

CAR T-Cell Therapy

Pediatric patients with relapsed and refractory acute lymphoblastic leukemia

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BACKGROUND: Immunotherapy provides a promising treatment option for children and adolescents with refractory or relapsed acute lymphoblastic leukemia (ALL).

OBJECTIVES: This article presents a hospital's experience with providing chimeric antigen receptor (CAR) T-cell therapy, followed by a detailed discussion of the trajectory of treatment provided for pediatric patients and their families.

METHODS: Clinical experience in delivering care to pediatric patients undergoing CAR T-cell therapy is described. Care coordination, patient and family assessment and education, and post-CAR T-cell infusion monitoring are presented.

FINDINGS: Of 59 patients having been treated with CAR T-cell therapy at the authors' institution, 93% had a complete response at day 28. The 12-month relapse-free survival rate is 55%. A multidisciplinary team of skilled clinicians is recommended to support patient and family needs throughout screening, treatment, and follow-up while coordinating care with the referring oncologist.

KEYWORDS

immunotherapy; CART-cell therapy; CART-19; acute lymphoblastic leukemia

DIGITAL OBJECT IDENTIFIER

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PEDIATRIC ACUTE LYMPHOBLASTIC LEUKEMIA (ALL) is the most common childhood cancer. About 6,000 new cases of ALL are diagnosed in the United States each year, with half of those cases involving children and adolescents (Hunger & Mullighan, 2015). Significant improvements in pediatric ALL survival rates, from less than 10% in the 1960s to as high as 90% today, have occurred because of ongoing clinical and bench scientific research. Factors contributing to improved survival include improvement in the efficacy of multi-agent chemotherapy; development of risk-stratified treatment intensity; and the addition of craniospinal radiation, cranial radiation, and intrathecal chemotherapy (Hunger & Mullighan, 2015).

About 15% of patients with pediatric ALL relapse, and cure rates are much lower after relapse. For patients who relapse after completion of therapy, the cure rate is 50%. For those who relapse while still undergoing therapy, the chance of obtaining a second remission is 50%–70%, and the cure rate is only 20%–30% (Hunger & Mullighan, 2015).

Survival rates based on risk stratification have shown that it is necessary to identify high-risk patients sooner and administer therapy based on risk. With risk-adapted therapy, the goal is to give patients the best chance of cure while minimizing unnecessary toxicity (Shalabi, Angiolillo, & Fry, 2015). Better understanding of the biology of pediatric ALL has aided the development of risk-stratified treatment regimens to administer the appropriate therapy (Tasian & Gardner, 2015). The toxicity of conventional therapy has limited the potential for dose escalations in relapsed and refractory ALL therapy. Poor salvage rates following relapse suggest that this may be because of ALL being refractory to conventional chemotherapy (Maude, Shpall, & Grupp, 2014). The decreased chance of cure because of chemotherapy resistance and poor treatment tolerance indicates the need for novel targeted therapies.

Continued research in genomics, ALL biology, and immunology has affected the discovery of more effective and less toxic targeted therapy for pediatric cancer (Lee, Barrett, Mackall, Orentas, & Grupp, 2012). This research in targeted therapies and immunologic therapies has led to phase 1 and phase 2 trials using targeted immunotherapies. The current article discusses one pediatric tertiary care hospital's experience with providing chimeric antigen receptor (CAR) T-cell therapy to patients with relapsed or refractory ALL. An