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THE CANCER LETTER

Inside information on cancer research and drug development

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MaineHealth Physician Recruitment Center



Associate Medical Director, Medical Oncology/Hematology and Cancer Genetics

Many choose to spend their vacations where we call home. Known for rocky coastlines, sandy beaches, sparkling lakes and breathtaking mountains, Maine offers much more to those lucky enough to live, work and raise families here. Come practice in a location that provides unsurpassed natural beauty, safe communities, excellent schools and nearly unlimited four-season outdoor recreation.

We are actively seeking physicians with expertise in general medical oncology/hematology, cancer genetics, and physician leaders as Associate Medical Directors to join Maine Medical Center's Division of Medical Oncology and our expanding statewide oncology program – the MaineHealth Cancer Care Network (MHCCN). The network is a coordinated system of care in which 11 MaineHealth partner hospitals and organizations work together to deliver the highest quality cancer care to patients as close to home as possible. The network provides a complete array of cancer care, including surgery, radiation and chemotherapy.

The MaineHealth Cancer Care Network (MHCCN) is rapidly growing a highly integrated care delivery network across the southern, central, and coastal regions of Maine and eastern New Hampshire. The network is comprised of 11 hospital partners and provides care to more than 6,300 analytic cancer cases annually. Maine Medical Center (MMC), the flagship of MaineHealth's integrated delivery system, an affiliate of Tufts University School of Medicine, has 637 licensed beds and is the state's leading tertiary care hospital and Level I Trauma Center, with a full complement of residencies and fellowships. MHCCN has expanding clinical trials portfolio greatly afforded by our recent inclusion in the NCI's Community Oncology Research Program (NCORP).

We are seeking individuals with a track-record of successful training, scholarship, commitment to cancer clinical trials, and/or clinical care in a progressive academic setting/health system environment.

For more information, please contact Gina Mallozzi, Physician Recruiter at (207) 661-2092 or gmallozzi@mainehealth.org.

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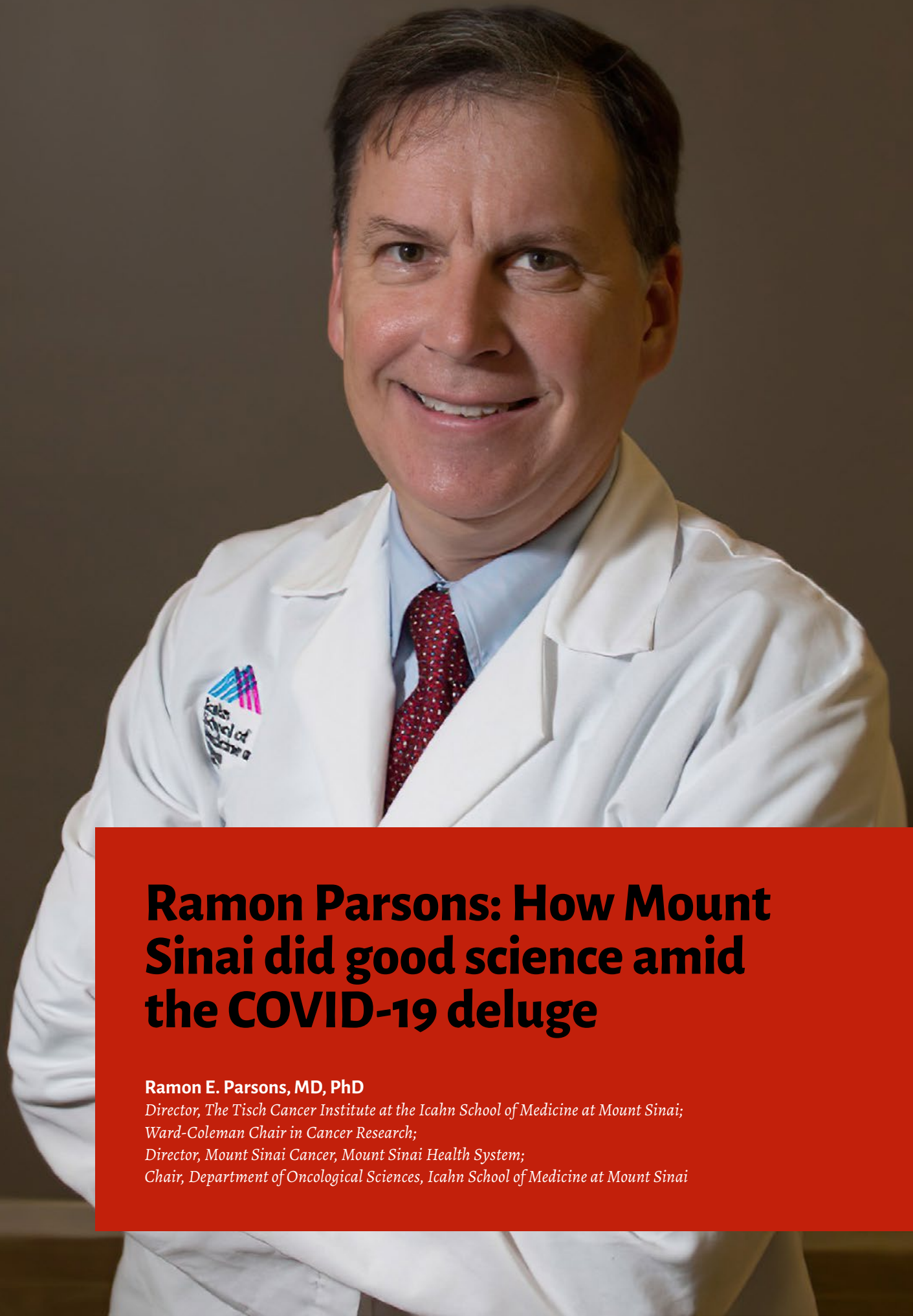
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Ramon Parsons: How Mount Sinai did good science amid the COVID-19 deluge

Ramon E. Parsons, MD, PhD

Director, The Tisch Cancer Institute at the Icahn School of Medicine at Mount Sinai;

Ward-Coleman Chair in Cancer Research;

Director, Mount Sinai Cancer, Mount Sinai Health System;

Chair, Department of Oncological Sciences, Icahn School of Medicine at Mount Sinai

Q

&

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

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CONVERSATION WITH THE CANCER LETTER

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Almost half of our physicians were redeployed to take care of COVID patients, with the rest needing to cover our cancer patients, of course, with a lot of telemedicine.

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The first COVID-19 patient walked into a Mount Sinai ER on March 1.

“It was somebody who had some foreign travel under their belt, and they’d returned, and they weren’t even that sick, actually. But they showed up in the ER, because they were suspicious,” Ramon E. Parsons, director of The Tisch Cancer Institute at the Icahn School of Medicine at Mount Sinai, said to *The Cancer Letter*.

Over the three months that followed, half of Mount Sinai’s cancer doctors became COVID doctors, taking care of the sick at the hospital system’s 45 COVID centers, contributing to the standards of managing the disease.

“Right in the heart of this, we had several of our fellows deployed into the ICUs, and at the same time we were speaking with the renal staff and some of the other physicians in the other disciplines on how to manage these patients,” Parsons said. “There was this really cool thread of emails that we went through our Deputy Director William Oh, where the health system basically in one week changed the standard of care for our patients to include anticoagulation.”

Looking at in-hospital deaths, Parsons doesn’t see much difference by race, a finding that suggests that equal treatment produces equal outcomes.

“The bottom line is, even though there are absolute differences, they’re not like what we’ve been seeing in the news about very, very markedly different outcomes,” Parsons said. “Obviously, some people could come in here sicker than others, but we have one system that applies the same standard of care to everybody.”

On the basic science side, Mount Sinai has developed a serology test and provided its components to NCI, where it was used to standardize and validate a panel of sera for use in evaluating serol-

ogy devices submitted to the FDA from multiple manufacturers.

“The materials that Mount Sinai sent enabled us to get started much faster in evaluating these devices for the FDA,” NCI Principal Deputy Director Doug Lowy said to *The Cancer Letter*.

NCI is designing a serology research program, funded with \$306 million in new funds. The money will be used “to develop, validate, improve, and implement serological testing and associated technologies” under the Paycheck Protection Program and Health Care Enhancement Act (P.L. 116-139). On May 12, the NCI Board of Scientific Advisors approved concepts for an RFA and an RFP to support research in serological testing (*The Cancer Letter*, [May 15, 2020](#)).

“Because we were able to set this test up and published it early on, a lot of other centers have been asking for the test from around the country,” Parsons said. “I think we’ll need to do this trial to measure the seroprotection of titres, because once we know a number or a cutoff that is generally seroprotective for people so that they can’t be reinfected, we’re hoping to see, with any luck, some herd immunity, as long as these titres are long-lasting. We don’t know that yet.”

“As you can imagine, we basically were down to roughly 40% volume at the low point. From the point of view of patient volume, we had to stop screening for cancer. So, there are very few new patients coming into our hem/onc treatment centers and of course we limited in person visits during the peak as much as possible,” Parsons said. “Recently, we’ve actually seen a spike in radiation oncology treatment, because of postponed surgeries, and we’ve opened our surgical efforts, starting a couple of weeks ago for some really pressing cases. With more last week, and even more this week.

“We’re starting to reopen, but, basically, it’s been a very tough time. All our department chairs and institute directors are taking temporary pay cuts. We’ve asked some of our staff to furlough, using a one-day-a-week furlough policy through New York State’s Shared Work Program.”

Cancer patients are returning.

“We’ve been screening them for COVID-19 symptoms by phone the day before, and then at the door when they come in. All patients receiving chemo are getting tested. It’s a safe environment, but as you can imagine, there’s some reticence, I think, after this crisis, to come into a medical center,” Parsons said. “But I think it is safer, frankly, than going to the supermarket, in my opinion, at this point.”

This conversation is part of an informal series of stories, interviews, and commentaries that track cancer institutions as they seek to reopen, reorganize, and reinvent in the wake of the COVID-19 pandemic:

- Programs designed to meet the NCI Community Outreach and Engagement requirements for cancer center designation have positioned the University of Miami Sylvester Comprehensive Cancer Center to monitor the prevalence of SARS-CoV-2 in South Florida (*The Cancer Letter*, [May 22, 2020](#)).
- Three months after the start of the COVID-19 pandemic, the Seattle Cancer Care Alliance is ramping up plans for a comeback of cancer services (*The Cancer Letter*, [May 15, 2020](#)).
- Health systems and academic cancer centers are cutting expenses to make up for operational shortfalls resulting from the pandemic—laying off employees, furloughing staff, and cutting salaries and benefits (*The Cancer Letter*, [May 8, 2020](#)).

- Community oncology practices are experiencing a significant decrease in patient volume, as weekly visits dropped by nearly 40%, while cancellations and no-shows have nearly doubled (*The Cancer Letter*, [May 1, 2020](#)).

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

Paul Goldberg: What role did Mount Sinai play in managing the pandemic in New York?

Ramon Parsons: On March 1, we had our first patient here at Mount Sinai. It was somebody who had some foreign travel under their belt, and they’d returned, and they weren’t even that sick, actually. But they showed up in the ER, because they were suspicious.

We just had our site visit from NCI at the end of January, and gotten our site visit pink sheet back, which had said we had gotten a good preliminary verbal score. So, we had a retreat on March 6, where we were very excited about our effort to develop our cancer center themes and programs—and it was all good.

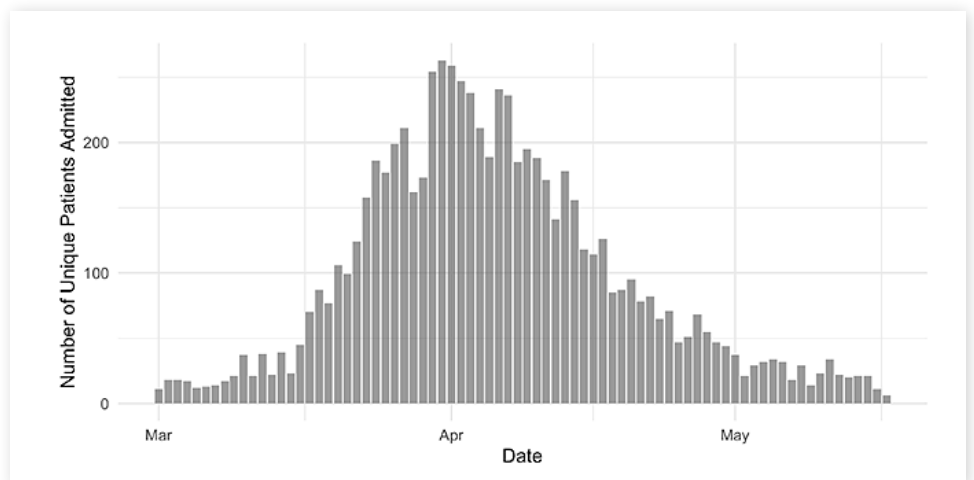
At that point, the news was circulating that COVID-19 and SARS-CoV-2 was in New York City, but it was just a few patients. What you’ll see here, in this slide, by the middle of March, new cases began to rise rapidly. Testing was not readily available yet, because we had to develop the ability to test for the virus in house. The graph includes patients at the multiple hospitals in our health system, the Mount Sinai Health System.

You can see, we had a plateau from early April to mid-April, and then it’s been sort of gradually going down. This data is now from last week. In the past week it’s come down a little bit, not much. It’s a very gradual decline, but we are seeing a lot fewer patients coming into our health system.

So, that’s the big picture.

First of all, we had to redeploy a lot of our cancer physicians to the COVID units. They were at the front line. We generated a COVID-19 cancer floor in the hospital and an outpatient infusion center for COVID-19 patients. On March 20, we shut down our research laboratories, and at the same time shut down as many clinical trials for cancer as possible.

We went from roughly 140 open trials down to 19, and the research laborato-



Mount Sinai Leading in COVID-19 and Cancer

Dr. Ramon Parsons



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EUROPEAN SOCIETY
OF MEDICAL ONCOLOGY

ANNALS OF
ONCOLOGY

EDITORIAL

COVID-19 infection in cancer patients: early observations and unanswered questions

The coronavirus disease 2019 (COVID-19) pandemic has no true precedent in modern times and is a rapidly evolving crisis worldwide. Risk factors for severe outcomes and death from COVID-19 infection include older age and medical comorbidities, characteristics that are common in cancer patients. The study by Zhang and colleagues published in this issue of the *Annals of Oncology* represents the first detailed report of the clinical outcomes of cancer patients—all with solid tumors—infected with COVID-19. The only previous published report included 18 cancer cases from 575 hospitals, with limited clinical information.¹ Zhang and colleagues retrospectively identified 28 infected cancer patients among 1276 COVID-19 patients admitted to three hospitals in Wuhan, China, during January and February 2020. This prevalence (2.2%) is 1.7 (95% confidence interval, 1.2–2.4) times higher than that of the Chinese population of the same age.² This report provides a first estimate of the probability of dying in infected cancer patients, with a mortality rate (28.6%) that is more than ten times higher than that reported in all COVID-19 patients in China.³ In addition, Zhang and colleagues identified that the recent use of anticancer therapies within 14 days of infection (including chemotherapy, immunotherapy and radiation) was an independent predictor of death or other severe events with a hazard ratio >4. Another important and novel finding was the high proportion of patients who acquired

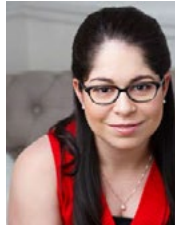
solid tumors may not mimic clinical practice in the United States and elsewhere, where most standard treatments occur in outpatient settings. The hospitals involved in this study were also COVID-19 referral centers, which may have led to more critically ill patients at these centers than elsewhere. Finally, severe complications and mortality from COVID-19 may be higher in some European countries, such as Italy and Spain, compared with China for reasons that remain unclear.

