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REMDESIVIR, IL INHIBITORS EMERGE AS FRONTRUNNERS IN RACE TO TREAT COVID-19

PHASE III RESULTS FOR REMDESIVIR EXPECTED WITHIN WEEKS

By Matthew Bin Han Ong



Experts in infectious diseases and investors on Wall Street are honing in on two potential treatments for COVID-19: interleukin inhibitors and remdesivir.

On April 21, NIH published [treatment guidelines](#) for COVID-19. The guidelines, which were developed by a panel with representatives from federal agencies, health care and academic organizations, and professional societies, include a [review](#) of experimental antivirals, host modifiers, and immunotherapies.

No drug has been proven safe and effective for treating COVID-19, and the panel notes that clinical trial data are insufficient to recommend either for or against any investigational treatment currently available.

The new guidelines include dismissive critiques of some investigational treatments, but remdesivir and two interleukin inhibitors have been spared—at least for now. These agents are in phase III trials.

The guidelines include strong recommendations against using the following therapies in any setting other than clinical trials:

- The combination of hydroxychloroquine plus azithromycin, because of the potential for toxicities,
- Lopinavir/ritonavir or other HIV protease inhibitors, because of unfavorable pharmacodynamics and negative clinical trial data,
- Interferons, because of lack of efficacy in treatment of severe acute respiratory syndrome (SARS) and Middle East respiratory syndrome (MERS) and toxicity, and
- Janus kinase inhibitors (e.g. baricitinib), because of their broad immunosuppressive effect.

“The NIH’s recommendation is standard from anybody who is in the establishment and understands clinical research,” Don Berry, a professor in the Department of Biostatistics and founding chair of that department at MD Anderson Cancer Center, said to *The Cancer Letter*. “And the busi-

ness with HCQ is just horrible. It probably is ineffective, and worse, with cardiovascular issues. It’s a horror, and it’s based on a rumor and innuendo.

“I hate seeing medicine and science politicized. Politicians seem uniquely ignorant of both,” Berry said. “The good politicians are the ones who know they’re ignorant.”

A conversation with Berry appears on [page 10](#).

Therapeutic options that didn’t receive a negative recommendation from the NIH panel are:

- Remdesivir, an antiviral drug sponsored by Gilead Sciences,
- Interleukin-6 and interleukin-1 inhibitors, agents that are used to regulate pro-inflammatory cytokines,
- Convalescent plasma or hyper-immune immunoglobulin, and
- Chloroquine or hydroxychloroquine, as single agents.

“Yes, I would agree with [NIH’s evaluation of remdesivir],” said Berry, who is also senior statistical scientist and founder of Berry Consultants, a company that is playing a key role in providing statistical guidance for multiple COVID-19 trials. “I have a probability distribution on the benefits of remdesivir. Thirty-five percent of my probability is on the positive side. But of course, reflecting my uncertainty, as soon as I see some randomized controlled results, this may change dramatically.”

On April 24, FDA issued a [safety communication](#) cautioning against the use of hydroxychloroquine or chloroquine for COVID-19 outside the hospital setting or a clinical trial.

“Hydroxychloroquine and chloroquine can cause abnormal heart rhythms such

as QT interval prolongation and a dangerously rapid heart rate called ventricular tachycardia,” FDA officials said in the advisory. “These risks may increase when these medicines are combined with other medicines known to prolong the QT interval, including the antibiotic azithromycin, which is also being used in some COVID-19 patients without FDA approval for this condition.

“Patients who also have other health issues such as heart and kidney disease are likely to be at increased risk of these heart problems when receiving these medicines.”

COVID-19 investigators are also in the process of initiating studies focused on other types of antivirals, as well as host-modifying agents that have broad immunosuppressive effects. The NIH guidelines are expected to be continually updated as published data and other authoritative information become available.

Multiple trials for the interleukin inhibitors, especially for IL-6, are underway.

At least three drugs, tocilizumab, sarilumab, and siltuximab, are being assessed in late-stage trials for treatment of acute respiratory distress syndrome (ARDS) caused by immune response to SARS-CoV-2 infection (*The Cancer Letter*, [March 27, 2020](#)).

NCI is finalizing plans to use its clinical trials networks to administer a compassionate use protocol for distribution of tocilizumab to cancer patients (*The Cancer Letter*, [April 10, 2020](#)).

What’s up with remdesivir?

Remdesivir, an investigational nucleotide analog that inhibits RNA-dependent RNA polymerase, is not approved anywhere globally for any use.

The drug, which was found to disrupt replication of RNA viruses, including coronaviruses, was previously tested as an antiviral therapy for the Ebola virus. After encouraging early-stage studies, it underperformed in comparison to several monoclonal antibodies in a multi-arm randomized trial reported in 2019.

Studies and news reports about remdesivir in COVID-19 are closely watched by public health and financial communities.

On April 10, a [study](#) published in The New England Journal of Medicine concluded that clinical improvement was observed in 36 of 53 patients (68%) who received remdesivir on a compassionate-use basis. The study was not designed to assess efficacy, which is measured in randomized, placebo-controlled trials.

As data accumulate, Gilead is scaling up production of the drug, with a target of more than 1 million treatment courses by December and, if needed, several million treatment courses in 2021.

While remdesivir is available through several expanded access protocols, phase III randomized trials evaluating the safety and efficacy of the antiviral for treatment of COVID-19 include:

- [SOLIDARITY](#), a multi-arm study coordinated through the World Health Organization—a Norwegian version of the trial that includes a remdesivir arm is available [here](#),
- [Adaptive COVID-19 Treatment Trial \(ACTT\)](#), sponsored by the National Institute of Allergy and Infectious Diseases, and
- Two studies initiated by Gilead, one for patients with [moderate](#) manifestations of COVID-19, and the other for patients with [severe](#) manifestations.

“We expect to share results at the end of this month from our open-label study

of remdesivir in patients with severe COVID-19 disease,” Merdad Parsey, Gilead’s chief medical officer, said in a statement April 23. “This randomized clinical trial is fully enrolled and will compare treatment outcomes and safety following five or 10 days of remdesivir treatment.

“We expect data at the end of May from our open-label study in patients with moderate disease that is studying five or 10 days of remdesivir versus standard of care,” Parsey said. “We also anticipate data at the end of May from NIAID’s double-blind, placebo-controlled study of remdesivir in patients across a range of disease severity.”

Two phase III trials of remdesivir in China, sponsored by the Capital Medical University in Beijing—also delineated by [moderate](#) or [severe](#) COVID-19—have been stopped April 15, citing inability to accrue patients as rationale for terminating or suspending the trials.

On April 23, the results from the China clinical trial for severe COVID-19 were posted, prematurely, on WHO’s website:

“237 patients with laboratory-confirmed COVID-19 underwent randomization (158 remdesivir; 79 control); one patient in the control group withdrew before receiving any study treatment. Remdesivir use was not associated with a difference in time to clinical improvement (hazard ratio 1.23, 95% CI 0.87-1.75), mortality at 28 days (13.9% vs. 12.8%, difference 1.1; 95% CI, -8.1, 10.3), or in time to SARS-CoV-2 PCR. :

“In this study of hospitalized adult patients with severe COVID-19 that was terminated prematurely, remdesivir was not associated with clinical or virological benefits. negativity. [sic] Adverse events were reported in 65.2% of remdesivir recipients versus 64.1% in placebo recipients. Remdesivir was stopped early in 19 (11.6%) patients because of adverse effects, compared to 4 (5.1%) in the control group.”

The assessment, which lists the outcome of the trial as “NEGATIVE,” has since been removed from WHO’s website. The apparent slipup, [reported by STAT](#), immediately led to a plunge in share prices for Gilead on April 23.

Gilead officials disputed the assessment of the trial’s results, which were provided to WHO in a draft document by study authors.

“The results of this trial in China, along with those of the compassionate use cohort of more critically ill patients published on April 10, add to a growing but still inconclusive body of evidence for remdesivir,” Merdad Parsey, Gilead’s chief medical officer, said in a [statement](#) April 23. “We believe the [WHO] post included inappropriate characterizations of the study.

“The study was terminated early due to low enrollment and, as a result, it was underpowered to enable statistically meaningful conclusions,” Parsey said. “As such, the study results are inconclusive, though trends in the data suggest a potential benefit for remdesivir, particularly among patients treated early in disease.”

The company’s stock price had spiked on April 16 as a result of coverage by STAT, which [published preliminary data](#) from the two Gilead-sponsored trials that were accruing at the University of Chicago. In an internal video discussion among UChicago investigators, a researcher characterized early data as encouraging, based on information from her site.

Although “only” two patients died in the UChicago cohort, one of the phase III Gilead trials—for severe COVID-19—does not randomize patients to a control arm, with only placebo or standard of care treatment.

The STAT story quoted a grateful patient, who declared that “remdesivir was a miracle.”

"I'm tied to the conventional wisdom in this regard, because of examples like this. The stuff that we heard about remdesivir from University of Chicago is whim and innuendo and anecdotes," MD Anderson's Berry said. "That, of course, was a travesty—as a measure of impact, Gilead's stock price increased 14% at one point on the basis of this story that came out of the STAT publication.

"To announce trial results prematurely can have grave consequences, including affecting the trial's integrity. In the case of remdesivir, leaking some of the results was inappropriate," Berry said. "The investigators are being, and should be, criticized for announcing their narrow experiences in the trial."

NIAID's Adaptive COVID-19 Treatment Trial

With 1,063 patients, NIAID's multicenter ACTT closed to enrollment on April 19. All patients accrued on the trial were randomized to remdesivir vs. placebo (*The Cancer Letter*, [April 17, 2020](#)).

According to ClinicalTrials.gov, the study is conducted in up to approximately 100 sites globally.

"The patients are being randomized approximately 1:1. Randomization is stratified by site and the severity of clinical illness," NIAID officials said to *The Cancer Letter*. "Randomization is also done in blocks of participants, so there is not a predictable pattern to the randomization.

"NIAID will share results when they are available, and will also provide an update on plans for the ACTT moving forward."

The pathogenesis and disease course of COVID-19 in symptomatic patients means that it's possible to get results rapidly, Berry said.

"The patient's experience in COVID-19 is not like cancer. It's over with quickly, one way or the other," Berry said. "The primary endpoint may be evaluated at 21 days (or sooner in the case of death). So, provided accrual is fast, there's no reason the trial results can't be announced in a matter of a few months."

The primary outcome measure for the NIAID trial is "time to recovery" within 29 days. Day of recovery is defined as the first day on which the subject satisfies one of the following three categories from the ordinal scale:

1. Hospitalized, not requiring supplemental oxygen i.e. no longer requires ongoing medical care;
2. Not hospitalized, limitation on activities and/or requiring home oxygen; or
3. Not hospitalized, no limitations on activities.

The Gilead trials use a seven-point ordinal scale to assess primary outcomes, beginning with death. The Norwegian version of WHO's SOLIDARITY is designed to primarily assess all-cause in-hospital mortality within three weeks, followed by seven secondary outcome measures.

"My own attitude is to focus on death. It's the easiest endpoint to address and it's the easiest to understand," Berry said. "Mortality is not the only possible benefit of a therapy, of course. Generally speaking, most therapies that move patients away from mortality also have a beneficial effect on patients not destined to die. So, you'd look for some sort of movement on that ordinal scale, not just death.

"But especially in view of the high case-fatality rate for COVID-19, death would be quite a reasonable primary endpoint, with an ordinal scale being supportive."

Like the WHO trial, the ACTT uses adaptive design, which enables investigators to add arms to the trial. While the current version of the ACTT has enrolled patients only for remdesivir vs. placebo, other investigational therapeutic agents may be added if the trial resumes enrollment and interim analyses are conducted.

"All participants in ACTT were given standard of care, and if the standard of care at an institution included other medications, these were allowed in ACTT," NIAID officials said. "A randomized, placebo-controlled trial is the gold standard for determining if an experimental treatment can benefit patients.

"We can make the protocol available after the trial is complete. Since the protocol may contain proprietary information, there is a process to ensure the protocol is suitable for public dissemination."

It is typical in many diseases to randomize experimental treatments against the standard of care, Berry said.

"On the other hand, it would be unethical to deprive a patient from receiving a therapy that is known (or widely regarded) to be effective," Berry said.

The adaptive design of the ACTT allows for early termination of any arm on the basis of futility, efficacy, or safety. On the flip side, if one therapy proves to be efficacious, then the treatment may become the control arm for comparison with new experimental treatments.

"As therapies begin to show that they are better than other therapies, then they are assigned with higher probability to subsequent patients," Berry said. "This obviously benefits patients in the trial. But it also moves better-performing therapies through the trial faster, graduating them from the trial to general use.

"For me, there is no alternative. Non-adaptive trials are destined for oblivion."

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

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CONVERSATION WITH
THE CANCER LETTER

Berry: “Designing clinical trials doesn’t have high priority when there’s no pandemic. And then, when there’s a pandemic, there’s panic”

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”



Donald A. Berry, PhD

*Professor, founding chair,
Department of Biostatistics, Division of Basic Sciences,
MD Anderson Cancer Center;
Senior statistical scientist, founder, Berry Consultants, LLC*

After a series of global epidemics, Don Berry has spent the past several years preparing for a serious pandemic that would be caused by yet another viral pathogen.

“People have long said that we’re not prepared for the next pandemic. We get a pandemic and then it goes away,” Berry, a professor in the Department of Biostatistics and founding chair of that department at MD Anderson Cancer Center, said to *The Cancer Letter*. “And so everybody says, ‘Well, okay, the next pandemic is way in the future, and so let’s not worry about it.’”

Well, SARS-CoV-2 is here—on the heels of Ebola, MERS, the H1N1 influenza pandemic in 2009, and SARS-CoV in 2003.

“Designing clinical trials doesn’t have high priority when there’s no pandemic. And then, when there’s a pandemic, there’s panic,” said Berry, who is also senior statistical scientist and founder of Berry Consultants, a company that is playing a key role in providing statistical guidance for multiple COVID-19 trials. “But 10 or so years ago, global infectious disease researchers decided to take planning seriously.

“In 2014, Berry Consultants worked with a European group called PREPARE. It’s an acronym that means essentially get ready for the next pandemic,” Berry said. “They focused on community-acquired pneumonia, recognizing that these pandemics are mostly associated with respiratory problems. So, they set up something called REMAP-CAP.”

REMAP-CAP stands for a Randomized, Embedded, Multifactorial, Adaptive Platform trial focused on Community-Acquired Pneumonia. The trial has a network of over 60 participating sites across 13 countries.

To respond to COVID-19, the trial has implemented an [appendix](#) to the core pro-

ocol to allow the platform to respond rapidly to the ongoing pandemic.

“On March 11, 2020, when the WHO declared a pandemic for COVID-19, the first patient accrued in REMAP-COVID,” Berry said. “[REMAP-COVID] started out considering 72 different combinations of therapies and sequences of therapies.

“It’s running, it’s randomizing, less so in Australia and New Zealand, because they don’t have many cases. But, of course, except the United States, Europe is leading the way in numbers of cases and deaths.”

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

Matthew Ong: NIH’s new treatment guidelines for COVID-19, including for investigational agents, notably recommend against a hydroxychloroquine combination and HIV protease inhibitors outside the context of a clinical trial. What’s your take on their assessment of the evidence?

Don Berry: The NIH’s recommendation is standard from anybody who is in the establishment and understands clinical research. And the business with HCQ is just horrible. It probably is ineffective, and worse, with cardiovascular issues.

But on the basis of, essentially, a whim, doctors have been hoarding it. And so, clinical trials have had problems trying to get the drug, because everybody is using it for COVID-19 and hoarding it. And patients who have major problems and lean on the drug for help, can’t get it.

It’s a horror and it’s based on a rumor and innuendo. There’s a trial, but I hate

to even call it a trial. The French trial was 15 patients, and okay, they seemed to do okay. But patients by and large, do okay.

So, you really need to have a control, not necessarily randomized, but you’ve got to have some sort of thing to base your conclusion that it’s effective on.

What about remdesivir? The NIH guidelines state that there are insufficient clinical data to recommend either for or against.

DB: Yes, I would agree with that. And again, the stuff that we heard about remdesivir from University of Chicago is whim and innuendo and anecdotes.

That, of course, was a travesty—as a measure of impact, Gilead’s stock price increased 14% at one point on the basis of [this story](#) that came out of the STAT publication.

About that, I’ll have to circle back. What have you been working on as a scientist and statistician in this pandemic?

DB: A number of things, through Berry Consultants. We designed the REMAP-CAP trial for the International Consortium, not including the United States, but many European countries plus Australia, New Zealand, Canada. Berry Consultants are working on a dozen or so COVID trials. I’m not personally working on many of them.

Most researchers want platform trials, which is what we’re sort of known for, including I-SPY 2, and GBM AGILE, and Precision Promise in cancer.

Just a bit of history: people have long said that we're not prepared for the next pandemic. We get a pandemic and then it goes away. And so everybody says, "Well, okay, the next pandemic is way in the future, and so let's not worry about it."

Designing clinical trials doesn't have high priority when there's no pandemic. And then, when there's a pandemic, there's panic.

But 10 or so years ago, global infectious disease researchers decided to take planning seriously. This was shortly after the H1N1 pandemic.

There was a meeting in Toronto that was attended by researchers from around the world. I gave a presentation about platform trials, including I-SPY 2. The conferees decided that was what the kind of trial they wanted to build.

In 2014, Berry Consultants worked with a European group called PREPARE. It's an acronym that means essentially get ready for the next pandemic.

So, we designed a trial for them—mainly Scott Berry, my son, who's the president of Berry Consultants, and other Berry consultants—more than just a trial for preparing for the pandemic, but to have a functioning trial in place when a pandemic arrives.

They focused on community-acquired pneumonia, recognizing that these pandemics are mostly associated with respiratory problems.

So, they set up something called REMAP-CAP, an acronym. The CAP is community-acquired pneumonia; the REMAP has something to do with preparation, and adaptive and platform trials. The protocol had an appendix that is specific to a future pandemic.

