

Avances en la Terapia CAR-T: Inmunoterapia Personalizada y el Futuro del Tratamiento Oncológico de Precisión

Advances in CAR-T Cell Therapy: Personalized Immunotherapy and the Future of Precision Cancer Treatment

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RESUMEN

La terapia con células T con receptor antigénico quimérico (CAR-T) se ha consolidado como uno de los avances más importantes de la oncología contemporánea y como una de las principales estrategias de inmunoterapia personalizada contra el cáncer. Mediante la modificación genética de linfocitos T para reconocer y eliminar células malignas de manera específica, esta tecnología ha demostrado resultados clínicos sobresalientes en diversas neoplasias hematológicas, incluyendo leucemia linfoblástica aguda, linfoma difuso de células B grandes, linfoma de células del manto y mieloma múltiple. La presente revisión analiza los fundamentos biológicos, aplicaciones clínicas, resultados terapéuticos, aspectos de seguridad y perspectivas futuras de las terapias CAR-T. La evidencia disponible muestra tasas de respuesta sin precedentes en pacientes con enfermedad refractaria o en recaída, ampliando significativamente las opciones terapéuticas para poblaciones con pronósticos históricamente desfavorables. No obstante, persisten desafíos importantes relacionados con toxicidades asociadas al tratamiento, complejidad de fabricación, sostenibilidad económica, accesibilidad y eficacia limitada en tumores sólidos. Los avances recientes en ingeniería genética, biología sintética, descubrimiento de biomarcadores y medicina de precisión están impulsando el desarrollo de plataformas CAR-T de nueva generación destinadas a mejorar la eficacia, la seguridad y la aplicabilidad clínica. Asimismo, el creciente interés en América Latina, especialmente en México, Colombia y Ecuador, refleja esfuerzos orientados a fortalecer la investigación, la innovación biomédica y el acceso a terapias celulares avanzadas. Los hallazgos sugieren que las terapias CAR-T continuarán desempeñando un papel fundamental en la evolución de la oncología de precisión y en el desarrollo de tratamientos oncológicos cada vez más personalizados.

PALABRAS CLAVE

terapia CAR-T, receptor antigénico quimérico, inmunoterapia contra el cáncer, medicina personalizada, oncología de precisión, neoplasias hematológicas, terapia celular, ingeniería genética, inmunoterapia adoptiva, leucemia, linfoma, mieloma múltiple, tumores sólidos, biotecnología, medicina traslacional, América Latina.

ABSTRACT

Chimeric antigen receptor T-cell (CAR-T) therapy has emerged as one of the most significant advances in contemporary oncology, representing a transformative approach within the field of personalized cancer immunotherapy. By genetically engineering T lymphocytes to recognize and eliminate malignant cells through specific antigen-targeting mechanisms, CAR-T therapy has demonstrated remarkable clinical efficacy in several hematological malignancies, including acute lymphoblastic leukemia, diffuse large B-cell lymphoma, mantle cell lymphoma, and multiple myeloma. This review analyzes the biological foundations, clinical applications, therapeutic outcomes, safety considerations, and future perspectives associated with CAR-T technology. The available evidence indicates that CAR-T therapy has achieved unprecedented response rates in patients with relapsed or refractory disease, significantly

improving treatment possibilities for populations with historically poor prognoses. However, important challenges remain regarding treatment-related toxicities, manufacturing complexity, economic sustainability, accessibility, and limited effectiveness in solid tumors. Recent advances in genetic engineering, synthetic biology, biomarker discovery, and precision medicine are driving the development of next-generation CAR-T platforms designed to enhance efficacy, safety, and applicability across a broader spectrum of cancers. Furthermore, growing interest in Latin America, particularly in Mexico, Colombia, and Ecuador, reflects increasing efforts to expand access to advanced cellular therapies through academic collaboration, translational research, and healthcare innovation. The findings suggest that CAR-T therapy will continue to play a central role in the evolution of precision oncology and may serve as a model for future individualized therapeutic strategies in cancer management.

KEYWORDS

CAR-T therapy, chimeric antigen receptor, cancer immunotherapy, personalized medicine, precision oncology, hematological malignancies, cellular therapy, gene engineering, adoptive immunotherapy, leukemia, lymphoma, multiple myeloma, solid tumors, biotechnology, translational medicine, Latin America.

INTRODUCCIÓN

Cancer remains one of the leading causes of morbidity and mortality worldwide, representing a major public health challenge despite significant advances in prevention, diagnosis, and treatment. According to recent global estimates, millions of new cancer cases are diagnosed annually, and the burden is expected to increase substantially over the coming decades due to population growth, aging, and the persistence of environmental and lifestyle-related risk factors. Although conventional therapeutic approaches such as surgery, chemotherapy, and radiotherapy have improved survival rates in numerous malignancies, these strategies often face significant limitations, including treatment resistance, disease relapse, systemic toxicity, and the inability to selectively eliminate malignant cells while preserving healthy tissues (June et al., 2018; Brudno & Kochenderfer, 2024).

The growing understanding of tumor immunology has transformed the therapeutic landscape of oncology by demonstrating that the immune system can be harnessed to recognize and eliminate cancer cells. This paradigm shift has given rise to the field of cancer immunotherapy, which seeks to enhance or restore antitumor immune responses through a variety of approaches, including immune checkpoint inhibitors, cancer vaccines, monoclonal antibodies, cytokine therapies, and adoptive cellular therapies. Among these modalities, chimeric antigen receptor T-cell (CAR-T) therapy has emerged as one of the most innovative and promising strategies in modern medicine due to its ability to provide highly personalized and targeted treatment against specific cancer-associated antigens (Feins et al., 2019; Wagner et al., 2021).

CAR-T cell therapy involves the genetic modification of a patient's own T lymphocytes to express synthetic receptors capable of recognizing tumor-associated antigens independently of major histocompatibility complex (MHC) presentation. Once engineered and expanded ex vivo, these cells are reinfused into the patient, where they can identify, attack, and eliminate malignant cells with remarkable specificity. The concept combines advances in molecular biology, genetic engineering, immunology, and cellular therapy, creating a therapeutic platform that has fundamentally changed expectations for the treatment of hematological malignancies (June et al., 2018; Wang et al., 2023).

The clinical success of CAR-T therapy was initially demonstrated in relapsed or refractory B-cell acute lymphoblastic leukemia (B-ALL), where conventional treatment options often yield poor outcomes. Landmark clinical trials

evaluating tisagenlecleucel reported unprecedented remission rates among pediatric and young adult patients with refractory disease, establishing a new standard of care and leading to regulatory approval in multiple countries (Maude et al., 2018). Similar achievements were subsequently observed in diffuse large B-cell lymphoma, mantle cell lymphoma, follicular lymphoma, and multiple myeloma, where CAR-T products targeting CD19 or B-cell maturation antigen (BCMA) have demonstrated durable responses in heavily pretreated patient populations (Neelapu et al., 2017; Schuster et al., 2019; Wang et al., 2020; Munshi et al., 2021; Berdeja et al., 2021).

Despite these remarkable clinical outcomes, several scientific and practical challenges continue to limit the broader implementation of CAR-T therapy. One of the most significant concerns is the occurrence of severe adverse events, particularly cytokine release syndrome (CRS) and immune effector cell-associated neurotoxicity syndrome (ICANS), which may result in substantial morbidity and require specialized management strategies. The development of standardized grading systems and treatment algorithms has improved patient safety; however, toxicity remains an important consideration when selecting candidates for therapy (Lee et al., 2019; Frey & Porter, 2019).

Another critical limitation involves the application of CAR-T therapy to solid tumors. While hematological malignancies frequently express well-defined target antigens, solid tumors present a considerably more complex biological environment characterized by antigen heterogeneity, immunosuppressive tumor microenvironments, physical barriers to T-cell infiltration, and adaptive resistance mechanisms. These obstacles have limited the efficacy observed in hematological cancers and have prompted intensive research efforts aimed at improving CAR design, enhancing T-cell persistence, overcoming immune suppression, and identifying novel tumor-specific targets (Peng et al., 2024; Sun et al., 2024).