Despite these limitations, this early report by Zhang and colleagues represents an important preliminary contribution to our understanding of the risk and effects of COVID-19 infection in cancer patients, and may allow oncologists to tailor clinical management of COVID-19 to our patients. At the very least, cancer patients must practice social distancing or isolation and be candidates for early and rapid evaluation for symptoms suspicious for COVID-19, including testing for virus and chest radiography.

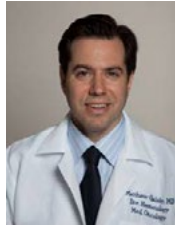
We expect that in the months to come, more detailed studies will be forthcoming on the impact of COVID-19 infection in cancer patients, including the risk of infection, the clinical impact of COVID-19 and concurrent cancer, the effect on different types of cancer, and the ability to deliver appropriate and even curative cancer treatments in the setting of infection.



Editorial by Dr. Oh featured in European Society for Medical Oncology (ESMO) *Annals of Oncology*



Dr. Debbie Doroshow featured in American College of Physicians (ACP) *Annals of Internal Medicine*



Dr. Matthew Galsky participation in The COVID-19 and Cancer Consortium



Dr. Cardi Smith invited to join National American Society of Clinical Oncology (ASCO) Task Force on Pandemic and Clinical Care Delivery

ries were only allowed to have a skeleton crew to maintain mouse colonies and other stocks that needed to be maintained—and to do COVID-19 research.

The students and faculty and postdocs not directly involved in COVID-19 research were asked to work from home, and they have been productive. Here's just a snapshot of some of the papers and activities that have been coming out from our investigators.

I focus on our clinical investigators, because these clinical investigators were serving on the front line, seeing patients with COVID, or actually going into the hospital and working hospital shifts.

For example, Elisa Port, [associate professor of surgery], a breast surgeon who's head of our Dubin Breast Center worked in Mount Sinai Brooklyn, which was hit really hard, for a long weekend, and where she helped out in the emergency room, admitting patients and triaging them.

This is a photograph in one of our outpatient centers.

This is the Dubin Breast Center with chairs turned around to have some social distancing. The picture shows how empty it was in April, when people just didn't want to come into the hospital.

One of the things that we're pretty astounded by is looking at the racial

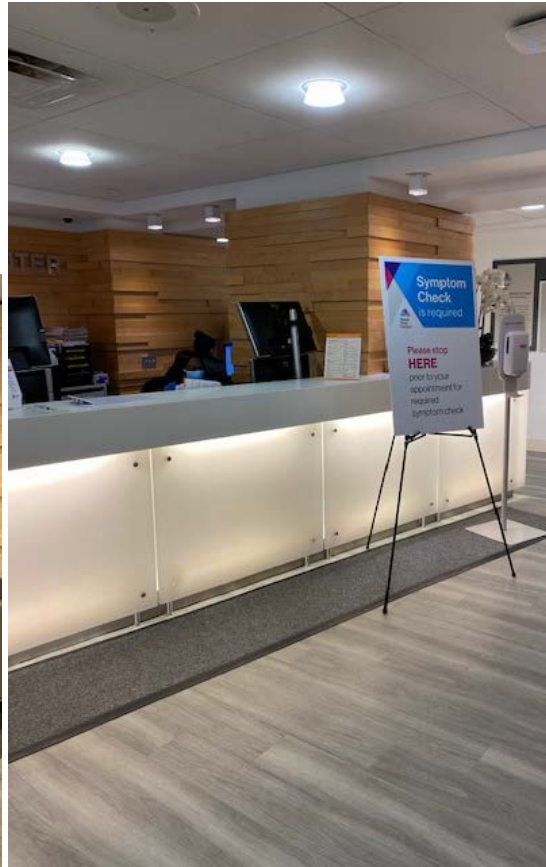
breakdown in our hospital system. You can see the red line for Hispanic, Latino, the green line is for Caucasian white, and then you can see African-American is the purple line.

Basically, what you can see is these are the margins of error for all these different subtypes, based on the numbers, because you can see that they're pretty wide out here, when you have higher ages. But the bottom line is, even though there are absolute differences, they're not like what we've been seeing in the news about very, very markedly different outcomes.

Obviously, some people could come in here sicker than others, but we have one

Looking to the Future: Breast and Surgical Patients

Dr. Elisa Port



system that applies the same standard of care to everybody.

Right in the heart of this, we had several of our fellows deployed into the ICUs, and at the same time we were speaking with the renal staff and some of the other physicians in the other disciplines on how to manage these patients.

There was this really cool thread of emails that we went through our Deputy Director William Oh, where the health system basically in one week changed the standard of care for our patients to include anticoagulation.”

This is just a study that came out of that effort already showing that it

does seem to provide some protection. [J Am Coll Cardiol. 2020 May 5;S0735-1097(20)35218-9. doi: 10.1016/j.jacc.2020.05.001.]

Valentin Fuster, [professor of cardiology and director of the Zena and Michael Wiener Cardiovascular Institute], is leading this effort. But we—through William Oh, [chief of the Division of Hematology and Medical Oncology at the Mount Sinai Health System and deputy director of The Tisch Cancer Institute]—had a lot to do with changing this policy, and, obviously, it looks like that has been helpful in terms of the survival for patients.

This next slide is an anecdotal story, but here’s a very interesting story of one of

our physicians, Thomas Marron, who, in early March, got COVID-19. He’s an assistant professor medical oncologist—one of our young stars. He’s an MD, PhD cancer immunologist, and he’s been opening up a lot of phase I trials in the cancer immunology space for the last few years.

This is just his journey. He told us about his journey, about how he got the disease early on, how he helped out with the biorepository, where now we’ve collected from over 500 patients that were acutely ill here in the hospital.

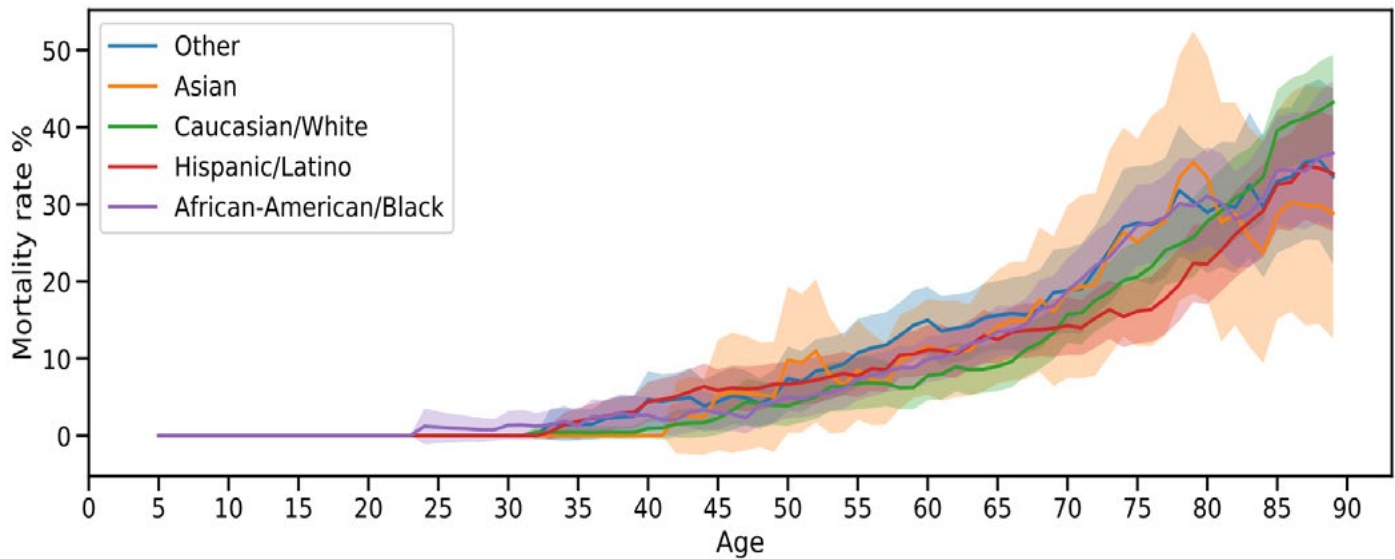
This effort was led by the co-leader of our cancer immunology program, Miriam Merad, [the Mount Sinai Endowed professor in Cancer Immunology, direc-

Health Equity Across the Mount Sinai Health System

Dr. William Oh



No Difference in In-Hospital Mortality By Self-Reported Race for COVID-19 Patients Admitted to MSHS (n=3,273)



tor of the Precision Immunology Institute at Mount Sinai School of Medicine and is the Director of the Mount Sinai Human Immune Monitoring Center], who was interested in seeing how the immune system was causing morbidity and mortality in this disease, which is apparent because many of the cytokines that are being released when patients are infected are nearly the same level you see when you have cytokine release syndrome in the setting of a variety of immunotherapies that are given to people. By the way Dr. Merad was just elected to the National Academy of Sciences.

He then volunteered on the COVID-19 unit. We had to expand to 45 COVID

units here at Mount Sinai Hospital alone. Normally, of course, there are no COVID units, and so the number of units in the hospital had to expand.

Almost half of our physicians were redeployed to take care of COVID patients, with the rest needing to cover our cancer patients, of course, with a lot of telemedicine. Also, we had to help out with the clinical trial efforts. Our clinical trial office was redeployed to help out with one of the trials that we're quite proud of, our convalescent plasma trial that we helped set up, which is looking like it is having some impact, although, we're still having to wait to see what that is.

Only a small subset have been studied so far, which does show some benefit for patients.

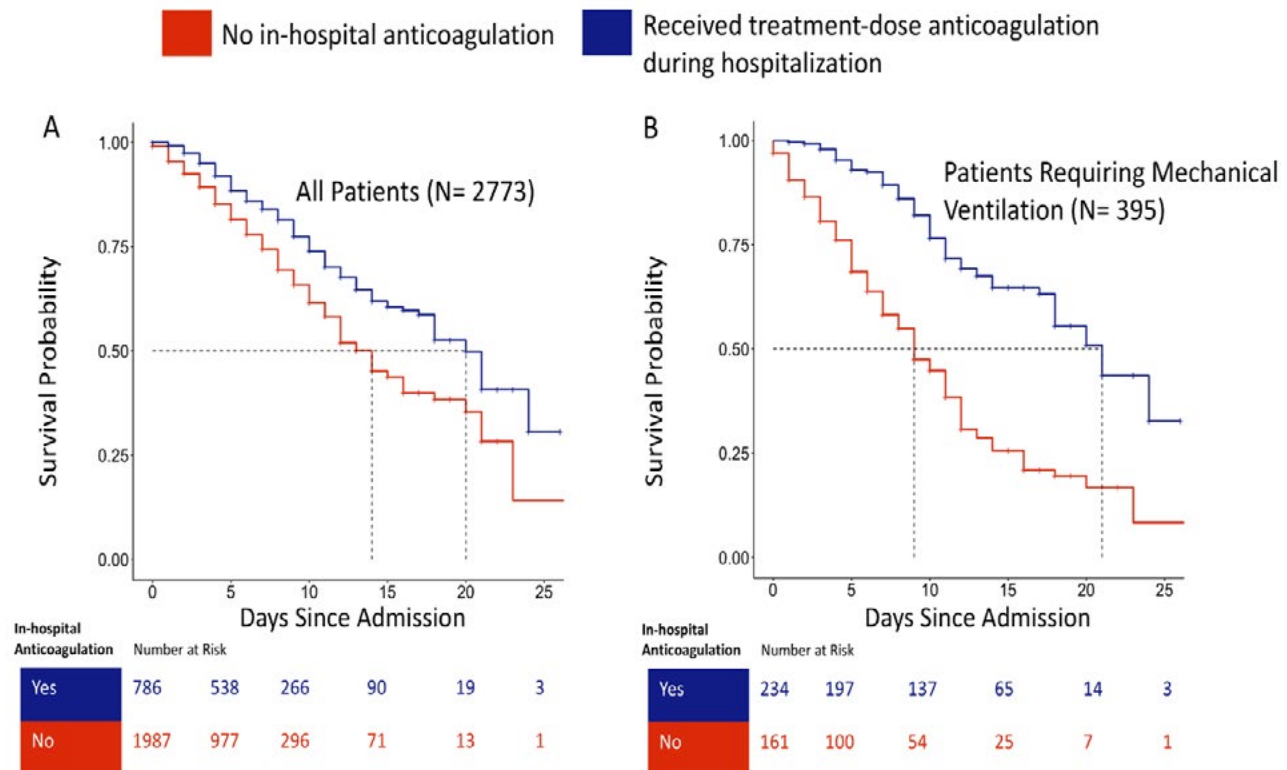
We've been helping out with clinical trials for moderate and severe COVID-19, including immunomodulating trials. This is just some of the types of trials he's interested in.

Basically, the first phase of infection is there's just not enough immune response, and the virus can grow unabated.

Then, once it's recognized, the hypothesis is that there's too much immune response, even when the virus is already slowing down, and this causes blood

Anticoagulation and COVID-19

Dr. William Oh



clots, hypoxia, multi-organ failure and loss of macrophages, and pus in the lungs.

He's got a trial that he's going to be opening or has opened for using lambda interferon to affect the first phase, and then another trial using an inhibitor, an immune-modulatory inhibitor for the second phase, where the immune system is over-reactive.

We are very fortunate to have a wonderful microbiology department here at Mount Sinai. It's led by [Peter Palese](#), [professor and chair of the Department of Microbiology]. We also have [Adolfo Garcia-Sastre](#), [professor in the Department of Microbiology and director of the [Globe-](#)

[al Health and Emerging Pathogens Institute](#)]. They're both members of the National Academy of Sciences, experts on viral infections, particular influenza, but they've been studying the SARS viruses.