REMAP-CAP has been running since 2015. On March 11, 2020, when the WHO

declared a pandemic for COVID-19, the first patient accrued in REMAP-COVID. The investigators had amended the appendix in January and February to apply specifically to COVID-19. And it started out considering 72 different combinations of therapies and sequences of therapies.

It's running, it's randomizing, less so in Australia and New Zealand, because they don't have many cases. But, of course, except the United States, Europe is leading the way in numbers of cases and deaths.

Many groups have contacted Berry Consultants wanting to do something like a platform trial. Most of them are talking about treatment, but I got one this morning that's considering vaccines and having a platform trial for vaccines.

We've also been analyzing data for people, and I hope that the latest analysis will come out in major medical publications very soon.

As well as for investigational agents?

DB: And investigational agents, yes. Everything really, but not randomized. And so, how do you do it? Data scientists and real-world evidence researchers tend to be unsophisticated. I saw something that was announced recently about HCQ. I thought the study was fundamentally flawed.

When dealing with RWE, it is essential to address the physicians' biases regarding who gets one treatment and who gets another. And there are biases in both directions. Sometimes the better-prognosis patients are given these investigational agents. Sometimes it's the worst patients who are given the agents.

So, you have to figure that out to the extent possible and adjust your analyses accordingly. People do multivariate analyses with no apparent understanding that it generally gives a nonsense answer. Real-world evidence is the cat's meow, but the cat also bites.

And that means—

DB: Which means, to mix metaphors, there are landmines all along the way, or there are cats jumping out from behind the corners and biting. To get the cat to meow, you have to know what you're doing. You have to know how to handle the cat.

Some news organizations, as you mentioned, have been publishing preliminary trial data for remdesivir and interpreting the results as positive. Is that okay?

DB: This is a big, big problem in medical research. What do you tell people when. The clinical trial system has been clear.

If it's a phase III trial, you don't tell anything. You don't tell the investigators. You blind them to the trial's results.

The remdesivir study with the anecdotes coming out, that was not a blinded trial. It was open-label. So, clinicians knew what drugs they were giving and saw what the results were. They talked out of turn and it leaked out.

Is it okay that it leaks out? That's a very, very difficult ethical, social, and unfortunately, political question. There have been issues with some organizations arguing that everybody should be told everything that's happening in a trial.

That would kill medical research as we know it. In a similar vein, some have argued that patients should have access to experimental drugs as soon as they become available, even before phase I trials. And then misinterpreting the real-world evidence in the way that I just described.

There has to be some kind of compromise here. We all believe in transparency. The clinical trials structure is not transparent. But for good reason. When I say good reason, it doesn't mean that I buy into conventional clinical trials hook, line, and sinker.

But we have to ensure that whatever changes we make in clinical research preserves the scientific method. There has to be some sort of compromise, but I don't know what it is.

I do know that the issues of transparency, trial sample size, and so on, differ depending on the rareness of the disease or condition. It also depends on the severity of the disease or condition.

To announce trial results prematurely can have grave consequences, including affecting the trial's integrity. In the case of remdesivir, leaking some of the results was inappropriate. The investigators are being, and should be, criticized for announcing their narrow experiences in the trial.

Because it was too early in the process to do so?

DB: Yes. I'm tied to the conventional wisdom in this regard, because of examples like this.

But it is something that we should keep talking about. And as we're going along, we have to figure out something that can be a way to let people know what the data are showing when it's moving

in a direction that could affect patients in important ways.

We don't want to hide something important just to hide it. We don't want to sit on data that are compelling. But the word compelling is obviously subjective, depending on who is looking at the data.

I know "compelling" when I see it, but giving an objective definition is such a difficult problem that I don't know how to do it.

One thing that the answer is most assuredly not is statistical significance. That's a concept that is essentially irrelevant for decision-making.

Not too long ago, we were bombarded by headlines about the "promise" of remdesivir in Ebola, only to see it fall behind monoclonal antibodies in phase III trials. How would you characterize the evidence on remdesivir to date for COVID-19?

DB: I have a probability distribution on the benefits of remdesivir. It's not a cure, so I associate no probability with that.

The probability distribution is on benefit at least for one level of the disease, whether it's in the ICU or in the severe stage where the patients are hospitalized but not in the ICU, and all the way back to prevention.

Does the drug have a role anywhere? My distribution is very spread out, representing my uncertainty. The mean of my distribution is small but not zero.

Thirty-five percent of my probability is on the positive side. But of course, re-

flecting my uncertainty, as soon as I see some randomized controlled results, this may change dramatically.

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The NIH has an ordinal scale, seven or eight categories where death is the worst one. My own attitude is to focus on death. It's the easiest endpoint to address and it's the easiest to understand.

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Of note are the remdesivir arm in WHO's SOLIDARITY trial, the two Gilead studies, and NIAID's ACTT. What did I miss and which phase III trials for remdesivir should we be paying attention to?

DB: You've got everything that I know about.

Most of the remdesivir trials randomize the antiviral vs. placebo or standard of care, but the primary endpoints may differ in order, i.e., death vs. clinical improvement. What's important for us to consider here?

DB: The NIH has an ordinal scale, seven or eight categories where death is the worst one. My own attitude is to focus on death. It's the easiest endpoint to address and it's the easiest to understand.

Mortality is not the only possible benefit of a therapy, of course. A therapy could reduce the rate of mortality, but incapacitate those who live, such as the celebrity patient who survived COVID-19 but had to have his leg amputated. And, too, there are outcomes worse than death.

However, and generally speaking, most therapies that move patients away from mortality also have a beneficial effect on patients not destined to die. So, you'd look for some sort of movement on that ordinal scale, not just death.

But especially in view of the high case-fatality rate for COVID-19, death would be quite a reasonable primary endpoint, with an ordinal scale being supportive.

Some of these trials are designed to be adaptive. For instance, WHO's and NIAID's trials leave room for the creation of new arms to test potential new drug combinations. This is a rhetorical question, but can you explain the utility of these designs?

DB: There are many kinds of potential adaptive aspects of clinical trial designs.

REMAP-CAP includes weekly interim analyses, including the possibility of announcing results if a particular therapeutic regimen is good, bad, or ugly.

And new therapies are added as they become available.

Another kind of adaptation is adaptive randomization. As therapies begin to show that they are better than other therapies, then they are assigned with higher probability to subsequent patients. It's something that we use in I-SPY 2, and in the first stages of registration trials Precision Promise, and GBM AGILE.

This obviously benefits patients in the trial. But it also moves better-performing therapies through the trial faster, graduating them from the trial to general use.

All types of adaptations require looking at the data that's accumulating from the trial. And the more looks the better. These looks and the actions that occur as a result of the looks are planned in advance.

So, an algorithm that dictates what decisions can be made runs the trial. In effect, a robot runs the trial. That means we can address various statistical matters, like the trial's Type I error (false positive rate).

REMAP-COVID addresses many questions, including combination therapy and sequential therapy. All adaptively.

For me, there is no alternative. Non-adaptive trials are destined for oblivion.

And the interim analyses also allow you to terminate any arm with an experimental agent that isn't showing meaningful effect.

DB: Right. Actually, that's an extreme version of adaptive randomization. You're adaptively randomizing therapies based on their performance.

And suppose one therapy is doing very badly, but the design hasn't given up on it completely. Perhaps some patients have been treated with it and their results may turn things around.

The algorithm may set its randomization probability to zero; so patients would no longer be assigned to that therapy, at least until more evidence becomes available. Or, it could be zero for patients in intensive care, but the therapy may still have a place in less severe disease.

Trials initiated by academic or public health institutions tend to include multiple arms for multiple investigational agents, or at least remain open to the possibility of adapting. The trials sponsored by Gilead test only remdesivir plus standard of care for different durations, dependent on clinical status. But, of course, it's their drug.

DB: It's their drug. And it's tradition. But I'm trying to change that tradition.

I-SPY 2, for example, has evaluated or is still evaluating 20 therapies in neoadjuvant breast cancer. And from 15 or so different companies. We built Precision Promise in pancreatic cancer and GBM AGILE in glioblastoma in the same way.

These trials consider lots of therapies and they use a variety of adaptations in each therapy's first stage. Success-

ful therapies move seamlessly into a phase-III stage.

An obvious benefit is the shared control arm. So, even if you don't do anything clever, you have potentially, up to a 50% reduction in trial cost, because many experimental therapies are sharing the controls.

Adaptive platform trials like REMAP-CAP have become part of the world, especially in Europe. They've funded adaptive platform trials beyond REMAP-CAP, including a major initiative in Alzheimer's disease, called IMI EPAD.

Speaking of accrual and completion, the two remdesivir trials by the Capital Medical University in Beijing have either been ended or halted, because "the epidemic of COVID-19 has been controlled well in China, no eligible patients can be enrolled at present." Are you seeing similar issues elsewhere?

DB: The nice thing about REMAP-COVID is it is far reaching across the globe.

In particular, and as you know, except for the United States the leading countries in terms of cases and mortality are Spain, Italy, France, the UK, and Germany, although Germany stands apart from the others in terms of mortality. So, accrual is not an issue.

Moreover, when and if COVID-19 moves south, REMAP-COVID has got it covered in Australia and New Zealand. So, the trial is flexible and adaptive, but it's also encompassing.

When do you expect investigators to present reliable, early analyses of the results from the remdesivir trials? I'm hearing late May, early June latest, but what does that mean for the strength of the evidence by then?

DB: I don't know what the accrual is. But this time frame is possible. The patient's experience in COVID-19 is not like cancer. It's over with quickly, one way or the other.

The primary endpoint may be evaluated at 21 days (or sooner in the case of death). So, provided accrual is fast, there's no reason the trial results can't be announced in a matter of a few months.

Right, NIAID's ACTT has exceeded its initial accrual goals. So, are there any contributions from oncology that you would like to note, in terms of expertise, innovation, for the development of these trials?

DB: Absolutely. The grandmother of adaptive platform trials is I-SPY 2. The grandfather is the BATTLE trial that was designed by Jack Lee and conducted at MD Anderson some years ago.

Many modern adaptive platform trials in other diseases are clones of I-SPY 2, including, like I mentioned earlier, Europe's Innovative Medicines Initiative's EPAD.

The IMI issued an RFP that said specifically that they wanted an I-SPY 2 in Alzheimer's. And I've already mentioned Precision Promise and GBM AGILE that have blazed pathways in the registration setting.

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For me, there is no alternative. Non-adaptive trials are destined for oblivion.

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So, all of these designs grew out of oncology to begin with.

DB: In a real sense, yes.

Finally, do you have any thoughts about the politics of this pandemic?

DB: Only that I hate seeing medicine and science politicized. Politicians seem uniquely ignorant of both. The good politicians are the ones who know they're ignorant.



GUEST EDITORIAL

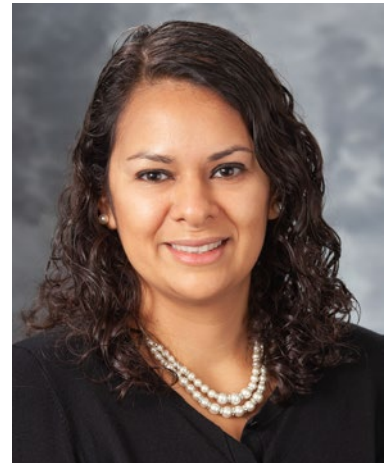
When disparities widen: COVID-19 in minority patients with cancer



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In late December, rumors regarding a dangerous virus that originated in a seafood market in Wuhan, China started spreading across the world. At the time, all we knew was that the virus resembled the severe acute respiratory syndrome, better known as SARS, and that it was aggressive and deadly.

Back then, it only seemed to be a distant thought in the Western World. By January, news about this novel coronavirus or SARS-CoV-2 causing the COVID-19

infection became more prevalent when it continued to spread aggressively, affecting countries all throughout Asia and Europe. Then, on Jan. 20, our biggest fear became a reality when the first person in the United States tested positive.

Since then, this novel coronavirus has reared its ugly head all across the country. When we were first made aware of this virus threatening our country, our fear as oncologists became one: “What

will happen to our patients with cancer?” Initial data from China and Italy about the infamous COVID-19 infection suggested that the virus tended to be especially dangerous to our older adult patients. That changed quickly when data later supported that pre-existing medical conditions also placed individuals at higher risk for contracting the infection and developing complications.

Recently, troubling trends and data from across the country started to

suggest that minority populations, especially Hispanic and black, are experiencing higher risk for COVID-19 infections and mortality that outpace the different state's population. Data released from New York City revealed that Hispanics make up 29% of the city's total population, but account for 34% of COVID-19 deaths.

Blacks, on the other hand, account for 28% of COVID-19 related deaths, but make up 22% of the city's total population.¹ Similar trends were seen in Chicago, where black residents comprise 29% of the city's population, but account for 72% of the COVID-19 deaths.² In California, the Latinx/Hispanic community, which makes up 39% of the state's population, has accounted for 38% of confirmed COVID-19 cases and 31% deaths. The black population, which makes up 6% of the California population, account for 7% of COVID-19 cases and 12% of deaths.^{3,4}

The trends reported above represent only the confirmed COVID-19 infections in Hispanics and blacks. This early data can be expected to be confounded by unequal access and availability of testing. One can presume that the actual numbers and percentages of minority patients affected is higher than what is reported, as it is likely that many have yet to be diagnosed.

Racial and ethnic minorities are often from lower socioeconomic backgrounds and commonly live in higher-density households and communities, which increases their exposure to the virus and limits the possibility of practicing social distancing.

We have also seen minority populations be targeted and negatively affected by an unfair health system that gives them inadequate access to care. Minority patients have higher tendencies to be uninsured. Reports have showed that the

uninsured rate for blacks was 11% and 18% for Hispanics as of 2018.⁵

As physicians, we have experienced the implications this can have on the health of these patients. It is well-documented that race/ethnic minorities have a higher prevalence of diabetes and hypertension than non-minority individuals.^{6,7} In 2011-2014 47% of Hispanic and 46.8% of non-Hispanic black adults had higher prevalence of obesity than non-Hispanic white adults⁸. These are all associated with increased risk for complications from the virus.

As of yet, there are no published data regarding COVID-19 affecting minorities with cancer, but we can safely presume how these trends will impact our patients. If otherwise non-cancer Hispanic and black people are at increased risk of infection and mortality, we can only imagine what that could mean to our minority patients who also happen to suffer from cancer. Even the thought of it makes us fear 10 times harder for our patients who have already in their battles gone through so much.

In attempts to protect our patients, we have changed the way cancer centers practice and have transitioned physical visits into virtual or telehealth ones. But how can one say that this transition can be beneficial to all?

Since the COVID ordeal started, we have heard statements such as "we are all on the same boat." However, as many have interestingly pointed out, we might all be in the same waters, but, in the midst of this pandemic, we are certainly not in the same boat. Not all of us have the same means when it comes to facing this pandemic. Some are in yachts, others in sailboats, and some can find themselves in river rafts.

We recall the story of our patient, a 75-year-old Spanish-speaking female with high blood pressure, and heart

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disease who in early February had been diagnosed with acute myeloid leukemia (AML). She was due to start chemotherapy after her initial diagnosis, but she contracted COVID-19 and required a prolonged hospitalization. One with no visitors allowed and no one to speak her native language.

After weeks alone in the hospital, battling her leukemia and COVID-19, she was successfully discharged to rehab. Unfortunately, treatment for her AML continued to be delayed due to ongoing cytopenias and deconditioning from her terrible diseases, recalls Dr. Olazagasti. Like this patient, many others are experiencing delays in diagnosis and treatments since this pandemic started.

For some lower socioeconomic status' patients with cancer, clinical trials are the only possible option to receive cancer-directed treatment and access to medication. Pausing clinical trials means no other possible treatment available for these patients.

For others, halting physical visits and transitioning to telehealth might not be as convenient. Often, they don't have the luxury of having smartphones or laptops with internet access to be able to see their oncologist face-to-face during virtual visits. Commonly, they find themselves owning prepaid phones that can run out of available minutes at any time. Even if they have more advanced smartphones, they may lack the knowledge as to how to access newer technology.

In many instances, Hispanics and blacks, are part of essential work force with occupations like cleaning and maintenance, food preparation and serving, transportation, health care support⁹—occupations that may not allow them to take paid sick leave or the needed time off to check in with their oncologists through virtual visits.

Also, data has shown the risk for contracting COVID-19 according to occupations, accounting for the proximity to others during the workday. Besides health care workers, many people who do service jobs like care aides, cashiers, fast-food workers and janitors make up the bulk of some of the most at risk and lowest income occupation¹⁰.

As physicians, we all wish we could do more for our patients during these arduous times. As oncologists, we have an innate desire to tend to our patients and provide comfort. The way we practice has drastically changed, and we have all had to adapt during this uncertain time.

All we can hope for is that we are still able to provide the support and care that our patients so desperately need. All we can strive for is to be available for our patients and show them that we are all in this fight together, and that their care and safety remain our main priority, even from afar. Every patient, regardless of their background, deserves equal treatment.

The holistic and integrative approach of cancer care has never been more essential than it is today.

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GUEST EDITORIAL

COVID-Lung Cancer Consortium:

An example of how the lung cancer community came together in a challenging time



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The COVID-19 pandemic has created a host of diagnostic, treatment, and follow-up problems for patients with cancer of all types, and this is particularly true for patients with lung cancer, their families, and health care providers.

Everyone wanted to know and was worried—would patients with lung cancer be more or less likely to contract COVID-19, and if they did so, would they have more serious disease?

Would their susceptibility to and course with COVID-19 be influenced by the type of treatment they received, such as checkpoint inhibitor blockade, chemotherapy, radiotherapy, or surgery? How would COVID-19 in lung cancer patients respond to COVID-19-targeted therapy?

To address these concerns, voiced by our patients and the large cadre of thoracic oncologists treating lung cancer patients, the COVID-Lung Cancer Consortium (organized through Icahn School of Medicine at Mount Sinai), was established to bring the lung cancer community together during the COVID pandemic.

In addition, it was clear that many of the resources created by the lung cancer translational research community could, in turn, be of potential benefit to studying and understanding SARS-CoV-2 virology.

