Call Made to Speed Cell-Therapy Development

Two organizations have called upon the FDA to update guidance on the pathway for investigational new drug (IND) studies of exploratory T cell-based therapies that would ease manufacturing requirements and offer more flexibility to make changes as studies progress. Specific recommendations were outlined in a white paper written by the Friends of Cancer Research (FOCR) and the Parker Institute for Cancer Immunotherapy (available at: https://www.focr.org/).

Current IND requirements limit the study of investigational cell therapies to a select few candidates, according to the paper. For example, engineered T-cell receptor and chimeric antigen receptor T-cell therapies have been approved for certain types of lymphoma and leukemia.

Now, “there is great interest in exploring these new treatment modalities to encompass the treatment of solid tumors, which comprise 90% of all cancers and the majority of cancer deaths,” the groups state.

“To potentially help a much larger number of patients, in particular those patients with solid tumors and no remaining treatment options,” the groups add, “it would be desirable to advance small, data-intensive clinical exploratory studies to differentiate which approaches warrant further focus.”

So many factors play into immune responses that cell therapies can be accurately characterized only in living and human systems, notes Jeff Allen, president and CEO of FOCR. Animal models cannot exactly replicate what happens in humans and thus cannot reliably predict safety and efficacy.

With hundreds of drug candidates in the pipeline, researchers are looking to the FDA for more specific guidance on early-stage development, says Allen. For example, greater flexibility around good manufacturing practices could allow studies to proceed more rapidly without sacrificing safety.

“As we see the potential for cures with some cell therapies, it’s timely to reflect on what could be done to accelerate the pace of discovery without taking undue risks,” says Michel Sadclain, MD, PhD, director of the Center for Cell Engineering at Memorial Sloan Kettering Cancer Center in New York, NY, who was not involved in preparing the white paper. “The field has accumulated enough of a solid track record and experience that we could, in some cases and in some settings, be less stringent on requirements to conduct trials and make modifications after trials have been initiated.”

The FDA already grants amendments to trial protocols on a case-by-case basis, notes Sadclain. The white paper proposes formalizing that process into standard IND filing requirements instead of granting modifications ad hoc. However, he cautions against imposing manufacturing standards that could potentially stifle innovation by imposing undue restrictions on the nascent field.

The white paper also makes several recommendations to expedite product development—for example, developing a “parent-child” IND framework to speed testing of multiple, highly related products, and establishing a consortium comprised of academia, government, nonprofit, and industry to share data.

“Our goal was to emphasize areas where there could be additional flexibility around filing INDs in the early stages of development and making modifications later in the process,” says Allen. “With the field evolving so quickly, it’s important to think collectively about the best ways of collecting data, characterizing the emerging evidence, and putting processes into place that ensure safety while also allowing the science to evolve.” —Janet Colwell

TCR Gene Therapy Improves AML Prognosis

Treatment with T cells engineered to express a receptor for Wilms tumor antigen 1 (WT1) helps prevent relapse in patients with acute myeloid leukemia (AML) who have received an allogeneic stem-cell transplant.

The finding, from a 12-person trial of JTCR016 (Juno/Celgene), highlights the potential for T-cell receptor (TCR) gene therapy to improve outcomes in AML—a disease for which chimeric antigen receptor-modified T cells have had little clinical impact, in part owing to the lack of surface markers unique to leukemic blast cells (Nat Med 2019;25:1064–72).

“The study is really small, but it’s very promising,” says Marcel van den Brink, MD, PhD, of Memorial Sloan Kettering Cancer Center in New York, NY, who was not involved in the research. “Our field is desperate for meaningful strategies to overcome a relapse, so a therapy like this is incredibly important—and can lead to real progress.”

Researchers from the Fred Hutchinson Cancer Research Center in Seattle, WA, developed the technology behind JTCR016. The bespoke therapy involves transducing CD8+ T cells...
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