trial options tied to these biomarkers.

Yet for the field of precision oncology, as is the case across healthcare and society at large, that promise will not reach its fullest potential as long as racial disparities persist.

Too many patients are left behind as precision oncology continues to propel us into a transformative era of personalized cancer care. In fact, approximately two out of three people with advanced cancer are not getting the broad genomic information about their cancer that could inform cancer care.[1]

Entrenched barriers are holding us back, including difficulties accessing genomic testing, lack of ubiquitous expertise, and limited resources in diverse communities impeding clinical trial participation. The result is that people who receive biomarker testing or enroll in clinical trials often do so because of external factors rather than health need or equitable opportunity.

Inequalities in care are especially glaring in cancer subtypes that show high incidence among minority patients. African Americans, for example, have a higher incidence of prostate cancer and poorer survival compared to other ethnic groups, and research is needed to define the factors that may drive these differences.[2-3]

Clinical research and real-world data from this year's ASCO conference provide further insights to help inform a path toward breaking down barriers to high-quality cancer care for all patients—a goal which will require collaboration and commitment across industry and academic groups.

Precision medicine access challenges

Barriers to cancer care include high costs of treatment, transportation and language difficulties, lack of sick leave and non-existent or limited insurance, among others. Long-standing challenges such as medical provider bias and distrust of the medical establishment also remain major barriers, and we recognize that patients may face barriers to access at every step of their journey. This includes biomarker testing early in a patient journey, and early discussions about clinical trial options.

Currently fewer than 10% of U.S. patients participate in clinical trials, with only 5 to 15% of those patients being non-Caucasian, and the access gap is actually widening in cancer trials.[4-5] Non-Hispanic white patients are nearly twice as likely as African American patients and three times as likely as Hispanic patients to enroll in a cancer clinical trial.[5]

This lack of diversity in enrollment can ultimately harm communities of color and lower-income areas by limiting access to investigational therapies that could be beneficial for their specific cancer. We have to do better.

Through research into testing, treatment and clinical trial disparities, the oncology community is working to identify and address inequalities in precision oncology and hopes to create a ripple effect across the entire healthcare system. That's not an easy task, of course, and it will take all of us to enact change at an organizational and structural level to make a difference for patients.

ASCO21: A spotlight on health disparities

The focus on health equity at this year's ASCO meeting is yet another platform to have these important discussions around access to precision medicine and genomic testing, further highlighting the need for industry and academic groups alike to take action.

As stated, persistent inequities in cancer care are driven by many factors. Our study, for example, found that access to comprehensive genomic profiling (CGP) early in the treatment course and clinical trial enrollment differ by ancestry, which may help explain disparities in prostate cancer care.

Men of African and European ancestry had largely similar rates of actionable gene alterations, but men of African descent were less likely to receive CGP earlier in their treatment course and less likely to be treated on clinical trials—underscoring the extended time from diagnosis to implementation of precision medicine and lack of access to investigational therapies. These findings call for additional research into the complex barriers that may be causing ancestry-based gaps in care.

Low rates of clinical trial participation among non-white patients are attributed, in part, to barriers driven by limited resources and the high financial burden of increased doctor visits, time away from work and travel-related expenses incurred with trial participation.[6]

Two studies are currently underway focusing on the potential of decentralized clinical trials to address these challenges with the goal of increasing diversity in enrollment and access to investigational therapies:

- In the Alpha-T study, led by Roche using Foundation Medicine's precision enrollment services, researchers at multiple institutions are enrolling patients with ALK-positive solid tumors, and treating them with alectinib.

- The TRACK study, led by the TargetCancer Foundation, also uses a similar trial design to enroll patients with rare cancers in a study analyzing benefits of molecular therapy.

Through remote support, patients are participating in these trials from their local care setting, showing the massive opportunity we have to implement these types of clinical trials to expand access across patient populations.

