ICl Impact on COVID-19 Severity Modest at Best

In an ongoing global pandemic, one question oncologists have been investigating is whether their patients—already vulnerable to COVID-19—may be at risk of more severe viral disease if their cancer therapy includes immune checkpoint inhibition (ICI). The emerging answer is that, at least for now, halting or modifying ICI-related treatment is unwarranted.

Rather, vigilance with SARS-CoV-2 testing is “what we suggest for patients who are on or about to start ICI,” said Jedd Wolchok, MD, PhD, of Memorial Sloan Kettering Cancer Center (MSKCC) in New York, NY. He coauthored two recent retrospective studies showing that “any signal we’ve observed that ICI may worsen COVID-19 outcomes is modest, to say the most.”

One set of findings was presented by Jia Luo, MD, at the American Association for Cancer Research (AACR) Virtual Meeting: COVID-19 and Cancer, held July 20–22. The analysis focused on patients with lung cancer, identifying 69 who were diagnosed with COVID-19 between March 12 and April 13 (Cancer Discov 2020;10:1121–8). Of these, 41 had received prior ICI, primarily PD-1 blockade.

“We wanted to see if there might be differences between recent or more remote exposure to ICI, in terms of impact on COVID-19 severity,” Luo said. As such, the 41 patients included those dosed within 6 months of a COVID-19 diagnosis and those who had started ICI within 3 months of developing it. Virus “severity” was defined by the following outcomes: hospitalization rate, the need for intensive care, and death. After adjusting for potentially confounding factors—chiefly smoking history—the investigators found no significant association between PD-1 blockade and an increased risk of severe COVID-19.

On the other hand, such a link was uncovered in a second, broader study of 423 patients with various cancers and COVID-19 (Nat Med 2020;26:1218–23). The researchers reported that two predictors for hospitalization and severe respiratory illness—defined as requiring supple-
second waves, perhaps we’ll be better prepared with uniform ways of querying patient outcomes, to reduce heterogeneity.” – Alissa Poh

Gilead Buys into Tizona’s Anti–HLA-G Strategy

Gilead announced plans in July to pay $300 million for a 49.9% stake in Tizona Therapeutics, with the option to pay another $1.25 billion for the remainder of the company. Whether Gilead follows through with the acquisition will hinge on results of a first-in-human trial involving Tizona’s investigational checkpoint inhibitor, TTX-080.

The antibody therapy is the first clinical-stage candidate designed to block the interaction of HLA-G, a histocompatibility antigen displayed on the surface of tumor cells, with corresponding receptors found on immune cells.

Because HLA-G and PD-L1 have distinct but overlapping expression patterns, Tizona’s HLA-G antagonist may help patients who do not respond to current anti–PD-1/PD-L1 treatments and deepen responses among those sensitive to existing immunotherapy agents. Receptors for HLA-G are also found on many different cell types—including T cells, B cells, natural killer cells, monocytes, and dendritic cells—so TTX-080 could promote antitumor immunity through several pathways at once.

Although the company has not publicly presented any preclinical TTX-080 data, onlookers are enthusiastic about the HLA-G–targeting approach. “It’s definitely something worth trying,” says Kerry Campbell, PhD, of Fox Chase Cancer Center in Philadelphia, PA. “Clearly HLA-G is expressed on a lot of tumors, and I think it’s worth a test.”

Yet, given the structural similarity between HLA-G, a nonclassic MHC class I molecule, and its classic counterparts involved in antigen presentation, some experts worry about the potential for cross-reactivity. “Going for an HLA molecule? Boy, you want to make sure that specificity is good,” says Mary Carrington, PhD, of the NCI.

First described for its role in protecting fetuses from their mothers’ immune systems, HLA-G was later shown to be expressed on a lot of tumors, and I think it’s worth a test.”

Researchers discovered osteosarcoma in the fibula (shown in red) of a horned dinosaur, Centrosaurus apertus, estimated to be 76 million years old.

A Discovery 76 Million Years in the Making

A deformed leg bone discovered in Alberta, Canada, offers the first histologically confirmed example of a malignant tumor diagnosed in a dinosaur (Lancet Oncol 2020;21:1021–2). The osteosarcoma, identified in the fossilized fibula of a plant-eating horned dinosaur called Centrosaurus apertus, shows that unregulated neoplastic growth is not a modern physiologic problem, but a vulnerability rooted deep in the genomic history of cellular development.

Those evolutionary insights could help narrow the search for genomically drivers of osteosarcoma, says hematologist Mark Crowther, MD, of McMaster University in Hamilton, ON, Canada, who co-led the study. Because all birds alive today descended from dinosaurs, and because osteosarcoma has been documented in birds, “it suggests to us strongly that the best place to look is in the genetic material that is shared between humans and birds.”

Paleontologists who found the 76-million-year-old fibula in the late 1980s chalked up the bone’s strange bulbous shape to a fracture that had not healed properly. The specimen then sat in a museum drawer for close to 30 years until Crowther—working with paleobiologist David Evans, PhD, of the Royal Ontario Museum in Toronto, Canada, and a multidisciplinary team of pathologists, radiologists, and orthopedic surgeons—decided to take another look.

The specialists formed a kind of paleo-oncologic tumor board and, using modern diagnostic techniques, offered a second opinion on their dinosaur “patient.” They compared its bone to one from a 19-year-old male, now deceased, who had confirmed osteosarcoma and had undergone lower-leg amputation. Although the dinosaur sample, unlike the human one, lacked preserved soft tissue, morphologic, radiographic, and histologic examinations of the two fibulae revealed similar patterns of abnormal bone formation, with blood vessels...
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