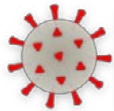
Then, finally, [Florian Kramer](#), [professor of vaccinology at the Department of Microbiology and the principal investigator of the Sinai-Emory Multi-Institutional Collaborative Influenza Vaccine Innovation Center], who developed, fortunately, a two-step ELISA test, which turns out to be apparently the most sensitive and specific test that's available right now, and becoming available nationally. [Nat Med. 2020 May 12. doi: 10.1038/s41591-020-0913-5.]

One of the exciting things that we've been contributing is our chair of pathology, [Carlos Cordon-Cardo](#), [the Irene Heinz Given and John LaPorte Given Professor and chairman for the Mount Sinai Health System Department of Pathology], a cancer scientist for many years, and a long-time colleague and collaborator of mine, going way back, started to take this test and put it in the clinic so that we could measure titres for the antibodies, IgG and IgM antibodies that result from an infection that has mounted some immune response.

Now, they also have an assay for measuring antibodies' ability to block infection in a microscale infection test, where

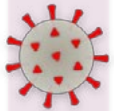
SARS-CoV-2 Has a Varied Course

Dr. Thomas Marron

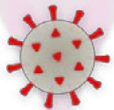


Non-Critical Symptoms
(fortunately most people, but who?)

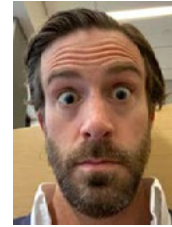
COVID-19
(life threatening)



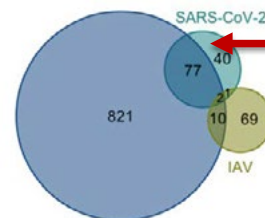
First Phase (not enough)
Inadequate induction of IFN
(virus stymies normal anti-viral response)



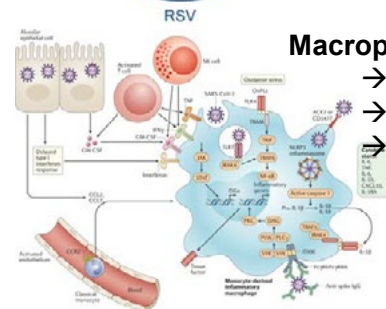
Second Phase (too much)
Exuberant inflammatory response
(inflammation causing the damage)



March 2, 2020



SARS-CoV-2 Lacks:
Type I & III IFNs
Downstream ISG



Macrophages accumulate
→ Hypoxia
→ Blood Clots
→ Multi-organ failure

they can see if the antibodies have the ability to block cellular infection.

Because we were able to set this test up and published it early on, a lot of other centers have been asking for the test from around the country.

He sent our blood samples as examples of positives, known positives, and negatives from prior to the infection. Carlos Cordon-Cardo organized this and sent them to the NCI Frederick, which is coordinating an effort to identify which tests are the best in this area.

The impression I've gotten on calls with the NCI director, who is very excited about this, basically they want us to be

part of a national effort, working with NIAID, to test in a prospective clinical trial using our test at multiple centers throughout the country, to determine at what level response correlates with seroprotection from infection.

Because this will be a very important study that will allow us to get back to work in safe way—and this could potentially also be used for vaccines—to know what amount of antibody titre to the virus is sufficient to lead to protective immunity.

So, that's very, very important. That's something that Florian is now championing, and is getting federal funding for in the process of expanding it. I think he's already opened the trial here, locally.

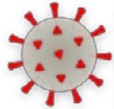
We also have been in conversation with NCI, who's been trying to work with us to get the test into the federal government agencies that are going to be able to help propel this at a national level, so that this test, which appears to be very specific and very sensitive, can be disseminated through a commercialization effort. That's really a very exciting thing that we're hoping to make this widely available through that effort. It's happening as we speak with efforts to start a new company that would be able to really ramp this up and scale it to a level that we've been doing really at a mom and pop level here at Mount Sinai.

In fact, cancer center labs including my own lab, one of my technicians, has been

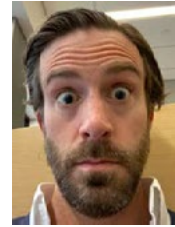
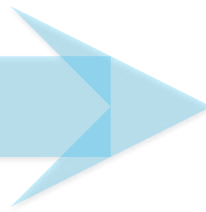


SARS-CoV-2 Has a Varied Course

Dr. Thomas Marron

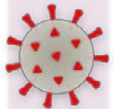


Non-Critical Symptoms
(fortunately most people, but who?)



March 2, 2020

COVID-19
(life threatening)

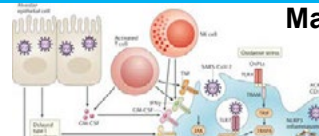


First Phase (not enough)

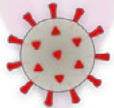
A randomized phase 2 trial of peginterferon lambda-1a (Lambda) for the treatment of hospitalized patients infected with SARS-CoV-2 with non-critical illness



SARS-CoV-2 Lacks:
Type I & III IFNs
downstream ISG



Macrophages accumulate
→ Hypoxia
→ Blood Clots
→ Multi-organ failure



Second Phase (too much)

A randomized placebo-controlled phase 2 trial of an oral CCR2/5 inhibitor for the treatment of hospitalized patients infected with SARS-CoV-2 with non-critical illness

MOUNT SINAI HOSPITAL CLINICAL LABORATORY COVID-19 ELISA ANTIBODY TEST

Antibody	Performance Measure	Estimate of Performance	95% Confidence Interval
Combined	Sensitivity (PPA)	92.5% (37/40)	(80.1%; 97.4%)
Combined	Specificity (NPA)	100% (74/74)	(95.1%; 100%)
Combined	PPV at prevalence = 5%	100%	(46.2%; 100%)
Combined	NPV at prevalence = 5%	99.6%	(98.9%; 99.9%)

Developer: Mount Sinai Hospital Clinical Laboratory
Test: Mt. Sinai Laboratory COVID-19 ELISA Antibody Test
Technology: 2-Step ELISA
Target: Spike

Test Facts:
[Information for Healthcare Providers](#)
[Information for Recipients](#)
[EUA Summary](#)

Source: FDA

helping out with making the protein that coats the surface of the virus. It's called the spike protein that coats the virus that's involved in the infection process. The full-length protein is very hard to make.

So, we've been helping out with making it, and that's used in the second step of the ELISA test.

Just to explain the ELISA test. Importantly, it's a two-step test, and the first step screens and is going to have some false positives.

So, if you get a positive on the first round, you then have the second round of testing, which is the full length. The first one uses the RBD, receptor binding domain, of the spike protein. And then the second one is the full-length spike protein, and you need to be positive for both tests to be considered a positive in this assay. Then, obviously, there's a titre possibly associated with the strength of the immunity, which we still don't understand exactly, if it does protect against viral infection. And that's, as I mentioned earlier, an ongoing effort.

At the same time, NCI has just started a new [serology] program [(*The Cancer Letter*, [May 15, 2020](#))]. There's going to be an RFA for it.

Basically, in that effort, they've been reaching out to us, and they want us to put together a team of investigators to compete for U54 and also for U01s, but also to expand are CLIA lab infrastructure, so that we can scale beyond what we currently have for serology testing on campus. So, we're in the midst of putting that together.

How did the pandemic affect the cancer center financially?

RP: Well, it's been a pretty big hit. As you can imagine, we basically were down to

roughly 40% volume at the low point. So, from the point of view of patient volume, we had to stop screening for cancer. And, there were very few patients coming into our hem/onc treatment centers.

We've recently seen a spike in radiation oncology treatment, because of postponed surgeries, and we've opened our surgical efforts, starting a couple of weeks ago for some really pressing cases. With more last week, and even more this week.

We're starting to reopen, but, basically, it's been a very tough time. All our department chairs and institute directors are taking temporary pay cuts. We've asked some of our staff to furlough, using a one-day-a-week furlough policy through New York State's Shared Work Program. But we're starting to see increased volume in the clinics now, and we've created, I believe, a very safe place for our patients. Our physicians here on campus have almost half the rate of infection that is seen in the general population here in New York City. So, our PPE is working, and we've created, as I mentioned earlier, spaces where our COVID patients are seen separately from our non-infected patients to protect the non-infected patients.

To answer your question, yes, it's been a big financial hit. We're very worried about it, frankly, going forward, because, as you know, revenue is lagging from billing. So, that part of the wave has not really hit our shores yet, but the institution is doing everything it can right now to weather the storm.

I guess you were taking care of the COVID patients. That was billing too; no?

RP: Yeah, the difference, though, is COVID remuneration is not the same level as you would get from surgery, and

some of the infusion that we're getting. It's really a matter of, frankly, our cash flow changed.

If you think about it, it's just a matter of how insurance companies compensate physicians generally. They're compensated for elective surgeries more than inpatient care. It is what it is, even though we've been very busy in the hospital.

That said, remember our outpatient revenue is much more important for our bottom line than inpatient revenue.

Are cancer patients returning?

RP: Yes, they are.

Actually, during this period I've been rounding in the hospital, in the clinics, and the outpatient clinics have been open the whole time and there are patients coming in. We also have telemedicine visits, but, of course, patients that are getting chemo need to come in.

We've been screening them for COVID-19 by phone the day before, and then at the door when they come in. All patients receiving chemo are getting tested. It's a safe environment, but as you can imagine, there's some reticence, I think, after this crisis, to come into a medical center.

But I think it is safer, frankly, than going to the supermarket, in my opinion, at this point.

What's been the impact on basic science?

RP: We had to, obviously, shut down the labs for cancer research since the end of March. So, it's going to be almost two months.

We just opened up this week. Research now can open up with social distancing, but the labs are only at 25% of normal capacity, to make sure that happens. I think, fortunately, we did not cull our mouse colonies, like some institutions have and, also fortunately, I think a lot of our students, because of our housing, live nearby.

So, they walk to work and don't have to get public transportation.

It's not great for everybody, but now I think we're going to get back to work in our cancer research, and I think a lot of people have taken this time to write grants and papers. We've seen a lot of grants being submitted. I've checked: to a scientist, with maybe just a few exceptions, scientists have something planned for submission, either with the federal government or through a foundation in the coming cycle.

Is there a connection between COVID-19 research and cancer research?

RP: There is. Many viruses have given us important clues about how the immune system works, and here, I believe that the information we're going to understand about how the virus can act as a Trojan horse and shut down the local immune response probably is going to give us lessons that we're going to learn from on how cancers are able to change the microenvironment for the same purpose.

If we could talk a little more about serology testing. I understand from people at NCI that Mount Sinai played a key role in this, basically as a partner of NCI. You mentioned some of that. Is there anything else to say? Anything you haven't mentioned?

RP: I am so proud to have such smart, resourceful and resilient colleagues, who have adapted to the crisis to take care of both cancer and COVID-19 patients.

I would say it was really dramatic. They asked us for blood products on March 27. Urgently, when this was happening.

We promised to deliver it a week later, and they hadn't received them yet. They were just really nervous about where they were, and I was worried when we were going to deliver. The place was chaotic, because all these patients were dying, and it was really crazy here. It was the right thing to do, but at the same time, a lot of people were under a lot of stress here.

But Carlos Cordon-Cardo was able to get the samples. A federal courier from Frederick came and picked them up on April 6, and then drove right back to Frederick, MD, to drop them off. They had started testing them literally, I think, as soon as he got back to Frederick.

So, it was really very dramatic that we were able to get them that, and then we had follow-up calls with the NCI director. One on a Saturday, in fact.

First, during the week to tell us that they really had great results and that they wanted to scale this test nationally. Then, with HHS, to try to figure out how do we get into the health system to actually operationalize that.

That's been super exciting for us, and we're very proud of that effort, and I'm very proud of the people who've worked on that here. I mentioned everybody's name already who was involved in that.

The other thing that you might be aware of is that we've had at Mount Sinai a bio-bank collected from our patients. It's called BioMe, which is basically a serum sample that's collected and some DNA that's collected on a volunteer basis with

informed consent for basically mostly healthy patients, but also patients that somehow interact with our health system at various levels, including several thousand cancer patients.

Those were collected pre COVID-19, and also, we collected into March of 2020, when we shut down the project. So, they're very interested in studying those samples, because many of those people now have gone on to get infected, and to figure out when did COVID-19 really first hit our shores, because we'll have a canary in the coal mine with those patients. And also, to see if we can identify various either genetic risk factors, and that's something that [Steven Chanock](#), [director of the NCI Division of Epidemiology and Genetics] is very interested in following up with.

I'd like to mention the people we've worked with at NCI. In addition to Ned Sharpless. Doug Lowy, the NCI deputy director, was very much involved in these conversations and so was Jim Cherry [scientific program director, Office of Scientific Operations, NCI at Frederick], and Ligia Pinto, [director of the Vaccine, Immunity and Cancer Program at the Frederick National Laboratory], who is involved in standardization of serologic testing at NCI Frederick. We've had a lot of conversations with them that have been very helpful and also with Steven Chanock.

So, it's been an exciting time. We feel like we're really helping out. One thing I would like to end with is our cancer center just went through the renewal process. The site visit was in, as I mentioned, Jan. 30. We should be getting our final summary statement anytime now in May, and our score is such that we're going to get renewed.

So, our plan is really a multipronged plan to expand our efforts to understand the tumor microenvironment and its role in cancer progression and also treatment.

We're also very interested in understanding the disparities that are occurring in our city—our catchment area is New York City—and trying to figure out what they are and ways we can address them.

Then a third area that we're very excited about is, because in the past this cancer center was focused only on East Harlem, Central Harlem, and the Upper East Side as its catchment, now that we've expanded to all of New York City, we wanted to expand our clinical trial network across our health system.

One thing that we've really done here is our CTO, working particularly with Karyn Goodman, [professor of radiation oncology and associate director for clinical research], was really lifted a lot, and our CTO helped out, the convalescent plasma clinical trial tremendously that the ID department led.

We've helped consent patients throughout the health system for that trial, and so we feel like we've learned from that experience, and now, we're going to be able to open up trials; obviously, not every trial, but trials that would be amenable to multi sites, perhaps oral medications for instance, we're going to be trying to open up throughout the health system. So, that's a very exciting development that is a consequence of our experience with COVID.

Looking at the recent FDA guidance about the serology tests, your test, of course, is mentioned as one of the great tests to use. Obviously, it couldn't have possibly existed before the spread of the disease. Did it just sort of happen very, very quickly that you developed it?

RP: The virus sequence was published sometime in early February, from China.

Basically, just based on they are very adept cloners, I believe that they simply just cloned the sequence based on the DNA sequence.

As I was saying, this microbiology department is really interested in influenza, and as you know, influenza has been one of these intractable diseases that we still don't have an effective vaccine for. The vaccine has to be changed every year, and it's never very good, to be honest. So, they're fascinated with this problem, and similarly they're fascinated with other viruses that can cause similar morbidity and mortality.

So, they were, I'd say, intellectually primed to be very interested in working on this,

As you know, COVID-19 affects cancer patients just as much as anybody else, and we are very concerned about that, as is everybody who works with cancer. But we've put together a COVID-19 registry at the institution, and there's a cancer subcommittee that includes the associate director for population science and other cancer center members that's part of that committee.