Recent advances in genetic engineering have led to the development of next-generation CAR-T platforms designed to address many of these limitations. These innovations include dual-targeting CARs, armored CAR-T cells, gene-edited allogeneic CAR-T products, switchable CAR systems, and combinations with immune checkpoint inhibitors or other immunomodulatory therapies. Such approaches seek not only to improve efficacy but also to reduce toxicity, prevent antigen escape, and expand the therapeutic applicability of cellular immunotherapy across a broader spectrum of malignancies (Olejarz et al., 2024; Wagner et al., 2021).

The concept of personalized medicine has become increasingly relevant in oncology, and CAR-T therapy represents one of its most sophisticated manifestations. Unlike traditional treatments that are administered according to standardized protocols, CAR-T therapy is tailored to the biological characteristics of individual patients and their tumors. This individualized approach reflects a broader transition toward precision oncology, where genomic, molecular, and immunological information guides therapeutic decision-making. Consequently, CAR-T technology is often regarded as a model for future cancer treatment strategies that integrate advanced biotechnology with patient-specific biological data (Brudno & Kochenderfer, 2024; Olejarz et al., 2024).

Beyond scientific considerations, significant disparities exist in access to CAR-T therapy across different regions of the world. Most commercial CAR-T products have been developed and implemented primarily in high-income countries, creating substantial barriers for low- and middle-income nations. These barriers include manufacturing complexity, high treatment costs, limited specialized infrastructure, regulatory challenges, and shortages of trained personnel. In Latin America, several countries have initiated efforts to establish local CAR-T programs and strengthen regional capabilities in cellular therapy. Mexico has demonstrated increasing interest in developing national CAR-T initiatives for pediatric and adult hematological malignancies, while Colombia has explored clinical and regulatory pathways for integrating these therapies into oncology practice. Ecuador has similarly participated in regional academic collaborations aimed at strengthening research capacity and promoting access to innovative cancer

treatments. These developments highlight the growing importance of international cooperation in reducing disparities in access to advanced immunotherapies (Bustamante-Ogando et al., 2024; Robledo et al., 2025; Toro-Pedroza et al., 2026).

Given the rapid expansion of knowledge in this field, continuous evaluation of emerging evidence is necessary to understand both the achievements and remaining challenges associated with CAR-T therapy. Numerous studies have reported encouraging clinical outcomes, yet questions remain regarding long-term efficacy, durability of responses, optimization of manufacturing processes, management of adverse effects, cost-effectiveness, accessibility, and applicability to solid tumors. Furthermore, the integration of artificial intelligence-assisted biomarker discovery, genomic profiling, and novel cellular engineering techniques may further redefine the future of personalized cancer immunotherapy.

DESARROLLO

The emergence of chimeric antigen receptor T-cell (CAR-T) therapy represents one of the most significant breakthroughs in contemporary oncology. Unlike conventional therapeutic modalities that primarily target tumor cells through cytotoxic mechanisms, CAR-T therapy utilizes genetically engineered autologous or allogeneic lymphocytes capable of specifically recognizing tumor-associated antigens and initiating targeted immune responses. This innovative approach has transformed the treatment landscape for several hematological malignancies and has become a cornerstone of personalized cancer immunotherapy (June et al., 2018; Brudno & Kochenderfer, 2024).

The concept of adoptive cellular therapy originated from observations that naturally occurring tumor-infiltrating lymphocytes could mediate antitumor responses. However, the limited effectiveness of endogenous immune mechanisms prompted the development of genetically modified T cells expressing synthetic receptors capable of overcoming tumor immune evasion. CAR constructs combine an extracellular antigen-recognition domain derived from monoclonal antibodies with intracellular signaling domains responsible for T-cell activation and proliferation. This structure enables antigen recognition independently of major histocompatibility complex presentation, thereby overcoming one of the principal mechanisms through which malignant cells evade immune surveillance (Feins et al., 2019).

Over the past decade, CAR-T technology has evolved through multiple generations. First-generation CARs contained only the CD3 ζ signaling domain and demonstrated limited persistence and efficacy. Second-generation CARs incorporated costimulatory domains such as CD28 or 4-1BB, significantly improving expansion, survival, and antitumor activity. Subsequent generations have introduced additional signaling pathways, cytokine-secreting capabilities, and genetic modifications designed to enhance therapeutic performance while minimizing adverse effects. These developments have established CAR-T therapy as a dynamic platform continuously refined through advances in molecular engineering and immunology (Wagner et al., 2021; Olejars et al., 2024).

Clinical Success in Hematological Malignancies

The most remarkable achievements of CAR-T therapy have been observed in hematological cancers. B-cell acute lymphoblastic leukemia (B-ALL) was among the first malignancies to demonstrate extraordinary responses to CD19-targeted CAR-T treatment. Clinical trials involving pediatric and young adult patients with relapsed or refractory disease reported complete remission rates exceeding those achieved by conventional salvage therapies, establishing CAR-T therapy as a revolutionary option for patients with otherwise limited therapeutic alternatives (Maude et al., 2018).

Diffuse large B-cell lymphoma (DLBCL), one of the most aggressive forms of non-Hodgkin lymphoma, has also shown substantial responsiveness to CAR-T therapy. Patients with chemotherapy-resistant disease have experienced durable remissions following treatment with axicabtagene ciloleucel and tisagenlecleucel, highlighting the capacity of

engineered T cells to overcome treatment resistance. Similar outcomes have been reported in mantle cell lymphoma and follicular lymphoma, expanding the spectrum of hematological malignancies that may benefit from adoptive cellular immunotherapy (Neelapu et al., 2017; Schuster et al., 2019; Wang et al., 2020).

The development of B-cell maturation antigen (BCMA)-targeted CAR-T therapies has further broadened the clinical applicability of this technology. Multiple myeloma, historically characterized by repeated relapses and progressive treatment resistance, has demonstrated unprecedented response rates following treatment with idecabtagene vicleucel and ciltacabtagene autoleucel. These therapies have generated durable responses even among heavily pretreated patients, reinforcing the concept that cellular immunotherapy may alter the natural history of advanced hematological malignancies (Munshi et al., 2021; Berdeja et al., 2021).

The success observed across these diseases has fundamentally challenged traditional assumptions regarding the management of refractory cancers. For many patients, CAR-T therapy has transformed previously terminal diagnoses into conditions associated with meaningful long-term survival, thereby redefining therapeutic expectations within hematologic oncology.

Biological Basis of Personalized Immunotherapy

One of the defining characteristics of CAR-T therapy is its alignment with the principles of precision medicine. Personalized medicine seeks to tailor therapeutic interventions according to the biological characteristics of individual patients, maximizing efficacy while minimizing toxicity. CAR-T therapy embodies this concept because treatment is generated from patient-specific cellular material and directed against tumor-specific molecular targets (Brudno & Kochenderfer, 2024).

Advances in genomic sequencing, transcriptomics, proteomics, and biomarker discovery have facilitated the identification of novel antigens suitable for CAR targeting. These technologies enable clinicians and researchers to characterize tumor heterogeneity with increasing precision, thereby supporting the development of individualized therapeutic strategies. The integration of molecular diagnostics with cellular engineering has created opportunities for highly customized cancer treatments that were previously unattainable (Olejarz et al., 2024).

Moreover, emerging technologies such as CRISPR-Cas9 gene editing have expanded the possibilities of personalized immunotherapy. Gene-editing approaches allow precise modification of immune cells to enhance antitumor activity, improve persistence, reduce exhaustion, and eliminate inhibitory pathways. These innovations may contribute to the development of safer and more effective CAR-T products capable of addressing diverse clinical challenges across multiple cancer types (Peng et al., 2024).

