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THE CANCER LETTER

Inside information on cancer research and drug development

Vol. 46 No. 42

NOVEMBER 6, 2020

www.cancerletter.com

STEVEN LIBUTTI: TRUSTING SCIENCE AS COVID'S NEW WAVE LOOMS OVER NEW JERSEY

As he watches COVID-19 numbers climb in New Jersey, Steven K. Libutti reviews all the things he had learned last spring, when the pandemic first slammed the state.

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University of New Mexico Comprehensive Cancer Center

DIRECTOR, CLINICAL TRIALS OFFICE

The University of New Mexico NCI-Designated Comprehensive Cancer Center (UNMCCC), one of the nation's National Cancer Institute (NCI) designated Comprehensive Cancer Centers, invites applications for the Director of the Clinical Trials Office (CTO). This position is responsible for assuring the strategic vision, direction, and management of all cancer clinical trial operations for the UNMCCC. The Director will provide expert management of the cancer clinical trials operational and budgetary needs of the CTO and oversee data management, regulatory compliance, quality assurance and safety, the integration of research into clinical operations, and scientific review for NCI-sponsored, pharmaceutical-sponsored, and investigator-initiated trials. May also serve as Executive Director of the New Mexico Cancer Care Alliance (NMCCA), a collaborative university-community clinical trials consortium which oversees all cancer clinical trial activity in a statewide network of community-based affiliate sites.

Located in Albuquerque, New Mexico, UNMCCC is the Official Cancer Center of New Mexico and the only NCI-Designated Comprehensive Cancer Center within a 500-mile radius. The Center has 131 board-certified oncology physicians and surgeons, forming New Mexico's largest cancer team which provides care to over 65 percent of New Mexicans diagnosed with cancer. Through its statewide cancer clinical trials network, considered an "exemplary national model for cancer clinical trials and health care delivery research," the UNMCCC offers access to more than 175 clinical trials. The UNMCCC has 132 members engaged in three research programs: Cancer Control & Population Science; Cellular and Molecular Oncology; and Cancer Therapeutics. National centers and programs at UNMCCC include: Project ECHO and Molecular Discovery and High Throughput Target Screening Center, one of the nation's Chemical Biology Consortia in The NCI NExT Program. The UNMCCC is also a member of the ORIEN National Network of NCI Cancer Centers engaged in precision oncology, data sharing, and collaborative research. Focused on discovering the causes and the cures for cancers disproportionately affecting the multiethnic peoples of the American Southwest, the UNMCCC has a robust early phase clinical trials program and an experimental therapeutics unit and has developed new diagnostics and early phase interventional trials for leukemia, and cancers of the breast, lung, ovary, prostate, liver, pancreas, brain, and melanoma.

Learn more at cancer.unm.edu.

MINIMUM JOB REQUIREMENTS

Master's degree in Healthcare or Business Administration with at least 5 years of clinical research experience, with at least 2 years of management in an NCI designated cancer center, preferably in a comprehensive cancer center. Experience in managing clinical trials operations specifically in areas surrounding clinical trial regulatory functions, research subject enrollment, research data collection and reporting, patient outcomes, quality assurance, research compliance, and process improvement.

OTHER DUTIES AND RESPONSIBILITIES

- Establishes and maintains processes and procedures of the CTO, which includes the UNMCCC Clinical Protocol Data Management & Informatics Shared Resource (CPDM&I; a Shared Resource component of the NCI P30 Cancer Center Support Grant). Ensures that actions and initiatives are consistent with University policies, and all institutional, state, and federal auditing, monitoring, reporting, and compliance requirements for the conduct of cancer clinical trials and cancer clinical research involving human subjects.
- Identifies operational parameters and requirements established by local, state & federal laws, and participates in the formulation of general operating policies; implements policy and develops appropriate procedures for the CRO/CPDM&I and participant sites.
- Identifies and solicits potential new clinical trials and participant sites, in conjunction with faculty and affiliated physicians; establishes and implements participant and sponsor agreements for all participants, as needed.
- Responsible for all fiscal control activities for the CTO/CPDM&I unit; develops and manages budgets, performs long-range financial and business planning, develops metrics to measure the ongoing status of the unit, and develops and prepares monthly operating reports.
- Designs, establishes, supervises, and maintains an organizational structure and staffing to effectively accomplish the organization's goals and objectives, including senior managers, research nurses, research and data coordinators, and other technical and fiscal staff.
- Responsible for the recruitment, education and training, supervision, performance management, and performance evaluation of subordinate managers and staff. Develops metrics to determine appropriate staff workloads and staff mix.
- Responsible for the monitoring, oversight, and review of all clinical trials conducted at UNMCCC and affiliate sites; develops and implements policies and procedures that are consistent with SOM Human Research Protections policies, FDA Good Clinical Practice guidelines, and all institutional, state and federal auditing and compliance requirements.
- Interacts with pharmaceutical and clinical research organization leaders to promote the UNMCCC and the CTO/CPDM&I and gain access to appropriate clinical trials; interacts with faculty, staff, and other cancer-related organizations to raise awareness of clinical trial offerings.

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COMPREHENSIVE CANCER CENTER

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

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

Steven Libutti: Trusting science as COVID's new wave looms over New Jersey

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Q & A

Libutti spoke with Paul Goldberg, editor and publisher of The Cancer Letter.

THE CANCER LETTER | NOVEMBER 6, 2020 | VOL 46 | ISSUE 42

CONVERSATION WITH THE CANCER LETTER

As he watches COVID-19 numbers climb in New Jersey, Steven K. Libutti reviews all the things he had learned last spring, when the pandemic first slammed the state.

There is a lot he knows in November that he didn't know in March. But the greatest insight he has gleaned from the experience isn't surprising in the least: "There was an urgency to try something to treat patients. And I respect that as a clinician, that you're standing in front of an otherwise young person who is fairly healthy and suddenly is needing to be put on a respirator and may not make it," Libutti, director, Rutgers Cancer Institute of New Jersey and senior vice president of oncology services, RWJBarnabas Health, said to *The Cancer Letter.*

"The scientific method is of critical importance. Because many of the treatments that were first believed to be effective turned out not to be effective, even though 'common sense' might have indicated they would be. But, when you apply the rigor of a well-designed clinical trial, you learned that they weren't."

Challenge No. 1 is not to allow the hospitals to be overwhelmed.

"The reason I think [mortality] was so high in New York and New Jersey back in the spring is we just became overwhelmed. There were just too many patients requiring hospitalization or intensive care. And that overwhelming of the system is certain to increase morbidity and mortality," Libutti said.

"The way to keep from getting overwhelmed is somewhat straightforward. You've got to wear masks. You've got to try to limit the number of people in close spaces. You've got to wash your hands. And you've got to keep your distance. If we can do all those things on a national level, I think we can buy ourselves the time we need to get to vaccines being deployed more broadly."

> My prediction is at the moment, just looking at the pace, and I have to admit some of this is hope, that the peak will be far lower than what we saw in March and April, stretched out over a longer period of time.

Last April, as the pandemic was about to peak in New Jersey, *The Cancer Letter* similarly checked in with Libutti (*The Cancer Letter*, April 6, 2020)

Cancer services at RWJBarnabas Health remained open through the spring spike, but volumes declined as patients were reluctant to come to the healthcare facilities. However, during the summer, the magnitude of services caught up, and the health system will likely have the same patient volumes or have a slight increase over last year, Libutti said.

Libutti said he is offended by the attacks on science that he has heard in recent months. "Our economy thrives with a healthy populace. And a healthy populace is based on our understanding of disease, which is rooted in science," Libutti said. "And so, it gets a little concerning and a little frustrating when you see a pushback against science. Some think that if you silence science or you ignore it, bad things will go away. And, we obviously know that's not the case.

"So, I hope folks like Tony Fauci and others that have seen a fair amount of at least verbal assault during this period don't lose hope and lose faith. I think the majority of us understand the important progress we make when we pay attention to scientific findings."

On Nov. 5, the United States reported over 120,000 new coronavirus cases, the highest number ever reported by a single country in a single day.

Libutti spoke with Paul Goldberg, editor and publisher of *The Cancer Letter.*

Paul Goldberg: How was your summer?

Steven Libutti: It was good as it could be expected, given everything we're dealing with. Obviously, the case numbers in New York and New Jersey were down throughout the summer months. And so, that meant that we got busy with catching up with patients who had deferred less acute follow-up issues or less acute diagnoses, to handle that backlog of patients that was a challenge to get in in March, April and May.

And so, we were pretty busy over the summer, although in a good way, in the way you want to be busy, as opposed to what we were dealing with in March, April and May. It did give us a little bit of a break from the very acute footing that we were on in March, April and May that you and I talked about. And, from a personal note, it was nice to see my kids on occasion, because folks were downshifted a little bit from work over the summer.

But, we're right back in it now. As you can see, from listening to the news or checking out the Hopkins website that tracks case numbers, we're seeing an increase in cases in New York and New Jersey, not to the same extent as in other areas of the country, but the number of diagnosed cases and hospitalizations is increasing, albeit slowly. And so, we're going back onto a more aggressive footing, to be ready.

I think when I spoke to you last, I had mentioned we had established a command center for cancer services across the health system. And, we were having weekly calls. At one point, it was twice-a-week calls. So, we just re-instituted our command center to have every other week calls right now. And, we'll obviously increase the frequency of that if we see the numbers go up. But we want to begin to share information across the hospitals within our system, with respect to oncology services and where things are being strained, et cetera, as we begin to see increased cases.

I'm guessing that you're looking at the COVID projections as often as you've been looking at FiveThirtyEight. What are your thoughts?

SL: When I look at what the numbers look like in New Jersey, and we've seen case positivity rates now go up between 4 and 5%, and R naught or Rt levels, that is number of patients potentially infected by a single patient go up to the 1.2, 1.3 range. And then, when you look at the daily case counts that come in from the Department of Health, we've seen day over day increases over the last month. It's obvious, as we're getting into the fall and winter, and people are going indoors more, we're seeing an increase in cases. And hospitalization numbers across our system, although they're nowhere near where they were at the peak, in April, they are increasing as well.

