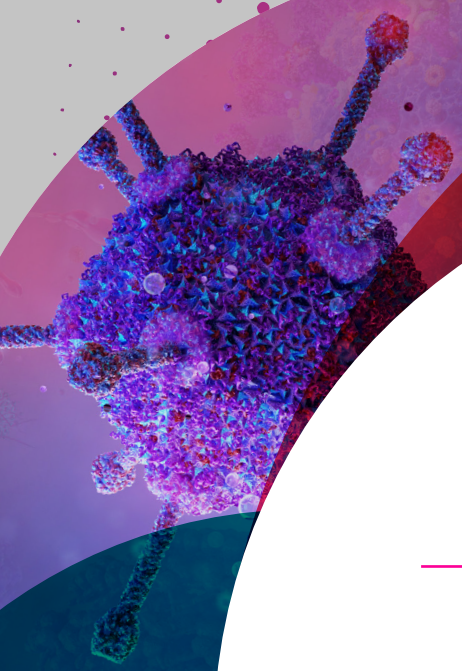
Vision Report



CAR T VISION

It's Time for CAR T

We believe every eligible patient should have the opportunity for cure with CAR T-cell therapy.

By 2030, we aim to double the proportion of eligible patients treated with CAR T-cell therapy.

Executive Summary

This report serves as an urgent call to action to enhance patient access to CAR T-cell therapy – an innovative, individualized and potentially curative treatment for certain blood cancers.* While progress has been made in expanding availability of CAR T-cell therapy, many patients still face significant barriers that prevent them from receiving this life-changing therapy when they need it most.

CAR T-cell therapy involves the engineering of a person's own immune cells to target and treat cancer.[1] These individualized medicines offer a different approach from conventional therapies, involving a one-time treatment that is intended to provide long-lasting remission. For some patients with certain forms of aggressive and difficult-to-treat blood cancers, CAR T-cell therapies have enabled them to remain cancer free for more than five years[2,3,4,5] – a significant milestone.

Despite its curative potential, many patients who could benefit from CAR T-cell therapy and want to access this treatment do not get the opportunity. In the US, as well as in European countries where CAR T-cell therapy is available to treat patients with large B-cell lymphoma (LBCL), only about two out of 10 eligible patients receive access to CAR T-cell therapy.[6,7]

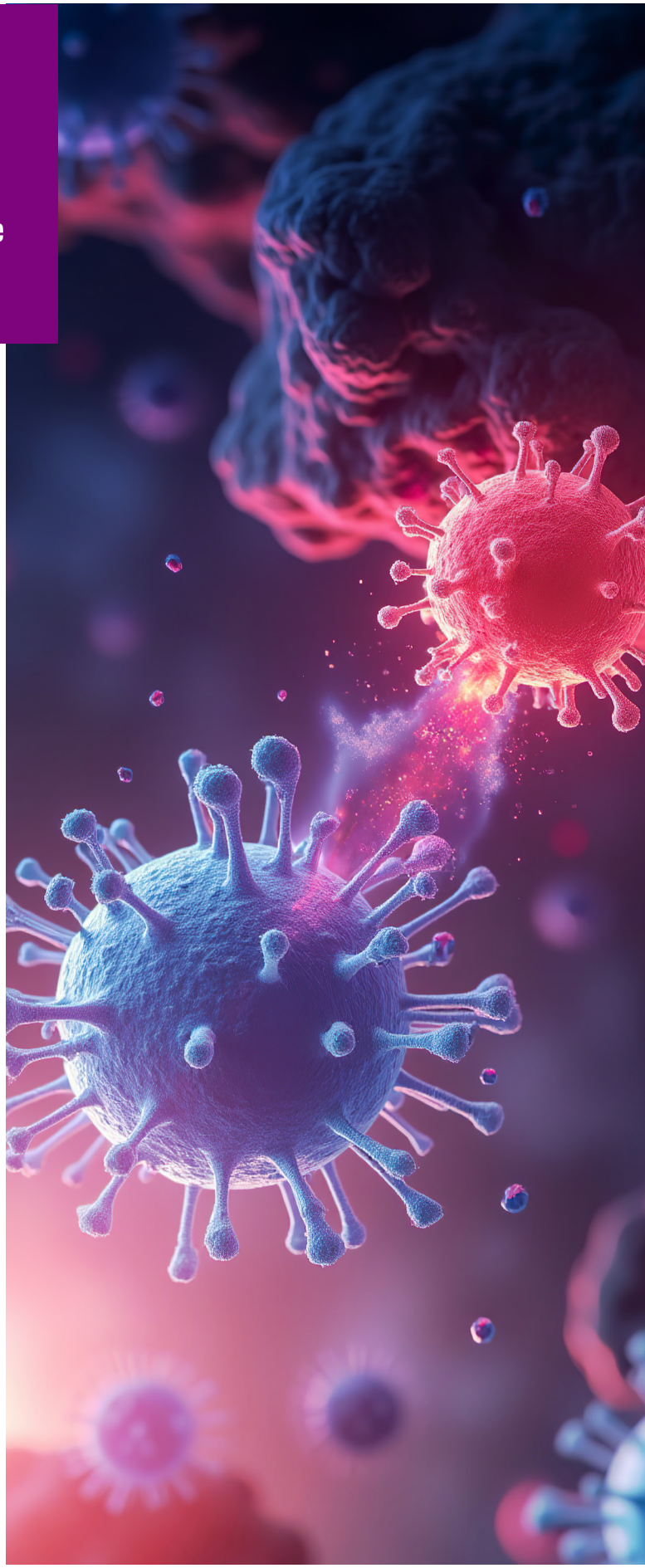
There are several reasons why patients do not get access to CAR T-cell therapy in the crucial treatment window when they are eligible. Limited knowledge of and capacity for CAR T-cell therapy outside specialized treatment centers,[8] limited capacity at treatment centers,[9] delays in referral,[9] long journeys for treatment,[9] financial and logistical burden on patients and caregivers,[10] significant upfront investment and total cost of treatment and care,[11] and funding and reimbursement challenges[8] are just some of the barriers that either prevent people from accessing treatment altogether or cause delays that risk a patient's cancer progressing before they access treatment. As experience with CAR T-cell therapies has grown, so too have the strategies and initiatives aimed at addressing access hurdles. In the future, as more therapies are approved across broader indications, there will be more need as well as more opportunities to address access challenges, including the cost of care, through innovation and system-level efficiencies. But patients needing treatment today cannot wait.