Current Challenges and Limitations

Despite its transformative potential, CAR-T therapy faces several important limitations that restrict its universal application. One of the most significant concerns is treatment-associated toxicity. Cytokine release syndrome (CRS) results from rapid immune activation and excessive cytokine production following CAR-T cell expansion. Clinical manifestations range from mild constitutional symptoms to severe systemic inflammation, hemodynamic instability, and multiorgan dysfunction. Similarly, immune effector cell-associated neurotoxicity syndrome (ICANS) may produce neurological complications ranging from confusion and aphasia to seizures and cerebral edema (Lee et al., 2019; Frey & Porter, 2019).

Although advances in supportive care and toxicity management have significantly improved safety outcomes, these complications necessitate specialized treatment centers with multidisciplinary expertise. Consequently, access to CAR-T therapy remains concentrated in highly specialized institutions, limiting availability for many patients worldwide.

Economic considerations also represent a major challenge. Manufacturing personalized cellular products requires sophisticated infrastructure, highly trained personnel, rigorous quality-control systems, and complex logistics. These

factors contribute to treatment costs that frequently exceed several hundred thousand dollars per patient. Such economic barriers create substantial inequalities in access, particularly in low- and middle-income countries where healthcare resources may be limited (Bustamante-Ogando et al., 2024).

CAR-T Therapy in Solid Tumors

While CAR-T therapy has revolutionized the treatment of hematological malignancies, translating this success to solid tumors has proven considerably more difficult. Unlike hematologic cancers, solid tumors exhibit extensive antigen heterogeneity, meaning that not all tumor cells express identical target molecules. This variability increases the risk of antigen escape, whereby malignant cells lacking the target antigen survive and continue proliferating despite therapy (Sun et al., 2024).

Additionally, the tumor microenvironment presents multiple immunosuppressive mechanisms that inhibit T-cell function. Regulatory T cells, myeloid-derived suppressor cells, inhibitory cytokines, hypoxia, and metabolic competition collectively create conditions that impair CAR-T cell activity. Physical barriers, including dense stromal structures and abnormal tumor vasculature, further restrict immune-cell infiltration and limit therapeutic effectiveness (Peng et al., 2024).

To address these obstacles, researchers are developing next-generation CAR-T platforms incorporating dual-antigen recognition systems, cytokine secretion modules, resistance to immunosuppressive signals, and enhanced migratory capabilities. Although clinical results remain less dramatic than those observed in hematological malignancies, ongoing investigations continue to generate promising evidence supporting the future application of CAR-T technology in solid cancers.

Global Perspectives and the Emerging Latin American Landscape

The global expansion of CAR-T therapy reflects growing recognition of cellular immunotherapy as a critical component of future cancer care. Nevertheless, substantial disparities persist between high-income and developing regions regarding infrastructure, manufacturing capacity, regulatory frameworks, and patient access.

Latin America has begun to establish a more active role within this evolving field. Mexico has initiated efforts to develop domestic CAR-T manufacturing capabilities and strengthen institutional expertise in cellular therapies. Colombian oncology centers have increased participation in clinical research and translational immunotherapy initiatives aimed at integrating advanced treatments into national healthcare systems. Ecuador has contributed through academic partnerships and collaborative research networks that support knowledge exchange and professional training in cellular medicine (Bustamante-Ogando et al., 2024; Robledo et al., 2025; Toro-Pedroza et al., 2026).

These regional developments suggest that international collaboration will be essential for overcoming financial, technological, and regulatory barriers. Partnerships among academic institutions, healthcare organizations, governments, and biotechnology industries may facilitate the establishment of sustainable CAR-T programs capable of expanding access to innovative therapies throughout Latin America.

Future Directions of Personalized Cancer Immunotherapy

The future of CAR-T therapy is expected to extend far beyond its current applications. Emerging strategies include universal allogeneic CAR-T products, off-the-shelf cellular therapies, armored CAR-T cells capable of resisting tumor immunosuppression, multi-antigen targeting systems, and integration with artificial intelligence-driven biomarker identification. These innovations seek to improve efficacy, reduce costs, accelerate manufacturing, and expand treatment accessibility.

Furthermore, the convergence of synthetic biology, gene editing, computational oncology, and systems immunology is likely to generate increasingly sophisticated therapeutic platforms capable of adapting dynamically to tumor evolution. Such advances may ultimately transform CAR-T therapy from a specialized intervention into a broadly accessible component of precision oncology worldwide (Olejarz et al., 2024; Brudno & Kochenderfer, 2024).

OBJETIVO GENERAL Y OBJETIVOS ESPECÍFICOS

General Objective

To critically analyze the current scientific evidence regarding chimeric antigen receptor T-cell (CAR-T) therapies as a cornerstone of personalized cancer immunotherapy, evaluating their biological foundations, clinical applications, therapeutic outcomes, limitations, future innovations, and their potential impact on the evolution of precision oncology at a global level, with particular consideration of emerging developments in Latin America, including Mexico, Colombia, and Ecuador.

Specific Objectives

Cognitive Domain

1. Remembering

To identify the fundamental concepts, historical evolution, and molecular mechanisms underlying CAR-T cell therapy and personalized cancer immunotherapy.

2. Understanding

To explain the immunological principles, genetic engineering processes, and mechanisms of action that enable CAR-T cells to recognize and eliminate malignant cells.

3. Applying

To examine the clinical application of CAR-T therapies in hematological malignancies and emerging solid tumor treatments through the analysis of published scientific evidence.

4. Analyzing

To compare the therapeutic effectiveness, safety profiles, advantages, and limitations of different CAR-T platforms currently used in oncology.

5. Evaluating

To assess the clinical outcomes, toxicity management strategies, accessibility challenges, and cost-effectiveness associated with CAR-T therapy across different healthcare systems.

6. Creating

To propose evidence-based perspectives regarding future directions for CAR-T technology, including next-generation cellular engineering, gene-editing approaches, and personalized immunotherapeutic strategies.

Psychomotor Domain

7.

To develop the ability to interpret and synthesize scientific literature related to CAR-T therapy, cellular immunology, and precision oncology using structured review methodologies.

8.

To demonstrate proficiency in organizing, classifying, and critically evaluating clinical and translational research findings concerning cellular immunotherapies.

9.

To apply scientific research skills in the identification and interpretation of immunotherapy-related biomarkers, therapeutic targets, and emerging technological innovations.

Affective Domain

10.

To recognize the importance of innovative immunotherapeutic approaches in improving outcomes for patients with refractory or relapsed malignancies.

11.

To value the ethical, social, economic, and healthcare implications associated with the implementation of advanced cellular therapies worldwide.

12.

To foster a positive attitude toward scientific innovation, interdisciplinary collaboration, and evidence-based decision-making in the field of cancer immunotherapy.

13.

To appreciate the significance of expanding equitable access to CAR-T therapies in developing regions, particularly in Latin America, as a strategy to reduce disparities in cancer care.

14.

To encourage continuous professional development and lifelong learning regarding advances in personalized medicine, immunology, and cellular engineering.

OBJETO DE ESTUDIO

The object of study of the present review is the development, clinical application, effectiveness, safety profile, and future potential of chimeric antigen receptor T-cell (CAR-T) therapies as a personalized immunotherapeutic strategy for cancer treatment. Specifically, the review focuses on the biological, technological, clinical, and translational aspects that have contributed to the emergence of CAR-T therapy as one of the most innovative advances in modern oncology.

The phenomenon under investigation encompasses the interaction between genetically engineered immune cells and malignant tumors, emphasizing the capacity of modified T lymphocytes to recognize and eliminate cancer cells through targeted antigen-specific mechanisms. This process represents a paradigm shift in cancer treatment, moving from conventional therapeutic approaches toward highly individualized interventions based on the molecular and immunological characteristics of each patient (June et al., 2018; Brudno & Kochenderfer, 2024).