And so, what is hard to predict right now is going to be the ultimate amplitude of this wave, like how high are we going to get in daily cases, and then what the mortality curve is going to look like. My prediction is at the moment, just looking at the pace, and I have to admit some of this is hope, that the peak will be far lower than what we saw in March and April, stretched out over a longer period of time.

Our waves that we saw in the spring began in March, peaked in April, and was back down to a low baseline by June. So, March, April, May, June, over about a four-month period, we saw this bell-shaped curve, rising up rapidly, then coming back down to a new steady state. Never going away completely, but coming back down to a new steady state. Now, we're seeing that rise begin to happen, but it doesn't look as acute a rise or as high a slope of that rise as it did back in March and April. I think we were really overwhelmed with this big wave. And my bias is that that's what drives the mortality.

We don't have that many more tools than we did in April now for treating the disease. Although, I think we do have a much better understanding and appreciation of this virus and the disease it causes. I say that because there's only one FDA-approved agent now, remdesivir, which has some modest activity. There's a number of agents in clinical trials, I think a few antibody therapy agents in trials look very promising. But still, the verdict is not yet in. That is, I believe, a very logical and promising strategy towards treatment. There's still trials ongoing with convalescent plasma. There are vaccines, which, hopefully, are imminent.

But in terms of treating patients, we've learned a lot, but it's not like we have a bunch of new agents we can pull off the shelf that are really effective. But the reason I believe we could perhaps, if we can keep that slope low and not overwhelm the hospitals, I think we can keep that mortality rate down. Because, the reason I think it was so high in New York and New Jersey back in the spring, is we just became overwhelmed. There were just too many patients requiring hospitalization or intensive care. And that overwhelming of the system is certain to increase morbidity and mortality.

And, I think if we can again keep from getting overwhelmed.

I'll tell you, Paul, from my perspective, the way to keep from getting overwhelmed is somewhat straightforward. You've got to wear masks. You've got to try to limit the number of people in close spaces. You've got to wash your hands. And you've got to keep your distance. If we can do all those things on a national level, I think we can buy ourselves the time we need to get to vaccines being deployed more broadly.

And, it seems so simple. I don't know why or how the simple act of wearing a mask … I mean, to me it's like, if it's raining out, you take an umbrella, or if it's snowing out, you put your boots on, why the simple act of putting on a mask has generated such passion among different groups, and it's a sign of independence and resistance to not wear a mask.

It's common sense. This is an airborne virus. If we all wore masks and followed these fairly straightforward recommendations, I don't think you'd have to worry about shutting things down, because you'd keep it at a reasonable pace.

So, again, not having a crystal ball, my sense is we are going to see an increase even in New York and New Jersey over the next several months. I'm hopeful that since at least in New York and New Jersey, we've been pretty good about getting the message out for masks and distance and hand-washing. And, I can tell you at our own facilities, and even when I go out shopping, I live in New York, in my community, when I go out to stores, everybody's got masks on. I think if we can adhere to that, we'll be able to control this until we're able to deploy vaccines, which is going to be the exit ramp for this.

Widespread deployment of vaccines, I believe, is how we bring this to a close at some point.

But you also know some things you didn't know in March. For example, steroids, remdesivir, anticoagulation.

SL: It's a great point, Paul. While we didn't necessarily approve a bunch of new drugs that you can pull off the shelf yet for treating it, we certainly learned a lot about the disease. And, that definitely factors into our ability to improve mortality, decrease morbidity.

Steroids are an important part. Obviously, patients with significant lung disease, there's good evidence now in randomized studies and retrospective studies that the addition of dexamethasone can improve survival. And, I think that's a key in our armamentarium. There is some benefit to remdesivir as well in trials, although some recent studies have questioned its impact on mortality. It's still a tool that we have that we didn't have then in treating patients.

And also, an understanding of when to intubate and when, maybe, you don't need intubation. There's some evidence from studies that it may not be in the patients' best interests to quickly put them on supportive ventilation, because of the damage caused to the lungs by positive pressure, et cetera, that perhaps there are some patients that can be maintained before being intubated.

So, I think all those things, you're absolutely right, are going to improve patient outcomes, and maybe avoid as high a mortality as we might otherwise get. But, I still believe the key in all of that is maintaining capacity. That is, if you don't overwhelm your system or overwhelm an individual hospital, they're much more likely to have better outcomes, even with modest improvements over what we had in March and April with respect to therapeutics or approaches, than if you overwhelm the system.

If the system becomes overwhelmed, like we are seeing now in Utah, where folks are beginning to contemplate difficult decision-making, based on triage criteria, likelihood of survival in terms of who gets in the ICU, who has to be discharged from the ICU—that's when I think you really start to see compounding morbidity and mortality.

Do you have enough PPE? Have you been able to build up a stash?

SL: Yes. That's a great question. We spent much of the summer months, when numbers were more easily managed and at a low steady state, to really begin to prepare and stock up, so we wouldn't be caught in the situations we found ourselves in in March and April.

So, right now systemwide, and certainly at the cancer institute, we are appropriately stocked with N95 masks, KN95 masks, surgical masks, gowns, shields, gloves, all the necessary PPE equipment to protect our faculty and staff that are patient-facing.

We ramped up our testing. Obviously, there's more testing nationwide. Certainly, New Jersey has significantly ramped up its testing. We're still in a posture where we test asymptomatic cancer patients that are going to be started on therapy to get a sense of whether those patients are positive or negative. We've been using PCR-based testing to this point.

About three weeks ago, we began to test patients with both PCR and an antigen test, since the antigen tests gives a result within 15 minutes. My hope is that if we show that antigen testing is good enough for us to make decisions around patients, compared to PCR, that we can reserve the PCR as a confirmatory test when needed. That will improve capacity in our emergency room to be testing folks with respiratory symptoms that begin to come in, in the winter months, when there's confusion as to whether it may be COVID or flu.

And, as you know, the supply chain, especially for PCR testing has been strained. And so, ideally if we can show

that antigen testing can be utilized as a frontline for the asymptomatic population at the cancer center, we can help to preserve the supply chain for PCR testing as it's needed. So, that's an area we're moving forward with, and we'll hopefully have some sense of that over the next couple of weeks, once we've got enough patients tested with both.

Are you able to set up COVID-free zones? Is that useful? Is that even feasible in such a huge health system?

SL: Certainly, for very at-risk patients, cancer patients under active treatment, transplant patients, we've thought a lot about how do we protect those vulnerable patients. We have COVID free units in all of our facilities. I think it's ultimately a challenge to have truly COVID-free zones beyond the unit level.

That is to say, this hospital's not going to admit COVID patients, just because things are becoming so widespread that—number one—you may not know that a patient is positive until they begin to undergo treatment. And, you may be the main hospital treating a particular community. And to have those patients shifted someplace at a distance regionally may complicate the care of those patients.

Ultimately, once our new cancer pavilion is completed, our goal will be to have many of our inpatient cancer patients at that facility.

Obviously, it will not have the capacity to have every cancer inpatient. But, certainly, during a period like this, an infectious disease epidemic or pandemic, a specialty-based hospital can be a focal point of trying to have that kind of a zone.

But for now, we're looking more at strategically protecting, or separating, those very vulnerable patients, immunocompromised patients, patients under active therapy within each institution, and keeping those units free of infectious disease. So, I think that's our main strategy right now.

How much telemedicine are you doing?

SL: Telemedicine is still a critically important component. It's actually my hope that the government, both federal and state, look to keep us on a more accessible posture for telemedicine. As you know, the hurdles for the use of telemedicine were higher before the pandemic. I'm hoping that those hurdles that have been lowered remain lowered.

I feel that telemedicine is here to stay now. It is an important tool, and I think fits especially well into how we deliver care for cancer patients. Many of our patients are in a period of survivorship, or long-term follow-up. And, oftentimes, when you meet with those patients, you're giving them good news. "We reviewed your scans, we reviewed your labs, everything looks great. There's no evidence of recurrence."

Sometimes, those appointments could be a telemedicine appointment, as opposed to the patient coming in. I mean, we certainly want to see our patients. We want to examine those patients. I'm not suggesting that telemedicine completely substitutes for that. But, there are opportunities, I think, and situations where telemedicine is very helpful. You know, second opinions, specific specialty input. You have a patient at one location who's being seen, and you'd like to get an opinion from your expert in heme malignancies or in GI oncology at another location. That's an ideal situation for a telemedicine consult on a patient.

And so, we're still using it. We're seeing some patients for initial visits for telemedicine, depending on where they are located. A lot of our initial visits though are in-person again now. We're seeing some follow-up patients still with telemedicine. And, it's my hope that we continue to have telemedicine as a tool, moving forward. I think it's really helped.

Would you be able to keep cancer services going at a normal rate if this thing hits us the way you think it's going to hit?

SL: We, surprisingly, during March, April and May, during that peak, while we saw a drop-off in volume for sure, same as many of our other colleagues in the region, we never closed down cancer services.

We continually treated patients with chemotherapy, with radiation therapy. The state had a mandate: no elective surgical procedures. But, they considered most cancer operations as urgent. So, we continued to operate on patients. Most of the access issues were not that we weren't open for business, it was more that patients were fearful of going out and about, because of what was happening with the pandemic.

Hopefully, we've lowered a lot of that concern with knowledge and reality. We published two studies, one in *JAMA Oncology*. The one in *JAMA Oncology*, our radiation oncology team did surface testing for the virus throughout all of our radiation oncology facilities—waiting rooms, treatment areas, et cetera—and then, we did the same for our infusion units and our waiting rooms.

And, we found no evidence of viral contamination on surfaces in those areas, which I think is reassuring to patients, that there's lower risk in coming in to be seen or to get treated.

We are very strict, as are many other cancer centers, in everyone wearing masks, having things rearranged so there's appropriate social distancing, limiting the number of folks that come along with the patient, to try to decrease person density within spaces. And so, our message is and has been that patients should not be fearful of coming to be treated, or to be diagnosed, or to see us, because we're taking every possible precaution to decrease their risk.