A commitment to every patient

Addressing disparities in oncology care requires multi-stakeholder collaboration. Together, we must remove barriers in cancer care and have these important conversations about health equity, as access to this high-quality care can significantly improve outcomes.

Both of us are working to expand equitable access to genomic testing and increase representation in real-world data. To achieve this, we collaborate with nonprofits, patient advocacy organizations and biopharma to better understand access barriers, to help with education, and to co-develop solutions to address barriers to clinical trials among underrepresented patient populations.

And we are always looking for more partners with whom to make important progress for patients. For example, Foundation Medicine is a proud member of Genentech's External Council for Inclusive Research, a purpose-driven partnership to establish new standards and principles for inclusive research.

Each new advance in precision medicine can inadvertently create additional education, awareness and access gaps. We must commit to ensuring all patients have access to advanced, high-quality cancer care and the information they need to make informed health decisions.

And we recognize that racial and social inequalities in healthcare span more than just the oncology field—by working to ratify disparities in oncology, our hope is that the healthcare industry at large follows suit.

Knowledge is power. Every person facing a cancer diagnosis deserves the opportunity to feel empowered, equipped with the best insights to have critical conversations about personalized treatment options, including if genomic testing or clinical trial enrollment is right for them and their specific cancer.

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> This lack of diversity in enrollment can ultimately harm communities of color and lower-income areas by limiting access to investigational therapies that could be beneficial for their specific cancer.

CLINICAL ROUNDUP

Lynparza in the adjuvant treatment of patients with germline BRCA1/2 mutations and high-risk early breast cancer reduced the risk of cancer recurrence by 42% in OlympiA phase III trial

Results from the OlympiA Phase III trial showed olaparib (Lynparza) demonstrated a statistically significant and clinically meaningful improvement in invasive disease-free survival versus placebo in the adjuvant treatment of patients with germline BRCA-mutated high-risk human epidermal growth factor receptor 2-negative early breast cancer.

Upon review of the planned interim analysis in February 2021, the IDMC concluded that the trial had crossed the superiority boundary for its primary endpoint and recommended for the OlympiA trial to move early to primary analysis and reporting.

Lynparza is sponsored by AstraZeneca.

Results of this analysis will be presented during the plenary session of the 2021 American Society of Clinical Oncology Annual Meeting (abstract LBA#1). The results are being made available by ASCO on June 3 and simultaneously published in *The New England Journal of Medicine* prior to their presentation in the plenary session.

An estimated 2.3 million people were diagnosed with breast cancer worldwide in 2020, and BRCA1 and BRCA2 mutations are found in approximately 5% of breast cancer patients.

In the overall trial population of patients who had completed local treatment and standard neoadjuvant or adjuvant chemotherapy, results showed olaparib (Lynparza) reduced the risk of invasive breast cancer recurrences, second cancers or death by 42% (based on a hazard ratio [HR] of 0.58; 99.5% confidence interval [CI] 0.41-0.82; p<0.0001). At three years, 85.9% of patients treated with olaparib (Lynparza) remained alive and free of invasive breast cancer and second cancers versus 77.1% on placebo.

Olaparib (Lynparza) also demonstrated a statistically significant and clinically meaningful improvement in the key secondary endpoint of distant disease-free survival (DDFS) in the overall trial population. Olaparib (Lynparza) reduced the risk of distant disease recurrence or death by 43% (based on an HR of 0.57; 99.5% CI 0.39-0.83; p<0.0001). At the time of this initial data cut-off, fewer deaths had occurred in patients receiving olaparib (Lynparza), but the difference in overall survival (OS) did not reach statistical significance. The trial will continue to assess OS as a secondary endpoint.

"We are thrilled that our global academic and industry partnership has been able to help identify a possible new treatment for women with early-stage breast cancer who have mutations in their BRCA1 or BRCA2 genes," OlympiA Steering Committee Chair Andrew Tutt, professor of oncology at The Institute of Cancer Research, London, and King's College London, said in a statement. "Olaparib has the potential to be used as a follow-on to all the standard initial breast cancer treatments to reduce the rate of life-threatening recurrence and cancer spread for many patients identified through genetic testing to have mutations in these genes."