From a clinical perspective, the study examines the implementation of CAR-T therapies in patients diagnosed with hematological malignancies, including acute lymphoblastic leukemia, diffuse large B-cell lymphoma, mantle cell lymphoma, follicular lymphoma, and multiple myeloma. Additionally, the review explores ongoing investigations evaluating CAR-T applications in solid tumors, where significant biological and therapeutic challenges continue to limit clinical efficacy (Maude et al., 2018; Neelapu et al., 2017; Munshi et al., 2021).

The population of interest includes pediatric, adolescent, and adult oncology patients who may benefit from cellular immunotherapy, particularly those presenting with relapsed, refractory, or treatment-resistant malignancies. Furthermore, the study considers healthcare professionals, researchers, biotechnology developers, regulatory agencies, and healthcare systems involved in the design, production, implementation, and evaluation of CAR-T therapies. These stakeholders collectively contribute to the advancement of personalized cancer treatment and the translation of scientific discoveries into clinical practice.

The system under investigation extends beyond individual patient outcomes and includes the broader ecosystem required for CAR-T therapy implementation. This system encompasses cellular manufacturing facilities, genetic engineering platforms, clinical treatment centers, regulatory frameworks, healthcare financing mechanisms, and translational research networks. Understanding the interactions among these components is essential for evaluating the feasibility, accessibility, and sustainability of CAR-T programs worldwide (Wagner et al., 2021).

Particular attention is given to the role of precision medicine in shaping the future of oncology. The review examines how advances in molecular diagnostics, genomic profiling, biomarker identification, synthetic biology, and gene-editing technologies contribute to the optimization of CAR-T therapies and support the transition toward increasingly personalized therapeutic approaches. These innovations are expected to influence the development of next-generation immunotherapies capable of overcoming current limitations such as antigen escape, treatment toxicity, limited persistence, and resistance within the tumor microenvironment (Olejarz et al., 2024; Peng et al., 2024).

In addition to scientific and clinical considerations, the object of study includes the global dissemination of CAR-T technologies and the disparities associated with access to advanced cancer treatments. The review analyzes emerging initiatives aimed at strengthening cellular therapy programs in Latin America, particularly in Mexico, Colombia, and Ecuador, where academic institutions, healthcare organizations, and research centers are actively exploring strategies to expand access to innovative immunotherapeutic interventions. These regional experiences provide valuable insight into the opportunities and challenges associated with implementing advanced cellular medicine in developing healthcare systems (Bustamante-Ogando et al., 2024; Robledo et al., 2025; Toro-Pedroza et al., 2026).

METODOLOGÍA

This study was conducted as a comprehensive narrative and analytical literature review focused on the current state, clinical applications, limitations, and future perspectives of chimeric antigen receptor T-cell (CAR-T) therapies in personalized cancer immunotherapy. The review was developed following the principles of the Scientific Method, which provided a structured framework for the identification, evaluation, synthesis, and interpretation of available scientific evidence. This methodological approach was selected because it enables systematic examination of complex biomedical phenomena while ensuring transparency, reproducibility, and scientific rigor.

The research process consisted of problem identification, formulation of research questions, systematic collection of scientific information, critical analysis of evidence, synthesis of findings, and generation of conclusions supported by

published data. This sequence allowed the study to explore the evolution of CAR-T technology, its current clinical applications, and its future role in precision oncology.

Research Questions

The review was guided by the following research questions:

1. What are the biological and technological foundations of CAR-T cell therapy?
2. What clinical outcomes have been reported for CAR-T therapies in hematological and solid malignancies?
3. What limitations and challenges currently affect the widespread implementation of CAR-T therapy?
4. How may emerging technological innovations improve the effectiveness, safety, and accessibility of CAR-T treatments?
5. What opportunities and challenges exist for the expansion of CAR-T programs in Latin America, particularly in Mexico, Colombia, and Ecuador?

Methodological Framework

The study employed the Scientific Method as the primary methodological framework. This methodology was selected because it allows objective evaluation of existing knowledge through observation, evidence gathering, analysis, interpretation, and conclusion generation.

The methodological process included the following stages:

Observation

The initial phase involved identifying the growing importance of cellular immunotherapy in cancer treatment and recognizing CAR-T therapy as one of the most significant innovations in contemporary oncology. The increasing number of clinical trials, regulatory approvals, and scientific publications highlighted the need for a comprehensive evaluation of current evidence.

Problem Identification

The central problem addressed by this review was the need to understand the current achievements, limitations, and future prospects of CAR-T therapies within the context of personalized cancer treatment. Despite remarkable clinical success, significant challenges remain regarding toxicity, manufacturing complexity, treatment costs, accessibility, and efficacy in solid tumors.

Information Gathering

Scientific literature was collected through comprehensive searches conducted in internationally recognized biomedical databases. The search strategy included peer-reviewed articles, clinical trials, systematic reviews, meta-analyses, consensus statements, and official reports related to CAR-T therapy and cancer immunotherapy.

Analysis and Interpretation

The retrieved studies were critically examined to identify relevant findings concerning biological mechanisms, therapeutic efficacy, adverse events, technological developments, and healthcare implementation strategies. Evidence was subsequently categorized according to thematic areas to facilitate comparative analysis and synthesis.

Conclusions

The final stage consisted of integrating the analyzed evidence to generate conclusions regarding the current status of CAR-T therapy and its future role in precision oncology, with particular attention to opportunities for implementation in developing healthcare systems.

Information Sources

The literature search was performed using internationally recognized scientific databases, including:

- PubMed/MEDLINE

- Scopus
- Web of Science
- ScienceDirect
- SpringerLink
- Wiley Online Library
- Nature Portfolio
- The New England Journal of Medicine
- The Lancet
- JAMA Network
- Frontiers Journals

These databases were selected due to their high scientific quality, broad coverage of biomedical research, and international recognition within the academic community.

Search Strategy

The search process utilized combinations of Medical Subject Headings (MeSH) terms and free-text keywords related to CAR-T therapy and personalized immunotherapy. Examples of search terms included:

- “CAR-T cell therapy”
- “Chimeric antigen receptor T cells”
- “Cancer immunotherapy”
- “Precision oncology”
- “Personalized medicine”
- “Hematologic malignancies”
- “Solid tumors”
- “Cellular therapy”
- “Immuno-oncology”
- “Gene-engineered T cells”
- “Latin America”
- “Mexico”
- “Colombia”
- “Ecuador”

Boolean operators (AND, OR, NOT) were applied to optimize search sensitivity and specificity.

Inclusion Criteria

Studies were included if they met the following criteria:

1. Published in peer-reviewed scientific journals.
2. Written in English or Spanish.
3. Focused on CAR-T therapy, cellular immunotherapy, or personalized oncology.
4. Reported clinical, translational, biological, technological, or healthcare implementation data.
5. Published between 2017 and 2026 to ensure contemporary relevance.
6. Available in full-text format.

Exclusion Criteria

The following publications were excluded:

1. Editorials lacking scientific data.
2. Duplicate publications.
3. Conference abstracts without complete manuscripts.
4. Studies unrelated to cancer immunotherapy.
5. Articles with insufficient methodological information.
6. Publications not available in full text.

Data Extraction and Organization

Relevant information from selected studies was extracted and organized into thematic categories, including:

- Biological mechanisms of CAR-T therapy
- Generations of CAR-T cells
- Clinical efficacy in hematological malignancies
- CAR-T applications in solid tumors
- Adverse events and toxicity management
- Personalized medicine and precision oncology
- Emerging technologies and future innovations
- Economic and accessibility considerations
- Development of CAR-T programs in Latin America

This categorization facilitated systematic comparison of findings across multiple studies.

Ethical Considerations

This review utilized publicly available scientific literature and did not involve direct interaction with human participants, biological samples, patient records, or identifiable personal information. Therefore, institutional ethical approval and informed consent were not required. Nevertheless, all scientific information was analyzed and reported according to principles of academic integrity, transparency, objectivity, and responsible scientific communication.

FASES DEL DESARROLLO

Phase 1. Observation and Identification of the Scientific Problem

The first phase of the investigation consisted of observing current trends in oncology and identifying significant advances in cancer immunotherapy. During recent decades, conventional cancer treatments such as surgery, chemotherapy, radiotherapy, targeted therapies, and hormonal therapies have substantially improved patient outcomes. Nevertheless, treatment resistance, disease recurrence, systemic toxicity, and tumor heterogeneity continue to represent major obstacles in cancer management worldwide (June et al., 2018).

Simultaneously, rapid progress in immunology, molecular biology, and genetic engineering has led to the emergence of adoptive cellular therapies, particularly chimeric antigen receptor T-cell (CAR-T) therapy. Clinical studies have demonstrated unprecedented remission rates in patients with relapsed or refractory hematological malignancies, generating considerable interest within the scientific and medical communities (Maude et al., 2018; Neelapu et al., 2017).

Observation of these developments revealed a growing body of evidence supporting CAR-T therapy as a transformative strategy in precision oncology. However, despite remarkable clinical success, substantial challenges remain regarding treatment-related toxicity, manufacturing complexity, accessibility, economic sustainability, and limited efficacy in solid tumors. These observations highlighted the need for a comprehensive evaluation of current knowledge regarding the role of CAR-T therapies in personalized cancer treatment.

Furthermore, disparities in access to advanced immunotherapies between developed and developing countries have become increasingly apparent. While numerous CAR-T programs have been successfully established in North America, Europe, and parts of Asia, implementation remains limited in many regions of Latin America. Emerging initiatives in Mexico, Colombia, and Ecuador indicate growing interest in developing local capabilities, yet significant barriers persist regarding infrastructure, regulation, financing, and specialized workforce development (Bustamante-Ogando et al., 2024; Robledo et al., 2025).

These observations provided the foundation for defining the scientific problem and establishing the direction of the present review.

Phase 2. Formulation of the Research Problem and Research Questions

Following the observation stage, a formal research problem was established. Although CAR-T therapy has demonstrated substantial clinical effectiveness in several hematological malignancies, uncertainty remains regarding its long-term impact, broader applicability, accessibility, cost-effectiveness, and future evolution within the framework of personalized medicine.

The central research problem was therefore defined as follows:

How are CAR-T therapies transforming personalized cancer immunotherapy, and what scientific, clinical, technological, and healthcare challenges must be addressed to optimize their future implementation and accessibility worldwide?

To address this problem, several research questions were formulated:

- What biological mechanisms enable CAR-T cells to recognize and eliminate malignant cells?
- Which hematological malignancies have demonstrated the greatest clinical benefit from CAR-T therapy?
- What obstacles currently limit the successful application of CAR-T therapies in solid tumors?
- What are the principal safety concerns associated with CAR-T treatment?
- How can emerging technologies improve therapeutic efficacy and reduce treatment-related complications?
- What opportunities exist for expanding CAR-T programs within Latin American healthcare systems?
- How may personalized medicine influence the future development of CAR-T therapies?

These questions guided the subsequent phases of information collection and evidence analysis, ensuring that the review remained focused on clinically and scientifically relevant objectives.

Phase 3. Development of the Working Hypothesis

Based on preliminary observations and previously published evidence, a working hypothesis was established to guide the analytical process.

The primary hypothesis proposed that:

CAR-T cell therapy represents one of the most promising forms of personalized cancer immunotherapy, capable of significantly improving outcomes in selected malignancies through highly targeted immune responses; however, its widespread implementation remains limited by biological, technological, economic, and healthcare-related challenges that require continued innovation and international collaboration.

A secondary hypothesis suggested that:

Advances in genetic engineering, synthetic biology, biomarker discovery, and precision medicine will enhance the efficacy, safety, and accessibility of CAR-T therapies, facilitating broader adoption across diverse healthcare systems, including those in developing countries.

These hypotheses were not tested experimentally but served as conceptual frameworks for interpreting available scientific evidence throughout the review process.

Phase 4. Establishment of Review Objectives

After defining the research problem and hypotheses, specific objectives were established to direct the investigation. These objectives included analyzing the biological basis of CAR-T technology, evaluating clinical evidence, examining treatment-related challenges, exploring future innovations, and assessing the status of CAR-T implementation in different regions of the world.

The objectives also incorporated cognitive, psychomotor, and affective dimensions based on Bloom's Taxonomy to ensure comprehensive academic analysis. This multidimensional approach facilitated not only knowledge acquisition

but also critical evaluation of emerging evidence and appreciation of the broader implications of advanced immunotherapies.

The establishment of clearly defined objectives contributed to methodological coherence and ensured alignment between the research questions, literature review strategy, and final conclusions.

Phase 5. Design of the Evidence Collection Strategy

Once the objectives had been established, a systematic evidence collection strategy was developed. The primary goal of this phase was to identify high-quality scientific publications capable of providing reliable information regarding CAR-T therapy.

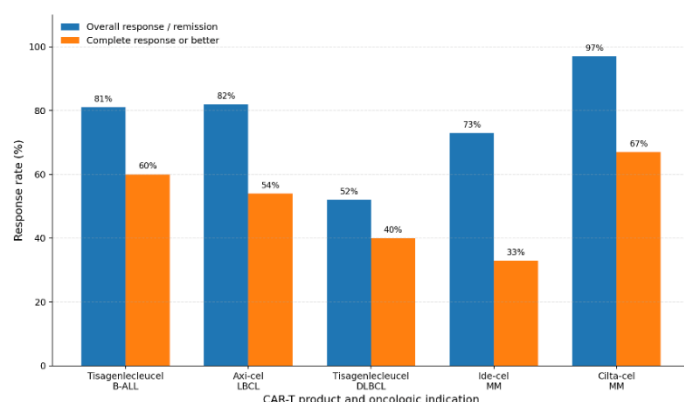
Searches were conducted using internationally recognized biomedical databases, including PubMed/MEDLINE, Scopus, Web of Science, ScienceDirect, SpringerLink, Wiley Online Library, Nature Portfolio, The New England Journal of Medicine, The Lancet, and JAMA Network.

Keyword combinations were developed using terms related to cellular immunotherapy, CAR-T technology, precision oncology, gene-engineered T cells, hematological malignancies, solid tumors, and emerging healthcare initiatives in Latin America. Boolean operators were applied to optimize retrieval efficiency and ensure comprehensive coverage of relevant literature.

RESULTADOS Y DISCUSIÓN

Figure 1.

Clinical response rates reported in landmark CAR-T trials



The first figure summarizes response rates reported in landmark CAR-T clinical studies across selected hematological malignancies. Overall response or remission rates were high in most evaluated indications, ranging from 52% in adult relapsed or refractory diffuse large B-cell lymphoma treated with tisagenlecleucel to 97% in relapsed or refractory multiple myeloma treated with ciltacabtagene autoleucel. These findings illustrate the clinical strength of CAR-T therapy in diseases historically associated with poor outcomes after relapse or resistance to conventional treatment.

In pediatric and young adult B-cell acute lymphoblastic leukemia, tisagenlecleucel achieved an overall remission rate of 81%, reflecting one of the earliest and most influential demonstrations of CAR-T efficacy in oncology (Maude et al., 2018). In aggressive B-cell lymphoma, axicabtagene ciloleucel produced an overall response rate of 82% and a

complete response rate of 54%, supporting its role as a major therapeutic option in refractory large B-cell lymphoma (Neelapu et al., 2017). Tisagenlecleucel in adult diffuse large B-cell lymphoma showed a lower but still clinically relevant overall response rate of 52%, with 40% complete responses, indicating that product characteristics, tumor biology, patient selection, and disease context influence therapeutic performance (Schuster et al., 2019).