And, as I mentioned, there's a biorepository for COVID-19 that's led by the co-leaders of our cancer immunology program, Miriam Merad.

So, we are in a position to follow the trajectory of the health of our patients and understand better who's going to be at risk. We have some clues from China, but we're going to really understand, I think, from our experience, and also pooling our data with other centers, who is really the most at risk for this disease.

At this point, there's a lot of anecdotal information, but codifying that is going to be very helpful.

Do you think better and more widespread use of serology testing would help to get doctors and nurses back to work and patients back to the clinic?

RP: I do think so. I think we'll need to do this trial to measure the seroprotection of titres, because once we know a number or a cutoff that is generally seroprotective for people so that they can't be reinfected, it's almost like we're going to see, with any luck, some herd immunity, as long as these titres are long-lasting. We don't know that yet.

So, yes, I think this is going to be very helpful. It's also going to help our economy get back to work, too, and reduce the spread, be able to trace contacts much better.

How soon will you get the data do you think?

RP: That's a really, really good question, and I don't know the answer to that. Again, that's something that Florian Krammer would be able to tell you. I just spoke to him about maybe a week ago, where we heard it most recent. Still not enough information to know for sure about seroprotection yet in a large study.

Thank you very much.



GUEST EDITORIAL

CCC19 data point to extensive use of hydroxychloroquine, azithromycin, or both, by patients with cancer and COVID-19



By **Otis W. Brawley, MD, MACP, FASCO, FACE**

*Bloomberg Distinguished Professor of Oncology and Epidemiology,
Johns Hopkins University*

Nicole Kuderer and colleagues are to be congratulated for their report—in [The Lancet](#) and at the [ASCO 2020 Annual Meeting](#)—on the impact of COVID-19 on a cohort of patients with cancer.

In a very short time, these researchers used social media and novel ways of communicating to bring together healthcare providers from over 100 institutions in the US, Canada, and Europe to form the [COVID-19 and Cancer Consortium \(CCC19\)](#) database.

This group is actively collecting data, and this publication represents an initial study of outcomes in cancer patients infected with SARS-CoV-2. It is an observational study, with all the caveats of an observational study, but it is data. It provides fact and understanding of the disease in cancer patients. It allows the medical community to change our practices for the betterment of patients during the pandemic.

We already know that studies show that SARS-CoV-2-infected older persons with comorbid diseases, especially diabetes, lung and cardiovascular disease are at

higher risk of poor outcomes. This study shows that patients with active cancer or progressing cancer have a higher risk of death after contracting the SARS-CoV-2, compared to the general population with the infection.

Most importantly, this study suggests that that elective surgery does not put patients at increased risk of adverse outcomes if infected postoperatively. It also suggests that cancer treatment with non-cytotoxic chemotherapy, and maintenance chemotherapy can continue with caution during the pandemic. It does support frequent testing for

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SAR-CoV-2 infection in those receiving cancer treatment.

Future analysis of the cohort will likely yield more information on risk of specific cancers or risk following myelosuppression associated with cytotoxic chemotherapy or immune activation associated with immunotherapy.

A most disturbing finding is that 40% of the 928 (371) patients in the cohort, were taking hydroxychloroquine, azithromycin, or both, and only two did so

outside of a well-designed clinical trial was and is appalling.

It is known that there are risks associated with “gun-slinger medicine.” This paper is now one of several studies to suggest that use of these drugs, especially in combination, is associated with increased risk of death.

I am less critical of the patients taking these drugs. They are afraid and desperate. I am outraged at the “so-called” doctors who prescribe these treat-

“

It is known that there are risks associated with “gun-slinger medicine.” This paper is now one of several studies to suggest that use of these drugs, especially in combination, is associated with increased risk of death.

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while enrolled on a clinical trial of these drugs. While we cannot assume an exact proportion, this finding means a lot of people with SARS-CoV-2 are taking these medicines. It speaks volumes to societal failure to appreciate the importance of using the scientific method to guide the practice of medicine.

There are some who say that desperate patients have the “right to try” a medicine that might help. Fact is, the data to support efficacy of these drugs to treat or prevent COVID-19 infection is pitifully poor. Indeed, the theory on why it would work is weak. In February, March, and April of this year, one could just barely justify a clinical trial to establish efficacy, but taking these drugs

ments. They ought to know better. Every patient prescribed these drugs is an experiment: each one is a “guinea pig” in a poorly designed clinical trial of one subject. Failure to support the science-based practice of medicine and the conduct of clinical trials slows progress in figuring out how to best treat our patients.

This paper and its publication provide an example of the best of medicine and the worst of medicine. The healthcare providers who prescribe medicines without scientific basis are doing the exact opposite of those physicians and scientists who formed the [COVID-19 and Cancer Consortium](#) database.

Radiation oncology appointments plummeted in the COVID-19 pandemic—but seem to be rising again

By Alexandria Carolan

Radiation visits—much like preventative screenings, surgery, chemotherapy and screening—were delayed or canceled at the peak of COVID-19 in the United States.

Now, the patients are returning, in some cases creating small upticks in demand for treatments that were delayed in March, April and May. In a few institutions, the return of the patients is creating wick-welcomed backlogs.

In a [survey](#) conducted by the American Society for Radiation Oncology April 16-30, 85% of oncology practices said radiation oncology appointments at their practices had decreased by about a third, even though their doors remained open through the pandemic. ASTRO received responses from 222 physician leaders of radiation oncology practices.

In the survey, 82% of respondents cited delayed/deferred treatment and 81% cited decreases in the number of patients being referred for radiation therapy.

“What we’re trying to do with the survey data is to dive deeper into that. We don’t have the answers yet, because we simply are still collecting the data. But one of the questions we do want to ask is—if there is a differential impact of

COVID specific to cancer care, and to radiation delivery, that may or may not require some kind of policy-level intervention, or practice-level intervention,” David Schwartz, co-author of the ASTRO study, said to *The Cancer Letter*.

“This is where it’s now a global, community-wide freakout. What impacts some of these things is not just the physicians, nor even the disease—it’s also the patient and community’s response to an overwhelming threat. You’re seeing people not showing up for surveillance,” said Schwartz, professor and chair of the Department of Radiation Oncology at University of Tennessee Health Science Center.

Data from another [survey](#), conducted by the American Cancer Society Cancer Action Network, showed that 79% of patients in active cancer treatment reported a delay to their health care (up from 27% in a previous survey). Seventeen percent of patients in active treatment reported delays to their cancer therapy—chemotherapy, radi-

ation, or hormone therapy. The survey polled more than 1,200 cancer patients and survivors.

“There are certain feeder cancers that keep the radiation oncology units busy. Those need to be diagnosed as a process. That process was broken—is broken,” Len Lichtenfeld, deputy chief medical officer at ACS, said to *The Cancer Letter*. “A breast cancer patient needs radiation following a lumpectomy, a prostatectomy that needs radiation, lung cancer patients that may benefit from radiation.”

In the ACS CAN survey, 17% reported that the threat of COVID-19 prevented them from seeing a doctor for an illness or injury for which they would have otherwise sought treatment. Among those who delayed or canceled care, 59% said the decision was made by their health care provider.

Nearly half (46%) of cancer patients and survivors reported a deterioration to their financial situation that affected

their ability to pay for care, an increase from 38% in the ACS CAN survey released in April.

“What we’re going to see is a backlog of more advanced presentations in the future, with patients whose care has been affected and delayed by the pandemic,” Sue S. Yom, professor in the Departments of Radiation Oncology and Otolaryngology-Head and Neck Surgery at University of California, San Francisco, said to *The Cancer Letter*.

“Radiation oncology is unique in that it requires such a specific commitment of time and resources over a very intensive period. I don’t think that that is something that all patients have the ability to do right now,” Yom said.

The uptick in demand for services is especially dramatic at New York’s Mount Sinai Health System. Mount Sinai deferred appointments at the beginning of the crisis, and made room in its hospitals for an expected overflow of COVID-19 cases in the city. That overflow never came.

“We have some outpatient facilities that patients were able to go to. Once we realized we were on the other side of the peak, and there wasn’t really going to be a need to use our clinical areas, we started opening them up again and ramping up,” Kenneth Rosenzweig, professor and system chair of radiation oncology at Mount Sinai Health System, said to *The Cancer Letter*.

“As of today, the end of May, we’re actually at a higher volume of patients on treatment than our typical average,” Rosenzweig said. “I think part of that, another reason is that some of the patients who had been delayed are now on treatment. So, there was a bit of a backlog—and now that’s opened up.”

Radiation appointments at Memorial Sloan Kettering Cancer Center plummeted during the peak of COVID-19.

Now, MSK is seeing increases in radiation oncology appointments.

“It was certainly expected that during that time where you would see, particularly in April—when the incidence [of COVID-19] was so high here, and we were seeing the ER flooded with patients—that we would see a reduction in radiation oncology visits,” Daniel Gomez, director of thoracic radiation oncology, and chief of radiation oncology, Manhattan Service, at MSK, said to *The Cancer Letter*.

“Now that that’s subsided, you’re seeing the opposite effect, and with regard to patients wanting to come in and get their cancers treated.”

“Patchwork quilt”

On a policy level in the U.S., it is up to the states and counties to institute COVID-19 guidelines.

“As the country learns how to deal with this—in policies, we’re downstream with those things. What might be going up in Tennessee might not be going up in New York or Chicago,” Daniel V. Wakefield, co-author of the ASTRO survey, said to *The Cancer Letter*.

“What we’ll see as a patchwork quilt of changes based on local government ordinances across the country, on not just a state level, but really, on city-to-city level,” said Wakefield, chief resident in the Department of Radiation Oncology at University of Tennessee Health Science Center and MPH ’20 candidate at Harvard University.

Cancer hospitals are a part of this patchwork quilt.

“What you are seeing is different phases of a pandemic. Everyone’s been in different acute and recovery phases,” UCSF’s Yom said. “And I will say that now that San Francisco is sort of officially in

reopening and recovery, we definitely are seeing a very dramatic uptick in our consultations. But, remember, the time from consultation to initiation of treatment can be a week to several weeks.”

“What we’re seeing now isn’t reflected yet, but our numbers have been trending up for about the past week or two.”

Many cancer experts have pointed out that COVID-19 has exacerbated health disparities, making the underserved more underserved (*The Cancer Letter*, [May 22](#)).

“The maps that we see of COVID infection rate positivity can actually be overlaid onto cancer incidence and cancer mortality,” said Schwartz, who is also in charge of COVID-19 testing and data collection in Memphis. “It comes down to one overriding issue: social determinants of health.”

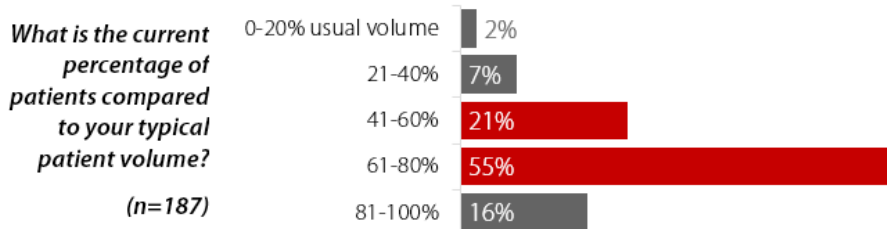
“This can be manifested as cancer, but also as chronic disease. And that’s another issue that we see here in Memphis—is that cancer incidences also overlap very tightly with the incidence of hypertension, especially uncontrolled hypertension, diabetes, stroke, heart attack, obesity, food insecurity—all of those things,” Schwartz said.

Rural vs. urban

David Beyer, medical director of radiation oncology at the Cancer Centers of Northern Arizona Healthcare, has delayed radiation treatments and pivoted to telehealth whenever possible out of concern for the health of his staff and patients.

Beyer is the only physician at his clinic.

“We don’t know what’s going to happen. We don’t know who in our department is going to get sick. We are a small rural clinic,” Beyer said. “If I get sick or have to quarantine myself for two weeks, we



On average, radiation oncology practices reported seeing two-thirds of their typical patient volume in late April. — Source: ASTRO.

have a serious problem. We have two radiation therapy technologists, and they actually deliver the treatments on a day-to-day basis to each patient. We have two of them. If one of them gets sick, or God forbid both of them get sick or have to self-quarantine, we have a problem.”

Beyer’s clinic used to treat 25-30 patients per day—now he sees about 15-20.

“There is one place where you can get screening mammograms. They are not doing screening mammograms right now,” Beyer said. “They made the same choice to shut down routine screening mammography. So, we’re not seeing breast cancer patients that otherwise might’ve been diagnosed right now with an asymptomatic breast cancer.”

Still, Beyer’s location in Sedona has been relatively spared from the coronavirus. As of May 25, his local hospital had one confirmed case of the disease. His staff members have been asking, “When are we going to start seeing our new patients in person, instead of over the computer?”

“My answer is, ‘Not yet,’” Beyer said. “We’re still sticking with the telehealth options as much as possible, so that we reduce the risk of exposing us and exposing them.”

“The next county over is the Navajo Nation. It exploded there. They have one of the highest rates of COVID anywhere in the country right now. It’s not that it’s not close—it’s not right here. What we’re doing works right now, for us,” Beyer said.

In Memphis, where ASTRO study architects Schwartz and Wakefield treat cancer patients, the spread of COVID-19 has been moderate. Nonetheless, the number of radiation oncology appointments at their clinic has declined.

“Ours is a center where we don’t have high concentrations of people living on top of each other like New York, or San Francisco, or Washington or Los Angeles—and we experienced a much different pandemic,” Wakefield said. “Ours was more of a slow burn. And to be frank, now I think it’s starting to have more effect than what we were seeing in New York six weeks ago.”

The population in Memphis tends to be poor and rural, Wakefield said. People drive their cars to the clinic rather than walk or take public transportation. High poverty rates and accompanying social risks leave its population and rural practices vulnerable.

In Memphis, there is a rural-urban divide, Schwartz said.

“Memphis is in an agricultural area, but it represents the largest metropolitan area in this region of the mid-South. We do get rural populations, and do refer back patients to referral to rural practices,” Schwartz said. “My impression is that rural practices probably have been struggling, simply because they do depend very much on a steady stream of referrals to maintain the nuts and bolts of their practices.”

What comes next?

Now, Schwartz and Wakefield are conducting a follow-up survey for ASTRO. That study is likely to show that demand for radiation oncology is continuing to rise.

“Now, as the general relaxing of social distancing and restrictive measures have kind of been released at least to some degree, and the nation slowly returns to business, we’re starting to see a larger influx of patient numbers,” Schwartz said. “I also think, probably, the patients are more comfortable to come in.

“Whatever loss of volume and losses of referrals that we got, I have to believe that the patients, too, are part of that issue. They simply did not feel comfortable coming in anywhere, let alone to a healthcare facility that was seeing patients with COVID,” Schwartz said.