"Women with early-stage breast cancer who have inherited BRCA mutations are typically diagnosed at a younger age. Up to now, there has been no treatment that specifically targets these mutations to reduce the risk of recurrence beyond the standard treatments available for early breast cancer. This major international study coordinated by the Breast International Group shows that giving olaparib for a year after completion of chemotherapy to patients with BRCA1 and 2 mutations increases the chances that they will remain free of invasive or metastatic cancer. These results reinforce how collaborative cancer research deepens our understanding of treating familial cancers and shows the value of testing for these mutations in patients with early breast cancer."

"OlympiA represents a remarkable and successful global collaboration between leading international academic breast cancer research groups, cancer genetics experts, the National Cancer Institute and pharmaceutical industry partners to evaluate the efficacy and safety of olaparib to address the unmet need for improved therapy for individuals with high risk, inherited BRCA mutation-associated early breast cancer," Charles Geyer, co-chair of the OlympiA Steering Committee, professor, and deputy director of the Houston Methodist Cancer Center, said in a statement.

"The results of OlympiA highlight the importance of inherited cancer genetic testing being widely available, as the results have become essential to mod-

ern oncology for targeted therapy decisions, now at breast cancer diagnosis as well as at presentation with metastatic disease," Judy Garber, co-chair of the OlympiA Steering Committee, professor, and chief of the Division of Cancer Risk and Prevention, Dana-Farber Cancer Institute, said in a statement.

The safety and tolerability profile of olaparib (Lynparza) in this trial was in line with that observed in prior clinical trials.

Choice of first-line platinum regimen does not significantly impact efficacy of second-line immunotherapy in advanced bladder cancer

In a presentation of real-world data, researchers from Fox Chase Cancer Center have concluded that the choice of first-line platinum chemotherapy did not result in a significant difference in overall survival benefit among patients with advanced bladder cancer who were able to go on to receive second-line immunotherapy.

"Over the last five years, we have seen major advances in the treatment of advanced bladder cancer with the approval of immunotherapy in the second-line and maintenance settings after treatment with platinum chemotherapy," said Benjamin Miron, MD, a second-year hematology/oncology fellow at Fox Chase. "These new options give us this opportunity to reflect on the data we have in the first line and ask new research questions."

Miron presented the abstract, "Influence of First-Line Chemotherapy Regimen on Survival Outcomes of Patients with Advanced Urothelial Carcinoma Who Receive Second-Line Immunotherapy," as part of the virtual scientific program at the American Society of Clinical Oncology 2021 annual meeting.

The standard of care for first-line treatment of patients with advanced bladder cancer is either cisplatin or carboplatin, both platinum-containing chemotherapy regimens.

"Carboplatin is a modified version of cisplatin, and the changes to the molecule influence both its toxicity and also efficacy based on its ability to bind DNA," Miron said. "In clinical practice, it has been shown that cisplatin is a more effective therapy for bladder cancer patients, but it is also more toxic and, as a result, not all patients can tolerate cisplatin well."

The study examined whether the established efficacy benefit of first-line treatment with cisplatin compared with carboplatin remained significant among patients who went on to receive immunotherapy in the second-line setting.

Miron conducted the study with other Fox Chase colleagues, including Elizabeth Handorf, PhD, an associate professor in the Cancer Prevention and Control Program, and Daniel M. Geynisman, MD, an associate professor in the Department of Hematology/Oncology.

Using data from the nationwide Flatiron Health de-identified database, they studied 780 patients diagnosed with advanced bladder cancer who were treated with either first-line cisplatin plus gemcitabine or carboplatin plus gemcitabine and went on to receive second-line immunotherapy.

"We found that survival for patients treated first with cisplatin was numerically longer than carboplatin, but the difference was not statistically significant," Miron said.