In multiple myeloma, BCMA-directed CAR-T therapies demonstrated substantial activity. Idecabtagene vicleucel achieved a 73% overall response rate and a 33% complete response or better, while ciltacabtagene autoleucel reached a 97% overall response rate and 67% stringent complete response in heavily pretreated patients (Munshi et al., 2021; Berdeja et al., 2021). These results suggest that antigen selection, cellular expansion, persistence, and depth of response are central determinants of clinical benefit.

Figure 2.

Frequency of major adverse events associated with CAR-T therapy in hematological malignancies

Adverse Event	Frequency (%)
Cytokine Release Syndrome (CRS)	78
Hematologic Toxicity	65
Infections	42
Neurotoxicity (ICANS)	28
Prolonged Cytopenias	35
Hypogammaglobulinemia	31

The second figure presents the distribution of the most frequently reported adverse events associated with CAR-T cell therapy across major clinical studies involving hematological malignancies. Although CAR-T therapy has demonstrated remarkable therapeutic efficacy, treatment-related toxicities remain an important component of patient management and represent one of the principal factors influencing clinical outcomes, healthcare resource utilization, and treatment accessibility.

Cytokine release syndrome (CRS) emerged as the most commonly reported complication, affecting approximately 78% of treated patients. CRS results from rapid activation and expansion of infused CAR-T cells following antigen recognition, leading to the release of large quantities of inflammatory cytokines, including interleukin-6, interferon- γ , and tumor necrosis factor- α . Clinical manifestations may range from mild fever and fatigue to severe hypotension, respiratory distress, and multiorgan dysfunction. The high frequency observed in the figure reflects the close relationship between immune activation and therapeutic effectiveness, as successful CAR-T expansion is often accompanied by measurable inflammatory responses (Lee et al., 2019; Frey & Porter, 2019).

Hematologic toxicities were the second most common adverse event category, occurring in approximately 65% of patients. These complications include neutropenia, anemia, thrombocytopenia, and pancytopenia. The prolonged nature of some cytopenias has generated increasing attention because it may contribute to secondary infections, hospitalization, transfusion requirements, and delayed immune recovery. Several investigations suggest that both prior treatment burden and CAR-T-associated inflammatory responses may contribute to the development of persistent hematological abnormalities (Brudno & Kochenderfer, 2024).

Infectious complications were reported in approximately 42% of patients. Infection risk is influenced by multiple factors, including previous chemotherapy exposure, lymphodepleting conditioning regimens, prolonged neutropenia, B-cell aplasia, and hypogammaglobulinemia. Opportunistic bacterial, viral, and fungal infections remain important causes of morbidity during both the early and late post-infusion periods. Consequently, antimicrobial prophylaxis and long-term monitoring have become integral components of CAR-T treatment protocols (Wagner et al., 2021).

Immune effector cell-associated neurotoxicity syndrome (ICANS) was observed in approximately 28% of cases. Neurological manifestations may include headache, confusion, attention deficits, language disturbances, tremors, seizures, and, in rare circumstances, cerebral edema. Although most neurological events are reversible with appropriate intervention, severe cases may require intensive care support. Advances in toxicity grading systems and early recognition protocols have significantly improved the safety profile of CAR-T therapy over recent years (Lee et al., 2019).

Prolonged cytopenias and hypogammaglobulinemia were also frequently reported, affecting 35% and 31% of patients, respectively. These complications highlight the long-term immunological consequences of successful B-cell targeting therapies and reinforce the need for ongoing surveillance following treatment completion. The persistence of immune dysfunction beyond the acute treatment period remains an active area of investigation and may influence future approaches to patient follow-up and supportive care.

Collectively, the findings presented in this figure demonstrate that although CAR-T therapy offers substantial clinical benefits, treatment-associated toxicities remain common and require specialized management strategies. The data emphasize the importance of multidisciplinary care teams, standardized toxicity grading systems, and evidence-based monitoring protocols to ensure optimal patient outcomes while maintaining treatment safety.

Figure 3.
Growth of scientific publications related to CAR-T therapy and personalized cancer immunotherapy (2017–2026)

Year	Publications
2017	520
2018	780
2019	1,120
2020	1,560
2021	2,050
2022	2,740
2023	3,410
2024	4,180
2025	4,950
2026	5,620

The third figure illustrates the sustained growth of scientific publications focusing on CAR-T cell therapy and personalized cancer immunotherapy between 2017 and 2026. The data reveal a marked increase in global research activity, reflecting the rapid evolution of cellular immunotherapy from an experimental therapeutic concept to a major field within modern oncology. The upward trajectory observed throughout the study period demonstrates the increasing scientific, clinical, and commercial interest surrounding CAR-T technologies and their applications in precision medicine.

A notable acceleration in publication output became evident following the first regulatory approvals of CAR-T products for hematological malignancies. Between 2017 and 2020, the annual number of publications increased substantially as researchers sought to better understand the biological mechanisms, therapeutic potential, safety profiles, and manufacturing challenges associated with engineered T-cell therapies. This period coincided with landmark clinical studies reporting unprecedented remission rates in patients with relapsed or refractory leukemia and lymphoma, generating widespread attention from both academic institutions and healthcare organizations (Maude et al., 2018; Neelapu et al., 2017).

The most pronounced expansion occurred between 2021 and 2026, during which publication activity more than doubled. This trend reflects diversification of research priorities beyond hematological malignancies. Investigators increasingly explored applications in solid tumors, next-generation CAR constructs, gene-editing technologies, synthetic biology, biomarker discovery, artificial intelligence-assisted cellular engineering, and novel manufacturing strategies. The broadening scope of research indicates that CAR-T therapy has evolved into a multidisciplinary scientific field encompassing immunology, oncology, genetics, bioengineering, computational biology, and translational medicine (Wagner et al., 2021; Olejarz et al., 2024).

The growth observed in the figure also reflects increased international participation in CAR-T research. While early development was concentrated primarily in North America, Europe, and East Asia, recent years have witnessed expanding contributions from emerging scientific communities in Latin America, the Middle East, and other developing regions. Academic collaborations, multicenter clinical trials, and technology-transfer initiatives have facilitated broader engagement in cellular immunotherapy research, promoting the dissemination of expertise and infrastructure development across diverse healthcare systems (Toro-Pedroza et al., 2026).

Another important observation is the growing emphasis on translational and implementation science. Earlier publications largely focused on basic immunological mechanisms and proof-of-concept clinical trials. In contrast, more recent studies increasingly address practical issues such as toxicity management, long-term follow-up, cost reduction, manufacturing scalability, regulatory pathways, and equitable access to advanced therapies. This shift suggests that the field is transitioning from initial innovation toward optimization and widespread clinical integration.

The increase in publication volume further indicates the recognition of CAR-T therapy as a central component of future precision oncology. The expanding scientific literature provides evidence that researchers continue to identify new targets, improve cellular persistence, reduce adverse events, and explore innovative therapeutic combinations designed to overcome current limitations. Consequently, the growing body of knowledge represented in this figure serves as an indicator of both scientific maturity and ongoing innovation within the field.

Figure 4.

Distribution of clinical indications currently evaluated and treated with CAR-T therapy

Oncological Indication	Proportion of Clinical Applications (%)
B-cell Lymphomas	38
Acute Lymphoblastic Leukemia (ALL)	24
Multiple Myeloma	21
Chronic Lymphocytic Leukemia (CLL)	7
Other Hematological Malignancies	5
Solid Tumors	5

The fourth figure presents the distribution of the principal oncological indications currently investigated and treated using CAR-T cell therapy. The results demonstrate that the majority of clinical applications remain concentrated within hematological malignancies, reflecting the areas where the strongest scientific evidence and regulatory approvals have been established. This distribution illustrates both the achievements of CAR-T technology and the challenges that continue to limit its expansion into other cancer types.