Time is of the essence and urgent action is needed. This is why a group of clinical, patient support, provider and health system experts came together to develop the Vision for CAR T-cell therapy with recommendations for interventions that, if adopted and scaled, will help many more patients get the opportunity of treatment. This expert Steering Committee has set an ambitious goal: to double the proportion of eligible patients who are treated with CAR T-cell therapy by 2030. The aim is to unite diverse stakeholders behind this Vision and the meaningful changes that are needed to support more eligible patients in reaching the outcomes that CAR T-cell therapy can offer.

It's Time for CAR T

We believe every eligible patient should have the opportunity for cure with CAR T-cell therapy.

By 2030, we aim to double the proportion of eligible patients treated with CAR T-cell therapy.



We call on every person and organization with the ability to shape patient journeys – policymakers, regulators, health system leaders, payors, health technology assessment (HTA) bodies, providers, healthcare professionals (HCPs), patient advocates and industry – to act with urgency to ensure every eligible patient has the opportunity for cure with CAR T-cell therapy, doubling the proportion of eligible patients treated in the next five years.

This report is the first publication of the Steering Committee. Its purpose is to inspire further discussion and exploration about how the CAR T Vision could be achieved and provides a foundation for collaboration between country stakeholders on the actions needed to address specific barriers to patient access.

We define **eligible patient as a person who meets the regulatory criteria for treatment with CAR T-cell therapy – this may vary by country or region and the Vision is meant to be adaptable to local contexts.*

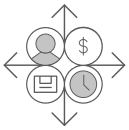
Recommendations

The following recommended imperatives aim to dramatically increase the proportion of eligible patients accessing CAR T-cell therapy. They provide the foundations for advocacy and action by local stakeholders to address the specific access challenges faced by patients in different geographies.

1. Increase awareness and understanding of CAR T-cell therapy

IMPERATIVES

- HCPs in referral centers identify potentially eligible patients for CAR T-cell therapy early and refer to specialists with urgency
- Eligible patients and their caregivers understand the clinical benefits and risks, as well as logistical and financial considerations of CAR T-cell therapy to make informed choices about treatment
- Policymakers and payors understand the value of CAR T-cell therapy and collaborate with stakeholders to address systemic barriers to treatment and care



2. Expand resources and capacity to deliver CAR T-cell therapy

IMPERATIVES

- Decentralized care delivery models – with the capital and infrastructure necessary to deliver care in accordance with quality and safety standards – are in place to bring care closer to people's homes
- Formalized processes and dedicated resources for coordination and communication between referral and treatment centers are in place, supporting eligibility assessment, referral and swift transfer of patients
- Manufacturer requirements for treating centers are harmonized to reduce duplication
- Qualification processes for treating centers are streamlined to maximize efficiency and reduce administrative burden, while maintaining quality and safety standards consistent with larger, integrated medical systems already administering CAR T-cell therapies
- Forecasting and demand planning processes are in place to support staff and expand health system capacity as more cell therapies are approved for expanded indications

3. Develop sustainable and innovative financing approaches to manage the costs of treatment and care

IMPERATIVES

- Economic models reflect that the upfront budget impact of CAR T-cell therapy can be mitigated in the long-term by reductions in healthcare spending
- Robust real-world data to support decision making on the clinical and economic value of CAR T-cell therapy is continually collected and utilized
- Innovative and sustainable contracting models ensure that patients have access to innovative treatments now and as more treatments become available
- Reimbursement for CAR T-cell therapy happens in a timely way to enable swift treatment, and covers the full cost of hospital treatment and care
- The long-term sustainability of CAR T-cell therapy is achieved by reductions in the total cost of care, expanded access and innovative financing partnerships

CAR T VISION

Join us in making the Vision a reality.

CAR T Vision Steering Committee

Dr. Miguel Perales

CO-CHAIR

American Society for Transplantation and Cellular Therapy (ASTCT)

Dr. Anna Sureda

CO-CHAIR

Clinical hematologist, professor and cell therapy researcher

Jacqueline Barry

Cell and Gene Therapy Catapult (CGT Catapult)

Yelak Biru

Immediate Past-President of International Myeloma Foundation (IMF)

Prof. John Gribben

Barts Cancer Institute, London and Past-President of European Hematology Association (EHA)

Meghan Gutierrez

Lymphoma Research Foundation (LRF)

Prof. Michael Hudecek

Universitätsklinikum Würzburg, Germany and T2EVOLVE IMI Consortium

Tim Hunt

Alliance for Regenerative Medicine (ARM)

Meagan O'Neill

Association of Cancer Care Centers (ACCC)

Brian O'Rourke

Independent healthcare advisor and expert in the science and practice of HTA

David Schmahl

Foundation for the Accreditation of Cellular Therapy (FACT)

Lorna Warwick

Lymphoma Coalition

Dr. Jason Westin

Medical oncologist, professor and cell therapy researcher

CAR T Vision Community

In developing the CAR T Vision and this report, the Steering Committee has consulted with experts and advocates to understand how the Vision can support their work and advocacy. We want to hear from more organizations in this field and expand the Vision community to include everyone working to enable access to CAR T-cell therapy for eligible patients.

The below organizations have endorsed the CAR T Vision:

APSHO Advanced Practitioner Society for Hematology and Oncology

Alliance for Regenerative Medicine

AACI Association of American Cancer Institutes

ACCC Association of Cancer Care Centers™

Barts Cancer Institute

CancerCare®

Cancer Support Community

CAR-TAPULT Cell and Gene Therapy

Fact Foundation for the Accreditation of Cellular Therapy

International Myeloma Foundation

Leukemia & Lymphoma Society®

Lymphoma Coalition

Disclaimer

This report and the initial activities of the CAR T Vision Steering Committee have been funded by Gilead and Kite, as the inaugural supporter of CAR T Vision. Report content has been reviewed by Gilead and Kite. However, the Steering Committee has editorial control of the CAR T Vision and its outputs, including this report.

Contents

1. Introduction

CAR T-cell therapy is a potentially curative treatment that is currently available to treat certain types of aggressive and advanced blood cancers. However, many eligible patients do not get the opportunity to benefit from this treatment.

The CAR T Vision Steering Committee was established to tackle this challenge – bringing together leaders from top North American and European patient advocacy groups, medical society organizations, academic and community treatment centers, and health technology assessment, policy and other subject matter experts. Its aim was to develop a Vision that would unite stakeholders behind shared goals with a renewed sense of urgency for action. This report is the first publication of the CAR T Vision Steering Committee. It details the Vision and how it was developed, the challenges to address, and the priority areas where progress is needed to make the Vision a reality.

The recommendations in this report are divided under three focus areas identified by the Steering Committee:

1. Awareness and understanding of CAR T-cell therapy
2. Resources and capacity to deliver CAR T-cell therapy
3. Sustainable and innovative approaches to manage the costs of treatment and care

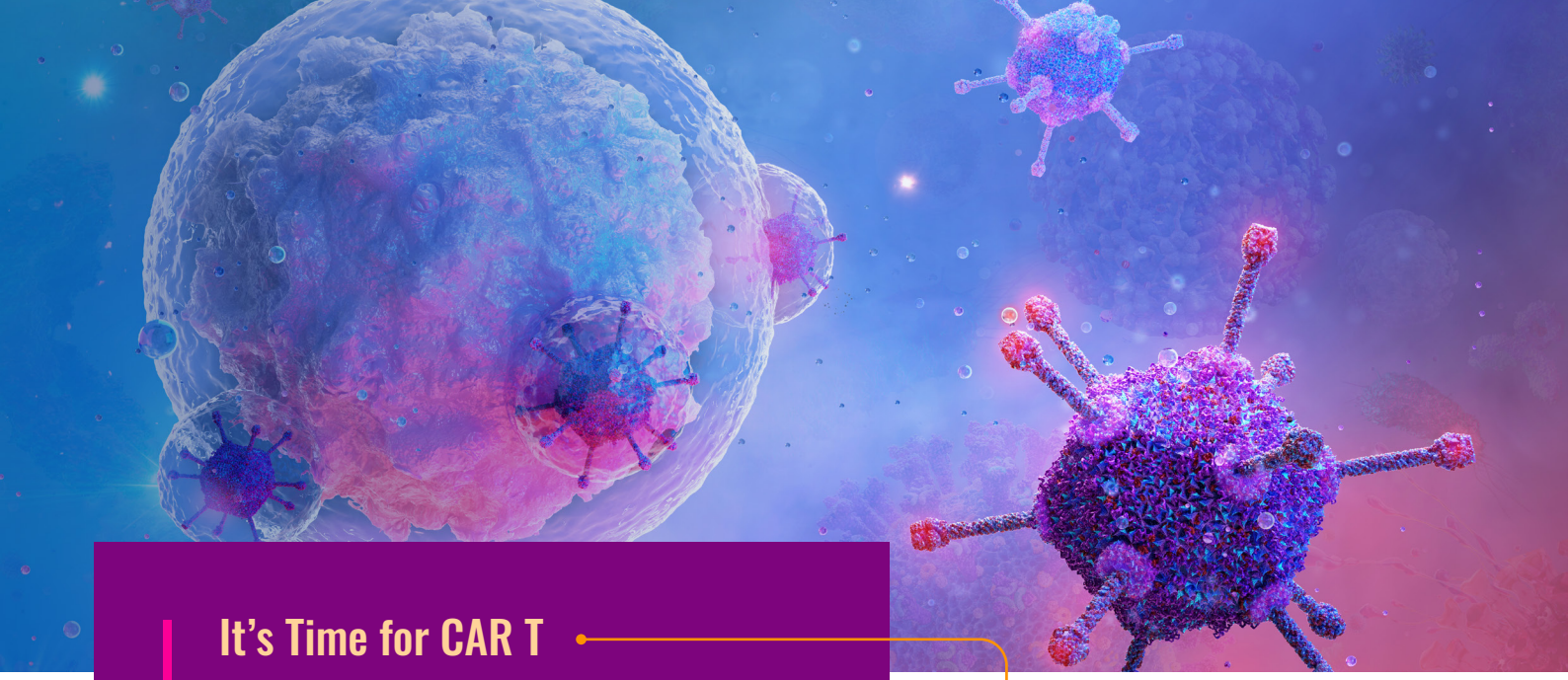
The recommendations section includes imperatives to dramatically increase the proportion of eligible patients accessing CAR T-cell therapy. They provide the foundations for advocacy and action by local stakeholders to address the specific access challenges faced by patients in different geographies.

2. Vision for improving patient access to CAR T-cell therapy

The Vision defines ***access*** as the proportion of eligible patients treated with CAR T-cell therapy. This is a milestone that can be benchmarked and measured in different geographies to assess the impact of interventions aimed at improving patient access. We define ***eligible patient*** as a person who meets the regulatory criteria for treatment with CAR T-cell therapy – this may vary by country or region and the Vision is meant to be adaptable to local contexts.

The phrase ***opportunity for cure*** was chosen because it articulates the ambition for transformative outcomes that is the intent of CAR T-cell therapy, while also recognizing that not all patients may reach the five-year survival mark. It also incorporates the importance of patient autonomy and choice – all eligible patients should have the opportunity to choose CAR T-cell therapy, if that is the appropriate option for them and it is available in their health system.

The Vision does not seek to supplant ongoing initiatives by the many organizations working in the CAR T-cell therapy space. Rather, it hopes to build on them by providing a new focal point and an urgent call to action for policymakers, health system leaders, payors, providers and industry for better access to this form of therapy. It also sets the strategic direction for a series of Vision Working Groups, which will draw on more experts from the CAR T-cell therapy community to turn the Vision goals into local action. While the initial focus of the Vision is on North America and Europe (where CAR T-cell therapies are available), its scope may be expanded to other geographies in future.



It's Time for CAR T

We believe every eligible patient should have the **opportunity for cure** with CAR T-cell therapy.

By 2030, we aim to **double the proportion** of eligible patients treated with CAR T-cell therapy.

Communicates the urgency to act now to ensure that patients who could benefit from CAR T-cell therapy get access when they need it

Our ambition

to address access for patients who could benefit from the curative potential of CAR T-cell therapy

Our Vision

goal for increasing access in the near term

OUR GOALS TO HELP US ACHIEVE OUR VISION:

- Increase awareness and understanding of CAR T-cell therapy
- Expand resources and capacity for CAR T-cell therapy
- Develop sustainable and innovative financing approaches to manage the costs of treatment and care

To realize the Vision, we need to see action across these three areas. The Vision goals will provide a framework for action via dedicated Working Groups, comprising members of the Steering Committee and additional experts, that will define specific objectives, actions and progress indicators to turn the Vision into local action. Other individuals and organizations may also use these Vision goals to guide their own efforts to drive progress.

3. Overview of CAR T-cell therapy

T-cells are a type of white blood cells that play a crucial role in the immune system by targeting and eliminating infected cells and directing other immune responses.[12] CAR T-cell therapy involves a process called apheresis, where blood is drawn from a vein and T-cells are separated from the blood.[13] These T-cells are then engineered to add a new piece of genetic code, which creates chimeric antigen receptors (CARs). When the cells are infused back into a person's body, they may be able to recognize and target cancer cells more effectively.[1]

In 2017, two CAR T-cell therapies received US Food and Drug Administration's (FDA) approval – one for patients up to 25 years old with B-cell precursor acute lymphoblastic leukemia (ALL) that is refractory or in second or later relapse,[14] and the other for adults with relapsed or refractory (R/R) large B-cell lymphoma (LBCL) after two or more lines of systemic therapy, including diffuse large B-cell lymphoma (DLBCL).[15]

Since then, the CAR T-cell therapy landscape has expanded rapidly. Seven CAR T-cell therapies have been approved by the US FDA[16,17,18,19,20,21,22] and six by the European Medicines Agency (EMA)[23,24,25,26,27,28] and the UK's Medicines and Healthcare products Regulatory Agency (MHRA)[29,30,31,32,33,34] to treat blood cancers, including ALL, LBCL, mantle cell lymphoma (MCL), follicular lymphoma (FL), chronic lymphocytic leukemia (CLL) and multiple myeloma (MM).[35]

In the near future, it is expected that CAR T-cell therapies may be approved in new and expanded indications, in blood cancers and beyond. Today, there are hundreds of clinical trials underway to explore CAR T-cell therapies for other serious conditions, including solid tumor cancers, HIV and autoimmune diseases.[36,37,38,39,40]

It is estimated that more than **50,000 patients** have been treated to date with commercial CAR T-cell therapy

– many of whom would have likely had few, if any, other treatment options available with curative intent.[35] CAR T-cell therapy has demonstrated its ability to induce prolonged remissions in patients with B-cell malignancies,[41] and one of the earliest patients treated in clinical trials has experienced remission of more than a decade.[42]

Data have demonstrated long-term overall survival rates* associated with CAR T-cell therapy.[2,3,5,43,44,45,46,47] For those still alive at four years, it is possible that treatment with CAR T-cell therapy may be curative.[48]

As more patients are treated with CAR T-cell therapy across the world, our understanding of the treatment is also expanding. In one real-world study (n=551), the median overall survival

with CAR T-cell therapy in older adults over 75 was observed to be comparable to those in younger patients.[49] Real-world data showed that CAR T-cell therapy favorable responses and survival outcomes for patients with DLBCL were observed in both the second-line and third-line or later settings.[50] Researchers understand much more about early predictors of safety profiles.[51] The knowledge base is growing.

Unlike many other blood cancer therapies, CAR T-cell therapy is designed to be a one-time treatment. While not without its own side effects, for most patients, these side effects are generally reversible and time limited.[52]

Patients treated with CAR T-cell therapy often recover more quickly than those treated with standard of care,[53,54,55] due to time without symptoms of disease progression or treatment toxicities, thereby allowing for a faster return to their daily lives.[56]

However, the nature of CAR T-cell therapies and the processes required for their manufacture and delivery, create challenges along the patient pathway that urgently need to be addressed.

In **third-line setting for R/R LBCL, the estimated five-year overall survival rate was 38.1% in the TRANSCEND trial (n=270) and 42.6% in the ZUMA-1 trial (n=101). In the Juliet trial (n=115), survival probability at three years was 36.3%.*

*In **second-line setting for R/R LBCL**, estimated four-year overall survival rate was 54.6% in the ZUMA-7 Trial (n=180) and three-year survival rate was 62.8% in the TRANSFORM trial (n=92).*

*In **R/R MM**, the estimated five-year overall survival rate was 49.1% in the LEGEND-2 trial (n=74), and the observed 30-month overall survival rate was 76.4% in CARTITUDE (n=419). Median overall survival observed in KarMMa-3 (n=386) was 41.4 months.*

Cross-trial comparisons cannot be made because studies were done in differing patient populations. Any direct comparison is limited without head-to-head data.

4. Patient access to CAR T-cell therapy: a mismatch between eligible patients and actual patients treated

Despite the potential of CAR T-cell therapies, a large proportion of eligible patients struggle to access them.

A real-world retrospective study observed that between 2022 and 2024, only 25% of eligible LBCL patients (n=205) deemed fit for second line CAR T-cell therapy received treatment, and non-curative intent treatments were often used instead.[57] A 2022 survey of US CAR T treatment centers (n=17) also revealed that only 25% of patients with MM referred for CAR T-cell therapy are believed to receive the treatment.[58]

In Europe, a 2020 comparative analysis study estimated that across France, Germany, Italy and Spain, an average of only 33% of third line and beyond relapsed or refractory LBCL patients received CAR T-cell therapy. The rate varied considerably across countries, with an average of 17% in Italy and 42% in France.[59] A recent IQVIA Institute report assessing Australia, Canada, France, Germany, Italy, Spain and the UK found that only 13% of relapsed or refractory large B-cell lymphoma patients who had beyond two lines of therapy received CAR T-cell therapy in 2022, within the EU countries and UK combined. The rate rose to just 18% in 2023.[6] Analysis in Germany using a patient-level simulation also found that an estimated 21% of potentially eligible LBCL patients (n=2191) were misallocated to another treatment approach due to clinical and non-clinical reasons, leading to reduced overall survival.[60]

In short, there are still too many barriers preventing eligible patients from accessing CAR T-cell therapy. These barriers can be summarized under the three following areas:

1. **Awareness and understanding of CAR T-cell therapy**
2. **Resources and capacity for CAR T-cell therapy**
3. **Sustainable and innovative financing approaches to manage the costs of treatment and care**

The next section brings focus to areas where there are opportunities for change, outlining the strategic imperatives that support and drive that change.

5. Opportunities for change

The Steering Committee discussion was complemented by a comprehensive literature review to identify the key barriers to treatment across these three areas, informing this section of the report. Published literature was retrieved through a literature search in PubMed while other literature including policy documentation was collected through interaction with Steering Committee members and handsearching.

While some challenges are more specific to certain regions, the Steering Committee has focused primarily on those that are applicable across countries and indications. Progress has been made in all these areas, and case studies are included here and in an appendix to provide inspiration and demonstrate how and where change is possible.

5.1. Awareness and understanding of CAR T-cell therapy

5.1.1. Limited knowledge or experience of CAR T-cell therapy among some HCPs and preference for other treatments

For many patients, community-based HCPs (those beyond designated treating centers) make the initial referral for CAR T-cell therapy. In the US, more than half of people with cancer receive care within community-based practices,[61] and CAR T-cell therapy treatment centers depend on community-based hematologists or oncologists for referrals.[62]

However, knowledge gaps among some HCPs around CAR T-cell therapy and the need for timely treatment may limit referrals for eligible patients.[8] A 2024 IQVIA Institute analysis covering seven countries (Australia, Canada, France, Germany, Italy, Spain, and the United Kingdom) found that ~70% of referring physicians stated they would benefit from more, or a lot more, information about CAR T-cell therapy.[6]

In addition, HCP preferences for other treatment options and established standards of care can be a barrier to referral for CAR T-cell therapy – in one US study, physician preference for conventional treatments was the primary barrier to CAR T-cell therapy for 32% of patients (n=493) treated in community practices.[63]

Nonetheless, the use of CAR T-cell therapy has increased in recent years,[64] and educational initiatives, such as online educational materials, peer-to-peer best practice sharing,[65,66] and dedicated educational sessions at congresses[67] are being implemented, and knowledge gaps are being filled. CAR T-cell therapy specialists are also proactively educating referring centers to improve patient care and optimize the referral and treatment process.[68] It is vital that this happens consistently across geographies and on an ongoing basis.

5.1.2. HCP reservations in referring people for CAR T-cell therapy

A survey of two groups of US community oncologists interviewed at two separate time points (Feb 2019 (n=59), Nov 2019 (n=55)) found that 46% and 29% had not referred any patients for CAR T-cell therapy, citing cumbersome logistics, high cost and toxicity as the main barriers.[62] While referring HCPs' knowledge of and experience with CAR T-cell therapy have improved over time, reservations about CAR T-cell therapy may persist.[62]

Another survey of US community-based hematologists and oncologists (n=45) in 2021 found they had limited experience with CAR T-cell therapy in multiple myeloma and expressed concerns about its safety and potential toxicity (33%), access (24%) and cost (18%).[69]

Community healthcare professionals are on the frontlines of cancer care, serving as trusted partners to patients and their families throughout their treatment journey. Ensuring these clinicians and their patients have access to clear, consistent, and evidence-based information about CAR T-cell therapy is essential for advancing equitable cancer care."

Meagan O'Neill

Executive Director, Association of Cancer Care Centers

CASE STUDY

Supporting community oncology to deliver CAR T-cell therapies in the US

Access to CAR T-cell therapy is still concentrated in large academic medical centers, creating logistical challenges for patients in rural or underserved areas.[70]

In 2021, the Association of Cancer Care Centers (ACCC) launched the "Bringing CAR T-cell Therapies to Community Oncology" initiative to help community cancer programs and practices obtain the education and tools they need to offer CAR T-cell therapy locally.[71]

The ACCC resources offer guidance and tips on the operational infrastructure needed for a successful CAR T-cell therapy program.[71,72] By bridging knowledge and infrastructure gaps between academic and community settings, the ACCC initiative is helping to expand access to CAR T-cell therapy, enabling more patients to receive treatment closer to home.

Further details available in the Appendix.

5.1.3. Patient reservations around the safety profile and efficacy of CAR T-cell therapy

Patients who are eligible for CAR T-cell therapy may also have some reservations about the treatment. In a study assessing key barriers to CAR T-cell therapy, patient refusal was a barrier in approximately 33% of cases.[63]

It is understandable that the decision to receive CAR T-cell therapy raises uncertainties for some people. These may include concerns around the management of potential side effects and the long-term safety profile of genetically modified T-cells,[73] worries about travel, time off work, and financial burden.[74] In an HCP survey in seven countries (Australia, Canada, France, Germany, Italy, Spain, and the United Kingdom), patient choice (due to clinical or side effect considerations) was a key reason for patients not receiving CAR T-cell therapy according to treating physicians (n=129) (ranging from 17% in Australia to 54% in the UK). Patient choice due to logistical or administrative reasons was also cited by HCPs in most countries (ranging from 4% in France to 46% in the UK).[6]

Providing clear accessible information can help people understand their treatment options, including the balance between adverse event risks and survival improvements.[75] While patients report an initial drop in quality of life and increase in psychological distress when initiating CAR T-cell therapy, both measures improve significantly within six months post-infusion ($p<0.001$) based on longitudinal model (n=103). In fact, at six months, reported quality of life is no different from that of the general US adult population.[76] CAR T-cell therapy has also demonstrated clinically meaningful improvements in quality of life compared to standard of care therapy after 100 and 150 days.[55] A meta-analysis revealed that CAR-T cell therapy improves patient-reported outcomes (PROs) in six domains including general health status, pain, fatigue, depression, social function, and cognitive function.[77] In the TRANSFORM study, the proportion of patients (n=90) with meaningful improvement in quality of life, cognitive functioning, and fatigue was higher at six months in patients provided with CAR T-cell therapy than those given standard of care.[78]

There are also concerns around the demands on caregivers.[79] The role of a dedicated caregiver is essential, particularly to provide care and support after CAR T-cell therapy, recognize early signs of treatment effects and immediately seek medical attention if needed. In the US (n=80) and UK (n=53) respectively, 36% and 27% of HCPs reported lack of caregiver support as a barrier to referral for CAR T-cell therapy.[9]

The burden on caregivers should not be overlooked. A longitudinal study of caregivers (n=69) of patients undergoing CAR T-cell therapy revealed that they have significant impairments to quality of life, with a substantial proportion experiencing psychological distress, highlighting the need for more supportive care interventions.[79]

> Patients have the fundamental right to consider their treatment options and choose what works best for them and their loved ones. To support them in making an informed choice, we need to make sure they have access to digestible, culturally sensitive and evidence-based information about CAR T-cell therapy, at the right time in their care journey."

Lorna Warwick

CEO, Lymphoma Coalition

5.1.4. Identifying patients that are eligible for CAR T-cell therapy

Early and accurate identification of eligible patients is crucial for the success of CAR T-cell therapy, maximizing its potential benefits. Delays can lead to disease progression, and can sometimes mean that people are no longer eligible for treatment.[80] Data has shown that in LBCL, when used earlier in the pathway, CAR T-cell therapy could potentially improve rates of sustained remission when compared with stem cell transplant, the historical standard of care, in refractory patients or in patients that relapse within 12 months from previous line of therapy.[41]

While the use of CAR T-cell therapy in the real-world setting has expanded beyond the criteria used in clinical trials, a lack of knowledge among some non-specialist or referring HCPs about the patient selection criteria may limit referral of eligible patients.[8] For example, some HCPs may use transplant eligibility criteria to assess patient eligibility for CAR T-cell therapy, but the two are not the same.[81]

The eligibility criteria for CAR T-cell therapy can vary based on multiple factors, including type of product, prior therapies, comorbidities, Eastern Cooperative Oncology Group (ECOG) performance status and organ function.[82,83] Interpretation of these eligibility criteria is often dependent on the experience of the HCPs and centers with administering CAR T-cell therapy. In one study, 17% of US HCPs (n=64) and 27% of UK HCPs (n=49) cited lack of clarity over eligibility criteria as a key challenge with the CAR T-cell therapy eligibility determination process.[9]

Given the rapidly evolving evidence in the real world, there is growing recognition that a multidisciplinary discussion between referring and treating clinicians should take place to enable early and accurate identification of eligible patients, particularly in situations with borderline parameters for some of the criteria.[8] Supporting accurate, efficient and early identification and referral of patients eligible for CAR T-cell therapy can also be done through the development of clinical guidelines and clinical education programs.

“A person’s potential eligibility for CAR T-cell therapy should be assessed on a case-by-case basis, with referring and treating physicians working together. This is one of the core principles of the RECUR framework for large B-cell lymphoma, developed by the American Society for Transplantation and Cellular Therapy, the Association of American Cancer Institutes and the Association of Cancer Care Centers.”

Dr. Miguel Perales

Past President, American Society for Transplantation and Cellular Therapy;
CAR T Vision Steering Committee Co-Chair

CASE STUDY

Identifying people who are eligible for CAR T-cell therapy in the US

For CAR T-cell therapy, timely identification and referral are important first steps in helping eligible patients get the most out of treatment. Delays in referral could lead to disease progression, making some people ineligible for treatment.[8]

In 2024, the American Society for Transplantation and Cellular Therapy (ASTCT), the Association of American Cancer Institutes (AACI), and the Association of Cancer Care Centers (ACCC) launched the RECUR initiative – a multidisciplinary program that aims to empower oncologists, HCPs and patients with a strong understanding of the factors needed for successful CAR T-cell therapy.[84]

The three organizations involved recognized that an effective framework for patient identification should include both clinical and non-clinical factors that could influence eligibility. With a focus on large B cell lymphoma (LBCL), they created the RECUR framework to support rapid identification in community settings and referral to accredited treatment centers.[85]

If they RECUR, you should refer:[85]

1. **R**elapsed/refractory LBCL: Any person with relapsed or refractory LBCL should be referred for a consult with a CAR T-cell therapy specialist
2. **E**very age and comorbidity: Age and comorbidity should be evaluated on a case-by-case basis by a CAR T-cell therapy specialist
3. **C**aregiver support: Discuss the need for support and continuum of care throughout the patient journey
4. **U**rgency to recommend consult: Rapid identification and referral is important for people to undergo timely evaluation for CAR T-cell therapy
5. **R**eceive patients returning post-CAR T: Streamline communication across teams within the local network to optimize local care of patients' local teams to optimize care for people returning after CAR T-cell therapy

Building on the above, the RECUR initiative hosts educational programs, provides resources and acts as a platform for knowledge exchange to support HCPs and patients in navigating CAR T-cell therapy.[84]

Further details available in the Appendix.

CASE STUDY

Supporting early identification and referral in Spain

Timely identification and referral are an important first step in the patient journey to CAR T-cell therapy. The delivery of CAR T-cell therapy is influenced by both clinical and system factors, which determine whether eligible patients are offered treatment.[86]

In 2024, three leading professional societies in Spain launched the IDEaL project (Identificación y Derivación Temprana de Pacientes con Linfoma Candidatos a Terapias CAR-T). Its aim was to analyze the CAR T-cell therapy landscape in Spain, and to develop recommendations to improve identification and referral for eligible people living with lymphoma. The experts involved represented the Spanish Society of Hematology and Hemotherapy (SEHH), the Spanish Group for Lymphoma and Bone Marrow Transplants (GELTAMO) and the Spanish Group for Hematopoietic Transplant and Cell Therapy (GETH-TC), with funding provided by Gilead and Kite.[86]

The IDEaL project's CORE working group consisted of nine hematology specialists, who developed practical recommendations and specific guidance for each type of lymphoma with a European Medicines Agency-approved indiciation for CAR T-cell therapies. They are available online and free to use, supporting hematology specialists around Spain in determining eligibility for CAR T-cell therapy.[86]

Further details available in the Appendix.

Vision Goal

Increase awareness and understanding of CAR T-cell therapy

To expand access, it is critical to continue to enhance knowledge and awareness of CAR T-cell therapy across all stakeholders so that:

- HCPs in referral centers can identify potentially eligible patients for CAR T-cell therapy early and refer to specialists for consultation with urgency
- Eligible patients and their caregivers understand the clinical benefits and risks, as well as logistical and financial considerations of CAR T-cell therapy to make informed choices about treatment
- Policymakers and payors understand the value of CAR T-cell therapy and collaborate with stakeholders to address systemic barriers to treatment and care

5.2. Resources and capacity to deliver CAR T-cell therapy

5.2.1. Treatment delivery limited to large, accredited treatment centers

Some countries concentrate the use of cellular therapies like CAR T-cell therapy to a limited number of centers. A review of 25 countries revealed that CAR T-cell therapy center density varied significantly, from 0.3 to 11.4 per 10 million inhabitants – a much higher variation when compared to allogeneic or autologous hematopoietic cell transplantation (HCT) centers.[87] In the US, some centers are situated within miles of each other, while other states have no centers.[88]

Distance from treatment centers may restrict patient access to CAR T-cell therapies particularly for those in smaller communities and rural areas. One study found the likelihood of receiving a CAR T-cell therapy was reduced by 40% when patients lived two to four hours from their nearest treatment center.[89]

Patients receiving CAR T-cell therapy are currently required to be closely monitored for treatment-related side effects and to stay near the treatment center for four weeks post-infusion,[90,91] despite recent evidence that a reduced monitoring period may be appropriate.[92]

Furthermore, patients are expected to refrain from driving for eight weeks post-infusion. Such restrictions may impose significant logistical and financial burden for many patients and caregivers, particularly for those in lower socioeconomic households.[93] In one US study, 7.3% of CAR T-cell therapy recipients (n=4,396) were from neighborhoods with a median income less than $40,000, suggesting people from lower socioeconomic status may not have the means to meet the FDA-mandated requirement of travelling and living close to a treatment center for up to four weeks.[94]

HCPs recognize the logistic considerations for patients, and in some cases, it prevents them from referring people for CAR T-cell therapy. In a survey of hematologists and oncologists, 36% of those in the US (n=80) and 38% of those in the UK (n=53) stated that 'travel distance' was a challenge that impacted their decision to refer eligible patients.[9]

Therefore, a more widespread distribution of centers, such as establishing new centers in community hospitals and outpatient settings,[95] would enable more equal opportunities for patients to access CAR T-cell therapy and improve care.[96]

People who choose CAR T-cell therapy should have access to local resources and support services that can help them manage any travel, accommodation or financial considerations, including for their care partners. That type of support and information is crucial to tackle socioeconomic inequalities in access to CAR T-cell therapy."

Meghan Gutierrez

CEO, Lymphoma Research Foundation

One US study showed that average travel time and distance were significantly reduced by 23% and 30%, respectively, when access was expanded to include community hospitals and other oncology specialty treatment centers.[93] A systematic literature review of outpatient administration of CAR T-cell therapy revealed that comparable outcomes in safety profile, efficacy, and quality of life were observed to inpatient administration while a reduction in the economic burden was also observed.[97]

With demand for CAR T-cell therapies likely to expand in the future, advanced planning is needed across indications to define the evolution of the CAR T-cell therapy center footprint to meet this demand. One such consideration includes the setting up of infrastructure to ensure the safe delivery of CAR T-cell therapy. The application and compliance of quality and safety standards, set by accreditation bodies such as Foundation for Accreditation of Cellular Therapy (FACT) in the US and the Joint Accreditation Committee (JACIE) in Europe, is a key step. Pharmaceutical manufacturers, too, have specific qualification procedures that centers must complete before offering CAR T-cell therapies. For new and smaller centers, navigating the complexity of initial accreditation, ongoing audits, provider training, outcomes reporting, and product logistics can be overwhelming.[98] A review in the US identified repetitive processes in both initial and ongoing evaluations, pointing to an opportunity to streamline duplicative accreditation and auditing of clinical sites[98] – particularly as HCPs gain experience with CAR T-cell therapy and become more adept at managing adverse events. Standards addressing care delivery in decentralized models and efficient corresponding accreditation processes will be essential to reducing delays to patient access to CAR T-cell therapy. Best practices can also be shared to enhance knowledge and build capability.

Other practical factors such as upfront investment in infrastructure expansion and staffing will also need to be considered when establishing new centers.[99] Rigorous financial planning and access to capital is essential to support the long-term viability of outpatient or decentralized CAR T-cell therapy models.[100]

“

We see a real opportunity for stakeholders in the CAR T-cell therapy community to continue working together to move towards greater standardization and harmonization of processes, to maximize efficiency while protecting the highest standards of care and patient safety.”

David Schmahl

CEO, Foundation for the Accreditation of Cellular Therapy (FACT)

CASE STUDY

Harmonizing qualification schemes to reduce inspection burden in Europe

CAR T-cell therapy is delivered by select treatment centers, which are formally evaluated by bodies such as the Foundation for Accreditation of Cellular Therapy (FACT) in the US and the Joint Accreditation Committee (JACIE) in Europe.[101] Commercial manufacturers also conduct their own inspections to authorize a center to provide a treatment[102] – the criteria for these inspections can differ between manufacturers and products.

In 2022, the GoCART Coalition launched an expert-led working group to reduce the inspection workload for centers, while protecting product quality and patient safety. The coalition – founded in 2020 by European Hematology Association (EHA) and the European Society for Blood and Marrow Transplantation (EBMT) – is a multi-stakeholder group working together to maximize the potential of cellular therapies in Europe.[103]

The expert working group consisted of industry representatives, researchers, clinicians, nurses and JACIE colleagues. It compared FACT-JACIE standards against manufacturer requirements for treatment centers and found substantial overlap. As a result, centers holding JACIE accreditation can now opt for a reduced or remote audit focused on product -specific requirements for cell therapies from several global manufacturers (subject to market authorization holders' agreement and obligations).[103]

Further details available in the Appendix.

CASE STUDY

Streamlining onboarding processes for CAR T treatment centers in the US

The US Food and Drug Administration (FDA) mandates product-specific education and training to ensure the safe use of CAR T-cell therapies.[104] This is delivered through the Risk Evaluation Mitigation Strategies (REMS) program.[104] As the number of approved CAR T-cell therapies increases, treatment centers will face a growing inspection burden.

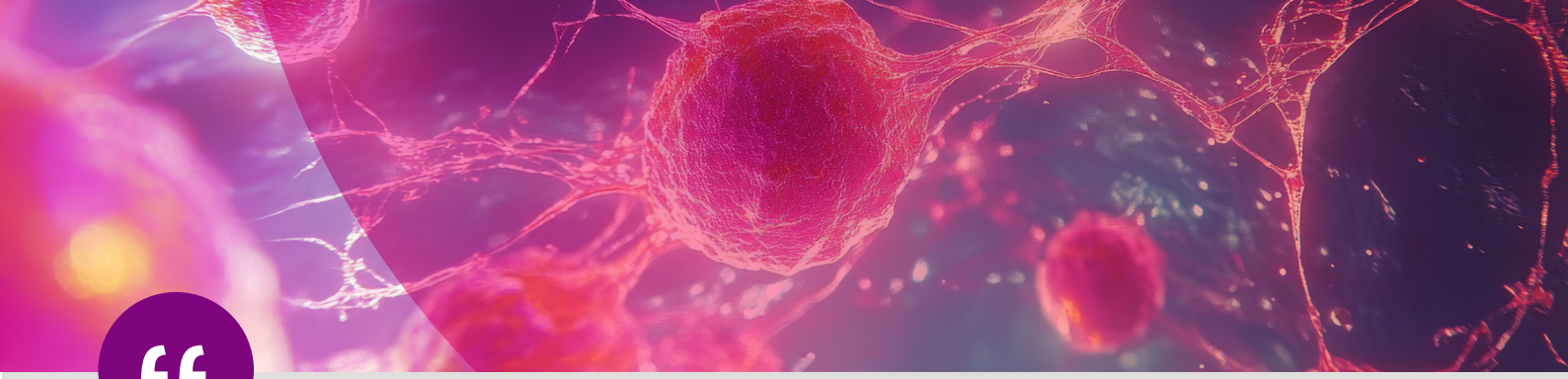
Recognizing that approximately 80% of the requirements for clinical site onboarding and ongoing operations are common across different manufacturers, the American Society for Transplantation and Cellular Therapy (ASTCT) launched the 80/20 Initiative. The initiative aims to standardize procedures to improve efficiency of onboarding and cost-effectiveness.[98]

The 80/20 Task Force convened multi-stakeholder workshops to identify and prioritize common challenges in the onboarding and maintenance of operations at treatment sites, and ways to streamline the process.[98,104] Key recommendations from the second workshop included:[104]

- Conducting training programs led by treatment centers and/or professional societies to replace manufacturers' product training
- Reporting standardized data points into a central, accessible repository for tracking of safety trends and identification of new signals
- Enabling accrediting bodies to attest to programs' quality and ongoing compliance with field safety expectations to replace initial manufacturer evaluation and ongoing REMS audit

The Task Force's recommendations were shared with the FDA at the Cell Therapy Liaision Meeting and in multiple professional society meetings and public forums with regulators, manufacturers, and FDA representatives.[104] Recently, the FDA scaled back several of the features of existing CAR T-cell therapy REMS programs redundant to standard clinical practice, including requirements related to manufacturer-created training, product-specific testing of trained staff and data reporting to manufacturers.[104]

Further details available in the Appendix.



> Undergoing treatment for any type of cancer is an intense experience for people and their families. Having the option to be treated or monitored closer to home can help relieve some of the additional stressors and reduce some of the inequities in access to CAR T-cell therapy."

Yelak Biru, MSc

Immediate Past President, International Myeloma Foundation

5.2.2. Referral challenges and efficiency of referral networks

Inefficiencies in the referral process create barriers to timely patient access to CAR T-cell therapy, even where referral networks exist. Network efficiency is often related to the structure and size of healthcare delivery systems. Large, fragmented systems, such as in the US, will likely have more challenges in care coordination and streamlining processes compared to centralized systems.[105]

Referring centers should have direct lines of communication to treatment centers to discuss questions regarding patient eligibility, facilitate referrals, and ensure a smooth transfer of care.[8] Rapid referral is vital, especially for higher-risk patients, to prevent delays that may jeopardize a person's ability to receive CAR T-cell therapy. In one study, more than one-third (37%) of respondents (n=371) said that improved communication between community HCPs and CAR T treatment centers would facilitate prescription of CAR T-cell therapies.[106] In another survey, 57% of UK HCPs (n=49) and 27% of US HCPs (n=64) indicated that the time required to communicate between referring and treatment centers was a challenge in determining eligibility.[9]

Formalized guidance may help to enhance coordination of care between CAR T-cell therapy treatment centers and referring centers.[107] Additionally, stated goals may also help to expedite referral times – for example, some large cancer institutes in the US have set goals to accept new patients within 24 hours.[108] While such goals may not be achievable in every case, a statement of intent helps to set expectations for all parties involved.

CASE STUDY

Reducing disparities in access to cell therapy in the US

Equitable access to cell therapy (CT) and hematopoietic cell transplantation (HCT) remains a challenge due to sociodemographic factors, including race and poverty.[109]

To address this in the US, the American Society for Transplantation and Cellular Therapy (ASTCT) and the National Marrow Donor Program (NMDP) created the ACCESS Initiative in 2022. The initiative aims to reduce barriers to CT and HCT and promote equal access through changes in practice and policy.[110]

The ACCESS initiative formed three multi-stakeholder committees to drive the program:[109]

1. