Car-t cell therapy: Transforming the treatment of hematologic malignancies.

Tim Greil*

Department of Dermatology and Venereology, Martin-Luther-University Halle-Wittenberg, Germany

Introduction

CAR-T cell therapy, or chimeric antigen receptor T cell therapy, has revolutionized the treatment landscape for hematologic malignancies, offering hope to patients with certain types of blood cancers that have been resistant to traditional treatments. This advanced immunotherapy involves genetically modifying a patient's T cells to express receptors that specifically target cancer cells, leading to targeted and potent anti-tumor responses. Since its introduction into clinical practice, CAR-T cell therapy has demonstrated impressive efficacy in treating refractory or relapsed leukemia, lymphoma, and multiple myeloma. This article explores the mechanism, clinical applications, challenges, and future directions of CAR-T cell therapy in the treatment of hematologic malignancies [1].

CAR-T cell therapy involves a multi-step process designed to harness the patient's immune system to target and eliminate cancer cells. The key steps include: T cells are collected from the patient's blood through a procedure known as leukapheresis. In the laboratory, T cells are genetically modified to express a chimeric antigen receptor (CAR) that specifically recognizes antigens present on cancer cells. For example, in treating B-cell malignancies, the CAR is often engineered to target CD19, a protein found on the surface of B cells [2].

The modified T cells are expanded to millions of cells and reinfused into the patient, where they seek out and destroy cancer cells expressing the target antigen. Once in the patient's body, the CAR-T cells recognize and bind to the target antigen on cancer cells, triggering their activation and proliferation. They release cytotoxic molecules, such as perforin and granzymes, leading to the destruction of the cancer cells [3].

CAR-T cell therapy has shown remarkable results in clinical trials and has been approved by regulatory agencies for the treatment of several hematologic malignancies: The success of CAR-T cell therapy in pediatric and young adult patients with relapsed or refractory B-cell ALL was one of the first major breakthroughs. Tisagenlecleucel (Kymriah) was the first CAR-T therapy approved by the FDA for this indication, demonstrating high remission rates in patients with limited treatment options [4].

Axicabtagene ciloleucel (Yescarta) and lisocabtagene maraleucel (Breyanzi) are CAR-T therapies approved for DLBCL, a form of non-Hodgkin lymphoma. These therapies have been particularly effective in patients who have relapsed after two or more lines of therapy, with complete response rates significantly higher than those seen with standard treatments [5].

CAR-T cell therapy targeting B-cell maturation antigen (BCMA), such as idecabtagene vicleucel (Abecma), has shown promising results in heavily pretreated patients with multiple myeloma. These therapies provide a new option for patients whose disease has progressed despite other therapies [6].

Despite the promising results, CAR-T cell therapy is not without challenges. These include: One of the most common side effects is CRS, a systemic inflammatory response caused by the rapid activation of CAR-T cells. Symptoms can range from mild flu-like symptoms to severe, life-threatening conditions such as high fever, hypotension, and multi-organ failure [7].

Neurotoxic effects, including confusion, seizures, and encephalopathy, can occur in some patients. This condition, known as immune effector cell-associated neurotoxicity syndrome (ICANS), can be challenging to manage [8].

CAR-T cell production is a complex process that requires individualized manufacturing for each patient. This results in high costs, making it challenging to provide access to this therapy for all eligible patients. Tumor cells can lose the expression of the targeted antigen, leading to "antigen escape" and disease relapse. This is a significant challenge in cases where the tumor evolves to avoid detection by the engineered T cells [9].

The field of CAR-T cell therapy is rapidly evolving, with ongoing research focused on overcoming current limitations and expanding its applications: Researchers are developing next-generation CARs with dual or multi-targeting capabilities to reduce the risk of antigen escape. These CARs can target multiple antigens simultaneously, improving the durability of responses. The development of off-the-shelf allogeneic CAR-T cells, derived from healthy donors, aims to overcome the challenges of manufacturing complexity and reduce costs. These therapies could make CAR-T cell treatment more accessible to a broader patient population. Combining CAR-T cell therapy with immune checkpoint inhibitors, chemotherapy, or targeted therapies is being explored to enhance its effectiveness and reduce relapse rates. These combinations may help modulate the tumor microenvironment and improve the persistence of CAR-T cells [10].

***Correspondence to:** Tim Greil, Department of Dermatology and Venereology, Martin-Luther-University Halle-Wittenberg, Germany. E-mail: tim.g@med.uni-tuebingen.de

***Received:** 27-Sep-2024, Manuscript No. AAJCIT-24-150271; **Editor assigned:** 28-Sep-2024, Pre QC No. AAJCIT-24-150271(PQ); **Reviewed:** 14-Oct-2024, QC No AAJCIT-24-150271; **Revised:** 19-Sep-2024, Manuscript No. AAJCIT-24-150271(R); **Published:** 28-Sep-2024, DOI:10.35841/aajcit-7.5.231*

***Citation:** Greil T., Car-t cell therapy: Transforming the treatment of hematologic malignancies. J Cancer Immunol Ther. 2024;7(5):231*

Conclusion

CAR-T cell therapy has transformed the treatment of hematologic malignancies, offering new hope to patients with few options. Its success in treating B-cell ALL, DLBCL, and multiple myeloma highlights its potential to provide long-lasting remission in patients with refractory or relapsed disease. However, challenges such as toxicity management, manufacturing complexity, and antigen escape need to be addressed for broader adoption. As research continues, innovations such as next-generation CARs and allogeneic CAR-T cells hold promise for expanding the reach and effectiveness of this ground breaking therapy. With continued advancements, CAR-T cell therapy is poised to remain a cornerstone of hematologic cancer treatment, offering a personalized approach to targeting and eradicating cancer.

References

1. Maude SL, Laetsch TW, Buechner J, Rives S, Boyer M, Bittencourt H, Bader P, Verneris MR, Stefanski HE, Myers GD, Qayed M. Tisagenlecleucel in children and young adults with B-cell lymphoblastic leukemia. N Eng J Med. 2018;378(5):439-48.
2. Grupp SA, Kalos M, Barrett D, Aplenc R, Porter DL, Rheingold SR, Teachey DT, Chew A, Hauck B, Wright JF, Milone MC. Chimeric antigen receptor–modified T cells for acute lymphoid leukemia. N Eng J Med. 2013;368(16):1509-18.
3. Neelapu SS, Locke FL, Bartlett NL, Lekakis LJ, Miklos DB, Jacobson CA, Braunschweig I, Oluwole OO, Siddiqi T, Lin Y, Timmerman JM. Axicabtagene ciloleucel CAR T-cell therapy in refractory large B-cell lymphoma. N Eng J Med. 2017;377(26):2531-44.
4. Abramson JS, Palomba ML, Gordon LI, Lunning MA, Wang M, Arnason J, Mehta A, Purev E, Maloney DG, Andreadis C, Sehgal A. Lisocabtagene maraleucel for patients with relapsed or refractory large B-cell lymphomas (TRANSCEND NHL 001): a multicentre seamless design study. Lancet. 2020;396(10254):839-52.
5. Munshi NC, Anderson Jr LD, Shah N, Madduri D, Berdeja J, Lonial S, Raje N, Lin Y, Siegel D, Oriol A, Moreau P. Idecabtagene vicleucel in relapsed and refractory multiple myeloma. N Eng J Med. 2021;384(8):705-16.
6. Park CH. Making potent CAR T cells using genetic engineering and synergistic agents. Cancers. 2021;13(13):3236.
7. Lee DW, Gardner R, Porter DL, Louis CU, Ahmed N, Jensen M, Grupp SA, Mackall CL. Current concepts in the diagnosis and management of cytokine release syndrome. Am J Hematol. 2014;124(2):188-95.
8. Neelapu SS, Tummala S, Kebriaei P, Wierda W, Gutierrez C, Locke FL, Komanduri KV, Lin Y, Jain N, Daver N, Westin J. Chimeric antigen receptor T-cell therapy—assessment and management of toxicities. Nat Rev Clin Oncol. 2018;15(1):47-62.
9. Gust J, Hay KA, Hanafi LA, Li D, Myerson D, Gonzalez-Cuyar LF, Yeung C, Liles WC, Wurfel M, Lopez JA, Chen J. Endothelial activation and blood–brain barrier disruption in neurotoxicity after adoptive immunotherapy with CD19 CAR-T cells. Cancer Discov. 2017;7(12):1404-19.
10. Majzner RG, Mackall CL. Tumor antigen escape from CAR T-cell therapy. Cancer Discov. 2018;8(10):1219-26.

Citation: *Greil T., Car-t cell therapy: Transforming the treatment of hematologic malignancies. J Cancer Immunol Ther. 2024;7(5):231*