So, we never, even in the heat of our surge, in April, we didn't have to deploy or detail any of our cancer providers to COVID activity.

We were able to maintain enough physician support for COVID issues, and we never had to go to final level of defense and take providers away from the cancer activity. We're hopeful that will be the same case now, that the cancer program will continue to be able to move ahead, even with another wave.

That's important, as you know, Paul, because as Ned Sharpless has stated and published, there's the concern that decreased screening occurred during this pandemic, because of either sites being closed or patients being fearful of going in for routine screening.

It was not necessarily that patients with known cancers were avoiding appointments, but rather these were patients who needed routine cancer screening. For example, getting a colonoscopy when you turn 50, or patients going for mammograms, other sort of screening activity, was really impacted by this pandemic, and will lead to anywhere from 5,000 to 10,000 additional cancer cases nationwide.

We're trying to really be in a posture now, having learned what we've learned, having prepared now for how to manage patients safely, to try to keep the screening going, keep the first visits going, keep the treatments going, because cancer is not going away. I think we talked about that the last time we spoke.

There are still roughly 50,000 new cancer cases a year in New Jersey, 16,000 to 17,000 deaths. That's not taking a holiday because of the pandemic. We're obligated to continue driving this forward and making a safe place for our patients to come.

Ned's numbers are national projections. What about New Jersey numbers? Have you looked at those? Can you see it now?

SL: It's a little early in terms of screening numbers for us to get a sense. As you know, Rutgers Cancer Institute co-manages the New Jersey State Cancer Registry, with the New Jersey Department of Health. There's now a COVID registry with the New Jersey Department of Health as well. We have a memorandum of understanding making its way through approval process, which will give access to cross-reference between those two registries, which I think will be an important research tool for understanding the impact of one on the other.

But in terms of increased incidence of cases or where things have been in terms of impact on screening or mortality, I think we'll only be able to get a true sense of that when we look back at the 2020 data, when we get midway through 2021. But when we get midway through 2021, once all the registry data has been cultivated across the state, once it's been validated at the state level, I think we'll be able to take a look back and get a sense of what immediate impact we have seen of COVID on cancer screening.

We also run a program with the state called, Screen NJ, which is a cancer screening program for lung cancer and colon cancer. We will begin now to look at our screening data over the last six months. But we've doubled our efforts in our Screen NJ program to try to get patients to their screening appointments over the last four or five months since the case numbers for COVID had gone down.

So, we're trying to be very aggressive about that, with messaging, with information, with outreach, with navigation, to try to maintain as normal a posture for cancer screening as we possibly can.

What was the impact on your institution on the health system in terms of maybe patient volume or in terms of money?

SL: So, during March, April and May, we saw a dip in cancer patient volume.

And, I'll speak specifically to the cancer patients across the system, since those are the numbers I have most completely. But, since May, we have seen that rebound back in terms of cancer volumes. And, right now, I believe, we will likely finish this year at- or slightly above what our volumes were in 2019.

So, we've come back quite a bit in terms of patient volume, especially over the last three months. And, obviously, we have two more months to go in the year—November and December—and depending on how rapidly new COVID cases, that new second wave, occurs in New Jersey, can have some impact. But, if I were going to project it out now, I think we'll finish the year very close

or maybe slightly ahead of where we were in 2019.

I think we've come back, certainly on the cancer service side. The system certainly saw decreases in especially surgical services, especially elective surgical cases during March, April and May, while the state had a no-elective-surgical-procedure order in place.

But, those cases came back over the summer in terms of the delays for those acute cases. I just don't know where that will hit related to 2019 data, just because that's outside of my sphere of responsibility.

But, I can tell you, with the cancer cases, fingers crossed, as long as the curve stays about at the slope it's at right now, we should finish 2020 back to where we were or slightly ahead of 2019.

In terms of money, or in terms of cases?

SL: These are cases, and cases correlate to revenue to some degree. Because, each case has treatments associated with it.

Overall, I think every system was strained financially. Certainly, federal government assistance, CARES Act, et cetera, was extraordinarily helpful and necessary for all of our health systems. I think our health system, like every other health system, was challenged across different service lines.

And, as I said, especially hard hit were elective cases during March, April and May. And so, you can't help but take a hit to your bottom line. And, certainly, as other not-for-profit health systems derived some benefit from the investments made by the federal government through the CARES Act, et cetera, in assisting, and that was critically important.

I think in terms of cancer volumes, which are the volumes again that I'm most responsible for and most intimate with, we've been able to maintain those volumes.

I will tell you this, though, our long-term strategic plans, and you and I have spoken in the past about the new cancer pavilion that we're building, the first freestanding cancer hospital in the state, the pandemic has not impacted that project or that timeline.

We're on time and on target for that project. We are on budget for that project. And still hoping to have the project completed toward the end of 2023—so about three years from now. So, fortunately, we were able to have the wherewithal to continue to navigate that in a positive direction.

But yes, obviously, the pandemic has hit our system financially. But, the system is healthy enough that I think we are weathering that storm.

What have you learned from this as a scientist? I've picked your brain as an administrator, that hemisphere of your brain. What about science?

SL: It's a great question. And, I like the way you frame it. Because, as you know, I wear a couple of different hats. But, I came originally from the National Cancer Institute and the Intramural Program. So, I'm always, at my heart, a scientist. I think like a scientist, or at least I hope I do.

So, I've learned a few things. I've certainly learned the power of a well-run or well-designed clinical trial. With the overwhelming numbers of cases that we saw in March, April and May, there was a tendency to have a sense of panic, or panic prescribing, so called "kitchen sink medicine", not understanding the disease, not understanding what might or might not work.

There was an urgency to try something to treat patients. And I respect that as a clinician, that you're standing in front of an otherwise young person who is fairly healthy and suddenly is needing to be put on a respirator and may not make it. And so, there was a big sense of urgency in trying anything.

The scientific method is of critical importance. Because many of the treatments that were first believed to be effective turned out not to be effective, even though "common sense" might have indicated they would be. But, when you apply the rigor of a well-designed clinical trial, you learned that they weren't.

And, I think it's as important to rule out agents that are not effective as it is to find ones that are. Because otherwise, you spend a lot of time giving patients agents or cocktails of agents that all might have toxicity, or add to their morbidity, without any benefit. And so, it's important to eliminate those agents from our armamentarium, or at least learn better how you might use them or how you might combine them. So, I think the scientific method is critically important there.

I was very impressed with how quickly we learned about this virus and this disease. It's unprecedented how quickly the sequence of this virus was available—freely available online—that folks could access it to begin to learn about what the unique characteristics of this coronavirus are.

I don't think we would have been able to see potentially three or four vaccines very close to being ready for use had it

not been for that science. I mean, think about it, there's never been a time in history, where vaccines were developed this quickly and validated through well-designed clinical trials.

And then, very basic things that the science taught us. How is this virus transmitted? Airborne transmission. How do we try to minimize the infectivity, person-to-person infectivity until we have a vaccine? And, I think simple things like wearing masks came from that.

And then finally, one of the most important things we're learning through science is how long does it appear folks are immune to a possible second infection after they've been infected once?

And, I think the notion that you could treat this disease with the morbidity we know it's associated with and the mortality we know it's associated with, and just essentially think that letting folks just infect each other—so-called herd immunity—to get the virus to burn out, I think is inconsistent with what we now understand about this virus scientifically.

The fact that a patient with a symptomatic infection may only be immune from a second infection for four to six months, and a patient with an asymptomatic infection may only be immune for less time than that, the idea that you'd somehow ever reach herd immunity, where folks were actually immune long term, I don't think is consistent with what we understand about this virus.

I think the only way to get to herd immunity will be through effective vaccines, if we can really optimize a vaccine. It looks like several of the vaccine candidates will fit this bill. If we are able to optimize the vaccine and squeeze out 12 or 14 months of sustained immunity from a vaccination, then folks could get boosters each year that truly could get us to the concept of herd immunity.

I think a vaccination, if the population gets vaccinated, and that would be real important, once we have a safe and effective vaccine identified and confirmed, socializing the notion that it's important to get vaccinated, once we got the 60% of the population either vaccinated or exposed, we'd probably get to that number.

Most of the population would need to be vaccinated to get to a number that would deliver the promise of the concept of herd immunity, that is that you get it under control.

I do get concerned when we see an assault on science. Our culture, our history is rooted in advances we've made over time, whether it's science that led to sanitation, whether it's science that led to the development of engines. We've evolved from horses to cars to space flight, et cetera. That's all grounded in science. And, so is health. We've developed treatments for many diseases. We've eradicated diseases. And that's really been the foundation of the progress of our society, our economy included.

Our economy thrives with a healthy populace. And a healthy populace is based on our understanding of disease, which is rooted in science. And so, it gets a little concerning and a little frustrating when you see a pushback against science. Some think that if you silence science or you ignore it, bad things will go away. And, we obviously know that's not the case.

So, I hope folks like Tony Fauci and others that have seen a fair amount of at least verbal assault during this period don't lose hope and lose faith. I think the majority of us understand the important progress we make when we pay attention to scientific findings.

Speaking of which, what happened in your trial of hydroxychloroquine? How did that come out?

SL: As I told you, as soon as I had results, you'd be one of the first to know what those results were.

Do you have them?

SL: We had some early challenges both from a supply chain perspective and also some technical hurdles with respect to the viral quantification, which is the endpoint of the study. We've dealt with those issues and successfully put in place the supply chain that we needed, and, certainly, the decrease in cases over the summer helped us with that. And, we overcame some of the technical issues. And, we are now almost complete with analyzing those viral levels in the patients that received those agents.

Certainly, there's a lot of evidence now that hydroxychloroquine as a single agent did not appear to have any clinical benefit in randomized studies.

What I'm hoping to learn from the completion of this study is whether there was any indication at all of an antiviral activity. Because perhaps, that agent could be used with other agents as part of a combination if there's any evidence that there's any activity from a virus quantification perspective.

