Editorial Commentary

Three-year update outcomes of the first chimeric antigen receptor-T therapy for children and young adults with relapsed/refractory acute lymphoblastic leukemia

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Keywords: Tisagenlecleucel; chimeric antigen receptor-T cell therapy (CAR-T cell therapy); relapsed/refractory B-cell acute lymphoblastic leukemia (R/R B-ALL)

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Acute lymphoblastic leukemia (ALL) is the most common childhood cancer, accounting for over 70% of acute leukemia cases. Treatment outcomes for pediatric ALL have improved dramatically over the past 40 years, with an event-free survival rate of approximately 70–85% and an overall survival (OS) rate of approximately 90% (1). This was largely due to the optimization of classical drug combinations developed from more than 30 years ago. Recurrence of disease is observed in approximately 20% of pediatric ALL patients, and the long-term OS of relapsed ALL is approximately 30–40% (2).

With the advent of anti-CD3/CD19 antibodies, blinatumomab (3) and inotuzumab ozogamicin which combines an anti-CD22 antibody with the anticancer drug calicheamicin (4) are effective against B-cell ALL (B-ALL), further improvements in treatment outcomes for relapsed and refractory cases are expected. In 2013, chimeric antigen receptor (CAR)-T cell therapy targeting CD19 (tisagenlecleucel) was introduced for cases in which there has been little hope of cure, including a case with recurrence after hematopoietic cell transplantation (HCT) (5). Tisagenlecleucel was tested for children and young adults with relapsed/refractory (R/R) B-ALL in the ELIANA (ClinicalTrials.gov identifier: NCT02435849) as an international phase II trial (6). In its initial analysis, tisagenlecleucel demonstrated an 81% remission rate and a 59% relapse-free rate at 12 months in children and young adults with R/R B-ALL (7). This report had a median follow-up period of 13.1 months. Here, they demonstrate favorable long-term safety in 79 children and young adults with a median follow-up of 38.8 months. This suggests that it is one of the options for consolidation treatment for patients with ALL (8). Evaluating treatments for leukemia, there is no doubt that results obtained 3 years or more after treatment are more reliable than results 1 year after treatment. Although this paper is an updated version of the previous one, it is more valuable than the previous one. Immediately, Tong and Mertens have responded to this paper and requested further updates, including statistical improvements (9). Compared with childhood cancer survivors without HCT, HCT survivors have a substantially increased burden of serious chronic conditions and impairments (10). CAR-T therapy is highly expected as a consolidation treatment with fewer late complications

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than in HCT. The role of HCT for R/R B-ALL is shifting to the treatment of patients who are unable to receive CAR-T therapy or who have relapsed after CAR-T therapy. Currently, there is growing interest in what treatments, such as blinatumomab and inotuzumab ozogamicin, can be used to bridge to CAR-T therapy or HCT after recurrence, and the development of more effective and safer treatment schedules will likely be considered in the near future.

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