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NCTN GROUP CHAIRS: CANCER TRIALS TAKE BACKSEAT TO CLINICAL CARE AMID COVID-19 PANDEMIC

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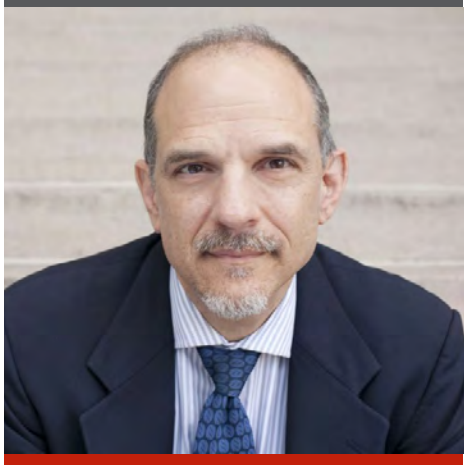
GUEST EDITORIAL

NCTN GROUP CHAIRS: CANCER TRIALS TAKE BACKSEAT TO CLINICAL CARE AMID COVID-19 PANDEMIC

While the National Clinical Trials Network (NCTN) groups remain open for business during the pandemic, it's not business as usual. For good reason, clinical trials are taking a backseat to clinical care. Leadership and members themselves face significant challenges treating oncology patients, as attention and resources are diverted to minister to those with COVID-19.

SWOG CANCER RESEARCH NETWORK



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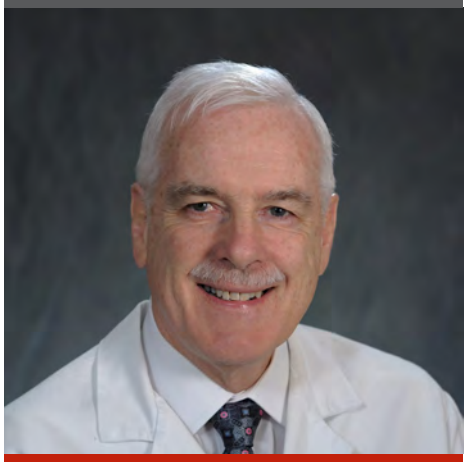

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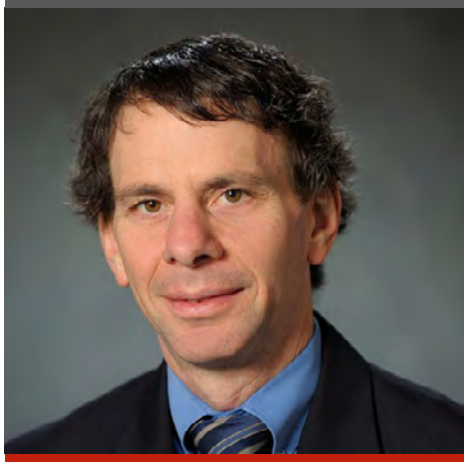

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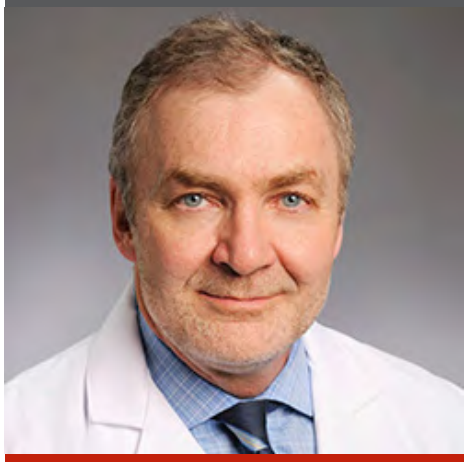

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Some are quietly creating formulas to consistently determine who gets chemotherapy, tumor resection, irradiation, or transplant. It's an unprecedented time. But for now, we plan to continue to treat patients with cancer who are already on study, and as circumstances permit, to accrue new patients to existing trials, and even to continue to open new, high-priority studies.

Our enrollment levels began to decline during the week of March 23, and we expect a decrease in overall accrual to continue for the duration of this pandemic. Some of our key member institutions cannot currently conduct research or have to limit clinical trial enrollment to those patients likely to get an "immediate benefit."

No treatment or population science trial has completely closed due to coronavirus. However, a few studies have been suspended—one NCTN trial due to a drug shortage; one due to concerns over patients coming in for infusion of possible placebo; and three National Community Oncology Research Program (NCORP) studies due to disruptions in cancer screening and cancer care delivery.

In the NCORP cases, we felt we could not collect reliable data at this time, so good science demanded the suspensions. One major example: Work has halted on ECOG-ACRIN Cancer Research Group's landmark Tomosynthesis Mammographic Imaging Screening Trial, or TMIST, which compares 2D and 3D mammography to determine the best way to detect early breast cancers.

We have spent the last month reacting and adapting. The Alliance for Clinical Trials in Oncology, the Children's Oncology Group (COG), and SWOG Cancer Research Network have changed their semi-annual face-to-face meetings to virtual spring conferences that can be conducted via video conference, while the Canadian Cancer Trials Group (CCTG) and ECOG-ACRIN cancelled their spring meetings altogether.

We've completely transitioned employees to work from home, all the while maintaining staffing and keeping trial operations going.

NCI relaxes rules during crisis

With help from the NCI, which has relaxed some rules during the crisis, we've been allowing member sites to suspend audits, and we have pushed back data submission deadlines. We now allow telehealth visits or delays for in-person appointments called for under protocols.

“With help from the NCI, which has relaxed some rules during the crisis, we've been allowing member sites to suspend audits, and we have pushed back data submission deadlines.”

Certain oral agents are being shipped directly to patients' homes via trackable methods, such as FedEx. All of these moves can potentially free up physicians and keep oncology patients out of our hospitals and clinics.

In addition, the network groups have also developed special forms for sites to record protocol deviations or note a COVID diagnosis for a patient on study. Some groups are reviewing active protocols to see if there are ways to make changes that can save members time, while maintaining trial integrity. For example, the FDA is allowing alternate dose schedules for certain drugs.

The groups are similarly exploring less frequent drug administration and spaced-out imaging, which we hope to adopt without going through the normal lengthy and sometimes bureaucratic protocol amendment process.

To accommodate sites that may become overwhelmed with COVID-19 care, or to protect patients who can't or won't travel for their treatments, the NCI's Cancer Therapy Evaluation Program (CTEP) is allowing local physicians to aid trial providers. Local doctors can administer standard therapies, conduct exams, and run the customary laboratory tests called for on the studies—as long as they follow protocol rules and get agreement from a treating physician approved to participate in the trial. We applaud the NCI for making this unprecedented allowance, and for doing it so quickly.

Communication is mission-critical during a crisis. That's why we're reaching out directly to member sites with guidance memos. The Alliance created a members-only coronavirus resource page, and CCTG, NRG, and SWOG created open access pages, which include information for sites, patients, and the public.

SWOG is also maintaining an online clearinghouse with an up-to-the-minute list of labs and biobanks still open and able to process tissue and other samples required by its protocols. ECOG-ACRIN and CCRG created special email addresses that members can use to ask COVID-related trial questions, while COG produced a guide for parents with children, teens and young adults with cancer, explaining how they can protect their kids from COVID-19. The guide is available in English, Spanish, and French.

We are proud of—and humbled by—the response of our members. From New Orleans to Detroit, New York City to San Francisco, the physicians, nurses, and clinical site staff in our groups are on the frontlines of healthcare during this public health emergency. Not only are they continuing to care for oncology patients, often under challenging conditions, but some are caring for patients with COVID. Some have switched their focus to clinical trials testing new antiviral therapies, lending valuable expertise from the oncology research community to the search for life-saving treatments.

CCC19: COVID-19 and Cancer Consortium

Just two weeks after the first COVID-19 death was recorded in the United States, a group of cancer physicians and scientists launched the COVID-19 and Cancer Consortium (CCC19), a national and soon-to-be international research project.

CCC19 uses an online form to collect de-identified, HIPAA-exempt data from oncology patients with COVID-19. The online survey was created at Vanderbilt University Medical Center and approved at the Fred Hutchinson Cancer Research Center and a number of other cancer centers and hospitals.

The survey collects patient demographics, clinicopathologic factors, coronavirus diagnosis and treatment details, and health care provider information. Patients, and their outcomes, can be tracked over time.

By collecting data now, we can conduct meaningful research later. Scan the roster of the CCC19 steering committee, and the project's list of collaborators, and you'll see a number of NCTN and NCORP researchers who have led our trials for years. We applaud these members, and the leadership of Vanderbilt, Fred Hutch, Dana-Farber, MD Anderson and more for their fast, forward-thinking efforts.

> "Medical lessons learned on the battlefield have often led to major improvements in civilian medicine. We are, surely, now in a war. We pledge to take what we learn and use that knowledge to better serve our members and the public."

Lessons learned from the CCC19 project, as well as from teleconferencing and telemedicine, will help us create and run better operations systems and manage smarter, faster trials later. The concept itself is not unique. Medical lessons learned on the battlefield have often led to major improvements in civilian medicine. We are, surely, now in a war. We pledge to take what we learn and use that knowledge to better serve our members and the public.

After six decades of clinical research, the network groups have built a massive scientific enterprise that includes large data sets, specimen banks, and a wealth of shared expertise. We have improved and lengthened lives, and even increased cure rates, in a number of childhood and adult malignancies.

For now, our committees continue to discuss new research ideas, protocols are being written and approved, data are being analyzed and manuscripts prepared. Since most CTEP and Division of Cancer Prevention functions have also been transitioned to remote participation, communications have been excellent and momentum maintained. Studies, even if not immediately activated, are being moved through regulatory processes at sites to ensure their immediate opening upon lifting of various embargos.

Decreasing the burden of disease and human suffering largely are achieved through clinical trials, even during the COVID era. Along with new studies to test COVID vaccines and drugs, network oncology research will continue.

Now, perhaps more than ever, this work is vital.

The authors acknowledge Wendy Lawton, SWOG Cancer Research Network communications director, for aid in writing and gathering background data.

GUEST EDITORIAL

Chernobyl doctor's view of COVID-19: Trump threatens 267 years of progress in biomedical research

By Robert Peter Gale, MD, PhD, DSc (hc), FACP, FRCP
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Governments respond differently to crises which threaten the health of their citizens. For example, during the current SARS-CoV-2 pandemic, some countries instituted an immediate lockdown whilst others have not restricted social activities, or have done so too late to be maximally effective.

The question is: What prompts these different policies?

I have been involved in mitigating the health effects of several catastrophes, including the nuclear power facility accidents in Chernobyl and Fukushima-Daiichi, a radiation accident in Goiania, Brazil, and earthquakes in Armenia and Mexico City. A consistent feature of the leaders of countries where these events occurred was to seek—and mostly follow—the advice of scientific and medical experts.

For example, my Soviet colleagues and I met frequently with members of a special committee of the Politburo, including General Secretary Mikhail Gorbachev, immediately after the Chernobyl accident. We kept them advised of our interventions at least weekly, if not daily. When we proposed using a molecularly-cloned hematopoietic growth factor (sargramostim) to treat the most severely affected victims, they wanted to see the evidence that this posed no danger.

At that time, we had only treated monkeys exposed to high-dose ionizing radiation, but the results were encouraging. Still, the Politburo was conservative and science-based, and it was only after two of us self-administered the drug (and survived) that we were allowed to proceed.

This is not to say the Soviet government was forthcoming with details of the accident, but they acted rationally when it came to medical interventions.

My experience after the Fukushima accident was similar. Japanese colleagues and I met frequently in the Prime Minister's Office and with Diet members to evolve a science-based strategy for evacuations, interventions, etc.

Contrast this with President Donald Trump's promotion of chloroquine and hydroxychloroquine to treat people with COVID-19. His recommendation to Americans is based on anecdotal data of *in vitro* anti-SARS-CoV-2 activity from two studies in China and uncontrolled clinical trials in China and France. In the French trial, 20 subjects received hydroxychloroquine with or without azithromycin and were compared with 14 controls who declined the intervention.

The endpoint in the French study was virus clearing, an unvalidated surrogate endpoint.

Add to this lack of randomization and blinding and a few other methodological issues. In contrast, a double-blind, placebo-controlled randomized trial of more than 1,500 subjects in Singapore at risk for influenza reported no benefit, despite similar in vitro anti-influenza virus activity. Importantly, 45% of subjects in the chloroquine arm reported adverse events.

Despite these shaky data, a tweet by President Trump on 21 March declared that the combination of hydroxychloroquine and azithromycin "has a real chance to be one of the biggest game changers in the history of medicine." (Don't tag Lister, Jenner, Pasteur, or Fleming.)

Gadzooks! How would Trump know?

The French study is so flawed that on April 3 the International Society of Antimicrobial Chemotherapy, publisher of the Journal of Antimicrobial Agents, issued this expression of concern about the paper that convinced Trump of the efficacy of chloroquine and hydroxychloroquine:

"The ISAC Board believes the article does not meet the Society's expected standard, especially relating to the lack of better explanations of the inclusion criteria and the triage of patients to ensure patient safety," the statement reads. "Although ISAC recognises it is important to help the scientific community by publishing new data fast, this cannot be at the cost of reducing scientific scrutiny and best practices."

"This morning, in the clinic, two people asked me whether they should be taking chloroquine, which they said they could obtain on the black market for an exorbitant price. I cautioned against this."

Although many scientists, myself included, share this concern and can pile on a few others, President. Trump's enthusiasm hasn't been dampened. When a person of his stature promotes a therapy, the endorsement has serious consequences.

This morning, in the clinic, two people asked me whether they should be taking chloroquine, which they said they could obtain on the black market for an exorbitant price. I cautioned against this.

One could see Trump's science advisors cringe as he continued to argue for this therapy.

Anthony Fauci, a respected scientist and infectious disease expert, tried to moderate this claim, but was restrained by the president on several occasions. Fauci, director of the National Institutes of Allergy and Infectious Diseases (NIAID), who supervised U.S. responses to epidemics such as AIDS and the 2009 influenza A(H1N1)pdm09 pandemic, serves at the will of the president, limiting what he can say—lest he be transferred to the Bethesda Post Office.

Being a smart guy, Fauci probably thinks it's better for the nation if he stays calm than if he gets tossed out. (I agree.) God knows what he says when he gets home, poor man. His wife must be a saint.

To quote *The New York Times*, "Day after day, the salesman turned president has encouraged people with COVID-19 to try hydroxychloroquine with all of the enthusiasm of a real estate developer selling time shares. The passing reference he makes to the possible dangers is usually overwhelmed by the full-throated endorsement. 'What do you have to lose?' he asked five times on Sunday."

President Trump isn't alone in his enthusiasm.

His co-promoters include such scientific luminaries as Peter Navarro (his trade adviser), Dr. Mehmet Oz (a television doctor), Larry Ellison, of Oracle, Laura Ingraham and co-conspirators on Fox News, as well as Rudolph Giuliani, who has interrupted stamping out corrup-

tion in Ukraine to help stamp out the SARS-CoV-2 pandemic.

With the numbers of crises Trump creates almost daily, we've already forgotten about the detention of migrants, the border wall, the Russia inquiry, impeachment, scrubbing the EPA of scientists with knowledge of climate change, reducing air pollution control standards, etc. Who can keep up? The administration's cavalier attitude toward science may ultimately cost the nation many more lives than the SARS-CoV-2 fiasco.

Recently, Trump turned a visit to the Centers for Disease Control and Prevention (CDC) into political theater by wearing a MAGA hat. One shudders to think what scientists and epidemiologists there made of this carnival.

attitude as leadership in the tradition of FDR and Winston Churchill.

The president used his bully pulpit to speed approval of this unscientific approach through the FDA, another public service agency part of the Executive Branch. Failure to take orders could earn FDA Commissioner Stephen Hahn a position beside Fauci in the Bethesda PO, along with HHS Secretary Alex Azar. They would make a formidable team.

A randomized clinical trial of hydroxychloroquine and azithromycin in persons with COVID-19 has begun at Rutgers Cancer Institute [See related story on page 18]. Unfortunately, the study design, with the primary endpoint of virus load, is unlikely to provide a definitive answer to questions of safety and efficacy. There is no arm receiving placebo-only, which may reflect the misguided belief of potential subjects that they need these drugs, thanks to the president's unfounded and unbounded enthusiasm.

> “Apparently, the concept of evidence-based medicine has not reached the White House, where some members of the Trump administration also recommended prayer to stop an AIDS epidemic amongst intravenous drug abusers.”

The latest insult to common sense and the importance of leadership came at a SARS-CoV-2 briefing on Friday, April 3, when the president announced the CDC recommendation that Americans wear face masks, but emphasized that this was voluntary: "You don't have to do it. I'm not going to do it." It would be difficult to classify this count-me-out

Sadly, we have been down this path before, thanks to political support for "amazing cancer cures," including shark cartilage, laetrile, coffee enemas, and vitamin C. Once such myths are created, it takes many years and many studies to eradicate them.

And let's not forget the potential to do harm directly, because Dr. Trump's Amazing COVID Cure has created shortages of these drugs for people with diseases where they are proven safe and effective—and has led to the poisoning (and death) of people drinking a chloroquine formulation designed to kill fish parasites.

Trump *et al.* are chipping away at the 267-year tradition of responsible experimentation in medicine.

In 1753, the British naval surgeon James Lind published his account of the comparative treatment of sailors with scurvy: "their cases as similar as I could have them." He divided 12 sick sailors into six pairs, giving each pair a different dietary supplement: cider, diluted sulfuric acid, vinegar, sea water, two oranges and a lemon or a purgative.

He noted: "The most sudden and visible good effects were perceived from the use of the oranges and lemons." So much for power calculations. (One can only wonder what an Institutional Review Board would make of the sulfuric acid cohort.)