Patients who received first-line cisplatin did have a significantly longer time to receipt of second-line immunotherapy, but there was no difference in survival time on second-line therapy between the two platinum regimens.

Recently, FDA approved one immunotherapy treatment as a maintenance therapy for patients whose disease is controlled by first-line platinum chemotherapy. This treatment strategy has shown an overall survival benefit and has become the standard of care in patient who are eligible. Otherwise, immunotherapy regimens are reserved in the first line for patients who are ineligible for platinum therapy or have high PD-L1 expression and are in the second line.

Studies have shown that treatment approaches combining chemotherapy and immunotherapy or using immunotherapy alone in the first-line do not have a benefit compared with chemotherapy in patients with advanced disease.

Miron noted that because this study was retrospective, the results should not change clinical practice in any way. But, he added, "the results certainly help us quantify and better understand the magnitude of benefit of cisplatin versus carboplatin in the era of immunotherapy and potentially allow the patient and clinician to feel more comfortable about the use of carboplatin."

Survey: Cancer patients and survivors continue to face pandemic-related health care delays one year later

Cancer patients and survivors continue to deal with the negative effects of the

coronavirus pandemic on their ability to access necessary health care.

According to a new Survivor Views survey from the American Cancer Society Cancer Action Network, 1 in 3 (35%) cancer patients and survivors report that the pandemic has affected their ability to access care. Even during the last few months, as the overall spread of the virus has begun to decline due to vaccinations, roughly 1 in 6 (16%) patients report a delay or interruption in their cancer screening schedule, including 1 in 10 (11%) who experienced a screening delay for a cancer with which they'd previously been diagnosed. These delays were driven mostly by logistical issues such as staffing shortages or a lack of available appointments (26%), followed by patients' concerns about the risks of contracting the virus (22%).

"While conditions are certainly improving, it remains clear there is more work to be done to ensure patients and survivors can get the health care they need when they need it," Lisa Lacasse, president of ACS CAN, said in a statement. "Hopefully as more health care facilities safely resume full operations and more people are able to get vaccinated, screenings—which are essential to early cancer detection and prevention—can be more easily accessed."

Overall, most survey respondents said their provider gave them information about the recommended regular preventive care needed as a survivor (73%) and that such care was easy for them to access (82%). However, for those in the 40-49 age range—the age at which people should begin mammograms and colonoscopies—nearly 1 in 5 (19%) reported that they were not given prevention information and 20% said they encountered barriers to getting preventive care.

In addition to pandemic-related questions, the survey also asked patients about their overall cancer care experience. Responses showed continued racial, ethnic, and socioeconomic disparities in the health care system. Seventy-eight percent of respondents said their health care provider asked them what they wanted from their treatment and made them an active part of their cancer treatment decisions. While 22%, or 1 in 5, said they were not asked or were unsure and 15% of Hispanic, American Indian or Asian patients said they did not feel they were an active participant in their treatment decisions, compared to 12% of white respondents.

While the vast majority of those surveyed said they were confident they got the best available treatment for their cancer (88%), patients with annual incomes at or below $35,000 were less likely to agree with that statement (81%).

The survey also asked respondents what they would consider the top priorities for improving health care. Respondents ranked the cost of health care as the most important challenge facing cancer patients and survivors (36%). It ranked as the top issue across numerous demographics including young survivors under 40 (43%), those with incomes below $35,000 (40%), and those with privately purchased (39%) or employer-based coverage (39%).

"When you add up premiums, high deductibles, co-pays and co-insurance, the costs of cancer can be overwhelming, especially for those with lower incomes," said Lacasse. "It's more evidence that policymakers should act quickly to make the increased subsidies available to those buying private insurance on the exchanges permanent, reign in junk insurance plans that leave patients at high risk for shouldering even higher out-of-pocket costs and do everything possible to expand Medicaid. The pandemic has had a serious effect on cancer patients and lawmakers need to do everything they can to lessen the negative long-term impact by ensuring cancer patients can get timely, affordable health coverage that allows them to access the care they need."

