



**TCL**

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## **THE COVID CHALLENGE: MAINTAINING PROGRESS IN MULTIPLE MYELOMA CLINICAL INVESTIGATION**

The past two decades have brought hope to myeloma patients, as the majority benefit from the significant advances in chemotherapy.

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*"The cancer care community must seize this opportunity to build a new knowledge base that will inform cancer care and treatment decisions during future disease outbreaks. We encourage every practice to share their experience."*

– Richard L. Schilsky, MD, FSCT, FACP, FASCO  
ASCO Chief Medical Officer and Executive Vice President

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GUEST EDITORIAL

# THE COVID CHALLENGE: MAINTAINING PROGRESS IN MULTIPLE MYELOMA CLINICAL INVESTIGATION

The past two decades have brought hope to myeloma patients, as the majority benefit from the significant advances in chemotherapy.



## Hearn Jay Cho, MD, PhD

*Associate professor, Multiple Myeloma Center of Excellence,  
Tisch Cancer Institute, Icahn School of Medicine at Mt. Sinai;  
Chief medical officer, The Multiple Myeloma Research Foundation*

According to data from the NCI Surveillance, Epidemiology, and End Results Program, the risk of death from multiple myeloma declined by 18.75% between 2000 and 2017, the last year for which numbers are available. During that time, incidence went up from 6 to 6.7 cases per 100,000 while deaths dropped from 3.8 to 3.2 per 100,000.

This decline in mortality can be attributed to the introduction of novel agents for induction and maintenance therapy and the standardization of consolidation therapy in this disease.

This journey is not finished, and we are in the midst of the next revolution in myeloma therapy. Rational development of combination immunotherapy for myeloma coupled with diligent translational science will lay the path to a cure for this disease.

Progress will come against the backdrop of the COVID-19 pandemic and its aftermath. This unprecedented healthcare crisis upended the conduct of clinical trials, slowing screening and enrollment to a trickle, and presenting logistical challenges to management of enrolled patients.

Investigators had to balance two imperatives that at times seemed opposed:

- Decreasing or eliminating clinic visits and infusions to minimize risk of exposure to SARS-CoV-2, and
- Safe continuation of investigational therapy.

The past five months have demonstrated that satisfying these two requirements is both feasible and scalable. For the Myeloma-Developing Regimens Using Genomics (MyDRUG) trial (NCT03732703, sponsored by the Mul-

tiple Myeloma Research Consortium), many of the investigational agents are oral, and we secured agreement from our pharmaceutical partners to allow direct shipping of investigational agents to patients' homes, utilizing local labs for monitoring to minimize trips to urban areas and tertiary care centers, and telemedicine for investigator follow-up visits.

Some health systems went even further in the management of COVID-19 patients, implementing "virtual hospital" plans in which patients received hospital-level care at home, utilizing visiting health care professionals, home therapy, including infusions, and remote lab monitoring.

These innovative responses to an extraordinary crisis show that clinical care may be safely delivered without undue risk or burden to patients. Therefore, it is worthwhile to incorporate such practices into clinical trial design to preserve patient safety and minimize barriers to patient consent such as frequent travel, which in turn may accelerate enrollment.

It is worthwhile to note that the subcutaneous formulation daratumumab faspro was just approved, and that similar injectable formulations are under clinical investigation for isatuximab and several bispecific T cell engaging agents, predicting much shorter treatment visits and possibly even home administration.

These innovations, along with companion oral medications, telemedicine and remote vitals monitoring (e.g. wearables), and flexibility in lab monitoring (local labs, mailer kits), may speed accrual and decrease costs for future IO trials in multiple myeloma.

## Immunologic therapy

Research into immunologic therapy for multiple myeloma is based on

clinical evidence that it has the potential for cure.

In a landmark series of reports in the late 90s, patients undergoing allogeneic bone marrow transplantation for multiple myeloma demonstrated a plateau in long-term disease-free survival, proving that the graft-vs-myeloma effect could control the disease.

Furthermore, patients who had relapsed after allogeneic transplant could be put into durable remission with donor lymphocyte infusion, indicating that anti-tumor lymphocyte activity was responsible for these remarkable results.

Despite this, clinical research in myeloma was dominated by the introduction of proteasome inhibitors (bortezomib, carfilzomib), IMiDs (thalidomide, lenalidomide, pomalidomide), and the acceptance of high-dose chemotherapy and autologous stem cell rescue (auto-transplant) as standard consolidation therapy. These innovations had a dramatic effect on survival and quality of life, but have not yet produced broadly applicable curative therapy.

The urgent need for immunologic agents that could replicate the outcomes in allogeneic transplant without the significant morbidity and mortality risks went unfulfilled until the introduction of elotuzumab, a monoclonal antibody (mAb) that recognized SLAMF7, and the anti-CD38 mAb daratumumab (a second anti-CD38 mAb, isatuximab, was recently approved by the FDA).

These agents were introduced based on the hypothesis that they would act as "targeting antibodies" that opsonized myeloma cells expressing the respective ligands on their cell surface, making them vulnerable to antibody-dependent, cell-mediated cytotoxicity (ADCC) and complement-dependent cytotoxicity (CDC). Emerging clinical and laboratory data indicate that these agents also have powerful effects on the immune

system. SLAMF7 is an activating receptor expressed on natural killer (NK) cells, and crosslinking with elotuzumab rendered NK cells capable of killing myeloma cells even if they were not coated with elotuzumab. CD38 is an ectoenzyme that catalyzes the rate-limiting step in the conversion of extracellular nicotine adenine dinucleotide (NAD) to adenosine, and inhibition of this activity with daratumumab may inhibit regulatory T cell (Treg) and promote cytotoxic T lymphocyte (CTL) activity.

Interestingly, upregulation of immune checkpoint molecules, including PD-L1, LAG-3, and TIGIT, are associated with progression of disease during treatment with daratumumab, further supporting a T cell-mediated mechanism for efficacy.

Furthermore, the immunomodulatory drugs are living up to their name. In addition to their cytotoxic effects on myeloma cells, ImiDs have a broad range of favorable effects on the immune system mediated by modifying the activity of the ubiquitin ligase cereblon.

ImiDs promote maturation of dendritic cells, the principle antigen-presenting cells, and activation of B, T, and NK cells. These agents are attractive partners for combination immunotherapy. In fact, combinations of elotuzumab and daratumumab with either lenalidomide or pomalidomide produced unprecedented response and progression-free survival results in relapse/refractory multiple myeloma that support the current investigations into daratumumab-based combination therapy in frontline treatment.

We are now in the midst of an explosive proliferation in immune-based therapies for multiple myeloma, including engineered Chimeric Antigen Receptor (CAR) T cells, bi-specific T or NK cell engaging agents, antibody-drug conjugates (ADCs), and novel mAbs tar-

getting immune checkpoints and other functional immunologic molecules.

Many of these agents are in late stage clinical trials, and the FDA's Oncologic Drugs Advisory Committee earlier this month unanimously voted in favor of approval of the BCMA ADC belantamab mafodotin (*The Cancer Letter*, [July 17, 2020](#)).

## Novel strategies

This dazzling array of novel strategies highlights both the promise and the challenges in developing curative therapy for myeloma.

This may be conceptualized in the context of the "Cancer-Immunity Cycle" proposed by Chen and Mellman in a review article in 2013 (*Immunity* 39:1, 2013), which posited that the initiation and propagation of successful anti-tumor immunity depended on an orderly succession of events: immunogenic tumor cell death and the release of tumor-associated antigens at the tumor site, uptake of these antigens by APC and trafficking to secondary lymphoid tissue, interactions with Ag-specific CD4 T helper and CD8 cytotoxic T cells, egress of these Ag-specific T cells to the circulation and homing back to the tumor site, recognition of Ag displayed on the tumor in the context of major histocompatibility complex (MHC) class I, and activation of T cell killing mechanisms to induce immunogenic cell death, thus continuing the cycle.

This model highlights two critical concepts.

First, anti-tumor immunity requires multiple steps that are dissociated in both space and time, and second, that tumors may have resistance mechanisms that interfere with one or more of these steps. An immunologic agent that acts at one or a few of these steps will only demonstrate clinical activi-

ty if all the other steps are favorably aligned, which explains the relatively low response rates of single agents in this context. Therefore, combination therapy is the logical goal to achieve robust response rates and durable remissions in a large population of myeloma patients.

The elotuzumab experience is instructive in this context. In phase 1 studies, elotuzumab showed no single agent activity whereas the combination with lenalidomide had a significant response rate. The phase 1b/2 ELOQUENT-2 study of elotuzumab vs lenalidomide in relapsed/refractory myeloma, the elotuzumab combination had a 79% response rate and median progression-free survival of 21 months, both showing superiority over the control arm.

Furthermore, the POLLUX study of daratumumab lenalidomide vs lenalidomide in relapsed/refractory myeloma demonstrated a remarkable 93% response rate and median PFS of 44.5 months, vastly superior to the control arm. Long term follow-up of both of these studies showed favorable 4-year progression-free and overall survival benefit, particularly in the POLLUX study, indicating that for a subset of myeloma patients, these combinations contributed to long-term control of their disease.

We are now faced with the challenge of converting these remarkable results in small subsets of patients into regimens that are effective in larger populations. The approved and investigational agents act at every point in the Cancer-Immunity Cycle and many of them can neutralize or bypass mechanisms of tumor immune evasion. Rational combinations of immunologic therapies may favorably align the cycle and confer long term remission as was promised by the allogeneic transplant experience.

These combinations may include approved myeloma drugs such as ImiDs and even conventional cytotoxic agents

such as cyclophosphamide, which can induce immunogenic cell death and reduce Treg cell numbers and activity.

These clinical trials must be paired with robust correlative science as we need to understand the actions of these therapies on myeloma cells and the tumor microenvironment in the bone marrow. Leading edge technologies such as high dimensional immunophenotyping by mass cytometry or single cell RNA sequencing, immune-oncology proteomics, and T cell clonal diversity by T cell receptor sequencing brings powerful, data-driven analysis of the immune response at a level comparable to genomics and gene expression analysis of tumor cells.

These studies may verify mechanisms of action, reveal novel biomarkers of response or resistance, and identify associated targets in these trials. These studies may also identify novel methods of patient selection that, in concert with tumor intrinsic factors such as cytogenetic abnormalities, may categorize patients that may be best served by specific therapies. Understanding this complex biology is essential to further advances.

There also needs to be broader thinking about the design of such trials, as therapies designed to modulate the anti-myeloma immune response are fundamentally different than cytotoxics or small molecule inhibitors intended to kill tumor cells. The Cancer-Immunity Cycle is a complex orchestrated process, and manipulations may be better accomplished with measured sculpting rather than hammer strikes. The concept of "maximum tolerated dose" may be less applicable compared to "minimum effective dose."

Again, the elotuzumab experience is instructive.

In phase 1b studies, two dose levels of elotuzumab, 10 mg/kg and 20 mg/kg IV



weekly were tested in combination with lenalidomide. The 20 mg/kg dose combination had both a lower response rate and shorter PFS compared to the 10 mg/kg dose, indicating that the higher dose, while tolerable, adversely affected the overall activity of the combination.

It is also time to revisit the concept of sequential therapy. There is already widespread acceptance of sequential therapy for myeloma, as we routinely treat patients with induction, consolidation, and then maintenance therapy. For immunotherapy, there is a strong rationale to leverage the cyclic nature of the Cancer-Immunity Cycle to sequence or alternate immunologic cell death by cytotoxics, ImiD/proteasome inhibitor combinations, or novel agents such as CAR-T cells or ADCs, with promoters of T cell immunity such as anti-CD38 mAbs, bi-specifics, or immune checkpoint inhibitors.

This concept may be extended, for example, to sequence cytotoxic induction therapy with immunologic maintenance. These novel trial designs may fall outside the normal registration path of a new agent, but in order to fulfill the potential of a given therapy, the biology of the agent must be respected. It is likely that novel diagnostic approaches such as combined immune and tumor genomic profiling and innovative trial designs will yield rationally-designed combination therapies that are tailored for specific myeloma populations.

Finally, the criteria upon which these trials are assessed is in evolution.

## Approval criteria evolve

Prior to the introduction of lenalidomide and bortezomib, median survival for myeloma patients was three years or less.

Therefore, demonstration of overall survival benefit was a reasonable goal of a registration trial.

The remarkable pace of progress has raised this bar very high.

It is notable that the last two multiple myeloma drugs to receive regular approval based on endpoints that included OS were approved in 2015, in the beginning of a surge of approvals.

Both were approved based on OS and progression-free survival.

Since 2015, 11 drugs received regular approval based on PFS alone, one based on PFS and overall response rate, and one based on ORR alone.

The only previous regular approval based on OS in multiple myeloma occurred in 2005.

A table listing two decades' worth of accelerated and regular approvals in multiple myeloma appears on [page 10](#).

In this time frame, we see that mortality in multiple myeloma overall has dramatically decreased, and it is likely that this figure is in evolution, as the full effect of newer immune therapies, both approved and investigational, are manifest.

This fact strongly supports the concept that surrogate endpoints—particularly PFS—are appropriate in assessing the efficacy of novel myeloma therapies.

Validation of endpoints continues.

There is now a vigorous debate on the use of Minimal Residual Disease (MRD) as a surrogate endpoint in myeloma clinical trials, as overall survival may unreasonably extend the assessment period and delay introduction of needed agents to standard care.

Although the FDA has not accepted this as a surrogate endpoint yet, it is critical to build these novel measures into myeloma immunology trials to understand their relation to traditional measures such as overall response rate and PFS. Further complicating matters, there are competing MRD assays, including flow cytometry, B cell receptor sequencing, and mass spectrometry detection of the M-protein in peripheral blood, and further clinical investigation is needed to determine the best assays and applications.

Laboratory and clinical investigation have yielded a remarkable array of novel agents, treatment regimens, and diagnostic technologies. The challenge is to find the rational combinations, sequences, and clinical trial practices that will finally deliver curative therapy.



We see that mortality in multiple myeloma overall has dramatically decreased, and it is likely that this figure is in evolution, as the full effect of newer immune therapies, both approved and investigational, are manifest.