For example, there are very few human lung epithelial cell strains where SARS-CoV-2 replicates. The large panel of human lung cancer and lung epithelial cell strains that also express ACE2 could provide a totally new resource for SARS-CoV-2 preclinical studies, such as drug testing.

Thus, we needed an organized format for discussing response to urgent patient issues during the current situation,

how different institutions, organizations and investigators could collaborate on issues related to unforeseen changes in patient care, clinical trials and to develop collaborative relevant scientific projects.

The forum has representation from thoracic oncology investigators at multiple academic institutions, patient advocacy organizations, NCI, NIH, professional organizations such as the American Society of Clinical Oncology, American Association for Cancer Research, and the International Association for the Study of Lung Cancer.

More than 70 people are participating in virtual meetings every second week. The initiators, Drs. Bunn, Hirsch and Minna, think this demonstrates an outstanding example for how the patient care and cancer translational research community can come together to help our lung cancer patients and learn from this epic event.

We think it is likely that many practices we are being forced to develop in response to the pandemic will be adapted and stay even after the pandemic is over.

From a patient care point of view, we need to develop an in-depth understanding of issues involved in telemedicine, wearable device monitoring at a distance (e.g. pulse oximetry, temperature), health disparity challenges, surgical and diagnostic procedures, development, accrual to and execution of clinical trials, patients understandable fear of contracting COVID-19 infection during clinical interactions, the role of diagnostic and surveillance COVID-testing.

A key aspect of this is prospectively collecting data on large numbers of lung

cancer patients to have data down the road to answer these questions through trials, such as:

- **TERAVOLT** [Co-PI: Leora Horn, MD, MSc, FRCPC, is an Ingram Associate Professor of Cancer Research at Vanderbilt Ingram Cancer Center and associate professor of medicine in the Division of Hematology/Oncology at the Vanderbilt University Medical Center], and
- **COMBAT-COVID-19** [PI: John Heymach John V. Heymach, MD, PhD, chair, Department of Thoracic/Head and Neck Medical Oncology, the David Bruton, Jr. Chair in Cancer Research, and professor, Department of Cancer Biology, MD Anderson Cancer Center].

A variety of perspectives and information on the approaches, educational aspects, and scientific projects and opportunities being developed at different locales are discussed. The consortium also has collaborations with infectious disease and epidemiology experts.

NCI is providing new funding opportunities and advice on how to deal with the sudden change of scientific focus and questions brought by the pandemic.

Overall, the consortium provides a venue to identify challenges and opportunities, harmonize activities, and facilitate collaborations on these urgent scientific matters.

If you would like to join the COVID-Lung Cancer Consortium, contact fred.hirsch@mssm.edu.

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

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CONVERSATION WITH
THE CANCER LETTER

Feist-Weiller mammography vans repurposed to screen for COVID-19 in northwest Louisiana

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In many of these underserved communities, this van is their sole source of medical support. It goes out and does normal health care, normal screening, cancer screening, and we have a good rapport within those communities.

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Andrew D. Yurochko

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At least for now, Feist-Weiller Cancer Center at the Louisiana State University Health Sciences Center at Shreveport has repurposed the three vans that were used to provide cancer screening and essential health care to medically underserved communities.

In some areas of northwest Louisiana, the Feist-Weiller program, called Partners in Wellness, while focused on mammography and other cancer screening, also provided the only health care available. Now, the program's three vans offer testing for COVID-19.

"In many of these underserved communities, this van is their sole source of medical support. It goes out and does normal health care, normal screening, cancer screening, and we have a good rapport within those communities," Andrew D. Yurochko, director of research at Feist-Weiller Cancer Center, said to *The Cancer Letter*. "Many of the drivers have been there many years, maybe as the vans have been around. The community knows the drivers. Many of the nurses and the clinicians that go out are also well known. Within the community, it's a trusted asset."

Yurochko is also professor and Carroll Feist Endowed Chair in Viral Oncology, vice chairman in the Department of Microbiology and Immunology at Feist-Weiller Cancer Center, and director of Research at the Center of Excellence for Arthritis and Rheumatology at Louisiana State University Health Sciences Center.

COVID-19 provides a lens into the deep health disparities between rural and urban populations in northwest Louisiana, parts of Arkansas, and Texas—all regions that Feist-Weiller Cancer Center serves.

"Many in the underserved communities, again whether suburban or rural, don't have a primary care physician and don't

really have a strong access to health care. So, they can't reach out to find out whether this is a common cold, or flu, or really COVID-19," Yurochko said.

"That same idea, whether it's a virus or a cancer, heart disease, or any element—it's been emphasized and exacerbated with the virus. You get the virus, and you get symptoms five to 10 days later. If it gets severe, it's a very rapid onset—and with a cancer it can be months, years or decades. That same thing that we're seeing with the virus is just extended in cancer," Yurochko said.

What does COVID-19 teach us about these disparities?

"If we don't address the issues from a standpoint of dollars and cents, we won't be able to have expanded health care availability," Yurochko said. "I hope this issue with negative acute outcomes in the underserved community really highlights that we need to do something."

"If it does highlight that point, and if money were to be available, I think we could have, via this very sad current outcome, a better positive outcome long-term in the context of cancer or any other type of chronic disease," Yurochko said. "If I had a crystal ball, I'd probably be a rich man, but I wish that that crystal ball would tell us that we will see expanded health care. I just don't know if that's the case."

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

Alex Carolan: How is Feist-Weiller Cancer Center addressing disparities of COVID-19 in Louisiana? Can you tell me about the vans you send out for rural areas for COVID-19 testing?

Andrew D. Yurochko: We serve both urban and rural communities. It was originally set up for women's health and mammography, but it's been expanded to cancer across many spectrums, as well as normal health care—in the context, that if you're going to do a cancer screening, you need to have normal background for blood work and body weight, etc.

And the vans, through our Partners in Wellness, have a series of steps we use to promote health care in our parish communities. The vans were purchased for the Louisiana State University Health Sciences Center via private money in a public-private partnership. These vans are designed to go out to the underserved in the context of cancer screening. In addition to the cancer screening and health care, there's also education. We have an education component as part of Partners in Wellness, that does talk about health care. It talks about obesity and cancer, smoking and cancer, diet and cancer, etc.

All of this goes hand-in-hand. What we've done in the context of COVID-19, the pandemic disease caused by infection with SARS-CoV-2, we've utilized the setup that this van has—both in the actual physical aspect of having a van that's set up for medical health care—and the partnership that the cancer center has set up with the community.

In many of these underserved communities, this van is their sole source of medical support. It goes out and does normal health care, normal screening, cancer screening, and we have a good rapport within those communities. Many of the drivers have been there many years, maybe as the vans have been around. The community knows the drivers. Many of the nurses and the clinicians that go out are also well known. Within the community, it's a trusted asset.

What we are trying to do in the context of community health with the pandemic is utilize these vans and the community outreach that's set up to sort of repurpose these vans, if you want to call it, to go out collect samples for our new viral diagnostic labs. The vans are already in play or already available. There are three different ones.

We have the appropriate nursing staff through our new diagnostic lab, the Emerging Viral Threat lab. These trained personnel who know how to do the appropriate swabs to get testing for the virus. We can send in our vans using the existing infrastructure, the vans, the communities that these vans already work within.

Whether it's a rural or urban community that has maybe a single health care system, or a clinic that we know the physician or they know the physician, we can coordinate with them to have meetings spots—and basically utilize a format and a structure in place and a community trust can go out and do this community service, which would be to get nasopharyngeal swabs and test for the presence of the virus.

We obviously follow all CDC, federal and state guidelines on testing right now. For the current situation, we are testing with the knowledge of a physician saying we need someone to be tested via a series of guidelines that they have. Eventually, we'd like to move from the now of targeted screening, to a more broad screening plan as we open up the state. We'll be able to use the same van, following expanded guidelines to do greater testing—say in nursing homes, or underserved communities, to get local businesses back online to be able to test the workers, the owners, and other community members in this underserved population.

The vans don't just go to the Shreveport and rural and urban aspects of our local

parish—it really handles the entirety of northern and central Louisiana. We're right smack in the middle between Jackson, the capital of Mississippi, Little Rock, the capital of Arkansas, and Dallas, Houston, and Baton Rouge. We are the one city in the middle—and can reach all the underserved within, really, three states. A lot of these areas in Louisiana, southern Arkansas, eastern Texas, and even as we go towards eastern Louisiana along the Mississippi River Delta, these are very poor areas. There are a lot of people who are in the classic sense underserved. The van really is their only source of medical assistance, medical health, diagnoses.

By utilizing the van for the context of the SARS coronavirus diagnosis and/or helping those citizens out, we can of course make a difference in their health, but also give them a diagnosis in an area where there's very little testing. We can go forward as we try to open up the state, to provide these rural parishes, or smaller cities, and the underserved in both urban and rural environments—provide them with a chance to receive a diagnosis for the virus and/or serology testing for the presence of a past infection with the virus.

Your cancer center is really in this unique position and has the unique resources to get testing to areas that may not otherwise have access.

AY: Correct.

What does COVID-19 teach us about addressing these disparities?

AY: In regard to health disparities, it has been reported in various newspapers and by the [Louisiana Department of Health](#) that in the context of racial disparities, the African American community in Louisiana has a higher incidence of infection and a higher case fatality rate.

And the numbers are very striking, based on the ones that I have seen. It tells us really when you look at the root causes, that the inability to access health care has a major impact on health outcome. This is an issue I think our cancer center and our medical school, which was really set up as a charity hospital to cover the indigent for the underserved in this part of the state—have always recognized.

It's obviously a very sad situation and very unfortunate situation, but I think it highlights the need for additional care and real need to reach out to our underserved community members.

It would be great if we'd go back in time and address this 20 to 30 years ago and be in a better situation now, but I think what it's telling us is emphasizing what we know to be true and what we need to address. It's putting it front and center in the news, that the African American community is seeing a much greater rate of infection than the caucasian community, and we're seeing a higher rates of fatalities too.

As a human and as a faculty member at a medical school, I hope that the state, the federal government and all of us can do more to help solve this problem. In fact, our governor just set up a task force to address this issue. Members of our cancer center outreach programs are on that task force. That's really what our mission of the cancer center has always been. It is also what our new lab that's partnering with the van and aspects of the cancer center is hoping to do via some of our community money that we received to specifically meet the

needs this underserved members of our community in the context of viral diagnosis and appropriate care.

It certainly doesn't address all the health care issues, but I think at least gets us a little closer to addressing community health care and community outreach. It provides chance of getting people in all communities back to work. Obviously, if they're sick, we hope to get them identified as testing positive for the virus and provide them with appropriate health care.

If you don't get treated early enough, that is a problem. Things can go from difficulty breathing to much, much worse, and it can happen very quickly—and really, in a matter of hours. And in the community that doesn't have access to health care or for people who don't have cars, this can result in a fatal outcome very quickly.

Essentially, these vans are able to be proactive for treatment. They can be screened for COVID-19, find out whether they have it, and maybe seek treatment earlier.

AY: Correct. That's our goal. Now, initially, we have to follow CDC and state guidelines on testing, which being a physician or somebody in that sort of role has to identify the patient with symptoms.

Now, as we open up and they relax the guidelines so that we can start screening more in the community, then we will absolutely be able to expand that ability to be proactive in the underserved community. All the first responders are always going to get tested, physicians on the frontline, health care workers, faculty at the medical school to be able

to go back to work—are going to have a much easier chance because we're required to be tested to actually be in a medical school and/or hospital setting.

But this opens up, as you mentioned, proactively, the ability to screen community members that work in many aspects of the jobs that we want to be opened up—from trash collection to restaurant workers, to workers that work in grocery stores, or other appropriate businesses. It really has an effect or will have an effect on the entire city, and the entire parish and the region.

To broaden this a bit, how have protocols changed at your cancer center since the start of the COVID-19 outbreak?

AY: In the context of cancer treatment, anything that's required for life, to maintain life, so anyone with a severe cancer who's undergoing chemotherapy, all those things that are important to keep a patient alive will certainly continue.

What has certainly stopped in the context of cancer center is anything that could be put off. For instance, some sort of skin cancer that obviously was not metastatic, hadn't broken the layers and wasn't going to be a significant issue. Those sort of things that they say we can deal with this next month, or so. None of that will be handled now.

Before, many people, they saw a little lesion and said "Can I take it off next week?" Assuming you could see a physician, they would do that. All that sort of stuff's being postponed. My guess is, if you had some significant issues and you had an emergency, and needed to see an oncologist, they would definitely make time for you.

If someone had serious leukemia or something that needed to be treated now, they're not going to prevent that from taking place. I hate to say anything cancer-related is not essential, but in that context, anything that can be postponed at least safely, will not be handled right now.

And that seems to be the case across the country. As a result of COVID-19, how might these disparities in cancer patients be exacerbated down the line?

AY: That is a difficult question to answer, and it's obviously very relevant. I think the issues that we've seen—COVID-19 as a disease, and the health disparities in the context of infection and fatalities—have highlighted how lack of health care access is a significant problem. If we don't address the issues from a standpoint of dollars and cents, we won't be able to have expanded health care availability.

Like I said, our cancer center does that, but we have to work within the confines of the money that we have—private donations, public donations, health care dollars from the state and the federal government. To do this, there is a limit.

I think emphasizing the issues with the viral infection says that if we don't do a better job in the context of reaching out with community health, identifying stigmas, identifying issues that require attention—what is something that you need to go see a physician for, what is not?

Again, remember many people in our communities don't even have a primary care physician to talk to. This is something that was emphasized with COVID-19, that when someone has a

fever and/or symptoms, potentially, of COVID-19, everyone says, “Oh, call your doctor and ask if it’s a problem and what should you do.”

Many in the underserved communities, again whether suburban or rural, don’t have a primary care physician and don’t really have a strong access to health care. So, they can’t reach out to find out whether this is a common cold, or flu, or really COVID-19.

That same idea, whether it’s a virus or a cancer, heart disease, or any element—it’s been emphasized and exacerbated with the virus. You get the virus, and you get symptoms five to 10 days later. If it gets severe, it’s a very rapid onset—and with a cancer it can be months, years or decades. That same thing that we’re seeing with the virus is just extended in cancer.

Now I hope, again, as a person who’s interested in community health and working in the public health care setting, I hope this issue with negative acute outcomes in the underserved community really highlights that we need to do something.

If it does highlight that point, and if money were to be available, I think we could have, via this very sad current outcome, a better positive outcome long-term in the context of cancer or any other type of chronic disease.

Again, that’s going to require community health outreach and funds to support that mission. I hope that that will happen. It’s going to be a very difficult, as we all know, economic time in the next year or two. If I had a crystal ball, I’d probably be a rich man, but I wish that that crystal ball would tell us that we will see expanded health care. I just don’t know if that’s the case.

I know our mission in our Emerging Viral Threat lab, will be to help these

diagnoses, both PCR for detection of the virus and serology to detect possible evidence of infection will continue. We will also continue to meet our mission to care for the underserved and do education and outreach within that community.

How could COVID-19 change how treatment works in a post-pandemic setting? Whether this means expanding your Partners in Wellness program, among other things.

AY: I think many things will change, as we see things that worked and things that didn’t work, by staying home we saw benefits of telemedicine, and of online learning at college and high school settings. In the context of education, I think we’ll see a lot more online education. I bring that up not just for elementary or high schools, colleges, but that also means community outreach could be done via that online mechanism.

On the other hand, I think we have to be careful not to overreach with that, because in communities that don’t have strong access to the internet and computers, that sort of element will be delayed. We’ll have to find a way to reach out whether that be through a local community clinic and churches in underserved communities, maybe we could have teleconferences with multiple people on the context of education.

Again, these are just some ideas and people have to think about them going forward.

But in a broader sense, I think telemedicine is going to be a way to move forward as we continue to maintain social distancing, which seems like it’s going

to be an issue for the next few years at the very minimum.

I think it also provides more rapid and easy access to health care. A rural physician will be able to have access to all of the modern tools as a large health care setting, such as a medical school, where you could call in and say, here’s my patient, what do I need to do? What do I need to check on? Here’s their number—rather than send a patient to the city or to our med school, we could almost do that from a distance.

As I said, in communities that don’t have access to a computer, we still need to have boots on the ground and thus we will have to be able to consider all elements. So whether they’re boots on the ground needed with the face-to-face, as much as you can deal with that in a pandemic or post-pandemic environment, as well as an electronic mechanism. I think those are things we will have to consider.

I’d like to switch gears a bit to discuss research-related endeavors at Feist-Weiller Cancer Center. You mentioned the Emerging Viral Threat lab. What is it, exactly? How does it work?

AY: We, being many folks at LSU Health Sciences Center, created it from scratch. We had some open labs that we used to build this lab, using the expertise of researchers in virology, microbiology, and immunology. It was a multi-talented series of folks that put this together. It’s not one single person that was involved in this. Many people came together to make this work.

What we did, we set up a lab where we can get samples from the hospital,

from clinics, from van swab patients, and other sources. We could then process those samples into our electronic records. We then take those samples into what we call the hot room, which is where the vials from patients with potentially live virus are processed via a robot. These samples go from virus in the swab to RNA, which can then be taken to the next room for the next step of the processing.

Obviously, everyone's using proper protective equipment in the lab, and especially in the hot room. We can then take those samples and do what we're asked to do, whether it be detecting the virus through some mechanism like PCR—and we have done this in a validated clinical setting. Our lab is validated to do these tests, and we try to get answers out in 36 to 48 hours. But we've been really pretty close to 24 hours from the onset of the sample testing to the outcome, which is a bonafide report that's been medically verified, and is then sent to the physician in charge.

This Emerging Viral Threat lab, or the EVT that we set up, has short-term goals—being to diagnose the virus via PCR as well as serology to test for antibodies to the virus. That's our short-term goal. For the mid-term, our goal is to get people back to work, to do more community screening as you see and hear in the news. This ability to go out in the community and do wider spread testing will help with this goal.