And, that may or may not be the case. That's why I think it's important that we complete our analysis and that we publish this work so it can be another building brick towards understanding what options we have.

One of the areas, Paul, that's real important is as we talked already, we have things like remdesivir, we have dexamethasone, et cetera. Those are mostly used for patients who have become hospitalized. I think the key for us, in addition to a vaccine, is we need some effective therapies that we can give to patients once they become infected, but they're not even yet symptomatic.

Because, I really believe the key is keeping patients out of the hospital. So, better outpatient therapies are a challenge and something we need to make progress on.

I think these antibody therapies, again, the antibodies, monoclonal antibodies have shown promise in their early studies. And those might fit the bill.

I think we're going to have to look at other agents in combination, strategies like those used for HIV now, to be able to come up with the right combination that can be given to an asymptomatic positive patient to prevent the chance that they would develop the disease. I think that and a combination of an effective vaccine is going to be our exit ramp from what we're dealing with now.

Would it be useful to have more negative studies of hydroxychloroquine?

SL: Having data supporting one or the other is equally important. You want to eliminate agents from your repertoire as much as you want to find new ones that work so you're not distracted with something that's just not going to be effective. That's why it's critical that we complete the analysis and we publish this study, whether it's a positive or a negative finding. Either way, I think it's going to be important.

I know you're thinking about this as a scientist and as a human being, what about Thanksgiving? Should people have Thanksgiving dinners, or is it better to take a break for a year?

SL: That's a tough one, Paul. I don't want to overstep my knowledge, expertise or my role in terms of presuming to tell folks what to do around their own personal activity or behaviors.

I'm asking you as a human being.

SL: That's how I'm going to answer it. I can only tell you how I'm going to approach it with my family and what makes sense to me. So, we know how this virus is spread. We know the virus is spread person to person as an aerosol, meaning if you're in an enclosed space with another person who's infected, and you have 15 minutes of exposure to that person without wearing a mask and without social distancing, over a 24-hour period, that cumulative 15 minutes over a 24-hour period, you have a very high chance of contracting the virus.

And, we still know that this virus causes a disease which has a much higher mortality than the flu, and much higher risk of hospitalization.

And, we also know that otherwise healthy folks can get very sick from this virus. And, we don't know that they completely recover, because some of the long-term effects, myocarditis, lung disease, etc, we are yet to fully understand. It will take us years to really understand the consequences of what it means to have been infected.

The way I'm approaching this with my own family is my immediate family will likely gather for Thanksgiving, because we've either spent a lot of time together, sort of co-quarantined, or my daughters, who live and work in Manhattan, will isolate themselves.

After several days of isolation, they will test themselves. They already have home saliva tests sitting in their apartments. They will test themselves, and then remain isolated until they get their test results back. And, if they're negative, I'll drive into the city and pick them both up—they both live in the same apartment building—and bring them back for our Thanksgiving dinner.

We are taking precautions that we are either having Thanksgiving with the nuclear family with those that have been quarantined together already for the most part, or have tested before they come back.

Thanksgiving is my favorite holiday. And, I usually have extended family all over to my house for Thanksgiving from all over the country. I have cousins up from Florida, my aunt up from Florida. I have my mom over who is in her 80s, everybody over to my house. It's one of my favorite times of the year.

But this year, we're just not doing that. And, it's not making a statement about it. It's because I don't want to put those family members at risk or any members of my family at risk. We all know how we care about each other. We may get on Zoom at each of our tables to do a toast and to share warm feelings with each other. But I think we have to be responsible as we move forward.

Everybody has to weigh their decisions. But, I would hope part of what factors into those decisions is risk and safety to each other. And, I think we owe that to each other as our families, and we owe that to each other as our larger socie-

tal family that we have to use common sense and take care of each other, take the right precautions, even though it's a bummer not to be able to have everybody around at the table. But you have to make certain sacrifices for the good of each other and for the good of everyone.

Is there anything we missed? Anything we didn't cover?

SL: The only thing I would add to this is I had mentioned to you when we spoke last, that we had set up a statewide call of all the cancer programs, and that during the heat of the pandemic, we were meeting every week. We've continued that call. During the summer we made it once-a-month. And now, as we're getting back into the heat of things, it's every other week, and we'll move back to once a week if we need to.

But that call has been incredibly useful, not just for the pandemic, but getting all the cancer leaders from the state together on a call every Friday morning has allowed us to exchange ideas, best practices, that's led to a number of interesting, collaborative research efforts that we are going to undertake. It's led to a lot of collegiality and assistance between the programs.

And, I think it will be of benefit to the patients and population of New Jersey that all of us are trying to work together in pursuit of more effective ways to screen, treat, and understand cancer in our population.

I'm very grateful to the other leaders of cancer centers across New Jersey for their commitment to this, and their collegiality and support in making certain that these lines of communication stay open and that we continue to share best practices on these calls.

Obviously, you try to look at the bright side of dark times. And certainly, this pandemic, there's been a lot of dark times. But one of the bright sides has been this connection that we've all made and that we're sustaining. And so, that's something I think is important to put into what we are discussing. Because, it shows that some positives can come out of a challenging situation.

Well, thank you so much for talking with me.

> “I think the key for us, in addition to a vaccine, is we need some effective therapies that we can give to patients once they become infected, but they're not even yet symptomatic.”

NEWS ANALYSIS

Election results notwithstanding, Trump stands poised to deliver blows to NIH, FDA, public health, research

By Matthew Bin Han Ong

The future of American health care, pandemic response, and sustained funding for cancer research hangs in the balance as the final votes are being counted and legal challenges launched in the 2020 presidential election.

At this writing, former Vice President Joe R. Biden is projected to win the election, but President Donald J. Trump, claiming election fraud, is unlikely to concede.

Much is at stake in this election, as the United States recorded over 120,000 new coronavirus cases on Nov. 5—the highest number of cases ever reported by a single country in a single day—as surges overwhelm hospitals in the upper Midwest. According to exit polls, most Americans ranked the economy and COVID-19 as top priorities that informed their decisions at the ballot.

Credible public health experts—including many oncologists—have openly criticized Trump's handling of the COVID-19 pandemic (*The Cancer Letter*, May 8, 2020, Coronavirus vs. Oncology). The deadly disease, caused by the SARS-CoV-2 virus, has claimed over 234,000 lives in the U.S. since March.

Congressional support for biomedical and cancer research is likely to remain solid no matter who is sworn in as the U.S. president in January. However, a potential second term for Trump may embolden him to act on his feud with NIH and FDA and make another effort to cut research funding.

Also, Trump would be expected to continue to chip away at operational aspects of the Affordable Care Act, even as he pushes for lower drug prices, as well as transparency in hospital billing practices and insurance reimbursement.

A Biden win would defend the ACA, and, possibly, lay down the foundations for a public healthcare framework, as per his campaign promise.

Of particular significance is Biden's record of securing $1.8 billion in a sweeping bipartisan deal to fund cancer research via the Beau Biden Cancer Moonshot, which was folded into the 21st Century Cures Act of 2016. The Moonshot has enabled the creation of a dedicated cancer center at FDA, led by Richard Pazdur (*The Cancer Letter*, Dec. 16, 2016, Jan. 20, 2017, To the Moon).

In spite of multiple budget proposals by the White House to slash domestic spending—including funding for biomedical research—over the past five years, Congress delivered some of the largest annual increases to NIH, growing the agency's budget by $11.6 billion, or 39%.

In 2018 alone, congressional appropriators added $3 billion to NIH, the largest increase in 15 years since the doubling

effort led by then Rep. John Porter (R-IL). In that same year, Trump's budget proposed slashing NIH funding by 27% (*The Cancer Letter*, July 10, 2020, April 6, 2018, March 16, 2018, March 17, 2017).

Porter, U.S. Congressman from the 10th district in Illinois for 21 years, who served on the U.S. House Committee on Appropriations and chairing the House Appropriations Subcommittee on Labor, Health and Human Services, Education and Related Agencies, had this to say about Trump's proposed budget cuts in 2018:

"Oh God. It would devastate medical research. Definitely devastate it," Porter said at the time to *The Cancer Letter*. "I can't tell you how they get their numbers. They look at the overall spending rate, and then they determine where they're going to suggest cuts and the hopeful message is to the people who want to cut down on the size of government and its reach, that they are doing what they were elected to do."

For many cancer patients, a repeal of the ACA could eliminate access to care—an outcome prevented by the late Sen. John McCain (R-AZ), who cast the deciding vote in July 2017 against a Republican effort to gut the healthcare law. With Democrats retaining control of the House of Representatives in the 2020 elections, another attempt at a repeal is unlikely to succeed over the next four years, even if Trump is re-elected.

To date, it remains unclear whether the White House and congressional Republicans have a replacement plan for the ACA, despite their vows to repeal the healthcare law and preserve subsidized insurance premiums and access to health care for an estimated over 20 million Americans who are covered under ACA provisions (*The Cancer Letter*, Jan. 20, 2017).

For career scientists at NIH and FDA and civil servants across the federal government, a hypothetical second term for Trump may prove devastating, pursuant to an Oct. 21 executive order that would strip civil service and due process protections for some federal employees.

On Nov. 2, a day before the election, Trump indicated that he may fire Anthony Fauci, the head of the National Institute of Allergy and Infectious Diseases and the face of the federal response to the COVID-19 pandemic. Fauci recently warned that the U.S. is badly positioned to cope with a winter surge, saying, "We're in for a whole lot of hurt. It's not a good situation."

Fauci said he and Deborah Birx, the coronavirus task force coordinator, have not spoken with Trump since early October.

Observers describe the Oct. 21 executive order as an attempt to purge Washington of "disloyal" career employees under the guise of "poor performance"—in a city that consistently and overwhelmingly votes Democratic. According to the latest tally, 92.6% of counted ballots in the District of Columbia favored Biden in the presidential election.

The White House said Trump's EO would "promote good governance and accountability within the federal workforce" by giving agencies more "flexibility to hire 'Schedule F' employees" and "to remove them without going through a lengthy appeals process."

