When a Global Pandemic Complicates Cancer Care

Although oncologists and their patients are accustomed to fighting tough battles against a lethal disease, Coronavirus Disease 2019 (COVID-19) has posed an unprecedented challenge.

Since the first cases of Coronavirus Disease 2019 (COVID-19) were reported in China in early January and the disease subsequently spread to the United States and nearly 200 countries, the oncology community has had to adapt to an ever-evolving medical emergency while trying to ensure the health and safety of patients with cancer.

However, faced with limited data on how the virus specifically affects people with cancer and other unknowns that surround a new disease, clinicians say that they have struggled at times to make decisions about care and have found themselves second-guessing treatment strategies.

“Our initial reaction was to avoid patient and health care worker exposure to infection, and we canceled as many visits and procedures as possible,” says Antoni Ribas, MD, PhD, president-elect of the American Association for Cancer Research (AACR) and director of the Tumor Immunology Program at the Jonsson Comprehensive Cancer Center at the University of California Los Angeles. Of course, withholding active therapies and giving cancer a chance to progress also pose a risk, so Dr. Ribas tried to strike a balance. He continued to treat patients who recently had started immunotherapy while advising others on maintenance therapy to stop treatment temporarily. “But I don’t know if it was the right thing to do,” he says.

Patients have also raised concerns about treatment in a world reshaped by the coronavirus. At the 24-hour support line of the American Cancer Society (ACS), 80% of calls, as of press time, are related to COVID-19, says ACS Deputy Chief Medical Officer J. Leonard Lichtenfeld, MD, with patients voicing fears about access to and interruptions in care.

Researchers and cancer organizations have responded by carefully examining early data from some of the most heavily affected regions and identifying key questions that require further study. They are also working to create a clearer picture of how the virus is affecting day-to-day cancer care and the areas in which patients may need additional support.

For example, to better understand how people with cancer are faring in the pandemic, the ACS Cancer Action Network conducted a nationwide survey of more than 1200 patients between March 25 and April 8. Consistent with questions that the ACS has fielded through its hotline, this survey found that:

- Approximately 27% of patients currently in active treatment have reported a delay in treatment.
- Approximately 13% have had their treatment delayed without knowledge of when it would be rescheduled.
- One-third of all patients say that they are worried about the impact the virus will have on their ability to get care; this is especially true for those in active treatment (40%).
- Nearly 4 in 10 (38%) have said that COVID-19 is affecting their ability to afford care, mostly because of reduced work hours.

“We’ve pivoted in no small way to address some of the questions raised by COVID-19 and have partnered with various cancer registries to study its impact on cancer patient care,” Dr. Lichtenfeld says. He notes that the ACS is also developing recommendations for how physicians can safely resume cancer screenings.

Major cancer conferences have shifted their focus to the coronavirus as well even as organizers have moved proceedings online to prevent its spread. The AACR’s annual meeting, for example, was originally scheduled for April 24 to 29 in San Diego, California, but was rescheduled as 3 virtual meetings held on April 27 to 28 and June 22 to 24, with a third, 3-day meeting in July dedicated to COVID-19 and cancer.

At the AACR’s April meeting, Dr. Ribas chaired a plenary session in which clinicians and researchers from China, Italy,
France, Spain, and New York City shared their early findings on outcomes for patients with cancer and COVID-19 infections. “Putting together a session like this and including places that were starting to collect data was important for understanding the gaps in knowledge so that we can focus on the right questions and collect the right information,” he says. “A lack of information is stimulating a lot of people to be very proactive.”