Progress toward understanding whether therapies were effective was slow, but steady. For example, 145 years later Johannes Fibiger, a Danish physician, studied 484 persons with diphtheria, giving them a serum treatment or not based on what day they were admitted to a Copenhagen hospital.

Fibiger argued for the need "to eliminate completely the play of chance and the influence of subjective judgment," indicating a clear understanding of the hazards of uncontrolled comparisons.

Many scientists, physicians, epidemiologists and statisticians, too numerous to mention, realized the need for scientific rigor in the evaluation of the safety and efficacy of medical interventions.

In 1990, Gordon Guyatt introduced a concept he called "scientific medicine" where one would evaluate the quality of data supporting a therapy decision. The response of his colleagues was less than enthusiastic, because of the implication prior medical decisions were unscientific. Undaunted, Guyatt tried a new term: "evidence-based medicine."

It's difficult to believe this term first appeared in the biomedical literature in 1991, only 30 years ago. Today, evidence-based medicine is taken for granted. Evidence-based medicine is, in fact, the alternative to voodoo-based medicine.

What physician would recommend a therapy not evidence-based, except in the context of a controlled trial? All too many, it seems, given reports of physicians prescribing chloroquine and hydroxychloroquine prophylactically and therapeutically.

Apparently, the concept of evidence-based medicine has not reached the White House, where some members of the Trump administration also recommended prayer to stop an AIDS epidemic amongst intravenous drug abusers. This is not to say that every intervention needs to be proven safe and effective in a double-blind randomized placebo-controlled clinical trial. (Consider the use of parachutes when jumping out of a plane at 10,000 meters.) However, we need an organized, structured, statistically validated approach to know whether a new therapy works.

In Hamlet (Act 4; Scene 3), Claudius remarks: "Diseases desperate grown, / By desperate appliance are relieved, / Or not at all." Certainly, the SARS-CoV-2 pandemic is a desperate disease, and we may need desperate appliances to save the lives of people with COVID-19.

However, this challenge requires a considered approach. There are many approved drugs, and we need our best scientists and physicians to carefully and quickly use modern analytical techniques to identify a hierarchy for testing. Resources are limited and time is of the essence.

How are these drugs more compelling than all the other drugs?

Testing chloroquine or hydroxychloroquine based on a hunch from someone with no scientific credentials means another, perhaps more promising, drug will not be tested.

In critical situations such as the current SARS-CoV-2 pandemic, large randomized controlled trials are not always feasible, and empirical therapy may be justified.

However, physicians need to demand careful and critical interpretation of data from such uncontrolled trials, and the trials should be structured as best possible to give definitive answers.

Judgments about safety and efficacy should not be made by persons lacking appropriate expertise, and certainly shouldn't be promoted to the public. Continued study of chloroquine and hydroxychloroquine in persons with COVID-19 in the context of a clinical trial is reasonable. However, their use to prevent SARS-Cov-2-infection or prevent COVID-19 is without scientific basis.

"The human cost of the SARS-CoV-2 pandemic is considerable, but most of us will survive. However, we may not survive the politically motivated desecration of the carefully constructed 267-year-old methodology for advancing human health."

President Trump might take a lesson from Lionel Trilling, who said: "I defeated myself long ago when I rejected the way of chutzpah and mishegass in favour of reason and diffidence."

The human cost of the SARS-CoV-2 pandemic is considerable, but most of us will survive. However, we may not survive the politically motivated desecration of the carefully constructed 267-year-old methodology for advancing human health.

And, in these holy days of Easter and Passover, please join me in prayer for the health of Anthony Fauci.

NCI to distribute IL-6 inhibitor for cancer patients with COVID-19 lung inflammation

By Matthew Bin Han Ong

NCI is finalizing plans to use its clinical trials networks to administer a compassionate use protocol for distribution of tocilizumab, a drug that blocks the inflammatory protein IL-6.

Tocilizumab, an immunosuppressive agent also known by its brand name Actemra, is sponsored by Genentech. Under NCI's protocol, the drug will be made available to cancer patients at institutions that are not participating in Genentech's phase III trial of the drug.

The IL-6 inhibitor was approved by FDA for rheumatology indications in 2011, and has been used for mitigation of cytokine release syndrome caused by CAR T-cell therapy.

According to Genentech, the federal government has obtained 10,000 vials of tocilizumab for the U.S. Strategic National Stockpile "for potential future use at the direction of the HHS."

It is one of three drugs—the other two being sarilumab and siltuximab—that are now being rushed into late-stage clinical trials for assessment of efficacy in treatment of acute respiratory distress syndrome caused by immune response to SARS-CoV-2 infection (*The Cancer Letter*, March 27, 2020).

"We are going to, in concert with Genentech, run a treatment referral trial for the Genentech Roche IL-6 receptor antibody for COVID-related ARDS," James Doroshow, deputy director for clinical and translational research at NCI, said April 9 in an emergency virtual joint meeting of the NCI Board of Scientific Advisors and the National Cancer Advisory Board.

"We wrote a trial, I would like to say—just like in the old days—in four days, a trial was put up. It's been reviewed by Genentech Roche," said Doroshow, who is also director of NCI's Division of Cancer Treatment and Diagnosis and head of the Oxidative Signaling and Molecular Therapeutics Group of NCI's Developmental Therapeutics Branch. "I hope to be able to have a final version of this to the central IRB very quickly."

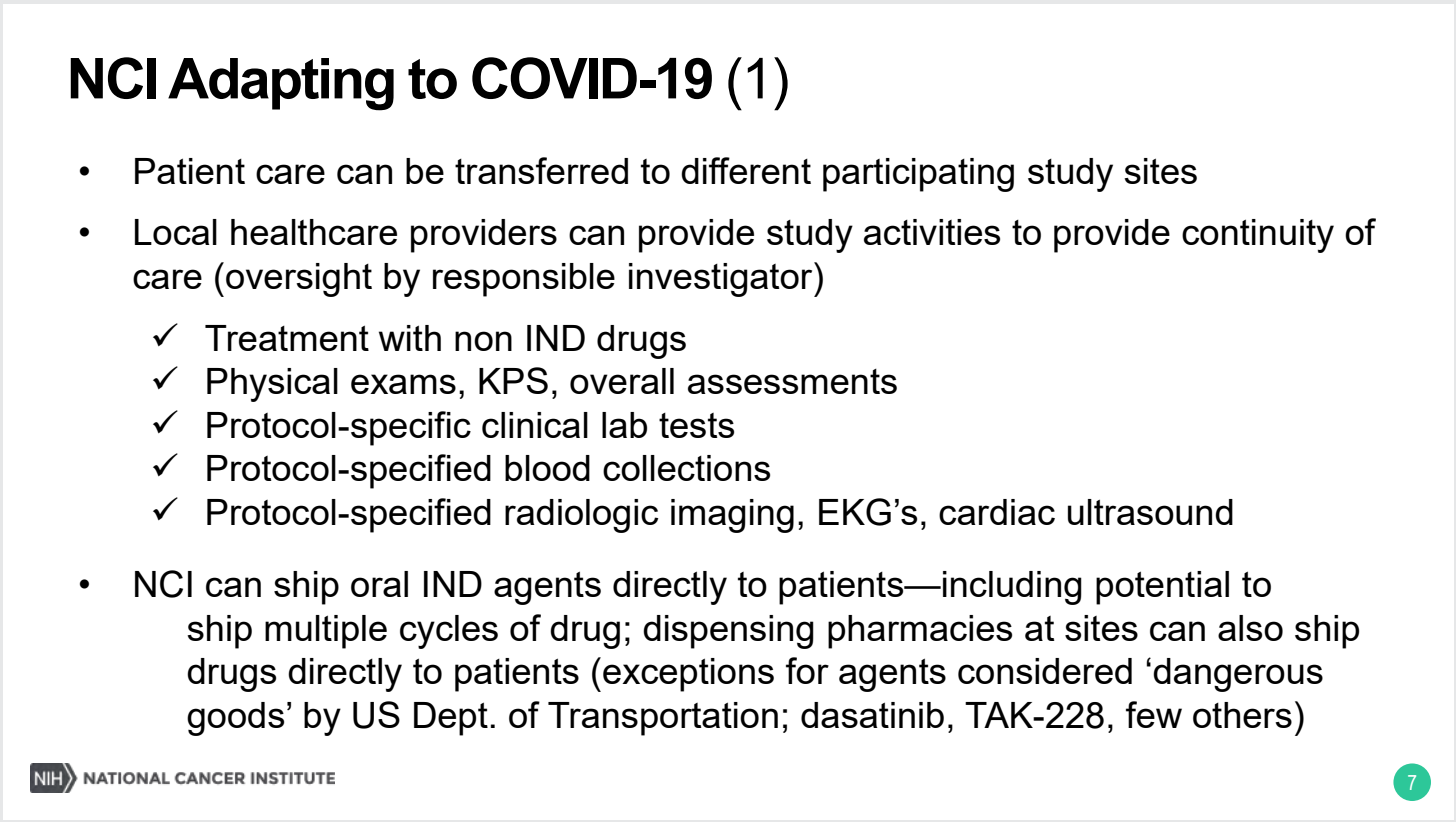
NCI's protocol for tocilizumab is designed to rapidly make the drug available to cancer patients, who face a particularly high fatality risk from severe complications stemming from COVID-19.

"Why do this? Well, because we know that there are multiple randomized trials and multiple institutional trials," Doroshow said. "There are some folks who simply can't afford to get this drug, and we wanted to have a very broadly eligible study, eligible even for patients very young in age, which is not addressed by most of the trials that are out there, to try to see whether we can move the needle in terms of decreasing ICU time, ventilator time, time in the hospital.

"We will collect some clinical data. It'll be a modest set of data," Doroshow said. "There will be blood obtained for biomarker evaluation.

"We hope to activate this across all of our networks, and all institutions that are not already participating in one of the various phase III randomized trials that are out there for tocilizumab, or any other IL-6-related agent."

An excerpt of Doroshow's remarks to BSA and NCAB follow:



I appreciate very much the opportunity to talk to you about what's gone on over the past three to four weeks, for the NCI to address, what it can do in its clinical trial networks to respond to this terrible crisis.

I'm going to review the modifications to the NCI clinical trial processes that have taken place over the last 10 to 14 days to try to address the ability to do studies in this patient population.

I'm going to discuss a trial that will soon be onboarded for IL-6 receptor antibodies, as a compassionate use trial.

Let me just say what we're trying to do to adapt to this current situation. While it may be obvious, but now it was clarified in a series of memoranda that came from Meg Mooney in [the Cancer Therapy Evaluation Program] and Worta McCaskill-Stevens in [the Division of Cancer Prevention], to try to address how individual investigators and sites can deal with this problem.

So, of course, it's clear that patient care can be transferred relatively easily to different participating sites, where, perhaps, the burden of the virus is less. That's really not as important a degree of change as is required.

What has happened is that we have made it clear that a much broader range of activities can be performed close to home to allow patients not to travel, and to continue on clinical trials with maintaining the oversight for the study by the responsible investigator, but allowing local physicians to provide treatment on study with non-IND drugs, to do physical exams, perform performance assessments, overall assessments, and performance status assessments, to do protocols, assist with the clinical lab tests, to collect, to actually research blood specimens, and to do radiologic imaging studies, EKGs, ultrasound, and the like.

And, all of that to be sent back to the responsible investigator, and done in such a way, if the patient only needs those drugs, to obviate the patient coming to the site where that individual was registered.

We've also, in concert with the FDA and with the NCI Central IRB, begun a process in which we can ship oral IND agents—I underscore, IND agents—directly to patients and to sites, so that the sites can then subsequently submit, send those drugs on to patients—and in fact, even multiple cycles of drugs—so that we can, again, limit the amount of time, the amount of travel that the patients need to do, and keep them on study.

There are only a few exceptions to this rule. There are about a half dozen drugs, I can't tell you why, but the U.S. Department of Transportation lists those drugs as dangerous goods. Why they are specifically dangerous versus many other anticancer drugs, I can't tell you, but those drugs cannot easily be shipped. And, happily, those drugs make up a re-

NCI Adapting to COVID-19 (2)

- Injectable CTEP IND agents must be administered at a registered site (FDA)
- Alternative procedures that do not compromise safety or the integrity of the study will be considered minor deviations:
  - Documented in the medical record with reason (ie., travel restriction)
  - Include: study visits by telemedicine rather than in-person; delayed study visits; delayed lab or imaging tests; minimal treatment delays; biospecimen collections
- Major deviations may be unavoidable; must still be reported to CIRB
- On-site auditing visits are being re-scheduled; remote auditing has been adopted by NCTN groups
- NCI CIRB supports "remote" informed consent: telephone discussion in conjunction with patient signature on written document

NIH NATIONAL CANCER INSTITUTE 8

ally small minority of the drugs used in the vast range of our clinical trials.

Now, again, it's probably not a surprise to people who are listening to this talk that FDA regulations require that injectable IND agents must be administered at the registered site, and this is not something that we at the NCI can do differently.

What we can do, however, is to make sure that the current situation does not lead to an enormous compromise, either in the safety or the integrity of the studies, by racking up huge amounts of deviations to trials that will cause havoc in the eventual evaluation of the data.

So, basically, if minor deviations occur because of travel restrictions—the exact time for study visits is not exactly on schedule, or if those study visits are done by telemedicine rather than in person, if lab tests or imaging trial studies are done slightly off the mark, in terms of the timing required, if there are minimal treatment delays, if there are delays in biospecimen collections—all those will be viewed as minor deviations, and no institution participating in NCI-designated and supported trials will get significant hits for those kinds of things.

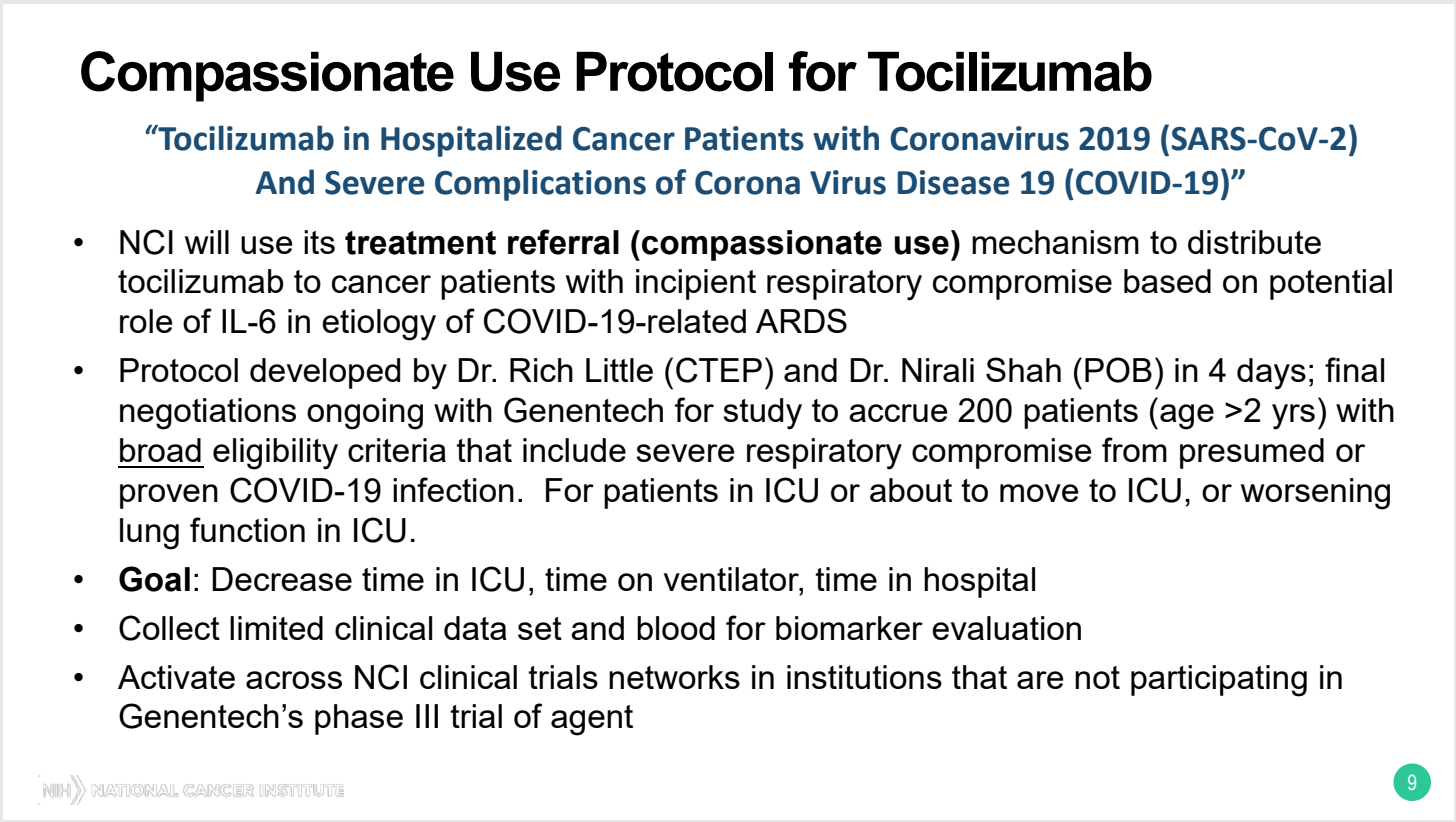
We understand that this is a really remarkable time in our history. We want to be able to get the big-picture understanding of the outcomes for our trials that have involved so many patients, without compromising those trials, but, at the same time, without compromising the ability of institutions to do their studies and not be affected by changes in practice that are unavoidable.

And, I'd like to say a specific word about acknowledging that major deviations to studies are clearly going to be unavoidable. We want those to be reported to the central IRB, but again, those things we have to be flexible,and understand the conditions in which we're trying to carry out clinical research for the population of institutions and patients who are still appropriate for entering on a clinical trial.

And so, again, I can give you my word that we will take into consideration the times, rather than the strict issues related to these deviations, as trials are reported out.

All of that we've talked at great length about, and we have weekly meetings with the NCTN group chairs, and all of the auditing visits for all of the major groups have been rescheduled. No face-to-face auditing will be done. All of the auditing will be done remotely until it's safe to be able to do that.

A major change that has been negotiated with the NCI Central IRB, where they have specifically, and in writing, supported remote informed consents, telephone discussions in conjunction with patient signatures, and return of written documents by fax or PDF are now viewed as appropriate and consistent with good clinical practice. I think this will help us not to require patients to come in multiple times for an informed consent visit versus a visit to get their initial treatment, if that is required.



Let me move on to a subject that represents something that I would love to be able to see. I think that we should understand that, if we're going to be flexible in this specific context, we ought to learn something about the entire process that we use for doing clinical trials, how that could be changed to make them more nimble.

And so, some of you remember the treatment referral protocols that the NCI ran. It started with distribution of Taxol. It went on to distribution of bevacizumab and other agents, but before they became available commercially.

We are going to, in concert with Genentech, run a treatment referral trial for the Genentech Roche IL-6 receptor antibody for COVID-related [Acute Respiratory Distress Syndrome].

We wrote a trial, I would like to say—just like in the old days—in four days, a trial was put up. It's been reviewed by Genentech Roche. I hope to be able to have a final version of this to the central IRB very quickly.

Why do this? Well, because we know that there are multiple randomized trials and multiple institutional trials. There are some folks who simply can't afford to get this drug, and we wanted to have a very broadly eligible study, eligible even for patients very young in age, which is not addressed by most of the trials that are out there, to try to see whether we can move the needle in terms of decreasing ICU time, ventilator time, time in the hospital.

We will collect some clinical data. It'll be a modest set of data. There will be blood obtained for biomarker evaluation.

So, we hope to activate this across all of our networks, and all institutions that are not already participating in one of the various phase III randomized trials that are out there for tocilizumab, or any other IL-6-related agent.

> "There are some folks who simply can't afford to get this drug, and we wanted to have a very broadly eligible study, eligible even for patients very young in age, which is not addressed by most of the trials that are out there."
>
> *– James Doroshow*

Q & A

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

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CONVERSATION WITH THE CANCER LETTER

Libutti: Rutgers studies COVID-19 while bracing for its surge

> “Cancer is not going to take a break or sit on the sidelines and wait for us to finish dealing with the pandemic.”

Steven K. Libutti, MD, FACS
Director, Rutgers Cancer Institute of New Jersey;
Senior vice president of oncology services, RWJBarnabas Health;
Vice chancellor for cancer programs, Rutgers Biomedical and Health Sciences;
Professor of surgery, Rutgers Robert Wood Johnson Medical School;
Affiliated Distinguished Professor in Genetics, Rutgers School of Arts and Sciences

As he manages the logistics of running Rutgers Cancer Institute of New Jersey and cancer services throughout RWJBarnabas Health, Steven K. Libutti has to worry about providing cancer care in a massive health system in the midst of the COVID-19 pandemic.

"We're watching what's happening in New York, because we know that's our future here in New Jersey," Libutti said to *The Cancer Letter*. "We're starting to see a significant increase in COVID-19 cases, hospitalizations and ventilator use, especially the last three or four days."

That day, April 3, New Jersey reported nearly 30,000 COVID-19 cases and nearly 750 deaths. The numbers have since climbed to 37,500 cases and over 900 deaths. The state is a distant second to New York, which has reported 122,600 cases and nearly 4,200 deaths.

In addition to making certain that the health system has enough beds, ventilators and N95 masks in anticipation of the surge, Rutgers and RWJBarnabas Health are initiating a clinical trial of azithromycin and hydroxychloroquine vs. hydroxychloroquine alone vs. supportive care for six days followed by hydroxychloroquine. The study's primary endpoint will be viral load at six days.

The Rutgers study will accrue 160 patients, with an early look after 80 patients are accrued. Ultimately, the answer may depoliticize the COVID-19 treatment aggressively touted by President Donald Trump at his White House briefings. The trial will test the findings of an earlier study by French researchers. The French study was open-label and not randomized. Altogether, 20 patients were treated.

"The French study, while small, looked promising. Both agents are readily available, FDA-approved, and, for the most part, well tolerated," Libutti said. "If a larger study can support the results seen in the French study, these agents can be quickly deployed as a component of the approach to treating COVID-19. If the larger study does not show activity, we can move on from these agents and focus on others."

Cancer centers are especially well suited for getting quick answers to scientific questions involving COVID-19.

"We are structured to do exactly what is needed right now: to quickly and efficiently deploy clinical trials in a very structured way, with an infrastructure that allows us to carefully monitor them, to collect data in a very organized, efficient and regulated way, to be able to support the infrastructure required to put together a trial, and then safely conduct it," Libutti said.

Libutti spoke with Paul Goldberg, editor and publisher of *The Cancer Letter*. The conversation took place on April 3.

Paul Goldberg: So, how are you?

Steven Libutti: So, we're hanging in there. This is like a nightmare that you just can't wake up from, but there's a lot of teamwork, not just across our own program at Rutgers and across our health system, but across the entire state of New Jersey.

And we're doing everything we can to keep caring for cancer patients amid this pandemic, and all the complexities that it brings in the care that has to be rendered to the folks suffering from COVID-19. We're slugging away.

We're watching what's happening in New York, because we know that's our future here in New Jersey. We're starting to see a significant increase in COVID-19 cases, hospitalizations and ventilator use, especially the last three or four days.

And we expect that we'll see a peak in northern Jersey first, and then it will begin to flow down the rest of the state, central and south. We're already seeing lots of cases in central Jersey, and we expect it to get worse before it gets better.

We're looking at a very large state that's your catchment area. What are the geographic patterns you are seeing?

SL: Not surprisingly, we're seeing COVID-19 cases increase significantly in the northern portions of the state, the ones in closest commuting proximity to New York, to Manhattan, and it's traveling south on I-95, the Jersey Turnpike.

And so, where a lot of our cases were in the northern portion of our catchment and our health system, we're now seeing more cases in the central region, and a slight pickup in cases, much like in locations further south.

We expect that those southern locations are going to see the wave as well. Probably, we'll see the peak, as best as we can assess by the trends, in the north over the next week. And then the central region, probably over the next week-and-a-half to two weeks, and then the southern part of the state in two-weeks-plus.

We're really bracing ourselves for a surge of cases. As everybody has predicted, this is a huge strain on resources, not just beds and ventilators and ICU, but personnel—nurses, providers, all being asked to now care for critically ill patients with COVID-19, and, as I said, we're doing everything we can to maintain cancer care, because that's still critically important.

Cancer is not going to take a break or sit on the sidelines and wait for us to finish dealing with the pandemic.

What's the number of cases you're expecting?

SL: It's hard to say, because the patterns are different from each hospital and each region. New Jersey caseloads right now, and all of us, I think, are essentially following the same data streams, [including] the Hopkins School of Public Health program, looking at case numbers across the world.

I track that every day, and New Jersey today [April 3] is close to 30,000 cases and almost 750 deaths.

And this is always lagging behind by about a day, as they catch up with all the data from the hospitals. New York state's over 102,000 cases [April 3] now. So, between New York and New Jersey, we make up just under half of all the cases in the United States. But I don't think it's going to be isolated to us.

I think that the rest of the country is looking at a preview of what to expect as the cases and the virus spread across the rest of the United States.

I don't know where we'll peak. As you know, we're one of the more densely populated states, but unlike New York, where Manhattan is very tightly and densely populated--a lot of apartment buildings etc., where it's ripe for transmission—we have urban areas and rural areas.

How this all maps out in New Jersey and what our ultimate peak is in terms of numbers is tough to say, but it's going to be more, we're not at the peak yet, and we will see a lot more cases.

Is your hospital capacity holding up?

SL: So far, we are. I think it's part of the strength of being a system, having 11 hospitals, geographically deployed across the state. Some of our hospitals are really bearing the brunt of large volumes of patients admitted, with a fair percentage at each of those hospitals in the ICU and on ventilators.

But, fortunately, some of the other hospitals in our system, especially some of the ones that are a little further south or west, aren't seeing the same numbers yet. And so, we're having to come up with a process to move patients around throughout the system, with respect to cancer care, trying to maintain cancer care at the hospitals that are busy with COVID, but also looking into how we move some of our cancer services to other hospitals within our system.

I'll also mention that a week ago, last Friday, we initiated a weekly statewide cancer teleconference across all the programs, or at least as many of the programs as we can get to participate—and it's almost 100% of the cancer programs across the state.

So, all the major health systems and their cancer programs, leadership and key players at their cancer programs get on a teleconference every Friday morning—today was our second one. We started last week.

We're sharing what experiences we are having, where we have common problems that we're facing, how we might all work together to try to come up with solutions to those problems, how we are looking at the surges we're seeing and how we can maintain cancer care.

We are trying to work together as a state, to make sure that we can continue caring for cancer patients, acute and otherwise, for as long as we possibly can, and, hopefully, continue to maintain cancer care throughout the pandemic.

Are you having any shortages of equipment so far?

SL: I think everyone is struggling with things like PPE (personal protective equipment), especially N95 masks, surgical masks.

I can't speak for the other systems across New Jersey, but I can say from our system's perspective, we have supplies. We're constantly keeping track of inventory, on a day-to-day basis, and leveling it up, both to the leadership at Rutgers and the leadership at the health system, to make sure that they're acquiring supplies as we need them, whether it's from the state or from vendors.

So, I think we're, right now at least, keeping ahead of the need for supplies. Ventilators right now, I think, we're keeping up, but, again, we're not at the peak yet, and how that plays itself out over the next couple of weeks, we'll see.

I know, the governor and his team are working hard to make sure that all the hospitals in the state have the equipment they need, but we're going to have to see how this plays out. Certainly, if we get the kind of numbers they're seeing in New York, it's going to stretch all of our systems very thin.

What about the underserved versus the wealthy? Are you seeing anything on that, or are you even looking yet? It's probably very early to look.

SL: We are, as a system, always need-blind and seek to serve our entire community. And we certainly don't turn folks away, and never have, coming to our ERs and coming to seek care from us. In terms of disproportionate numbers of infected or severity of disease, I don't think anyone has had time yet to take a deep breath and look at that.

I think we're seeing infections across all socioeconomic layers and all ethnic groups, etc.

This is, so far, an equal opportunity pandemic, in terms of the folks that are getting affected. So, right now, I wouldn't have any specifics in terms of demographics, but we're seeing patients from all over our system and all walks of life—all socioeconomic strata, in terms of those affected.

How are your cancer patients doing?

SL: We, fortunately, have not yet seen a lot of our cancer patients under care get infected or succumb to COVID-19. That is one of our principal concerns: staying ahead of that. I'm alluding mainly to our patients under active care.

I'm sure that if we went back in the histories of the patients that have been treated so far across the system and some of those that have succumbed to the disease, there may be cancer history in their background, because of how common cancer is.

But right now, our patients under acute cancer care, while we've had some patients infected, we have been keeping ahead of that, in terms of not having a lot of patients suffer mortality, in terms of our acute cancer patients.

Hopefully, that's not just a matter of time and numbers, that we can aggressively stay ahead, with the various practices we've put in place to try to mitigate spread of SARS-CoV-2 in cancer centers.

We are practicing social distancing. We are implementing telemedicine to try to minimize patients coming in for follow-up visits, routine visits. We are going to be launching this week using telemedicine for new patient visits. Again, we are trying to minimize the number of patients that have to be together.

And then, obviously, our patients getting radiation therapy or infusion therapy, we are trying our best to expand space, to increase distance between patients. We've implemented some policies minimizing or severely limiting folks that can accompany our patients, again to maintain social distancing, and then, making sure our providers and our staff are appropriately gowned and masked, eye protection, patients wearing masks, again, trying to minimize the risk of spread.

We've been talking to a physician in Milan, and their approach was to set up a COVID-free hospital, as best they can, for cancer patients. Is that doable? Is that the way other people should do it? Have you looked at them at all?

SL: You know, we talked a little bit about that on our statewide call, and I think it will be challenging to do that; maybe not impossible, but certainly challenging.

I think we're certainly going to try to—just because it will make it easier to treat COVID patients and to have teams focused on their critical care needs—I think we're going to try to coordinate certain hospitals across the state that will focus on COVID response.

And there's also plans in New Jersey, like there are in other states, to set up "field hospitals", or expanded locations for COVID patients. I think that will allow us to identify certain hospitals, where we can concentrate the non-COVID patients, and certainly cancer patients.

I don't know that we'll be able to totally segregate COVID patients, or create a single hospital that is only for cancer patients. As you probably know, we have plans in place now at Rutgers and RWJBarnabas Health to build a free-standing cancer hospital in New Jersey, but, obviously, that's three years away.

By then, hopefully, this is just a bad memory, in terms of what we've gone through here. But right now, there are no active plans to designate one or two hospitals purely for cancer care. But that may be something we have to think about. I'm aware of the data from Italy and from Spain, in terms of the mortality rate in lymphoma patients and in lung cancer patients, and that's why we're trying our best to keep our teams separate.

Right now, at least in New Brunswick, oncologists are not on the COVID acute care teams, even though there's a surge plan that's been put in place for docs that don't normally do critical care and infectious disease work to be able to surge to help with COVID care.

Our oncology doctors may ultimately have to participate in that, but right now, our whole mindset is to try to keep them separate and caring for the cancer

patients. At least for now, so we're not putting the cancer patients at risk.

Any other best practices you'd want to propose or any that you've benefited from?

SL: Well, most of them are the common-sense ones. We call all our patients that have appointments with us, whether it's radiation oncology or an infusion therapy, we call them the night before their visit—every patient—and we go through a questionnaire about any symptoms they may have, have them take their own temperature to note any fever.

We screen every patient at the door, before they come into the cancer center, with a history and another temperature check. We do the same with our providers that have clinical activity.

Every morning, everyone gets screened. Everybody—both provider and patient—are all masked, to try to decrease the risk of spread for anyone who's asymptomatic and might be a carrier.

We actually have a pretty interesting study ongoing through our CTSA [Clinical and Translational Science Award], led by Reynold A. Panettieri [vice chancellor for translational medicine, science director, Rutgers Institute for Translational Medicine, science professor of medicine, Rutgers Robert Wood Johnson Medical School, emeritus professor of medicine, University of Pennsylvania], Jeffrey Carson [provost, New Brunswick at Rutgers Biomedical and Health Sciences, the Distinguished Professor of Medicine and Richard C. Reynolds, M.D. Chair in General Internal Medicine] and Martin J. Blaser [director of Center for Advanced Biotechnology and Medicine, the Henry Rutgers Chair of the Human Microbiome, and professor at the Departments of Medicine and Microbiology, Rutgers Robert Wood Johnson Medical School] that is studying health care providers, or health care workers.

The study is looking at asymptomatic health care workers without necessarily a known exposure and testing all of them for SARS-CoV-2, and the idea is to enroll 700 providers or health care workers. So far, I think in the first week that trial has been open, they've enrolled 500 already, and the goal is to try to determine what the prevalence of SARS-CoV-2 infection is in an asymptomatic cohort of health care workers. Just so we can get a sense of how pervasive asymptomatic infection is.

I think that'll be a really important study in terms of understanding, risk mitigation and how well we are doing and what we might do better. That study dovetails into two other studies, one of which we launched this week. The other is going to launch in a week or so.

This week, we launched a therapeutic trial that's not just for cancer patients. It's for all patients that have SARS-CoV-2 and COVID-19. It's being run by Rutgers Cancer Institute. I am the study chair. [The study will randomize patients into three groups: 1) azithromycin and hydroxychloroquine; 2) hydroxychloroquine alone; or 3) supportive care for six days followed by hydroxychloroquine. Treatment will continue for 10 days. Once treatment is completed, participants will be followed monthly for six months to monitor for return of symptoms.]

I wrote the trial with collaborators, and a critical care doctor, Sabiha Hussain, is the PI, and we're essentially looking at hydroxychloroquine sulfate plus azithromycin versus hydroxychloroquine sulfate versus a supportive care arm, with the endpoint of the study being viral load at day six, compared to baseline, essentially trying to mirror the study that was done in France that seemed to indicate that there was some antiviral activity with the combination of azithromycin and hydroxychloroquine.

The trial will enroll 160 patients, and I think it's real important that in a prospective randomized way we understand if those agents are actually effective at reducing viral load, and if so, then make some solid recommendations on how to use them and when to use them. It's my own suspicion that the antiviral agents will best be applied early in the course of the disease, not when patients have had progressive pulmonary disease, ARDS, requiring ventilation.

At that point, we're probably dealing more with the consequences of the immune response and cytokine release and less so with viral load. But, certainly, early on in the disease, I think antivirals can play an important role. Agents like hydroxychloroquine, maybe with azithromycin, agents like remdesivir, and, obviously, there are many trials ongoing [*The Cancer Letter*, March 24, 2020].

I should mention that in the therapeutic trial that I just talked about, we're accruing now and went from concept to an IRB-approved protocol in nine days. The IRB and the FDA were just superb in working with us to try to get this done in a safe way, in a rapid way, so we could start answering that important question very quickly.

How and why did you choose these two drugs, as opposed to some other drugs? Is the French study intriguing enough? I am not trying to drag you into politics. We can just stay on science.

SL: The French study, while small, looked promising. Both agents are readily available, FDA-approved, and, for the most

part, well tolerated. If a larger study can support the results seen in the French study, these agents can be quickly deployed as a component of the approach to treating COVID-19. If the larger study does not show activity, we can move on from these agents and focus on others.

How quickly do you think you can get the answer?

SL: So, we have to accrue 160 patients—it's my goal to accrue all 160 in about 30 days. As I said, we started the trial this week, and our goal is to have patients completely enrolled, if we can, by the end of April. And then, since our endpoint is viral load on day six, compared to baseline, we hope to have all the data generated within the couple of weeks after the trial is completed.