The same "fact sheet" states that the order prohibits personnel actions against these employees, "including actions on the basis of the employee's partisan affiliation, other protected characteristics, or because of the employee's status as a whistleblower."

Even as a lame duck president, Trump is expected to launch these attacks on what he and his supporters describe as the "Deep State."

GUEST EDITORIAL

A slice of carrot cake with cream cheese frosting will not make the turmoil go away, but it can't hurt

By Chase Sloan
Author of "Cakes for Cancer Cookbook"

Tensions are running high, the soul of the country is at stake, the pandemic is afoot, the Thanksgiving dinner is in doubt, and winter is on its way to Cleveland, where I live.

Isn't this the perfect time for a nice slice of classic carrot cake with cream cheese frosting?

What follows is a recipe for this fall favorite and a story of how one 15-year-old—yours truly—put his extra time to the benefit of cancer research.

This past summer, in the midst of the COVID-19 pandemic, with all my plans cancelled, I was faced with the question that billions of people worldwide were asking themselves:

What do I do now?

Why not do something bigger than myself?

There are many worthy causes out there, and since both my parents are cancer researchers, cancer came to mind. Unfortunately, at age 15, there are a lot of things you can't really do too easily, and getting money to donate, or earning money at all are among them. Yet, if there's anything that the sports I participate in—Jiu Jitsu and bodybuilding—have taught me, it's that giving up is never the answer.

I thought of my mom's friend Anne Duli, who died of cancer. Anne, a long-time administrator at Case Comprehensive Cancer Center, became almost like a grandmother to me. I thought of her love for all things sweet, especially anything chocolate-flavored and her passion for using food to bring people together to show she cared.

I happen to be into baking and cooking and have been writing my own recipes, especially for cakes. Anne and I always

bonded over cooking and I would often bounce recipe ideas off of her. This is when it hit me, I thought to myself, "I have all these recipes just sitting around, waiting to be used...I should write a cookbook!"

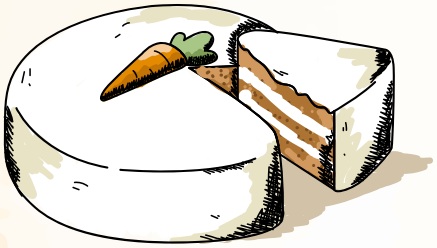
The goal was daunting, but I figured that if my father, a neurosurgeon, can save lives on the daily basis and my mother, a medical researcher, can publish dozens of papers a year, I can surely write one book and use the profits to raise money for cancer research.

If there's anything Anne taught me, it's that personal connection to food is what makes it special.

So, I spent the summer developing and editing recipes and personal vignettes that accompany them.

The book, *Cakes for Cancer Cookbook*, is available on Amazon as a Kindle e-book and also as a paperback. I am donating 75% of the proceeds to St. Jude Children's Research Hospital and the American Association for Cancer Research. It has received local and national media attention, enabling me to send sizable checks to St. Jude and AACR at the end of each month.

Whether you are baking for a big gathering, the nuclear family, or just yourself on this COVID-marred Thanksgiving, here is a recipe and a story:



Classic Carrot Cake

Carrot cake will always have a special place in my heart. The reason being that the recipe here is basically just an amped-up and even more moist version of a carrot cake recipe from my great grandma, which has been the staple at my family's Thanksgiving dinners for as long as I remember. For the longest time, it was something that we only made for Thanksgiving, which just made me look forward to it like crazy and crave it more. Now, this cake has become so popular among our family and close friends that it is requested year-round, and I gladly make it without thinking twice. Of course, we still make it every Thanksgiving as well, and I am honored to have my cake at a spot on the dessert table.

INGREDIENTS:

- *2 ¾ cup all-purpose flour*
- *1 ½ cup light brown sugar*
- *½ cup plus 2 tbsp sugar*
- *2 ¼ tsp baking powder*
- *½ tsp baking soda*
- *1 ¾ tsp cinnamon*
- *½ tsp nutmeg*
- *4 eggs*
- *1 tbsp molasses*
- *½ tsp ground ginger*
- *1 ⅓ cup vegetable oil*
- *½ cup milk*
- *2 ½ cups grated carrots*

STEPS:

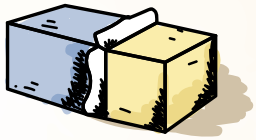
1. Put the eggs, oil, molasses and sugars in a large bowl and mix until the color lightens and the mixture is smooth.
2. Add in the spices and 1 ½ cups of flour and mix until combined.
3. Pour in the milk and mix until combined.
4. Fold in the last 1 cup of flour.
5. Divide the cake batter between 2 greased 9 inch round pans and bake at 325 degrees Fahrenheit until a toothpick comes out clean (about 40 minutes).

Cream Cheese Frosting

This one may only be five ingredients, but what a magical combination of five things it is. A frosting good and flavorful enough to eat on its own, this cream-cheese-heavy version of a classic Southern frosting tastes to me like a sweeter, thinner cheesecake batter and that is for sure not a bad thing. It was a no brainer for me to make this recipe more cream cheese-centric than most other recipes you'll find, but that gives it a prominent tang and impeccable richness that even my dog, Duke, loves. He may not be the toughest food critic, but he clearly loves this stuff, because he once broke a record two-month streak of not stealing food off the counter to lick this frosting off a cake's sides. Of course, I was too busy laughing to be mad, and I hold no grudges on him. Just a warning though, if you have a dog around, you may want to watch this frosting closely.

INGREDIENTS:

- *24 oz cream cheese*
- *1 cup softened salted butter*
- *1 ½ tsp vanilla extract*
- *1 ½ tsp vanilla paste*
- *5 ½ cups powdered sugar*



STEPS:

1. In a bowl, combine the butter and cream cheese until a cohesive mixture is formed.
2. Add in the vanilla and mix until incorporated.
3. Add the powdered sugar cup by cup and mix until smooth, adding milk as needed.

IN BRIEF

Timothy W. Mullett named chair of the Commission on Cancer of the American College of Surgeons

Cardiothoracic surgeon Timothy W. Mullett, medical director of the Markey Cancer Center Affiliate Network, was named chair of the Commission on Cancer of the American College of Surgeons.

Mullett has been serving as the chair-elect of the CoC for the past year.

Mullett is a surgical oncologist who specializes in the treatment of lung cancer. Although he began his career at the University of Kentucky as a cardiothoracic surgeon treating heart issues, he soon shifted his professional focus to treating lung cancer. Today, he is a co-leader and principal investigator of the Kentucky LEADS Collaborative to improve lung cancer survival.

In addition to his work in lung cancer research, Mullett serves as the chair of UK's cancer committee and the medical director of the Markey Cancer Center Research Network, a collaborative network that conducts high-priority trials, including therapeutic oncology trials and interventional and non-interventional studies for community centers.

In his role as chair, Mullett will serve as the spokesperson for oncology issues addressed by the organization, identify priorities for the CoC and National Cancer Database.

Donna D. Zhang receives $7.3 million NIEHS grant to research arsenic-induced lung cancer, Type 2 diabetes

Donna D. Zhang, of University of Arizona Health Sciences, has received an eight-year, $7.3 million grant from the National Institute of Environmental Health Sciences to determine how a family of proteins can be harnessed to prevent or treat arsenic-induced lung cancer and Type 2 diabetes.

Zhang is the Musil Family Endowed Chair in Drug Discovery at the UArizona College of Pharmacy, research member at the UArizona Cancer Center, and associate director of the UArizona Superfund Research Center.

Arsenic is present in almost all groundwater sources in Arizona, particularly in rural areas. Combined with occupational exposures, such as mining, more than 160 million people worldwide have been exposed to potentially unsafe levels of arsenic.

Zhang began studying NRF2 in 2000 as a research assistant professor at the University of Missouri-Columbia, and has continued her work since joining UArizona Health Sciences in 2005.

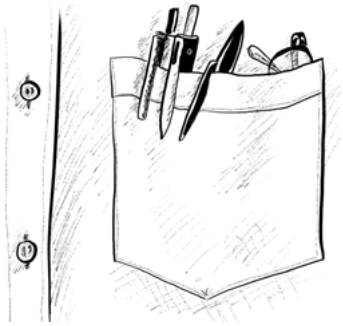
"Three types of cancer primarily are induced by exposure to arsenic: lung, skin and bladder," Zhang said in a statement. "This project will focus on lung cancer, and our goal is to identify new pharmaceuticals to prevent or treat adverse health effects resulting from arsenic exposure."

Zhang's past research has uncovered both positive and negative effects of NRF2, a protein that plays a critical role in protecting healthy cells because of its ability to control how certain genes are expressed in response to stressors. These genes help protect the cell from damage that can lead to cancer progression and resistance to therapy. NRF2 has been a therapeutic target for chemoprevention drugs to help slow or stop the spread of cancer and other diseases.

Zhang also has uncovered what she calls a "dark side" to NRF2. Although NRF2 has the positive benefit of protecting healthy cells, it also can protect cancer cells. This occurs when NRF2 is activated constantly, meaning it is not being properly regulated. The result of this hyperactivation can lead to cancer growth, spread and resistance to therapy. It also can promote a pro-diabetic shift in metabolism, which can lead to Type 2 diabetes.

"We are trying to better understand how arsenic disrupts the NRF2-mediated balance, resulting in lung cancer and Type 2 diabetes," Zhang said. "We want to rationally target NRF2 with a rigorous, multitiered approach to generate legitimate therapeutic options to mitigate these diseases."

THE CLINICAL CANCER LETTER



TRIALS & TRIBULATIONS

Living with cannabis: The goal of helping cancer patients live in comfort deserves data now

By Dylan M. Zylla, MD, MS
Medical director, HealthPartners/Park Nicollet Cancer Research Center; Adjunct assistant professor, University of Minnesota

In the election this week, voters said Yes to measures to legalize recreational cannabis (marijuana) in Arizona (60%), New Jersey (67%), and Montana (57%). Measures to legalize medical cannabis passed in Mississippi (68%) and South Dakota (54%).