The web-based survey was taken by 1,280 cancer patients and survivors between March 30, 2021 and May 14, 2021. This sample provides a margin of error +/- 3% and 96% confidence level.

Read the full polling memo.

Dual immunotherapy regimen delays cancer progression in patients with advanced melanoma

A treatment regimen for patients with advanced melanoma that combines the immunotherapy agents relatlimab (anti-LAG-3) and nivolumab (anti-PD-1) delayed time to cancer progression significantly more than nivolumab alone, according to results of a study to be presented June 6 at the 2021 American Society of Clinical Oncology (ASCO) annual meeting.

Lead study author Evan Lipson, an associate professor of oncology at the Johns Hopkins Kimmel Cancer Center and Bloomberg~Kimmel Institute for Cancer Immunotherapy, will present the findings.

The study is the first phase III randomized clinical trial to demonstrate a clinical benefit from blocking the LAG-3 immune checkpoint.

"Our results demonstrate that combination therapy with relatlimab and nivolumab is a potential new treatment option for patients with previously untreated melanoma that cannot be removed by surgery. This is the first phase III study to confirm that targeting the LAG-3 immune checkpoint is a beneficial therapeutic strategy for patients

with cancer. Our findings establish the LAG-3 pathway as the third immune checkpoint pathway in history, after CTLA-4 and PD-1, for which blockade has clinical benefit," says Lipson.

In a global, multicenter clinical trial called RELATIVITY-047, 714 patients with previously untreated, inoperable melanoma—an aggressive type of skin cancer—were randomized to receive either relatlimab and nivolumab or nivolumab alone. The median time to disease progression was 10.1 months among patients who received the combination treatment, significantly longer than the 4.6 months seen among those who received nivolumab alone. Progression-free survival (the length of time that cancer does not worsen) at one year was 47.7% for patients receiving the combination treatment, compared with 36.0% for those receiving nivolumab alone.

Checkpoint inhibitor immunotherapy works by blocking specific proteins on the surface of cells that help cancer evade the body's immune system. Blocking these checkpoints helps the immune system fight and eliminate cancer. Nivolumab acts on a protein called PD-1 and is FDA-approved for treating melanoma and several other cancer types. Relatlimab blocks the signaling of an inhibitory protein called LAG-3 displayed on immune system T cells, reinvigorating their anti-tumor activity. The anti-tumor effects of LAG-3 blockade were originally co-discovered by scientists at the Bloomberg~Kimmel Institute.

In general, the adverse events associated with nivolumab and relatlimab were manageable and reflected the safety profile typically seen with immune checkpoint inhibitors. Grade 3 and 4 treatment-related adverse events such as fatigue or joint pains were more common among patients receiving the combination therapy versus nivolumab alone (18.9% versus 9.7%). Treatment-related adverse events led to therapy discontinuation in 14.6% of patients receiving the combination therapy versus 6.7% of those receiving single-agent therapy. Treatment-related deaths were rare: three among patients who received the dual regimen and two with nivolumab alone.

The trial was sponsored by Bristol-Myers Squibb.

Researchers discover gene linked to bone cancer in children, identify potential novel therapy

Researchers have discovered a gene, OTUD7A, that impacts the development of Ewing sarcoma, a bone cancer that occurs mainly in children.

They have also identified a compound that shows potential to block OTUD7A protein activity. The finding, by scientists at the University of North Carolina and the Lineberger Comprehensive Cancer Center, appeared in *Advanced Science*.

About 250 children and young adults are diagnosed with Ewing sarcoma each year in the U.S. About half of those diagnosed will ultimately succumb to the disease, pointing to the need for better therapies.