If patients are beginning to receive treatment for cancer that requires radiation after the fact, it may take weeks from there to show up in the data.

“The number of cases of cancer—the screening test, the diagnoses, the visits starting with a primary care doctor, maybe a urologist—all of those visits are way down,” ACS’s Lichtenfeld said. “The normal progress of activity starts with diagnosis, and the treatment. And consequently, if the diagnoses are decreased because people aren’t going to see the doctor, then I wouldn’t be surprised to see that radiation therapy is decreased.

“One of the major messages that’s been so hard to deliver during this pandemic has been, if you have to a or symptom of cancer, you need to see somebody and you need to—withstanding concerns about the risk of going to see a doctor—you have to break through that concern and get yourself taken care of.”

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&

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

A



CONVERSATION WITH
THE CANCER LETTER

John Cleveland: How Moffitt will heal from conflict of interest trauma— and from COVID-19

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Given the press, the leadership changes that were associated with problems with the Thousand Talents Program, and then COVID-19, we're working very hard to make sure that all of our team members understand that inclusion is at our foundation.

”



John L. Cleveland, PhD

*Executive vice president, center director,
H. Lee Moffitt Cancer Center & Research Institute*

As a freshly-minted director of H. Lee Moffitt Cancer Center & Research Institute, John Cleveland has two items on top of his to-do list:

1. Rework the center's leadership, and
2. Deal with a crippling pandemic.

On April 28, after serving as interim director for over six months, Cleveland was appointed center director and executive vice president of the Tampa-based NCI-designated Comprehensive Cancer Center.

Cleveland, whose research is focused on the molecular pathogenesis of cancer, joined Moffitt in 2014 as the associate center director of basic science.

"We have a succession plan at Moffitt for all of our leadership positions, and I was part of the succession plan for Dr. Thomas Sellers. I stepped up to the plate and took over the role of center director," Cleveland said to *The Cancer Letter*. "Since Dec. 18, I was actually wearing three hats as the interim center director, the ACD of basic science, and the ACD of clinical science."

Sellers, Moffitt's former director, and Alan List, former president and CEO, stepped down Dec. 18, 2019, after an internal review alleged that they violated "conflict of interest rules through their work in China." Four other researchers were similarly implicated in the investigation. Two of the ousted researchers—Sellers, and Howard McLeod—are disputing the cancer center's allegations (*The Cancer Letter*, [Jan. 3](#), [Feb. 14](#), [March 6](#), 2020).

As is the case at many academic cancer centers, Moffitt's finances took a hit in the early months of the pandemic. Leadership and senior faculty took 10% to 15% pay cuts, and all employees were required to take 40 hours of paid time off.

"Yet we've weathered this storm, and we're starting to see an uptick in the number of patients coming in and we have reactivated surgeries at all levels, and radiology is coming back as well," Cleveland said. "We're confident we're going to weather the storm."

Guiding Moffitt through recovery from the COVID-19 crisis is the first step in Cleveland's program.

"I would like to grow by about 30%. More than this I worry that we may get too big for our britches and stop doing the things that make Moffitt remarkable, which really is team science," Cleveland said.

Prior to joining Moffitt, Cleveland was a professor and chair of the Department of Cancer Biology at The Scripps Research Institute. Before that, he held various leadership roles with St. Jude Children's Research Hospital.

Cleveland earned his bachelor's degree in biology from the University of Maine, and his doctorate in immunology and microbiology from Wayne State University School of Medicine. He began his career at NCI.

"I felt like I was coming home. At Moffitt, I had a remarkable run as the ACD of basic science," Cleveland said. "I think I've recruited about 60% of the current faculty in the division, including three new terrific chairs and program leaders and all of this was possible from the generous support from the state of Florida, who's investing in Moffitt to the tune of around \$25 million a year.

"It's been a place where you can come and put your footprints in the sand. I did that with basic science. Now, I want to do it for the whole cancer center. I have size 15 feet, so I hope I can leave large footprints."

Cleveland envisions significant investment in what he calls "five big pro-

grams" at Moffitt: immuno-oncology, cancer metabolism research, outreach and engagement and equity, cancer care delivery, and machine learning.

"Moffitt has experienced a rather staggering 9% growth per year in patient numbers," Cleveland said. "If you do the numbers, that will double the size of the clinical care component of the institute in about eight years."

In his first year, Cleveland plans to address the evolving controversy over the role of foreign state-funded programs in cancer research at Moffitt.

On May 13, the Federal Bureau of Investigation issued a public service announcement calling attention to targeting of research organizations by the People's Republic of China to obtain IP on COVID-19 related research.

Some changes at Moffitt include a new process for conducting background checks for all new international employees, regardless of country of origin, revising the institution's conflict of interest policy, and providing additional COI training.

"One of the things that's actually going to happen next week is I'm having an Open Forum on Inclusion, which is one of our core values, as about 10% of our workforce is of Asian heritage," Cleveland said. "Given the press, the leadership changes that were associated with problems with the Thousand Talents Program, and then COVID-19, we're working very hard to make sure that all of our team members understand that Inclusion is at our foundation.

"We're going to be talking about this next week to assure all our team members that, despite all of the things that have happened, we recognize that those of Asian descent and those from China are essential members of our Moffitt family."

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

Matthew Ong: Congratulations. What do you most look forward to doing as center director at Moffitt?

John Cleveland: Thank you very much.

Front and center are our strategic research initiatives that senior leadership, the Board and our External Advisory Committee have given a ringing endorsement.

There are five strategic research initiatives that I see as extremely important. First, is to double down on our investments in immuno-oncology. We want Moffitt as the number one destination center for immunotherapy. We're going to do that through strategic recruitments and building out an already exceptionally strong Immunology Program that's led by two remarkable co-leaders, Jose Conejo-Garcia and Frederick Locke.

We have one of the original FDA approved, CLIA-certified Cell Therapy Facilities that allows us to take immune cell products and put them back into patients. So, we're undergoing a big expansion on that front as well. And we're also rolling out a CRO called OncoBay that is specifically focused on the immunotherapy sector.

Second, we will be rolling out a Metabolism program, where we will target metabolism at three levels, specifically targeting (i) differences in metabolism that are intrinsic to cancer cells, and that are unique to different tumor types; (ii) the immune system, where we can manipulate T-cell metabolism to reprogram these cells to become more effective killers, and to generate

tissue resident memory T cells that have long lasting persistence and anti-tumor effects; and (iii) the metabolism of individual patients, which I think, is actually the most exciting.

Specifically, we've really ignored the fact that everything that we do to a patient actually affects their metabolism. Whether we give them chemotherapy, targeted therapy, or immune therapies, they're all affecting the metabolism of the patient. You and I are different in our metabolism. That is targeting metabolism becomes the fifth pillar of cancer therapy along with radiation, chemotherapy, targeted therapy and immunotherapy.

Third we also need to double down on our investment in Cancer Outreach, Engagement and Equity. We have a remarkable associate center director of Community Outreach, Engagement & Equity, Dr. Susan Vadaparampil, and she's a terrific leader in this space. Over the next six years, we'll be expanding our catchment area from 15 to 21 counties, and we'll be servicing and giving Moffitt Care to almost half the population of the state of Florida through our new partnership with AdventHealth, which is a very large primary health care system that's centered in Orlando, Florida.

Importantly, this partnership allows us to tackle the first part of our mission, which is to contribute to the prevention and cure of cancer. We're a tertiary cancer center, so we're very good at working on the cure part, but we're not very good at tackling cancer prevention, and our partnerships with AdventHealth will allow us to tackle this mission-critical goal. And we want to be leaders in this space.

Fourth, we want to invest in cancer care delivery, which focuses on the science, implementation, and economics of the delivery of cancer care to our patients. The COVID-19 pandemic underscored

the importance of this, because it's really affecting our ability to deliver cancer care to our patients. So this is clearly an area that we need to invest in, and in a big way. This is going to be led by our remarkable ACD of population science, Dr. Shelley Tworoger.

Finally, we're also investing in machine learning. We just hired a remarkable investigator, Dr. Issam El Naqa from University of Michigan, as the founding chair of the Department of Machine Learning. We believe that machine learning has the real potential to transform everything we do, in research and in clinical care, in community outreach, you name it. This is going to affect our entire enterprise. We're excited about rolling out this new initiative in the Division of Quantitative Science that is being led by another remarkable investigator Dr. Dana Rollison.

Also key to our success are new changes in leadership and infrastructure we've made. When I took over as interim center director, there were some leadership changes that had to happen for us to move forward with our CCSG submission next January. First, we were successful in recruiting Dr. Eric Haura, the new ACD of clinical science. Eric is an exceptional physician-scientist. He is the director of our Lung Cancer Center of Excellence, is PI of four grants, has over 190 peer-reviewed publications and is a very translationally focused investigator, one who is a great role model for physician scientists and clinical investigators at the institute. He was a key recruitment and the External Advisory Committee strongly endorsed his appointment.

Second, we have also created additional layers of leadership to oversee specific areas of the cancer center, which is growing rapidly. Specifically, reporting up to Eric will be an assistant center director of clinical research Review and Partnership, Dr. Nikhil Khushalani. Nikhil is a top-tier clinical investigator,

who serves as vice chair of the Cutaneous Oncology Department and is a member of the Moffitt Medical Board. He is a terrific clinical investigator, and he'll oversee the clinical trials regulatory arm of trials at Moffitt.

Third, we're doing a deep dive and looking at gaps and opportunities for building out more support for clinical trials. Clinical trials are a key recruitment tool at Moffitt for all researchers, where we have over 630 active clinical trials, and over 130 observational and behavioral intervention trials. Moffitt has a very clinical trial-rich environment where investigators can come and move their research into the clinic.

Indeed, as a "well-seasoned" investigator of 63 years, I'm now finally taking my basic research and moving it into the clinic in a lung cancer trial with Dr. Jhanelle Gray, our chair of Thoracic Oncology, and Dr. Doug Cress, a senior member of the Molecular Oncology Department. That's the kind of thing that really excites investigators about coming to Moffitt.

How has your journey as a researcher led you here? And why did you take this job?

JC: I first started out at the NCI, and trained with a remarkable investigator, Dr. Ulf Rapp. He was the discoverer of the Raf family of oncogenes. This was a really exciting time at the NCI, from '84 to '89, and it was a terrific experience, because there were a lot of new oncogenes being discovered, and the idea that oncogenes cooperate to cause cancer came out, and we were working on that topic as well.

While I was there, I collaborated with an amazing investigator named Dr. James Ihle, who was recruited to St. Jude Children's Research Hospital as the chair of

Biochemistry. Jim recruited me as his first faculty to that department at St. Jude's, which was a terrific career move. I was there for 17 years. I was mentored by Jim and I was also blessed to be mentored by Dr. Charles (Chuck) Sherr, who was an HHMI investigator, as was Jim. Chuck was an amazing force, an investigator who was famous for discovering oncogenes, cyclins and their inhibitors, and then for discovering a new tumor suppressor that regulates the p53 tumor suppressor called ARF, the alternative reading frame tumor suppressor. With Chuck and his wonderful lab partner and wife, Martine Roussel, who is also a remarkable investigator—they are both members of the National Academy of Sciences—we did some of our very best work.

After 17 years I began looking for leadership opportunities outside of St. Jude's, and I was recruited by Richard Lerner to the Scripps Research Institute, specifically to roll out a Cancer Biology Department at a new Scripps campus called Scripps Florida, which is in Jupiter in Palm Beach County.

With about \$520 million investment from the state of Florida and Palm Beach County, Scripps created a top-notch academic institute that continues to thrive today. It was exciting to be part of something new and to be part of Scripps, which is a world-renowned research institute. I was the founding chair at Scripps-Florida and was a member of the steering committee that helped recruit up to 62 investigators.

While I was at Scripps and leading the Cancer Biology Department, I got to know Moffitt, because we were looking for establishing partnerships between Scripps and Moffitt. We tried to establish a joint research enterprise. It didn't work out, but what did work out was establishing a relationship with Dr. James Mulé, the ACD of Translational Science here at Moffitt. Jim is also the guy who set up the Cell Therapies Facility and he

is truly the founder of the immunotherapy enterprise at Moffitt. He also had amazing training with the real grandfather of the field, Steve Rosenberg at the Surgical Oncology Branch at the NCI.

I got to know Jim, and he reached out to me in 2013, and asked me if I'd be interested in a new opportunity of being the associate center director of basic science. He said, "It's a division that needs some help, and needs some growth." I interviewed for that position in November 2013, and I started the job in July 2014.

One reason that sold me on coming to Moffitt was actually meeting the man himself, H. Lee Moffitt. Lee's really a remarkable individual (we call him "The Closer"), and he convinced me to come, through an inspiring recruitment dinner, but more so when he also dragged me over to the cafeteria to have lunch with patients.

That was an epiphany for me, I felt like I was coming home. Because I experienced the same kind of thing every day when I was at St. Jude's. You know why you're coming to work, right? You're going there to take care of the patients. When I was hired at St. Jude's, one of the first meetings I had was with the founder, comedian Danny Thomas, who was a remarkable man. He said, "I want you to take care of my kids. Don't ever forget that."

Then, when Lee took me over to the cafeteria, he told me the same thing, "I want you to take care of our patients. You're here to do this, never forget that." He says, "You've got a year to cure cancer." Of course, it's going to take longer than that, and there's 300 different types, but that's the kind of men that Lee and Danny are. These are the founders of cancer institutes that have become remarkable enterprises.

At Moffitt, I had a remarkable run as the ACD of basic science. I think I've re-

cruited about 60% of the current faculty in the division, including three new terrific chairs and program leaders and all of this was possible from the generous support from the state of Florida, who's investing in Moffitt to the tune of around \$25 million a year.

These monies come from a program initiated by former Gov. Rick Scott, who developed this to support cancer centers in Florida. We've invested in research, and this investment has led to a huge ROI.

Indeed, the institute has enjoyed about a 30% growth over the last five years in research. We anticipate that we'll have another 30% growth over the next five years as well. It's been a place where you can come and put your footprints in the sand. I did that with basic science. Now, I want to do it for the whole cancer center. I have size 15 feet, so I hope I can leave large footprints.

Speaking of large footprints, you served as interim director after the major change in leadership last year. What was it like stepping in—forgive the pun—at a crucial transition point? Was it challenging?

JC: Yes, it was challenging. I mean, first was the initial surprise and shock because I was not privy to the investigations that led to the change in leadership. I was told only two days before they were actually instituted and was asked at that time by the chair of the Institute Board of Directors, Timothy Adams, by our founder Lee Moffitt, and by the other executive vice presidents if I would consider taking over the role of interim cancer center director.

We have a succession plan at Moffitt for all of our leadership positions, and I was part of the succession plan for Dr. Thomas Sellers. It turned out that this was a very wise thing to do; and it's the wise thing for any institute.