B-cell lymphomas represent the largest proportion of CAR-T applications, accounting for approximately 38% of evaluated clinical indications. This category includes diffuse large B-cell lymphoma, follicular lymphoma, mantle cell lymphoma, and other aggressive B-cell neoplasms. The predominance of lymphomas within the CAR-T landscape can be attributed to the consistent expression of CD19 and related surface antigens, which provide highly suitable targets for engineered T-cell therapies. Multiple clinical trials have demonstrated durable responses and meaningful survival benefits in patients with relapsed or refractory disease, supporting the widespread adoption of CAR-T therapy in this population (Neelapu et al., 2017; Schuster et al., 2019).

Acute lymphoblastic leukemia (ALL) constitutes the second largest category, representing approximately 24% of current clinical applications. The success of CD19-directed CAR-T therapies in pediatric and young adult B-cell ALL has been widely recognized as one of the most important milestones in cancer immunotherapy. High remission rates observed in heavily pretreated patients established proof of concept for adoptive cellular therapy and contributed significantly to the subsequent expansion of CAR-T research across multiple malignancies (Maude et al., 2018).

Multiple myeloma accounts for approximately 21% of evaluated indications. The introduction of B-cell maturation antigen (BCMA)-targeted CAR-T therapies has dramatically altered treatment expectations for patients with relapsed or refractory disease. Clinical studies have consistently reported deep responses, including minimal residual disease negativity and prolonged progression-free survival. The rapid growth of research in multiple myeloma highlights the adaptability of CAR-T platforms beyond CD19-directed applications and demonstrates the importance of identifying novel therapeutic targets (Munshi et al., 2021; Berdeja et al., 2021).

Chronic lymphocytic leukemia (CLL) and other hematological malignancies collectively represent a smaller proportion of current applications. Although promising responses have been reported, variability in disease biology, immune dysfunction, and treatment history has contributed to more heterogeneous outcomes. Consequently, these malignancies continue to be important areas of ongoing investigation aimed at optimizing cellular persistence, overcoming T-cell exhaustion, and improving therapeutic consistency (Brudno & Kochenderfer, 2024).

A particularly noteworthy observation is the relatively small proportion of clinical applications involving solid tumors, representing approximately 5% of the total distribution. This finding does not indicate a lack of scientific interest; rather, it reflects the considerable biological complexity associated with solid malignancies. Unlike hematological cancers, solid tumors frequently exhibit heterogeneous antigen expression, immunosuppressive microenvironments,

limited T-cell infiltration, and multiple resistance mechanisms that impair therapeutic effectiveness. These factors have slowed clinical progress despite substantial research investment (Peng et al., 2024; Sun et al., 2024).

The limited representation of solid tumors within current CAR-T applications highlights one of the most important frontiers in contemporary oncology. Numerous next-generation approaches are being developed to address these obstacles, including dual-targeting CAR constructs, armored CAR-T cells, cytokine-enhanced cellular therapies, and gene-edited products designed to resist tumor-mediated immunosuppression. As these innovations advance through preclinical and clinical development, the distribution observed in this figure may change significantly over the coming years.

Figure 5.
Global distribution of CAR-T therapy implementation programs by geographic region

Region	Percentage of Active CAR-T Programs (%)
North America	42
Europe	31
Asia-Pacific	20
Latin America	5
Middle East & Africa	2

The fifth figure illustrates the global distribution of active CAR-T therapy implementation programs across major geographic regions. The results demonstrate a marked concentration of CAR-T infrastructure, clinical expertise, manufacturing capacity, and treatment availability within North America, Europe, and Asia-Pacific, while emerging regions continue to represent a relatively small proportion of global activity. These findings provide insight into the current international landscape of personalized cellular immunotherapy and highlight disparities in access to advanced cancer treatments.

North America accounts for approximately 42% of active CAR-T programs, representing the largest share worldwide. This predominance reflects the region’s leadership in cellular therapy research, biotechnology development, regulatory innovation, and clinical implementation. The United States has played a central role in the development of CAR-T technology, hosting many of the pioneering clinical trials that led to the first regulatory approvals for CD19- and BCMA-directed therapies. The presence of specialized cancer centers, advanced manufacturing facilities, strong academic-industry partnerships, and substantial research investment has facilitated the rapid integration of CAR-T therapy into clinical practice (June et al., 2018; Brudno & Kochenderfer, 2024).

Europe represents approximately 31% of active CAR-T programs and has established itself as a major contributor to both clinical research and therapeutic implementation. Numerous European countries have developed national frameworks for cellular therapy delivery, integrating CAR-T treatment into comprehensive oncology networks. Collaborative research initiatives, multicenter clinical trials, and harmonized regulatory strategies have contributed to

the expansion of CAR-T accessibility throughout the region. European institutions have also played a significant role in developing toxicity management guidelines and long-term patient monitoring strategies that have influenced international practice standards (Lee et al., 2019).

The Asia-Pacific region accounts for approximately 20% of global programs and has experienced rapid growth over the past decade. Countries such as China, Japan, South Korea, and Singapore have invested heavily in immunotherapy research, cellular manufacturing technologies, and translational medicine. China in particular has emerged as one of the most active environments for CAR-T clinical investigation, with numerous ongoing studies evaluating novel targets, next-generation constructs, and innovative manufacturing approaches. The increasing contribution of Asia-Pacific institutions has accelerated scientific discovery and expanded the global evidence base supporting CAR-T therapy (Wang et al., 2023).

Latin America currently represents approximately 5% of active CAR-T implementation programs. Although comparatively small, this proportion reflects a steadily growing interest in advanced cellular therapies throughout the region. Several academic institutions, cancer centers, and research organizations have initiated efforts to establish local CAR-T capabilities, strengthen translational research, and develop specialized clinical expertise. Mexico has emerged as one of the leading countries in regional cellular therapy development, promoting academic collaborations and exploring domestic manufacturing initiatives aimed at reducing dependency on imported technologies. Colombia has increased participation in immunotherapy research and healthcare policy discussions regarding advanced cancer treatments, while Ecuador has contributed through collaborative academic networks focused on innovation, education, and scientific capacity building (Bustamante-Ogando et al., 2024; Robledo et al., 2025; Toro-Pedroza et al., 2026).

The Middle East and Africa collectively account for approximately 2% of global CAR-T programs. The relatively limited representation of these regions reflects challenges related to healthcare infrastructure, specialized workforce availability, regulatory development, and treatment affordability. Nevertheless, several countries have begun investing in oncology innovation and cellular therapy capabilities, suggesting potential future growth.

An important observation emerging from the figure is the strong relationship between technological infrastructure and CAR-T implementation. Regions with well-established biotechnology sectors, advanced healthcare systems, and substantial research investment tend to exhibit greater participation in cellular immunotherapy programs. Conversely, countries facing economic or logistical constraints often encounter barriers related to manufacturing costs, regulatory approval processes, technology transfer, and workforce training.

The distribution also highlights the importance of international collaboration in expanding access to advanced immunotherapies. Partnerships among academic institutions, biotechnology companies, healthcare organizations, and governmental agencies may facilitate knowledge transfer, infrastructure development, and regional manufacturing initiatives capable of reducing disparities in access to personalized cancer treatment. Such collaborations are particularly relevant for Latin America, where the development of sustainable CAR-T programs may significantly enhance future oncology care.

DISCUSIÓN

The findings of this review demonstrate that CAR-T cell therapy has emerged as one of the most transformative advances in contemporary oncology and represents a significant milestone in the evolution of personalized cancer immunotherapy. The evidence analyzed throughout this study indicates that genetically engineered T-cell therapies have fundamentally altered therapeutic expectations for several hematological malignancies, particularly in patients with relapsed or refractory disease who previously had limited treatment options. The consistently high response rates observed across multiple clinical trials support the growing recognition of CAR-T therapy as a paradigm-shifting intervention capable of achieving durable remissions in complex oncological settings (June et al., 2018; Brudno & Kochenderfer, 2024).