If I can get an answer to this question by mid-May, I think it would be very helpful. And so, that's what we're shooting for. Obviously, you can't control a lot of things, like accrual and samples, etc. We have a really good team in place, a very good infrastructure. And so, that's my goal, hopefully, to have an answer within the next six or eight weeks.

You can probably shorten that by a few weeks, because it's not a rare disease you are treating.

SL: That's right. In fact, we have a stopping rule. After we've accrued 50%, we're going to look at the results—after 80 patients have been enrolled—and so, there's the possibility that we'll see such an extreme response that we might be able to make some decisions based on efficacy. Or if we see no difference between the arms—between the arms and our supportive care arm, we may be able to declare futility.

I think either answer is going to be important to know. If these agents are effective, we need to know that, because we need to use them, maybe earlier and more broadly. If they're not effective, we should also know that, because we shouldn't be spending time administering these drugs if they don't work.

***The Cancer Letter* would be the place to cover it—because we would get the answer right away to everybody.**

SL: When we know what's coming out, I'll reach out to you and let you know. We'll obviously prepare it as a manuscript, but it's so important we're not going to wait until it gets published to get the information out there, because it's going to impact and affect decision making. Well, I'd be happy to let you know as soon as we know.

We'll get it out within hours of you letting us know to everybody in the field.

SL: That would be great.

I'm wondering why you didn't choose to work with more sites or more institutions in accruing patients.

SL: We may very well do that. We've opened it at two sites within our system. We opened it at University Hospital in Newark and at Robert Wood Johnson University Hospital in New Brunswick.

We may yet open it at other sites across our system, and I've had conversations on our statewide call about opening it at other hospitals across the state. It is not an easy trial to do logistically, because these are highly infectious patients, and they're patients with symptoms, when we get these samples—and we get samples at baseline, day three and day six—our team has to be entirely in PPE. They have to take oral pharyngeal swabs, they take blood.

So, logistically there're some hurdles that you have to put in place to be able to do it. But I think if we have any trouble at all accruing at the pace we'd like to accrue, I will quickly reach out to open it at other sites.

You're an immunologist; what's your next trial? Because the next rabbit out of the hat is going to be immunology; no?

SL: I can't really honestly with a straight face carry the moniker of immunologist. While I have a strong interest in cancer immunology, and I am a basic scientist in addition to being a clinician, there are far more qualified immunologists that are actually trained, and have a much stronger background than I.

But I will say that I think this is obviously a problem of immunology and a problem of microenvironment and response to a pathogen. And so, it's been very interesting to me, in terms of the new collaborations I've been able to start at Rutgers, as we've all tried to rally together to face this pandemic.

I think that there are opportunities to understand better ways of vaccinating patients, and we have a collabora-

tive project that we just launched this week—looking at novel approaches to vaccinate patients. We're looking at how serology either indicates which patients will be at risk once they've had this disease to be re-infected, or which folks might already carry some immunity against this pathogen.

As you know, there've been some publications around, perhaps BCG immunization might confer some protection against this, and so collaborating with an investigator Maria Gennaro, [professor of medicine] who has a particular interest in this at Rutgers, these are going to be some of the questions we're going to look at moving forward. The idea of treating patients who are virus-positive but asymptomatic, prophylaxing patients against progressing into COVID-19 is something we're looking at.

Jeff Carson, one of my colleagues, is writing a protocol looking at hydroxychloroquine and azithromycin in the asymptomatic population as a means of potentially preventing COVID-19 disease.

Paul, I would have never predicted six months ago, as a cancer center director and a surgical oncologist, that I would ever write a trial looking at agents against an infectious disease. But we're in very strange times right now. But I have to say, everybody is standing up together to try to face this issue.

I emailed Ned Sharpless, the NCI director, on a Saturday two weeks ago to tell him about the trial we were writing, and asked for some guidance and support from NCI. And within literally 12 hours, he and Henry Ciolino [director of the NCI Office of Cancer Centers] put out a supplement RFA to all 71 cancer centers, essentially asking the cancer centers to submit ideas for going after SARS-CoV-2 or COVID-19 either directly related to cancer issues with it, or even not just cancer, but finding new therapies. And so, that was amazing.

The FDA and the NCI are working together to try to test new antibody assays, and we're going to be through an [Material Transfer Agreement] providing them with positive sera and negative sera to use as controls in that. So, the number of groups that are standing up and standing together to face this worldwide pandemic is amazing.

And it really is a testament to the power we have when we all try to work together to face an unprecedented challenge, and this certainly is an unprecedented challenge.

Let's talk about the cancer centers for just a moment, about the role they can play in this, because there's really nothing like this infrastructure anywhere else in medicine—the infrastructure for asking questions, setting up experiments, and getting the answers fast.

SL: You are absolutely right. That is spot-on, and I think the reason why I got involved with this four weeks ago, was essentially that recognition at Rutgers, and this is true at every cancer center, every NCI-designated cancer center across the country.

We are structured to do exactly what is needed right now: to quickly and efficiently deploy clinical trials in a very structured way, with an infrastructure that allows us to carefully monitor them, to collect data in a very organized, efficient and regulated way, to be able to support the infrastructure required to put together a trial, and then safely conduct it.

Whether it's clinical research assistants, or research nurses, or data managers, or our regulatory affairs folks, each of the NCI-designated cancer centers has been built to do the kind of fast, efficient and effective clinical research that's necessary to answer questions.

And right now, there are some critically important questions that are not necessarily related to cancer, but we serve as a resource to our communities, to our states and to the federal government, since we are NCI-sponsored and designated to pull together in an emergency like this and leverage our expertise to help in any way we can.

And it's not only on the clinical research side, but on the basic science side. As cancer immunology has become a major area of exploration at many cancer centers, you're right, we have some very strong immunology activity going on in our research labs, and to focus some of those assets that we have to particularly look at this question and this problem, and how we might tackle it, is something else that we can bring to the table.

So, we, and I think cancer centers across the country, are rallying to the cause. I think that many of them are stepping up and leveraging their infrastructure and their resources to help.

I guess one thing that I've noticed as an instant historian—because that's what journalists are—is that virology, immunology, rheumatology and oncology are stomping around on the same street corner. COVID-19 showed that more than anything ever could. Am I seeing something that's real?

SL: I think you are.

I think we in the cancer community have been gravitating closer and closer to folks that have for a long time been mavens of virology and immunology. We've been looking at it, not just virology as potentially causative agents of cancer, HPV is a great example, but also as vectors. How do we leverage vectors to immunize against cancer?

And it's not such a leap to apply some of the same principles to immunizing against pathogens. Although there are amazing experts that have dedicated their entire careers to immunizing against infectious disease, I think there's also things that have been learned in the cancer community that might help with that.

And I think HPV is a perfect example.

Here we have a virus that we know is a pathogen that leads to neoplasia and malignancy, and a lot of expertise has grown out of that, including the virology unit, an immunology unit at NCI Frederick. And now, that group is focusing on helping with the COVID-19, SARS-CoV-2 pandemic.

I think you're right that we have gravitated to certain overlaps with immunologists, infectious disease docs. The microbiome is a great example. We've started to really embrace studies in the microbiomes in understanding cancer risk and response to cancer therapy.

And, obviously, the microbiome plays a huge role in susceptibility to infection and response to infection. And so, Marty Blaser, who's a world-renowned expert in the microbiome, who's now at Rutgers, and I had begun some collaborations around the microbiome and cancer, and now we are talking to each other almost every day about how we're deploying efforts for SARS-CoV-2 and COVID-19.

So, I think you're right. I think these groups that began to interact, as you said, on the same corner, are now really seeing what each has to offer in the current emergency.

Is there anything we forgot, anything we need to focus on?

SL: No, only that I think now, more than ever, is a time for collaboration and working together. I think the only way we are going to defeat this current pandemic and be ready for future ones is to really look at ways that we can work across disciplines, work across specialties, work across state lines, and across institutions, and really see the strengths we have when we work together and collaborate.

This is truly a nightmare, and truly something that is beyond words to describe. I could never have imagined in my lifetime seeing something like this, but I am optimistic that working together, we are going to get through this, and if we do it right, we'll be that much stronger when we do.

Good luck and stay safe.

SL: Thank you, Paul. I appreciate it, and, as always, thank you for telling our story.

> “I would have never predicted six months ago, as a cancer center director and a surgical oncologist, that I would ever write a trial looking at agents against an infectious disease.”

Q & A

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

CONVERSATION WITH THE CANCER LETTER

COVID-19 lesson from Spain: Like the U.S., we failed to take this seriously before it came to us—we have to learn

Josep Tabernero, MD, PhD
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"We need to work a little bit harder in making health systems more efficient. Public health leaders and public health policymakers should think about how emergencies and diseases like these should be tackled in the future. We have to learn. There is no doubt about this."

While the world watched the pandemic unfold in China and Italy, SARS-Cov-2 spread exponentially in Spain, killing more people faster and earlier within a month, relative to many outbreaks in other Western countries.

Spain quickly surpassed Italy in the number of confirmed cases, even though the coronavirus began spreading rapidly in Italy a week or two earlier than in Spain. Both countries reached the "peak" almost simultaneously, as the epidemiological curves of total detected infections reach a plateau following nationwide lockdown and containment measures.

By April 10, over 157,000 cases had been confirmed in Spain, with nearly 16,000 deaths. Italy has logged nearly 144,000 detected cases, with over 18,000 deaths.

On April 10, with over 470,000 confirmed cases at this writing, the death toll in the United States, at nearly 18,000, has exceeded that of Spain—a number that is expected to continue rising.

"One of the things that we have failed, globally—and probably the United States as well—is to take this problem seriously before it came to our environment," said Josep Tabernero, director of the Vall d'Hebron Institute of Oncology (VHIO), head of the Medical Oncology Department of Vall d'Hebron University Hospital, and director of clinical research at VHIO.

"It's important to learn about and from others," Tabernero said to *The Cancer Letter*. "If you look at how the authorities dealt with it in South Korea, actually, they didn't confine the whole population—except for those that were positive—but they had available SARS-CoV-2 tests for the global population.

"This was not the case in Spain. At the end, the Spanish authorities decided to shut down, to lock down the country with most of the citizens confined."

The Vall d'Hebron University Hospital, located at the far northwestern edge of Barcelona, is the largest hospital complex in Catalonia, which, with a population of over 7.5 million, is the second most populous autonomous community in Spain.

"Right now, we have a total of 176 patients hospitalized in the intensive care unit; around 675 patients in total, not only those in the intensive care unit, but also in the conventional wards," Tabernero said. "We used to have, before the COVID-19 outbreak, 130 beds in the intensive care units, and this figure has been expanded through different facilities and resources up to 320—just in case more cases were coming and they needed intensive care unit support."

The VHIO has established separate clinics and care teams for patients with cancer to lower their risk of being exposed to the coronavirus.

"I think that it's important in cancer care to establish independent paths for our patients, just to prevent them from getting infected," Tabernero said. "Obviously, this is not something that we did early on, from the beginning, but learning about what our colleagues did in Italy and China was really very helpful."

Following discussions with cancer experts with experience in Wuhan, China, VHIO has also postponed surgical procedures for patients who were scheduled for elective surgery, while including neoadjuvant therapy for some patients.

"Especially for cancer care, one of the things that was raised as a risk for infection and for patients with cancer, and also for severe evolution of the disease, was, for example, to have elective surgery for patients with cancer," Tabernero said. "We have implemented in some diseases more new neoadjuvant treatments than we used to have.

"This is something that health authorities may consider in promoting policies like this."

As drastic containment measures were being implemented in Spain, government health officials moved quickly to expedite research and clinical trials on COVID-19.

"Our oncologists, especially medical oncologists, are used to do clinical trials for many new therapeutic options," Tabernero said. "So, we are used to rapidly designing and activating clinical trials.

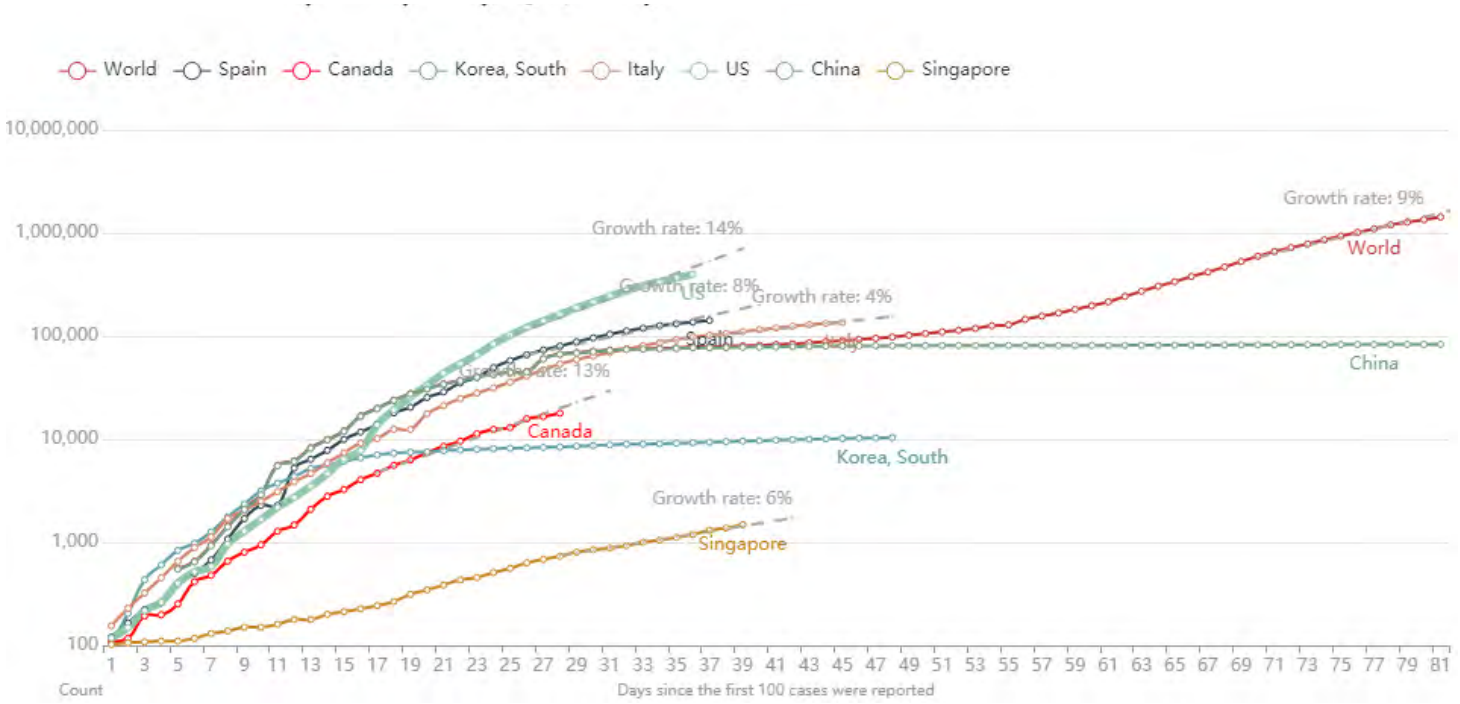
"Here in Spain, actually, now that our regulatory process has been sped up for clinical trials related to COVID-19, I can tell you the approval time—the time between the clinical trial protocol is submitted and the enrollment of the first patient—can be assured in three working days. You wouldn't have ever imagined a situation like this."

Tabernero said Spain's universal health care infrastructure ensures that all hospitals and community clinics can interface with each other, including through an established national telehealth program.

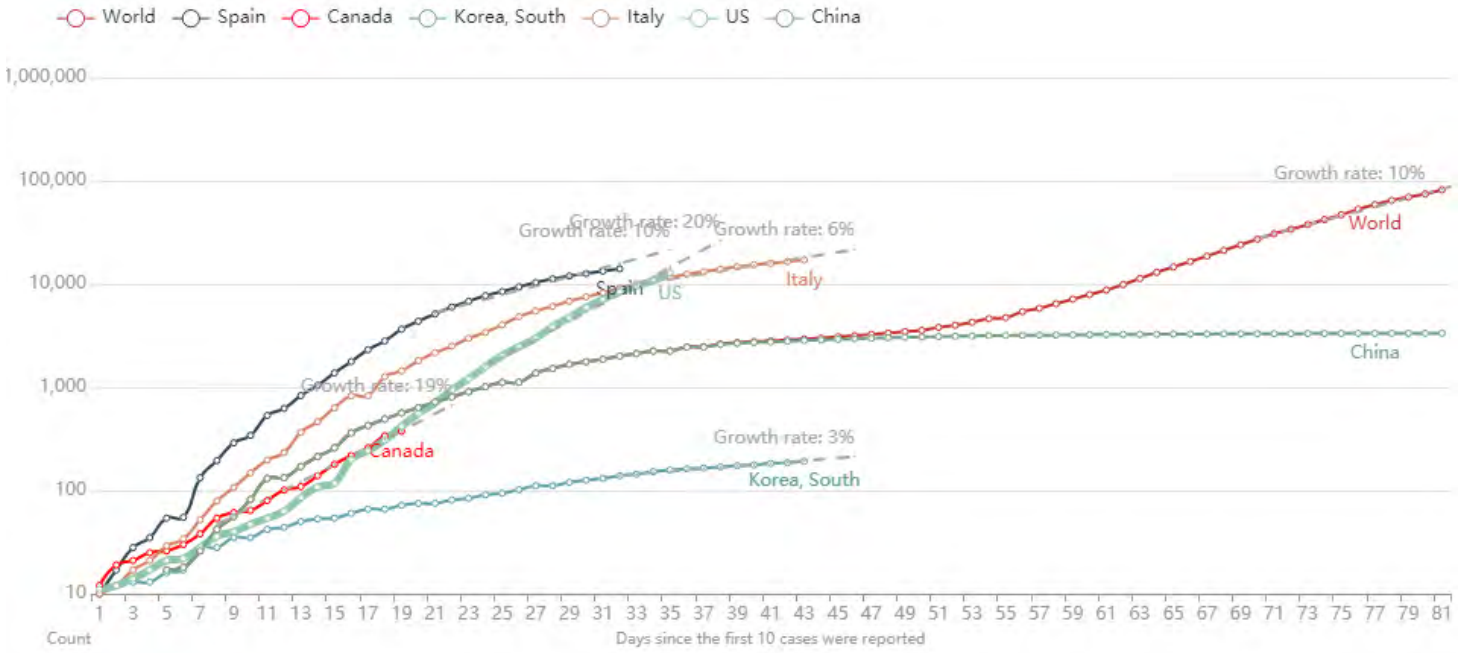
"Fortunately, on our side, the network was very well established before the pandemic, but this is not usually the case in all the countries," Tabernero said. "So, each region [in Spain] is trying to do its best to organize this thing in the best manner.