Patients with advanced cancer battle debilitating symptoms of pain, nausea, and anxiety, among others. Many patients have grown fearful of taking opioids despite experiencing severe cancer-related pain, because of the ongoing opioid epidemic.

Cannabis (marijuana) use is becoming more prevalent in patients with cancer[1], perhaps due to its ability to help manage multiple symptoms with minimal side effects.[2,3] Despite scant clinical evidence, other than case reports, nearly one-quarter of patients also use cannabis, with the hopes it will treat their cancer.[1]

Furthermore, nearly three in four patients want information about cannabis from their cancer care team, yet only 15% receive it. However, only 30% of oncologists feel they have sufficient training to make informed recommendations about cannabis[4], and 85% want more education.[5]

While robust randomized trial data does not exist with cannabis, since 2000, 19 clinical studies have assessed how cannabis containing products impact symptoms and global quality of life in patients with cancer.[6] Nabiximols (an oromucosal spray containing a 1:1 ratio of delta-9-tetrahydrocannabinol (THC) to cannabidiol (CBD) was evaluated in two large placebo-controlled trials for cancer-related pain[7], showing little overall impact in patients with refractory cancer-related pain.

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In addition, two large survey studies involving over 4,000 patients demonstrated cannabis may improve a variety of symptoms, and may lessen use of concomitant medications such as opioids and antiemetics.[2,3] The lack of clear dosing standards and delivery mechanisms make analyzing results across studies challenging.

For patients, the issues of safety, stigma, quality, and cost may be most important. Side effects of cannabis reported in the aforementioned studies were often mild. Cannabis may be safer than opioids as studies indicate lower opioid-related deaths in states that have enacted cannabis laws.

While cannabis has generally been considered safe with traditional cytotoxic agents, there is growing concern that the anti-inflammatory properties of cannabis may negatively impact immunotherapy.[8,9] Furthermore, little is known about how cannabis may impact metabolism of oral chemotherapy (e.g., "targeted agents"), such as those commonly used for breast and prostate cancer.

> For patients, the issues of safety, stigma, quality, and cost may be most important. Side effects of cannabis reported in the aforementioned studies were often mild.

The stigma of cannabis use may prevent more widespread implementation. Patients may be reluctant to disclose their cannabis use (or interest in potential use) for fear their oncologist may limit or alter the cancer-directed treatment plan. Determining the exact dose of THC or CBD patients are ingesting is difficult, unless laboratory testing of products becomes mainstream. Even less may be known about the ubiquitous over-the-counter CBD-only products where use is becoming widespread.

Finally, the costs of cannabis products can be prohibitive, with regular users paying $3,000 or more a year. In oncology, out-of-pocket costs for chemotherapy treatments and routine care already weigh heavily on patients.

In Minnesota, a randomized delayed-start trial of cannabis in patients with incurable cancer requiring opioids for pain was launched with a goal to minimize opioid requirements and improve quality of life.[10] The study used a novel design utilizing a state-sponsored cannabis program with 36% of eligible patients screened ultimately enrolling. Of the 30 patients enrolled, cannabis users showed a trend toward improved pain control and lower opioid use.

Patients with advanced malignancies often prefer to focus on quality of life over quantity. As such, finding safe, effective, cost-efficient ways to help them manage symptoms is paramount. Barriers to conducting interventional cannabis research include:

a. requirement of a schedule 1 DEA license,

b. the myriad cannabis products/ strains available, and

c. the lack of dedicated research funding opportunities.

In December 2020, the NCI Cannabis, Cannabinoids, and Cancer Research Symposium will bring together leaders in this field. Cannabis likely has a role, but determining which patients (and symptoms) benefit the most is currently challenging.

High-quality studies are needed to enable patients, providers and policymakers to make informed decisions on the use of cannabis. Without additional data, the true benefits and risks of cannabis use will remain clouded in smoke.

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A Recap:

The electorates in four states, New Jersey, South Dakota, Montana and Arizona, voted decisively to legalize recreational marijuana Nov. 3, 2020, and voters in Mississippi and South Dakota also approved initiatives to legalize medicinal marijuana. In Oregon, voters decriminalized small amounts of heroin, cocaine, and methamphetamine—becoming the first state to do so. In Washington, D.C., voters approved a ballot initiative to decriminalize psychedelic mushrooms, among other psychedelic plants.

> While cannabis has generally been considered safe with traditional cytotoxic agents, there is growing concern that the anti-inflammatory properties of cannabis may negatively impact immunotherapy.

CLINICAL ROUNDUP

Cancer patients, clinicians find value in electronic real-time symptom reporting

Cancer patients and their medical teams found it beneficial when patients shared their symptoms in real time using a web- or telephone-based reporting system, according to a national multi-institutional study, the PRO-TECT trial.

The PRO-TECT trial is evaluating the use of electronic patient-reported outcomes among adults receiving outpatient treatment for advanced and metastatic cancers. The study was published in *JCO Clinical Cancer Informatics*.

"Our prior research showed that using a web-based system for patients to self-report symptoms to their cancer care team improves patient satisfaction, quality of life, physical function, reduces emergency room visits and lengthens survival," Ethan Basch, director of UNC Lineberger's Cancer Outcomes Research Program and the Richard M. Goldberg Distinguished Professor and chief of oncology at the UNC School of Medicine, said in a statement. "However, it has not been clear whether this approach could be widely used in cancer practices across the U.S. or be seen as useful or valuable by patients and providers. It is essential with any strategy for improving care to make sure that people will actually use it and find it valuable."

In the new study, the researchers conducted a cluster-randomized controlled study at 52 community-based oncology practices across the United States. Half of the practices were assigned to use ePROs as part of the standard of care.

Participants in the study's intervention arm were prompted every week for a year to report their symptoms and well-being. This involved using a website or an automated telephone program to answer a series of questions about their symptoms, such as pain, nausea and depression, as well as their physical functioning and financial health.

The responses had a pre-assigned value on a five-point scale. When a patient reported worsening or severe symptoms, they were sent an email with information on symptom management and a nurse was alerted in real-time to intervene.

To measure whether the ePRO process and information gathered provided value, as well as to identify challenges, the researchers surveyed the patients and clinicians. Patients provided feedback three months after they started on the study and when they completed it. Nurses and physicians shared their assessment on clinical usefulness after they had worked with the system for six months or more.

The majority of the 496 patients surveyed found the PRO-TECT digital ePRO system was easy to understand (95%) and use (93%), and the questions were relevant to their care (91%). Most of the 57 nurses responded that the information was helpful for clinical documentation (79%) and useful for patient care (75%). Of the 39 oncologists surveyed, most found ePRO information useful (91%).

Though clinicians said the ePRO system was useful overall, some reported the information collected had limited value. Sixteen percent of the nurses surveyed said it rarely or never improved discussions with patients, and 14% said it didn't improve care quality. Nearly 30% of physicians said they rarely used patient-reported information to shape their discussions with patients. Also, some nurses felt they received too many symptom alerts, yet 93% wanted to receive future alerts for severe symptoms.

"There is clearly a lot of enthusiasm from patients to connect to their care team through electronic real-time approaches, and providers also recognize this value, but we know it isn't perfect," Basch said. "Our findings lay a path forward for determining the best ways to integrate patient-reported outcomes in oncology practice."

Basch said a number of issues need to be addressed to encourage clinics and hospitals to consider using ePRO systems. The technology must be easy for patients and providers to use. Workflows may need to be modified to give nurses more time to respond to symptom alerts.

Basch said it would be helpful to develop standardized ways to teach patients how to use the system and to remind them of the importance of using it. In addition, it is important to continuously monitor and troubleshoot a program while it is being implemented.

"Patient reported outcomes are well accepted and seen as valuable for quality care by patients and providers, and they improve patient engagement and experience," Basch said. "Models for health systems to successfully implement PRO programs are needed, likely based on quality improvement approaches. For

wide implementation to be effective, a financial model will also be helpful for PROs, most likely through direct reimbursement from insurance companies, or as a key component of value-based alternative payment arrangements between health systems and insurance payers."

Colon cancer surgery performed by highly skilled surgeons improves long-term survival for patients

Researchers found that colon cancer patients achieve better five-year survival rates when the surgeons who treat them are rated as highly skilled.

The study is published online in *JAMA Oncology* and was virtually presented as part of the American College of Surgeons Commission on Cancer's Annual Research Paper Competition.

"In the last few years, studies have shown that patients of more highly skilled surgeons have fewer immediate postoperative complications. This study moves to the next level and shows that patients of more highly skilled surgeons not only have fewer complications in the short term, they survive longer," lead author Brian C. Brajcich, a clinical scholar with the American College of Surgeons, research fellow at Northwestern University School of Medicine, said in a statement.

The study was conducted by the Illinois Surgical Quality Improvement Collaborative, a group of 56 hospitals that perform 80% of the complex surgical operations across the state. The ISQIC is a collaborative partner with the American College of Surgeons National Surgical Quality Improvement Program.

"A previous study done by our group found that lapses in surgical technique can result in a complication within a few days of surgery. This study is striking because no one has looked directly at the relationship between surgical skill and improved survival at the five-year mark, and, yes, surgeons with better skill achieve considerably better survival rates for their patients," Karl Y. Bilimoria, director of the Surgical Outcomes and Quality Improvement Center at Northwestern Medicine, and an ACS Faculty Scholar, said in a statement.

The type of surgery for colon cancer depends on the extent and location of the cancer and the goal of treatment. During a laparoscopic colectomy, for example, the surgeon removes the cancerous area of the colon, a small segment of normal colon on either side, and nearby lymph nodes.

Study investigators recruited surgeons from the ISQIC in 2016 to participate in a video-based technical skills assessment program. Each surgeon was videotaped while performing a minimally invasive right hemicolectomy (partial surgical removal of the colon). Videos were reviewed by 12 or more surgeons, including two colorectal surgeons experienced in evaluating surgical video tapes.