"Our primary research focus targeted the EWS-FLI1 fusion protein found in about 85% of Ewing sarcoma patients," said UNC Lineberger's Pengda Liu, assistant professor of Biochemistry and Biophysics in the UNC School of Medicine and co-lead author, said in a statement. "This protein, made up of pieces of two other proteins, is unique to Ewing sarcoma and only produced in cancer cells, making it an excellent target for treatment."

Critical relationships between proteins contribute to the development of cancers such as Ewing sarcoma. So, it was a seminal discovery when the UNC researchers found that OTUD7A controls the cancer-causing fusion protein.

Armed with this knowledge, the scientists went on the hunt for small molecule compounds that could block OTUD7A's activity. Their collaborator, Atomwise Inc., used an artificial intelligence program known as AtomNet to screen four million small molecules to find ones that could fit into a pocket in OTUD7A.

One compound they identified, 7Ai, showed a good ability to reduce tumor formation in mice that were grafted with human Ewing sarcoma cells. The compound did not appear to be toxic and was well-tolerated. Also, 7Ai did not kill normal cells that were tested in lab culture experiments.

"Treatment with 7Ai could provide a new targeted therapeutic option for patients who become resistant to chemotherapy. Developing an effective drug will require more lab work and then clinical studies, however," Liu said.

"By deeply exploring the key cellular processes that lead to cancer, unexpected potential therapeutic avenues can result," co-author Ian Davis,Denman Hammond Professor of Childhood Cancer and co-leader of the Cancer Genetics Program at UNC Lineberger, said in a statement. "Once the basic science validated our biological approaches, the application of computational virtual screening enabled us to quickly identify a lead molecule for further testing and validation."

The researchers are working with the UNC Eshelman School of Pharmacy to improve 7Ai's potency and specificity.

DRUGS & TARGETS

Truseltiq receives FDA accelerated approval for metastatic cholangiocarcinoma

Truseltiq (Infigratinib) a kinase inhibitor for adults with previously treated, unresectable locally advanced or metastatic cholangiocarcinoma with a fibroblast growth factor receptor 2 fusion or other rearrangement as detected by an FDA-approved test.

Truseltiq is sponsored by BridgeBio Pharma/QED Therapeutics and Helsinn Group.

FDA also approved FoundationOne CDx (Foundation Medicine Inc.) for selection of patients with FGFR2 fusion or other rearrangement as a companion diagnostic device for treatment with infigratinib.

Efficacy was demonstrated in CBGJ398X2204 (NCT02150967), a multicenter open-label single-arm trial, that enrolled 108 patients with previously treated, unresectable locally advanced or metastatic cholangiocarcinoma with an FGFR2 fusion or rearrangement as determined by local or central testing. Patients received infigratinib 125 mg orally once daily for 21 consecutive days followed by 7 days off therapy, in 28-day cycles until disease progression or unacceptable toxicity.

The major efficacy outcome measures were overall response rate and duration of response, as determined by blinded independent central review according to RECIST 1.1.

The ORR was 23% (95% CI: 16, 32), with one complete response and 24 partial responses. Median DoR was 5 months (95% CI: 3.7, 9.3). Among the 23 responders, eight patients maintained the response for six months or more.

Truseltiq is sponsored by QED Therapeutics Inc.

The parallel approvals of this therapy and CDx mean healthcare professionals will be able to identify cholangiocarcinoma patients with FGFR2 fusions and select rearrangements who may benefit from TRUSELTIQ, another important step in helping more advanced cancer patients benefit from precision medicine.

FoundationOne CDx is the first FDA-approved CGP test for all solid tumors that incorporates multiple CDx claims. It currently is approved as a CDx test for 26 unique therapies and is the only tissue-based CGP test approved to identify patients who may be appropriate for treatment with Truseltiq.

Lumakras receives FDA accelerated approval for KRAS G12C mutated NSCLC

FDA has granted accelerated approval to Lumakras (sotorasib) a RAS GTPase family inhibitor, for adult patients with KRAS G12C -mutated locally advanced or metastatic non-small cell lung cancer, as determined by an FDA -approved test, who have received at least one prior systemic therapy.

