CAR-T Therapy: A Novel Treatment for Patients with Relapsed Lymphoma or Leukemia

By: Aran Tavakoli, MSN, RN, CNS

Patients with relapsed or refractory-to-treatment Leukemia or Lymphoma face dire mortality rates and rarely achieve disease free outcomes. The majority of adults with acute lymphoblastic leukemia (ALL) will relapse at some point and up to 25% have resistance to treatment and will die of their disease (Up to Date, ALL 2017). Less than 10% of patients with relapsed diffuse large B cell lymphoma (DLBCL) will experience prolonged disease-free survival with second-line treatments. Though, over time, advancements have been made in the treatment of this disease, the majority of patients are not cured (Up to Date, Lymphoma 2017).

A new therapy called Chimeric Antigen Receptor T-Cells (CAR T) could improve the survival of patients with these diseases as well as other hematologic malignancies (e.g.: multiple myeloma). CAR-T belongs to a group of therapies called Immunotherapy that uses the help of a patient's own immune system to destroy cancer cells. The responses so far to this therapy, used after all other treatments have stopped working, have been remarkable for both adults and children. (NCI, 2017).

Initial CAR-T outcomes are promising. It has been reported in the literature that there is 40-50% complete response (CR). In the study that was open here at UCSD, phase 2 ZUMA-1 for patients that have DLBCL , the primary analysis of 101 patients showed an overall response rate of 82%, including a complete response (no evidence of disease) of 54% at greater than 6 months of follow-up (Locke FL, Neelapu SS, Bartlett NL, et al, 2017). In adult and pediatric heavily pretreated relapsed refractory ALL, high remission rates of 67-93% have been reported (Frey, 2017). These are outcomes that have not been seen for these diseases, ever.

CAR-T uses advanced cell transfer, where the patient's own immune system cells are collected via apheresis and shipped to a drug company. The drug company then isolates the T-Cells and exposes them to a virus that has been reprogramed with different content that is no longer infectious. The viral vector delivers a message to the T-cells to attack leukemia and lymphoma cells. These reprogramed T-cells are grown in culture, frozen and shipped back to UCSD (Frey, 2017).

After receiving conditioning chemotherapy, the patient's cells are defrosted at the bedside and infused through a central line. This is all very anti-climactic. What is climactic, are the acute side effects patients can get from this treatment. Patients can have severe cytokine release syndrome and neurotoxicity that require care in the Intensive Care Unit (ICU) including vasopressors and mechanical ventilation.

Cytokine release syndrome can include the following symptoms: Elevated temperatures, chills and rigors, tachycardia, hypotension, hypoxia, generalized body edema from capillary leak syndrome, headache, rash, nausea, weakness and increased C-reactive protein (Brudno Kochendefer, 2016). The patient's temperatures can also rise to greater than 103.0o F. If the patient requires vasopressors to maintain perfusion, or assistance with ventilation they are transferred to the Intensive Care Unit.

Aran Tavakoli, MSN, RN, AOCNS
is an Oncology Clinical Nurse Specialist. She has worked at UCSD Health since 2010. She earned her Bachelor's in Nursing from Loma Linda University and her Master's in Oncology Nursing from UCLA. She has been actively involved in the Oncology Nursing Society, holding local and national leadership positions and contributing to national think tanks on leadership. Aran is published and has given presentations at local and national conferences. Her current interests include care of the patient receiving immune effector cells, oncology nursing education and improving quality nursing care.

Neuro-toxicities can present as mild to life threatening. Mild toxicities can include somnolence, confusion, encephalopathy that can progress from mild, where it is not limiting activities of daily living, to severe disorientation, obtundation or stupor, combative delirium, seizures, and/or fatal brain swelling. Neuro-toxicities may mimic signs and symptoms of a stroke including dysphagia and acute change in level of consciousness. (Brudno Kochendefer, 2016). All patients have a neurology consult and examination so that a baseline is established, before needing neurology's services for an acute change.

Because of the severity of the side effects and unique patient management, a close relationship between the BMT unit and the ICU has developed. Prior to admission, the ICU is notified of these patients and the patient management guide is sent to nursing and the intensivist. RRT nurses proactively round on the patient while they are on the BMT unit. Then, when a patient is transferred to the ICU, BMT nursing staff does reverse proactive rounds. The BMT resource nurse will check on the ICU nurse each shift, see the patient, and answer questions about oncology-specific care or treatments.

When patients have life threating complications it is critical that the medical teams are communicating with each other. Patients may need to be started on high doses of methylprednisolone, but only at the correct stage of toxicity. Because patients can progress quickly to system failure, the BMT team needs to be continuously updated on the patient's condition if it worsens to provide treatment recommendations.

Though these agents have been used at UCSD on clinical trials, recently 2 drug companies have received approval for their product through the Federal Drug Administration (FDA). The first CAR-T therapy approved by the FDA on August 30, 2017 was Kymriah (tisagenlecleucel) that is indicated for certain pediatric and young adult patients (up to age 25) with a specific form of acute lymphoblastic leukemia (ALL). On October 18, 2017, Yescarta (axicabtagene ciloleucel) by Kite Pharma Inc., the CAR-T therapy being trialed at UCSD, was approved to treat adult patients with certain types of large B-cell lymphoma who have not responded to or who have relapsed after at least two other courses of treatment.

BMT Team

In summary, CAR-T therapy has significant life threatening side-effects, but once these side effects resolve, patients recover and have a higher chance at long term disease-free survival than in the past. These new immunotherapy treatments are improving the odds and the longevity of responses to these treatments will continue to be monitored as more patients are treated.

REFERENCES:

Brudno, J.N., & Kochenderfer, J.N (2016). Toxicities of chimeric antigen receptor T cells: Recognition and management. Blood, 127, 3321-3330. Doi:10.1182/blood-2016-04-703751

Freesman, A.S., & Friedberg, J.W. Treatment of relapsed or refractory diffuse large B cell lymphoma. Negrin, R.S. ed. UpToDate. Waltham, MA: UpToDate Inc. http://www.uptodate.com (Accessed on October 20, 2017.)

Frey, N. (2017). The what, when and how of CAR T cell therapy for ALL. Best Practice & Research Clinical Hematology, 30: 275-281.

Larson, R.A. Treatment of relapsed or refractory actue lymphoblastic leukemia in adults. Lowenberg, B. ed. UpToDate. Waltham, MA: UpToDate Inc. http://www.uptodate.com (Accessed on October, 20, 2017.)

Locke FL, Neelapu SS, Bartlett NL, et al. Primary results from ZUMA-1: a pivotal trial of axicabtagene ciloleucel (Axi-cel; KTE-C19) in patients with refractory aggressive non-Hodgkin lymphoma (NHL) Proceedings of the 107th Annual Meeting American Association Cancer Research; Washington (DC): AACR; 2017. p. CT019.

National Cancer Institute (NCI). CAR T Cells: Engineering Patients' Immune Cells to Treat Their Cancers. https://www.cancer.gov/about-cancer/treatment/research/car-t-cells Accessed on October, 20, 2017