"This is one of the advantages. We don't have one single public health system, but the systems are very similar, and they are all connected. They can interface with all the electronic medical records. So, it's easy to work with the primary physicians, and also with small community hospitals."

CORONAVIRUS CONFIRMED CASE TRAJECTORIES BY COUNTRY/REGION/TERRITORY



CORONAVIRUS DEATH CASE TRAJECTORIES BY COUNTRY/REGION/TERRITORY



Source: 1Point3Acres, April 8, 2020

With national coverage, the central and regional governments in Spain have been able to reliably track patients.

"We can follow up our patients, we can track them, if they are temporarily visited in other community hospitals or outpatient clinics by GPs," Tabernero said. "The bottom-line message here is that there is good coverage for the whole population. Public health leaders and public health policymakers should think about how emergencies and diseases like these should be tackled in the future. We have to learn. There is no doubt about this.

"The take-home message is that we have to work more in promoting better health care systems and adequate public health policies, because in the end—especially your country, but also other countries—we're all investing a huge proportion of the GDP in health care.

"And then, you realize that it does not work as you would like. We need to work a little bit harder in making health systems more efficient."

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

Matthew Ong: How are you doing, and what's the situation like in Barcelona at the moment?

Josep Tabernero: Well, actually, the situation is improving a little bit. We have probably reached the top of the peak in a way that the number of patients—that we diagnose and that come to our institution, in the emergency area and are hospitalized—it's reducing over the last five days.

The number of patients in the intensive care unit has been stable in the last seven days. We have a total of 176 patients in the intensive care units. Actually, one thing that I have to say is that the units were increased in number. So, Vall d'Hebron University Hospital, it's a general hospital.

We used to have, before the COVID-19 outbreak, 130 beds in the intensive care units, and this figure has been expanded through different facilities and resources up to 320—just in case more cases were coming and they needed intensive care unit support. Right now, we have a total of 176 patients hospitalized in the intensive care unit; around 675 patients in total, not only those in the intensive care unit, but also in the conventional wards.

And this is in your hospital alone?

JT: Yes, this is in our hospital alone. We have a total of 1,200 beds in the hospital with a comprehensive cancer area, but the hospital is a general hospital, and now a huge number of conventional and intensive care unit beds are dedicated to COVID-19 affected patients.

Is the observed flattening of the curve consistent with the models as well?

JT: I think that it is consistent with the model. In Barcelona, we have been confined at home for more than three weeks. In the rest of Spain, it's been two weeks since the central government ordered people to be confined at home. But in the Catalonia region, actually, it's three weeks, so we are starting to see the results of that decision.

Right now, the question is how we are going to be starting to allow people from the lockdown to start doing activities, and this has to be gradually, of course. The question is how you're going to be selecting the population, whether it's going to be done by age, of course, but also whether we will have good technologies to test by PCR, which percentage of the population has been infected symptomatically or asymptomatically, and also to know whether they have developed a good immune response by IgM levels and IgG levels.

So, there's discussion on that, because now, in two weeks, the lockdown will be stopped—I assume this is going to be the case—but gradually. It will not be the whole population, at once, but the numbers that you were referring to are consistent with the models.

The only problem is that, looking at several web pages, including, for example, the web page from John Hopkins, the Coronavirus Resource Center, actually, from the data continuously updated, it's difficult to understand the way that different countries count the patients affected by the disease, recovered, or deceased. If you look at the numbers, it's very clear that, right now, Spain is the second country, just after the United States, in the total number of patients that have been confirmed, something around 157,000.

But then, when you look at the number of deaths, actually, Italy, because they started a little bit earlier, they have more deaths. We are at the level of 16,000. But also, interestingly, in our country we have more patients that have recovered from the disease. The total number of patients recovered from the disease is around 55,000.

So, sometimes it's difficult to understand the numbers, as infected patients have been counted in different ways. But if you look at the evolution over the last few days, I think that we start to see the light of having achieved the plateau; so, the number of patients that come to

the emergency area has been reduced in the last five to seven days.

So, as Spain is thinking about reopening the economy, what are some strategies that are being considered? How does one warm up to regular business while preventing new spikes in infections, and a resurgence of the pandemic?

JT: Yes, this is the discussion that we are having right now. Basically, different opening models are being evaluated. None has been taken as the right one, but, as mentioned, there are lots of discussions about whether we'd be able to screen the population, especially the young population, for those markers that I mentioned.

One message is that it seems that the oldest population will still be confined for more time, because this is the population that, in principle, is at greater risk for developing severe complications.

So, at least in the U.S., it seems our lay news cycle has been focused on China, Italy, and then, of course, the exponential increase in cases here. And before we knew it, Spain appeared to suddenly climb up the charts in total cases and deaths. What happened?

JT: I think that what happened is that the pandemic evolved very rapidly. When we look at the epidemiology of the disease, it seems that the first cases actually came from Germany and later on from Italy, of people that had been in contact with the Chinese population. But then, it expanded very rapidly. It seems that it's important to enact measures as soon as possible. Different countries have evaluated these kinds of measures.

For example, if you look at how the authorities dealt with it in South Korea, actually, they didn't confine the whole population—except for those that were positive—but they had available SARS-CoV-2 tests for the global population.

This was not the case in Spain. At the end, the Spanish authorities decided to shut down, to lock down the country with most of the citizens confined, except those that were indispensable, like, obviously, all the health workers, but also all the food distribution workers, among others.

I don't know whether it depends also on the behavior of the population, but at least what the authorities did three weeks ago now, it shows that we are starting seeing the result for that. Probably we should have confined the population earlier. But now, it's easy to look back and say that.

What are your data on fatality rates telling you? What are the overall case fatality rates for Spain? Also, what proportion of these deaths are patients with cancer?

JT: The fatality, actually, if you look at the numbers, it's around 10%. It depends a little bit on the regions, but I don't think that these numbers are correct—the denominator is wrong, because we have not diagnosed all patients that have been infected.

We only diagnose those that actually come to the hospitals or to the primary care physicians, but there are some patients with middle symptoms that have not gone to see a doctor, either in the hospital or in the primary care service. So, I don't think that the denominator is real.

We can probably assume the same, over here.

JT: Yes, probably it's the same there. Actually, if you look at South Korea, it's the opposite. I think that the denominator in South Korea is really good. But then, if you go to different regions, the fatality rate is a little bit different. But again, I don't think that these numbers are correct. It's very difficult to prove the numbers, right?

I'd think so. In Italy, a sample of over 900 patients that are well characterized show that 16.5% of the deceased are patients with cancer.

JT: They have more mature data, because they started doing this one week and a half or two weeks before. Our perception, at least in the distribution of patients from our hospital, seems to be very similar.

Nevertheless, in our institution, as in other cancer institutions, we have different paths for the patients. Those patients that are visited for examinations in first visits, sequential visits, in our institution follow a different path.

We have adopted important measures, just to prevent the dissemination of the disease. And so, for example, as mentioned, we were clinically screening those patients when they came to the

facilities—before they enter the offices of the physicians and the nurses.

They were asked for all the symptoms, and also, their temperature was evaluated. If cancer patients did not wear a mask, we offered masks to them. I think that this would help to separate those patients that had symptoms and then had a better diagnosis for them, preventing the others from being infected.

I think that it's important in cancer care to establish independent paths for our patients just to prevent them from getting infected. Obviously, this is not something that we did early on, from the beginning, but learning about what our colleagues did in Italy and China was really very helpful.

So, keeping clinics and facilities for cancer patients separate from regular patients is best practice?

JT: Yes. And also, when we see patients that come to the emergency area, cancer patients, they are immediately separated—whether they have respiratory symptoms or symptoms that are similar to COVID-19 disease—from the others that do not have related symptoms. And the teams are different. This is another important thing, just to divide the professional teams as soon as possible.

The process here is to establish preventive measures, especially for the population of patients with cancer. As you know, a huge population of cancer patients have immuno-depression because of the disease, because of the treatments that they receive, so, this is a population at risk. So, it's one of the populations that we should take care of more precisely, with separated paths to evaluate them.

Also, what we have done, as many other centers, of course, is to increase our telemedicine practice, so with more virtual visits, especially for the controls or workups for patients that were in follow-up. We try to do this as much as possible.

We're also in collaboration with primary care physicians, and also small hospitals from the community. So, we try to prevent as much as possible that those patients that do not necessarily need to come to the hospital actually don't come to the hospital.

Of course, this needs good infrastructure and also to establish a good network. Fortunately, on our side, the network was very well established before the pandemic, but this is not usually the case in all the countries.

So, each region is trying to do its best to organize this thing in the best manner—because one of the messages that we are raising is that other peaks may come, and, unfortunately, the COVID-19 outbreak does not seem to be one single peak.

So, we have to be prepared for multiple peaks, or, at least, moderate outbreaks. We don't know whether they are going to be peaks or not. If there are not going to be peaks, the disease is still going to be there, so we have to try to invest our resources in organizing as much digital medicine and telemedicine as possible.

With universal health care in Spain, do you find conducting telehealth across the country to be easier? Is it more convenient to move and refer patients, and make their records easily transferable?

JT: Yes, I think so. This is one of the advantages. We don't have one single public health system, but the systems are very similar, and they are all connected. They can interface with all the electronic medical records.

So, it's easy to work with the primary physicians, and also with small community hospitals. We can follow up with our patients, we can track them, if they are temporarily visited in other community hospitals or outpatient clinics by GPs.

I have to say, also, that the whole health care professionals community has been very, very sensitive, and I'm really very thankful to all of them, because everyone has put their best to try to help our patients by different means. So, this is really very important. This is something remarkable and very reinforcing for all of us.

As you know, we don't really have an interoperable telehealth infrastructure here—and many health systems, not to mention community hospitals, may not have a robust program to begin with. Reimbursement is not assured, states have individual licensing requirements for physicians, and most EMRs don't interface, because they tend to be proprietary.

JT: Yes. We all have to learn about what has happened. Actually, one of the many things that we can learn, the take-home message is that we have to work more in promoting better health care systems and adequate public health policies, because in the end—especially your country, but also other countries—

we're all investing a huge proportion of the GDP in health care.

And then, you realize that it does not work as you would like. We need to work a little bit harder in making health systems more efficient.

So, early U.S. data seems to suggest that we're seeing high rates of severe complications, hospitalizations, and deaths across many age groups, not just in the elderly—a hospitalization profile that appears to differ somewhat from data in Italy and China, if I'm not mistaken. What can you infer from the unique characteristics of Spain's population and how they may inform outcomes? For instance, the median age in Italy is higher, which translates into a greater number of deaths in the elderly.

JT: Yes, actually, our population is quite aged. It's very similar to Lombardia's population. Again, if you look at the numbers, it's very clear that the population that has more comorbidities, concomitant conditions, you see more severe cases and higher fatality rate. Nevertheless, we have patients—and naturally, health care professionals, without any considerable risk at the beginning—that unfortunately have died from the disease.

But if you look at the fatality rates, there is a clear trend, proportionally increasing with conditions like age and some comorbidities, like previous medical history of hypertension and other chronic diseases, and of course, in patients with cancer, it's also the same. But one of the important points here, again, is to try to recognize those patients that have mild to severe COVID-19 disease and to provide them with the most rapid medical intervention or treatment.

If all patients come to the hospitals, then everything is more difficult. As you know, this is not only related to the infection. The infection, per se, is not the critical thing. The most critical fact appears to be the rapid onset of severe inflammation that, in some particular patients, appears in the lungs, probably related to the overactivity of the macrophages in combating the SARS-CoV-2 infection.

At this time, there are some treatment options that, when they are administered on time, they help to mitigate the severity of the respiratory insufficiency, the respiratory impairment. And then, you'll have more opportunities for these patients to survive and to recover well. That's why it's important to screen and capture those patients that are at major risk to develop this severe inflammation of the lungs, and therefore at risk of respiratory insufficiency.

Speaking of which, what are some notable scientific efforts in Spain, both locally or as part of international collaborations? Here, I see intense focus on antiretrovirals and antiviral drugs, IL-6 inhibitors and other immunosuppresants, perhaps more research now looking at the impact of ACE inhibitors and ARBs on fatality, etc.

JT: Yes. On top of the antiviral treatment options, as you mentioned, there's a huge international collaboration of promoting clinical trials on this.

What is really new is the approach of treating inflammation, as you mentioned, with new therapeutics directed to IL-6 or the IL-6 receptor, and even to other macrophage receptors that are critical for the macrophage function, among others.

This needs to be the cutting-edge research that we, and other centers of course, are implementing. Because, again, the infection, per se, it's important, but the most important thing is the secondary inflammatory reaction that the host has against the viral infection.

We've been covering this pandemic a lot, and the consensus seems to be that oncology, as a specialty, with its advanced clinical trials ecosystem and focus on immunology, is already set up to study this efficiently. I've also been told that cancers are way more complex than viruses, so the research should move quickly. What do you think?

JT: There are several things to mention about that. First of all, our oncologists, especially medical oncologists, are used to do clinical trials for many new therapeutic options. So, we are used to rapidly designing and activating clinical trials.

Here in Spain, actually, now that our regulatory process has been sped up for clinical trials related to COVID-19, I can tell you the approval time—the time between the clinical trial protocol is submitted and the enrollment of the first patient—can be assured in three working days. You wouldn't have ever imagined a situation like this.

This includes everything—IRB approval, the National Health Authority's approv-

al, and the completion of the contract, at least the preliminary contract. This is good for the patients, and it shows you how sensitive all the stakeholders are around this.

Also, as you mentioned, our population is a population that is at risk of having severe symptoms of infection from COVID-19, because of the immunosuppression related to the disease and related to the therapeutic options we have missed.

So, this is a population where you can easily see results, if they are positive, in international trials aimed to, number one, prevent the worsening of the COVID-19 disease; number two, to ameliorate the symptoms and the respiratory function impairment, and number three, the use of immunotherapy and other related agents in patients with cancer and COVID-19.

Certainly, we have invested in how important it is to mitigate this immune response that these patients have, especially as it relates to the macrophage functions. We have very rapidly and easily adapted some of the therapeutic strategies in these clinical trials.

You've watched the pandemic unfold in different countries and in their respective health systems. What can you say about how the universal health care system in Spain coped with this pandemic—in terms of the development of testing capabilities, dissemination of public health messaging, contingency plans and clinical guidelines, as well as the ability to provide standard, accessible care?

JT: This is an important factor, at least in our environment. Almost all patients are covered, by definition, by the public health system, but there are some patients that also have private insurance—around 25% of the population—that they use more or less, depending on the medical needs that you have.

For example, the uptake of private insurances for obstetrics is much higher than the uptake for severe diseases like the COVID-19 infection or myocardial infarction, or diseases like that

But the bottom-line message here is that there is good coverage for the whole population. But the second important thing is that it's not specifically related to the coverage, but to how comprehensive and how well public health policies are implemented in the different countries or regions. The regions where they have good public health policies, actually, have been more rapid in implementing the right measures for combating the disease.

So, this is also something important that we have to learn for the future. Public health leaders and public health policymakers should think about how emergencies and diseases like these should be tackled in the future. We have to learn. There is no doubt about this.

What are your impressions of how the U.S. has handled this pandemic, especially at the national level? Also, what have you learned that you think, perhaps, we should be paying attention to as well?

JT: First of all, the United States is a very big country with completely different states in the way that the people behave, and also with the health systems in place. One of the messages that we have learned from what has happened in Spain and Italy is that you cannot make global decisions and actions, because there are some communities where there is not so much population concentration, and therefore, cases of COVID-19.

For example, in New York City, the population is very much concentrated, but this is not the case in Arkansas or in other places, so you cannot make global decisions for the whole community, especially in big countries.

The principle should be similar in a way that you have to protect the population. The actions that you take may be different, according to the real facts of each state or region population and the COVID-19 spread. This is something that we have to take into consideration.

Of course, there is also a balance of how these decisions may affect the economy, right? This is an important discussion that we also have in our country, but obviously, there should be a balance on that. So, some measures that have to be taken in regions or cities where the population is highly concentrated do not necessarily have to be the same ones that you have to take in other regions.

That being said, I think that one of the things that we have failed globally—and probably the United States as well—is to take this problem seriously before it came to our environment.

I think that, for the future—and this was part of what I mentioned before about public health and the policymakers—this is something that has to be taken in consideration. But it's important to learn about and from others. Even if you may have rapid tests to screen patients for COVID-19 infection, simple things, like confinement and the use of masks and to stay at home, are really very important.

And I know how painful these decisions are, because we are not societies that are used to staying at home for four weeks, only to go outside just to get food in the supermarket—but these are important steps for mitigating the peak. Otherwise, it's going to be very difficult to have the best medical care if all the medical resources are saturated.

Many reports have focused on how a number of countries and regions in Asia—notably, South Korea, Taiwan, and Singapore—were primed to move more quickly, citing experience with the first SARS outbreak as a primary reason for their proactivity, swift public health measures, and high compliance by the general population. What are your thoughts?

