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Correspondence

CAR T-cell therapy in pediatric oncology: From leukemia to emerging promise in Wilms tumor and solid malignancies

Dear Editor,

CAR T cell therapy represents an advanced immunotherapeutic modality in pediatric oncology, involving genetic modification of a patient's own T cells to recognize and destroy cancer cells, offering highly targeted and personalized treatment. Originating from immunotherapy research in the 1980s, first-generation CARs were developed in 1989–1993, followed by second-generation CARs in the early 2000s with enhanced efficacy. FDA approval led to its first pediatric use in 2013, achieving complete remission in a child with acute lymphoblastic leukemia (ALL) [1–3]. Now approved for ALL and certain lymphomas, it provides hope for children with other cancers.

Leukemia is a blood cancer that begins in the bone marrow, characterized by abnormal proliferation of blood cells, occurring in both children and adults, and can be controlled with early diagnosis and treatment. Recurrence of leukemia after chemotherapy remains challenging. CAR T-cell therapy, a breakthrough in hematologic cancers, enables engineered T cells to recognize and directly attack tumor antigens without MHC dependence, offering promising salvage treatment options [4]. A meta-analysis evaluated long-term outcomes and adverse effects of CAR T-cell therapy in relapsed/refractory B-cell acute lymphoblastic leukemia (r/r B-ALL) using 10 clinical trials. Anti-CD19 CAR T-cell therapy achieved the highest minimal residual disease-negative complete remission (74.75 %), followed by anti-CD22 and CD19/CD22 combinations. The pooled remission rate was 70 %. Major adverse effects included cytokine release syndrome (81.8 %), hematologic toxicities (71.9 %), and neurotoxicity (33.2 %) [4].

Wilms tumor (nephroblastoma) is the most common pediatric kidney cancer, comprising over 90 % of childhood renal malignancies. Standard treatment—surgery, chemotherapy, and radiotherapy—achieves ~90 % 5-year survival in localized disease, but outcomes remain poor in high-risk or relapsed cases. CAR T-cell therapy offers a novel strategy, engineering patient T cells to target tumor-specific antigens. For Wilms tumor, promising targets include Wilms Tumor 1 (WT1), Glypican-3 (GPC3), and B7–H3 (CD276), all highly expressed in tumor tissue with limited presence in normal cells. Preclinical studies show these CAR T-cells can induce potent tumor cell killing. Challenges include antigen heterogeneity, the immunosuppressive tumor microenvironment, and limited CAR T-cell persistence. Strategies under investigation involve multi-antigen targeting, microenvironment modulation, and genetic enhancements (e.g., cytokine signaling domains) to improve durability. Several clinical trials are evaluating WT1-, GPC3-, and B7–H3-directed CAR T-cell therapies in pediatric solid tumors, including Wilms tumor. While still early in development, this approach holds promise for improving survival in high-risk and recurrent disease, potentially reducing the need for more toxic conventional therapies [5,6].

CAR T-cell therapy, while highly successful in hematologic cancers, faces significant challenges in pediatric solid tumors such as rhabdomyosarcoma, osteosarcoma, Ewing sarcoma, medulloblastoma, and gliomas. These challenges include tumor heterogeneity, a suppressive microenvironment, and difficulty identifying safe, consistently expressed antigens. Promising targets under investigation include B7–H3, GD2, and HER2, each evaluated in ongoing clinical trials for tumors like osteosarcoma and rhabdomyosarcoma [7–9].

CAR T-cell therapy has revolutionized treatment for pediatric hematologic malignancies and shows emerging potential in Wilms tumor through novel antigen targets like WT1, GPC3, and B7–H3. While significant challenges remain in solid tumors, ongoing innovations and clinical trials may expand its curative potential for high-risk and relapsed pediatric cancers.

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Declaration of competing interest

None.

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