

# Cancer Immunotherapy Paves Way for Better Understanding of COVID-19

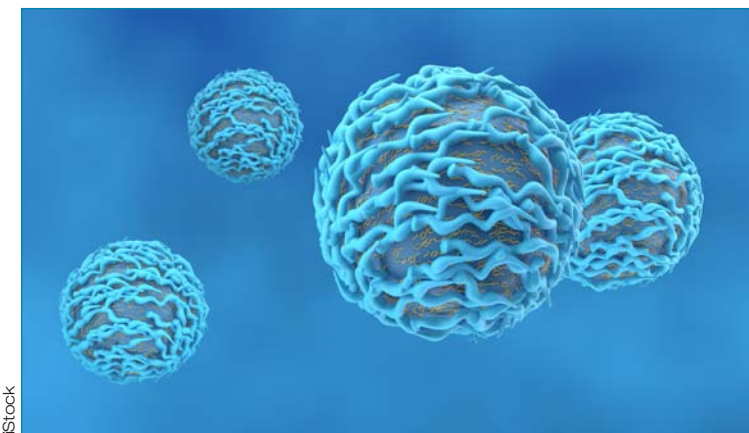
BY PEGGY EASTMAN

Insights gained from treating cancer patients with immunotherapy are helping to unravel the mysteries of the coronavirus pandemic, according to speakers at a webinar sponsored by the Cancer Research Institute, which is dedicated to advancing the field of immunotherapy. Specifically, knowledge learned in cancer immunotherapy may help physicians individualize treatments based on the different immune responses of their patients with COVID-19, which is a heterogeneous disease.

“You wouldn’t think cutting-edge cancer research has a lot to do with the COVID-19 pandemic,” said moderator Matthew Herper, Senior Writer in Medicine for STAT, a media company focused on medicine and science.

However, he noted that cancer research over the past 10 years has led to an increased understanding of immunology and how the immune system can be harnessed to fight cancer. “That means we’re facing some of the same problems as we try to understand how the immune system reacts to the virus,” Herper said.

“It’s been known for many years that in certain viral infections inflammation contributes to pathology,” said CAR T-cell therapy pioneer Carl June, MD, the Richard W. Vague Professor in Immunotherapy in the Department of Pathology and Laboratory Medicine, Director of the Center for Cellular Immunotherapies at the Perelman School of Medicine, and Director of the Parker Institute for Cancer Immunotherapy at the University of Pennsylvania.



“I think cancer has been from the beginning probably the proving ground for translational medicine, where things are rapidly taken from basic discoveries and tested right on patients, because there was no alternative—just like we have [COVID-19] patients piling up in ICUs with this pandemic,” added June, who himself contracted the coronavirus and recovered from it.

“Oncology is now about the host immune system reacting to the tumor, and there are technologies being developed at breakneck speed to study the host immune system in cancer patients...and those technologies can be applied to the benefit of understanding the host immune response in a pandemic. So we’re seeing real technology transfer there,” added June.

He said the infrastructure for immuno-oncology will be a benefit as researchers and clinicians seek to better understand the new pandemic virus, which has shown how widely people’s immune response varies to the same pathogen. While there are tailored therapies in cancer, “we don’t have that in viral diseases, and I think that’s where we need to go,” noted June.

“The immune system has enabled us to survive as a species; we can survive only if we have an immune response that can fight the viral

infection,” said Miriam Merad, MD, PhD, the Mount Sinai Endowed Professor in Cancer Immunology and Director of the Precision

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Immunology Institute at the Icahn School of Medicine at Mount Sinai, where she also co-leads the cancer immunology program at the Mount Sinai Tisch Cancer Institute and is Director of the Mount Sinai Human Immune Monitoring Center. Merad cited the complexity of the immune system, noting that “it is fundamental for health and homeostasis and repair and being able to resist this type of threat [the pandemic].”

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While a strong immune response is necessary to fight the coronavirus, it can be hyperactive and thus harmful. Merad has led the effort at Mount Sinai to develop a quick test that monitors a patient’s inflammatory response to COVID-19, and helped launch a clinical trial that uses sarilumab—typically given to treat rheumatoid arthritis—to manage those responses. By identifying severe immunological reactions in COVID-19 patients quickly, “we can speed the implementation of a cytokine blockade and significantly improve patient outcome,” she said.

“I think as cancer researchers, one of the things we bring to the table in this [pandemic] challenge is the real need to understand a lot of nuances and details about the immune system,” said E. John Wherry, PhD, the Richard and Barbara Schiffrin President’s Distinguished Professor, Chair of the Department of Systems Pharmacology and Translational Therapeutics in the Perelman School of Medicine, and Director of the UPenn Institute for Immunology.

That need to understand complex immune nuances and details, he said, has arisen because cancer immunotherapists “are fortunate to have many drugs at our disposal, and we have to match those drugs to the patient and the immune system and the type of cancer where the patient is going to respond the most.

“Over the past 10 years, the cancer immunotherapy field has gone into explicit detail to match therapies to the right kind of patient,” Wherry noted. “So applying that in COVID-19 gives us an opportunity to understand which patients are suffering from the hyperinflammatory state, and which patients may have failed to mount an appropriate immune response and may need antivirals and maybe immune activation.

