MedicalXpress

Immunotherapy pioneers reveal updated efficacy data of tisagenlecleucel CAR T-cell therapy

December 4 2018

Physician-scientists from Children's Hospital of Philadelphia (CHOP) presented updated efficacy and safety data on Kymriah(R) (tisagenlecleucel, formerly CTL019) —the first-ever U.S. Food and Drug Administration (FDA) approved personalized CAR T-cell gene immunotherapy for aggressive blood cancers at the 60th American Society of Hematology (ASH) annual meeting, as well as first-of-its-kind research on overcoming CAR T-cell resistance.

Together, the contributions further cement CHOP's aggressive pursuit of giving patients better options in this new field of personalized, cellular medicine.

An updated, longer-term analysis of ELIANA, the first pediatric global CAR-T cell therapy registration trial of Kymriah (tisagenlecleucel) in children and young adult patients with relapsed or refractory (r/r) acute lymphoblastic leukemia (ALL), shows an 82% remission rate within three months after a single infusion, and 62% relapse-free survival at 24 months, as presented by Stephan Grupp, MD, Ph.D., Director of the Cancer Immunotherapy Program and Section Chief of Cell Therapy and Transplant at CHOP, and a Professor of Pediatrics in the Perelman School of Medicine at the University of Pennsylvania.

The safety profiles observed for Kymriah, pioneered together with Novartis and the Perelman School of Medicine at the University of

Pennsylvania, remained consistent with previously reported results, with no emergence of new safety concerns.

"Before this personalized, cellular gene therapy, the patients we are treating with CAR T-cells had about a ten percent chance of surviving," said Dr. Grupp. "To see this 82 percent remission rate in our patients is beyond what I ever imagined when we treated our first patient in 2012. Hundreds of patients later, we're able to say those children who safely achieve durable remissions have a good chance of long-term disease control, and our hope is this is the last treatment they ever need."

Chimeric antigen receptor T (CAR-T) cell therapy genetically modifies a patient's immune cells to make them seek out and kill leukemia cells. The approach was developed by a team led by Carl June, MD, a professor of Pathology and Laboratory Medicine in the Perelman School of Medicine at the University of Pennsylvania and director of the Center for Cellular Immunotherapies in Penn's Abramson Cancer Center. In 2012, Penn and Novartis entered into a global collaboration to further research, develop and commercialize Kymriah. CHOP was the first institution to use the therapy in children with leukemia.

In other data presented at ASH, CHOP researchers found for some patients who do not achieve durable responses to CAR T-cell therapy due to T-cell exhaustion or cell death, which may be generated by the body's naturally occurring brake on the immune system, adding an inhibitor against the immune checkpoint PD-1 (programmed cell death 1) to CAR T-cell therapy could extend treatment response and improve outcomes for children with r/r ALL.

CHOP's small, single-center study evaluated 14 children ranging in age from 4 to 17 years, all of whom had received CD19-directed CAR T-cell therapy, and were given pembrolizumab or nivolumab. With the addition of the PD-1 blockade, 50 percent of patients maintained either partial or

complete disease responses, according to study lead Shannon Maude, MD, Ph.D., an oncologist and scientist in CHOP's Cancer Immunotherapy Program.

"When we give a checkpoint inhibitor, it seems to release the body's immune brakes on the

T-cell, allowing the T-cell to focus on its job of attacking cancer," Dr. Maude said. "This combination therapy could overcome that resistance in some CAR T-cell patients. Understanding these are children who would otherwise have no other therapeutic options, maximizing the response of the therapy, and overcoming resistance, are critical."

"Our unrivaled immunotherapy program treated the first patient, and now more patients than any other pediatric institution in the world, with this innovative therapy," said Stephen Hunger, MD, Chief of the Division of Oncology and Director of the Center for Childhood Cancer Research at CHOP. "Now, equally exciting, our clinical and research teams continue to move the dial, looking for ways to improve upon CAR T-cell therapy so even more young cancer patients benefit from it. Our institution remains unsurpassed in its efforts to introduce and perfect new gene therapies."

Dr. Grupp, Dr. Maude and their team will continue following these patients and exploring combination strategies to improve outcomes after CAR T-cell therapy, as more clinical research trials are underway at CHOP to further improve CAR T-cell therapy and apply it for use in more pediatric cancers.

Provided by Children's Hospital of Philadelphia

Citation: Immunotherapy pioneers reveal updated efficacy data of tisagenlecleucel CAR T-cell