

## Review Article

Open Access, Volume 4

# CAR T cell therapy of AML and ALL: A mini review

**Omid Moeini\***; Armit Hosseini; Amirali Rahmani; Mohammadmatin Nourikhani

Department of Laboratory Medicine, Faculty of Paramedical Sciences, Tehran Medical Sciences, Islamic Azad University, Tehran, Iran.

### \*Corresponding Author: Omid Moeini

Department of Laboratory Medicine, Faculty of  
Paramedical Sciences, Tehran Medical Sciences,  
Islamic Azad University, Tehran, Iran.  
Email: mr.omidmoeini@gmail.com

### Abstract

CAR T cell therapy is a promising immunotherapy that can target and eradicate leukemia cells with high specificity. While CD19, CD20, and CD22 CAR T cells have shown impressive responses in ALL patients, AML-specific CAR T cells are still being investigated. However, CAR T cell therapy can lead to serious adverse effects. Further research is necessary to optimize the efficacy and safety of CAR T cell therapy in AML and ALL.

Received: Mar 20, 2023

Accepted: Apr 05, 2023

Published: Apr 12, 2023

Archived: www.jcimcr.org

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DOI: www.doi.org/10.52768/2766-7820/2367

### Introduction

Acute Myeloid Leukemia (AML) and Acute Lymphoblastic Leukemia (ALL) are aggressive hematologic malignancies that can be difficult to treat, and many patients do not respond well to conventional therapies. However, recent advances in immunotherapy have led to the development of Chimeric Antigen Receptor (CAR) T cell therapy, an innovative treatment approach that harnesses a patient's own immune system to target and destroy cancer cells. CAR T cells are genetically modified to express a customized receptor on their surface that can recognize specific cancer cells, leading to their eradication. In the context of AML and ALL, targeting antigens such as CD19, CD20, CD22, and CD33 has shown promise, with CD19 CAR T cells in particular demonstrating impressive efficacy in treating ALL. However, CAR T cell therapy is not without risk, as it can also lead to potentially fatal side effects such as Cytokine Release Syndrome (CRS). As such, it is vital to continue studying and refining CAR T cell therapy in AML and ALL to optimize its efficacy and minimize its risks for patients.

### CAR T cell therapies in AML

Acute Myeloid Leukemia (AML) is a hematologic malignancy that can be difficult to treat with traditional therapies. Chimeric Antigen Receptor (CAR) T cell therapy is an emerging treatment that harnesses a patient's own immune system to eradicate cancer cells [1,2]. CAR T cells are genetically modified T cells that express a receptor targeting a specific cancer antigen. In AML, CAR T cells targeting the CD19, CD33, FLT3, and BAALC antigens have shown potential for treating this disease [3]. While promising, this approach is not without risks. CAR T cell therapy can cause Cytokine Release Syndrome (CRS), a potentially life-threatening condition that can result in fever, low blood pressure, and organ dysfunction [4]. Additionally, CAR T cell therapy may not work for all AML patients, highlighting the need for further research to improve CAR T cell therapy efficacy and understand which patients are most likely to benefit [5].

Recent research has demonstrated that combining CAR T cell therapy with other treatments may enhance its therapeutic potential for AML [6]. For example, preclinical studies have suggested that CAR T cells in combination with chemotherapy

agents such as fludarabine, cyclophosphamide, or dasatinib may increase sensitivity of AML cells to CAR T cells, leading to improved treatment outcomes [7]. While these combination therapies show promise, they are still in the early stages of development and require further investigation to establish their safety and efficacy [7].

The development of CAR T cell therapy for AML presents a unique set of challenges. Unlike in ALL, AML cells often exhibit heterogeneous antigen expression, which can limit the effectiveness of CAR T cells [8]. Additionally, the immunosuppressive nature of the AML microenvironment can lead to decreased CAR T cell persistence and functional impairment. Therefore, it is important to develop strategies that can overcome these challenges while maintaining treatment safety [9]. Recently, researchers have proposed using allogeneic CAR T cells or dual-targeting CAR T cells to improve CAR T cell efficacy while increasing treatment safety [10]. While promising, these approaches are still in the preclinical phase and require further research to establish their feasibility and safety [11].

Acute Lymphoblastic Leukemia (ALL) is a hematologic malignancy that typically affects children and young adults [12]. While traditional therapies for ALL have improved outcomes over the years, a significant proportion of patients still relapse or do not respond to treatment. Chimeric Antigen Receptor (CAR) T cell therapy has emerged as a promising new treatment approach for ALL [13]. CAR T cells are engineered immune cells that express a receptor targeting the CD19 antigen present on ALL cells. Clinical trials testing CAR T cell therapy for ALL have shown high response rates, especially in patients with relapsed or refractory disease [14]. However, CAR T cell therapy can cause severe side effects like Cytokine Release Syndrome (CRS) and neurotoxicity, underscoring the need for careful patient monitoring and management [15].

While CAR T cell therapy targeting CD19 has shown impressive results in the treatment of ALL, some patients eventually relapse due to antigen loss or other mechanisms of resistance [16]. To address this, researchers are developing CAR T cells that target multiple antigens or antigen combinations simultaneously [12]. For example, dual-targeting CAR T cells targeting both CD19 and CD22 have shown promising results in early clinical trials, with high response rates in relapsed or refractory ALL patients. However, this approach can also increase the risk of toxicity and reduce treatment safety [16,17].

CAR T cell therapy is rapidly evolving, and researchers continue to explore new avenues for improving CAR T cell therapy for ALL [18]. One emerging approach is the use of allogeneic CAR T cells, which are derived from healthy donors instead of the patient's own T cells. Allogeneic CAR T cells can be engineered to express safety switches or other features that increase treatment safety and reduce the risk of toxicity [19]. For example, a recent study reported successful clinical outcomes with off-the-shelf, CD19-directed allogeneic CAR T cells for ALL, suggesting that this approach may have therapeutic value. However, further research is needed to confirm the safety and efficacy of allogeneic CAR T cells in the treatment of ALL [20].

## Conclusion

In conclusion, CAR T cell therapy has emerged as a promising

immunotherapeutic approach for the treatment of Acute Myeloid Leukemia (AML) and Acute Lymphoblastic Leukemia (ALL). While CAR T cells targeting CD19 have shown impressive efficacy in treating ALL, AML-specific CAR T cells targeting antigens such as CD33, FLT3, and BAALC are also being investigated. Combining CAR T cell therapy with chemotherapy agents or developing dual-targeting CAR T cells may further enhance its therapeutic potential. However, CAR T cell therapy can also cause severe side effects such as Cytokine Release Syndrome (CRS) and neurotoxicity. Therefore, it is vital to carefully monitor and manage patients undergoing CAR T cell therapy to maximize treatment success and minimize treatment risk. Future research in CAR T cell therapy for AML and ALL will continue to refine the therapy, identify which patients are most likely to benefit, and broaden the use of this innovative treatment approach to improve patient outcomes.

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