It's actually something that I was aspiring to anyway. In fact, when I was hired by Dr. Sellers back in 2014, the first question he asked me is, "Why do you want this job?" I said, "Well, to be honest, I really don't want this job. I want your job." But what I didn't want was for it to happen this way, and in this fashion.

I stepped up to the plate and took over the role of center director. The following day, I called a meeting of all the other ACDs and they totally rallied. It was an exercise to see how close the Moffitt family really was. And the family was really, really tight, because we all really stepped up and helped each other out, to get through the crisis and the change of leadership.

On the day that it was announced to the institute, Dr. Doug Letson (physician-in-chief) and I got up there shoulder to shoulder and we told everyone, "Don't worry, we've got you. We're going to be alright. We're a strong cancer center. We're strong because of all of you, and because of the patients that we're here to care for. We can't let that mission stop."

Being such a mission-driven Institute helped us get through this. We just kept on forging right ahead. And this came shining through at the EAC site visit that we had in late April. I'm sure that they came into this with concerns about the changes in leadership. They wanted to know that we were strong and they came away from that meeting saying that we were exceptionally strong, and that we should submit our CCSG renewal.

It was really, really challenging. These leaders were also very dear friends and close professional colleagues, and it was also personally very difficult. But when things like this happen and you have patients counting on you, you have to move forward. There are challenges in life, but these also create opportunities. It's a new day and the future of Moffitt is very bright.

I have a remarkable group of peers in the EVPs at Moffitt who have greatly facilitated my transition into the center director position. Yvette Tremonti, who's the CFO, is incredible. And so are Jack Kolosky, the COO, and L. David de la Parte, general counsel. Doug Letson is a terrific mentor and friend, as is our foundation president, Maria Muller.

We meet every week, and together we've overcome the challenges caused by changes in leadership and the COVID-19 pandemic and the fiscal crisis that ensued. Mr. Adams really stepped up as well as our leader during these difficult times. He's been extremely engaged and is a dynamic leader of the board.

Looking back, what really saw us through were our succession plans and our remarkable cadre of leaders. This remarkable group of individuals helped the cancer center through these crises, and still rolled out dynamite research, clinical trials and clinical care.

It's been a time when we've all learned that we're very resilient, and we've truly come to appreciate the talents of each other. There's an incredible synergy between the leaders and our faculty. And all of our trainees and staff have stepped up to the plate.

Everyone has contributed at Moffitt to get by these crises. It is a very big family and a wonderful one, and it was created by the vision of Lee Moffitt. I feel

blessed to work here. It's a true honor and privilege to lead such a remarkable cancer center.

You spoke briefly about leadership changes and infrastructure changes when you took over as interim director—how have those changes affected your faculty and research enterprise?

JC: Some of the infrastructure changes are still in flight. And, some of the infrastructure changes have led to the creation of new positions.

We're also doing a deep dive to identify gaps and opportunities in clinical trial regulatory processes and in clinical trial operations, and this is ongoing. We're doing a similar deep dive in research administration infrastructure. Moffitt's had remarkable growth, but one of the things that we really haven't done very well, and that we're going to be doing well, is to grow infrastructure support at scale, to support all the research that's going on at Moffitt.

At the end of the day, we're going to come out much better—we're going to be a more proactive and less reactive institute.

Moffitt has experienced a rather staggering 9% growth per year in patient numbers. If you do the numbers, that will double the size of the clinical care component of the institute in about eight years.

I don't really want to grow that much on the research side, but I would like to grow by about 30%. More than this I worry that we may get too big for our britches and stop doing the things that

make Moffitt remarkable, which really is team science.

One of the cool things here is that everybody that has an appointment on the research side, whether it be in basic science, population science, or quantitative science, also has an appointment in a clinical department. Clinical investigators have appointments in basic, population or quantitative science. Team science is really part of the DNA of Moffitt.

You've thoroughly described your scientific vision for Moffitt. What are some of your top leadership priorities in terms of growing the faculty and staff over the next few years?

JC: After we get through with the CCSC submission next January, we're going to have a national search for the ACD of basic science. Since Dec. 18, I was actually wearing three hats as the interim center director, the ACD of basic science, and the ACD of clinical science.

Clinical science was actually the toughest part. Eric Haura in his new role as the ACD of clinical science has been doing a remarkable job. There was an interim ACD of basic science before I came on board that served for two years, and that was Dr. James Mulé. I've asked Jim to again step up to the plate as the interim ACD of basic science, and thankfully he's agreed to do so.

So, that's one big leadership opportunity. Another is to hire a co-leader in our Cancer Biology & Evolution Program, which is a remarkably unique program led by Dr. Elsa Flores that applies Darwinian principles to understand how cancer initiates, progresses, sustains it-

self, and how we should treat patients by, for example, adaptive therapy.

As I noted before, we want to roll out a new Metabolism Program in the 2026 cycle. We need two co-leaders for this, and the way we're envisioning this is that one co-leader would be at Moffitt and one would be with our partner at AdventHealth, which is remarkably strong in the metabolism arena. They have exceptional programs studying obesity and diabetes, which are the #2 and #3 risk factors for cancer.

There's lots of opportunity for interactions between AdventHealth and Moffitt in the metabolism arena. To help support this initiative, we've created an associate center director of AdventHealth-Moffitt partnerships. And in Dr. Steven Smith, the vice president and chief scientific officer of the AdventHealth Research Institute, we have the perfect leader to help us realize this vision. Steven is a remarkable investigator in the obesity and diabetes field, and a physician-scientist who translates his work in the clinic.

AdventHealth has developed a new CRU in partnership with Moffitt where we're also doing clinical trials together. Moffitt and AdventHealth have become one in this enterprise. We are jointly recruiting and Dr. Smith is a member of the Research Executive Committee.

We have a lot of positive vibes and we're in an area that's got a lot of positive vibes as well. Tampa is, probably to the surprise of many, a pretty young city. When I go into a restaurant, I'm always the oldest one there. And, there's a lot of culture, great restaurants and beaches and there's lots of things to do. It's easy to recruit faculty here from the Northeast, from Boston or from New York. The whole place has a lot of good mojo going on.

Do you expect to engage in more healing and more morale-building after what happened in December?

JC: Yes, I think we definitely need that. One of the things that's actually going to happen next week is I'm having an Open Forum on Inclusion, which is one of our core values, as about 10% of our workforce is of Asian heritage.

Given the press, the leadership changes that were associated with problems with the Thousand Talents Program, and then COVID-19, we're working very hard to make sure that all of our team members understand that inclusion is at our foundation.

We're going to be talking about this next week to assure all our team members that, despite all of the things that have happened, we recognize that those of Asian descent and those from China are essential members of our Moffitt family.

So, that's one kind of healing that we're still working on. I think other areas of healing will be more practical ones. We're building up more support for clinical trials and research administration that are needed to make a more efficient streamlined institute.

We're also working on being ultra-compliant. Given what happened, we did a deep dive on compliance, which is led by Donnetta Horseman. She reports up to David de la Parte, EVP and general counsel.

They've done a terrific job on reaching out to all the faculty and all the staff and giving us hyper-training in conflicts of interest training, to make sure that everyone is compliant.

The ubiquitous anti-Asian sentiment is part of an incredibly discouraging social and political reality that we're dealing with at this time—and I'm glad to hear that you're being proactive about countering mainstream anti-Asian rhetoric. Are there any other lessons to be learned from Moffitt's investigations on research and funding conflicts of interest?

JC: I think a major takeaway is that we actually have to provide the infrastructure for our investigators to help them receive the necessary training in this area.

I think a lot of us have been learning this on the fly and never really paid enough attention to it. But with the events that have transpired, it's become front and center, it's become a priority. I think that is something that's clear that we just have to pay a lot of attention to.

One of the things that we're doing now is that electronic forms used for when faculty take outside activities also go to corporate compliance, which can warn faculty if they are traveling to a country of concern that's been defined by the federal government. Then, they can step in and educate and provide advice to the faculty or staff member who might be traveling there.

We're also having more in-depth COI training as part of the onboarding process and then there's annual renewals of compliance training. Every year we're going to be rolling this out for all faculty and staff where we will get primers to make sure that everyone's compliant.

How has Moffitt been coping with the COVID-19 crisis, and what is your strategy for re-opening? Also, how have your center's finances and personnel retention been affected?

JC: Research has been shuttered for about eight weeks now since the last week in March, when the work-from-home orders came through. Laboratories have been allowed to have at least one essential person come in per day and we did not shutter our animal experiments or our animal facilities, as we anticipated that when we could restart, we'd want to be able to hit "go" as fast as we can.

Work-from-home has been a struggle for most wet bench investigators, but trainees and faculty have been focusing on data analyses and writing grants and manuscripts. I told all my faculty that I wanted June/July to be a record-setting grant submission cycle, and most PIs are submitting at least two RO1 grants. I think what we're going to see is an incredible influx of grant applications at the NIH and probably an overburdened system.

People have been working from home, but now, over the past two weeks, we're allowing more people in, as long as they're coming in on alternative hours or alternative days. They come in and do their job, and then they go home. Likely in June, we're going to be alternating shifts for the wet bench and probably for the dry labs as well.

There's a Return-to-Campus committee that's laid out guidelines that we need to have in place to return to work safely, and there's also an assessment of individuals that were working on campus, but who can really work from home forever. It's likely, our work-from-home

workforce will more than double as a result of COVID-19.

Fiscally, the pandemic did hit the cancer center pretty hard. EVPs took a 15% pay cut, chairs and ACDs took a 10% pay cut, and everyone was forced to take 40 hours of PTO. Yet, we've weathered this storm, and we're starting to see an uptick in the number of patients coming in and we have reactivated surgeries at all levels, and radiology is coming back as well. We're confident we're going to weather the storm.

It seems utterly superhuman that you've had to manage two major transitions in a span of five months—first, the leadership changes, and then COVID-19. You're the second pure PhD to become the director of Moffitt. What was the national search for candidates like?

JC: Tim Adams, the chair of the Institute Board of Directors, hired a national search firm called Russell Reynolds Associates to do a national search, and I applied for the position and was interviewed for the position by Russell Reynolds.

They did a thorough national assessment and a thorough assessment of my candidacy, which included a two-hour in-depth interview. After their review they came forward with recommendations to Mr. Adams and then to the Board of Directors, who indicated that I was the right candidate for the job.

The Board of Directors is also using the same firm to identify and recruit the new CEO/president as well. This is a very respected and talented search firm that has been involved in other major

recruitments, for example, like at the Hutch and at NYU.

I have experienced nothing but support from my peers and colleagues on both the research and the clinical side.

I think we went through that process pretty seamlessly. And the EAC indicated that they were very supportive of this decision, even before I got the job.

With your background as a distinguished basic scientist, what does your confirmation as director say about the research culture at Moffitt?

JC: The research culture of Moffitt is really remarkable. It's science driven and translation is part of our DNA. Our goal is to do clinical trials to get our work into patients and to have our clinical trials lead to FDA approval and to changes in the standard of care. We've done that over and over again at Moffitt. I think that's what really makes Moffitt remarkable.

Everyone knows that, that's why we're here—the mission is to cure cancer. That's what we're all about. The other part of our mission is a work in progress, which is preventing cancer. We need to double down on those efforts, and I firmly believe we can now tackle this through our partnership with AdventHealth. I'm very, very confident that we'll make big inroads in this space as well.

Thank you for speaking with me at length.

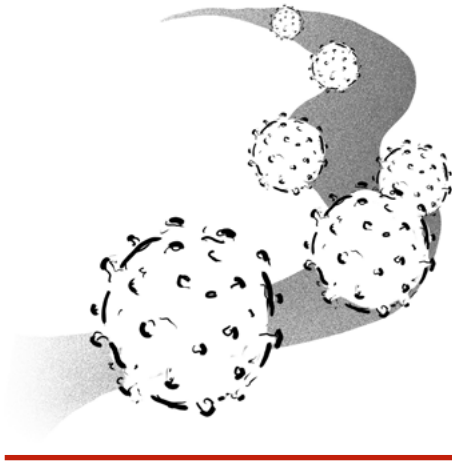
JC: Thank you as well.

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COVID-19 UPDATES



Study: Hydroxychloroquine doesn't improve survival in hospitalized COVID-19 patients, but tocilizumab does

An observational study of more than 3,000 patients hospitalized with COVID-19 at Hackensack Meridian Health has shown that hydroxychloroquine doesn't improve survival for hospitalized patients.

However, tocilizumab appears to improve survival among critically ill intensive care unit patients, the study showed. If confirmed, tocilizumab would become the first medication improving survival from COVID-19.

Hackensack Meridian Health released the findings on medRxiv, which allow researchers to share critical scientific information rapidly prior to publication in peer-reviewed journals.

The results are based on the new data analysis platform—the HMH Universal Observational Database for COVID-19, or RECOVERY, which compiles outcomes from 13 Hackensack Meridian Health hospitals throughout New Jersey.

“Our researchers’ observations that tocilizumab may improve survival among the most critically ill could alter the course of the pandemic if confirmed in randomized trials—and Hackensack Meridian Health is participating in those randomized trials as well,” Robert C. Garrett, chief executive officer of Hackensack Meridian Health, said in a statement.

The outcomes division of the John Theurer Cancer Center at Hackensack University Medical Center, under the leadership of Stuart Goldberg and Andrew Ip, created a database to guide the analysis of more than 3,000 patients admitted to Hackensack Meridian Health facilities for urgent care.

Results from the study follow:

- Among 2,512 hospitalized patients with COVID-19, 76% received at least one dose of hydroxychloroquine and 59% received hydroxychloroquine with azithromycin.
- After adjusting for imbalances via propensity modeling, compared to receiving no hydroxychloroquine, there was no significant differences in associated mortality for patients receiving any hydroxychloroquine during the hospital stay.
- Among 547 ICU patients, including 134 receiving tocilizumab in the ICU, an exploratory analysis found a trend towards an improved survival rate: 56% who received the drug compared to 46% who did not receive the therapy, and a propensity adjusted hazard ratio 0.76.

The Hackensack Meridian JTCC team worked with COTA Inc., to conduct propensity modeling to assess for potential effective therapeutic interventions. The data and statistical analysis were enhanced by Donald A. Berry, professor in the Department of Biostatistics at MD Anderson Cancer Center, and his statistical team at Berry Consultants.

“Our study adds to the emerging data finding no benefit for hydroxychloroquine among hospitalized patients, but now we will turn our database’s attention to exploring if the medication is beneficial earlier in the pre-hospital course,” Andre Goy, physician in chief at Hackensack Meridian Health Oncology and chairman and chief physician officer at John Theurer Cancer Center, said in a statement.

Researchers established an observational database through Epic–Hackensack Meridian’s electronic health records system—and collected a random sampling of COVID-19 patients who received treatment at one of 13 hospitals across the network. To date, Hackensack Meridian Health has cared for more than 10,000 patients with confirmed COVID-19 infections and has discharged more than 6,000 patients from network hospitals.

