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Letter to the Editor

CAR-T Cells: An Innovative Therapeutic Strategy Against Pediatric Acute Lymphoblastic Leukemia

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Dear editor

Acute lymphoblastic leukemia (ALL) is a prevalent and highly progressive cancer in children and adolescents associated with an excessive production of immature lymphocytes in the bone marrow, which causes a negative effect on the production of other blood components, such as red blood cells, platelets, and other white blood cells (1-3).

The survival rate of ALL was only 10% in children in the 1960s, but reached 90% by 2015; however, the survival rate remains 80–90% among very young children (2, 4-6).

Chemotherapy is the primary treatment for ALL, along with auxiliary therapies to ameliorate its severe side effects; however, hematopoietic stem cell transplantation and immunotherapy are two emerging and promising approaches for the treatment of ALL (6-9).

Immunotherapy for pediatric ALL involves the use of genetically modified T cells, called chimeric antigen receptor (CAR)-T cells, which are autologous or allogeneic immune T cells that have been produced to identify and eliminate cancer cells more specifically by targeting one or several cancer-related proteins, notably, CD19 and CD22, or both (Figure 1) (6, 10).

According to the data presented by clinicaltrials.gov, until 2018, twelve clinical studies have been performed on pediatric leukemia, especially ALL, involving the use of CAR-T cells on ~394 patients. However, these were all early-stage trials (Phase I or Phase I/II) (6).

Of these twelve studies, ten involved CD19-targeted CAR-T cells, while four involved CD22-targeted CAR-T cells (6).

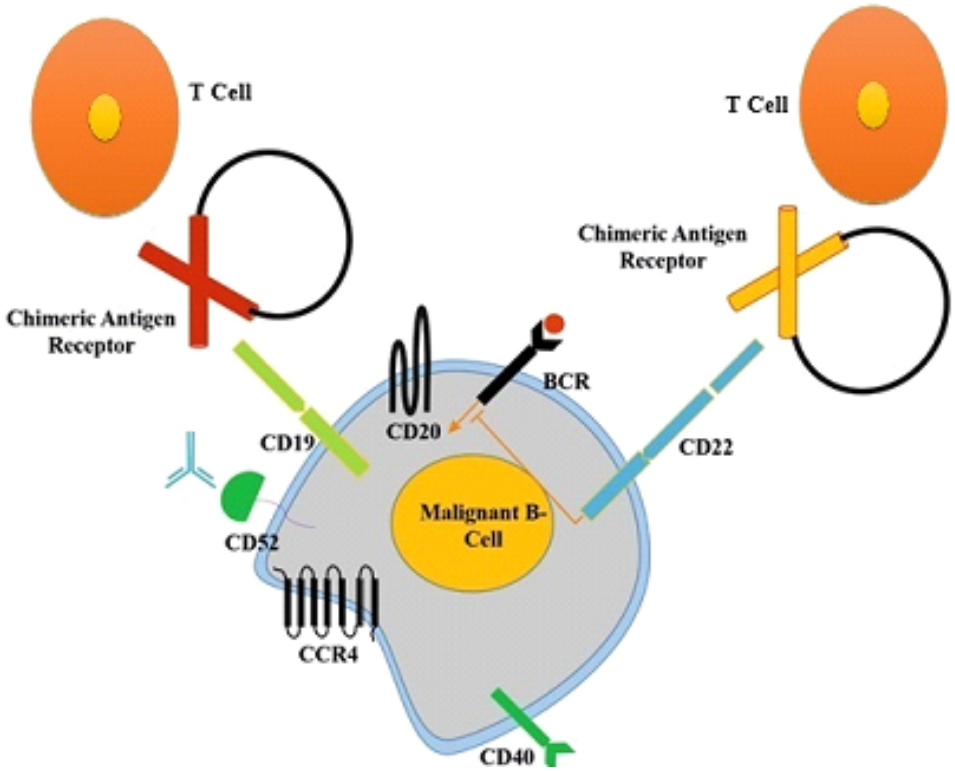

Figure 1: CAR-T Cells in the treatment of B-cell malignancies. BCR indicates B-cell receptor; CAR, chimeric antigen receptor; CCR4, CC chemokine receptor 4. CAR-modified T cells targeting the transmembrane proteins CD19 and CD22 on a malignant B cell. T-cell activation leads to the apoptosis of the cancer cell (22).

Furthermore, in a Phase I clinical trial, it was demonstrated that a bicistronic CAR-T cell therapy called AUTO3 served as a promising therapy for pediatric patients with relapsed/refractory (R/R) B-cell ALL, by simultaneously targeting CD19 and CD22 (11). Similarly, a Phase I clinical trial study has indicated the efficiency and safety of bispecific CAR-T cells, which simultaneously target CD19 and CD22, in pediatric ALL patients (12).

These data, along with those from previous studies, demonstrate the potential of CAR T-cells for treating leukemia, especially ALL (6, 13, 14).

In addition, tisagenlecleucel (Kymriah^{TM}), an autologous CD19-targeted CAR-T cell immunotherapy, has been recently introduced as a Food and Drug Administration- and European Union-approved cell-based therapy for use in pediatric patients with relapsed/refractory (R/R) B-cell precursor ALL (15-18).

According to previous studies, 83% of patients have demonstrated a partial or complete response to treatment following a single injection of tisagenlecleucel over a short period (19). Besides the high response rate to treatment, the time period after primary treatment without certain complications or adverse events in pediatric ALL patients was longer, and their overall survival was higher following tisagenlecleucel-based treatments than other cancer treatments (20).

However, the long-term efficiency and safety of this approach remains unclear and challenging (21). Additionally, thus far, cytokine release syndrome, neurological toxicity, and other toxicities have been recognized as the most commonly known complications of this method (22). Furthermore, cardiovascular and neurodegenerative disorders can be attributed to the toxic effects of CAR-T cells (23).

Hence, this modern treatment should be employed along with specialized medical care by medical groups with diverse expertise and the required facilities to certify optimal patient consequences (23).

Additionally, the cost of this treatment is very high, at ~€282,000 per patient (24).

Thus, CAR T-cells could aid the treatment of ALL patients and reverse the process of disease by identifying and killing cancer cells (6).

Clinical studies have demonstrated the potential of CAR-T cells to serve as a successful treatment strategy for pediatric ALL when chemotherapy has failed.

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Conflicts of Interest

The authors declare no conflicts of interest.

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