Then long-term, we like to set a tone of being a laboratory that continues surveillance—whether a year or five years from now—and opens us up not just to test for the current virus, but other things from the flu, to new pandemic-type viruses that might arise—as well as modulating research within the community that could be of fundamental importance through its ability to di-

rect, and new treatment options for this virus or others as well.

What other forms of research are being done at Feist-Weiller Cancer Center and Louisiana State University Health Sciences Center?

AY: We are doing clinical trials, and this is really the interwoven nature of all this stuff we've been talking about. By having our lab diagnose patients quickly, we're able to know who was positive, and therefore who had COVID-19, and to then open those patients up to clinical trials.

As you mentioned, these trials are not directly through the cancer center in the context of ongoing oncology type trials, but they are set up through the lab and the school—and since the lab was piggybacking off the genomics, the cancer genomics lab, it's all interwoven.

One such trial is inhaled nitric oxide, this is a gas that had been used in children, and it's an element that is important in preventing lung damage. The idea is, in a very colloquial sense, that the difficulty people have breathing is caused by lung damage due to a viral infection.

If there are products, in the case of this inhaled gas, it's very rapid. It gets in and it is hoped that it can mitigate some of the damage caused by the virus and improve lung function. It's also not a gas that gets rapidly taken up into the blood system in this case, but rather it can directly influence lung function.

So, by having this lab, and having a medical school willing to do this, we're one of only a few medical centers testing this inhaled gas for outcome in COVID-19 pa-

tients. There's no data yet on whether it has worked in the context of improving outcome. All other studies have shown that it should be efficacious.

In the context of convalescent plasma, that's the idea that someone who's had the virus has antibodies in their plasma. If you put those antibodies into a sick patient, those antibodies will run around the patient so to speak, and block viral infection and replication, mitigating disease and hopefully showing a positive outcome and a quicker recovery.

Again, through the lab we have set up serology, and this is a collaboration with our life share blood group here in Shreveport. We look for people who have recovered from the virus. We take some of their blood, we test it out in our serology assay, make sure they have antibodies to the virus and what that antibody titer really is, and then we can use that plasma as a treatment for others in our ICU who might be very, very sick.

I'd like to talk about how Louisiana got to the point where it is now in terms of the prevalence of COVID-19. What happened?

AY: Sure. As you know, everyone knows that Louisiana is a very festive state.

Mardi Gras is the same as Fasching, or Carnivale, which occurs in many countries around the world. It's a huge tourist draw. New Orleans's Mardi Gras is a big deal. People come from all over the world, all over the country. In Shreveport, the other end of the state, there are also multiple Mardi Gras parades and festivals and so forth.

From a virus standpoint, these are large groups of people where there

can be tens of thousands to hundreds of thousands, really over a period of several weeks. All of these people coming together in close proximity, and it's very likely there were a few people probably asymptomatic shedders in those large groups—with people shoulder-to-shoulder, involved in all the fun stuff that's Mardi Gras. It's very likely this allowed the virus to unfortunately just blow up from an infection standpoint, and thus get access to huge numbers of people that then dispersed going to multiple parishes in Louisiana, and multiple states around the country, and probably even multiple countries around the world.

The same thing holds true for Shreveport where I'm at. There are Mardi Gras parades here, and a lot of the local people from five or six different states—from Texas, Arkansas, Mississippi, Oklahoma—and probably as far away as Tennessee, and I'm sure other states as well come and have fun at these festivals. It's just a large group of people. Again it's what a festival is, to get together and have a good time.

From a virus standpoint, it's a giant incubator to rapidly spread virus. I think this is what happened, and we saw the first cases in New Orleans really about two weeks later, coming into emergency rooms with atypical pneumonias—and the same thing roughly happened here in Shreveport. It's just an unfortunate circumstance, and very sad.

Right now, I think Louisiana is in the top five or so when thinking of our population and numbers of tested positive patients as well as deaths—it's a very high level and we've been very heavily affected.

We've mentioned some of it in the context of overall numbers, but also the

disproportionate effect on underserved communities. So it's really a very sad situation and very unfortunate the way it is and at least elements of Mardi Gras contributed to this infection rate. I don't want to put all the onus on that, because, obviously, the virus was already here much earlier than we realized, which is based on new data, so there were kids in school, people shopping, etc that also contributed to viral spread.

I think when we go back and take a look, what we're going to see is it was probably more widespread in the community a lot earlier than we realized in what we are calling asymptomatic shedders.

It was really in those healthy individuals spreading below our limit of detection that helped spread the virus. It was only when it got in nursing homes and in people with some of these other illnesses that it really blossomed in a negative way as a virus.

And so at Mardi Gras, the virus just did what a virus does, which is spread and spread. I really think that Mardi Gras—and it's been in the newspaper here locally and throughout the state—was a breeding ground for dissemination of the virus.

It was just a perfect storm for the virus that people are wall-to-wall, bumper-to-bumper there. They're at parties, they're having a good time, all the frivolities that go with that. Then again, obviously, they came back home from Mardi Gras in February and spread it to kids, who went to school, who then spread it to other kids, who in turn brought it home to parents, and churches and work, etc.

You had a larger underlying viral load, so to speak, that that then allowed it to more quickly explode. That's at least, I think, a pretty viable explanation for what happened.

And you saw similar things in New York. They had the St. Patrick's Day celebrations. Nothing was shut down then yet. In Florida, you had spring break along the beaches. Many states weren't proactive enough in this whole scenario. So, where do we go from here? How do we get past this?

AY: So, I think that's truly a billion-dollar question.

How do we get by? There are a number of different models that are out there, and none of them at present, say, we're going to get rid of the virus. It's within our population, whether it's long-term, like some of the benign coronaviruses. Put in perspective, this particular coronavirus is in the beta coronaviruses.

The first SARS coronavirus, the MERS coronavirus and two of the four benign coronaviruses that cause some of the common cold are all grouped closely together. All of these viruses, jumped from animals, some from as early as the 13th century, and some up as you know just last year.

There are four benign coronaviruses.

Two of those, OC-43 and HKU-1 are the two mostly closely related to the SARS-COV-2, and they are in the normal community. They seasonally come in, cause the common cold, they disappear and come back year in, year out. And the questions then, are what's going to happen with this new virus? Is it going to be a seasonal player and show that type of a feature, a seasonality of every winter?

We do know that from studies in Brazil, Australia and other countries with warmer climates are seeing outbreaks right now, suggesting that the virus does fine in warmer climates. How does this country deal with it? A lot of it depends on unknown areas. Is this a virus that's going to slowly mutate like the benign coronaviruses and become less dangerous, to be a seasonal common cold, or would it become more dangerous? Is this virus going to be maintained in its somewhat nasty form and level of fatality?

There are a number of different variables. We just don't have the data, it seems like it might be five times worse than the flu, to maybe 20 or 100 times worse depending on what study you look at. We won't know until we have more data, but I think short-term, it's very likely to be around in the summer in some form and then to return in the fall. Kids are going to go back to school and we're going to have to continue social distancing or there will certainly be a flare up of viral infection.

We're going to have to continue screening. We've talked about the van. Part of our mission is going to be to continue going into the community, screening for the virus and for antibodies via serology, to keep our community safe. If there're outbreaks or hotspots, we're going to want to trace those infections to keep it from getting out of control.

Obviously in schools, we don't want it to be prevalent in schools. We don't know when a vaccine will be made. They're talking 12 to 18 months, but that would be the fastest vaccine ever made, and obviously every person probably on the planet is hoping that the vaccine actually meets that deadline. But most vaccines take five years, 10 years or longer—and so, it is a lot of unknowns. There's a lot of very interesting models

out there with information saying it will be a seasonal virus to saying it will be a biannual virus, obviously coming back every other year.

The new normal may just be that this virus is around us for the long haul. I hope, ultimately, from the virus standpoint, that it acts like the benign coronaviruses that did jump from animals and became one of the harmless causes of the common cold. The thing is, these other four coronaviruses did jump from farm animals and other animals. They know that from sequence and fingerprinting of the viral genomic sequence. So we hope this new virus will also become less a problem with time.

These coronaviruses jump species on a normal basis, and over time, when they do jump, they in the end usually become more benign. That's really the hope, that long-term they become more benign and just cause a common cold-like illness and normal upper respiratory infections, and not one that has the high rate of fatalities that the current one has. That would certainly be a hope, as is getting an effective vaccine that can mitigate infection. But yeah, right now we're going to have the new normal—this virus and dealing with elements of it for quite some time.

Absolutely. And is there anything else you'd like to add?

AY: It's important that we talk about the lab, in the context that it was set up as a real group effort by many people, from administrators to scientists, to clinicians, to nurses, to computer programmers, to try to help our community in this pandemic.

It started from a grass roots lab working with aspects of our cancer center, and expanded to an important element in community service, committee outreach, and community health. It's one of the things that we had talked about earlier, that since it's part of the LSU Health Sciences Center, the medical school, which is a state school and not part of the hospital, we can more easily perform community outreach and care for underserved—where the hospital's lab that does the same function is set up to care for patients that come only into the hospital.

I think that's an important distinction, and one that I think we can have really a strong effect on the community. It's a little bit of a model for at least the state, and maybe others, of how a collaborative endeavor between many different players can have a positive outcome and a positive effect on our community.

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Part of our mission is going to be to continue going into the community, screening for the virus and for antibodies via serology, to keep our community safe. If there're outbreaks or hotspots, we're going to want to trace those infections to keep it from getting out of control.

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

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CONVERSATION WITH
THE CANCER LETTER

Tulane Cancer Center chips away at the “digital divide” that keeps the underserved from benefiting from telemedicine

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The patients who do need to be seen, we are caring for, and that’s an important message as well. We’re not neglecting to take care of our cancer patients. We’re providing care as best we can under extenuating circumstances.

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A. Oliver Sartor

*Professor of medicine, medical director,
C.E. and Bernadine Laborde Professor of Cancer Research,
Tulane Cancer Center, Tulane University*

In the past, few patients had Oliver Sartor's personal cell phone number.

Since the COVID-19 outbreak in New Orleans, Sartor, professor of medicine and medical director of Tulane Cancer Center, C.E. and Bernadine Laborde Professor of Cancer Research, gives out his number to all patients as part of telehealth visits.

Telehealth can include scheduled calls on the landline or a full workup using electronic medical devices paired with the patient's laptop. But when standard telehealth approaches fail, the doctor and patient text each other.

"There is a divide by age. There's a divide in the city and the country with regard particularly to the internet," Sartor said to *The Cancer Letter*. "There's a socioeconomic divide, and to some extent, overlapping with that is probably a racial divide, given that African Americans are more likely to be at a poor socioeconomic strata. There are many African Americans in rural parishes in Louisiana as well."

"But you know what, you pick up the phone and you call. Everybody has a telephone," Sartor said.

Tulane Cancer Center has adapted in many ways to COVID-19, from providing testing to asymptomatic patients who receive chemotherapy, to transferring care from in-person visits to telehealth visits when possible.

Now, most patients have Sartor's cell phone number.

"The thing that has been tremendously helpful is texting, because so many patients can receive a text or an email and a lot of times just reaching out via text or email has been tremendously helpful," Sartor said. "I have avidly collected cell phone numbers from all patients, and have used texts and email as a relatively routine part of our communication.

But, obviously, we tilted that way now. What's a little bit unusual is that virtually every patient has my cell phone, so that if they need to reach out, they can reach me and we can handle the issue."

After the pandemic, telehealth will become a more routine part of care for cancer patients, Sartor said.

Of course, "there is certain testing that occurs in a specialized center. We're able to do genomics that are not typically done elsewhere. We're able to run very particular scans that are not done elsewhere," Sartor said. "I think there could be a greater use of telemedicine and a greater comfort with telehealth and telemedicine in this sort of post-COVID world."

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

Alex Carolan: How are things there?

Oliver Sartor: Well, I think the first piece you need to know is that we really have bent the COVID-19 curve, and our numbers of admissions are diminishing. The numbers of deaths are diminishing in New Orleans. The numbers of new cases are diminishing. We really have done a good job with the isolation—and actually, Louisiana has some of the highest per capita testing rates of any state.

We've done relatively well, I think, but did not have the density of population that a place like New York City does. New York has been really tough.

And when you say that these numbers have been decreasing in terms of deaths and positive cases, is this in your cancer center or statewide?

OS: This is both statewide and in our cancer center, too.

State-wide COVID-19 statistics are available at the Louisiana Office of Public Health Portal.

Our hospitals are nicely down in terms of admissions. That was a huge concern, initially—were we going to have capacity? The answer is we did have capacity through some rather amazing work at the hospital level, and our cancer center has made very substantial changes. We feel like the worst is over.

We have tested 135,000 people in the state of Louisiana, which per capita, is one of the highest testing rates in the country.

That's good to hear. What does this curve look like in Louisiana?

OS: The curve is bending throughout Louisiana but new cases are appearing now in the more suburban and rural areas.

Nobody has immunity to this thing. I mean, there is no natural immunity, and if you get exposures—inevitably, you're going to get infected. I think the social distancing has made a huge difference. But not everybody can socially distance with the same effectiveness.

If you live in a prosperous area, having a 4,000 square foot house with two people in it, that's very different than if you're six people in a small apartment. Crowding occurs for those people who don't have the financial resources to create more space at home, there's more interaction, and many people still must go to work to earn a living.

I'm working at home six days a week. I'm in the office only one day a week, where

I'm seeing my cancer patients, but only the prioritized cancer patients.

As you said, some people have the luxury of being able to social distance and some people just can't. Could you delve into what you've seen so far in terms of these disparities? What does that look like in Louisiana?

OS: There is a very significant African American disparity in terms of death rates. It's not really completely clear, other than age, what the risk factors are. It may be that African Americans are more likely to have multiple co-morbid risk factors, and it not clear whether or not African Americans are seeking care later in the disease cycle.

There's more obesity in the African American population. There's more type 2 diabetes. Both of those are factors that contribute to mortality when infected with the virus. One of the things that our teams noted relatively early on is that if you're obese and end up on a respirator, it's really, really, tough to get you off.

So, if there's more obesity, then there's more difficulty getting off of the ventilators, which means there's a higher risk of death. Diabetes seems to be an issue, whether or not that's a microvascular disease or something else or may be correlated. With obesity, issues aren't clear.

But there is clearly an African American predilection for dying from the COVID-19 disease. The other group that has been hardest hit are those with the hematologic malignancies, including the leukemias, lymphomas and multiple myelomas.

These patients are immunocompromised to a greater degree by their dis-

eases. They often have bone marrow dysfunction. They're often on more immunosuppressive therapies. All those under active cancer management, those with the hematologic malignancies, are unequivocally more likely to have died.



Crowding occurs for those people who don't have the financial resources to create more space at home, there's more interaction, and many people still must go to work to earn a living.



I'm glad you brought that up. We did a story last week about how patients are concerned about their care during coronavirus, because treatment is delayed or canceled. How has Tulane been addressing this?

OS: Well, first of all, we've tried to prioritize the patients that need to see us. With things like adjuvant therapy, there is flexibility. Prostate, which is where I focus, the good news is that we have some pretty active hormonal therapies and that we can use our hormonal therapies a little bit longer while waiting for the more definitive radiations to occur.

For surgery, it's been very problematic—because essentially, all of the surgeries have been canceled. One of the things that we instituted last week, is that we've been doing asymptomatic COVID-19 testing on all of our chemotherapy patients.

We've got the rapid Abbott 15-minute test, where we can actually do the test on the entry into the clinic.

The good news is, out of our initial three days of testing, I think we've tested around 65 or so. We only had one positive among our asymptomatic patients. That patient, by the way, was a hematologic malignancy case. We do have rapid testing available at the cancer center there and hope that can facilitate optimal care.

So, every chemotherapy patient receives testing if they're asymptomatic?

OS: Yes, but that only started last week.

Every chemotherapy patient is now getting COVID-19 testing prior to the infusion. We started that last week, like I said, it's just in the preliminary phases, but the good news is we've got the 15 minute test. We get a positive result in about five minutes, a negative result in about 15 minutes. We've got an analyzer dedicated to the cancer center so we could get those patients tested when they arrive at the cancer center.

And if a patient tests positive, like the one hematologic malignancy patient you mentioned, what are the next steps?

OS: The first thing is they should be notified, of course. It then becomes up to the individual physician to manage it. We don't have a policy on how a COVID-positive patient that's asymptomatic ought to be tested if they have cancer, because the individual physician can make decisions regarding how urgent is their therapy, what degree of risk it poses, etc.

For the asymptomatic patient in general, they're basically instructed to go home and segregate, and then report back if they become symptomatic. By basically putting somebody in self-quarantine, that's great for managing the virus—but what about the cancer? We did think about trying to put together a cancer center policy for positive patients.

But it really depends on whether or not you'd have an asymptomatic early stage prostate cancer patient who's under surveillance versus a myeloma patient under active chemotherapy. In general, we would not want to give chemotherapy to a patient with an active viral infection because that would lead to further immunosuppression.

But we are continuing to give chemotherapy. I have patients of mine that are under active immunotherapy or chemotherapy, patients who progressed rapidly after hormonal alternatives, and we really don't have a choice. I take care of kidney cancer patients who are getting infusions with immunotherapy, because quite frankly, their disease progressed rapidly on the alternative. Even though we're trying to utilize the alternatives to chemotherapy, when feasible—for some patients, chemotherapy is literally life-saving.

Of course. What changes has Tulane Cancer Center made as a whole in light of COVID-19?

OS: A wide variety of things.

First of all, we've really tried to prioritize our in-person patient visits to those people that absolutely need it. We've had a tremendous expansion in our telehealth, and they're using different platforms, either something as simple as FaceTime or a phone call. You can accomplish a great deal on a phone call—or actually having the more formal tablet visit, which is done through our EMR. Prioritizing the follow-up of patients in terms of televisits has been a huge change, and diminishing the number of physical visits to the cancer center has been required under this crisis.

Number two, we've created outside utilization of testing so they don't have to come into the cancer center for their laboratory testing. For our radiation patients, we instituted a patient flow where literally we were starting and are continuing to start radiation at 4:00 a.m. through 8:00 a.m. So that patients can come in and be socially-distanced. Then we restart it at about 4:00 p.m. going to 8:00 p.m. We literally have segregated our radiation patients in an effort to be able to continue their care, but to diminish the interactions that they might have with others.