JT: Yes, that's true. I think that they have learned more about SARS, and MERS, of course. One interesting country, maybe, is Canada, because they have those sorts of experiences with SARS, because of the Chinese population in Toronto, you may remember, in 2002 to 2004.

But it seems to me that they have taken more rapid actions than other countries. And this is a country that is close to you geographically.

Indeed. We've covered a lot. Did we miss anything?

JT: This is related to cancer care. We had discussions with some of the groups that were in Wuhan in China. Especially for cancer care, one of the things that was raised as a risk for infection and for patients with cancer, and also for severe evolution of the disease, was, for example, to have elective surgery for patients with cancer. We have implemented in some diseases more new neoadjuvant treatments than we used to have.

We learned this a lot from some of the Chinese colleagues. So, for example, in colon cancer, even in breast cancer, in patients that you would not do neoadjuvant treatment, now we are implementing more neoadjuvant protocols to treat these patients as much as possible, with chemotherapy or hormone therapy depending on the disease, and just to delay, as much as possible, surgery to a time where all the health resources come to a more normal situation.

For the time being, actually, we're delaying some of the surgeries, especially in the big diseases—colon cancer, gastric cancer, lung cancer as well, breast cancer, and others. This is something that health authorities may consider in promoting policies like this.

Is this done with equal weight of consideration for health care capacity as well as for managing severe complications that may result from surgery, even more so if the patient becomes infected by SARS-Cov-2? Or does one take greater precedence over the other?

JT: I think it's both. If you use most of your resources in intensive care units for patients with COVID-19 respiratory function impairment, you decrease the opportunity of having the resources for patients that have complications with elective surgical procedures. But also, if you have a major surgery, you are, in a way, also in a more immune-depressed status, and you don't want to put these patients at risk for having more severe COVID-19 infections.

So, I think there are multiple factors that favor decisions like this. Obviously, this is not something that we'll have to do forever. If we can delay right now, surgery for four, six weeks, this is something to consider, even if for that particular disease or for that particular patient, you were not planning neoadjuvant treatments in another situation outside the COVID-19 pandemic.

Thank you so much for taking the time to speak with me.

JT: You're welcome.

> One of the things that we have failed globally—and probably the United States as well—is to take this problem seriously before it came to our environment.

Q & A

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

CONVERSATION WITH THE CANCER LETTER

A view from the plateau: As Italy's cases drop, oncologists plan post-COVID-19 agenda

> I believe that following this coronavirus infection, we will use much more telehealth and we will use it much more for patients for whom you don't need to come to the hospital.

Giuseppe Curigliano, MD, PhD
Associate professor of medical oncology, University of Milano;
Head, Division of Early Drug Development, European Institute of Oncology, Italy

In Italy, the number of people dying from COVID-19 has dropped to about 500 per day—a decrease from the 900 to 1,000 patients who had been dying daily when the disease spread was at its peak.

For Giuseppe Curigliano, associate professor of medical oncology at University of Milano, and head of the Division of Early Drug Development at the European Institute of Oncology, this is positive news.

"Less mortality, less people infected, less hospitals overwhelmed by patients. We'll see if we survive, but it's something good," Curigliano said.

We've been reaching out to Curigliano regularly:

- What to expect: Oncology's response to coronavirus in Italy (*The Cancer Letter*, March 11).
- Curigliano: "I don't want to see more people dying" (*The Cancer Letter*, March 20).
- Curigliano: Italy's COVID-19 cases keep rising; maybe next week the curve will flatten (*The Cancer Letter*, March 27).
- As Italy's COVID-19 incidence curve flattens, Curigliano sees lessons for the U.S. (*The Cancer Letter*, April 3).

The curve of COVID-19 patients in Italy has reached "a clear plateau," Curigliano said.

So, what comes next?

"How to be sure that patients who survived COVID are really negative for the COVID infection," Curigliano said. "We are going to launch a program in my institution to perform a serological test. On those serological tests, we will test IgG and IgM—the antibodies against the coronavirus—in order to understand who is immunized and who is not.

"Now, we are going to launch a trial with 1,000 people," Curigliano said. "This is now important, because once the number of infected people goes down, what you have to do is to understand how many people are really immunized.

"We will do also this testing on a population of cancer patients, including five big hospitals in Regione Lombardia. And so the idea is also to study the immunization of cancer patients."

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

Alex Carolan: How have you been?

Giuseppe Curigliano: We are doing better. We are actually in a plateau, in a clear plateau.

Yesterday we had less than a 500 people dying. Usually the numbers were 900 or 1,000, and yesterday we had just 500. Less mortality, less people infected, less hospitals overwhelmed by patients. We are very happy about this. We'll see if we survive, but it's something good.

How are things in your hospital?

GC: In my hospital, we have also less cases.

Last week you had 10 positive patients with cancer?

GC: Yes. Now we have just one. In the last week, one new case.

And how are the other patients who were positive?

GC: Most of them are quarantined, actually. No one died. We have to repeat again the tests in order to understand if they are negative or not. After two weeks, we need to retest the patient.

The curve is going down. The maximum percentage was on March 21.

So, what is the most important topic now? What to do now—how to be sure that patients who survived COVID are really negative for the COVID infection. We are going to launch a program in my institution to perform a serological test. On those serological tests, we will test IgG and IgM—the antibodies against the coronavirus—in order to understand who is immunized and who is not. This is quite important. And we have to do this for both health professionals and for doctors.

Whom will the program be testing? Will it be testing everybody who tested positive?

GC: My idea is to design, specifically, a prospective trial in which we test all doctors and health professionals that have been positive for sure—or all doctors, patients, and health professionals who had symptoms and had never been tested. Because, you know, many had symptoms, but they were not tested, because there was no deterioration of the clinical status. And then, of course, also testing people who look healthy to understand if they have contact with the virus. Because you can be completely asymptomatic.

Right. How many people are we talking about here?

GC: Now, we are going to launch a trial with 1,000 people.

And what is the timeline for this trial?

GC: We submitted to the ethical committee last Friday, and we hope to have the approval by this Friday. So we will start next week with the trial.

There's been a lot of talk about antibody testing in the U.S. as well.

GC: Yes. This is now important, because once the number of infected people goes down, what you have to do is to understand how many people are really immunized.

And what is the scientific question that this trial is asking?

GC: The scientific question is how many people are immunized for coronavirus. The second question is looking at positive doctors or patients—what is the time when you need to be immunized with the serum conversion from IgM to IgG?

Our study is just to understand who is immunized. I mean, you test IgG and IgM in the patient, but you do not collect the plasma of those patients. But those are exactly the same patients that can donate the plasma, and to use their plasma to treat other patients.

Is there anything else our readers should know about this?

GC: What we will do, of course—we will do also this testing on a population of cancer patients, including five big hospitals in Regione Lombardia. And so, the idea is also to study the immunization of cancer patients. So, this is not only for health professionals, but also for patients.

Now that the curve has finally plateaued—and I know this may still be far out—when do you expect to resume follow-up visits and routine visits for your patients?

GC: Now, it's too early to start again the follow-up. We prefer to have zero infected people—like in China. And we hope to reach this number—zero—we hope at the end of May. Then, every activity will restart. The first priority will be, of course, to give opportunity to high-risk patients to come back for visits and follow-up. And then we will do a graduated recall for all the patients according to priority of visit.

Does that mean that's when the whole country will likely stop being on lockdown?

GC: The idea of the government is to start removing the lockdown for some specific areas of the country, and for some specific people. Everything will be normal first for younger people who have been immunized. For elderly populations, maybe it's too early, so we have to protect them.

There would be a national program in order to remove the lockdown. And this would be a gradual program that will consider, of course, the general testing of the serum. Who is immunized, or not? And, of course, also the specific population of our country—leaving at the end the elderly population that has been most affected by the virus infection.

Let's talk about telehealth. How does your hospital plan to move forward with this?

GC: Oh, this is a very good question. We had that discussion just this morning. So, our idea is to use much more telehealth. You know, you don't need to see a patient who has no symptoms, who did a lot of tests at home and they are negative. You can do a visit with telehealth. You can even weigh the patient and all the needs of the patient without coming directly to the hospital.

For monitoring safety of specific drugs, you can do the same. I believe that following this coronavirus infection, we will use much more telehealth and we will use it much more for patients for whom you don't need to come to the hospital.

So, you expect there to be fewer in-person visits?

GC: At least for asymptomatic patients for follow-up visits.

This sounds like good news going forward, yes?

GC: The patients are very happy. We did a lot of visits with telehealth. They can see you in the computer exactly like you are seeing me. It's the same. It's like being in person. The only thing that they are missing, maybe, is the human touch—because you will not visit them. But they know very well that if they have an abnormal finding, they will talk to you. And so, a patients that can come to the hospital will be the only ones that have abnormal findings, clinically or on tests.

In the U.S., there are hospitals that have considered establishing COVID-19-negative hubs similar to yours during coronavirus. How did your hospital make this decision? Was it difficult to go about this?

GC: No, because once the epidemic started, the first decision of the national health system was how to protect patients who are not COVID infected, and have other type of problems. So patients who need an orthopedic surgeon for fracture, patients who need cardiovascular intervention for cardiac asthenia, or other acute cardiac events, and finally—cancer patients.

The first decision was to have COVID hospitals, just COVID hospitals—and then hubs in order to accept patients with other disease that are COVID negative. Cardiovascular hubs, orthopedic hubs, and finally, cancer hubs.

Was this a quick process?

GC: It was decided in one day. Yes.

They communicated: In Milano, you have three hubs, that are the National Cancer Institute, European Institute of Oncology, and the Humanitas Cancer Center. So, in your hospital you will do checkpoints. Only COVID-negative patients will come. And all the cancer patients of the other hospitals will be sent to you for surgery, chemotherapy, and radiation oncology.

Do you think COVID-19-negative hospitals are feasible in the United States?

GC: In our experience, we are a COVID-free hospital since two and a half months ago. And this, you know very well, we had less than 20 patients positive overall—less than 20.

Right, and now you're down to one.

GC: So, in an endemic area where you have, in Regione Lombardia, 50,000 positive patients—we had less than 20. And in terms of health professionals, the health professionals that are positive in our hospital are less than 15. It works. This is an example. It's a very clean hospital with specific pathways. We did a lot of triage, and so you really protect the health professional and patients.

It sounds like an excellent model for others to follow if they're able to. On the topic of taking care of health professionals, your hospital was certainly successful doing so. Was this because of access to PPE?

GC: When I arrive in the hospital every morning, also for doctors, they take your body temperature and then they will give you a mask once a day like this and some gloves for the whole day. Every morning, every one of us will have a mask and gloves. For health professional involved in basic procedures, like bronchoscopy or direct contact, they have much more advanced personal protective equipment. It's very important to protect the health professionals.

Of course. And is there any advice you have for health care professionals in the United States?

GC: For my colleagues who are medical oncologists, my suggestion is really to create hubs in cancer centers for patients who are COVID-negative, and who should be treated according to the priority that they decide.

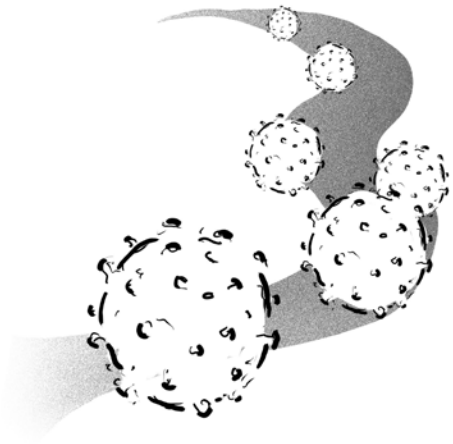
It's really important to have personal protective equipment, because the more you are protected, the more you can protect your patients. This is my message for my colleagues.

Before we end our conversation, is there anything else you'd like to add?

GC: For now, in my country, in order to restart, the first endpoint is to understand who is immunized or not. The next step will be to generate something like an immunological fingerprint or ID card—let's say immunological ID card—that can tell you that you are immunized, and so you can go back to work, and you don't have any risk for the patients you will take care of.

That sounds like a good next step. Well, thank you again for taking the time to speak with me.

COVID-19 UPDATES



ASCO publishes guidance on allocation of limited resources

The American Society of Clinical Oncology April 9 published a set of recommendations to support the oncology community as health care institutions across the United States face potentially difficult decisions around the allocation of scarce health care resources during the COVID-19 pandemic.

In some geographic areas, the crisis is expected to demand more resources—including ventilators, critical and intensive care beds, and medications—than the U.S. or local health care systems can supply, and institutions will need to develop allocation decision policies as they provide care for a growing number of patients.

ASCO's recommendations assert:

- Institutions should develop a fair and consistent prioritization and allocation policy before allocation becomes necessary. Decisions should be made at an institution-level, rather than at the bedside, so that oncologists can continue to maintain their duty to their patient.
- Allocation of resources in a pandemic should be based on maximizing health benefits. Rationing for lifesaving critical care resources should not use assessments about the perceived quality of a patient's life or perceptions about a patient's social worth.
- Oncologists should work with their institutions on how best to utilize scarce resources for care and support of cancer patients.
- Oncologists should communicate allocation plans and decisions to their patients with compassion and honesty, and health care institutions should offer support to oncologists in these communications.
- Oncologists should engage in advance care planning discussions with their patients and carefully document patient preferences for goals of care, particularly end of life care.

ASCO released the recommendations both in response to member reports that cancer care is being affected by the pandemic and to anticipate and inform the growing number of conversations happening at many institutions about resource allocation. The most critical aim is to ensure that the perspectives of patients with cancer and oncologists are included in all such discussions and decisions. The recommendations were developed by the ASCO Ethics Committee, approved by the board of directors, and accepted after peer review for future publication in the *Journal of Clinical Oncology*.

"As health care institutions make difficult decisions about where and how to deploy their resources during the COVID-19 crisis, they must ensure that allocation approaches don't unconditionally deny patients with cancer access to resources," ASCO President Howard A. "Skip" Burris III, said in a statement. "Every person with cancer has inherent worth and dignity. A cancer diagnosis alone should not keep a patient from a fair chance to access potentially life-saving resources, even in a public health crisis."

ASCO's recommendations aim to encourage the development of fair and equitable policies at the health system level for allocation of resources, especially critical care sources, and are not intended to guide individual treatment decisions. The recommendations also strive to promote the involvement of oncologists in the development and implementation of these policies to ensure that the needs of patients with cancer and their care teams are factored into the development of institutional policies. Individual oncologists will find guidance in ASCO's recommendations about their critical role in caring for and advocating for patients who could potentially benefit from resources that are in scarcity during this time of crisis.

"Oncologists have great skill and expertise in treating the individual patient in front of them, but in a public health emergency like this one, we need to expand our view to also protect the health of the larger patient population," Jonathan M. Marron, chair-elect of ASCO's Ethics Committee and lead author of the recommendations, said in a statement. "Oncologists have an important role to play to promote resource allocation plans that fairly, objectively, and consistently consider patients with cancer, and to work with their institutions to communicate those decisions clearly to patients, families, and surrogates."

COVID-19 cancer registry aims to track impact on patients during pandemic, inform care

The American Society of Clinical Oncology has launched an ASCO survey on COVID-19 in Oncology Registry to help the entire

cancer community learn about the pattern of symptoms and severity of COVID-19 among patients with cancer, as well as how COVID-19 infections impact the delivery of cancer care and patient outcomes.

The registry will collect both baseline and follow up data throughout the COVID-19 pandemic and into 2021.

"As this unprecedented public health crisis continues, we're seeing that certain populations – including individuals with cancer – are more likely to be vulnerable to the worst outcomes from COVID-19," ASCO President Howard "Skip" Burris III, said in a statement. "The cancer care community needs data on how the virus is impacting our patients, their cancer treatment, and outcomes to inform current cancer care and decision-making for future disease outbreaks. We encourage all oncology practices to participate so that we can learn from every patient, in every practice, in every state across the country."

Once sufficient patient data have been received and analyzed, ASCO will deliver periodic reports to the cancer community and the broader public on key learnings, such as characteristics of patients with cancer most impacted by COVID-19, estimates of disease severity, treatment modifications or delays, implementation of telemedicine in the cancer treatment setting, and clinical outcomes among patients related to both COVID-19 and cancer. ASCO also plans to develop peer-reviewed manuscripts based on the data provided.

The ASCO Registry is designed to capture not just point-in-time data on patients with cancer, but longitudinal data on how the virus impacts care and outcomes during the COVID-19 pandemic and into 2021.

"By looking at longitudinal data on patients, we'll be able to learn more about the longer-term of effects of COVID-19 and its impact on cancer care," Burris said. "We hope to learn if the virus resulted in specific complications for patients, delayed patients' ability to get a specific type of treatment, or if certain approaches resulted in better outcomes for patients."

Participating practices will be asked to complete a baseline data capture form on each patient with cancer who has a confirmed diagnosis of COVID-19, and subsequent follow-up information on status, treatment, and outcomes.

Limited patient identifying data, including zip code, date of birth, gender, race, ethnicity, type of cancer, and comorbidities, will be collected in a secure way to make longitudinal analysis possible. Data from practices participating in the registry will be collected and securely stored on the CancerLinQ platform. Additionally, CancerLinQ will be capturing data directly from CancerLinQ-participating practices on COVID-19 infection in their patients with cancer to allow for future analyses.

The web-based registry is open to all U.S. oncology practices, including physician-owned, academic, hospital/health system-owned practices, and hospitals, and will collect data from patients with all types of cancer who are undergoing all types of cancer treatment.

All participating practices will receive nominal financial support to cover research data-entry costs. The funding is supported by Conquer Cancer, The ASCO Foundation.