Each reviewer assigned a skill score to the video he or she reviewed. Skill scores were derived from the American Society of Colon and Rectal Surgeons Video Assessment Tool, which assesses factors such as gentleness of tissue manipulation, efficient and methodical performance of the procedure, and extent of surgical excision. Skill levels for the surgeons in the study reflected the mean skill score from all reviewers.

The study included 609 patients who underwent laparoscopic colectomy by one of the participating surgeons between 2012 and 2017. Five surgeons who achieved the highest technical skill scores also had the highest volume of procedures in the study, as well as the highest average annual number of surgical cases; the totals were more than two times higher than the number of procedures performed by other surgeons. Overall, five-year survival for these surgeons was 79%. Five-year survival rates were 55% for medium-skilled surgeons and 60% for low-skilled surgeons.

"This study demonstrates that surgical technical skill is an important driver of long-term outcomes in cancer surgery. When talking about ways to improve outcomes for patients, we surgeons should not only think about quality measures but ways to improve surgeons' skills through some form of surgical coaching," Brajcich said.

The Northwestern Medicine health system is bringing surgeons together in the Technical Excellence Collaborative to review one another's work, find opportunities for improvement in technique, and follow patients to track their outcomes, Bilimoria said.

"High surgical volumes have been shown to result in lower morbidity and improved outcomes for many types of surgery and this study shows that technical skill also results in improved survival for patients with colon cancer," Kelly K. Hunt, professor and chair of the Department of Breast Surgical Oncology at MD Anderson Cancer Center, said in a statement.

"The ACS Cancer Research Program has also shown that adherence to the critical elements of an operation [operative standards] also results in improved outcomes and quality of life for cancer patients," said Hunt, who is also vice-chair of the Cancer Surgery Program. Therefore, the Cancer Surgery Standards Program was formed to develop synoptic operative reporting templates, electronic documentation tools, and educational content around these operative standards. Ultimately, the program seeks to facilitate adoption

and utilization of synoptic operative reporting tools for improved outcomes in all major cancer operations."

Other study authors include Jonah J. Stulberg, MD, PhD, MPH; Bryan E. Palis, MA; Jeanette W. Chung, PhD; Reiping Huang, PhD; and Heidi Nelson, MD, FACS.

Active surveillance is safe for African Americans with low-risk prostate cancer

Researchers found that active surveillance is safe for African Americans with low-risk prostate cancer.

In the study, published Nov. 3 in *JAMA*, researchers hypothesized that African American men undergoing active surveillance are at a significantly higher risk of disease progression, metastases and death from prostate cancer compared to non-Hispanic white men.

Results demonstrate that that 59.9% of African American men experienced disease progression compared to 48.3% of white men. In addition, 54.8% of African Americans required treatment, compared to 41.4% of white men.

However, African American men and white men experience comparable rates of metastasis (1.5% vs 1.4%) and prostate cancer-specific death (1.1% vs 1.0%).

"Our research provides evidence that active surveillance is safe for African American men," senior author Brent Rose, assistant professor in the Department of Radiation Medicine and Applied Sciences at University of California San Diego School of Medicine, said in a statement. "This means more African American men can avoid definitive treatment and the associated side effects of urinary incontinence, erectile dysfunction and bowel problems."

The retrospective study looked at outcomes for 2,280 African American men and 6,446 non-Hispanic white men with low-risk prostate cancer who underwent active surveillance under the VA health care. The database included access to the health care records of 9 million veterans between 2000 and 2020 who received care at 1,255 health care facilities in the United States.

Previous studies have shown that African American men are 2.4 times as likely to die from prostate cancer compared to non-Hispanic white men. This, plus a concern that African Americans may develop cancers that are more aggressive, has led to fewer Black men being offered active surveillance as a treatment strategy.

One in nine men will receive a prostate cancer diagnosis in their lifetime. Prostate cancer is more likely to develop in older men and in African American men. While the average age for diagnosis is 66, the number of younger men diagnosed with this disease is increasing.

Active surveillance is the preferred treatment option for many men with low-risk prostate cancer in order to avoid or delay the side effects of definitive treatments.

"Physicians and patients should discuss active surveillance for African American men with low-risk prostate cancer," said Rose, a radiation oncologist at Moores Cancer Center at UC San Diego Health and senior author on the paper. "Overall outcomes are similar among African American men and white men. However, due to the increased risk of progression, African American men need to be carefully followed and promptly treated if their cancer progresses."

Co-authors are: Rishi Deka, Patrick T. Courtney, J. Kellogg Parsons, Tyler J. Nelson, Vinit Nalawade, Elaine Luterstein, Daniel R. Cherry, Daniel R. Simpson, Arno J. Mundt, James D. Murphy, Christopher J. Kane, Maria E. Martinez, all of UC San Diego; and Anthony V. D'Amico, of Harvard Medical School and Dana-Farber Cancer Institute.

This research was funded, in part, by NIH (TL1-TR001443) and the Department of Defense (W81XWH-17-PCRP-PRA).

Nerves keep pancreatic cancer cells from starving, study finds

Researchers found that pancreatic cancer cells avert starvation by signaling to nerves, which grow deeply into dense tumors and secrete nutrients.

The study, based on experiments in cancer cells, mice, and human tissue samples, was published Nov. 2 in *Cell*.

The study addresses pancreatic ductal adenocarcinoma, the deadliest cancer of the pancreas with a five-year survival rate below 10%. Such tumors encourage the growth of dense tissue that presses on blood vessels, reducing the supply of blood-borne nutrients like serine. This amino acid is used as a building block for proteins, and is required for cancer cells to multiply.

Led by researchers from NYU Grossman School of Medicine, the Department of Radiation Oncology at NYU Langone Health, and Perlmutter Cancer Center, the study found that starving pancreatic cancer cells secrete a protein called nerve growth factor, which sends signals to extensions of nerve cells, instructing them to grow deeply into tumors.

The researchers found further that such extensions, called axons, secrete

serine, which rescues pancreatic cancer cells from starvation and restores their growth.

"Our study offers more proof that pancreatic cancers are remarkable metabolic scavengers, which contributes to their deadliness," corresponding author Alec Kimmelman,the Anita Steckler and Joseph Steckler Chair of the Department of Radiation Oncology at NYU Langone, said in a statement. "The ability of nerves to funnel nutrients from the bloodstream to the more austere pancreatic tumor microenvironment is a fascinating adaptation, and could lead to therapeutic approaches that interfere with this unique flexibility."

The study found that pancreatic cancer cells starved of serine take advantage of the process by which messenger RNA strands are translated into proteins. Bases of mRNA molecular strands are decoded into amino acids using three-base units called codons.

Ribosomes read each codon as they link amino acids together in the right order, but ribosomes stall if there is a lack of available amino acids.

The researchers found that serine-starved pancreatic cancer cells more significantly slow the rate at which two of the six serine codons (TCC and TCT), but not all six as assumed, are translated into amino acid chains.

Under serine-starved situations, this variability lets cancer cells minimize the production of certain proteins, but continue to build stress-adaptive proteins like nerve growth factor, which happens to be encoded by few TCC and TCT codons.

NGF and other factors are known to encourage nerves to grow into pancreatic tumors, and to increase tumor growth as well. The study is the first to show that axons, extensions of neuronal cells that transmit their signals, provide metabolic support to cancer cells by secreting serine in nutrient-deprived areas.

In a glimpse of potential future applications for the study, mice with PDAC tumors fed serine-free diets saw 50% slower tumor growth. To go beyond what diet alone could achieve, the researchers also blocked the recruitment of axons into PDAC tumors using FDA-approved LOXO-101. The drug blocks the activation of a receptor protein on the surface of neurons that interacts with nerve growth factor (also called TRK-A), thereby inhibiting the ability of neurons to send their axons into tumors.

LOXO-101 alone did not slow PDAC tumor growth in mice, but slowed it by an additional 50% when combined with a serine-free diet, compared with the diet alone. This suggests that nerves were necessary to support PDAC cell growth in serine-deprived tumor regions.

"As TRK inhibitors are approved in the treatment of some cancers, they might have value in combination with a low serine diet following surgery in the perhaps 40% of patients with PDAC tumors that can't make serine," lead study author Robert Banh, a post-doctoral scholar in Kimmelman's lab, said in a statement. "Whether this approach could decrease tumor recurrence by limiting the nutrient supply would need to be confirmed in clinical trials."

Large-scale cancer proteomics study profiles protein changes in response to drug treatments

Through large-scale profiling of protein changes in response to drug treatments in cancer cell lines, researchers at MD Anderson Cancer Center have generated a resource to aid in predicting drug sensitivity, to understand therapeutic resistance mechanisms and to identify optimal combination treatment strategies.

Their findings, published in *Cancer Cell*, include expression changes in more than 200 clinically relevant proteins across more than 300 cell lines after treatment with 168 different compounds, making it the largest dataset available on protein responses to drug treatments in cancer cell lines.

"We've seen a number of perturbation studies that look at gene expression changes following drug treatments or CRISPR-mediated changes, but there is a significant gap in terms of proteomic profiling," senior author Han Liang, professor of bioinformatics and computational biology, said in a statement. "We hoped to fill that gap by profiling changes in major therapeutic target proteins, which provides a lot of insight in terms of drug resistance and designing drug combinations."

Perturbation biology measures how a system, such as cancer cells, responds to various stimuli. These types of experiments have proven useful in modeling cancer behaviors and understanding responses at a system level, Liang said. To profile protein perturbations, the researchers used a technique called reverse-phase protein array (RPPA), which enables the rapid quantitative analyses of a select group of proteins. Protein levels were measured at baseline and after treatment, often at multiple time points.

The study evaluated drugs targeting a variety of signaling pathways and cellular processes across 319 commonly used, well-characterized cell lines from many cancer types, including breast, ovarian, uterine, skin, prostate and hematologic cancers.

Rather than analyzing all possible drug-cell line combinations, the researchers

focused on those most likely to be relevant to the field. In total, they generated RPPA profiles of 15,492 samples, including 11,884 drug-treated samples and 3,608 control samples. The data was highly reproducible and verified by multiple independent pathways.