Then, we, of course, have both questionnaire and temperature checks at the time that any patient comes into the clinic, including all cancer center personnel. All the personnel that comes into the clinic gets a temperature check and a questionnaire for symptoms. If they are symptomatic, then they're questioned by a physician in order to determine what should be done next.

We've had a good volume of symptomatic testing available for some time here in Louisiana, so we can get symptomatic testing done in a variety of settings. But the asymptomatic testing is a change, we put that in the last week for the

chemotherapy patients and for the hemato-immunologic malignancy patients as a priority.

That's an overview—segregating those patients who need to be seen from those who don't, emphasizing televisits and checks into the clinic, moving the laboratory out as much as possible.

The patients who do need to be seen, we are caring for, and that's an important message as well. We're not neglecting to take care of our cancer patients. We're providing care as best we can under extenuating circumstances.

You said that follow-ups and appointments are replaced with telemedicine when possible. Have you seen a digital divide when it comes to disparities?

OS: I treat telemedicine as going all the way from a telephone call, to those patients going into the more formal EMR. There definitely is an age divide. First of all, because I take care of prostate cancer patients, my average patient is probably about age 70. For many patients in their seventies and eighties, they're simply not familiar with the technology that would involve a full televisit.

But you know what, you pick up the phone and you call. Everybody has a telephone. The thing that has been tremendously helpful is texting, because so many patients can receive a text or an email and a lot of times just reaching out via text or email has been tremendously helpful.

I haven't tracked the number of texts that I've sent patients, but I'll simply say that I have avidly collected cell phone numbers from all patients, and

have used texts and email as a relatively routine part of our communication. But, obviously, we tilted that way now. What's a little bit unusual is that virtually every patient has my cell phone, so that if they need to reach out, they can reach me and we can handle the issue.

It's good to hear that you're able to stay in touch and lessen the divide in terms of digital difficulties.

OS: There still is some degree of divide. I treat an African American patient who lives in the country, and he doesn't have a cell phone, doesn't text, but he has a home phone. That is a little more cumbersome, but nevertheless, we've been able to communicate. He's staying indoors, he's staying at home, so he's relatively easy to reach and we've communicated two or three times in the last month.

There is a divide by age. There's a divide in the city and the country with regard particularly to the internet. There's a socioeconomic divide, and to some extent, overlapping with that is probably a racial divide, given that African Americans are more likely to be at a poor socioeconomic strata. There are many African Americans in rural parishes in Louisiana as well.

Do you have an exact number of how many COVID-19 patients your hospital has seen?

OS: No, I don't have that exact number. This is one of the problems, patients are getting COVID-19 testing elsewhere. We're somewhat of a referral center, so patients will come here for their cancer

care, but they may get their ordinary care back at home.

One of the things that we've found out is that patients have had problems with cough or a fever and they don't come in to New Orleans, where their cancer care is. They go to their local doctor, who might be 200 miles away. If so, we know for a fact that we're not getting all the information in from the periphery. We can only comment about the testing done at our center, where we do know. Unfortunately, our hematologic malignancy patients have had a significant number of deaths.

If you have a patient with cancer who is positive in your center, do you treat them for COVID? How does this work?

OS: I don't consider myself to be a COVID doctor. We refer to the infectious disease specialists who admittedly have been overwhelmed. But nevertheless, generally what we've done is follow the CDC guidelines for symptomatic versus asymptomatic.

Mainly, what we've been doing is supportive care. They do have some protocols, they do have a corporate protocol. They do have the plasma protocol up and going from previously infected patients, and we have some other protocols as well. So there is a protocol directed therapy, but most of the care is supportive, as you know.

COVID-19 treatment has obviously changed the way cancer care is working right now. Looking past this, how do you think COVID-19 could change how cancer treatment works?

OS: I think that many patients and many physicians will be more comfortable with a telehealth paradigm. There is certain testing that occurs in a specialized center. We're able to do genomics that are not typically done elsewhere. We're able to run very particular scans that are not done elsewhere. I think there could be a greater use of telemedicine and a greater comfort with telehealth and telemedicine in this sort of post-COVID world.

That's a great point. And how are researchers in oncology equipped to respond to COVID-19?

OS: Almost all researchers are familiar with the paradigm of what it takes in order to prove that a drug is effective. Oncologists deal with life-threatening illnesses every day. We're accustomed to clinical trials. We understand clinical trial design, inclusion criteria, and the importance of clinical trials.

I do think that oncologists are uniquely informed through their training and experiences to deal with clinical trials, whereas many other physicians really are not. The idea that you would do a randomized trial is still, for primary care, they're not used to such matters. I think that we can understand the literature and the necessity for good data. All oncologists are accustomed to dealing with life-threatening illnesses, so in some ways, we may be a little less prone to panic than some of the other specialties

At Tulane, is there any research being done related to COVID-19 in cancer patients?



All oncologists are accustomed to dealing with life-threatening illnesses, so in some ways, we may be a little less prone to panic than some of the other specialties.



OS: We had, and I'd like to give an attribution to a Swiss colleague who looked at one of the binding proteins for the COVID-19 virus, and that binding protein is called TMPRSS2, which is ordinarily a fairly obscure protein unless you work in prostate cancer research. Here, TMPRSS2 is well known as an androgen responsive gene and it is also, TMPRSS2 is also expressed to the lung.

One of the things we're doing in the basic labs is to look at the androgen regulation of TMPRSS2 in the lung and to ask questions that may be relevant for viral entry. One of my colleagues has put forth a protocol to look at androgen manipulation of the TMPRSS2, and to determine if there might be an effect on COVID. That colleague is at the University of Minnesota.

The idea came in part from Switzerland, is where I first saw it. The idea that this TMPRSS2 gene, which is known to cancer researchers in the prostate field, can be manipulated by manipulating androgens now may actually be going into a clinical trial.

I'm not able to share the protocol; it's in the developmental phases and must be viewed in context of other available protocols. You'll quickly see that TMPRSS2 is an androgen-responsive gene, and so the virus uses it in terms of getting into the cell if it's part of the viral entry mechanism, which diminishes the expression of TMPRSS2 by manipulation of androgens—it's certainly a logical way to potentially impact the natural history of the viral disease, but we know little about androgen regulation of TMPRSS2 in the lung, and that needs to be shown.

Is there anything else you'd like to discuss regarding the science of this disease?

OS: I'm a little bit dismayed at the lack of viral research in general. It turns out that infectious disease divisions at many large pharmaceutical companies have been either cut back or abolished altogether. I think the government will need to take a unique place in terms of studying infectious diseases, and how they can influence populations—and how we need to intervene, even though the profitability of such research may be low.

The big pharma companies are, of course, trying to prioritize the research that gets the best return on investment for their shareholders. I think as a nation and as a government, we have to prioritize the viral diseases, even though it is not necessarily profitable.

I think everybody sees the wisdom of that now. There were certain cutbacks at the governmental level that were very unfortunate, that have already occurred, and we're going to need to be more vigilant in the future.

Is there anything else you'd like to add?

OS: The good news is that critical cancer care has been proceeding, but under different guises—and we've made a lot of changes in how we're delivering that care. Hopefully, the compromise of care is relatively minimal outside of the delays in surgery that, unfortunately, have become inevitable during this crisis.

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

A



CONVERSATION WITH
THE CANCER LETTER

As COVID-19 peaks in San Antonio, Mesa predicts gradual reopening

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Based on the case burden and the risk in San Antonio, which is clearly lower than it is in areas like New York and Boston, we have still preserved adjuvant therapy for individuals, but we continue to monitor the situation. The San Antonio burden is now just at about a thousand cases, and we're in a town of about 3 million.

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Ruben A. Mesa, MD, FACP

Director, Mays Cancer Center, home to UT Health San Antonio MD Anderson; Mays Family Foundation Distinguished University Presidential Chair, Professor of Medicine

News coverage of the COVID-19 pandemic in New York has lent urgency to social distancing efforts in San Antonio and South Texas, likely flattening the curve.

“We’re still really a bit in the peak as we speak. I don’t think we’re past the peak, but I think by all estimations we’re hopeful that we have had a flattened curve from the social distancing efforts. The social distancing efforts started in San Antonio and South Texas before they did for Texas as a whole,” Ruben Mesa, director of Mays Cancer Center at UT Health San Antonio MD Anderson Cancer Center, said to *The Cancer Letter*.

“I’ve shared this with my colleagues in New York, I think we all owe them an indirect debt of gratitude. Not that any of this was intentional, but I think the experience in New York, having been as severe as it was, frightened a lot of the rest of the country into much more genuine compliance than we would’ve had otherwise.

“I don’t think people would have taken the threat nearly as seriously if it had been just the communicated experiences from northern Italy and others. I think those of us in health care who have direct friends over there, clearly were getting the texts and emails and felt that very genuinely.

“But I think individuals just watching the news as to what was happening in Bergamo, it was not nearly as real for them as was the experience in New York. With people in San Antonio, seeing those images and other things, the compliance has been very good. I think that’s in large part because they saw what the stakes were from the terrible experiences in New York.”

Mesa said the reopening of the economy in San Antonio will likely move slowly.

“I certainly understand the economic pressures to try to reopen. Within our

region, the city and the county set the tone for that, more than the governor,” Mesa said.

“The city and county have set up a task force with many of the faculty from our university leading that. I think it’ll be a very gradual process. I think what they’re signaling will be very much baby steps. A wider range of businesses open, but in a to-go model a bit like the restaurants are working at right now. A bit of an increase in elective procedures, mandatory masks for all in public. Like in San Antonio, starting tomorrow, there’s a mandatory mask order and a \$1,000 fine for violation. So, I think it will be a very, very gradual process.”

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

Paul Goldberg: Thank you for taking the time to talk with me. How’s it going?

Ruben Mesa: So far so good. I’ve been very impressed with the efforts of San Antonio, coordinating with the Mays Cancer Center and with the state and the county resources to prepare. Our team has been working very hard to remain solely focused on how we care for our cancer patients and how we try to avoid individuals having worse outcome from their cancer, while trying to keep our patients, our faculty, and our staff safe.

As we try to navigate this process, as other centers have done, we try to keep that front and center in our minds in terms of what are the key things that will help to drive outcomes.

What do we need to preserve in terms of therapy?

So, for example, for radiation therapy we are trying to make it as safe as possible.

We clearly, like other centers, have the minimum number of people present in the outpatient environment. And everyone is working from home, except at those times that they are directly involved with patient care.

When we’ve been caring for patients who are receiving radiation therapy, we created a part of the parking lot directly across from radiation therapy, and we have people wait in their cars, and then we send a text them with both the vault number and when to come in.

They come in masked, and we screen everyone at the door, both for symptoms and temperature. They go straight to Vault Three, where they meet their radiation therapist. So, we have a kind of rotating waiting room in the parking lot and in our vaults.

We have a similar approach for infusions. And, again, we’ve tried to optimize infusions. We’ve looked through our schedules for infusions that could be deferred, some uses of Zometa, vitamin infusions, and any of those types of things that could be deferred safely, have been deferred until we’re past the surge. But other things we certainly have kept in mind and kept moving forward.

And all faculty and staff are screened each day, and everyone receives a sticker.

When do the cases peak?

RM: I think we’re still really a bit in the peak as we speak. I don’t think we’re past the peak, but I think by all estimations we’re hopeful that we have had a flattened curve from the social distancing efforts. The social distancing efforts started in San Antonio and South Texas before they did for Texas as a whole.

And I think that was very helpful. I think to some degree, and I’ve shared this with

my colleagues in New York, I think we all owe them an indirect debt of gratitude. Not that any of this was intentional, but I think the experience in New York, having been as severe as it was, frightened a lot of the rest of the country into much more genuine compliance than we would've had otherwise.

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But I think individuals just watching the news as to what was happening in Bergamo, it was not nearly as real for them as was the experience in New York. With people in San Antonio, seeing those images and other things, the compliance has been very good. I think that's in large part because they saw what the stakes were from the terrible experiences in New York.

What do you think about the pressure to reopen soon? Are you getting some of that in South Texas?

RM: I certainly understand the economic pressures to try to reopen. Within our region, the city and the county set the tone for that, more than the governor.

The city and county have set up a task force with many of the faculty from our university leading that. I think it'll be a very gradual process. I think what they're signaling will be very much baby steps. A wider range of businesses open, but in a to-go model a bit like the restaurants are working at right now. A bit of an increase in elective procedures, mandatory masks for all in public. Like

in San Antonio, starting tomorrow, there's a mandatory mask order and a \$1,000 fine for violation. So, I think it will be a very, very gradual process.

Are you still doing adjuvant care, or have you let that drop off a bit?

RM: Based on the case burden and the risk in San Antonio, which is clearly lower than it is in areas like New York and Boston, we have still preserved adjuvant therapy for individuals, but we continue to monitor the situation. The San Antonio burden is now just at about a thousand cases, and we're in a town of about 3 million.

So, we are trying to keep it as safe as possible, but again, trying to really map alternative therapy for those with particularly a curative course, would include adjuvant therapy. If we were in an area with a much higher risk and transmission rate, I certainly wouldn't fault centers for doing otherwise, but we have tried to preserve that piece.

What about the catchment area? Who is getting hit harder and who is less severely affected?

RM: I think what we do see is that there's a higher rate of patients becoming ill who are poor Hispanic patients from our catchment area. I think, as has been seen in the other urban areas where there's a higher rate of co-morbidities, a higher rate of challenges with social determinants of health.

We believe there's a higher rate of both ICU admission as well as ventilator use. Now, we're not totally seeing it to the degree that some of the other urban

areas have, but there does seem to be a health disparity piece. We certainly have been very active, as other centers have, in terms of ramping up what eHealth looks like with e-visits.

We've been working with community oncologists, trying to guide therapy both with second opinions and other guidance to have people treated as close to home as possible. Our catchment area is quite large. We have people coming to our practice that live as far as six hours away by car. Our catchment area of South Texas goes all the way down to the Rio Grande Valley and the Texas-Mexico border, where there's a fair amount of population.

So, we've been trying to be a resource through e-visits, and, if need be, even telephone visits to the greatest degree that we can. As well as, most certainly, for probably about 40% to 50% of our visits that can be done remotely, follow-up visits, patients on oral therapies. I deal with a lot of chronic leukemias, a lot of oral therapies—all of those haven't been moved over to electronic visits.

Are you finding that the digital divide is real? Is it affecting you? How can you move to telehealth when there is a disparity in access to technology?

RM: It clearly is a barrier. Our institution has re-tasked a variety of individuals to help prepare patients for those visits, including some of our early medical students that are not involved with active care. They have found that many have limitations in terms of access to a computer with a webcam, but many still do have a smartphone, and the ability to do video visits on their smartphones broadens that to a great degree but not 100%.

So, at the current time, just a straight telephone visit also is able to be done at a variety of rates. Currently, Medicare is still deciding as to whether it will cover those. I think they should, as certainly a backup during this time.

The video visits, I think clearly are of better quality: the direct ability to see the patient and to be able to look into their eyes and see how they're doing and connect. It's a better connection. But a telephone visit is much better than a canceled visit. So, we really tried to avoid canceling care by using the electronic and phone visits as an additional step and resource.

Which you may or may not be paid for?

RM: We think we likely will, but the telephone may well be at a discount. Again, we recognize during all of this period, the main goal, as I've shared with our staff, is to try to preserve outcomes for our patients—as well as to really diminish their anxiety.

Clearly, this is a terrifying time for all of us, but for cancer patients, I think, doubly so, in that they have all of the stresses everyone else has, including work-related stresses, etc., but then they have cancer, too. So they may be afraid of whether they will get the therapy they need as well as are they at increased risk of something they've taken for granted, such as going to the grocery store — even with a mask.

So, I found that, with many of these e-visits with patients, part of the time we really speak about the disease, but part of the time we speak about COVID, how it relates to them specifically and what measures they're taking.

Are you going to be able to do any studies in this, to learn from it, either on the role of certain types of care that may or may not be needed, or maybe on prevalence, or disparities? Is there any aspect of it that you'll be able to study?

RM: We've been very interested in trying to learn from this as best we can, particularly realizing that this is not going away anytime soon.

We're participating in Jeremy Warner's COVID-19 and Cancer Consortium and are sharing the data that we're aggregating from the San Antonio area. We're trying to learn from the consortium as well as compare and contrast our data with that from other centers.

Certainly, our center has been involved with a variety of the therapeutic research. We're involved with the remdesivir study, and potentially will participate with the ruxolitinib study. I was one of the investigators that was involved with getting ruxolitinib approved for myelofibrosis several years ago, so I am very pleased to see that ruxolitinib may have a role with its anti-inflammatory properties as part of a phase III study.

My colleagues and I through the MPN Research Consortium, which is an NCI-funded PO1, are putting together a trial looking at the potential impact of extra e-visits for monitoring these patients during this time, having conversations with them in a structured way in terms of both safety and trying to alleviate the anxiety during this time.

We are doing that with our nurse practitioners and PAs to try to see if we can have an impact in both diminishing anx-

ity, but also potential impact in terms of decreasing rates of infection and other things. So, we are trying to learn from this as much as we can.

What impact has it had on your institution in terms of your ability to do what you do—and in terms of the money. Are you getting harmed by this?

RM: Without question, I think every center is taking a significant financial hit from COVID-19. Our center is well run and well organized, so I think it's a hit that we will survive, but it clearly will have an impact.

So, one, is we are under a hiring freeze, and all aspects of growth and things of that nature that were planned, clearly, all of that is deferred for the time being.

It certainly has been tremendously disruptive, as it has, I'm sure, for all, in terms of the clinical research program. We have not stopped our clinical trials program, but we clearly have slowed to primarily enroll patients onto therapeutic clinical trials that we think are crucial in terms of being an option for those patients. But things like observational studies, biobanking studies—all of those are really in a holding pattern during this time.

There's clearly an impact in terms of the experience that trainees are receiving. There clearly will be an impact that I don't think we fully have felt yet in terms of the funding environment for research. I sit on the national board of the Leukemia and Lymphoma Society. The LLS like other foundations, are seeing a very sharp drop in philanthropic dollars because, one, much of that philanthropy frequently occurs in the

setting of people holding events. But second, with the dramatic challenges in terms of the market. Many people who are involved with philanthropy, clearly, are going to be reluctant to support those things at the same rate that they have in the past. I think we're going to see an impact on that.

The American Society of Hematology just had a conference call on this on Friday, getting people together, trying to understand what is the impact going to be in terms of on training grants, on junior faculty, in terms of a lot of those key resources they need early on in their careers. I think there will be an echo effect on disrupting some momentum in research that'll take some real intentional efforts to move forward.

It all sounds like things may be able to start getting back to normal at some point in the foreseeable future. What would that look like for you?

RM: I think the analogy that Governor Newsom of California used of a dimmer, as opposed to an on/off switch, is probably what we'll see. I think in medicine as a field, clinical care will bounce back much faster than in some other areas of society because of the clinical need, and I think the appreciation both by government and the public in terms of the importance of health care.

But I think it'll be gradual. I think we'll slowly ramp up on what elective procedures. I've had a great concern, as I'm sure many others have, in terms of the deferment of cancer screening that has occurred during this process.

We've pulled together under our cancer prevention screening committee, a

coordinated effort to keep track of everyone who had canceled or deferred colonoscopy, mammography, cervical cancer screening, or potentially lung or others, if they were scheduled for that, so that we can keep track of those folks.

We can contact them when we're able to bring them in for screenings. Another important part is trying to prevent people from presenting with late-stage cancers, because they missed their cancer screening due to COVID-19.

It's interesting, because you can look and see the inefficiencies in the American medical system more clearly in the middle of this crisis. Is this something you're seeing?

RM: I would say, without question, that we don't really have a coordinated system. I've seen a lot of creativity in terms of trying to make up something on the fly. So, for example, every morning here I participate in a call between the city, the county, the VA, our university and the large medical community in San Antonio.

A lot of the medical training for the U.S. is based in San Antonio, so there's a daily call that really helps to coordinate between these entities to discuss how many cases we have, the stress on the healthcare system, how many events are in San Antonio, where do we stand with that, ICU beds, etc.

So, that's a level of coordination that's really never existed before. But it makes you ask the question: Why have we never thought about these kind of things before in a much more coordinated way?

I speak with my colleagues in London, who were very much ahead of us on the curve with this—the coordination they've had at the NHS. They've had their own challenges in terms of shortfalls and other things, but their level of coordination is really interesting.

It certainly makes you wonder. We have a very large, well-organized, military system to help us defend against physical threats to the country, but we've not really had the equivalent in terms of doing that for a health threat.

So, will something like that evolve? I think it may well be necessary. As I've heard our infectious disease doctors speak, they feel that the rate of the mutations of the coronavirus from SARS, the original SARS, to this, potentially is an accelerating process, and that it may be somewhat predictable that another highly contagious variant of this—that is not cross-immune to this one—may come again in another handful of years. How do we evolve our system to be poised to deal with the next epidemic, because the next epidemic is likely, and how do we not repeat the mistakes of the past?

Well, the treatment is going to get better; wouldn't you think?

RM: Clearly, clearly. But, of course, if it evolves further, will the new treatments we evolve be as effective. I'm sure you've seen the little YouTube video from Bill Gates speaking about the Ebola crisis. One thing I have shared with folks is that I think there are a few things that are indirect positives, without question. I am hopeful our society is going to come out of this and have a much greater appreciation both for what ev-

everyone does in health care, but also for the value of biomedical research.

I'm hopeful that it'll be a time where people's efforts are really valued and that it'll open up other opportunities for both COVID- and non-COVID-related research.

Having covered this for months now, it's impossible to see a response to COVID without a major role for oncology.

RM: Oh, without a question. I think many of the therapies that have evolved from the cancer world clearly have real relevance here.

Between the role of viruses, and the role of the immune system and perhaps even the drugs are going back and forth between rheumatology, viral disease, hematology and oncology.

RM: Without a question. The JAK inhibitors, BTK inhibitors, trials with mesenchymal stem cells—obviously that's a variant of stem cell transplantation—a lot of the anti-infectives that again were developed for dealing with infectious complications of cancer therapy are very closely intertwined, without question.

Is there anything we forgot? Anything you wanted to mention?

RM: I'll mention one other thing that we did. We created a separate pathway early on in this in terms of caring for people who were not feeling well. If they're not feeling well it's as likely or more likely that they are feeling bad because of their therapy, a different infection, or their cancer than it is likely to be from COVID. And then we really did not want to be sending patients to the emergency room unless it really was a life-threatening emergency.

So, we created a separate pathway. In a different part of our building, we isolated a unit just to be able to do that sort of analysis with everyone with our people in full PPE. We evaluate patients for their symptoms, screen them for COVID if appropriate, use a separate elevator and be able to work that through a separate team. I think the realities of being able to evaluate potentially infected patients in our environment was something we had to react to on the fly.

We're trying to learn everything we can from this experience and our new processes to both help patients during this crisis but also moving forward.

Were you able to keep the hospital pretty much COVID-free?

RM: The way we're structured, we are in a shared university hospital and there are COVID units. Our cancer patients are on separate units, but it's not a COVID-free environment. Our cancer center, our outpatient facility, we don't have the luxury of being able to keep them completely separate. But we do have a workflow for COVID-positive patients to be treated in different spots. And then if they're receiving radiation, they receive it at the end of the day with a deep clean of the vault when appropriate.

You were able to keep those two worlds separate?

RM: Correct. And we work to keep those two worlds separate. We've also worked to try to have duplicate teams so that if we have individuals who became infected we would have backups particularly with some of the roles that are so sub-specialized, such as our radiation therapists.

I think it's well away from any large scale opening of venues or events or movie theaters or things of that nature. I think it will be very gradual baby steps. But I certainly hope that it's not premature.

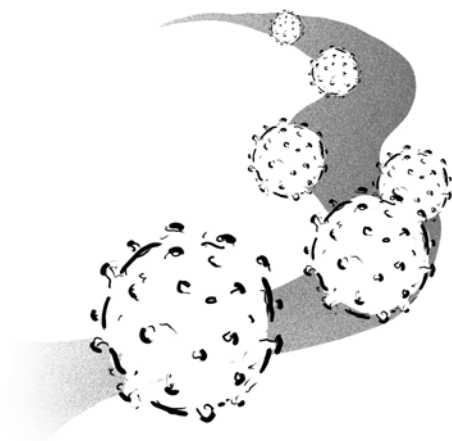
Well, thank you so much.

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COVID-19 UPDATES



FDA issues advisory on off-label use of hydroxychloroquine and chloroquine

FDA has issued a [Drug Safety Communication](#) regarding known side effects of hydroxychloroquine and chloroquine, including serious and potentially life-threatening heart rhythm problems, that have been reported with their use for the treatment or prevention of COVID-19, for which they are not approved by the FDA.

These risks, which are in the drug labels for their approved uses, may be mitigated when health care professionals closely screen and supervise these patients such as in a hospital setting or a clinical trial, as indicated in the [Emergency Use Authorization](#) for these drugs to treat COVID-19.

“We understand that health care professionals are looking for every possible treatment option for their patients and we want to ensure we’re providing them with the appropriate information needed for them to make the best medical decisions,” FDA Commissioner Stephen M. Hahn said in a statement. “While

clinical trials are ongoing to determine the safety and effectiveness of these drugs for COVID-19, there are known side effects of these medications that should be considered. We encourage health care professionals making individual patient decisions closely screen and monitor those patients to help mitigate these risks. The FDA will continue to monitor and investigate these potential risks and will communicate publicly when more information is available.”

The FDA has issued an EUA to allow hydroxychloroquine and chloroquine products donated to the Strategic National Stockpile to be distributed and used in limited circumstances, such as for certain hospitalized patients with COVID-19.

These drugs are able to be distributed from the SNS to states for doctors to prescribe to adolescent and adult patients hospitalized with COVID-19, as appropriate, when a clinical trial is not available or feasible. The EUA requires that fact sheets with important information about using these drugs in treating COVID-19, including the known risks and drug interactions, as well as appropriate screening and monitoring, be made available to health care providers and patients.

Hydroxychloroquine and chloroquine are FDA-approved to treat or prevent malaria. Hydroxychloroquine sulfate is also FDA-approved to treat lupus and rheumatoid arthritis. These medicines have not been proven safe or effective for treating COVID-19.

However, clinical trials are underway and additional trials are being planned to determine if these drugs can benefit patients with COVID-19. These trials are also examining whether the drugs can prevent COVID-19 among health care workers, first responders or people who have been in close contact with someone with COVID-19.

AACI annual meeting goes virtual

The Association of American Cancer Institutes has moved its July 7-8 annual meeting to a virtual format.

“The health and well-being of AACI meeting attendees, exhibitors, and cancer center patients is our top priority,” AACI said in a statement. “As we plan our 2020 meetings, we are closely monitoring the coronavirus pandemic—particularly the impact of COVID-19 on travel and professional conferences.

“We believe this decision will allow us to deliver the innovative, quality education our members expect from the CRI annual meeting, while prioritizing the health and safety of attendees.”

The association said it plans to announce information on registration and virtual sessions in the coming weeks.

Reagan-Udall Foundation and Friends of Cancer Research form COVID-19 Evidence Accelerator focused on RWE

The Reagan-Udall Foundation for the FDA and Friends of Cancer Research, created the Evidence Accelerator, a public-private partnership combining the efforts of academic, government, and private sector organizations applying data analytics to accelerate the understanding of COVID-19.

Mobilizing major data organizations, government and academic researchers, and health systems, the Evidence Accel-

erator builds on the work of its partners to maximize the use of real-world data. Contributing researchers will engage in weekly meetings to present and critically discuss findings from different data sources. In addition, the Evidence Accelerator will facilitate parallel analyses of questions to identify patient characteristics, treatment patterns, and management strategies for COVID-19.

Western NY researchers study COVID-19 using NGS to identify immune response biomarkers

Western New York health care and medical researchers are conducting a study that will use next-generation sequencing to identify biomarkers of immune response to COVID-19 that could be used to predict which patients are likely to progress to severe infection that would require more intensive care.

The goal is to provide medical professionals with a blood test that will help them to better prognose and triage patients with COVID-19. The study, the Western New York Immunogenomic COVID-19 Study, is conducted by Roswell Park Comprehensive Cancer Center, Catholic Health and the University at Buffalo.

The WNY Immunogenomic COVID-19 study originated from an exchange between two senior leaders at Roswell Park: Kunle Odunsi, and Carl Morrison.

“We believe we can limit COVID-19’s deadly impact by marrying thoughtful strategy to next-generation sequencing technology—an opportunity that we never had before with any previous pandemic, using technology that in a few short years has changed the way we detect, diagnose and treat cancer,” Odunsi, deputy director, the Robert,

Anne & Lew Wallace Endowed Chair in Cancer Immunotherapy, and chair of Gynecologic Oncology at Roswell Park, said in a statement.

“We’ve seen a huge variation in how COVID-19 affects people. Some are not sick at all, some get flu-like symptoms for a few days, and some become very sick and develop symptoms that can become life-threatening,” Morrison, who is senior vice president of Scientific Development and Integrative Medicine at the cancer center, said in a statement.

Three collaborating organizations will work with Roswell Park:

- Catholic Health will join Roswell Park as a clinical site for the study, providing blood from consenting patients who test positive for COVID-19 to be sequenced and analyzed.
- The University at Buffalo, through its Jacobs School of Medicine and Biomedical Sciences and School of Pharmacy and Pharmaceutical Sciences will focus on the interface of virus-cancer-immunology research initiatives that will help facilitate the study.
- Thermo Fisher Scientific will provide data analysis and defray the costs of the equipment and chemical reagents that are central to this work.

Gene Morse, SUNY Distinguished Professor, UB School of Pharmacy and Pharmaceutical Sciences, and director of the Global Virus Network Center of Excellence at The University of Buffalo, is building scientific collaborations that focus on the interface of virus-cancer-immunology research initiatives that will facilitate the study. He will examine the blood samples of COVID-19 patients for immune-pharmacodynamic markers to quantify antiviral and immune-therapeutics activity in relation to the stages of COVID-19 infection and

the development of antibodies following infection.

The team will sequence immune receptors from both T cells and B cells, the two major types of immune cells our bodies enlist in order to fight off viruses like SARS-CoV-2, the particular coronavirus that causes COVID-19.

A fund has been established to support the initiative, with 11 Day Power Play Inc., a nonprofit that raises funds for pressing medical research. It has provided a leadership gift of \$150,000 toward the project’s estimated cost of \$1 million.

Funds donated to Roswell Park’s COVID-19 Response Fund: [give.roswell-park.org/COVID-19](https://www.give.roswell-park.org/COVID-19).

Invitae develops tools to support telemedicine

Invitae has developed tools to help health care workers order genetic testing via telemedicine for patients with cancer and newly pregnant women.

Invitae’s clinical chatbot, Gia, provides telemedicine genetic testing framework that helps identify patients who need germline genetic testing.

Clinicians are turning to telemedicine for patients who face disruptions to clinic visits, such as women who are newly pregnant or patients with cancer. Adapting to remote care requires tools that make it easier to replace tasks that were previously handled in-person, such as patient education or information gathering. Invitae has added new telehealth workflows to Gia for clinicians.

“Genetic testing plays an important role in clinical care. We’ve expanded Gia’s capabilities to give clinicians a virtual

go-between that can handle many elements of patient education, identification and information gathering involved in genetic testing,” Robert Nussbaum, chief medical officer of Invitae, said in a statement. “Coupled with our ability to ship test kits to and from a patient’s home that use saliva and do not require phlebotomy, we can help clinicians continue to provide care from afar.”

Gia stands for “genetic information assistant” and streamlines communication between patients and clinicians. It automates pretest education and genetic testing. Gia is HIPAA-compliant and SOC-2 certified. It also has a 92% satisfaction rate.

Gia includes patient identification, pre-test education, post-test support and automated documentation that is available 24/7. Gia can also help identify patients that may be at increased risk for breast, endometrial, ovarian, pancreatic, colon and prostate cancer and may benefit from genetic testing as a screening tool.

Kennedy, former FDA commissioner and Stanford president, dies of COVID-19

Donald Kennedy, who served as FDA commissioner from 1977 to 1979, died this week of complications resulting from COVID-19. He was 88.

“I am sad to inform you of the passing of former FDA Commissioner Donald Kennedy, Ph.D., who passed away this week from complications resulting from COVID-19,” FDA Commissioner Stephen M. Hahn said in a statement. “Kennedy was a widely-recognized researcher, an admired teacher, an astute administrator, and a firm believer in the importance of public service. He

leaves an impressive and inspirational legacy. Words cannot express enough how much we value the contributions Dr. Kennedy made to public health.

“As we all cope with this pandemic, his passing strikes close to home.

“Under his leadership, the agency warned the public about, and seized as an illegal drug, the popular but ineffective cancer treatment, Laetrile. He also led the agency as it faced widespread reaction to the attempted ban of saccharin under the Food Additives Amendment. Among his accomplishments, Dr. Kennedy implemented the 1976 Medical Device Amendments; pursued a concerted—though in the end unsuccessful—effort to pass a comprehensive Drug Regulation Reform Act (though many provisions of that effort eventually found their way into the law); proposed restrictions against the use of antibiotics in animal feed; and removed, under the Secretary’s order, the antidiabetic drug, phenformin, as an imminent hazard under the law—the first time that provision had been applied.”

After he left the FDA, Kennedy returned to Stanford University as vice president for academic affairs and provost and then, from 1980 to 1991, served as president. He served as editor-in-chief of the journal *Science* from 2000 to 2008.

FAQs and Guidances

Federal government:

- NIH [COVID-19 treatment guidelines](#)
- 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 support-

ed 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
 - Centers for Medicare & Medicaid Services [FAQ](#): Interim final rule
- ### 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](#)
 - ◊ [ASCO/National Coalition for Cancer Survivorship FAQ](#)
 - 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](#)
 - National Coalition for Cancer Survivorship [webinar](#) with Otis Brawley
 - ◊ [NCCS resources](#) for survivors
 - 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
 - Joint [recommendations](#) for treatment of patients with breast cancer
 - American College of Surgeons [resources](#): For the surgical community
 - Multiple Myeloma Research Foundation [resources](#)
 - Society for Immunotherapy of Cancer [resources](#): Implications for patients, translational research
 - GO2 Foundation for Lung Cancer [resources](#)
 - Adolescent and young adult [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
- Journals:**
- [Journal](#) of the National Comprehensive Cancer Network: How to manage cancer care during COVID-19 pandemic
 - ◊ [NCCN best practices](#)
 - ◊ [Special Feature](#): How to keep cancer patients and healthcare workers safe
- Companies:**
- Advarra: Coronavirus [guidance](#)
 - Asbestos.com: Coronavirus [guidance](#)

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IN BRIEF



ASCO announces 2020 awards

Researchers, patient advocates, and global oncology leaders who have worked to transform cancer care around the world are among the recipients of the American Society of Clinical Oncology's Special Awards—the society's highest honors—and Conquer Cancer, the ASCO Foundation Women Who Conquer Cancer Mentorship Awards.

"It is an honor to recognize the inspiring achievements of this year's awardees, and their dedication to conquering cancer," Monica Bertagnolli, immediate past president of ASCO and chair of the Special Awards Selection Committee, said in a statement.

The 2020 Special Award Recipients are posted [here](#):

David A. Karnofsky Memorial Award and Lecture

George D. Demetri, MD, FASCO, is senior vice president for experimental therapeutics and Director of the Sarcoma Center at the Dana-Farber Cancer

Institute, a professor of medicine at Harvard Medical School, and co-director of the Ludwig Center at Harvard. Dr. Demetri has dedicated his career to translational research aimed at understanding and treating precisely defined subsets of cancers, and he was a pioneer in the development of the imatinib as the first cancer therapy targeting gastrointestinal stromal tumor (GIST) as a molecularly defined subset of sarcoma.