Six practices have already expressed interest in participating in the ASCO Registry: Oncology Hematology Care, Inc. (Cincinnati, Ohio), Winship Cancer Institute of Emory University (Atlanta, Georgia), Virginia Cancer Specialists (Alexandria, Virginia), Levine Cancer Institute, Atrium Health (Charlotte, North Carolina), Mayo Clinic (Rochester, Minnesota; Scottsdale and Phoenix, Arizona; and Jacksonville, Florida), and Hartford Healthcare Cancer Institute (Hartford, Connecticut).

AACR to split virtual annual meeting into two parts

The American Association for Cancer Research has split its virtual annual meeting into two sessions, which will be held in April and in June.

"AACR has been closely monitoring the rapid escalation of the COVID-19 pandemic," the AACR board said in a statement. "The health and safety of all annual meeting attendees and the patients and communities they serve are the AACR's highest priorities. Therefore, the AACR board of directors has made the decision not to move forward with an in-person annual meeting in August, and instead to present segments of the meeting program in two AACR virtual annual meetings."

Here is how the sessions will be split:

- **April 27-28, 2020: AACR Virtual Annual Meeting I**. This virtual meeting will feature a selection of high-impact proffered paper presentations. The program will include a number of clinical trial plenary sessions featuring more than 30 oral presentations along with perspectives on the science behind the clinical trials by expert discussants; clinical trial poster sessions; several minisymposia that showcase basic and translational science; and three New Drugs on the Horizon symposia that include first disclosures of innovative small molecules and biologics that have recently entered phase I clinical trials. Access to AACR Virtual Annual Meeting I will be made freely available. The abstracts of these proffered paper presentations will be posted online at 12:01 a.m. EDT (U.S.) on Monday, April 27.
- **June 22-24, 2020: AACR Virtual Annual Meeting II**. The second virtual

annual meeting will present thousands of proffered papers in minisymposia and in an e-poster platform. This meeting will also include an exciting opening plenary session with presentations on the latest developments in tumor biology and genetics (including the microenvironment), early detection, precision oncology, and cancer immunotherapies; the Presidential Address; the Presidential Select Symposium on precision pediatric cancer medicine; scientific merit and distinguished public service award lectures from individuals who have made extraordinary contributions to the cancer field; and a comprehensive educational program featuring about 70 educational sessions and methods workshops. Further details on the program, information regarding registration for AACR virtual annual meeting II, and guidance in obtaining any refunds of registration fees for the in-person April 2020 annual meeting will be communicated as soon as possible. Abstracts of the proffered paper presentations presented in this virtual meeting will be posted online at 12:01 a.m. EDT (U.S.) on Friday, May 15.

FDA approves first generic of commonly used albuterol inhaler to treat and prevent bronchospasm

FDA has approved the first generic of Proventil HFA (albuterol sulfate) Metered Dose Inhaler, 90 mcg/Inhalation, for the treatment or prevention of bronchospasm in patients four years of age and older who have reversible obstructive airway disease, as well as the prevention of exercise-induced bronchospasm in this age group.

"The FDA recognizes the increased demand for albuterol products during the novel coronavirus pandemic," FDA Commissioner Stephen M. Hahn, said in a statement. "We remain deeply committed to facilitating access to medical products to help address critical needs of the American public."

According to the National Heart, Lung, and Blood Institute, bronchospasms occur when the muscles surrounding the airways swell and tighten, causing them to squeeze the airways and make them smaller. Exercise and other physical activity can bring on symptoms in most people who have asthma and may occur either during or right after being active. Asthma causes recurring periods of wheezing (a whistling sound when breathing), chest tightness, shortness of breath and coughing. The coughing often worsens at night or early in the morning.

In March 2020, FDA issued a revised draft product-specific guidance for proposed generic albuterol sulfate metered dose inhalers, including drug products referencing Proventil HFA. Among other things, the draft guidance provides bioequivalence recommendations.

FDA requires applicants to submit appropriate data and information to demonstrate that complex generic drug-device combination products meet the agency's rigorous approval standards. These standards ensure quality generic drug products are as safe and effective as their brand name counterparts.

The FDA granted approval of this generic albuterol sulfate inhalation aerosol to Cipla Limited.

COA establishes practice referral service for patients seeking cancer treatment during COVID-19 pandemic

Hospitals have scaled back or closed cancer and blood disease services to make space for patients with COVID-19.

Recognizing that cancer care must continue, the Community Oncology Alliance has launched a referral service for patients seeking care in their communities.

Through the COA Patient-Practice Connector website, patients seeking care can fill out a brief contact form without sharing any personal health information. The COA team will then use that information to try to identify a practice that is still serving patients in their community within 24 hours.

The COA Patient-Practice Connector minimizes the amount of exposure that cancer patients may face when trying to find treatment. The website makes it easier to maintain social distance and find the provider that is the best fit for the patient.

No patient data will be stored or shared, and users can choose their provider. All data submitted to COA will be deleted immediately once a request is closed.

COA opposes home infusion for cancer, citing safety concerns

The Community Oncology Alliance board of directors released a position statement opposing the home infusion of chemotherapy, cancer immunotherapy, and cancer treatment supportive drugs because of serious patient safety concerns.

The home infusion of cancer treatments by a provider who may not be a trained oncology nurse and may not recognize or be prepared to treat any of the serious adverse reactions that frequently occur is of significant concern, the statement said.

Many of the side effects caused by cancer treatment can have a rapid, unpredictable onset that places patients

in incredible jeopardy and can even be life-threatening. Home infusion negates the benefits of the expertise and team approach to cancer care, which are the hallmarks of community oncology, within facilities specifically designed for safe and effective cancer drug infusions.

The COVID-19 pandemic has forced all health care providers and care settings to dramatically adjust operations. Independent, community oncology practices have quickly adapted and are taking extreme measures to keep their facilities and providers COVID-19 free so that their patients in active treatment can be assured of a safe environment. The recent, major expansion of telehealth services and relaxation of regulations has provided oncologists with a powerful tool to do this by monitoring patients and ensuring that only those that are in urgent need of treatment come into the practice.

The COA home infusion position statement notes that there are other medical specialties and diseases where the infusion of Medicare Part B drugs at home may be reasonable during the COVID-19 pandemic. As such, the position is currently limited to opposition for the home infusion of cancer treatments.

GO2 Foundation for Lung Cancer: COVID-19 patients with pre-existing conditions should receive same treatment as those without

GO2 Foundation for Lung Cancer is working with value-based coalitions to address the concerns of discrimination in access to treatment to make sure that our lung cancer community is not disadvantaged during the COVID-19 crisis.

"The Americans with Disabilities Act: Section 504 of the Rehabilitation Act and Section 1557 of the Affordable Care Act provides protection from healthcare discrimination.

- Because of concerns about pre-existing conditions and disability discrimination in access to treatment has been a major concern during the COVID-19 crisis, the Department of Health and Human Services' Office of Civil Rights issued guidance to covered healthcare entities (anyone that accepts federal funding) on protecting individual civil rights and privacy during the COVID-19 emergency.
- The guidance states that "persons with disabilities should not be denied medical care on the basis of stereotypes, assessments of quality of life, or judgments about a person's relative worth based on the presence or absence of disabilities. Decisions by covered entities concerning whether an individual is a candidate for treatment should be based on an individualized assessment of the patient based on the best available objective medical evidence."
- While this guidance is not a new law it is a step in addressing civil rights concerns as potential rationing of health services comes closer to reality.
- The guidance would be extended to persons with pre-existing or severe chronic health conditions.
- The "Know Your Rights" fact sheet explains protections and provides direction on filing a complaint of discrimination.

"We are adding the voice of the lung cancer community with the disabilities community in supporting these guiding principles," the foundation said in a statement. "These principles reinforce our civil rights laws that protect equal dignity for every human life and that healthcare providers should not discriminate against those with disabilities nor put at the end of the line for health services during emergencies."

Algorithm aims to protect surgical team members against infection with COVID-19 virus

Researchers from Stanford University's Department of Surgery have created an algorithm that aims to protect operating room team members who perform urgent and emergency operations from COVID-19, and rationally conserve the personal protective equipment they wear.

This best practice guideline is published in the *Journal of the American College of Surgeons* ahead of print. Stanford Health Care serves Santa Clara and San Mateo Counties, which saw their first cases of COVID-19 infection in early March.

The Stanford algorithm is based on the urgency of the procedure, potential for aerosolization and release of virus droplets at the surgical site, and evidence that a patient has been infected. The algorithm aligns with the goals of the ACS statement on PPE Shortages during the COVID-19 Pandemic, released April 1.

"We developed institutional guidelines based on how soon the surgical cases needed to be performed, the patient's condition, the risk that a surgeon would access an area of body where the amount of virus could be high, and the risk that a patient could be infected with COVID-19," Joseph Forrester, an assistant professor in general surgery and lead author of the algorithm article, said in a statement.

Forrester was a field agent in Liberia during the 2014 Ebola outbreak where he conducted several investigations of the Ebola burden and preparedness as an Epidemic Intelligence Service officer with CDC.

At Stanford, a PPE task force of hospital and medical school leaders from interventional suites, including the operating room, interventional radiology, and endoscopy, as well as quality improvement and infectious disease experts, convened on March 19 to create institutional guidelines that could be implemented within 72 hours. At that time, Stanford Health Care had approximately 10 patients infected with COVID-19. Guidelines incorporated current data about COVID-19 transmission in hospital and non-hospital settings and operating room risk during outbreaks of SARS and Ebola.

Patients were triaged by severity of illness into urgent and emergency procedures. Urgent cases were stratified into high- and low-risk procedures depending on the expected viral burden at the surgical site. Procedures categorized as aerosol-generating were classified as high-risk. These procedures include those that involve the aerodigestive tract, endoscopy, and open or laparoscopic surgery on the bowel with gross contamination.

The Stanford guideline assumes, above all, that any patient could be infected with COVID-19 unless proven otherwise by a negative RT-PCR test. When operating on COVID-19-positive patients or performing an AGP, the guideline requires operating room team members to be fitted with an N-95 respirator mask and wear a gown, gloves, and eye protection. Only when an RT-PCR test is negative for COVID-19 may surgical team members wear standard surgical clothing.

A surgeon may consider delaying an urgent or emergency procedure on a patient who exhibits viral symptoms (fever, cough, sore throat). If delay compromises the well-being of the patient, the surgeon orders in-house RT-PCR COVID-19 testing with a 24-hour turnaround. If the patient's status does not allow for a 24-hour wait, the case is considered to be an emergency and the patient is presumed to be COVID-19-positive.

Special considerations are made for the use of PPE during and after bag mask ventilation and endotracheal intubation, which both pose a high risk for viral transmission. All health care providers who are not directly involved with intubation are asked to leave the operating room beforehand. Anesthesiologists should be fitted with N-95 face masks and droplet-protective PPE because they are positioned at the head of the bed throughout the procedure. Cleaning staff should take droplet precautions when cleaning any operating room.

At the time the guideline was created at Stanford Health there was a nationwide shortage of N-95 face masks. To conserve the institution's supply, the algorithm requires a face shield to be placed over the mask.

Karyopharm to evaluate low-dose Xpovio as potential COVID-19 treatment

A global randomized clinical trial for low dose oral Xpovio (selinexor) in hospitalized patients with severe COVID-19 aims to evaluate the drug as a potential treatment option.

Karyopharm Therapeutics Inc. sponsors the drug.

FDA has approved Xpovio as a treatment for patients with relapsed or refractory multiple myeloma. Selinexor is an oral, selective inhibitor of nuclear export compound that blocks the cellular protein XPO1.

In addition to its roles in cancer, XPO1 also facilitates the transport of several viral proteins from the nucleus of the host cell to the cytoplasm, and it amplifies the activities of pro-inflammatory transcription factors.

SINE compounds have been shown to disrupt the replication of multiple viruses in vitro and in vivo. They have also been shown to mediate anti-inflammatory and anti-viral effects, including respiratory infections, in several animal models. In particular, SINE compounds have recently been identified as having the potential to interfere with key host protein interactions with SARS-CoV-2, the virus that causes COVID-19.2

Selinexor is the only XPO1 inhibitor approved for commercial use by the FDA and has been extensively tested in clinical trials across numerous cancer indications worldwide since 2012. The proposed clinical trial to treat hospitalized patients with COVID-19 would be the first study of an XPO1 inhibitor in patients with severe viral infections.

"While Karyopharm's clinical development strategy until now has been focused on patients with various types of cancer, there is increasing evidence that XPO1 inhibition could play an important role in the treatment of patients with viral infections including SARS-CoV-2," Sharon Shacham, president and chief scientific officer of Karyopharm, said in a statement.

"As the medical community is urgently seeking innovative ways to address the COVID-19 pandemic, based on recent scientific data, we have decided to evaluate the potential for selinexor in the treatment of patients with COVID-19. We look forward to working with clinical investigators and regulators across

the globe as expeditiously as possible to determine the next steps for this new initiative.

"Additionally, we continue to move our oncology programs forward including the expected submission of our BOSTON supplemental New Drug Application in the second quarter of this year," Shacham said.

"I am highly encouraged by the scientific rationale of studying selinexor, which targets both virus and immune-mediated injury, for treatment of patients with severe COVID-19," Thomas J. Walsh, professor of medicine, pediatrics, and microbiology & immunology, Weill Cornell Medicine, Cornell University, said in a statement.

SINE XPO1 inhibitors have demonstrated activity against over 20 different viruses, including the RNA viruses, influenza, respiratory syncytial virus and other common causes of respiratory infection. XPO1 inhibition has been identified in several assays as having potential activity against SARS-CoV-2, although specific animal models have not been available to date. One of the most important aspects of COVID-19 is the marked pulmonary inflammation with high levels of cytokines such as IL6, IL1, IFNg and others. Along these lines, selinexor and other SINE compounds have demonstrated potent anti-inflammatory activity through the inhibition of Nuclear Factor kB (NF-kB), leading to reductions in all of these cytokines in a variety of models, and this may be particularly beneficial to hospitalized patients with COVID-19.

GSK and Vir Biotechnology collaborate to find COVID-19 solutions

GlaxoSmithKline plc. and Vir Biotechnology Inc. are collaborating on research solutions for coronaviruses, including SARS-CoV-2.

The binding agreement will use Vir's proprietary monoclonal antibody platform technology to accelerate existing and identify new anti-viral antibodies that could be used as therapeutic or preventative options to help address the current COVID-19 pandemic and future outbreaks. The companies will leverage GSK's expertise in functional genomics and combine their capabilities in CRISPR screening and artificial intelligence to identify anti-coronavirus compounds that target cellular host genes. They will also apply their combined expertise to research SARS-CoV-2 and other coronavirus vaccines.

"Vir's unique antibody platform has precedented success in identifying and developing antibodies as treatments for multiple pathogens, and it is highly complementary with our R&D approach to focus on the science of immunology," Hal Barron, chief scientific officer and president of Research and Development at GSK, said in a statement.

The initial focus of the collaboration will be to accelerate the development of specific antibody candidates identified by the Vir platform, VIR-7831 and VIR-7832, that have demonstrated high affinity for the SARS-CoV-2 spike protein and are highly potent in neutralising SARS-CoV-2 in live virus-cellular assays. Subject to regulatory review, the companies plan to proceed directly into a phase II clinical trial within the next three to five months.

The collaboration will also utilise Vir's CRISPR screening and machine learning approach to identify cellular targets whose inhibition can prevent viral infection. Vir has identified multiple potential targets against flu and other respiratory pathogens, as well as hepatitis B virus, and will now focus on SARS-CoV-2.

Additionally, the companies have also agreed to conduct research into SARS-CoV-2 and other coronavirus vaccines by coupling GSK's vaccines technologies and expertise with Vir's ability to identify neutralising epitopes that are present across entire viral families. These efforts will be additive to other initiatives GSK is advancing to develop a potential vaccine for COVID-19.

"It is becoming increasingly clear that multiple therapeutic approaches, used in combination or in sequence, will be necessary to stop this coronavirus pandemic. It is likely that the current coronavirus outbreak will not be the last," George Scangos, CEO of Vir Biotechnology, said in a statement.

To gain access to Vir's technology, GSK will make an equity investment in Vir of $250 million, priced at $37.73, a 10% premium to the closing share price on March 27.

OncoSec collaborates with Providence Cancer Institute to conduct phase I study of COVID-19 vaccine

Providence Cancer Institute, a part of Providence St. Joseph Health, has launched a phase I study of OncoSec's novel DNA-encodable, investigational vaccine, CORVax12, designed to act as a prophylactic vaccine to prevent COVID-19.

CORVax12 consists of OncoSec's existing product candidate, Tavo (interleukin-12 or "IL-12" plasmid), in combination with an immunogenic component of the

SARS-CoV-2 virus recently developed by researchers at NIH's National Institute of Allergy and Infectious Diseases and licensed to OncoSec on a non-exclusive basis.

OncoSec's CORVax12 vaccine approach combines the co-administration of Tavo (plasmid IL-12) with a DNA-encodable version of the SARS-CoV-2 spike or "S" glycoprotein to enhance immunogenicity of the component developed by scientists at the NIAID Vaccine Research Center. CORVax12 is designed to drive a coordinated vaccine response, capable of drawing upon the innate, adaptive humoral, and adaptive cellular arms. We believe this multi-pronged innate, adaptive and cellular immune response is likely to be important in generating a robust anti-viral response.

"Previous vaccine efforts against coronaviruses, including the SARS coronavirus, have focused on the S glycoprotein, which facilitates interaction with the host cell through binding to the ACE2 receptor," principal investigator on the study Rom Leidner, co-medical director, of the Head and Neck Cancer Program at Providence Cancer Institute, and assistant member of the Earle A. Chiles Research Institute, said in a statement.

Providence investigators will evaluate the vaccination of healthy adult volunteers utilizing OncoSec's next-generation, investigational APOLLO generator technology for the first time clinically if FDA clears the APOLLO to enter the clinic. The trial will also include extensive immune monitoring.