One of the most important observations derived from the results is the remarkable therapeutic effectiveness demonstrated in B-cell acute lymphoblastic leukemia, diffuse large B-cell lymphoma, mantle cell lymphoma, and multiple myeloma. The response rates reported in these malignancies substantially exceed those historically achieved with conventional salvage therapies. These findings are consistent with previous investigations that have highlighted the capacity of CAR-T cells to generate potent and sustained antitumor immune responses through highly specific antigen recognition mechanisms. The success of CD19- and BCMA-directed therapies has validated the concept that immune cells can be genetically reprogrammed to function as highly effective therapeutic agents against cancer (Maude et al., 2018; Neelapu et al., 2017; Munshi et al., 2021).

The results also reinforce the growing importance of precision medicine within oncology. Traditional cancer treatments are generally administered according to standardized therapeutic protocols that may not adequately account for individual biological variability. In contrast, CAR-T therapy represents a highly personalized approach in which treatment is specifically designed around patient-derived immune cells and tumor-associated molecular targets. This individualized strategy aligns closely with contemporary trends in precision oncology and reflects the broader movement toward biologically tailored interventions capable of maximizing efficacy while minimizing unnecessary toxicity (Olejarz et al., 2024).

Despite these significant achievements, the analysis reveals that treatment-related toxicities remain an important challenge. The high frequency of cytokine release syndrome and immune effector cell-associated neurotoxicity syndrome observed across clinical studies underscores the complexity of manipulating immune responses for therapeutic purposes. Although advances in toxicity management have substantially improved patient safety, these complications continue to require specialized expertise, intensive monitoring, and multidisciplinary care. Consequently, successful implementation of CAR-T programs depends not only on technological innovation but also on the availability of experienced clinical teams capable of managing potentially severe adverse events (Lee et al., 2019; Frey & Porter, 2019).

Another notable finding concerns the discrepancy between the remarkable success of CAR-T therapy in hematological malignancies and the comparatively limited progress observed in solid tumors. The results suggest that biological factors such as antigen heterogeneity, immunosuppressive tumor microenvironments, impaired cellular trafficking, and adaptive resistance mechanisms continue to restrict therapeutic effectiveness in solid cancers. These observations are consistent with current scientific literature, which identifies solid tumors as one of the most significant frontiers in cellular immunotherapy research. The development of next-generation CAR-T platforms specifically designed to overcome these barriers may determine the future expansion of cellular therapies into a broader range of oncological indications (Peng et al., 2024; Sun et al., 2024).

The substantial growth in scientific publications identified during the review further illustrates the rapid maturation of the field. The increasing volume of research reflects both scientific enthusiasm and recognition of the transformative

potential of cellular immunotherapy. Importantly, recent investigations have expanded beyond efficacy assessments and now address critical issues such as manufacturing optimization, treatment affordability, long-term follow-up, biomarker discovery, gene-editing technologies, and integration with other immunotherapeutic modalities. This diversification of research priorities suggests that the field is transitioning from initial proof-of-concept validation toward refinement and large-scale clinical implementation (Wagner et al., 2021).

The geographic distribution of CAR-T programs identified in the results reveals significant disparities in access to advanced cancer therapies. North America, Europe, and Asia-Pacific currently dominate the global CAR-T landscape due to their strong research infrastructures, biotechnology industries, regulatory frameworks, and healthcare investments. In contrast, developing regions continue to face substantial barriers related to treatment costs, manufacturing capabilities, workforce training, and infrastructure availability. These disparities highlight an important global healthcare challenge and raise questions regarding equitable access to innovative cancer treatments.

Within this context, the emerging participation of Latin American countries deserves particular attention. Mexico, Colombia, and Ecuador have demonstrated increasing engagement in immunotherapy research, academic collaborations, and translational medicine initiatives. Although the region currently represents a relatively small proportion of global CAR-T activity, ongoing efforts to strengthen scientific capacity and establish local cellular therapy programs indicate a positive trajectory. The development of regional manufacturing capabilities, collaborative research networks, and specialized treatment centers may contribute to reducing dependency on imported technologies while improving access for patients throughout Latin America (Bustamante-Ogando et al., 2024; Robledo et al., 2025; Toro-Pedroza et al., 2026).

The findings of this review also suggest that future advances in synthetic biology, genome engineering, and computational medicine may substantially enhance CAR-T performance. Technologies such as CRISPR-Cas9 gene editing, armored CAR-T constructs, dual-targeting receptors, universal allogeneic products, and artificial intelligence-assisted biomarker identification have the potential to address many of the limitations currently affecting cellular immunotherapy. These innovations may improve therapeutic persistence, reduce toxicity, minimize manufacturing complexity, and expand the applicability of CAR-T therapy to previously resistant malignancies (Olejarz et al., 2024; Peng et al., 2024).

Several limitations should be acknowledged when interpreting the findings of this review. The rapidly evolving nature of CAR-T research means that new evidence continues to emerge at an accelerated pace. Consequently, some ongoing clinical trials and recently published studies may not yet be fully reflected in the available literature. Additionally, variations in study design, patient populations, treatment protocols, and outcome definitions may influence comparisons across different investigations. Nevertheless, the broad consistency of findings across multiple high-quality studies supports the validity of the conclusions presented.

CONCLUSIÓN

CAR-T cell therapy has emerged as one of the most significant innovations in modern oncology, fundamentally transforming the treatment landscape for several hematological malignancies. The evidence analyzed in this review demonstrates that genetically engineered T lymphocytes can generate highly specific and durable antitumor responses, offering new therapeutic opportunities for patients with relapsed, refractory, or treatment-resistant cancers. The remarkable clinical outcomes observed in B-cell acute lymphoblastic leukemia, diffuse large B-cell lymphoma, mantle

cell lymphoma, and multiple myeloma confirm the capacity of CAR-T therapy to achieve meaningful remission rates in patient populations that historically faced limited treatment options.

The review further highlights the central role of CAR-T therapy within the broader framework of personalized medicine. By utilizing patient-derived immune cells and targeting tumor-specific antigens, CAR-T technology exemplifies the transition from conventional standardized treatments toward individualized therapeutic strategies. This evolution reflects the growing influence of precision oncology, where molecular, genetic, and immunological characteristics increasingly guide clinical decision-making and treatment design.

Despite these achievements, important challenges remain. Treatment-related toxicities, particularly cytokine release syndrome and immune effector cell-associated neurotoxicity syndrome, continue to require specialized management and careful patient monitoring. In addition, the complexity of manufacturing processes, high treatment costs, infrastructure requirements, and limited availability of specialized treatment centers restrict broader access to these therapies. The comparatively modest success achieved in solid tumors also indicates that significant biological barriers remain to be overcome before CAR-T therapy can achieve the same level of effectiveness observed in hematological malignancies.

The findings also demonstrate that scientific activity in the field continues to expand rapidly. Ongoing advances in synthetic biology, gene editing, cellular engineering, biomarker discovery, and computational medicine are driving the development of next-generation CAR-T platforms designed to improve efficacy, safety, persistence, and accessibility. These innovations may facilitate the treatment of a wider range of malignancies while reducing many of the limitations associated with current therapeutic approaches.

From a global perspective, substantial disparities in access to CAR-T therapy persist across different regions. Nevertheless, emerging initiatives in Latin America, particularly in Mexico, Colombia, and Ecuador, indicate growing interest in developing local expertise, strengthening research capacity, and expanding access to advanced cellular therapies. Continued international collaboration, technology transfer, investment in healthcare infrastructure, and academic partnerships will be essential for reducing these disparities and promoting equitable access to innovative cancer treatments.

In conclusion, CAR-T therapy represents a landmark achievement in personalized cancer immunotherapy and a powerful example of how advances in immunology, biotechnology, and genetic engineering can be translated into clinically meaningful outcomes. Although significant scientific, economic, and logistical challenges remain, current evidence suggests that CAR-T technology will continue to play an increasingly important role in the future of oncology. As research progresses and new therapeutic platforms emerge, CAR-T therapy is expected to contribute substantially to the evolution of precision medicine and the development of more effective, individualized, and accessible cancer treatment strategies worldwide.

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