Genentech begins phase III trial of tocilizumab + remdesivir in hospitalized patients with severe COVID-19 pneumonia

Genentech, a member of the Roche Group, has launched a phase III, randomized, double-blind, multicenter study (REMDACTA) to evaluate the safety and efficacy of Actemra (tocilizumab) plus the investigational antiviral remdesivir, versus placebo plus remdesivir in hospitalized patients with severe COVID-19 pneumonia.

The trial, in collaboration with Gilead Sciences Inc., is expected to begin enrolling in June with a target of 450 patients.

“Based on our current understanding, we believe that combining an antiviral with an immune modulator could potentially be an effective approach to treating patients with severe disease,”

Levi Garraway, Genentech chief medical officer and head of global product development, said in a statement.

In addition to REMDACTA, Genentech is close to completing enrollment of the global randomized, double-blind, placebo-controlled phase III clinical trial (COVACTA, NCT04320615) to evaluate the safety and efficacy of intravenous Actemra plus standard of care, versus placebo plus SOC in hospitalized adult patients with severe COVID-19 pneumonia.

Approximately 450 patients will be enrolled in COVACTA. This is an increase from the original target of 330 patients. Actemra is not currently approved for this use by FDA.

The protocol for COVACTA allows the inclusion of patients who are being treated with antivirals, including investigational antivirals. Data from the REMDACTA trial are designed to supplement the COVACTA study.

The COVACTA study is conducted in collaboration with FDA and the Biomedical Advanced Research and Development Authority. Genentech is also a participant in the Accelerated COVID-19 Therapeutic Interventions and Vaccines partnership, led by NIH and the Foundation of the NIH.

Genentech has also initiated a national phase III double-blind, placebo-controlled randomized trial (EMPACTA, NCT04372186) that will focus on recruiting approximately 375 patients at trial sites known to provide critical care to underserved and minority populations that often do not have access to clinical trials.

UMich develops app that calculates risk of delaying cancer care during COVID-19

A team of data scientists and cancer doctors from the University of Michi-

gan Rogel Cancer Center and the U-M School of Public Health developed a free, web-based application to compare the long-term risk for a patient whose cancer treatment was postponed.

The OncCOVID app draws on national cancer data sets to help assess the risk of immediate treatment versus delayed treatment, depending on a patient's individual characteristics, as well as on COVID's impact on their local community.

"We also see the app providing additional reassurance to oncologists and their patients when the data show that delaying treatment will likely have little or no impact on a patient's long-term outcome," the project's lead researcher, Holly Hartman, a doctoral student in biostatistics at U-M, said in a statement.

OncCOVID could also be used by health care systems resuming care and need to prioritize a backlog of patients.

"Hospitals have basically been using a three-tiered system during COVID: treat, delay a little, or delay a lot," Daniel Spratt, associate professor of radiation oncology at Michigan Medicine and one of the senior researchers on the project, said in a statement. "Unfortunately, this tiered system is an extremely blunt instrument. Our goal was to create a resource that could be tailored both to the individual patient and to their local community."

The app allows doctors to enter more than 45 characteristics about a patient — including their age, location, cancer type and stage, treatment plan, underlying medical conditions, and the proposed length of a delay in care. It then calculates the patient's likely five-year survival following immediate treatment and delayed treatment.

Under the hood, the app draws on millions of records contained in the National Cancer Institute's Surveillance, Epidemiology, and End Results registry and the National Cancer Database, com-

bined with county-level COVID infection data from Johns Hopkins University.

Advanced features allow all of the app's underlying statistical assumptions to be adjusted, such as the baseline mortality risk from COVID and the disease's infection rate. In the future, the researchers plan to use the same data model to start looking at the effects that treatment delays due to the coronavirus pandemic may have on cancer mortality nationally, Hartman said.

ACS CAN survey: cancer patients increasingly face COVID-19 health impact

In a survey conducted by the American Cancer Society Cancer Action Network survey of cancer patients and survivors, 87% of respondents said the COVID-19 pandemic had affected their health care in some manner, up from 51% in an April survey.

Of those in active treatment 79% reported delays to health care (up from 27%), including 17% of patients who reported delays to their cancer therapy like chemotherapy, radiation or hormone therapy. The most commonly reported effects for those in active treatment were for changes to in-person cancer provider appointments (57%*); and delays in access to imaging services (25% up from 20%) and surgical procedures (15% up from 8%). Delayed access to supportive services, including physical therapy or mental health care, remained steady (20%).

Nearly one in four patients surveyed say the pandemic has made it more difficult to contact their providers with questions about their health care needs, and one in five say they are worried their cancer could be growing or returning

due to delays and interruptions caused by the COVID-19 outbreak.

Forty-six percent said the COVID-19 pandemic had impacted their financial situation and ability to pay for care in some way (up from 38%). And nearly a quarter (23%) said they worry they may lose their health insurance due to the pandemic and its effects on the economy.

While a majority of respondents said they are sheltering in place, 18% said they were working outside the home, including 11% of those still in active treatment. More than a third (34%) of patients say they are anxious the pandemic will make it hard to afford basic household expenses; concerns that are especially prevalent among lower-income patients with more than half (54%) of those earning \$30,000 or less reporting that they are worried about affording essentials, including rent, food and utilities.

This combined medical and financial stress has resulted in nearly half (48%) of patients saying the COVID-19 pandemic has had a moderate or major effect on their mental health. In particular, 67% said they worry it will be harder for them to stay safe when social distancing and other restrictions are relaxed in their area, and 70% of patients worry they will be unable to find protective equipment like gloves or masks to help keep them safe.

The survey also collected feedback from a small group of providers and caregivers who similarly reported concern about delayed care and difficulties providing support for patients while being unable to see them, as well as a lack of personal protective equipment. Caregivers, like patients, reported anxiety over reopening and the increased potential for their and their loved one's exposure to the virus.

The web-based survey was taken by more than 1,200 cancer patients and survivors. This sample provides a margin of error +/- 3% and 96% confidence level. Additional input was provided by 111

caregivers and 139 health care providers supporting cancer patients and survivors.

IN BRIEF



Catherine Alfano, Stacy Sanchez, Joseph Herman, Martin Karpeh recruited by Northwell Cancer Institute

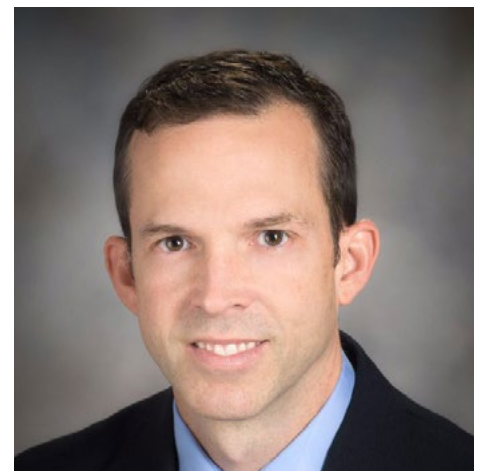
The Northwell Health Cancer Institute has recruited four experts to its cancer program:



- **Catherine Alfano** will serve at the Cancer Institute's new vice president of cancer care management and research. Alfano was previously vice president of survivorship at the American Cancer Society and, prior to that, deputy director of the NCI Office of Cancer Survivorship.

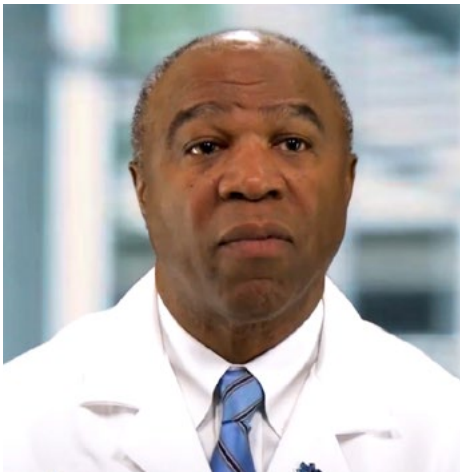


- **Stacy Sanchez** will assume the role of chief nursing officer. She is the former director of pediatric and critical care services, and interim director of acute care services at Memorial Sloan Kettering Cancer Center.



- **Joseph Herman** will become vice chair of clinical informatics for radiation medicine and director of clinical research integration for the cancer institute. He joins Northwell after serving as professor and division head of the Department of

Radiation Oncology at MD Anderson Cancer Center, a role he has held since 2016. He specializes in the treatment of pancreatic and hepatobiliary malignancies, and previously initiated and co-directed the Pancreatic Multidisciplinary Clinic at Johns Hopkins University. He currently serves as principal investigator for several institutional gastrointestinal protocols and is a co-investigator (radiation oncology lead) for the Alliance borderline resectable cancer trial, which is evaluating the role of stereotactic body radiation therapy.



- **Martin Karpeh, Jr.**, was named director of surgical oncology for Northwell's eastern region and chair of the department of surgery at Huntington Hospital. Overseeing surgical oncology for Northwell's Eastern Region on Long Island, he will direct programs at Huntington Hospital, Southside Hospital in Bay Shore and Peconic Bay Medical Center. Karpeh joined Northwell at the end of April to help colleagues during the COVID-19 pandemic. Karpeh comes to Northwell from Hackensack University Medical Center, where he was surgeon-in-chief from 2014-2019. He also was founding chair of surgery at the Hackensack Meridian School of Medicine at Seton Hall. Karpeh has held surgical oncology leadership positions at Beth Israel Medical Center/Continuum Health Partners

of New York; chief of surgical oncology at Stony Brook University and cancer center director at Stony Brook University Medical Center. In addition, he was an attending surgeon at Memorial Sloan Kettering Cancer Center for 11 years.

"We are laying the groundwork to create a survivorship program, bolster oncology nursing practice and initiatives, enhance the integration of clinical cancer research and advance surgical oncology," Richard Barakat, physician-in-chief and director of the Northwell Health Cancer Institute and senior vice president of cancer services at Northwell Health, said in a statement.

Pamela Hull joins Markey as associate director of population science and community impact



Medical sociologist Pamela Hull was named associate director of population science and community impact at the University of Kentucky Markey Cancer Center

She will also serve as the William Stamps Farish Endowed Chair in Cancer Research and join the UK College of Medicine as an associate professor of behavioral science.

Hull's expertise is in the development, testing and dissemination of behavioral interventions to promote cancer prevention behaviors, and she has more than 15 years of experience conducting community-engaged research. She specializes in HPV-mediated cancer prevention, childhood obesity prevention, community-engaged research, and health disparities.

In her role as associate director, Hull will oversee Markey's community outreach and engagement functions in addition to its population science research agenda and infrastructure, which includes Markey's Cancer Prevention and Control Research Program. She will also have oversight of the Kentucky Cancer Program-East and the Kentucky Cancer Consortium. The goal of Markey's community outreach and engagement efforts is to accelerate science-to-practice translation across the cancer care continuum, with an emphasis on the needs of Kentucky's citizens.

Two of Hull's extramurally funded grants will also move to the UK. The first is a grant from NCI focused on increasing HPV vaccination in community-based pediatric practices. The second is a grant from the U.S. Department of Agriculture funding the development and testing of a smartphone application featuring shopping tools and nutrition education tools intended for use by low-income and nutritionally at-risk families and their children.

Prior to joining the UK Markey Cancer Center, Hull was an associate professor in the Vanderbilt University School of Medicine's Division of Epidemiology and served as associate director of community outreach and engagement for the Vanderbilt-Ingram Cancer Center in Nashville. During her tenure at Vanderbilt, she led many community-engagement activities that helped reduce the cancer burden and health disparities with partners in the region.

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HIGH- VALUE OPPORTUNITIES

CLINICAL TRIAL DESIGN: STATISTICAL OPTIONS/CHALLENGES

BIOSIMILARS AND PATENT ISSUES

CREATING THE INFRASTRUCTURE FOR INTERVENTIONAL PHARMACOECONOMIC TRIALS

OPPORTUNITIES TO OPTIMIZE CANCER DRUG POLICIES

THE INTERVENTIONAL PHARMACOECONOMIC TOOLBOX

FOCUS ON OPTIMAL DOSING OF IBRUTINIB

WELCOME ADDRESS

Allen Lichter

Value in Cancer Care Consortium

KEYNOTE SPEAKER

Cliff Hudis

American Society of Clinical Oncology

Web Conference Organizers

Daniel Goldstein, MD – Davidoff Center, Rabin Medical Center, Israel

Mark J Ratain, MD – The University of Chicago

Hosted by:

The University of Chicago, Value in Cancer Care Consortium (Vi3C), Clalit Health Services

THE CLINICAL CANCER LETTER

CLINICAL ROUNDUP



AI could predict risk of lung cancer recurrence

Computer scientists working with pathologists have trained an artificial intelligence tool to determine which patients with lung cancer have a higher risk of their disease coming back after treatment—part of Cancer Research UK's landmark TRACERx study.

The AI tool was able to differentiate between immune cells and cancer cells, enabling researchers to build a detailed picture of how lung cancers evolve in response to the immune system in individual patients.

The paper was published in *Nature Medicine* May 27 and is showcased alongside eight other TRACERx publications on the Nature website.

Although this research is in its early stages, the approach could speed up how doctors predict which patients are

more likely to see their lung cancer return, so they can be closely monitored with tailored treatment plans.

The AI tool—developed by researchers at The Institute of Cancer Research, London, in collaboration with scientists at University College London Cancer Institute and the Francis Crick Institute—was trained by pathologists to pick out immune cells from cancer cells. This allowed the tool to map out areas in tumours where the number of immune cells were high compared to the number of cancer cells, in patients with lung cancer.

Using the AI tool, the team found that while some parts of the tumor were packed with immune cells, described as hot regions, other parts of the tumour appeared to be completely devoid of them, which they described as cold regions.

When the researchers followed the progress of patients who had a higher number of cold regions, they found patients were at a higher risk of relapse.

This study is part of the TRACERx* (Tracking Cancer Evolution through therapy [Rx]) lung study—a £14 million, 9-year study funded by Cancer Research UK.

In the study, led by Yinyin Yuan, of The Institute of Cancer Research, and researchers from the UCL Cancer Institute and the Francis Crick Institute, AI pathology image-mapping technology was combined with next-generation sequencing. They used this tool to analyse samples from 100 patients with non-small cell lung cancer who took part in the TRACERx study.

The team's work revealed that cancer cells found in immune cold regions may have evolved more recently than cancer cells found in immune hot regions that are packed with immune cells.

The researchers suggest that areas of the tumour with fewer immune cells may have developed a cloaking mechanism under evolutionary pressure from the immune system allowing them to hide from the body's natural defences.

Their AI tool can assess how many regions with this cloaking mechanism exist within a tumor.

“Our research has revealed fresh insights into why some lung cancers are so difficult to treat, and we wouldn't have been able to do this without the scale and scope of the TRACERx project,” Yuan said.