The data obtained from these analyses provides important insight into the mechanisms of drug response or resistance, highlighting signaling pathways that are activated or suppressed following treatment with a given drug. Further, having data on both baseline and post-treatment protein levels is much more useful in modeling to predict sensitivity to additional drugs, Liang said.

The researchers also constructed a comprehensive map of protein-drug connections to visualize responses and to better study relationships between different proteins and signaling pathways. The maps showcase which proteins have significant changes from a given drug, which drugs yield similar responses and which proteins saw similar patterns of change. Studying these complex relationships can reveal unknown connections and can point to potentially effective therapeutic combinations.

"Through this dataset, one can immediately see the consequences of a given drug, including perturbed pathways and adaptive responses, which can help to identify optimal drug combinations," Liang said. "As we continue working to expand the data, we think this will be a valuable starting place for researchers doing drug mechanism studies."

The protein response data is publicly available for researchers in a data portal, which provides various methods for visualizing and downloading the data.

Although the study includes only a subset of cancer types, the researchers hope to continue adding to the dataset in the future. In the long-term, the research team anticipates that proteomic profiling at baseline and following treatment may be a useful tool in clinical trials to better follow patient treatment responses and to optimize therapeutic strategies.

This study was supported by the National Institutes of Health (U01CA168394, U24CA143883, U54HG008100, P50CA098258, P50CA217685, U24CA209851, U01CA217842, P50CA221703, U24CA210950, U24CA210949, R50CA221675, UL1TR003167, and P30CA016672), the Dr. Miriam and Sheldon G. Adelson Medical Research Foundation, Susan G. Komen, the Ovarian Cancer Research Foundation, the Breast Cancer Research Foundation, the The Lorraine Dell Bioinformatics for Personalization of Cancer Medicine Program, the Department of Defense (W81XWH-16-1-0237), the Cancer Prevention & Research Institute of Texas (RP170593, RP160015 and RP170640), the Ovarian Cancer Research Alliance, the Fund for Innovation in Cancer Informatics, and NCI's Office of Cancer Genomics Cancer Target Discovery and Development (CTD2) initiative.

DRUGS & TARGETS

Lynparza approved in the EU as first-line maintenance treatment with bevacizumab for HRD-positive advanced ovarian cancer

Lynparza (olaparib) has been approved in the European Union for the first-line maintenance treatment with bevacizumab of patients with homologous recombination deficient-positive advanced ovarian cancer.

Lynparza is sponsored by AstraZeneca and MSD.

The approval by the European Commission was based on a biomarker subgroup analysis of the PAOLA-1 phase III trial, which showed that Lynparza, in combination with bevacizumab maintenance treatment, demonstrated a substantial progression-free survival improvement versus bevacizumab alone for patients with HRD-positive advanced ovarian cancer. It follows the recommendation for approval by the Committee for Medicinal Products for Human Use of the European Medicines Agency in September 2020.

The PAOLA-1 Phase III trial showed that Lynparza, in combination with bevacizumab maintenance treatment, reduced the risk of disease progression or death by 67% (based on a hazard ratio of 0.33; 95% confidence interval

0.25-0.45). The addition of Lynparza improved PFS to a median of 37.2 months versus 17.7 with bevacizumab alone in patients with HRD-positive advanced ovarian cancer. The data from the PAOLA-1 trial was published in The New England Journal of Medicine in 2019.

Further results recently presented at the European Society for Medical Oncology Virtual Congress 2020 showed a statistically significant improvement in the key secondary endpoint of the time to second disease progression. Lynparza with bevacizumab provided benefit beyond first disease progression, improving PFS2 to a median of 50.3 months versus 35.3 with bevacizumab alone.

The full EU indication is for Lynparza in combination with bevacizumab for the maintenance treatment of adult patients with advanced (FIGO stages III and IV) high-grade epithelial ovarian, fallopian tube or primary peritoneal cancer who are in response (complete or partial) following completion of first-line platinum-based chemotherapy in combination with bevacizumab and whose cancer is associated with HRD positive status defined by either a breast cancer susceptibility gene 1/2 (BRCA1/2) mutation and/or genomic instability.

Lynparza in combination with bevacizumab is approved in the U.S. and other countries as first-line maintenance treatment for HRD-positive advanced ovarian cancer and is currently under regulatory review in other countries.

Kymriah receives approval for commercial manufacturing in Japan

Japan's Ministry of Health, Labor and Welfare has issued marketing authorization for Foundation for Biomedical Research and Innovation at Kobe to manufacture and supply commercial Kymriah (tisagenlecleucel) for patients in Japan.

Kymriah is sponsored by Novartis.

Commercial manufacturing for Kymriah now takes place at five sites globally including at the Morris Plains, New Jersey facility, where FDA approved a further increase in manufacturing capacity.

Kymriah is the first-ever FDA-approved CAR T-cell therapy, and the first-ever CAR-T to be approved in two distinct indications. Kymriah is currently approved for the treatment of r/r pediatric and young adult (up to 25 years of age) acute lymphoblastic leukemia, and r/r adult diffuse large B-cell lymphoma (DLBCL).

Kymriah, approved in both indications by the Japan MHLW in 2019, is currently the only CAR T-cell therapy approved in Asia. Clinical manufacturing began at FBRI in 2019 and will continue alongside commercial manufacturing.

Kymriah was developed in collaboration with the Perelman School of Medicine at the University of Pennsylvania.

Kymriah is currently approved for use in at least one indication in 26 countries and at more than 260 certified treatment centers.

Merck to acquire VelosBio for $2.75 billion

Merck and VelosBio Inc. have entered into a definitive agreement, where Merck, through a subsidiary, will acquire all outstanding shares of VelosBio for $2.75 billion in cash.

VelosBio is a privately held clinical-stage biopharmaceutical company committed to developing first-in-class cancer therapies targeting receptor tyrosine kinase-like orphan receptor 1.

VelosBio's lead investigational candidate is VLS-101, an antibody-drug conjugate targeting ROR1 that is being evaluated in a phase I and a phase II clinical trial for the treatment of hematologic malignancies and solid tumors.

In October 2020, VelosBio began a phase II clinical trial (NCT04504916) to evaluate VLS-101 for the treatment of patients with solid tumors, including patients with triple-negative breast cancer, hormone receptor-positive and/or HER2-positive breast cancer, and non-squamous non-small-cell lung cancer.

In early clinical trials, VLS-101 demonstrated a manageable safety profile and early signs of anti-tumor activity. Results of a phase I clinical trial, to be presented virtually at the American Society of Hematology Annual Meeting (Dec. 5-8, 2020), showed that VLS-101 resulted in objective clinical responses, including complete responses, in 47% (n=7/15) of patients with mantle cell lymphoma (MCL) and 80% (n=4/5) of patients with diffuse large B-cell lymphoma.

Patients in this phase I trial had been heavily pretreated with other anticancer medications, and their cancers had failed to respond or had relapsed after initially responding to these other anticancer medications. In addition, VelosBio is developing a preclinical pipeline of next-generation ADCs and bispecific antibodies targeting ROR1 with the potential to complement VLS-101 by offering alternative methods of tumor cell killing.

The closing of the transaction, which is subject to approval under the Hart-Scott-Rodino Antitrust Improvements Act and other customary conditions, is expected by the end of 2020.

Merck was represented by Gibson Dunn & Crutcher LLP as legal advisor and J.P. Morgan Securities LLC as financial advisor. VelosBio was represented by Cooley LLP as legal advisor and Centerview Partners LLC as financial advisor.

NCI TRIALS

NCI Trials for Nov. 2020

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

For further information, contact the principal investigator listed.

Phase I - PED-CITN-01
3CI Study: Childhood Cancer Combination Immunotherapy. Phase Ib and Expansion Study of Nivolumab Combination Immunotherapy in Children, Adolescent and Young Adult (CAYA) Patients with Relapsed/Refractory Hypermutant Cancers

Cancer Immunotherapy Trials Network
Morgenstern, Daniel Alexander
(416) 813-7654

Phase II - A021804
A Prospective, Multi-Institutional Phase II Trial Evaluating Temozolomide vs. Temozolomide and Olaparib for Advanced Pheochromocytoma and Paraganglioma

Alliance for Clinical Trials in Oncology
Del Rivero, Jaydira
(240) 805-2888

Phase II - AMC-107
A Phase 2 Trial of Ixazomib for Kaposi Sarcoma

AIDS Malignancy Consortium
Mitsuyasu, Ronald T.
(310) 825-6689

Phase II - EA8184
A Phase II Randomized Double Blinded Study of Green Tea Catechins (GTC) vs. Placebo in Men on Active Surveillance for Prostate Cancer: Modulation of Biological and Clinical Intermediate Biomarkers

ECOG-ACRIN Cancer Research Group
Kumar, Nagi B.
(813) 745-6885

Phase III - EA9181
A Phase III Randomized Trial of Steroids + Tyrosine Kinase Inhibitor Induction with Chemotherapy or Blinatumomab for Newly Diagnosed BCR-ABL-Positive Acute Lymphoblastic Leukemia in Adults

ECOG-ACRIN Cancer Research Group
Ofran, Yishai
+972-4-7772541

Phase III - EAA181
Effective Quadruplet Utilization After Treatment Evaluation (EQUATE): A Randomized Phase 3 Trial for Newly Diagnosed Multiple Myeloma Not Intended for Early Autologous Transplantation

ECOG-ACRIN Cancer Research Group
Kumar, Shaji K.
(507) 284-2017

Phase III - NRG-BN009
Phase III Trial of Salvage Stereotactic Radiosurgery (SRS) or SRS + Hippocampal-Avoidant Whole Brain Radiotherapy (HA-WBRT) for First or Second Distant Brain Relapse After Upfront SRS with Brain Metastasis Velocity >/= 4 Brain Metastases/Year

NRG Oncology
Gondi, Vinai
(630) 821-6430

Phase Other - A231901CD
Improving Patient-Centered Communication in Breast Cancer: A RCT of a Shared Decision Engagement System (SHADES)

Alliance for Clinical Trials in Oncology
Hawley, Sarah
(734) 936-8816