“The reports we’re hearing now reflect the heterogeneity of the disease,” he added. “When you treat all hospitalized patients the same way, you may miss an opportunity to tailor a therapy to patients who will benefit the most.”

Asked whether cancer patients receiving immunotherapy are more susceptible to COVID-19 than cancer patients receiving chemotherapy

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## CANCER IMMUNOTHERAPY

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or no therapy, June said, “I have to resist making any kind of blanket statements. It certainly depends on the type of therapy—whether it’s cytotoxic chemotherapy, whether they are bone marrow transplant patients, or whether they are getting checkpoint inhibitor therapies.”

He noted that some chemotherapies can cause pulmonary damage, “and so we know that is a co-morbidity that can lead to a worse outcome if the patient gets COVID-19 and has had previous damage.” He said there is controversy on the effects of checkpoint inhibitors and susceptibility to the coronavirus in cancer patients taking these drugs.

There are some hints that lung cancer may make things worse for patients who contract COVID-19, but “I think the jury is still out,” said Wherry. “I think the take-home message is that cancer patients shouldn’t stop getting cancer treatment. It’s not obviously making things worse...and there are anecdotal reports of benefits in individual patients.”

He noted that the incidence of COVID-19 in his institution’s hospitalized patients is not increased in the cancer population, and “if anything, it may be a little reduced.”

Merad agreed. “What we’re seeing is that immunotherapy patients really have been underrepresented in those with severe COVID-19, suggesting that patients on inflammatory blockade seem to have done better,” she said. “This is a big issue for thousands of patients, and quite encouraging. We’ll definitely be looking at that.”

Speakers were asked whether they were surprised by the recent news that a steroid, dexamethasone, had a robust effect on seriously ill COVID-19 patients in the United Kingdom’s Recovery trial, suggesting that the drug had a modulatory effect on an overactive immune response in patients with severe disease. Specifically, preliminary results from the Oxford University trial showed that, in hospitalized COVID-19 patients with acute respiratory distress syndrome (ARDS), low-dose dexamethasone reduced deaths by one-third.

“I was astonished, actually, that that happened,” said June, noting that the results need to be reported in a peer-reviewed publication. “We have to be cautious, but our infectious disease specialists at Penn are going to put this into practice...I’m really surprised at how fast they’re going to adopt that.”

“I don’t know why this trial seemed to be so positive when in so many others, including previous trials of MERS and SARS, this wasn’t seen,” he added. “My bet is that they may just have threaded the needle perfectly with a low dose at the right time in the infection.”

Merad noted that, in looking at measurements of cytokine reduction with steroid drugs, dexamethasone seemed to have the strongest effect. But, she said, “I would like to see the data. I would caution everyone and say, ‘Please share the data with all of us.’ We need to really look at the details. I’m hoping they also have biology correlates, because this will help us understand why a specific group responded so well.”

Speakers were asked whether COVID-19 affects cancer patients differently depending on the type of cancer they have—or whether it is just too soon to know.

“The one thing I would like people to remember is that we can and should be measuring the immune system as part of our clinical care,” Wherry said. “We can measure the immune system with an unprecedented level of specificity and detail—driven a lot by the cancer immunotherapy field—and we can put that into practice to design therapies that are more finely tuned to a patient’s clinical presentation type.”

“So I think integrating the ability to use information about the overall immune health of the patient to tailor treatments is really what a lot of this has taught us, and it might be beneficial in diseases like COVID-19.”

Asked how the coronavirus has affected their laboratories and research programs, all three speakers decried the pandemic’s chilling effect on basic research and clinical trials, just when answers from science are so desperately needed.

“A lot of things have ground to a halt,” said Wherry. “A lot of the really key basic science that is the jet fuel and the engine of what we’re talking about for COVID-19 research and for cancer immunotherapy—a lot

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### Learning Objectives for This Month’s Activity:

After participating in this activity, readers should be better able to: 1. Evaluate how cancer research has contributed to our current understanding of COVID-19. 2. Assess how the COVID-19 pandemic has affected the current state of scientific research. 3. Summarize what we have learned about the role of immunology in our treatment of patients with COVID-19.

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of that basic discovery work has essentially stopped.” And, he warned, “We can’t restart on a dime. It’s going to take a long time to rebuild what we have lost over the last few months. I think one of the things this pandemic has, I hope, taught all of us is that science really matters. We’re going to get out of this mess because of science, data-driven science that points to answers and experimentally testing hypotheses, whether in the lab or the clinic.”

June agreed that the pandemic has been devastating for research. “It’s really ground to a virtual halt,” he said of his university, adding that “our biopsy core services have been shut down.”

June agreed with Wherry on the need to draw attention to the importance of science, especially now. “We’ve done a poor job of educating the public on why we need science...I think now is our opportunity to tell the public why they need science,” noting that “some people don’t know why you need a vaccine, for instance.”

Merad noted that, in addition to the pandemic’s damaging effects on the clinical trials infrastructure, the shutdown of schools caused by the pandemic has been devastating for the careers of some researchers who need to stay home with their children and cannot pursue their work.

“The pandemic has created a whole group of people who are parents of young children who need to stay home with them... so the pandemic has created a whole group of people who are unable to do research,” she noted. “This is going to affect their careers.” **OT**

*Peggy Eastman is a contributing writer.*