## ENDPOINTS FOR APPROVAL OF MULTIPLE MYELOMA DRUGS – SOURCE: FDA

Drug	NME or Novel Biologic?	Sponsor	Indication	Accelerated Approval Year	Regular Approval Year	AA Endpoint	RA Endpoint
Bortezomib	Yes	Millenium	MM with at least 2 prior therapies	2003	2005	RR	OS
Bortezomib	No	Millenium	MM, with dexamethasone 1 after at least one prior therapies	n/a	2005	n/a	TTP/OS
Lenalidomide	Yes	Celgene	In combination with dexamethasone for MM after at least one prior therapy	n/a	2006	n/a	TTP
Thalidomide	No	Celgene	In combination with dexamethasone for newly diagnosed MM	2006		RR	
Doxorubicin HCl liposome injection	No	Alza	In combination with bortezomib after at least one prior therapy	n/a	2007	n/a	TTP
Bortezomib	No	Millenium	Newly diagnosed MM	n/a	2008	n/a	TTP
Pomalidomide	Yes	Celgene	MM after at least 2 prior therapies, including lenalidomide and bortezomib	2013	2015	RR	PFS/OS
Pomalidomide	No	Celgene	MM, at least 2 prior lines, including lenalidomide and a proteasome inhibitor		2015		PFS/OS
Panobinostat	Yes	Novartis	In combination with bortezomib and dexamethasone after two prior regimens, including bortezomib and an immunomodulatory agent	2015		PFS	
Carfilzomib	No	Onyx	In combination with lenalidomide and dexamethasone for relapsed or refractory MM after one to three prior lines of therapy	n/a	2015	n/a	PFS
Elotuzumab	Yes	BMS	In combination with lenalidomide and dexamethasone for the treatment of MM in adults who have received one to three prior therapies	n/a	2015	n/a	PFS
Ixazomib	Yes	Millenium	In combination with lenalidomide and dexamethasone for MM after at least one prior therapy	n/a	2015	n/a	PFS
Daratumumab	Yes	Janssen	MM after at least 3 prior lines of therapy, including a proteasome inhibitor and an immunomodulatory drug or are double refractory	2015	2016	ORR	PFS
Carfilzomib	No	Onyx	In combination with dexamethasone for relapsed or refractory MM after one to three lines of therapy	n/a	2016	n/a	PFS
Daratumumab	No	Janssen	In combination with lenalidomide and dexamethasone in patients with relapsed or refractory MM who have received at least one prior therapy	n/a	2016	n/a	PFS
Daratumumab	No	Janssen	In combination with bortezomib and dexamethasone in patients with relapsed or refractory MM who have received at least one prior therapy	n/a	2016	n/a	PFS

Drug	NME or Novel Biologic?	Sponsor	Indication	Accelerated Approval Year	Regular Approval Year	AA Endpoint	RA Endpoint
Revlimid	No	Celgene	Maintenance therapy for MM following autologous stem cell transplant	n/a	2017	n/a	PFS
Daratumumab	No	Janssen	in combination with bortezomib, melphalan and prednisone in newly diagnosed patients who are ineligible for autologous stem cell transplant	n/a	2018	n/a	PFS
Daratumumab	No	Janssen	In combination with lenalidomide and dexamethasone for newly diagnosed patients ineligible for autologous stem cell transplant	n/a	2019	n/a	PFS
Daratumumab	No	Janssen	in combination with bortezomib, thalidomide, and dexamethasone for newly diagnosed multiple myeloma in patients who are eligible for autologous stem cell transplant (ASCT).	n/a	2019	n/a	ORR/PFS
Selinexor	Yes	Karyopharm Therapeutics	Relapsed/refractory MM after four prior therapies and resistant to at least two proteasome inhibitors, two immunomodulatory agents and an anti-CD38 monoclonal antibody	2019		RR	
Isatuximab-irfc	Yes	sanofi-aventis	In combination with pomalidomide and dexamethasone for adult patients with multiple myeloma who have received at least two prior therapies including lenalidomide and a proteasome inhibitor	n/a	2020	n/a	PFS
Daratumumab and hyaluronidase-fihj	Yes	Janssen	New product allows for subcutaneous dosing of daratumumab. For the same indications of daratumumab IV listed below: a. in combination with bortezomib, melphalan and prednisone in newly diagnosed patients who are ineligible for autologous stem cell transplant b. in combination with lenalidomide and dexamethasone in newly diagnosed patients who are ineligible for autologous stem cell transplant and in patients with relapsed or refractory multiple myeloma who have received at least one prior therapy c. in combination with bortezomib and dexamethasone in patients who have received at least one prior therapy d. as monotherapy, in patients who have received at least three prior lines of therapy including a proteasome inhibitor (PI) and an immunomodulatory agent or who are double-refractory to a PI and an immunomodulatory agent	n/a	2020	n/a	ORR and pharmacokinetic

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

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CONVERSATION WITH  
THE CANCER LETTER

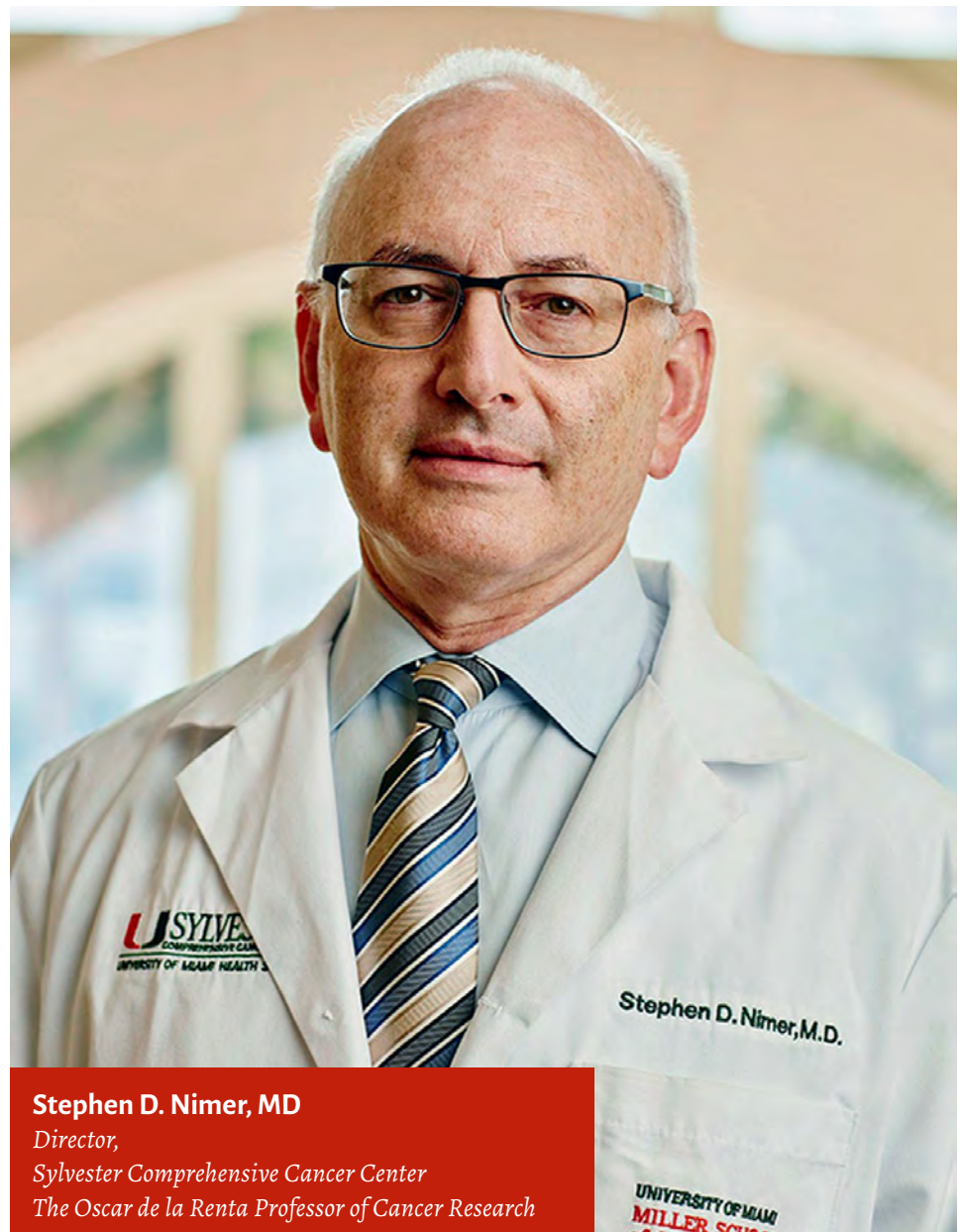
## Stephen Nimer: Cancer patients are coming in for treatment, Florida's COVID-19 spike notwithstanding

This story is part of *The Cancer Letter's* ongoing coverage of COVID-19's impact on oncology. A full list of our coverage is available [here](#).

“

Our concern is that people are going to show up with more advanced cancers, with metastatic disease or incurable disease. Like the rest of the country, we stopped doing screening mammographies and colonoscopies for a while. Those were thought to be elective procedures; right?

”



**Stephen D. Nimer, MD**

Director,  
Sylvester Comprehensive Cancer Center  
The Oscar de la Renta Professor of Cancer Research

“Our chemotherapy and radiation therapy volumes have been very robust. Probably because of the NCI designation, we are seeing significantly more patients than last year,” Stephen D. Nimer, director of Sylvester Comprehensive Cancer Center, said to *The Cancer Letter*. “Compared to last year, we seem to be up about 15%. We’ve been growing by about 8% to 9% for quite some years. This year is even more.”

Sylvester received the NCI Cancer Center designation last July (*The Cancer Letter*, [July 29, 2019](#))

Located in Miami-Dade County, Sylvester is in the hottest of hot spots of the pandemic. At this writing, Florida has had 461,371 cases of COVID-19, with 71,511 cases diagnosed in the past seven days—more than any state in the U.S. The number of deaths is at 6,586.

“Finally, this past week our numbers have started to come down. But throughout the pandemic we have stressed that if you come to see us, you’re not going to get COVID from someone in the hospital,” Nimer said. “As you know, Sylvester has an in-patient cancer only facility that has 40 beds, which we use primarily for stem cell transplant patients, CAR T-cell patients and leukemia patients. We don’t have any COVID patients in our Sylvester facility, and we have continued to conduct stem cell transplants and give chemotherapy and radiation therapy safely.

“Then, we have the university hospital, which has around 400 beds, including hundreds of beds available for cancer patients. We have several floors of the university hospital that are strictly devoted to COVID patients. The COVID floors are on top. It’s an isolated area; people aren’t traveling through it. We keep the COVID-19-positive patients and PUIs in separate surroundings from the rest of our patients the moment they arrive in the Emergency Department.”

Nimer said he worries about long-term effects of the pandemic.

“Our concern is that people are going to show up with more advanced cancers, with metastatic disease or incurable disease. Like the rest of the country, we stopped doing screening mammographies and colonoscopies for a while. Those were thought to be elective procedures; right?”

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

**Paul Goldberg:** How are you holding up?

**Stephen Nimer:** We are quite busy. Our chemotherapy and radiation therapy volumes have been very robust. Probably because of the NCI designation, we are seeing significantly more patients than last year.

In addition, I think that, based on the organizational structures we put in place for our pursuit of NCI designation, our health system and our university have been relying on the infrastructure, expertise and outstanding people within Sylvester to help develop a robust internal testing facility and program to help us deal with COVID-19.

As loyal and caring members of the University of Miami, we’ve been honored to help out.

Our nurse leaders have helped set up testing facilities and run our testing hotline, while our physicians have written guidelines for our patients and employees.

Our researchers have provided expertise, instruments and reagents, so we could quickly ramp up PCR testing capacity. We have also helped address key public health issues, like identifying and

isolating close contacts to reduce viral transmission.

To do this, we have worked extremely closely with executive leadership and with student health, employee health, athletics and with many departments across the university, especially the Department of Pathology, with whom we meet daily, to make sure our testing practices are appropriately validated, including our serologic testing platforms for seroprevalence studies.

**Why is Florida the hottest of the hotspots? What do you think went wrong?**

**SN:** I think we had a false sense of security.

I talk to my cancer researcher friends in New York all the time. Shortly after things got really bad in New York City, we peaked at about 49 COVID positive in-patients. So, we figured that maybe we had dodged the bullet; and everyone was saying we aren’t seeing so many cases...., “Oh, it’s the warm weather,” “It’s the UV light, because everyone’s out in the sun.” But those things didn’t turn out to be true.

We also heard that, like the flu, when it gets warmer in Florida, the virus will disappear. And that wasn’t true, either.

I guess we attribute our cases to the obvious retrospective conclusion that like many, many other states, we probably opened up too early.

You know, I would love to see data about the role that opening restaurants played in spreading the virus, because when I drove around getting takeout, I saw lots of people in restaurants that were not part of the same family—lots of young people sitting together and eating dinner. Of course, not wear-

ing masks while they were eating and talking and drinking.

I also think that the timing was against us. Based on what was happening in the Northeast, we were cooped up for months, with stay-at-home orders, etc.

Then, when the Northeast got better, people were feeling a little bit more confident, so they “let us out.” They opened up the beaches here, and people started getting together, because that’s what people do. And there were lots of conflicting directives about wearing masks, so many people hung out without masks.



I would love to see data about the role that opening restaurants played in spreading the virus, because when I drove around getting takeout, I saw lots of people in restaurants that were not part of the same family—lots of young people sitting together and eating dinner.



There are a lot of young people in Miami; it’s a young city. And I think that that had a great deal to do with it. But I also think there are several factors that maybe haven’t gotten enough attention.

First, Florida has a huge elderly population. About 20% of the 21 million people who live in Florida are 65 or older.

I believe the current numbers show that roughly 48% of the COVID-19 deaths in Florida have occurred among people who were in assisted living facilities.

While there was a several-week period where we were seeing a lot of younger people, once again, the COVID-19 patients we are seeing and hospitalizing are pretty sick—and they are elderly.

The second factor is that Florida, like California, has a huge agriculture industry, including the citrus industry, tomato industry, and others. These industries are dependent on migrant workers who often live in very close quarters, are transported to and from work together, and may be working shoulder-to-shoulder.

COVID infections in these workers has led to big increases in the numbers throughout Florida, not just South Florida, and probably in California, too.

What can you say about disparities? At Sylvester, you probably have the best view of disparities anywhere in the world.

**SN:** We’re seeing the same thing as everyone else is seeing.

Supermarket workers, bus drivers—many of these “essential jobs,” where people can’t work from home, are more often held by minorities. And, of course, like everybody else, we’re still seeing that the people who are dying have significant comorbid conditions that are more commonly seen in minority populations.

Florida is a big state, with a lot of people, and we are disappointed that people don’t wear masks the way they should.

There is good news, though; over the past week, the numbers now are going down. The number of COVID-positive patients in our hospital is going down. The number of COVID tests we are doing per day is going down. The percent of COVID tests that are positive is also going down.

It seems like we may be over a peak, but even after the earlier peak, the downside of the peak wasn’t very steeply down. So, this time, even if we’re no longer at the peak, we don’t know how long we will stay at this level, or something near this level.

Different models are showing different predictions.

It could be a plateau rather than a peak?

**SN:** Exactly.

And then there’s no guarantee that there will not be another peak.

**SN:** When kids go back to school, people have been predicting another bump up.

But we don’t know what that may look like. I do think people are scared. Seeing just how many cases are occurring in our county or our state.

We get a lot of winter visitors from the Northeast, and everyone said, “Well, there are subways in New York, and everyone is so jammed together.”

We don't have subways. We aren't all jammed together down here—but there's been a lot of illness in Florida, plus a lot of asymptomatic infections.

**How have your surveillance efforts been going? You were doing serology testing through the outreach (*The Cancer Letter*, [May 22, 2020](#)) Has that resumed?**

**SN:** We did some serologic testing early on, but more recently we have been largely focused on PCR-based testing. As you imply, we have done a couple of seroprevalence studies. Interestingly, we did a serologic study of our health-care workers.

We generated an IRB-approved protocol, 500 employees. The protocol got IRB-approved on a Tuesday. On Wednesday morning, we sent an email out to our employees that we were looking for 500 people. By the end of the day, we had roughly 3,000 employees volunteer to do the serology study.

And so, we found pretty much similar data to what Dr. Erin Kobetz [associate director for population science and cancer disparity at Sylvester and vice provost for research at the University of Miami] found in Miami-Dade County.

I don't want to quote the data precisely, as we are trying to publish it, but a single-digit percentage of our employees tested positive. This study concluded some time ago, and the numbers are no doubt higher. We are planning on doing additional seroprevalence studies that will include university students, when the college opens up in August.

We have a four-pronged testing program in place to monitor our students

for back-to-school. Currently, the university plans to begin school with a hybrid model, with some in-school classes and some online learning.

**Have your Game Changer vehicles been put back into use? (*The Cancer Letter*, [April 27, 2018](#))**

**SN:** I don't think it's in use. What would happen pre-COVID, is that when the Game Changer vehicle would show up someplace, it would draw a crowd.

We have been very concerned that the vehicle not be a place that would bring crowds together. However, the staff have been assigned to other duties, helping with our COVID-19 control efforts.

**You were doing serology testing, which you put on hold because of an FDA action. Have you started using different tests?**

**SN:** We have validated other serologic tests, and we have found some that work well, including a point of care (POC) test.

To some extent, you have to read the fine print for some of these testing platforms. One serologic test says it is very sensitive "if used 14 days after the onset of symptoms." Well, most of our patients won't be tested exactly on Day 14, and so the assay doesn't work "as well as advertised." Even for PCR machines, sometimes it states that this machine is 100% sensitive if used within five days of the onset of symptoms. Again, this instrument may not be as sensitive when used in real-life situations.

We believe that there are cases where serology helps us. And we do have some plans for more seroprevalence studies, but we're relying primarily on PCR-based virus detection methodologies.

And, obviously, there are lots of asymptomatic infections occurring, that nobody's identifying adequately.

**There's no way to do it, really, at this point, except through more testing.**

**SN:** Right. We are working with Weill Cornell and several other institutions to conduct environmental testing, using PCR, trying to detect where the virus could be on the rise within our undergraduate campus.

This effort is part of a pretty comprehensive plan, that we hope will reassure faculty and students, and parents, that we are doing everything that the science permits us to do right now.

We are testing a variety of point-of-care devices that could give you results in 15 minutes; these may not be as sensitive as traditional PCR-based assays, but they still can be very helpful.

**How has the cancer center been affected? What's the impact on the cancer center?**

**SN:** We're doing a lot more telemedicine, telehealth visits. As a medical center, we used to do maybe 100 a week, and now we do thousands a day.

Unfortunately, it was necessary for us to institute a no-visitor policy, which is really tough for our cancer patients



and their families, but necessary. That's still in place.

Given our robust in-house testing, we test everybody before they start chemotherapy, before they start radiation therapy, before they undergo a surgical procedure. The turnaround times for these tests is generally less than 24 hours.

That's been very helpful, to get people evaluated and screened. We've had a few of our employees come down with COVID. But then again, oftentimes it's traced back to their kids, as opposed to being acquired within the hospital setting.

Our hospital environment has been very safe. We've not had significant outbreaks; perhaps we've had a patient or two that's gotten a healthcare worker or two infected, but it's really very minimal.

We have some doctors who are quite concerned. They're over 60 or 65. They may have health problems. We've been very accommodating to our faculty, to make sure that people don't need to feel like they are jeopardizing themselves.

But especially as this goes on, it's putting a great strain on everybody. We have lots of employees whose kids are at home, which, while typical for the summer, is problematic during the fall and winter. People are concerned about whether school will be delayed or not.

Actually, the Miami-Dade School District announced just yesterday that they're pushing back the start of school a week. It now starts Aug. 31, and they are going to have only online classes until sometime in October. They will make another decision, probably in September, on what to do for the rest of the school semester. That will impact our ability to have all of our critical employees coming to work.

Everybody who can work from home is still working from home. The dedication of our people has been amazing—they really are heroes!

**You mentioned that patients are back, but are they back in the same numbers as before?**

**SN:** The number of patients we are seeing is virtually the same as before.

In some instances, we actually have more patient activity than a year ago, even though it takes more time and effort to see a patient. For every patient we see, the staff has to put on PPE and take it off properly. Everybody who comes into our facility is given a mask.

Because there are no family members allowed inside our facility, it takes a lot more effort on our part. For instance, we have to help navigate the patient from the front door of our facilities to their exam room.

We have streamlined things for patients; we have eliminated waiting rooms at many of our sites of practice. Instead, you can wait in your car. We'll text you and say, "The doctor's ready to see you."

And then you can come into the building, and you go right in to see the doctor. We have eliminated a lot of the chairs from our waiting rooms, but we decided to also eliminate almost all waiting, especially the sitting-in-a-chair waiting.

**You mentioned that patient volume is up from last year, because of the designation, but do you have some guess on the numbers?**

**SN:** Compared to last year, we seem to be up about 15%. We've been growing by about 8% to 9% for quite some years. This year our growth is even more. But we're very worried that there's a lot of cancer out there that's not being diagnosed.

I would say that our volumes are very good, and the number of chemo treatments we have been giving has been stable. If we're down at all, it's just a couple percent. Other parts of our health system were hurting, during the period when the governor declared there would be no elective procedures in the state, and that lasted for a few months.

We had to cancel a lot of surgeries. We had to institute some financial mitigation on the medical campus; top leadership took a salary cut, and the university chose not to contribute to our retirement accounts for this year. We have gotten some CARES money, which has helped. As is true at all other institutions, for many reasons travel is not allowed.

We are holding no in-person meetings. We used to serve lunch at some events and have recruitment dinners. So, I think we're probably saving money on food, and I think we're saving millions, because people aren't traveling. Also, as none of our physicians are traveling, they are able to see some more patients. But, at some point, people have to take some vacation, and I think that's been very tough for everybody.

I will say though that we continue to hire key cancer physicians and researchers, so we can advance our mission.

You mentioned that a lot of cancer is not getting diagnosed. How do you mitigate that later?

“

A lot of screening hasn't taken place. Also, people are afraid. People are afraid to donate blood. People are afraid to go to the Emergency Department for care. In the non-cancer arena, people are having heart attacks and strokes at home, because they don't want to go to a hospital.

”

**SN:** Our concern is that people are going to show up with more advanced disease, with metastatic disease or incurable disease. We stopped doing screening mammographies and colonoscopies for a while. Those were thought to be elective procedures; right?

A lot of screening hasn't taken place. Also, people are afraid. People are afraid to donate blood. People are afraid to go to the Emergency Department for care. In the non-cancer arena, people are having heart attacks and strokes at home, because they don't want to go to a hospital.

We have a confidence-building campaign. We need to get the message out that the hospital is a safe place.

Finally, this past week our numbers have started to come down. But throughout the pandemic we have stressed that if you come to see us, you're not going to get COVID from someone in the hospital.

As you know, Sylvester has an in-patient facility that has 40 beds, which we use primarily for stem cell transplant patients, CAR T-cell patients and leukemia patients.

Then, we have the university hospital, which has around 400 beds. So, we don't have any COVID patients in our Sylvester facility, and we have continued to conduct stem cell transplants and give chemotherapy and radiation therapy safely.

We have several floors of the university hospital that are strictly devoted to COVID. The COVID floors are on top. It's an isolated area; people aren't traveling through it. And we keep the COVID-19 positive patients in separate surroundings from the moment they arrive in the Emergency Department.

Have you done any cool science based on COVID?

**SN:** We have been very involved with the [COVID-19 and Cancer Consortium](#).

We have a manuscript about setting up our testing facility that's available on medRxiv, entitled "A How-to Guide to establishing a SARS-CoV-2 Testing Facility Within an Academic Health Center Setting."

We have been participating in driving convalescent plasma studies for patients in South Florida.

We're also a major site for the Moderna vaccine trial, and, in fact, Vice President Mike Pence was here on Monday of this week to kick it off. We have several other vaccine trials in the pipeline, and several efforts to develop new rapid SARS-CoV-2 testing instruments or technologies.

Obviously, the diversity of our population is very good in any effort to understand the efficacy of the vaccine in different populations, especially in minority populations that may be at increased risk for having bad outcomes once infected with the virus.

And so, VP Pence and the governor and lieutenant governor of the State of Florida and the commissioner of the FDA came to visit us to help kick off this effort.

**You're a blood cancer doc, are you seeing anything from your perspective on this?**

**SN:** We and our colleagues are trying to figure out what are the key risk factors for COVID-19 disease in patients with hematologic malignancies.

I believe we are identifying some specific risk factors in myeloma patients and in CLL patients. Even though cancer patients are often elderly, we really haven't seen specific groups of patients that are doing poorly.

**What about your basic science labs? Are they back to being open? Is it difficult to reopen them?**

**SN:** The university asked every PI to submit what they thought was the critical research that was being conducted. For those with labs, that often meant animal studies, or COVID-relevant research. We have also been able to conduct cancer clinical trials that are critical for the health of our patients, but generally not those trials that require hospitalization.

And so, throughout the pandemic, we have been able to continue the mouse MDS and AML work that has been ongoing for a while. Initially, we were not able to breed new mice strains but more recently, things have opened up.

We were also asked how many people work in your lab and how much lab space do you have. So, roughly, six to eight weeks ago, we have been al-

lowed one person for 200 square feet of lab space.

Also, to maintain social distancing, nobody in my lab is allowed to work more than 20 hours a week. So, we work seven days a week, and we stagger it, so we never have more than five or six people in the lab at the same time. Everyone has to have a mask on. You're not allowed to sit at your desk and play with your computer. If you want to do that, you should be at home, working remotely.

My lab has maintained its two lab meetings a week, but we now do all this by Zoom.

It's a significant difference, of course. Everybody's been impacted, and everyone would love to get back to doing more, but the university is going back slowly, and, of course, we've been in the middle of this surge.

But the lab work is critical. Cancer clinical trials are critical. Also, we have some people at our university that are working on COVID specifically, whether it be viral detection or studying aspects of immune function. We're all very anxious in the cancer center to get back to normal in the lab, but we don't know when that'll be.

**Is there anything in your life that might have prepared you for this?**

**SN:** The only thing I would say is when I look back at my medical training, when I was an intern and a resident in the "days of the giants," as they say. Hard work, focus, being willing to learn each and every day, the things that prepare you to be a physician, prepare you for dealing with emergencies like this.

Think of what we've learned about the science and the biology behind this infection. As our knowledge evolved, we have gone from an initial focus on surfaces, cleaning surfaces, to a focus on droplets and more recently on aerosols. We have identified some therapies that work.

Being a scientist is very helpful in all this.

But I do think that this is a once-in-a-lifetime thing. To see a pandemic that has killed more than 150,000 people in the United States, is incredible.

**Is there anything we forgot? Anything we didn't mention?**

**SN:** To wrap up, the only thing I would say is that the incredible teamwork that we've experienced at our cancer center, on a daily basis, has really been remarkable, as has all the hard work and long hours that people have put in.

We are continuously sending each other emails with information from medical journals, the FDA website, the CDC website, and other sources; the flow of information is incredible.

I think the message is that you can't ignore the science; right?

**Thank you.**

# UC Davis cancer researcher with ties to PRC military charged with visa fraud

By Matthew Bin Han Ong

A UC Davis cancer researcher was arrested July 24 on visa fraud charges.

Juan Tang, the researcher, had previously sought refuge at the Consulate General of the People's Republic of China in San Francisco, according to a July 23 statement from the Department of Justice.

When she applied for a non-immigrant J-1 visa in October 2019, Tang did not disclose her status as a uniformed officer in a branch of the PRC military, DOJ said.

"The UC Davis School of Medicine is providing all information requested by the authorities as they investigate this case," a UC Davis spokesperson said to *The Cancer Letter*. "Juan Tang was a visiting researcher in the Department of Radiation Oncology, funded by the Chinese Scholarship Council, a study-based exchange program affiliated with the China's Ministry of Education and Xijing Hospital in China. Her work was solely based in the research laboratory and she left the University at the end of June.

"It appears the investigation of Ms. Tang is focused on statements made in her visa application for travel to the U.S."

The details of Tang's case were publicly announced amid a recent flurry of prosecution involving individuals who had ties to the People's Republic of China:

- Three other researchers—at UCSF, Stanford, and Indiana University—were also charged with visa fraud, according to the July 23 DOJ announcement, and
- A Singaporean national, who reportedly admitted to working with PRC intelligence operatives, pleaded guilty July 24 to tapping U.S. government employees for sensitive information.

Earlier this year, six researchers at Moffitt Cancer Center were ousted after an internal review by Moffitt alleged that they violated conflict of interest rules through their work in China (*The Cancer Letter*, Jan. 24, 2020, Dec. 20, 2019). The Moffitt cases echo the COIs revealed in 2019 at MD Anderson Cancer Center, where three faculty members were sanctioned for failure to ensure confidentiality of review of NIH grants.

The MD Anderson scientists were also accused of failing to disclose outside funding, academic appointments and roles in laboratories outside the U.S. (*The Cancer Letter*, April 26, 2019).

Tang, the former UC Davis researcher, does not serve as a principal investigator on any NIH grant, NIH officials said.

"NIH does not comment on specific researchers or any investigations, whether or not they may be underway or completed," a spokesperson for the NIH Office of Extramural Research said to *The Cancer Letter*.

"As NIH Director Dr. Francis Collins noted in his Statement on Protecting the Integrity of U.S. Biomedical Research, NIH research is built on a set of bedrock principles of scientific excellence, unassailable integrity and fair competition," NIH officials said. "NIH expects applicants for and recipients of NIH-supported research—both domestic and foreign—to abide by these principles.

“

Juan Tang was a visiting researcher in the Department of Radiation Oncology, funded by the Chinese Scholarship Council, a study-based exchange program affiliated with the China's Ministry of Education and Xijing Hospital in China. Her work was solely based in the research laboratory and she left the University at the end of June.

”

– UC Davis statement

“More on NIH's efforts in this area can be found on the OER's [Protecting U.S. Biomedical Intellectual Innovation webpage](#) and this [recent related blog post](#) from Dr. Michael Lauer, NIH's deputy director for extramural research.”

The July 23 DOJ [statement](#) describing Tang's case follows:

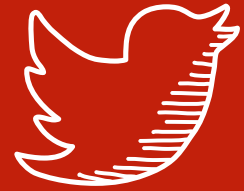
According to court documents unsealed in the Eastern District of California on July 20, Tang, a researcher at the University of California at Davis, applied for a non-immigrant J1 visa on or about Oct. 28, 2019. The visa was issued in November 2019, and Tang entered the United States on or about Dec. 27, 2019. Tang is alleged to have made fraudulent statements on her visa application. Specifically, to the question, 'Have you ever served in the military,' Tang responded 'No.'

In fact, Tang is a uniformed officer of the PLA Air Force (PLAAF). As set forth in the [Complaint](#), the FBI found a photograph of Tang in a military uniform and references to Tang's employment at the Air Force Military Medical University, which has also been known as the Fourth Military Medical University. The FBI interviewed Tang on June 20. Although Tang denied having been a member of the military, an additional photograph of Tang in a different PLA military uniform was found on electronic media seized pursuant to a search warrant.

The FBI is seeking to arrest Tang pursuant to an Arrest Warrant and Complaint that were filed on June 26, and unsealed on July 20. Tang has sought refuge at the Chinese consulate in San Francisco, where she remains.

On July 24, FBI reported that Tang was taken into federal custody.

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

A



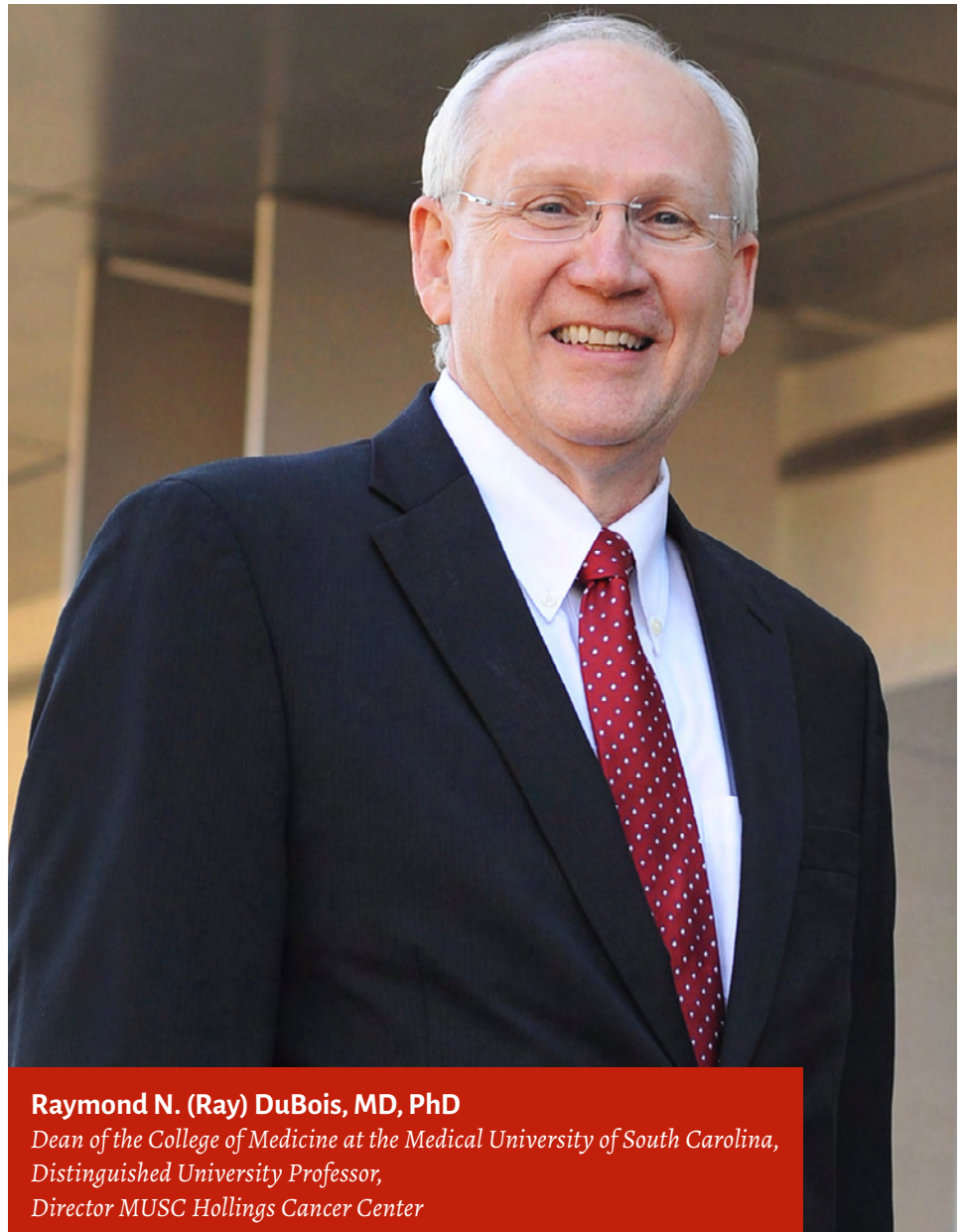
CONVERSATION WITH  
THE CANCER LETTER

## Raymond DuBois discusses his plans to navigate past the pandemic and take Hollings to comprehensive designation

“

In serving both as cancer center director and dean, I believe that I will be in a position to help develop more synergy and closer ties between both of these organizational units, which will ultimately benefit both.

”



**Raymond N. (Ray) DuBois, MD, PhD**

*Dean of the College of Medicine at the Medical University of South Carolina,  
Distinguished University Professor,  
Director MUSC Hollings Cancer Center*

Raymond N. DuBois was named director of MUSC Hollings Cancer Center effective Aug. 17.

This is an additional role for DuBois, who will continue his other job as the dean of the MUSC College of Medicine. He has held that position since March 2016.

“Our cancer center was established in 1993, and it has evolved over time. It was established to help support the vision of Sen. Fritz Hollings and his legacy of public service, serving our culturally and socio-economically diverse state,” DuBois said to *The Cancer Letter*. “My vision for the next five to ten years is to take our enterprise to a higher level and to try to integrate our activities more across the state, interfacing better with our state-wide clinical enterprise.

“We have several underserved populations in this state. We really want to have a major impact in approaching and solving many of our health disparity issues.”

DuBois, whose research is focused on elucidating the role of inflammation and inflammatory mediators in the progression of cancer, replaces the interim director, Denis C. Guttridge, who has served in the role since mid-January. Guttridge was appointed to the interim position when the previous Hollings director, Gustavo Leone, announced his intention to become director of the Medical College of Wisconsin Cancer Center.

Guttridge will continue his dual role as director of the Charles P. Darby Children’s Research Institute in the MUSC College of Medicine, and associate director of translational sciences for Hollings.

“Ray is a great choice for the Director of the Hollings Cancer Center at the Medical University of South Carolina in Charleston,” NCI Director Ned Sharpless said in a statement. “I have worked with him closely during his service as chair of the NCI Board of Scientific Counselors

and as a member of the Frederick National Laboratory Advisory Committee. He recognizes and promotes research excellence, has a proven track record, and strongly supports patient-centered cancer care. He will certainly elevate the Hollings Cancer Center as well as the whole cancer effort in the State of South Carolina.”

DuBois serves as chair of the NCI Board of Scientific Counselors and is a member of the Scientific Advisory Board for the NCI Frederick National Laboratory. He is vice chair for the Stand Up To Cancer Scientific Advisory Board and chair of the [SU2C Catalyst Program](#), where he oversees the selection and management of several early phase clinical cancer trials examining unique drug combinations in collaboration with the leadership from BMS, Genentech and Merck.

He serves as president of the AACR Foundation, chair of the AACR Foundation Board and is a past president of AACR, the Southern Society for Clinical Investigation, and the International Society for Gastrointestinal Cancer. He was named to the steering committee for the AACR Academy in 2018.

Before coming to MUSC, DuBois served as executive director of the Biodesign Institute in Arizona and as the Dalton Professor of Chemistry and Biochemistry with a joint appointment as professor of Medicine in the Mayo College of Medicine and Investigator at the Mayo Clinic Cancer Center.

From 2007 to 2012, he served as provost and executive vice president at MD Anderson Cancer Center and held the Ellen Knisely Distinguished Chair in Colon Cancer Research. He also oversaw their Global Academic Oncology Program.

Prior to that, DuBois spent 16 years at Vanderbilt University Medical Center, serving as director of Gastroenterology, Hepatology & Nutrition as well as director of the Vanderbilt-Ingram Cancer Center.

DuBois said his goals include setting Hollings on the path toward comprehensive designation.

Taking on the new role of cancer center director in addition to his duties as dean is not unique among academic medical centers today, DuBois said.

“There are currently over 150 deans of allopathic (MD granting) medical schools in the United States,” DuBois said. “And we looked at what all of their roles were at their respective institutions, in terms of duties and major administrative responsibilities.

“Over half of the deans are either CEOs of their health systems or serve as provosts, or, in some cases, even presidents of their institutions. Many also serve as VPs of clinical affairs for their health enterprise, and some serve as directors of research institutes or centers. I have not served in any of those roles here at MUSC.

“In serving both as cancer center director and dean, I believe that I will be in a position to help develop more synergy and closer ties between both of these organizational units, which will ultimately benefit both. However, the Hollings cancer center will remain a completely independent unit organizationally.”

As the Hollings director, DuBois will report to MUSC Provost and Executive Vice President Lisa Saladin and Patrick J. Cawley, CEO, of MUSC Health and vice president for Health Affairs, University.

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

**Paul Goldberg: First of all, congratulations.**

**Raymond DuBois:** Well, thanks. As you know, I’ve been interested in cancer for



a long time, and I've been involved in major leadership roles in a couple of cancer centers and national cancer organizations. So, it's exciting to be back in a position like this.

**And you're now a permanent cancer center director. You're not stepping in temporarily?**

**RD:** Yes, this is a permanent role, in addition to my current duty as the dean of the College of Medicine. So, it'll be an expansion of my role, to include leading the Hollings Cancer Center.

**I don't think I've ever seen the dean be a cancer center director. A dean is someone that a cancer center director fights against. How will you do that?**

**RD:** I agree that at some institutions there is friction between the school of medicine and the cancer center, but that won't happen here. We've solved that problem.

There are currently over 150 deans of allopathic (MD granting) medical schools in the United States. And we looked at what all of their roles were at their respective institutions, in terms of duties and major administrative responsibilities.

Over half of the deans are either CEOs of their health systems or serve as provosts, or, in some cases, even presidents of their institutions. Many also serve as VPs of clinical affairs for their health enterprise, and some serve as directors of research institutes or centers. I have not served in any of those roles here at MUSC.

At Vanderbilt, for example, the president of the medical center and the dean are the same person. There are a few deans who also run major research centers, such as a cardiovascular research center, for example, and others. So, it's not beyond the scope of what some deans do.

And many deans have a much broader scope of work as CEOs of their multi-hospital health systems that includes managing mergers and acquisitions as well as clinical network expansion. So, we didn't think that it was something beyond what would be possible.

In serving both as cancer center director and dean, I believe that I will be in a position to help develop more synergy and closer ties between both of these organizational units, which will ultimately benefit both. However, the Hollings Cancer Center will remain a completely independent unit organizationally.

**Being the CEO of a health system sounds like a bigger conflict, potentially.**

**RD:** Well, individuals in those positions take on the whole scope of the organization under one roof. There's a number of places, Michigan, and Vanderbilt and others, where the dean and the leader of the health system are the same person, but that is a much, much bigger job than directing a single cancer center.

**Did you apply for the job? Or did they say, "Dr. DuBois, we want you to do it."**

**RD:** The administrative leadership for MUSC and MUSC Health knew that I was already engaged as a member of

the Hollings Cancer Center and did ask me if I would be potentially interested.

And, obviously, having been here for almost five years, I had a pretty good feel for the cancer center, and scope of work, and some of the issues being addressed.

Also, I have a pretty well-developed leadership team in the College of Medicine. We have several associate and senior associate deans that take care of education, research and clinical activities.

The cancer center has a fairly robust senior executive committee that helps oversee programs and operations there.

It's a matter of managing things and delegating appropriately to make sure all the work gets done. In fact, I am a strong believer in the team approach, because I have seen great things happen when a team of professionals with complementary skills and backgrounds work together toward common goals. Our common goal is the fight against cancer!

**Because, I mean, most of us have 24 hours in a day. Did they give you more?**

**RD:** Well, there's a lot that needs to be done. It's a big job, but I think I'm up for the task, and with my current team in place we have things under reasonably good control in the college.

We still have all of the issues that we're dealing with the COVID pandemic—and that has caused a lot of challenges.

**Well, let's get to that in a minute. You also have a lab, an active lab.**

**RD:** I do direct a research lab. I have pared it down quite a bit, and only maintain a group of about four to six individuals that I'm working with now so that when I work on those issues I can more easily focus on a smaller number of projects.

I meet regularly with the lab group, and am very involved in evaluating data, troubleshooting and deciding on future experiments needed. It's worth noting that most members of my lab team have been with me for several years, so we are a well-oiled machine.

My research effort is a fraction of what it was at MD Anderson or at Vanderbilt. Thus, it is easier to manage, but very important for me to continue. I've given up my Program Project Grant and one of my RoIs to make administrative time for managing the CCSG.

**What about the cancer center itself? What is it like? I mean, every cancer center is different. What's Hollings like, and what are your thoughts on what you want it to be?**

**RD:** It's a matrix center, similar to several other institutions. Obviously, these matrix centers are much different from cancer centers like MD Anderson, Memorial Sloan Kettering or the Fred Hutchinson Cancer Center in Seattle.

We currently have 110 to 150 members of the cancer center, so it's one of the smaller of the NCI-designated centers. It encompasses the clinical care of patients, clinical research, basic science research and translational research.

Hollings has organized research programs with a clinical trials office. Hollings also supports a significant community outreach effort, because South

Carolina has a large rural population with a huge underserved population.

Hollings has established a well-organized community outreach effort for cancer screening, cancer education, and other activities across the state, because there's such a big underserved need.

The Hollings Cancer Center is the only NCI-designated cancer center in the state of South Carolina.

**Is there anything you do that nobody else does? Anything about Hollings that's just totally unique? And what are your goals for where you want to take it?**

**RD:** Paul, that is a great question. We have a very well-developed and sophisticated group working on health disparities, and we do have a lot of health disparities research underway.

The outcomes for some of the people in our state are much worse than for other citizens of the state in higher socio-economic brackets.

We're constantly looking to try to solve some of those problems with outreach and other programs. There also are some unique populations that seem to have a higher incidence of cancer because of a variety of factors including gender, race, lifestyle or geographic differences.

We are trying to investigate that and understand what causes it: is it environmental, genetic, or what are the other etiologic factors that lead to such a susceptible population?

**What happens five years from now? By the way, when is your grant renewal?**

**RD:** Well, I just came on board Friday, so, I'm working through that. We have three years to submit it, so that's not a lot of time in terms of getting these things prepared. We'll have to start working on it right away.

We do not currently have comprehensive status. Obviously, one of the big goals here is to work towards getting comprehensive status at some point, when it's appropriate.

**What needs to happen?**

**RD:** Well, we need to build and develop our clinical operation to a much greater extent.

Our health system has recently acquired four new hospitals in rural areas of the state. In order to step up and care for that increased need, we're going to have to build the clinical enterprise to a greater extent, as well as our clinical research operation to reach out to these other areas in the MUSC network within the state.

And then, we will need to develop a broader group of investigator-initiated trials to go along with that.

**I don't think that many people who know more about how science and clinical operations overlap than you do. You've done this in so many places.**

**RD:** I think that's one of the reasons why I was interested in this, because I have had a lot of experience with the areas of need for the cancer center. And I have a real passion and purpose in the cancer field. So, I'm very excited about rolling up my sleeves and getting to work on these issues.

I officially take over the directorship on Aug. 17, but we've already started having preliminary meetings and planning.

And, obviously, we'll have to come up with a more tailored strategic plan to address the main issues that we want to focus on. I would like to hear from all members of the cancer center and solicit their input.

**Is this a good time to be recruiting?**

**RD:** Well, COVID has slowed down recruiting across the whole nation, Paul, as you would suspect, people are hunkering down and trying to deal with the pandemic right now. Although, folks are continuing to get trained and looking for jobs.

One of the advantages we have here in the Charleston area is that it's a wonderful place to live. This region of the country offers a very nice lifestyle and quality of life for professionals and their families.

We've actually been doing quite well in recruiting faculty for the whole College of Medicine in general. And, there is a close link between the college and the cancer center, because almost all of the faculty and researchers in the cancer center have appointments in the College of Medicine.

So, I had already been involved in a lot of those recruitments prior to this and will continue to focus on that going forward.

**But as far as COVID, how has the pandemic affected the institution on the cancer side and all around?**

**RD:** Like most other cancer centers, it has impacted our research operations overall and slowed things down a bit during the shutdown.

One of the biggest impacts on the institution has been the financial impact. And, as you know, when we shut down all of our outpatient clinics and a lot of our inpatient surgical procedures, we lost a significant amount of revenue since the pandemic started.

Charleston was not hit that hard initially, so we were able to restart those activities fairly quickly. And we're back up to almost 100% of our clinical activity that we had prior to the pandemic.

However, we have had a significant increase in the surge of cases over the past few weeks, which has taken quite a toll. It puts a lot of pressure on our intensive care units.

That's put a strain on our operations and faculty, although we've been able to continue with our clinical activities over this time, and that's really improved our financial situation and allowed continuity of care for our patients.

With regard to cancer, it's had a big impact, Paul, and I think you've heard from Ned Sharpless and Otis Brawley and others about some of these issues. Some cancer patients are afraid of getting the virus and hesitate to come in and get treatment in order to avoid exposure.

For patients who must come for an in-person appointment, we are taking a lot of precautions, like social distancing, masking, and separating patients with COVID from those without.

We test all inpatients and people who come in for procedures, to make sure they're negative for the virus and thus not spread it to our staff and faculty.

There's data in many different medical areas: cardiovascular, diabetes,

cancer—that regular exams and procedures are getting greatly delayed. So, there's more and more data that's coming out all the time.

I just saw a huge piece by the American Cardiology Association this morning about problems with women having more heart attacks and more severe heart damage after their heart attack, just because of the fear of getting COVID when they come to a clinical facility.

**Are cancer patients coming in now, even despite the resurgence?**

**RD:** Yes. Because if you're on a defined treatment regimen, it's really important not to disrupt that. And so, within the cancer center, we've taken extra precautions, because many cancer patients are immunocompromised and need special attention.

**It must be even more complex to be both a center director and the dean at this time, because of COVID.**

**RD:** Yes, it has complicated everybody's lives. It has disrupted education of medical students and training of residents. And it's been very difficult, because our third and fourth year medical students must be involved directly in patient care in order to achieve proper training.

And there has been some concern about getting the students back into the clinical setting, because of their potential exposure. But we've been able to accomplish that since May 18, and things are working reasonably well.

Everyone is trying to do the best they can given the current circumstances we are dealing with. Everyone's situation is

more complex now. And as mentioned before, we're doing everything we can to provide a safe environment and continuity of care for our patients.

**So third and fourth year medical students returned to campus on May 18th. And you were shut down when?**

**RD:** Well, it was from that initial date in March, when all the clinical activities were shut down in several states because of the stay-at-home order and that initial reaction to the pandemic.

**So, it's two months.**

**RD:** Yes. On the education side, we had to adjust our curriculum. We had to do a lot of our teaching online. We had to initiate virtual teaching for some subspecialties.

We have just tried to adapt the best we could. It's just nothing that you're ever really totally prepared for.

**But you're able to recruit, right? Even with the financial challenges?**

**RD:** Well, we've gotten our financial footing back on solid ground. We made up almost all of the loss that we had during the stay-at-home order.

I suspect that there will be future surges in the fall based on what is happening now in Australia and other times of the year, and that we will have to adjust our clinical activity based on the severity of the pandemic. We are now in hurricane

season and that is always one of threats along the Atlantic coast. So, yes, we are in a position to recruit.

**But if you're able to even out the finances this at this time, with the element of surprise, at the next COVID spike it would be just a matter of managing it, applying what you have learned.**

**RD:** Yes. We have great faculty and very dedicated staff. We are extremely committed to delivering patient-centered care. So, we've been able to adjust, make it work, and continue to care for our patients. And we're in a better position to do so if we experience another surge in the future.

**Is there anything we've missed? Is there anything you want to address?**

**RD:** Our cancer center was established in 1993, and it's evolved over time. We are well configured here and an ideal size to support team science and nurture the careers of young cancer scientists and we do promote innovation to a great extent.

And then there are underserved populations in the state, and we really want to try to have a major impact in approaching and solving some of these health disparity issues and increasing our community outreach and engagement efforts.

**Well, thank you so much.**

**RD:** Thank you Paul and we do appreciate all you do to spread the cancer

message across the country and keep everyone adequately informed.

I must give a shout-out to our physicians, nurses, staff, researchers and volunteers here at MUSC and at Hollings. They have been working days, nights, and weekends during the pandemic to try and resolve a myriad of problems and issues that unexpectedly crop up every day.

These people now have the hardest jobs in the world, yet they come in, roll up their sleeves and devote themselves to serving their patients and people all across the community with skill and compassion, despite the great risk to themselves and their families.

It makes me very proud to be a member of this medical community. It has been inspirational.

““

**Our health system has recently acquired four new hospitals in rural areas of the state. In order to step up and care for that increased need, we're going to have to build the clinical enterprise to a greater extent, as well as our clinical research operation to reach out to these other areas in the MUSC network within the state.**

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Director of Administration – Wake Forest Baptist Comprehensive Cancer Center

The Wake Forest Baptist Comprehensive Cancer Center (WFBCCC), located in Winston-Salem, North Carolina, is seeking a Director of Administration who serves as the WFBCCC Associate Director for Administration for the NCI Cancer Center Support Grant. This position reports to the Comprehensive Cancer Center Director and is a member of the leadership team of the WFBCCC. This position has broad responsibilities which unite faculty and staff members from within WFBCCC and from various other Centers, Departments, and Institutes within Wake Forest and collaborating institutions around a common strategic vision. The Director of Administration helps facilitate the vision of the Director and other senior WFBCCC faculty leaders by creating an environment of collaboration and interaction for the membership across departmental, school, and institutional boundaries. S/he is also responsible for ensuring that all WFBCCC activities meet National Cancer Institute Cancer Center Support Grant (CCSG) guidelines and essential characteristics.

The WFBCCC was founded in the 1960's and was one of the first to receive NCI designation in 1974. The WFBCCC has been continuously funded through the CCSG mechanism since inception and was awarded Comprehensive status in 1990. The WFBCCC catchment area consists of 58 counties located in rural and Appalachian regions within central and western North Carolina, southwestern Virginia, and West Virginia.

Candidates should have a master's degree and at least six years of significant administrative experience. PhD is preferred. The preferred candidate will have experience with CCSG renewals and significant knowledge of oncology clinical and basic research. Other requirements include excellent written and oral communication skills, and outstanding interpersonal skills.

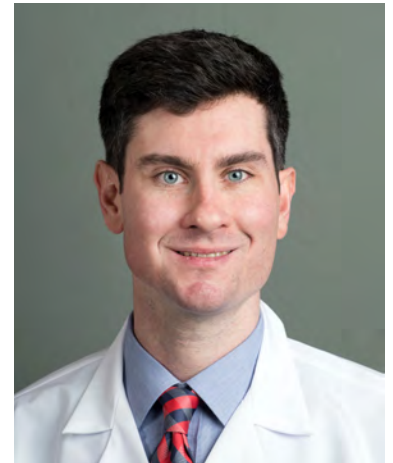
To apply, click [here](#).



GUEST EDITORIAL

# The billion-dollar scrotal cosmesis solution: LHRH analogues, androgen suppression, and adherence

Two articles in the [July 24](#) issue of *The Cancer Letter* referenced a April 1 *Journal of Urology* manuscript (doi:10.1097/JU.0000000000000577) describing frequent delays in administration of LHRH agonists and the potential clinical impact as assessed through recovery of testosterone.

**Walter M. Stadler, MD, FACP***Fred C. Buffet Professor of Medicine**Dean for Clinical Research,**Deputy Director, University of Chicago Comprehensive Cancer Center***Brian Heiss, MD***Clinical Instructor, Oncology,**Fellow, Clinical Pharmacology,**University of Chicago Comprehensive Cancer Center.*

The [interview](#) with Jason Hafron further emphasized that this issue has the potential for becoming even worse during the COVID-19 pandemic, given patients' reluctance to come to clinic or physician offices for routine care.

Given the well-known association of adherence with socioeconomic status, it is further interesting to speculate on the differential impact of late LHRH agonist administration in socioeconomically deprived communities, a factor that was not investigated by Hafron and colleagues, but is almost certainly relevant, based on our anecdotal observations.

The clinical relevance of the modest observed impacts on testosterone is debatable, but the randomized Level 1 data of intermittent versus continuous androgen ablation strongly argues that this is important. Dr. Hafron, and other commentators, also discuss potential causes for delays in treatment and focus on reimbursement schedules that place institutions and practices at financial risk with these very expensive medications.

That in itself is an interesting claim for those of us old enough to recall the illegal, sponsor-supported, schemes of providing discounted leuprolide to practitioners who then sold them to patients (and their insurance carriers) at a handsome profit.

While one can certainly consider multiple policy, business, and health system approaches to better financially support appropriate medical therapy, the authors and commentators seem to have forgotten a far cheaper, permanent, and potentially more effective approach to androgen ablation; namely, surgical orchiectomy.

The economic impacts of LHRH agonists, in an era with increasing attention to medical costs, are staggering. A 2001 article estimated an orchiecto-

my cost per case of \$2,479, compared to an annual cost of depot leuprolide of \$7,136 (doi:10.1097/00005392-200101000-00026). Not only do patients with advanced disease receive these treatments for many years, drug prices have continued to escalate, despite the availability of several medically equivalent LHRH agonists.

Perhaps most relevant is that in 2018



The clinical relevance of the modest observed impacts on testosterone is debatable, but the randomized Level 1 data of intermittent versus continuous androgen ablation strongly argues that this is important.



Medicare alone spent over \$358 million for leuprolide and goserelin under [Medicare parts B and D](#). When private insurance and patient out-of-pocket costs are additionally considered, an annual United States expenditure of a billion dollars is at least the correct order of magnitude.

Is there any true value to this expenditure?

From an economic and medical perspective, it is hard to justify. Surgical orchiectomy is a rapid, permanent, and highly effective method for de-

creasing testosterone levels; nevertheless, its use is low and has been decreasing over the last two decades (doi:10.1097/JU.0000000000000684).

There have been arguments that LHRH agonists may have additional beneficial impacts; however, this is not borne out in randomized studies (doi:10.1016/S0090-4295(99)80197-6). In fact, comparative studies suggest that adverse effects of LHRH agonists may actually be higher than orchiectomy (doi:10.1001/jamaoncol.2015.4917).

Similarly, a recent study of a novel LHRH antagonist suggested a higher risk of cardiovascular morbidity with a LHRH agonist, compared to the antagonist (doi:10.1056/NEJMoa2004325). A review of the event curves in this study suggests that this increased risk occurs early, raising the hypothesis that it is associated with the testosterone flair that occurs with initial LHRH agonist therapy.

We are thus using an expensive drug that is no more effective, and potentially more lethal, than a simple surgical procedure.

Clearly, there are body image and patient-related issues with surgical orchiectomy. Many of these are associated with the physiologic effects of androgen ablation in general rather than orchiectomy specifically; however, the absence of palpable and notable testicles is noteworthy.

Interestingly, subcapsular orchiectomy has an equivalent impact on testosterone, compared to simple orchiectomy, but leaves residual tissue, and is associated with potentially less psychologic stress and less of the so-called postoperative empty scrotum feeling (doi: 10.1016/S0090-4295(99)80460-9), (doi: 10.4274/uob.925).

Here, it is perhaps important to point out that medical castration also leads

to involution and marked shrinkage of the testicles to approximately half the pretreatment size (doi: 10.1097/O1.ju.0000135831.19857.5c).

Based on our experience, patients seem more willing to consider surgical orchiectomy after a period of exposure to medical castration. Therefore, to more carefully study these issues, we are opening a clinical trial assessing feasibility and acceptance of performing subcapsular orchiectomy in patients on long-term medical castration.

In this trial, eligible patients will be approached to participate in a short education session about orchiectomy, and the fraction of patients who eventually undergo the procedure will be the primary endpoint.

Other important endpoints include change in body image perception, sexual function and satisfaction, and decision regret. The total institutional and out-of-pocket costs of one year of therapy with medical versus surgical castration will be compared.

The cost of medical care in general and oncologic care specifically continues to dominate the headlines, and in oncology the cost of drugs is becoming an increasing component of medical expenditures.

While it is not politically expedient to discuss appropriate maximum healthcare spending, at least in the United States, there is little doubt that tradeoffs are necessary. Fundamentally, money spent on a specific treatment will likely preclude alternative spending.

In a field that continues to be dominated by men, one might ask if scrotal cosmesis is worth a billion dollars.

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# Senate committee proposes \$15.5 billion in COVID-19 relief for NIH

By Alexandria Carolan

The Senate appropriations subcommittee July 27 proposed a fifth COVID-19 pandemic relief package that includes \$15.5 billion in supplemental funds for NIH.

The measure, introduced in the Senate Appropriations Subcommittee on Labor, Health and Human Services, Education and Related Agencies seeks to give NIH \$15.5 billion as part of the Health, Economic Assistance, Liability Protection, and Schools (HEALS) Act.

“ASCO is encouraged by the inclusion of \$15.5 billion in funding for the NIH proposed in the Senate,” Richard L. Schilsky, ASCO executive vice president and chief medical officer, said to *The Cancer Letter*.

“We continue to urge Congress to come to a bipartisan, bicameral agreement this year that provides both emergency relief funding to restart stalled research programs as well as necessary increases to the baseline NIH and NCI budgets to ensure continued progress in the vital research necessary to protect and improve the health of the American people.”

Nearly two-thirds of these proposed new NIH funds—\$10.1 billion—would be set aside to reopen NIH-funded research laboratories and reconstitute lost research. The total cost of the package comes to \$1 trillion.

At a Senate appropriations hearing July 2, NIH Director Francis Collins estimated that it would cost about \$10 billion to restart the labs and resume activities that were halted during the COVID-19 pandemic, “just on the basis of the research that’s been lost (*The Cancer Letter*, July 10, 2020).

This action is separate from the FY21 appropriations process.

“If we’re going to bring these institutions back up to where they need to be on top of that, I think there’s a wide variety of areas that NIH really would like to also put more efforts into, to compensate for

this in terms of our efforts in COVID-19,” Collins said at the Senate hearing.

The amount proposed in the Senate version of the spending package for the departments of Labor, HHS, Education, and other agencies is \$10.8 billion more than what the House proposed in emergency funding for NIH in a COVID-19 spending bill passed May 15.

“This funding increase for NIH in the Senate is significantly larger than the \$4.7 billion for NIH that House Democrats included in their bill, the Health and Economic Recovery Omnibus Emergency Solutions (HEROES) Act, that passed this past May, even though the House bill included \$2 trillion more in overall funding than what the Senate is proposing to spend,” Jon Retzlaff, chief policy officer and vice president of science policy and government affairs for the American Association for Cancer Research, said to *The Cancer Letter*.



This funding increase for NIH in the Senate is significantly larger than the \$4.7 billion for NIH that House Democrats included in their bill, the Health and Economic Recovery Omnibus Emergency Solutions (HEROES) Act, that passed this past May.



—Jon Retzlaff

Cancer groups had expressed frustrations with the House appropriations bill, because it uses emergency funding to get around FY21 budget caps. As a result, the majority of proposed House funding for NIH—\$4.7 billion—cannot count toward the base used to determine future appropriations.

The House bill would increase the FY21 NIH base budget by \$500 million. To compare, over the past five years, NIH grew by \$11.6 billion, or 39%.

The Department of Health and Human Services receives \$118.4 billion under the spending bill. This includes:

- \$3.4 billion for the Centers for Disease Control and Prevention. The proposal provides \$3.4 billion to CDC, including \$1.5 billion to continue supporting state, local, and territorial public health needs; \$500 million to enhance seasonal influenza vaccination efforts; \$200 million to enhance global public health security efforts; and \$200 million to modernize public health data reporting.
- \$15.5 billion for NIH:
  - ▶ \$290 million for National Heart, Lung, and Blood Institute
  - ▶ \$200 million for National Institute of Diabetes and Digestive and Kidney Diseases
  - ▶ \$480.56 million for National Institute of Allergy and Infectious Diseases
  - ▶ \$172.68 million for Eunice Kennedy Shriver National Institute of Child Health and Human Development
  - ▶ \$200 million for National Institute of Mental Health
  - ▶ \$64.33 million for National Institute of Minority Health and Health Disparities

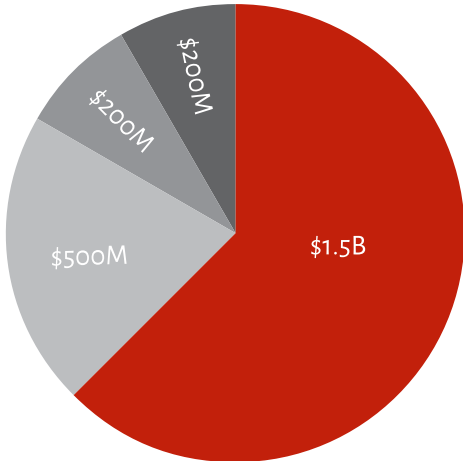
- ▶ \$1.22 billion for National Center for Advancing Translational Sciences

The Senate bill slates \$12.91 billion for the NIH Office of the Director. This includes:





- \$10.1 billion for NIH-funded labs and research,
- \$1.24 billion for the ACTIV public-private partnership to prioritize and speed the development of treatments and vaccines,
- \$240 million to provide resources targeting young researchers who need additional research time as post-doctoral candidates because of lost research/training due to COVID-19,
- \$1.33 billion for COVID-19 specific research to smaller ICs at the direction of the NIH director.

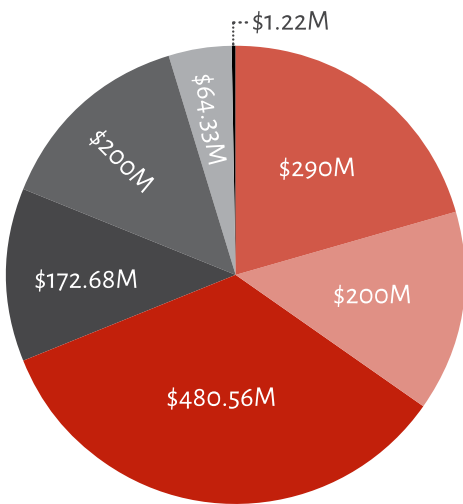
“Bottom line, the entire medical research advocacy community is very much indebted to Chairman Roy Blunt (R-MO) and his colleague, Sen. Richard Shelby (R-AL), who serves as chairman of the full Senate Appropriations Committee, for their willingness to fight for NIH funding in this urgent piece of legislation that is aimed at alleviating the burden and impact from the COVID-19 health and economic crisis,” Retzlaff said.

“We applaud the inclusion of \$15.5 billion to ensure NIH-funded research stalled by COVID-19 can move forward,” Research!America President and CEO Mary Woolley said in a statement. “We encourage Congress and the administration to quickly agree on a supplemental package, equipping our nation’s research ecosystem to defeat COVID-19 and jumpstart medical and scientific progress.”










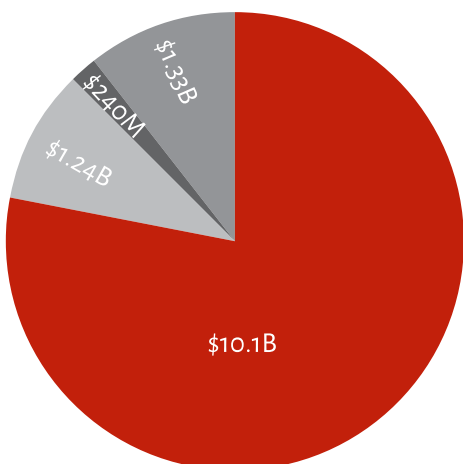
### \$3.4 billion for CDC

-  Modernize public health data reporting
-  Enhance global public health security efforts
-  Enhance seasonal influenza vaccination efforts
-  Support state, local, and territorial public health needs







### \$15.5 billion for NIH

-  National Center for Advancing Translational Sciences
-  National Institute of Minority Health and Health Disparities
-  National Institute of Mental Health
-  Eunice Kennedy Shriver National Institute of Child Health and Human Development
-  National Institute of Allergy and Infectious Diseases
-  National Institute of Diabetes and Digestive and Kidney Diseases
-  National Heart, Lung, and Blood Institute



### \$12.91 billion for the NIH Office of the Director

-  COVID-19 specific research to smaller ICs at the direction of the NIH director
-  Resources targeting young researchers who need additional research time as post-doctoral candidates because of lost research/training due to COVID-19
-  ACTIV public-private partnership to prioritize and speed the development of treatments and vaccines
-  NIH-funded labs and research

## LETTER TO THE EDITOR



““

Telehealth is meeting the promise of patient care that is more affordable, accessible, and satisfactory. America's health insurance providers will continue to advocate for policies which encourage its growth.

””

## AHIP: Health insurance providers are committed to improving access to telehealth

In a July 24, 2020 letter to the editor entitled, “Insurers’ moves to limit telehealth amid COVID-19 are inhumane and must be stopped,” the authors use disjointed logic to reach an inaccurate conclusion. [*The Cancer Letter*, July 24, July 17, 2020]

Health insurance providers have, in fact, been committed to improving access to telehealth for years, and those efforts have been greatly expanded during the COVID-19 crisis.

With the entire world in the grips of a global pandemic, there has been an explosion in the demand for and use of telehealth. The benefits of telehealth are clear—it can improve access to high quality care and help keep patients and their providers safe.

Health insurance providers have known this for years and have worked hard to improve access to and coverage of telehealth care. The claim that health insurance providers are looking to eliminate or deny members access to telehealth services is patently false. Here are just a few examples among many of the actions health insurance providers are taking in support of telehealth:

- Centene has created a Medicaid Telehealth Partnership with the national Association of Community Health Centers and has committed \$5 million to the partnership's efforts to purchase equipment and provide training and technical assistance to federally qualified health centers in order to deliver care to underserved communities.
- CVS Health has expanded its virtual strategy during COVID-19, offering clinical monitoring, virtual support, and oversight through telehealth to complement existing in-home care.
- Dozens of health plans, including Piedmont Community Health Plan, Sutter Health Plus, and University Health Alliance, will waive out-of-pocket costs for consumers when they access care via telehealth.

Telehealth is meeting the promise of patient care that is more affordable, accessible, and satisfactory. America's health insurance providers will continue to advocate for policies which encourage its growth.

We invite you to visit <https://www.ahip.org/search/?q=telehealth> to learn more about how America's health insurance providers support growing and strengthening telehealth.

**Christopher Regal**  
 Director, Clinical Innovation  
 America's Health Insurance Plans  
[www.ahip.org](http://www.ahip.org)

## IN BRIEF



## Winship receives \$7.8 million for multiple myeloma research

Winship Cancer Institute of Emory University received \$7.8 million from the Paula and Rodger Riney Foundation to fund the Riney Family Multiple Myeloma Research Program Fund.

The two-year project will support fast-tracked research projects at Winship in multiple myeloma.

Rodger Riney, founder of the brokerage firm Scottrade Financial Services, was diagnosed with multiple myeloma in 2015. Rodger and his wife Paula Riney have made substantial gifts to the Washington University School of Medicine in St. Louis and to Dana-Farber Cancer Institute in Boston to accelerate research into multiple myeloma and improve outcomes for patients.

Winship has played a role in the development, testing, and approval of multiple myeloma treatments in recent years, including several recently approved immunotherapy drugs.

For the two-year funding period, Lonial and the Winship myeloma team have proposed projects in fundamental research in the underlying biology of multiple myeloma, translational research in the development of new treatments, and clinical research in understanding response rates and drug resistance, among other areas.

The Riney Family Multiple Myeloma Research Program Fund will engage faculty from all four Winship research programs: cancer immunology, cancer prevention and control, cell and molecular biology, and discovery and developmental therapeutics.

## Jin, Wang receive \$3.7 million from NCI to support research exploring link between cancer and HIV/AIDS

Ge Jin and Bingcheng Wang received a \$3.7 million five-year grant to explore why those living with HIV have a higher risk for certain kinds of cancers, such as lung cancer.

Jin and Wang, co-principal investigators of the grant, are members of the Case Comprehensive Cancer Center's Molecular Oncology Program. Jin is a professor at the School of Dental Medicine and Wang is the John A. and Josephine B. Wootton Endowed Chair of Research, professor at the School of Medicine, and a researcher at MetroHealth System.

The U.S. Department of Health and Human Services estimates more than 1.7 million people are newly infected with HIV every year. These 1.7 million people are more likely to get cancer at an earlier age and at a higher frequency, Jin said.



“We want to look at the molecular events involved in these processes, and find out why,” Jin said in a statement. “We need to find a better way to detect cancer in these patients at an earlier stage.”

Jin and Wang found that the immune cells from HIV patients secrete exosomes and attack lung cells, thus promoting the growth of cancer.



Wang said he believes the grant from NCI will “further investigate this novel mechanism of lung cancer promotion by HIV and develop new therapeutic agents to treat the disease among people living with HIV.”

## The Prostate Cancer Foundation and Robert F. Smith plan to address health disparities for African American men

The Prostate Cancer Foundation and Robert F. Smith, founder, chairman and CEO of Vista Equity Partners, plan to collaborate on research to reduce deaths from prostate cancer.

“As African American men are at an increased risk for being diagnosed or dying from prostate cancer, understanding their risk profile and applying this knowledge earlier with strategic detection, care, and decisions about cancer risk management is of utmost importance to address health inequity in the U.S.,” Smith said in a statement. “This is why I made a personal commitment to help accelerate research, encourage

African American men to participate in the study and subsequent testing, and develop new detection strategies that have the power to transform how we diagnose and treat this disease and help save lives.”

The research Smith is supporting will lead to the development of the Smith Polygenic Risk Test for Prostate Cancer, a non-invasive, early detection test that will identify a man’s lifetime prostate cancer risk using a combination of more than 250 genetic variants obtained from a single sample of saliva or blood. The Smith Test is expected to cost less than \$90 USD and will be made available in PCF’s dedicated Veterans Affairs network of Centers of Excellence, including the Robert Frederick Smith Center of Precision Oncology Excellence at the VA Chicago.

The test is part of a larger PCF research initiative to improve the understanding of genetic risk in African American men and transform early detection and imaging strategies, risk management,

and clinical-decision making by men at highest lifetime risk of prostate cancer. The research, led by Chris Haiman, a genetic epidemiologist at the University of Southern California, and international colleagues, is aimed at accelerating the reduction of prostate cancer disparities for African American men by 2030.

Most genomic studies of prostate cancer have focused on men of European ancestry, and there is a need for additional resources to develop and optimize a polygenic risk score in those disproportionately affected. The new Smith-PCF initiative plans to increase the representation of African American men in the study and expand research to allow Haiman to quadruple the size of his study cohort, a step to providing access to the Smith Polygenic Risk Test as soon as possible.

African American men are 76% more likely to develop prostate cancer than Caucasian men, and are more than twice as likely to die from the disease compared to men of other ethnicities.

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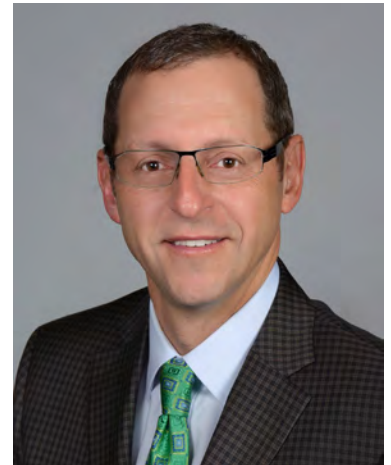
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# THE CLINICAL CANCER LETTER



## TRIALS & TRIBULATIONS

# Cancer care in the COVID-19 world: Adjusting to a new reality



### Marcus Neubauer, MD

Chief medical officer,  
The US Oncology Network

Oncology practices face difficult challenges while delivering care in the middle of COVID-19, as they care for patients who are at higher risk for this potentially deadly disease. While there is still much to learn about how COVID-19 impacts various patient populations, early studies of COVID-19 patients with a history of cancer provide some insight.

In one study, researchers examined data based on 928 COVID-19 patients with active cancer, or who were in remission, and found that 13% died.<sup>1</sup> A second study

analyzed data on 800 cancer patients with COVID-19 and reported a 28% death rate.<sup>2</sup> In contrast, the COVID-19 case fatality of patients without cancer in the U.S. is 5.9%.<sup>3</sup>

The higher death rates of cancer patients are not surprising because these individuals tend to be older with compromised immune systems. Consequently, it is imperative for all of us who provide cancer care to do everything possible to ensure a safe environment for this vulnerable population.

## Implementing changes for the safety of patients and staff

Healthcare providers have had to adjust their way of doing business to accommodate the new reality created by COVID-19. Across The US Oncology Network we have seen innovation, creativity and a good deal of common sense applied to protect patients and staff. Practices have made a few of the following adjustments, adhering to CDC guidelines whenever possible:

- **Screening procedures:** All people entering the facility have their temperatures checked and are questioned about symptoms.
- **Contact tracing and quarantines:** For patients and staff who test positive, efforts are made to identify whom they might have exposed to the virus. Employees who are exposed and are deemed medium to high-risk are quarantined, which is extremely disruptive but necessary. In order to keep our essential health care professionals on the front lines, those exposed, but deemed low risk, are expected to stay on-site, at work.
- **Visitor restrictions:** Gone are the days when family and friends encircle the patient to offer support during an infusion session. Today, no visitors are allowed, with an occasional exception.

## Personal protection equipment

Early on, PPE was used to some extent; but now, everyone wears masks—either homemade, surgical, or N95 respirators. Patients are required to wear masks as well. Consistent with CDC guidelines, employees who do not have close contact with patients or those working behind a Plexiglass shield wear homemade face coverings because the supply of N95 and surgical masks is limited.

Providers who interact closely with patients, such as nurses and physicians, are primarily wearing N95 respirators, using a lot of hand sanitation and wiping surfaces frequently. Gowns are generally not used, unless a patient is at particularly high risk. Phlebotomists have very close contact with patients and are fully donned with N95 respirators, face shields, gowns and gloves.

Lately, we have had enough PPE, but it has taken quite some time for the sup-

ply to catch up with our needs. Before the pandemic, masks were discarded after each patient visit, but the limited supply prohibits us from doing this today. We have seen some creative strategies employed to reuse masks. Some practices are decontaminating them with UV light, while others are storing them in brown paper bags for use over several days.



Lately, we have had enough PPE, but it has taken quite some time for the supply to catch up with our needs. Before the pandemic, masks were discarded after each patient visit, but the limited supply prohibits us from doing this today.



Practices have implemented social distancing as much as possible by positioning chairs six feet apart from one another in the waiting room. Some practices have patients wait for their appointment in their cars, keeping them out of the waiting room. Infusion room chairs are placed as far apart as possible. Practices have gotten creative by mounting large Plexiglass shields on rollers and positioning these barriers between chairs for extra protection. Onsite schedulers and front desk receptionists are also protected by Plexiglass.

One-quarter to one-third of employees are working from home, greatly reducing the number of individuals in the clinics. Practices are scheduling patients remotely, enabling patients to leave the clinic directly after their appointment rather than walking through the facility to a scheduler's desk.

Social distancing and PPE have proven to be better options to minimize exposure and infection than performing broad scale testing. Access to testing has simply not been available the way we had hoped. With several days needed for results and a large number of false negatives, relying on testing alone is not prudent. People with symptoms and high-risk individuals are advised to get tested.

## Positives from the pandemic

While COVID-19 has been devastating to our world, it is important to look for anything positive we can learn from the experience. The following are a few things that hopefully will carry forward post-COVID:

- **Greater awareness of germs**

People may continue to be more respectful of germs by covering their mouths when coughing and sneezing and by being more vigilant about hand washing and using sanitizers. Social distancing will likely exist into the future for cancer care, with practices developing new ways to keep patients and staff safe from all pathogens and viruses, not just COVID-19. Physical redesigns of facilities may be necessary to accommodate this new way of caring for patients.

- **The growth of telemedicine**

Telemedicine could be a new normal if Medicare and commercial payers continue to reimburse, and The Network will continue to strongly advocate for it. Our practices are using telemedicine very



effectively to engage with patients, and we believe it can continue to play a vital role in providing comprehensive care. Of course, not all visits for cancer care are conducive to telemedicine, but some are.

- **Increased use of technology**

Post-COVID-19, more technology will likely emerge around scheduling tracking positive cases and contact tracing.

## Patients and practices are meeting the challenge

Patients know they are immune-compromised and at a higher risk of getting this infection, yet most are continuing treatment. Infusion volume across The US Oncology Network is down less than 5%, and radiation volumes have not changed. Patients, for the most part, are appreciative of the extra steps practices are taking to ensure their safety. While a few may object to wearing a mask, they are the exception.

Overall, our practices are doing well. Providers are rising to the occasion, as they understand that as front-line workers, they need to be present. Some staff shortages occurred early on when a few practice employees tested positive, but infections have been limited since stringent safety measures were implemented. These protocols help protect everyone from asymptomatic individuals who may not know they have the virus.

Some employees missed work because they were concerned about their own health or were caring for a child or a sick family member. The situation really is quite complex, as employees are trying to juggle all of these new concerns, while still doing their jobs.

Frankly, I am proud of the resilience and commitment I have seen from practice staff at The US Oncology Network, as they continue to keep patient care the number one priority while often expe-

riencing turmoil in their personal and/or professional lives.

## Getting back to value-based care

While there are a lot of uncertainties to deal with during this pandemic, one thing we know for sure is that cancer care cannot wait. For some cancers, treatment delays of just a few weeks can impact outcomes. For the most part, practices have been able to continue to deliver high-quality care.

While there have been disruptions along the way and probably more to come, that will not keep us from providing the care people need. We are working around the obstacles with PPE, shields, social distancing and new policies to protect patients and staff.

Practices were in the middle of the Oncology Care Model and various value-based programs when the pandemic hit, interrupting the great progress we were making. We need to get back into the rhythm of delivering care in the value-based world while accommodating this new way of doing business.

The US Oncology Network is committed to doing everything possible during these uncertain times to provide all aspects of high-quality care while still supporting value-based initiatives. Society and the patients we serve deserve no less.

### References

1. <https://www.cidrap.umn.edu/news-perspective/2020/05/studies-highlight-covid-19-impact-cancer-patients>
2. *Ibid.*
3. <https://khn.org/morning-breakout/new-study-confirms-patients-with-cancer-or-in-remission-have-higher-death-risk-from-covid-19/>



Access to testing has simply not been available the way we had hoped. With several days needed for results and a large number of false negatives, relying on testing alone is not prudent. People with symptoms and high-risk individuals are advised to get tested.



## CLINICAL ROUNDUP



## FDA, Syapse real-world study reveal higher risk of hospitalization and death among cancer patients with COVID-19, underscore health disparities

The FDA's Oncology Center of Excellence and Syapse presented data at the American Association of Clinical Research [COVID-19 and Cancer](#) meeting on an analysis of more than 212,000 health records of people living with cancer across two major health systems in the Midwestern United States.

The analysis found that cancer patients who also had COVID-19 are more likely—compared to those without COVID-19—to have: (1) other health conditions (e.g., kidney failure, obesity and heart disease), (2) increased rates of hospitalization and invasive mechanical ventilation, and (3) a 16-fold increased mortality risk. The researchers also underscored evidence for health care disparities among cancer patients with COVID-19.

This presentation is part of OCE's partnerships with experts in healthcare

data and analytics to investigate characteristics and clinical outcomes of patients with cancer who are infected with SARS-CoV-2, the virus that causes COVID-19.

This work builds upon several initiatives underway across FDA that leverage real-world data to improve understanding of COVID-19. These efforts include FDA's participation in the [COVID-19 Evidence Accelerator](#), organized by the Reagan-Udall Foundation for the FDA in collaboration with Friends of Cancer Research.

## ACS updates guideline for cervical cancer screening

An updated cervical cancer screening guideline from the American Cancer Society reflects the rapidly changing landscape of cervical cancer prevention in the United States, calling for less and more simplified screening.

The guideline appears in [CA: A Cancer Journal for Clinicians](#).

The updated guideline recommends that individuals with a cervix initiate cervical cancer screening at age 25, continuing through age 65, and that primary human papillomavirus testing every 5 years be the preferred method of testing.

The guideline says using HPV testing in combination with a Pap test (called cotesting) every five years or Pap tests alone every three years are acceptable options for now, as not all labs have transitioned to primary HPV testing.

"These streamlined recommendations can improve compliance and reduce potential harms," Debbie Saslow, managing director of HPV & GYN Cancers for ACS, said in a statement. "They are made possible by some important de-

velopments that have allowed us to transform our approach to cervical cancer screening, primarily a deeper understanding of the role of HPV and the development of tools to address it."

Virtually all cases of cervical cancer are caused by infection with high-risk strains of HPV. Evidence shows the HPV test is more accurate than the Pap test and can be done less often; one HPV test every five years is more effective than a Pap test every three years, and even every year as was recommended in the 1980's and 1990's, in reducing the risk of cervical cancer.

A negative HPV test is linked to a very low cervical cancer risk. In addition, a vaccine for HPV has been in use for nearly 15 years, and more women of screening age are now vaccinated and protected from the majority of cervical cancers.

The previous ACS guideline, released in 2012, called for screening starting at age 21. Since then, HPV vaccination rates have improved in the United States. Data suggest vaccination has led to a drop in rates of precancerous cervical changes, the precursors to cancer. In addition, cervical cancer incidence is low in this age group. Cancer registry data from 2011 to 2015 indicates an estimated 108 cases of invasive cervical cancer in women 20 to 24 years in the U.S. each year, a number that is expected to continue to fall as vaccine use increases.

There are also potential harms related to the treatment of precancerous cells identified by screening including preterm birth, and screening has not been shown to lower the rate of cancer in women in this age group. Also, most HPV infections in women in this age group become undetectable in 1-2 years. Those factors led the ACS to move the recommended age to initiate cervical cancer screening to 25.

"We estimate that compared with the currently recommended strategy of

cytology (Pap testing) alone beginning at age 21 and switching to co-testing at age 30 years, starting with primary HPV testing at age 25 will prevent 13% more cervical cancers and 7% more cervical cancer deaths,” Saslow said. “Our model showed we could do that with a 9% increase in follow-up procedures, but with 45% fewer tests required overall.”

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## Clinical trial tests oral cancer drug to combat respiratory symptoms of COVID-19

Researchers at The Ohio State University Comprehensive Cancer Center – Arthur G. James Cancer Hospital and Richard J. Solove Research Institute and The Ohio State University Wexner Medical Center are conducting a clinical trial to determine if ibrutinib (Imbruvica) can help patients with cancer or other immunocompromised conditions recover from COVID-19.

Imbruvica is sponsored by Janssen Scientific Affairs.

For this phase II clinical trial, physicians at the OSUCCC – James will enroll up to 78 patients with cancer or a precancerous condition who have been hospitalized as a result of a COVID-19 infection. Patients will be randomized to receive either 14 days of standard treatment plus the study drug ibrutinib, or standard treatment alone.

Ibrutinib is an oral therapy in a class of drugs known as Bruton’s tyrosine kinase inhibitors. These drugs work by blocking specific chemical reactions in the body involved in cellular processes. Use of this drug is considered experimental for this study; however, ibrutinib is approved by FDA for treatment of certain cancers, including mantle cell lymphoma, chronic lymphocytic leukemia/small lymphocytic lymphoma and others.

Jennifer Woyach, an OSUCCC – James hematologist and co-principal investigator of the study, said preliminary data suggests ibrutinib has the potential to reduce rates of respiratory failure and death in COVID-19-infected patients.

“Ibrutinib targets and blocks a specific kinase related to lung inflammation, so we believe it could have real potential to help decrease this inflammation by shutting down the inappropriate cytokine release we see in COVID-19—a sort of overreaction from the immune system that can cause many problems, including life-threatening respiratory challenges,” Woyach said in a statement.

Patients will be monitored throughout study treatment with bloodwork to measure inflammatory markers, immune response and other bodily functions.

“Individuals with cancer or certain precancerous conditions can have lower immunity to diseases and infection, due to treatment or the nature of the disease. It is critically important that we perform clinical trials to try to improve COVID-19 care in these patients, because a COVID-19 infection can be even more dangerous for those who are immunocompromised,” Zeinab El Boghdady, infectious disease physician at the Ohio State University Wexner Medical Center and co-principal investigator for the trial, said in a statement.

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## Fox Chase researchers examine treatment toxicities in older esophageal cancer patients

Researchers at Fox Chase Cancer Center found that older patients who underwent chemoradiation therapy followed by removal of their esophagus due to

cancer had toxicities and outcomes similar to younger patients.

The study, “[Treatment-Related Toxicity and Outcomes in Older Versus Younger Patients With Esophageal Cancer Treated With Neoadjuvant Chemoradiation](#),” was published in the *Journal of Geriatric Oncology*.

Chemoradiation followed by an esophagectomy is considered the standard of care for locally advanced esophageal cancer.

“Clinical trials tend to enroll younger patients. Therefore, it’s hard to extrapolate and treat older patients based on the results of trials in younger patients,” Rishi Jain, lead author on the study and assistant professor in the Department of Hematology/Oncology at Fox Chase, said in a statement.

“We wanted to take a closer look at how older patients did with esophageal cancer, specifically in terms of side effects or toxicities and survivals. These results are important to know, because unfortunately sometimes people use age to decide how to treat patients and maybe older patients aren’t offered aggressive treatments,” Jain said.

Jain worked on the study with Joshua E. Meyer, an associate professor in the Department of Radiation Oncology, Efrat Dotan, an associate professor in the Department of Hematology/Oncology, and other researchers at Fox Chase.

The study examined 125 patients with early stage esophageal cancer who were treated at Fox Chase. Patients were split into age groups of individuals over 65 and individuals under 65. Of those 125 patients, Jain said 58 were over the age of 65 and 25 percent of the trial population were over 70.

Researchers compared side effects of the age groups, which were broken

down into categories of hospitalizations related to the treatment, hematologic toxicities—or blood count issues—as well as others.

Similar toxicities and outcomes between younger and older patients in the study suggest that preliminary chemoradiation before esophagectomy is safe in select older adults with esophageal cancer, Jain said.

Additionally, the researchers found that older patients did have a higher rate of blood count issues, specifically lower platelets. Jain said, however, that this can be expected because older individuals have lower reserves of bone marrow with which to rebound after a blood count issue. Researchers said platelet-to-lymphocyte ratios and neutrophil-to-lymphocyte ratios may be able to serve as prognostic markers of aging, toxicity, and outcomes.

Jain said the study highlights the fact that by using practices like comprehensive geriatric assessments, physicians can effectively assess what problems an older patient may have and make sure they are addressed while treatment for cancer is being pursued.

“It’s helpful to know that if you carefully select older patients, you can safely get them through the treatment without putting them at much higher risk for complications in comparison to younger patients who are almost always treated aggressively,” said Jain.

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## Artificial intelligence identifies prostate cancer with near-perfect accuracy

A study by UPMC and University of Pittsburgh School of Medicine researchers demonstrates the highest accuracy

to date in recognizing and characterizing prostate cancer using an artificial intelligence program.

The results were published in the *Lancet Digital Health*.

“Humans are good at recognizing anomalies, but they have their own biases or past experience,” senior author Rajiv Dhir, chief pathologist and vice chair of pathology at UPMC Shadyside and professor of biomedical informatics at Pitt, said in a statement. “Machines are detached from the whole story. There’s definitely an element of standardizing care.”

To train the AI to recognize prostate cancer, Dhir and his colleagues provided images from more than a million parts of stained tissue slides taken from patient biopsies. Each image was labeled by expert pathologists to teach the AI how to discriminate between healthy and abnormal tissue. The algorithm was then tested on a separate set of 1,600 slides taken from 100 consecutive patients seen at UPMC for suspected prostate cancer.

During testing, the AI demonstrated 98% sensitivity and 97% specificity at detecting prostate cancer—significantly higher than previously reported for algorithms working from tissue slides.

This is the first algorithm to extend beyond cancer detection, reporting high performance for tumor grading, sizing and invasion of the surrounding nerves. These all are clinically important features required as part of the pathology report.

AI also flagged six slides that were not noted by the expert pathologists.

But Dhir explained that this doesn’t necessarily mean that the machine is superior to humans. For example, in the course of evaluating these cas-

es, the pathologist could have simply seen enough evidence of malignancy elsewhere in that patient’s samples to recommend treatment. For less experienced pathologists, though, the algorithm could act as a failsafe to catch cases that might otherwise be missed.

“Algorithms like this are especially useful in lesions that are atypical,” Dhir said. “A non-specialized person may not be able to make the correct assessment. That’s a major advantage of this kind of system.”

While these results are promising, Dhir cautions that new algorithms will have to be trained to detect different types of cancer. The pathology markers aren’t universal across all tissue types. But he didn’t see why that couldn’t be done to adapt this technology to work with breast cancer, for example.

Additional authors on the study include Liron Pantanowitz, of the University of Michigan; Gabriela Quiroga-Garza, of UPMC; Lilach Bien, Ronen Heled, Daphna Laifefeld, Chaim Linhart, Judith Sandbank, Manuela Vecsler, of Ibex Medical Analytics; Anat Albrecht-Shach, of Shamir Medical Center; Varda Shalev, of Maccabbi Healthcare Services; and Pamela Michelow, and Scott Hazelhurst, of the University of the Witwatersrand.

Funding for this study was provided by Ibex, which also created this commercially available algorithm.

Pantanowitz, Shalev and Albrecht-Shach report fees paid by Ibex, and Pantanowitz and Shalev serve on the medical advisory board. Bien and Linhart are authors on pending patents US 62/743,559 and US 62/981,925. Ibex had no influence over the design of the study or the interpretation of the results.

## DRUGS &amp; TARGETS



## Tecentriq approved by FDA for BRAF V600 unresectable or metastatic melanoma

Tecentriq (atezolizumab) received FDA approval in combination with cobimetinib and vemurafenib for patients with BRAF V600 mutation-positive unresectable or metastatic melanoma.

Tecentriq is sponsored by Genentech Inc.

Efficacy in combination with cobimetinib and vemurafenib was evaluated in a double-blind, randomized (1:1), placebo-controlled, multicenter trial (IMspire150, NCT02908672) in 514 patients. After a 28-day cycle of cobimetinib and vemurafenib, patients received atezolizumab 840 mg intravenous infusion every 2 weeks in combination with cobimetinib 60 mg orally once daily and vemurafenib 720 mg orally twice daily, or placebo in combination with cobimetinib 60 mg orally once daily (21 days on/7 days off) and vemurafenib 960 mg orally twice daily.

The primary efficacy outcome measure was investigator-assessed progression-free survival (PFS) per RECIST 1.1. Median PFS was 15.1 months (95% CI: 11.4, 18.4) in the atezolizumab arm and 10.6

months (95% CI: 9.3, 12.7) in the placebo arm (HR 0.78; 95% CI: 0.63, 0.97;  $p=0.0249$ ).

This application was granted priority review and atezolizumab was granted orphan product designation. FDA collaborated with Switzerland's Swissmedic on the review of this application as part of Project Orbis.

## FDA approves first cell-based gene therapy for adult patients with relapsed or refractory MCL

Tecartus (brexucabtagene autoleucel), a cell-based gene therapy, received FDA approval for treatment of adult patients diagnosed with mantle cell lymphoma who have not responded to or who have relapsed following other kinds of treatment.

Tecartus is sponsored by Kite Pharma Inc. Tecartus, a CAR T-cell therapy, is the first cell-based gene therapy approved by FDA for the treatment of MCL.

MCL is a rare form of cancerous B-cell non-Hodgkin's lymphoma that usually occurs in middle-aged or older adults. In patients with MCL, B-cells, a type of white blood cell which helps the body fight infection, change into cancer cells that start to form tumors in the lymph nodes and quickly spread to other areas of the body.

Approval was based on ZUMA-2 (NCT02601313), an open-label, multicenter, single-arm trial of 74 patients with relapsed or refractory MCL who had previously received anthracycline- or bendamustine-containing chemotherapy, an anti-CD20 antibody, and a Bruton tyrosine kinase inhibitor. Patients received a single infusion of brexucabtagene autoleucel following completion of lymphodepleting chemotherapy. The primary efficacy outcome measure was objective response rate

per Lugano [2014] criteria as assessed by an independent review committee.

Of the 60 patients evaluable for efficacy based on a minimum duration of follow-up for response of six months, the ORR was 87% (95% CI: 75, 94), with a complete remission (CR) rate of 62% (95% CI: 48, 74). The estimated median duration of response was not reached (range of 0+ to 29.2+ months) after a median follow-up time for duration of response of 8.6 months. Of all 74 leukapheresed patients, the ORR as assessed by an independent review committee was 80% (95% CI: 69, 88) with a CR rate of 55% (95% CI: 43, 67).

Tecartus is being approved with a risk evaluation and mitigation strategy, which includes elements to assure safe use. The risk mitigation measures for Tecartus are identical to those of the current REMS Program for another CAR-T therapy, Yescarta.

To further evaluate the long-term safety of Tecartus, FDA is also requiring the manufacturer to conduct a post-marketing observational study involving patients treated with Tecartus.

Tecartus was approved under the Accelerated Approval pathway and was granted Priority Review and Breakthrough Therapy designations. Tecartus also received Orphan Drug designation, which provides incentives to assist and encourage the development of drugs for rare diseases.

## Keytruda receives two sBLA acceptances from FDA in TNBC in indications

Keytruda has received two sBLA acceptances from FDA for the treatment of triple negative breast cancer:

- FDA has accepted and granted priority review for a new sBLA seeking

accelerated approval for Keytruda in combination with chemotherapy for the treatment of patients with locally recurrent unresectable or metastatic triple-negative breast cancer whose tumors express PD-L1 (Combined Positive Score [CPS]  $\geq 10$ ), based on the phase 3 KEYNOTE-355 trial. FDA has set a target action date of Nov. 28, 2020.

- FDA also accepted for standard review a new sBLA for Keytruda for the treatment of patients with high-risk early-stage TNBC, in combination with chemotherapy as neoadjuvant treatment, and then as a single agent as adjuvant treatment after surgery, based on the phase 3 KEYNOTE-522 trial. The target action date for this application is March 29, 2021.

Keytruda is sponsored by Merck. These are the first U.S. applications for Keytruda in breast cancer.

The applications are based on data from the KEYNOTE-355 and KEYNOTE-522 trials, respectively. In KEYNOTE-355, Keytruda plus chemotherapy demonstrated a statistically significant and clinically meaningful improvement in progression-free survival compared with chemotherapy alone in patients whose tumors expressed PD-L1 at CPS  $\geq 10$ .

Approximately 38% of patients enrolled in KEYNOTE-355 had tumors expressing PD-L1 at CPS  $\geq 10$ . As previously announced, the trial will continue without changes to evaluate the other dual primary endpoint of overall survival.

In KEYNOTE-522—the first randomized trial of an anti-PD-1 therapy in the neoadjuvant/adjuvant setting for TNBC—neoadjuvant Keytruda plus chemotherapy resulted in a statistically significant increase in pathologic complete response in patients with early-stage TNBC, regardless of PD-L1 expression.

The Keytruda regimen also demonstrated a favorable trend for the other dual primary endpoint of event-free survival. As previously announced, Keytruda plus chemotherapy was granted Breakthrough Therapy designation by FDA for the neoadjuvant treatment of patients with high-risk early-stage TNBC.

## **HIF-2 $\alpha$ inhibitor MK-6482 receives FDA Breakthrough Designation for Von Hippel-Lindau Disease-associated RCC**

The hypoxia-inducible factor-2 alpha (HIF-2 $\alpha$ ) inhibitor MK-6482, a novel investigational candidate, received Breakthrough Designation from FDA for the treatment of patients with von Hippel-Lindau disease-associated renal cell carcinoma with nonmetastatic RCC tumors less than three centimeters in size, unless immediate surgery is required.

HIF-2 $\alpha$  inhibitor MK-6482 is sponsored by Merck.

FDA also granted orphan drug designation to MK-6482 for VHL disease. These designations are based on data from a phase II trial evaluating MK-6482 in patients with VHL-associated clear cell RCC.

## **Engineered macrophage immunotherapy receives IND clearance from FDA**

FDA has cleared an investigational new drug application for CT-0508, an

anti-human epidermal growth factor receptor 2-targeted chimeric antigen receptor macrophage.

CT-0508 is sponsored by Carisma Therapeutics Inc.

Under this IND, Carisma intends to initiate its phase I, first-in-human, multi-center study in patients with recurrent or metastatic HER2 overexpressing solid tumors after failure of approved HER2 targeted agents.

“This will be the first time that an engineered macrophage has progressed successfully to the in-patient study phase and represents a new chapter for Carisma: advancing from a preclinical discovery-stage company to a clinical development stage company,” Steven Kelly, president and chief executive officer, said in a statement.

Historically, cell therapies have encountered key challenges treating solid tumors, including limited trafficking to the tumor site, an immunosuppressive tumor microenvironment, and the heterogeneous expression of tumor-associated antigens, but Carisma’s preclinical findings suggest that CAR-M therapy could overcome these challenges.

“Our preclinical findings indicate that CAR-M have the ability to mount a broad immune response against cancers, and the acceptance of the CT-0508 IND brings this technology to patients with incurable solid tumors,” Michael Klichinsky, co-inventor of the CAR-M technology, scientific co-founder, and vice president of discovery at Carisma Therapeutics.

The planned clinical trial will be conducted at two trial sites—University of Pennsylvania in and University of North Carolina—and will enroll patients with different types of recurrent or metastatic cancers with HER2 overexpressing solid tumors.

“HER2 is overexpressed not only in breast and gastroesophageal cancers, but in a wide variety of epithelial origin solid tumors, such as non-small cell lung, colorectal, bladder, and pancreatic cancers,” Debora Barton, chief medical officer at Carisma Therapeutics, said in a statement.

## **BDTX-189 receives FDA Fast Track Designation for solid tumors harboring HER2 or EGFR mutations**

BDTX-189 has received Fast Track Designation from FDA for the treatment of adult patients with solid tumors harboring an allosteric human epidermal growth factor receptor 2 mutation or an epidermal growth factor receptor or HER2 Exon 20 insertion mutation who have progressed following prior treatment and who have no satisfactory treatment options.

BDTX-189, an orally available, irreversible small molecule inhibitor, is sponsored by Black Diamond Therapeutics, Inc. BDTX-189 is Diamond Therapeutics lead product candidate designed to selectively inhibit the activity of a broad range of previously unaddressed oncogenic driver mutations of the ErbB kinases in EGFR and HER2.

“While targeted therapies, such as kinase inhibitors, have transformed the treatment of cancer, only a small percentage of patients with metastatic cancer have tumors with genetic profiles that could make them eligible for an approved precision oncology medicine,” David M. Epstein, president and chief executive officer of Black Diamond Therapeutics, said in a statement.

## **Tagrisso receives FDA Breakthrough Therapy Designation for adjuvant treatment of stage IB-III A EGFR-mutated lung cancer**

Tagrisso (osimertinib) has received Breakthrough Therapy Designation from FDA for the adjuvant treatment of patients with early-stage (IB, II and IIIA) epidermal growth factor receptor-mutated non-small cell lung cancer after complete tumor resection with curative intent.

Tagrisso is sponsored by AstraZeneca.

“Patients with early-stage EGFRm lung cancer often experience recurrence even after successful surgery and adjuvant chemotherapy, yet there are currently no approved targeted treatments to improve outcomes,” José Baselga, executive vice president of Oncology R&D said in a statement.

FDA granted the Breakthrough Therapy Designation based on data from the phase III ADAURA trial.

In the trial, Tagrisso demonstrated a statistically significant and clinically meaningful improvement in disease-free survival in the adjuvant treatment of Stage IB-III A EGFRm NSCLC patients, reducing the risk of disease recurrence or death by 79% (HR 0.21; 95% CI 0.16-0.28;  $p < 0.0001$ ) in a key secondary endpoint. In April 2020, an independent data monitoring Committee recommended the trial to be unblinded two years early based on its determination of overwhelming efficacy.

Tagrisso is approved for the first-line treatment of patients with metastatic EGFRm NSCLC and for the treatment of metastatic EGFR T790M mutation-positive NSCLC in the U.S., Japan, China, and the EU.

## **Piqray receives approval in Europe for HR+/HER2- advanced breast cancer with a PIK3CA mutation**

Piqray (alpelisib) received approval from the European Commission in combination with fulvestrant for the treatment of postmenopausal women, and men, with hormone receptor positive, human epidermal growth factor receptor-2 negative (HR+/HER2-) locally advanced or metastatic breast cancer with a PIK3CA mutation after disease progression following endocrine therapy as monotherapy.

Piqray is sponsored by Novartis.

Piqray is the first and only treatment specifically approved for people with advanced breast cancer whose tumors harbor a PIK3CA mutation, which stimulates tumor growth and is associated with poor response to therapy.

This approval follows a positive opinion granted in May by the Committee for Medicinal Products for Human Use of the European Medicines Agency based on the phase III SOLAR-1 trial showing that Piqray nearly doubled median progression-free survival compared to fulvestrant alone.

Overall response rate was more than doubled when Piqray was added to fulvestrant compared to fulvestrant alone.