Making Sense of the Research

One of the earliest questions that investigators had was whether patients with cancer and COVID-19 infections have more severe outcomes than patients who do not have cancer. The answer will help to guide clinicians in deciding whether cancer treatment should be temporarily stopped to limit patients’ exposure risk. Two abstracts presented at the AACR’s April meeting by researchers from Wuhan, China, suggest that it may depend, in part, on the type and stage of cancer. Investigators reported that patients with hematologic, lung, or metastatic cancers had the highest frequency of severe events. However, patients with other cancer types and nonmetastatic cancers experienced frequencies of severe conditions similar to those observed in patients without cancer.1

In another AACR presentation, Italian researchers reported on a new global registry called the Thoracic Cancers International COVID-19 Collaboration (TERAVOLT), which was established to gather data and provide guidance to oncologists on managing thoracic malignancies while understanding COVID-19 risk factors. Initial results from 200 patients in 8 countries show that patients with thoracic malignancies and COVID-19 infections are less likely to be admitted to intensive care and are at increased risk of prolonged hospitalization and mortality from the virus.

More recent abstracts with a shorter follow-up period presented by French, Spanish, and Italian researchers compared patients who were infected with COVID-19 and had a prior cancer diagnosis but were no longer being treated with those who were actively being treated for cancer. Scientists found that the 2 groups had similar outcomes. According to Dr. Ribas, the only patients who did worse were those who had undergone very recent chemotherapy (eg, in the past 2 weeks) and had hematologic malignancies that lowered their ability to fight infections or had a history of smoking or another comorbid condition such as chronic inflammatory disease or hypertension.

“There’s still no consensus on whether cancer patients with COVID-19 infections do worse,” he adds. “I still question that myself after hearing the presentations.”

Furthermore, because these studies assessed only COVID-19–infected patients who had recently undergone chemotherapy for their cancer, scientists did not yet know about the outcomes for those who had undergone radiation, immunotherapy, surgery, or targeted therapy for their disease, Dr. Ribas notes.

On May 1, a Montefiore Health System and Albert Einstein College of Medicine study published in Cancer Discovery found that people with cancer who develop COVID-19 infections are more likely to die from the virus than those without cancer.2 It was the largest study that had been reported to date and involved 218 patients who tested positive from March 18 to April 8. However, investigators found mortality to be related more to frailty, age, and comorbidities than active cancer therapy. Moreover, they qualified that the patients were treated at a time when testing was almost exclusively performed for sicker, symptomatic people requiring hospitalization, which could explain the higher fatality rates.

Whether or not clinicians should be withholding immunotherapy from patients with cancer during the pandemic is another unknown. On the one hand, immune system cells reject viral infections, and anti-PD1 and anti-CTLA4 therapies have been shown to be effective against RNA viruses such as hepatitis C. Because the coronavirus that causes COVID-19 is also an RNA virus, blocking these pathways could potentially be effective in fighting it. In that case, withholding these therapies during the pandemic may not be a good idea, Dr. Ribas notes.

On the other hand, he adds, investigators do not yet have enough data on the immune responses of patients with COVID-19 to these therapies. Potentially, these responses could lead to worse complications with the virus.

In addition to seeking answers for how best to manage patients with cancer during the pandemic, researchers also are investigating whether specific cancer drugs can be used to treat COVID-19 infections. “There are a lot of parallels between a virus that infects cells and cell mutations that cause cancer,” Dr. Ribas says. Although the data are still early, there is some evidence that the immunosuppressive drug tocilizumab, which is used to treat patients with cancer who experience respiratory distress syndrome associated with chimeric antigen receptor T-cell therapies, may also help patients infected with COVID-19 who experience the same syndrome. Moreover, JAK and BTK inhibitors, which are used to treat hematologic malignancies and rheumatoid conditions, are now being studied in patients infected with the coronavirus because some of the same issues exist in the pathogenesis of COVID-19.

Unfortunately, at the same time that COVID-19 research is being prioritized, many types of cancer research have come to a screeching halt. “Most lab experiments cannot be done, and fewer patients will be going on clinical trials,” Dr. Ribas says. “Temporarily, that will have an impact on cancer research as a whole, but it’s a necessary measure. We’re fighting cancer in a different way by not allowing the virus to spread.”

