Navigating Cancer Care in the COVID-19 Era

Experts allay initial concerns about immunotherapy use, push virtual trials

Since the COVID-19 pandemic began nearly 2 years ago, clinicians, researchers, industry leaders, and federal regulators in oncology have had to adapt to an evolving landscape of patient care and trial management. Lessons have been learned along the way, and some were highlighted during the 2021 Society for Immunotherapy of Cancer (SITC) Annual Meeting in Washington, DC, in November.

"A key question, early on, was whether immunotherapy might increase cancer patients' risk of severe illness or death if they contracted COVID-19," said Jeffrey Weber, MD, PhD, of New York University's Langone Medical Center in New York. "We wondered if this treatment might be a double-edged sword. It could boost the antiviral immune response and decrease T-cell exhaustion, but also exacerbate the virus's detrimental effects, including pneumonitis and cytokine release syndrome."

Guidelines issued by the American Society of Clinical Oncology and the National Comprehensive Cancer Network urged oncologists to consider less frequent dosing—for instance, giving pembrolizumab (Keytruda; Merck) in 6-week cycles, not every 3 weeks. "In addition, we backed off using combination therapy, which tends to be more immunotoxic, and tried single agents first," Weber said.

Analyses of patient cohorts have since indicated that "our worries were theoretical—immunotherapy doesn't appear to significantly worsen outcomes related to COVID-19," he added.

Margaret Callahan, MD, PhD, of Memorial Sloan Kettering Cancer Center in New York, NY, agreed that "the data across thousands of patients so far are very reassuring, and the concerns we had at first haven't been borne out." Rather than the treatment itself, patients who are immunocompromised—usually from high-dose steroids to manage immunotherapy's side effects—present a more pertinent risk when it comes to COVID-19 morbidity or mortality, she pointed out.

"It's something we now think about, trying to avoid immunosuppressants, if at all possible, for our patients," Weber said. With the advent of COVID-19 vaccines, too, "we've learned to ask patients if they got a shot recently, to not confuse vaccine-related adenopathy with disease progression," given that they look similar in radiographic imaging.

For clinical trials, Weber noted that "we've recovered extremely well" from the steep decline in patient accrual due to strict mitigation measures, including treatment and follow-up delays, that most cancer centers adopted at the start of the pandemic. Whether such measures affected data from ongoing trials "would be interesting to see in retrospective analyses," he mused. "My gut tells me there'll be no real impact, but this hasn't been rigorously studied."

Although steps to keep COVID-19 at bay "were quickly instituted under the stress of 'wartime' conditions, they'll leave a legacy in terms of how we do business in clinical cancer research," Weber said, "and that's not a bad thing."

STREAMLINING TRIALS

Both Weber and Callahan would like to see some of the specific mitigation measures around trial conduct, including increased use of online consent forms and fewer nonessential tests, retained as a pandemic legacy.

"We've been buried under paperwork; standardized electronic order sets, auditing, and data entry would improve operational efficiency," Weber said. Reevaluating mandatory requirements for reporting certain data, whether relevant or not, would also be welcome, he added. "Maybe we shouldn't get bent out of shape about minor protocol deviations, for instance."

"COVID-19 has shined a light on the trials process: Is each step necessary, and what does it really contribute?" Callahan remarked. "We should look at the risk–benefit ratio differently, maybe refocus it in a more patient-centric way."

Also speaking at SITC, Kannan Natarajan, PhD, a senior vice president at Pfizer, agreed that "the pandemic is providing an opportunity to transform how we conduct studies" and advocated moving toward virtual trials. With this approach, patients' data would be obtained digitally or through local labs and imaging centers, so "their participation isn't hampered by study site inaccessibility or other logistical constraints," he said. "I think we'd accelerate recruitment and potentially increase trial population diversity."

Web-based trials have already proven feasible outside oncology, Natarajan noted, citing a randomized study across the United States and Canada that concluded, like many others, that hydroxychloroquine did not reduce COVID-19 severity (Ann Intern Med 2020;173:623–31). All aspects of the trial were remote, from screening participants and shipping the study drug directly to them, to collecting their data electronically.

"Seamless communication is critical" for successful virtual trials, Natarajan said, "and digital technology will play a big role here. At Pfizer, we've begun implementing ePRO [electronic patient-reported outcomes], which involves patients using their own mobile devices. We've done local language translations where needed for our global trials, and overall, it's been adopted well."

The FDA is similarly interested in decentralized trials, said Lorraine Pelosof, MD, PhD, a SITC panelist representing the agency's Office of Oncologic Diseases. For new drug or biologics license applications, "we now request that investigators voluntarily flag their datasets to distinguish between assessments done remotely or at the study site," she said. "We're hoping to learn about the challenges and opportunities of remote modifications made during the pandemic, so in [the] future, more aspects of oncology trials can be prospectively decentralized."

COVID-19 "has been a catalyst of greater adaptability and flexibility," Pelosof observed, "and it may soon be possible that even if you don't live in a city with a huge medical center, you can still participate in cancer trials and help move the field forward." *–Alissa Poh* ■

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