Science of Oncology Award and Lecture

Pasi A. Jänne, MD, PhD, MMSc, is a professor of medicine at Harvard Medical School and co-scientific director of the Belfer Center for Applied Cancer Science, director of the Lowe Center for Thoracic Oncology, and a member of the Executive Committee for Research at the Dana-Farber Cancer Institute. Dr. Jänne was one of the co-discoverers of epidermal growth factor receptor (EGFR) mutations and he has led the development of therapeutic strategies for patients with EGFR-mutant lung cancer.

Gianni Bonadonna Breast Cancer Award and Lecture

George W. Sledge Jr., MD, FASCO, is a professor and chief of the Division of Oncology at Stanford University Medical Center. Dr. Sledge is an expert in the areas of antiangiogenic drug development and breast cancer murine models of growth and metastasis, as well as breast cancer genomics, and has devoted much of the past two decades in the clinic to the development of novel biologic agents for breast cancer.

ASCO-American Cancer Society Award and Lecture

Timothy Rebbeck, PhD, is the Vincent L. Gregory, Jr. Professor of Cancer Prevention at the Harvard T.H. Chan School of Public Health and the Dana-Farber

Cancer Institute. He is founding director of the Zhu Family Center for Global Cancer Prevention at the Harvard T.H. Chan School of Public Health and leads the Cancer Outreach and Engagement activities for the Dana-Farber Harvard Cancer Center. His work has led to an understanding of the genetic and environmental causes of breast, prostate, skin, endometrial, and ovarian cancers, as well as interventions intended to reduce the burden of these cancers in individuals and populations.

Allen S. Lichter Visionary Leader Award and Lecture

Hyman B. Muss, MD, FASCO, is the Mary Jones Hudson Distinguished Professor of Geriatric Oncology at the University of North Carolina School of Medicine, and the director of the Geriatric Oncology Program at the UNC Lineberger Comprehensive Cancer Center Program. He is an internationally recognized expert on the treatment of breast cancer in older patients, breast cancer survivorship, and long-term toxicity of treatment. He is exploring the role of biomarkers of aging and their potential role as predictors of toxicity and survival.

Distinguished Achievement Award

Robin Zon, MD, FACP, FASCO, is president of Michiana Hematology Oncology and serves on the Trinity Oncology Excellence Committee. Dr. Zon received ASCO's Advocate of the Year Award for her health care advocacy efforts, and she has been called upon by the Institute of Medicine, the National Cancer Institute, and the federal government to offer guidance and share her expertise. Dr. Zon meets with local and federal elected officials on a routine basis to promote cancer care policies.

Pediatric Oncology Award and Lecture
Alice L. Yu, MD, PhD, is the Distinguished Chair Professor and co-director

of the Institute of Stem Cell & Translational Cancer Research at the Chang Gung Memorial Hospital at Linkou and Chang Kung University, a Distinguished Visiting Fellow in the Genomics Research Center of Academia Sinica in Taiwan, and a professor in pediatrics at the University of California, San Diego. Dr. Yu has more than 40 years of experience in developing cures and understanding the biology of childhood cancer, is a pioneer of anti-GD2 therapy, and has either led or significantly contributed to numerous clinical trials to develop novel cancer therapeutics.

B.J. Kennedy Award and Lecture for Scientific Excellence in Geriatric Oncology

Andrew E. Chapman, DO, FACP, is a professor of medical oncology in the Department of Medical Oncology of the Sidney Kimmel Cancer Center at Thomas Jefferson University Hospital, and a clinical professor in Jefferson's College of Nursing. Dr. Chapman is the chief of cancer services for the Sidney Kimmel Cancer Center, the enterprise senior vice president of the Jefferson Health system for medical oncology, and vice chair for clinical operations for the Department of Medical Oncology. Dr. Chapman is the co-founder/co-director of the Jefferson Senior Adult Oncology Center, specializing in the multidisciplinary evaluation and treatment of older adults with cancer.

Excellence in Teaching Award

Anthony V. D'Amico, MD, PhD, is the Eleanor Theresa Walters Distinguished Chair, chief of Genitourinary Radiation Oncology at the Dana-Farber Cancer Institute and Brigham and Women's Hospital, chair of the residency executive committee in the Harvard Radiation Oncology Program, and advisory dean and chair of career advising and mentorship at Harvard medical School.

Dr. D'Amico is an internationally known expert in the treatment of prostate cancer and has defined combined modal-ity staging.

Partners in Progress Award

Carlos Gil Moreira Ferreira, MD, PhD, is the chief scientific officer at Oncoclinicas, president of Oncoclinicas Institute, and chair of the Oncoclinicas Medical Board, in Rio de Janeiro, Brazil. He is a lung cancer specialist and is active in oncology drug development, health policy, health economics, and health innovation.

Humanitarian Award

Gary W. Unzeitig, MD, FACS, is a breast surgeon and principal investigator practicing in the South Texas border community of Laredo since 1983. He is active staff at Doctors Hospital of Laredo. Dr. Unzeitig has been active in the Alliance for Clinical Trials, serving on the Board of Directors and Executive Committee, as co-chair of the Health Disparities Committee, and on the Community Oncology, Breast, Prevention, and Audit Committees.

Walther Cancer Foundation Palliative and Supportive Care in Oncology Endowed Award and Lecture

Betty R. Ferrell, PhD, MA, CHPN, FAAN, FPCN, is the director and professor of nursing research at City of Hope Medical Center and associate director of the City of Hope Comprehensive Cancer Center. Dr. Ferrell's background is in palliative care, quality of life, spirituality, and oncology research. She has successfully developed and disseminated local, national, and international programs related to systems change, quality of life, symptom management, and transitions to palliative care.

Hologic, Inc Endowed Women Who Conquer Cancer Mentorship Award

Dawn L. Hershman, MD, MS, FASCO, is a professor of medicine and epidemiology and leader of the Breast Cancer Program at Herbert Irving Comprehensive Cancer Center, Columbia University Medical Center. Dr. Hershman is a nationally recognized expert in breast cancer treatment, prevention, and survivorship. Her research focuses on improving cancer care delivery, reducing disparities, and improving the quality of life and quality of care of breast cancer survivors.

International Women Who Conquer Cancer Mentorship Award

Lillian L. Siu, MD, FRCPC, FASCO, is a senior medical oncologist and clinician scientist in the Cancer Clinical Research Unit at Princess Margaret Cancer Centre and a professor of medicine at the University of Toronto, Canada. Dr. Siu's primary research focus is in the area of new anticancer drug development, particularly phase I trials and head and neck malignancies.

Fellows of the American Society of Clinical Oncology (FASCO)

The Fellow of the American Society of Clinical Oncology (FASCO) distinction recognizes ASCO members for their extraordinary volunteer service, dedication, and commitment to ASCO. The following members are being recognized in 2020:

- Peter Adamson, MD, FASCO
- Banu Arun, MD, FASCO
- Elizabeth Blanchard, MD, FASCO

- Marcia Brose, MD, PhD, FASCO
- David Carbone, MD PhD, FASCO
- Ronald Chen, MD, MPH, FASCO
- Anne Chiang, MD, PhD, FASCO
- Linus Chuang, MD, FASCO
- Kelly Cooke, DO, FASCO
- Neelima Denduluri, MD, FASCO
- Laurie Gaspar, MD, MBA, FASTRO, FASCO
- Pamela Goodwin, MD, MSc, FRCPC, FASCO
- Bruce Haffty, MD, FACR, FASTRO, FASCO
- Michael Hassett, MD, MPH, FASCO
- Ralph Hauke, MD, FACP, FASCO
- Heather Hylton, MS, FASCO
- Reshma Jagsi, MD, DPhil, FASCO
- Jeffrey Kirshner, MD, FASCO
- Stuart Lichtman, MD, FACP, FASCO
- Jennifer Ligibel, MD, FASCO
- Merry Jennifer Markham, MD, FACP, FASCO
- Howard McLeod, PharmD, FASCO
- Kathy Miller, MD, FASCO
- Anne Moore, MD, FASCO
- Kevin Oeffinger, MD, FASCO
- Nathan Pennell, MD, PhD, FASCO
- Todd Pickard, MMSc, PA-C, DFAAPA, FASCO
- Brian Rini, MD, FASCO
- Mark Robson, MD, FASCO
- Gabrielle Rocque, MD, FASCO

- Robert Siegel, MD, FASCO
- David Spigel, MD, FASCO
- Vered Stearns, MD, FASCO
- Keith Thompson, MD, FASCO
- Mary-Ellen Taplin, MD, FASCO
- Jeremy Warner, MD, MS, FASCO

Serody and Basch named to leadership roles at UNC

Jonathan Serody was named chief of hematology and Ethan Basch was named chief of oncology at University of North Carolina School of Medicine Department of Medicine.

Melba Ribeiro will serve both divisions as associate chief for administration.

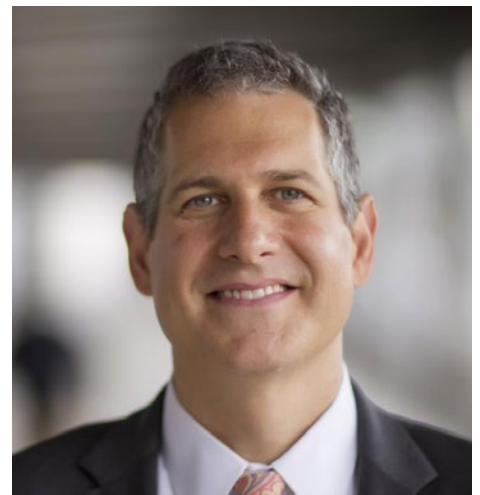
The appointments are part of a realignment of the Division of Hematology and Oncology that will form two divisions from one.

“The division of hematology and oncology has grown substantially under the leadership of Dr. Lisa Carey,” Ron Falk, chair of the University of North Carolina School of Medicine’s Department of Medicine, said in a statement. “As Dr. Carey transitions to her new role as deputy director of clinical sciences at [UNC Lineberger Comprehensive Cancer Center], we’ve determined that having two divisions, tightly linked, will help us more efficiently manage administration for these subspecialties and position them for future growth.”

The North Carolina Cancer Hospital is the clinical home for the Lineberger Comprehensive Cancer Center.



Serody, the Elizabeth Thomas Professor of Medicine, Microbiology and Immunology, is the associate chief of malignant hematology, bone marrow transplant and cellular therapy and the director of UNC’s Bone Marrow Transplantation & Cellular Therapy Program. He also serves as the associate director for Translational Science at the UNC Lineberger.



Basch is the Richard M. Goldberg Distinguished Professor in Medical Oncology and is focused clinically on the treatment of prostate cancer. He leads a longstanding research program focused on cancer care delivery transformation and patient-centered care, and directs

the Outcomes Research Program for UNC Lineberger.

His group established that integrating patient-reported outcome symptom monitoring into routine cancer care improves patients' quality of life, reduces emergency department visits, and lengthens overall survival. Basch developed a system for patient adverse event reporting in clinical trials, the PRO-CT-CAE, that is now a standard in oncology drug development.

Poynter, Harki appointed to leadership team at Masonic Cancer Center

Jenny Poynter and Daniel Harki were appointed to the leadership team of Masonic Cancer Center April 15.



Poynter was named Masonic Cancer Center's first associate director for Community Outreach and Engagement. Poynter is an associate professor in the Department of Pediatrics, Division of Epidemiology and Clinical Research of the Medical School at the University of Minnesota. She also serves as the vice chair of the Children's Oncology Group Epidemiology Committee and is a re-

search member of the Masonic Cancer Center's Screening, Prevention, Etiology, and Cancer Survivorship Program.

She will be joining Chris Pennell, the center's associate director for Community Outreach and Education. That role will be divided into two associate director roles. Poynter is the associate director of Community Outreach, and Pennell will assume the position of associate director for Education.

Poynter is a molecular epidemiologist whose research is focused on genetic susceptibility and epigenetic alterations in pediatric germ cell tumors and myeloid malignancy.



Harki, an associate professor in the Department of Medicinal Chemistry within the College of Pharmacy at University of Minnesota, will become a co-leader of the Masonic Cancer Center, University of Minnesota's Cellular Mechanisms Program. He will join Carol Lange, professor in the Department of Medicine, Division of Hematology-Oncology and Transplantation within the Medical School.

Harki succeeds long time co-leader James McCarthy, professor in the Department of Laboratory Medicine and Pathology in the Medical School.

Harki has published widely on the development of novel small molecules, nucleosides and nucleic acids, and in particular, his program focuses significant efforts developing chemical probes for the APOBEC family of DNA cytosine deaminases.

American Heart Association grants \$17 million for studies on health impact of e-cigarettes and nicotine on youth

The American Heart Association has awarded \$17 million in scientific research to be led by scientists from Boston University, the Ohio State University and Yale University to study the health impacts of e-cigarettes and other nicotine delivery systems on youth and young adults.

The studies are funded through a program called ENACT: End Nicotine Addiction in Children and Teens Research Initiative.

The research projects will be high-impact and fast tracked, only two years in length and funded at levels among the highest individual grants awarded in the association's history. The initiative is designed to produce programs to support youth as well as provide clear evidence to inform policy decisions.

Research teams from Boston University, the Ohio State University and Yale University will work over the next two years to identify the biological impacts of vaping on multiple organ systems (heart, brain, lungs, vascular, etc.), behavioral factors and specific social influencers of health to reverse these trends.

The projects include:

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VAPERACE

Led by Naomi Hamburg, the Joseph A. Vita, MD Professor at the Boston University School of Medicine, this team will establish the Rapidly Advancing Discovery to Arrest the Outbreak of Youth Vaping Center and will include four intersecting projects at Boston University, Johns Hopkins University, Stanford University and the University of Louisville.

These projects include: basic research using human induced pluripotent stem cell samples to test the toxicity of the components of e-cigarettes; mobile health technology to measure the physiological cardiovascular impacts of e-cigarettes on youth in real-world settings and a virtual reality and text messaging delivered e-cigarette cessation program for youth developed by combining social media methods with focus groups.

VERIFY: A Comprehensive Approach to Understanding and Ending Youth E-cigarette Addiction

Led by Peter Mohler, the vice dean for research and director of the Davis Heart & Lung Research Institute at the Ohio State College of Medicine and Wexner Medical Center. This team comprised of investigators in the Colleges of Medicine, Nursing, Public Health and Engineering and the Comprehensive Cancer Center will work to provide answers about the short- and long-term health effects of e-cigarettes, including their impact on the brain, lungs, and heart; the most effective regulations to reduce the appeal and addictiveness of e-cigarettes for youth; and the best methods to help youth addicted to e-cigarettes quit.

Team VERIFY: Vaping's End through Research and Innovation For Youth will recruit youth for a year-long study to look

at the relationship between nicotine form, concentration and flavorings on youth e-cig use, addiction, neurocognitive outcomes and pulmonary health compared to healthy peers.

They will also study the influence of nicotine form, concentration and flavor on youth puffing behavior, nicotine delivery, abuse liability, toxicant exposure and acute cardiovascular and pulmonary effects; and they will develop and test a multi-point, scalable vaping cessation program to include quit-line-delivered phone counseling, text-based cessation, nicotine replacement therapy and online cessation support.

Understanding and Treating E-cigarette Use Among Youth

Led by Suchitra Krishnan-Sarin, a professor of psychiatry at Yale University School of Medicine. This team will develop and test several youth-based programs and conduct clinical and behavioral research to learn more about the effect of youth e-cigarette use.

They plan to develop a high school-based intervention to educate youth about e-cigarettes, prevent initiation of vaping, promote quitting among those who already use e-cigarettes and change attitudes and perceptions toward e-cigarettes school-wide. They will also develop a cessation program that will use smartphone-based contingency management for nicotine abstinence in combination with individualized, cognitive behavioral therapy.

Further, they plan to develop and pilot a computerized cognitive behavioral therapy intervention for youth e-cigarette users. Finally, the team will develop a measure of e-cigarette withdrawal in youth and assess the relationship between withdrawal, dependence, treatment outcomes and e-cigarette characteristics such as flavors and devices.

THE CLINICAL CANCER LETTER

CLINICAL ROUNDUP



Phase III CheckMate-743 study of Opdivo and Yervoy meets primary OS endpoint in mesothelioma

CheckMate-743, a phase III trial evaluating Opdivo (nivolumab) in combination with Yervoy (ipilimumab) in previously untreated malignant pleural mesothelioma met its primary endpoint of overall survival.

Bristol-Myers Squibb sponsors both drugs.

Based on a prespecified interim analysis conducted by the independent data monitoring committee, Opdivo in combination with Yervoy resulted in a statistically significant and clinically meaningful improvement in OS compared to chemotherapy (pemetrexed and cisplatin or carboplatin).

The safety profile of Opdivo plus Yervoy observed in the trial reflects the known safety profile of the combination.

“These topline results from the CheckMate-743 trial demonstrate the potential of Opdivo plus Yervoy in previously untreated patients with malignant pleural mesothelioma, and is another example of the established efficacy and safety of the dual immunotherapy combination seen in multiple tumor types,” Sabine Maier, development lead of Thoracic Cancers at BMS, said in a statement.

CheckMate-743 is an open-label, multi-center, randomized phase III trial evaluating Opdivo plus Yervoy compared to chemotherapy (pemetrexed and cisplatin or carboplatin) in patients with previously untreated malignant pleural mesothelioma. The primary endpoint of the trial was OS. Secondary endpoints included objective response rate, disease control rate, progression-free survival, and efficacy measures according to PD-L1 expression level.

Phase III CheckMate-9ER meets primary PFS endpoint in RCC

The phase III CheckMate-9ER trial evaluating Opdivo (nivolumab) in combination with Cabometyx (cabozantinib) compared to sunitinib in previously untreated advanced or metastatic renal cell carcinoma met its primary endpoint of progression-free survival at final analysis.

CheckMate-9ER has also met secondary endpoints of overall survival at a pre-specified interim analysis, and objective response rate.