Assessing the Road Ahead

Like most nonprofit organizations during the pandemic, the ACS has experienced a significant blow to both its operations and its fundraising efforts, Dr. Lichtenfeld says. Social distancing concerns have also curtailed some of its initiatives. As the coronavirus became increasingly widespread in March, the organization suspended its Road to Recovery program, which provides patients with cancer free rides to and from treatment, and it closed all 36 of its Hope Lodges, which provide free accommodations for patients and caregivers during treatment. At press time, it was working to reopen several Hope Lodges as soon as possible, depending on local circumstances.
Still, the ACS has found new ways to support patients and the medical community, and it is continuing many of its core services. For example, it repurposed some of the Hope Lodges so that health care workers who needed a place to stay could use the facilities. Furthermore, although the ACS suspended its next extramural research funding cycle, its internal research and virtual fundraisers will continue, as will patient, caregiver, and physician education efforts supported by webinars and media outreach.

While remaining hopeful that specific recommendations soon will be developed for safe operations at outpatient cancer centers along with rapid COVID-19 testing, Dr. Lichtenfeld notes that primary care practices and rural hospitals will likely face particularly daunting challenges in providing screenings and treatment.

“These are all pieces of a large puzzle that won’t be coming together in any neat fashion as we move forward,” he adds.

**References**

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### New Guidance for Treating Patients With Lung Cancer and COVID-19

Treating patients with lung cancer who also have COVID-19 is a unique hurdle for oncologists who must address not 1 but 2 potentially severe, life-threatening diseases. In light of this, the *Journal of Thoracic Oncology* published a review of treatments for this patient group in its May issue.

The work is a practical, multidisciplinary, and international overview. However, researchers note that evidence is still lacking in many areas, says lead author Chandra Belani, MD, chief science officer for the International Association for the Study of Lung Cancer, which publishes the journal, and professor of medicine and oncology at the Penn State College of Medicine and Cancer Institute in Hershey, Pennsylvania.

Patients with lung cancer tend to be older and at greater risk for relative immunosuppression from both their malignancy and anticancer treatments. They also may have comorbid conditions such as a smoking history or preexisting lung disease, which make them even more vulnerable to COVID-19 complications.

Balancing the risk between treatment and exposure to infection is always top of mind, Dr. Belani notes, and the risk of rapid COVID-19 onset requires oncologists to make urgent treatment decisions. There are also contradictions to consider: self-isolation, for example, runs contrary to best-practice care for patients with cancer, who benefit from joining support groups, receiving help from loved ones, and staying active. The overview offers advice to clinicians on treating all stages and types of lung cancer and on dealing with COVID-19 and immunotherapy.

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### Research Notes Largest Yearly Decline in Melanoma Deaths

Major advances in treating melanoma have led to a significant decline in mortality for the disease according to research published in the *American Journal of Public Health* in March. Metastatic melanoma death rates had increased by 7.5% between 1986 and 2013 among white Americans, who account for nearly all cases of the disease. However, the rate dropped by 17.9% from 2013 to 2016 according to researchers from the NYU Grossman School of Medicine, its Perlmutter Cancer Center, and Harvard University. In 2014, mortality rates started to sharply decline in particular among men older than 50 years.

The decline surpasses comparable reductions in 3 other common forms of cancer—prostate, breast, and lung—and is unprecedented in the cancer medicine field. The authors note that it occurred in tandem with the introduction of 10 new treatments for the disease, which include immune checkpoint inhibitors and treatments that target the *BRAF* gene, which is mutated in slightly less than half of patients with melanoma.

The therapies have transformed the treatment of metastatic melanoma and dramatically reduced deaths, says cosenior study author David Polsky, MD, PhD, professor of dermatologic oncology at NYU Langone Health. The study is the first to highlight how these new drugs are improving American survival rates for the disease, he notes.

Dr. Polsky and his colleagues analyzed new melanoma cases and deaths in 9 US Surveillance, Epidemiology, and End Results registry areas that recorded data between 1986 and 2016. The dramatic decline in mortality cannot be explained merely by improved early-detection rates, which have been occurring for some time, although they are still important in enabling less toxic treatments, he says.

The authors add that future research should focus on developing even more effective treatments, identifying biomarkers to select those patients most likely to benefit from various therapies, and continuing to emphasize public health approaches in prevention and early detection to reduce advanced disease incidence.

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