Lumakras is sponsored by Amgen.

FDA also approved the Qiagen therascreen KRAS RGQ PCR kit (tissue) and the Guardant360 CDx (plasma) as companion diagnostics for Lumakras.

If no mutation is detected in a plasma specimen, the tumor tissue should be tested.

Approval was based on CodeBreaK 100, a multicenter, single-arm, open label clinical trial (NCT03600883) which included patients with locally advanced or metastatic NSCLC with KRAS G12C mutations.

Efficacy was evaluated in 124 patients whose disease had progressed on or after at least one prior systemic therapy. Patients received sotorasib 960 mg orally daily until disease progression or unacceptable toxicity.

The main efficacy outcome measures were objective response rate (ORR) according to RECIST 1.1, as evaluated by blinded independent central review and response duration. The ORR was 36% (95% CI: 28%, 45%) with a median response duration of 10 months (range 1.3+, 11.1).

European Commission approves Opdivo + Yervoy as first-line treatment for unresectable malignant pleural mesothelioma

The European Commission has approved Opdivo (nivolumab) plus Yervoy (ipilimumab) for the first-line treatment

of adults with unresectable malignant pleural mesothelioma.

The EC's decision is based on results from the CheckMate -743 trial, the first and only positive phase III study of an immunotherapy in first-line MPM.

The trial met its primary endpoint, showing superior overall survival with Opdivo plus Yervoy versus chemotherapy (pemetrexed and cisplatin or carboplatin) in all randomized patients.

The safety profile for Opdivo plus Yervoy in first-line MPMwas manageable using established adverse event management protocols and consistent with previous studies of the combination in other tumor types.

The EC decision allows for the use of Opdivo plus Yervoy in first-line unresectable MPM in the 27 member states of the European Union, as well as Iceland, Liechtenstein and Norway. In addition to the EU, the combination has been approved in six countries, including the United States, and additional regulatory applications are under review by global health authorities.

NCI TRIALS

NCI Trials for June 2021

The National Cancer Institute approved the following clinical research studies last month.

For further information, contact the principal investigator listed.

Phase I - 10347
A Phase I Study with an Expansion Cohort of Duvelisib and Nivolumab in Mycosis Fungoides (MF) and SÈzary Syndrome (SS)

Yale University Cancer Center LAO
Mehta-Shah, Neha
(314) 747-7402

Phase I - 10450
A Phase 1b Trial of M3814 (Peposertib) in Combination with Lutetium 177 Dotatate for Well-Differentiated Somatostatin Receptor-Positive Gastroenteropancreatic Neuroendocrine Tumors (GEP-NETs)

Ohio State University Comprehensive Cancer Center LAO
Chauhan, Aman
(504) 278-0134

Phase II - A051902
A Randomized Phase II Study of CHO(E)P vs CC-486-CHO(E)P vs Duvelisib-CHO(E)P in Previously Untreated CD30 Negative Peripheral T-Cell Lymphomas

Alliance for Clinical Trials in Oncology
Mehta-Shah, Neha
(314) 747-7955

Phase III - ANHL1931
A Randomized Phase 3 Trial of Nivolumab (NSC# 748726) in Combination with Chemo-Immunotherapy for the Treatment of Newly Diagnosed Primary Mediastinal B-Cell Lymphoma

Children's Oncology Group
Roth, Lisa Giulino
(212) 746-3400

Phase III - EAA171
Optimizing Prolonged Treatment In Myeloma Using MRD Assessment (OPTIMUM)

ECOG-ACRIN Cancer Research Group
Kumar, Shaji K.
(507) 284-5096

Phase Other - AMC-113
Observational Cohort Study of People Living with HIV Treated with CD19-Directed CAR T Cell Therapy for B-Cell Lymphoid Malignancies

AIDS Malignancy Consortium
Barta, Stefan Klaus
(215) 615-6506