Opdivo is sponsored by Bristol-Myers Squibb, and Cabometyx is sponsored by Exelixis. The trial is sponsored by BMS and Ono Pharmaceutical Co. and co-funded by Exelixis, Ipsen and Takeda Pharmaceutical Company Ltd.

CheckMate-9ER is an open-label, randomized, multi-national phase III trial evaluating patients with previously untreated advanced or metastatic renal cell carcinoma. Patients are randomized 1:1 to Opdivo and Cabometyx or sunitinib. The primary endpoint is progression-free survival. Secondary endpoints include overall survival and objective response rate. The primary efficacy analysis is comparing the doublet combination versus sunitinib in all randomized patients.

The safety profiles of Opdivo and Cabometyx observed in the trial reflect the known safety profiles of the immunotherapy and tyrosine kinase inhibitor components in first-line RCC.

“The results from the pivotal CheckMate-9ER trial clearly demonstrate the combination of cabozantinib plus nivolumab provides a clinically meaningful benefit in the key efficacy measures of progression-free survival and overall survival for previously untreated kidney cancer patients,” Toni Choueiri, director of the Lank Center for Genitourinary Oncology at Dana-Farber Cancer Institute and Jerome and Nancy Kohlberg Professor of Medicine at Harvard Medical School, said in a statement.

New targeted agent produces responses in trial with patients with uterine serous carcinoma

In its first clinical trial in patients with a hard-to-treat form of uterine cancer, a targeted drug that subjects tumor cells to staggering levels of DNA damage caused tumors to shrink in nearly one-third of patients, investigators at Dana-Farber Cancer Institute report.

The preliminary results, presented online April 23 at the virtual session of the Society for Gynecologic Oncology Annual Meeting on Women's Cancer, demonstrated strong activity of WEE1-directed therapy in uterine serous carcinoma (USC), which accounts for about 10% of uterine cancers but up to 40% of deaths from the disease, trial leaders say.

The drug tested in the study—adavosertib—takes advantage of an inherent weakness in the relentless growth of some cancer cells. Their non-stop proliferation creates a condition known as replication stress, where their ability to duplicate their DNA effectively is significantly impaired.

In USC, more than 90% of cases are marked by a mutation or other abnormality in the TP53 gene, which plays a critical role in the checkpoint between the first phase of cell growth and the DNA-duplication phase. Without a working TP53 gene, cells can barrel into the DNA-duplication phase with extensive DNA damage on board.

The absence of functional TP53 places enormous strain on a checkpoint further on in the cell cycle called G2/M. Providing a final quality check, G2/M, guards the entry to mitosis, the act of dividing into two daughter cells. Hobbiling G2/M by blocking one of the proteins involved in it could burden tumor

cells with so much DNA damage that they cannot survive.

That is the strategy behind adavosertib, which targets a protein called WEE1 that helps regulate the G2/M checkpoint. The new trial marked the first time the drug, which has been tested in patients with other cancers, including breast and ovarian cancer, was tested in patients with USC.

The trial involved 35 patients, all of whom had previously been treated with platinum-based chemotherapy. They took adavosertib orally on a set schedule. At a median follow-up of 3.8 months, 10 of 34 patients who could be evaluated, had shrinkage of their tumors—a response rate of almost 30%. In some cases, the responses were exceptionally durable, with some patients still responding more than a year after undergoing treatment, study leaders say.

RVD Therapy shows substantial benefit in large myeloma study

A team of investigators from Winship Cancer Institute of Emory University has shown outstanding long term survival results for multiple myeloma patients from a 3-drug induction regimen in a [study](#) published in the *Journal of Clinical Oncology*.

The study describes the largest cohort of patients treated with a combination of lenalidomide, bortezomib, and dexamethasone (RVD) with the longest follow up reported to date.

The study followed 1,000 consecutive patients with newly diagnosed myeloma, both transplantation-eligible and -ineligible, who were treated with RVD induction therapy from January 2007 until August 2016.

“Looking at a large cohort of patients over a long period of time, we were

able to provide a more comprehensive picture of the overall treatment course with RVD as induction therapy,” senior author and Winship hematologist, Ajay K. Nooka, said in a statement. “We have seen our patients attain excellent results from RVD, so it’s gratifying to corroborate those results in this study.”

The study describes the RVD induction regimen as part of the significant therapeutic advances in myeloma over the past few decades that have led to an improved survival benefit for patients.

“Our study demonstrates not only the efficacy of the RVD induction regimen in attaining deep responses, but also the benefit of risk-stratified and continuous maintenance therapy in positively impacting long-term survival,” first author and Winship hematologist Nisha S. Joseph, said in a statement.

The study’s outcomes are based on genetic risk at diagnosis, progression-free survival, overall survival, and the impact of genetics on the quality and depth of response. African American patients made up 35.2% of study participants, which is consistent with the demographics of the myeloma population served by Winship.

“Large data sets like ours with 352 African-American patients receiving uniform therapy help to reassure that AA patients derive a similar benefit as their white counterparts if offered the same therapeutic care,” Nooka and Joseph said.

Cue Biopharma and Merck to evaluate CUE-101 + Keytruda in head and neck indication

Cue Biopharma Inc. and Merck are evaluating the combination of Cue Biopharma’s investigational product candidate CUE-101, a first-in-class biologic, with

Merck's Keytruda in patients with advanced head and neck cancer.

Cue Biopharma is a clinical-stage biopharmaceutical company engineering a novel class of injectable biologics to selectively engage and modulate targeted T cells within the body.

Under the terms of the agreement, Cue Biopharma will conduct a phase I study, KEYNOTE-A78, evaluating CUE-101 in combination with Keytruda in first-line HPV+ advanced head and neck cancer.

KEYNOTE-A78 will be conducted alongside the ongoing phase I monotherapy study of CUE-101 post first-line treatment. The early monotherapy PK data from the first two dosing cohorts

demonstrates dose-related drug exposure consistent with preclinical modeling. Subsequent to the respective dose escalations, expansion cohorts evaluating CUE-101 as a monotherapy and in combination with Keytruda will be conducted at optimized dosing regimens.

"Through the monotherapy and combination studies, we believe we will be able to demonstrate the mechanistic advantages of our approach and platform for modulating disease-relevant T cells directly in the patient's body to safely enhance efficacy over current standards of care," Daniel Passeri, chief executive officer of Cue Biopharma, said in a statement.

"Based on a novel mechanism of action designed to induce and expand

tumor-specific T cells in the patient's body, we believe CUE-101 may lead to enhanced anti-tumor activity in combination with KEYTRUDA," Ken Pienta, acting chief medical officer of Cue Biopharma, said in a statement.

CUE-101 is a fusion protein comprised of a human leukocyte antigen complex, an HPV16 E7 peptide epitope, reduced affinity human interleukin-2 molecules, and an effector attenuated human immunoglobulin G (IgG1) Fc domain. In preclinical studies, CUE-101 has demonstrated selective induction and expansion of HPV16 E7-specific cytotoxic T cells with both in vitro and in vivo evidence supporting its potential for clinical efficacy both as a monotherapy and in combination with anti-PD1 checkpoint blockade.

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DRUGS & TARGETS



FDA approves Tukysa in breast cancer indication

FDA has approved Tukysa in combination with chemotherapy (trastuzumab and capecitabine) for the treatment of adult patients with advanced forms of HER2-positive breast cancer that can't be removed with surgery, or has spread to other parts of the body, including the brain, and who have received one or more prior treatments.

Seattle Genetics sponsors Tukysa.

FDA collaborated with the Australian Therapeutic Goods Administration, Health Canada, Health Sciences Authority (HSA, Singapore) and Swissmedic (SMC, Switzerland) on this review.

This is the first Project Orbis partnership between the FDA, HSA and Swissmedic. While FDA approved Tukysa, the application is still under review at the other agencies.

Collaboration among international regulators may allow patients with cancer to receive earlier access to products in other countries where there may be significant delays in regulatory submissions, regardless of whether the product

has received FDA approval. Early availability of new therapies and adoption as standard of care around the world may have an impact on the increasingly international conduct of cancer clinical trials, potentially accelerating the development of anticancer products.

"The FDA's Project Orbis provides a framework for concurrent submission and review of oncology drug applications among the FDA's international collaborators," Richard Pazdur, director of the FDA Oncology Center of Excellence and acting director of the Office of Oncologic Diseases in the FDA Center for Drug Evaluation and Research, said in a statement.

"We are pleased to work with our Singapore and Switzerland colleagues for the first time, and to continue working alongside our Australian and Canadian colleagues as we facilitate new treatment options for patients—like today's first new molecular entity under Project Orbis," Pazdur said.

"The clinical trial supporting this approval enrolled and specifically studied patients with active brain metastases in addition to the overall population enrolled, which also demonstrated benefit in this subgroup," Pazdur said.

More than 25% of women with metastatic HER2-positive breast cancer will develop brain metastases.

"We recognize that patients with cancer constitute a vulnerable population at risk of contracting the coronavirus disease," said Pazdur. "In this critical time, we remain steadfast in our commitment to patients with cancer and doing everything we can to expedite oncology product development. Tukysa was approved four months prior to the FDA goal date, providing an example of this commitment and showing how our regular work in reviewing treatments for patients with cancer is moving forward without delay."

Tukysa is a kinase inhibitor, and was approved for treatment after patients have taken one or more anti-HER2-based regimens in the metastatic setting. The FDA approved Tukysa based on the results of a clinical trial enrolling 612 patients who had HER2-positive advanced unresectable or metastatic breast cancer and had prior treatment with trastuzumab, pertuzumab and ado-trastuzumab emtansine (T-DM1).

Patients with previously treated and stable brain metastases, as well as those with previously treated and growing or untreated brain metastases, were eligible for the clinical trial, and 48% of enrolled patients had brain metastases at the start of the trial.

The primary endpoint was progression-free survival. The median PFS in patients who received Tukysa, trastuzumab, and capecitabine was 7.8 months compared to 5.6 months in those patients who received placebo, trastuzumab, and capecitabine.

Overall survival and PFS in patients with brain metastases at baseline were key secondary endpoints. The median overall survival in patients who received Tukysa, trastuzumab, and capecitabine was 21.9 months compared to 17.4 months in patients who received placebo, trastuzumab, and capecitabine. The median PFS in patients with brain metastases at baseline who received Tukysa, trastuzumab and capecitabine was 7.6 months compared to 5.4 months in patients who received placebo, trastuzumab and capecitabine.

FDA grants accelerated approval for Trodelvy in previously-treated metastatic TNBC

FDA has approved Trodelvy (sacituzumab govitecan-hziy) for the treatment of adult patients with metastatic triple-negative breast cancer who have received at least two prior therapies for metastatic disease.

Patients must have received at least two prior therapies before taking Trodelvy. Trodelvy is the first ADC approved by the FDA specifically for relapsed or refractory metastatic TNBC and is also the first FDA-approved anti-Trop-2 ADC.

Trodelvy, which was granted Breakthrough Therapy Designation and Priority Review, was approved under the FDA Accelerated Approval Program based on the objective response rate and duration of response observed in a single-arm, multicenter phase II study.

“Metastatic triple-negative breast cancer is an aggressive form of breast cancer with limited treatment options. Chemotherapy has been the mainstay of treatment for triple-negative breast cancer. The approval of Trodelvy today represents a new targeted therapy for patients living with this aggressive malignancy,” Richard Pazdur, director of the FDA Oncology Center of Excellence and acting director of the Office of Oncologic Diseases in the FDA Center for Drug Evaluation and Research, said in a statement. “There is intense interest in finding new medications to help treat metastatic triple-negative breast cancer. Today’s approval provides patients who’ve already tried two prior therapies with a new option.”

Continued approval may be contingent upon verification of clinical benefit in the confirmatory phase III ASCENT study, which was recently halted by the independent data safety monitoring Committee for compelling evidence of efficacy across multiple endpoints.

“In our trial, Trodelvy demonstrated clinically meaningful responses in pa-

tients with difficult-to-treat metastatic TNBC and moves the needle towards better outcomes for patients with metastatic breast cancer,” lead investigator Aditya Bardia, director of Precision Medicine at the Center for Breast Cancer, Massachusetts General Hospital Cancer Center, and assistant professor of Medicine at Harvard Medical School, said in a statement.

In the single-arm phase II study, Trodelvy demonstrated an ORR of 33.3% (95% CI: 24.6, 43.1) and a median DoR of 7.7 months (95% CI: 4.9, 10.8), as determined by local assessment, in 108 adult TNBC patients who had previously received a median of three prior systemic therapies in the metastatic setting (range: 2-10).

FDA approves first targeted treatment for patients with cholangiocarcinoma

FDA has granted accelerated approval to Pemazyre (pemigatinib), the first treatment approved for adults with certain types of previously treated, advanced cholangiocarcinoma.

FDA also approved the Foundation-One CDX (Foundation Medicine Inc.) as a companion diagnostic for patient selection.

Incyte Corp. sponsors the drug.

“This approval demonstrates that while we continue to focus our efforts on addressing the COVID-19 pandemic, the FDA remains committed to the important work of reviewing treatments for patients with cancer and other serious conditions,” said Richard Pazdur, director of the FDA Oncology Center of Excellence and acting director of the Office of Oncologic Diseases in the FDA’s Center

for Drug Evaluation and Research, said in a statement.

“With Pemazyre, we considered the observed efficacy results to be clinically meaningful and the overall risk to benefit assessment for patients with tumors harboring FGFR2 gene fusions and other rearrangements to be favorable, particularly when we considered that these patients have no other good options following first line treatment with chemotherapy,” Pazdur said.

The approval is for locally advanced or metastatic cholangiocarcinoma in patients who have tumors that have a fusion or other rearrangement of the FGFR2 gene.

At diagnosis, a majority of patients with cholangiocarcinoma have advanced disease. Prior to the April 17 approval, there were no FDA-approved therapies for the disease. FGFR2 fusions have been found in the tumors of approximately 9% to 14% of patients with cholangiocarcinoma. Pemazyre is a tablet that works by blocking FGFR2 in tumor cells.

Efficacy was investigated in FIGHT-202 (NCT02924376), a multicenter open-label single-arm trial, in 107 patients with locally advanced unresectable or metastatic cholangiocarcinoma whose disease had progressed on or after at least one prior therapy and had an FGFR2 gene fusion or rearrangement. Patients received pemigatinib, 13.5 mg orally, once daily for 14 consecutive days, followed by 7 days off therapy.

The major efficacy outcome measures were overall response rate and duration of response determined by an independent review committee using RECIST 1.1. Among the 107 patients, the ORR was 36% (95% CI: 27%, 45%), including three complete responses. The median DOR was 9.1 months with responses lasting ≥ 6 months in 24 of the 38 (63%) responding patients and ≥ 12 months in 7 (18%) patients.

FDA approves Imbruvica in CLL/SLL indication

FDA has approved Imbruvica (ibrutinib) in combination with rituximab for the treatment of previously untreated patients with chronic lymphocytic leukemia or small lymphocytic lymphoma.

AbbVie sponsors Imbruvica.

“The FDA approval of ibrutinib and rituximab regimen is welcome news for these previously untreated patients who have been looking forward to a non-chemotherapy treatment option. The results from ECOG-ACRIN’s E1912 clinical trial in previously untreated, younger adult patients and today’s milestone represent a paradigm shift in how physicians can treat patients with CLL and may enable many to choose a non-chemotherapy treatment option,” Brian Koffman, chief medical officer and executive vice president of CLL Society, said in a statement.

Approval was based on the E1912 trial (NCT02048813), a 2:1 randomized, multicenter, open-label, actively controlled trial of ibrutinib with rituximab compared to fludarabine, cyclophosphamide, and rituximab (FCR) in 529 adult patients 70 years or younger with previously untreated CLL or SLL requiring systemic therapy. Patients with 17p deletion were excluded. Ibrutinib was administered at 420 mg daily until disease progression or unacceptable toxicity.

The main efficacy outcome measure was progression-free survival (PFS). The trial demonstrated a statistically significant improvement in PFS for patients receiving ibrutinib plus rituximab compared with those receiving FCR (HR 0.34; 95% CI: 0.22, 0.52; $p < 0.0001$). Median PFS was not reached in either

arm after a median follow-up duration of 37 months.

In addition to the Real-Time Oncology Review pilot program and priority review, the approval was granted under the FDA’s recently established Project Orbis, an initiative of the FDA Oncology Center of Excellence, which provides a framework for submission and review of oncology medicine applications among multiple regulatory agencies worldwide.

For this application, a modified Project Orbis was undertaken because of the timing of submission to other regulatory agencies. FDA is collaborating with the Australian Therapeutic Goods Administration, Health Canada, and Swissmedic as they review the application.

“Imbruvica enables long-term disease management and now has demonstrated superior progression-free survival compared to a standard chemoimmunotherapy regimen. Today, many patients who were previously considered appropriate for chemotherapy now have an alternative treatment option,” Danelle James, Imbruvica Clinical Development Lead, Pharmacyclics LLC, an AbbVie company, said in a statement.

The E1912 study demonstrated that previously untreated patients (ages 70 or younger) with CLL have superior progression free survival Imbruvica plus rituximab compared to those treated with fludarabine, cyclophosphamide and rituximab (FCR).

At a median follow-up of 37 months, Imbruvica plus rituximab significantly improved PFS compared to FCR (hazard ratio [HR] 0.34; 95% confidence interval [CI]: 0.22-0.52; $p < 0.0001$). With a median follow-up time of 49 months, median overall survival was not reached with a total of 23 deaths: 11 (3%) in the IMBRUVICA plus rituximab and 12 (7%) in the FCR treatment arms.

FDA approves Keytruda companion diagnostic

FDA has approved PD-L1 IHC 22C3 pharmDx as a companion diagnostic to identify patients with non-small cell lung cancer who are appropriate for first-line monotherapy with Keytruda on the Dako Omnis platform.

Agilent Technologies Inc. sponsors PD-L1 IHC 22C3 pharmDx. Dako Omnis is Agilent’s fully automated, walk-away solution for staining tumor samples that provides a flexible, high-throughput diagnostic service integrated into the core of the laboratory workflow.

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