OncoSec will supply CORVax12 and its investigational APOLLO electroporation device to Providence as part of this effort and does not anticipate any additional capital commitment at this time. Additionally, OncoSec will contribute manufacturing, preclinical, and prior clinical information and data for TAVO, along with manufacturing data for its APOLLO technology, to support FDA's allowance of the Providence IND. Providence will hold the IND, if cleared by FDA, and perform the preclinical and clinical development work.

FAQs and Guidances

Federal government:

- NCI source book and resources: clinical and laboratory operations
- NCI Emergency Resources: What people with cancer should know about the coronavirus
- NCI guidance: Interim guidance for patients on clinical trials supported by the NCI Cancer Therapy Evaluation Program (CTEP) and the NCI Community Oncology Research Program (NCORP).
- CTEP coronavirus guidance
- COVID-19 scientific interest group
- FDA guidance: Conduct of clinical trials of medical products during COVID-19 pandemic
- FDA guidance update: Blood donations
  - More FDA updates: Medical Countermeasures Initiative, on COVID-19
  - FDA continues to facilitate access to crucial medical products, Including ventilators
  - FDA provides update on patient access to certain REMS drugs during COVID-19 public health emergency
  - A message to patients with cancer and Health Care Providers About COVID-19
  - Update: Diagnostic testing for COVID-19
  - Resources for patients and caregivers
  - FDA enforcement policy for extracorporeal membrane oxygenation and cardiopulmonary bypass devices

Professional societies:

- American Society of Clinical Oncology FAQ: Emerging issues and challenges in caring for patients with cancer during the coronavirus pandemic
  - ASCO recommendations for the oncology community
  - ASCO COVID-19 in oncology registry
- American Association for Cancer Research FAQ: Information on virtual annual meetings
- American Cancer Society FAQ: Common questions about the new coronavirus outbreak
  - ACS clinical guidance: COVID-19 elective case triage guidelines for surgical care
  - Create a surgical review committee for COVID-19-related surgical triage decision making
  - COVID-19 and 2020 ACS Grants
- Society for Immunotherapy of Cancer Resources: Patient management and basic and translational research

- Community Oncology Alliance resources: Coronavirus (COVID-19) practice resources and protocols
- Leukemia & Lymphoma Society FAQ: Resources and what you should know about the coronavirus
- American Society for Radiation Oncology FAQ: COVID-19 recommendations and information
- American College of Surgeons resources: For the surgical community
- Society for Immunotherapy of Cancer resources: Implications for patients, translational research
- GO2 Foundation for Lung Cancer resources
- American Society for Transplantation and Cellular Therapy resources
- European Blood and Marrow Transplantation Society recommendations
- World Marrow Donor Association resources
- National Institute for Health Care Management Foundation resources

Research centers:

- St. Jude Children's Research Hospital FAQ: COVID-19 and children with cancer
- Journal of the National Comprehensive Cancer Network: How to manage cancer care during COVID-19 pandemic
  - NCCN best practices

Companies:

- Advarra: Coronavirus guidance

IN BRIEF

Frederic Pla named COO of The Parker Institute for Cancer Immunotherapy

Frederic Pla was named chief operating officer of The Parker Institute for Cancer Immunotherapy.

In this role, Pla will lead day-to-day operations and work with PICI's leadership team to establish comprehensive goals for performance, expansion and sustainable growth of the organization. Pla will focus on business development to expand PICI's external partnerships, and will oversee PICI's business operations, legal, strategic alliances and communications areas.

Pla most recently served as COO at Genomic Health. Under his leadership, the company implemented "Genomic Health 2.0," putting in place new operating processes, tools and workstreams to support its growth.

In another development, Jeffrey Bluestone, stepped down from his role as president and CEO at The Parker Institute. He has joined its board of directors as vice chairman and a member of the executive committee.

PICI is looking for his replacement.

ACS awards research and training grants

The American Cancer Society has approved funding for 79 research and training grants totaling $36,2 million in the first of two grant cycles for 2020.

Grant applications were reviewed and approved remotely in light of the coronavirus epidemic. The grants will fund investigators at 59 institutions across the U.S.; 73 are new grants while 6 are renewals of previous grants. The grant starting date was moved from July 1 to Sept. 1, 2020 to accommodate institutions that are partially shut down due to the epidemic.

Highlights of the latest cycle include:

- **Matthew J. Sikora** of University of Colorado, Denver, and his team will work to identify strategies and potential drugs to undermine estrogen receptor activity in invasive lobular carcinoma, which affects more than 44,000 women in the U.S. every year. They

hope their work targeting the MDC1 protein will allow them to combat resistance to drugs that target estrogen in this cancer.

- **Haiying Cheng**, Albert Einstein College of Medicine. Cheng will focus on metastatic lung cancer, specifically how a particular gene (RICTOR) may contribute to the spread and survival of cancer cells in distant metastatic sites. Their findings have shown that RICTOR amplification may be a new target in lung cancer metastases could open up a new avenue for the discovery of novel treatment strategies that could eventually lead to better treatment outcome and longer survival for some lung cancer patients.
- **Ankur Nagaraja**, of Dana-Farber Cancer Institute. This research aims to address what Dr. Nagaraja believes is a fundamental cause of most stomach and esophageal (gastroesophageal) cancers: that most gastroesophageal cancers arise following a catastrophic disruption of the genome where the cancer cell acquires extra copies of many chromosomes They hope to gain a better understanding of how a normal stomach or esophagus cell transforms into stomach or esophageal cancer, with the ultimate goal of using this knowledge to develop new, more effective therapies that attack gastroesophageal cancer cells where they are most vulnerable.
- **Cassandra E. Callmann**, of Northwestern University. Callman's lab hopes to harness the power of nanotechnology to accelerate the development of a cancer vaccine for triple-negative breast cancer. Their early studies have found nanoscale vaccines show remarkable anticancer efficacy in mouse models of TNBC, with 6 of 9 animals being completely cured.
- **Alejandra H. de Mendoza**, of Georgetown University. De Mendoza will evaluate whether a culturally targeted video can increase genetic testing and counseling in Latina women, who have double the risk of having a BRCA1 or BRCA2 mutation compared to the general population yet have lower awareness and use of genetic counseling and testing. A pilot study showed the video led to significantly increased knowledge, and 60% of viewers subsequently attending genetic counseling, compared to national estimates of <10%.
- **Carolyn S. Harris**, University of California, San Francisco/ Patients with cancer, as well as cancer survivors, often experience more than one symptom at the same time. Harris's research shows that it is very common for cancer patients and survivors to report having 10 symptoms at the same time, with those symptoms having a negative impact on patients' and survivors' ability to function and overall quality of life. This research will be the first to investigate whether changes in three genes are associated with two common symptom clusters; this knowledge could then be used to develop new interventions to prevent or treat them.

Van Crocker Jr. named president and co-founder of CTCA Oncology Data, Analytics & Research Business

Percy Van Crocker Jr. was named Cancer Treatment Centers of America's Oncology Data, Analytics & Research Business as President and Co-Founder.

In this role, Crocker will lead a team focused on harnessing genomic and clinical data.

FUNDING OPPORTUNITIES

DOD Ovarian Cancer Research Program FY20 funding opportunity

The FY20 Defense Appropriations Act is anticipated to provide funding to the Department of Defense Ovarian Cancer Research Program to support patient-centered research to prevent, detect, treat, and cure ovarian cancer.

The FY 2020 Defense Appropriations Bill has not been signed into law—and although FY20 funds have not been appropriated for the Department of Defense Ovarian Cancer Research Program, the OCRP has published information to allow investigators time to plan and develop ideas for submission to the anticipated FY20 funding opportunities.

FY20 OCRP program announcements and general application instructions for the following award mechanism is posted on the Grants.gov website.

THE CLINICAL CANCER LETTER

CLINICAL ROUNDUP

Phase III TNBC ASCENT study to be stopped for compelling efficacy

The phase III confirmatory ASCENT study—designed to validate the promising safety and efficacy data of sacituzumab govitecan observed in a phase II study of heavily pretreated patients with metastatic triple negative breast cancer—will be halted due to compelling evidence of efficacy.

The primary endpoint for the study is progression-free survival, and secondary endpoints include overall survival and objective response rate, among others. This decision was based on the unanimous recommendation by the independent data safety monitoring committee during its recent routine review of the ASCENT study.

Immunomedics Inc. sponsors the trial.

"The remarkable results we observed across multiple endpoints in the ASCENT study warranted early discontinuation of the trial and are indicative of a potential major advance in the treatment of this devastating disease that affects younger women and African American women at higher rates," Julie R. Gralow, Jill Bennett Endowed Professor of Breast Cancer, University of Washington School of Medicine and member of Fred Hutchinson Cancer Research Center, said in a statement.

A biologics license application resubmission seeking accelerated approval of sacituzumab govitecan for the treatment of patients with mTNBC who have received at least two prior therapies for metastatic disease is under FDA review, with a PDUFA target action date of June 2, 2020. The FDA previously granted Breakthrough Therapy Designation for sacituzumab govitecan in this disease setting.

Roswell Park reports extended survival among breast cancer survivors who exercise regularly

Following physical activity guidelines from the U.S. Department of Health and Human Services can improve clinical outcomes for patients with high-risk breast cancer, according to a study published in the *Journal of the National Cancer Institute.*

Researchers at Roswell Park Comprehensive Cancer Center conducted the study, which was led by Rikki Cannioto, assistant professor of oncology in the Department of Cancer Prevention and Control at the Buffalo cancer center.

Among people with high-risk breast cancer, those who engaged in moderate-to-vigorous levels of physical activity before and after their diagnosis had a statistically significant reduction in their chance of cancer recurrence or death. The work is the first report to show that physical activity measured at time points before, during and after chemotherapy is associated with outcome in those with high-risk breast cancer.

The HHS' Physical Activity Guidelines for Americans recommend that adults engage in at least 2.5 to 5 hours of moderate-intensity physical activity or 1.25 to 2.5 hours of vigorous-intensity aerobic physical activity per week.

Cannioto *et al.* surveyed 1,340 people with high-risk breast cancer who were enrolled in the Diet, Exercise, Lifestyles and Cancer Prognosis (DELCaP) Study to determine whether meeting those minimum levels of activity at four time periods before diagnosis, during treatment and after treatment was associated with disease recurrence and/or mortality.

"When considering activity from before diagnosis and after treatment, we found that patients meeting the minimum Guidelines at both time points experienced significantly reduced hazards of disease recurrence and mortality—55% and 68%, respectively," Cannioto said in a statement.

Importantly, patients who did not meet the physical activity guidelines before

diagnosis, but who reported meeting the guidelines at their two-year follow-up experienced a significant survival advantage of 46% decreased chance of recurrence and 43% decreased chance of mortality.

When combining physical activity data from all four time points before, during and after treatment, they found striking inverse associations between mortality and physical activity at all activity levels, demonstrating that patients who consistently engaged in lower volumes of regular, weekly physical activity experienced similar survival advantages as patients who met or exceeded the guidelines.

"Taken collectively, these findings have important implications in the clinical oncology setting, because they suggest that a cancer diagnosis may serve as an impetus for increasing physical activity in some patients, and among these patients, beginning an exercise program after treatment resulted in a survival advantage," Cannioto said.

"These observations coincide with previous findings from our group showing that lower levels of regular, weekly activity were associated with a significant survival advantage—which is encouraging given that patients and survivors can be overwhelmed by the current physical activity Guidelines," Cannioto said.

Drug combination fights resistance to lung cancer treatment

A drug combination discovered by the UT Southwestern Simmons Cancer Center may extend the effectiveness of a lung cancer treatment and make it available to many more patients.

The findings, published in *Nature Cancer,* focused on epidermal growth factor receptor, EGFR, a protein that has a prominent role in the growth and survival of cancer cells, and resistance that builds up against inhibitors used to battle it. The researchers found that adding an interferon blocker, normally used to treat lupus, effectively wiped out this resistance in mice.

"This could be very important because it could expand the reach of the drug from about 15% to the majority of patients with lung cancer. That's millions of people worldwide," Amyn Habib, associate professor of Neurology and Neurotherapeutics at UT Southwestern Medical Center, a member of the Harold C. Simmons Comprehensive Cancer Center, and a staff physician at the Dallas Veterans Affairs Medical Center, said in a statement.

About 15% of lung cancer patients have a mutation in EGFR that makes it more active.

Habib's lab discovered that the signaling pathways release interferons that resist the EGFR inhibitor. It was an unexpected finding because oncologists normally see interferons as allies in fighting cancer.

Their broad search included drugs outside of cancer treatment and found an interferon blocker used in lupus patients called anifrolumab. The researchers used anifrolumab to block interferons in mice, crippling the signaling pathway and wiping out the resistance to the EGFR blocker.

They also found that patients who did not have mutated EGFR also increased their interferon levels in response to EGFR inhibitors. This has kept those patients from responding to the EGFR inhibitor drugs. If the lupus drug could block the interferons, it would also open those patients up to the benefits of the EGFR blocking drugs.

Habib's lab made the discovery by focusing on about 3,000 genes in the lung cancer cell and charting that were turned on or off. The data clearly led the researchers to increased activity with interferons.

This was previously unknown to medical science, and it is significant because EGFR signaling plays a role in other cancers including breast cancer and glioblastoma. Habib says his next step is to pursue clinical trials in lung cancer patients.

Other authors of the study from UT Southwestern are Ke Gong, Gao Guo, Nishah Panchani, Matthew Bender, David E. Gerber, John D. Minna, Farjana Fattah, Boning Gao, Michael Peyton, Kemp Kernstine, Cheng-Ming Chiang, Adwait Amod Sathe, Chao Xing, and Esra A. Akbay. Authors from other institutions are Kathryn H. Dao of Baylor Research Institute in Dallas, Dawen Zhao of Wake Forest School of Medicine in Winston-Salem, North Carolina, and Sandeep Burma and Bipasha Mukherjee, both at the University of Texas Health Science Center at San Antonio.

DRUGS & TARGETS

FDA approves Braftovi + cetuximab for BRAFV600E-mutant metastatic CRC indication

FDA has approved Braftovi (encorafenib) in combination with Erbitux (cetuximab) for the treatment of adult patients with metastatic colorectal cancer with a BRAFV600E mutation, as detected by an FDA-approved test, after prior therapy.

The approval is based on results from the BEACON CRC trial, the only phase III trial to specifically study patients with previously treated metastatic CRC with a BRAFV600E mutation.

Braftovi is sponsored by Pfizer.

Based on results from the BEACON CRC trial, Braftovi plus cetuximab showed a median overall survival of 8.4 months (95% CI: 7.5, 11.0) compared with 5.4 months (95% CI: 4.8, 6.6) for Control (irinotecan with cetuximab or FOLFIRI with cetuximab) ([HR 0.60, (95% CI: 0.45, 0.79), p=0.0003]). Additionally, BRAFTOVI plus cetuximab showed an improved objective response rate (ORR) of 20% (95% CI: 13%, 29%) compared with 2% (95% CI: 0%, 7%) for Control (p<0.0001) and median progression-free survival (mPFS) was 4.2 months with BRAFTOVI plus cetuximab (95% CI: 3.7, 5.4) versus 1.5 months with Control (95% CI: 1.4, 1.7) ([HR 0.40, (95% CI: 0.31, 0.52), p<0.0001]).

"BRAF mutations are estimated to occur in up to 15% of people with metastatic colorectal cancer and represent a poor prognosis for these patients,"Scott Kopetz, associate professor of gastrointestinal medical oncology at MD Anderson Cancer Center, said in a statement. "As the first-and-only targeted regimen for people with BRAFV600E-mutant metastatic CRC who have received prior therapy, BRAFTOVI in combination with cetuximab is a much-needed new treatment option for these patients."

The most common adverse reactions (AR) (≥ 25%) seen in patients treated with BRAFTOVI in combination with cetuximab were fatigue, nausea, diarrhea, dermatitis acneiform, abdominal pain, decreased appetite, arthralgia and rash. The full prescribing information for BRAFTOVI can be found here.

FDA approves luspatercept-aamt for anemia in adults with MDS

FDA has approved luspatercept-aamt (Reblozyl, sponsored by Celgene Corp) for the treatment of anemia failing an erythropoiesis stimulating agent and requiring 2 or more red blood cell units over 8 weeks in adult patients with very low- to intermediate-risk myelodysplastic syndromes with ring sideroblasts or with myelodysplastic/myeloproliferative neoplasm with ring sideroblasts and thrombocytosis.

Efficacy was demonstrated in the MEDALIST trial (NCT02631070), a randomized, multi-center, double-blind, placebo-controlled trial in 229 patients with IPSS-R very low, low, or intermediate-risk myelodysplastic syndromes who had ring sideroblasts and required RBC transfusions (2 or more RBC units over 8 weeks). Patients were randomized 2:1 to luspatercept-aamt or placebo. All patients received best supportive care, which included RBC transfusions.

The main efficacy endpoint in MDS-RS and MDS-RS-T was the proportion of patients who were RBC-transfusion independent, defined as the absence of any RBC transfusion during any consecutive 8-week period between Weeks 1 and 24.

Of the 153 patients who received luspatercept-aamt, 58 (37.9%, 95% CI: 30.2, 46.1) were RBC-TI for at least 8 weeks, compared to 10 patients (13.2%, 95% CI: 6.5, 22.9) who received placebo (treatment difference 24.6% (95% CI: 14.5, 34.6; p<0.0001.)

Myriad receives reimbursement for the BRACAnalysis Diagnostic System in Japan

Myriad Genetics has received reimbursement and launched the BRACAnalysis Diagnostic System in Japan to help physicians determine which people affected with breast and ovarian cancer have hereditary breast and ovarian cancer syndrome and qualify for additional diagnostic and medical management.

BRACAnalysis was approved by Japan's Ministry of Health, Labour and Welfare in November 2019 for this indication.