TRACERx is Cancer Research UK's single biggest investment in lung cancer.

Study confirms effective, less toxic alternative to standard treatment for adults with Burkitt lymphoma

In a study, an alternative treatment regimen that is less toxic than standard dose-intensive chemotherapy was found to be highly effective for adults with Burkitt lymphoma across all age groups and independent of HIV status.

In addition to being better tolerated, the regimen, called dose-adjusted (DA) EPOCH-R, is already an option for diffuse large B-cell lymphomas and can be administered in an outpatient setting.

The findings were published May 26, 2020, in the *Journal of Clinical Oncology*. The study was led by researchers in the Center for Cancer Research at NCI, and sponsored by NCI's Cancer Therapy Evaluation Program. It was conducted at 22 research centers across the country. The DA-EPOCH-R regimen was originally developed by NCI researchers led by Wyndham Wilson, at the NIH Clinical Center in Bethesda, Maryland.

"We knew Burkitt lymphoma is curable with dose-intensive chemotherapy, but that treatment can be acutely toxic for adult patients," lead author Mark Roschewski, of NCI's Lymphoid Malignancies Branch, said in a statement. "With this finding, we not only have a potentially curative treatment option for these patients that's less toxic, but one that appears effective for most adults, including elderly patients and those with HIV and other comorbidities who might not be able to receive standard treatment."

Burkitt lymphoma is a rare but aggressive B-cell lymphoma that is more common in children than adults. The dose-intensive chemotherapy that's been developed to cure Burkitt lymphoma in pediatric patients is much better tolerated by children than adults, who can have severe side effects, especially if they are older or have other serious health conditions, such as being infected with HIV. People living with HIV/AIDS have an increased risk for Burkitt lymphoma.

NCI researchers have tested several approaches to determine whether less toxic treatments could still be effective for Burkitt lymphoma in adults. In an earlier pilot study with 30 adult patients treated only at NCI, the DA-EPOCH-R

chemotherapy regimen was effective. The DA-EPOCH-R regimen is tailored to an individual patient's ability to tolerate chemotherapy.

The regimen infuses chemotherapy over 96 hours for each cycle, and "dose-adjusted" means that later cycles can use higher doses of chemotherapy if it is well tolerated. This is compared to "dose-intensive" chemotherapy, which uses very high doses in all patients from the beginning.

To confirm these findings, the researchers conducted a larger, multicenter phase II study, enrolling 113 patients identified as having low- or high-risk disease, based on characteristics such as tumor bulk and performance status. The median age was 49 years, and 62% were 40 years or older. At a median follow-up of almost 5 years, the researchers calculated that the 4-year rate of event-free survival was 84.5%, meaning that percentage of patients had not seen any sign of their cancer's return.

Overall survival was 87%. For low-risk patients, event-free survival was 100%, and for high-risk patients it was 82%. The treatment was effective across age groups, including patients in their 70s and 80s, and regardless of HIV status. The treatment was well-tolerated with a relatively low number of patients experiencing the severe side effects commonly associated with dose-intensive chemotherapy.

These findings suggest that highly dose-intensive chemotherapy may not be necessary for cure, and that carefully defined low-risk patients may be treated with limited chemotherapy. Furthermore, patients can receive EPOCH-R in an outpatient setting, an alternative to the prolonged hospitalization required to receive highly dose-intensive chemotherapy.

Five treatment-related deaths occurred in the study.

The researchers found that patients in the study who had disease in the central nervous system, specifically in cerebrospinal fluid (CSF), had the highest risk of treatment-related death or treatment failure.

Fox Chase researchers investigate perceived barriers to discussing sexual issues in breast cancer patients

Researchers at Fox Chase Cancer Center found that breast cancer patients describe having thoughts and feelings that can prevent them from discussing cancer-related sexual issues with their healthcare providers, even if they would like to.

"Overall, there is growing interest in the importance of women's sexual health after breast cancer because of the impact it can have on women's quality of life," Lauren Zimmaro, lead author on "Patients' perceived barriers to discussing sexual health with breast cancer healthcare providers," published in *Psycho-Oncology*, said in a statement.

Zimmaro is a senior postdoctoral fellow with Jennifer Barsky Reese, of the Cancer Prevention and Control Research Program at Fox Chase, who was the principal investigator and senior author on the paper.

Zimmaro said sexual issues, including those directly resulting from treatment, are common among breast cancer patients. In some cases, chemotherapy and hormonal treatments may cause vaginal dryness, discomfort during sexual activity, and loss of sexual desire, she said. In other instances following mastectomies and other breast cancer surgeries, sexual concerns may include body image issues or changes in breast

sensation, which can negatively impact women's sexual arousal.

"These changes are often very distressing, and although they seem to be quite common, we know that women are rarely bringing up these concerns with their cancer providers, so we were interested in learning more about why this might be," Zimmaro said.

This paper is part of a program of research in Reese's lab focusing on understanding and improving patient-provider communication about sexual health. The researchers sought to learn more about the kinds of barriers that were preventing women from feeling comfortable discussing sexual concerns with their healthcare providers.

A total of 144 women treated for breast cancer at Fox Chase who were participating in a trial of a sexual health communication training program led by Reese completed questionnaires assessing their beliefs about discussing sexual issues with providers.

The researchers found that women cited two major barriers to discussing sexual issues with their healthcare providers. One was their own thoughts or feelings, which could impede them in discussing sexual issues with their providers, and the other was the women's beliefs about their providers' reactions to discussions of sexual health.

"Overall, women tended to view their own discomfort in discussing sexual concerns as the bigger barrier to discussing these issues with their providers than discomfort they attributed to their breast cancer providers," Zimmaro said.

She said these results could be helpful in showing patients that it is common to have some doubts or hesitations about their ability or comfort in discussing sexual concerns. However, it may be important for women to recognize these

barriers so that they can have their sexual concerns addressed appropriately.

"Now that we have a clearer understanding of the types of barriers preventing women from raising the topic of sexual issues with their providers, we can work towards addressing them," said Zimmaro. "In fact, the findings helped confirm the need for programs that can help women feel more comfortable discussing sexual issues with their providers like the ones being evaluated in Dr. Reese's lab."

Evidence from two studies demonstrates efficacy of Immunoscore

Two Immunoscore clinical studies in stage III colon cancer patients validated the clinical value of Immunoscore to refine patients stratification and predict which patients benefit most from 6 months adjuvant chemotherapy.

Immunoscore is sponsored by HalioDx SAS.

Published in *JNCI Cancer Spectrum*, the Immunoscore-NO147 study was conducted in collaboration with clinicians and researchers from the Mayo Clinic. The Immunoscore-IDEA France study, published in *Annals of Oncology*, was conducted in collaboration with PRODIGE, a digestive oncology intergroup gathering the GERCOR, the FFCD and UNICANCER organizations. Objectives of these retrospective studies in prospectively conducted trials were to examine and validate the ability of Immunoscore to identify patients at high-risk of relapse and investigate survival differences according to Immunoscore in predefined subgroups, including Tumor/Node Stage and treatment duration.

The two studies were performed on independent large phase III randomized clinical trials cohorts, and included 559 patient samples from the FOLFOX alone arm of the NCCTG N0147 trial³, and 1062 patient samples from both arms (3 versus 6 months) of the IDEA France trial⁴ (as part of the IDEA international collaborations⁵). Consistent prognostic performances were obtained, and Immunoscore predictive performance was demonstrated for FOLFOX therapy duration.

MK-6482 induced positive response in Hippel-Lindau disease-associated kidney cancer

In an international trial led by researchers at The University of Texas MD Anderson Cancer Center, treatment with MK-6482, the small molecule inhibitor of hypoxia-inducible factor (HIF)-2 α was well tolerated and resulted in clinical responses for patients with von Hippel-Lindau disease-associated renal cell carcinoma.

The results of the phase II trial were shared today in an oral presentation May 28 at the 2020 American Society of Clinical Oncology virtual annual meeting by principal investigator Eric Jonasch, professor of genitourinary medical oncology at MD Anderson.

The trial met its primary endpoint and showed an objective response rate in RCC tumors per RECIST by independent review. The confirmed response rate was 27.9%. When also considering the eight patients with unconfirmed response, the objective response rate was 41.0%. Additionally, 86.9% of patients had a decrease in the size of their target lesions. The median time to response was 5.5 months.

RCC affects approximately 40% of people with VHL disease and is one of the most common causes of disease-related death in people with VHL disease.

The VHL mutation causes cells to lose their ability to respond to oxygen levels properly, and leads to a buildup of HIF proteins inside the tumor cell. This process incorrectly signals that the cells are starved of oxygen, causing the formation of blood vessels and driving tumor growth. The inactivation of the VHL tumor-suppressor protein also is observed in more than 90% of sporadic RCC tumors. MK-6482 directly targets HIF-2 α , hindering cancer cell growth, spread and abnormal blood vessel development.

Treatment of VHL disease-associated renal tumors consists of active surveillance until surgery is required for tumors larger than 3 cm to prevent metastatic disease. Repeated surgical procedures can carry significant complications as many patients develop renal insufficiency. Surgery will not cure VHL disease patients with RCC; surgery only is intended to prevent death from metastatic kidney cancer.

As of data cut-off, the single-arm clinical trial had enrolled 61 patients. The study enrolled adult patients with a germline mutation diagnosis of VHL disease, no prior systemic cancer therapy, measurable non-metastatic RCC tumors and Eastern Cooperative Oncology Group (ECOG) performance status of 0 or 1.

Patients received MK-6482 orally once daily until disease progression, unacceptable toxicity, or investigator's or patient's decision to withdraw. Tumor size was evaluated at screening and every 12 weeks thereafter. No patients had progressive disease on treatment and 58 patients (95.1%) remain on treatment.

DRUGS & TARGETS



Opdivo + Yervoy receive FDA approval combined with limited chemotherapy as first-line treatment of metastatic or recurrent NSCLC

FDA has approved Opdivo and Yervoy (nivolumab + ipilimumab) in combination with two cycles of platinum-doublet chemotherapy as first-line treatment for patients with metastatic or recurrent non-small cell lung cancer, with no epidermal growth factor receptor or anaplastic lymphoma kinase genomic tumor aberrations.

Opdivo and Yervoy are sponsored by Bristol-Myers Squibb Co.

Efficacy was investigated in CHECKMATE-9LA (NCT03215706), a randomized, open-label trial in patients with metastatic or recurrent NSCLC. Patients were randomized to receive either the combination of nivolumab plus ipilimumab and 2 cycles of platinum-doublet chemotherapy (n=361) or platinum-doublet chemotherapy for 4 cycles (n=358).

The trial demonstrated a statistically significant benefit in overall survival (OS) for patients treated with nivolumab plus ipilimumab plus chemotherapy compared to those who received chemotherapy. Median OS was 14.1 months (95% CI: 13.2, 16.2) versus 10.7 months (95% CI: 9.5, 12.5), HR 0.69; 96.71% CI: 0.55, 0.87).

Median progression-free survival per blinded independent central review (BICR) was 6.8 months (95% CI: 5.6, 7.7) in the nivolumab plus ipilimumab and chemotherapy arm and 5 months (95% CI: 4.3, 5.6) in the chemotherapy arm (HR 0.70; 95% CI: 0.57, 0.86). Confirmed overall response rate (ORR) per BICR was 38% (95% CI: 33, 43) and 25% (95% CI: 21, 30) respectively. Median response duration was 10 months in the nivolumab plus ipilimumab and chemotherapy arm, and 5.1 months in the chemotherapy arm.

FDA collaborated with the Australian Therapeutic Goods Administration, Health Canada, and Singapore's Health Sciences Authority on the review of this application as part of Project Orbis. FDA approved this application 2 months ahead of schedule. The FDA and HSA decisions are near-simultaneous, while the review of the applications is ongoing for the Australian TGA and Health Canada.

This review used the Real-Time Oncology Review. This application was granted priority review and fast track designation.

Brigatinib receives FDA approval for ALK-positive metastatic NSCLC

Brigatinib (Alunbrig) has received FDA approval for adult patients with

anaplastic lymphoma kinase-positive metastatic non-small cell lung cancer as detected by an FDA-approved test.

Alunbrig is sponsored by Ariad Pharmaceuticals Inc.

FDA also approved the Vysis ALK Break Apart FISH Probe Kit (sponsored by Abbott Molecular Inc.) as a companion diagnostic for brigatinib.

Efficacy was investigated in ALTA 1L (NCT02737501), a randomized (1:1), open-label, multicenter trial in adult patients with advanced ALK-positive NSCLC who had not previously received an ALK-targeted therapy. The trial required patients to have an ALK rearrangement based on a local standard of care testing. The trial randomized 275 patients to receive brigatinib 180 mg orally once daily with a 7-day lead-in at 90 mg once daily (n=137) or crizotinib 250 mg orally twice daily (n=138). A subset of the clinical samples was retrospectively tested with the Vysis ALK Break Apart FISH Probe Kit. Of the enrolled patients, 239 had positive results using the Vysis diagnostic test (central results were negative for 20 patients and unavailable for 16 patients).

The major efficacy outcome measure was progression-free survival evaluated by a blinded independent review committee according to RECIST 1.1. Additional efficacy outcome measures as evaluated by the BIRC was confirmed overall response rate.

Estimated median PFS for patients treated with brigatinib was 24 months (95% CI: 18.5, NE) compared with 11 months (95% CI: 9.2, 12.9) for those treated with crizotinib (HR 0.49; 95% CI: 0.35, 0.68; p<.0001). Confirmed ORR was 74% (95% CI: 66, 81) and 62% (95% CI: 53, 70), respectively.

CLR 131 receives fast track designation in lymphoplasmacytic lymphoma/Waldenstrom's macroglobulinemia

CLR 131 was granted FDA Fast Track Designation in lymphoplasmacytic lymphoma (LPL)/Waldenstrom's macroglobulinemia in patients having received two prior treatment regimens or more.

CLR 131 is sponsored by Cellectar Biosciences Inc.

CLR 131 is a small-molecule, cancer-targeting radiotherapeutic Phospholipid Drug Conjugate designed to deliver cytotoxic radiation directly and selectively to cancer cells and cancer stem cells. It is being evaluated in Cellectar's phase II CLOVER-1 clinical study in patients with relapsed or refractory multiple myeloma and lymphoplasmacytic lymphoma/Waldenstrom's macroglobulinemia.

"LPL/WM patients that do not respond optimally or are intolerant of ibrutinib, currently have limited treatment options and poor survival rates," James Caruso, president and CEO of Cellectar, said in a statement.

All four LPL/WM patients treated in our CLOVER-1 phase II study to date achieved a 100% overall response rate and a 25% complete response rate.

"This strong response rate may represent an important improvement in the treatment of relapsed/refractory LPL/WM as no approved or late-stage development treatments for relapsed or refractory patients have reported complete responses," Caruso said.

FDA granted CLR 131 in LPL Orphan Drug Designation earlier this year.

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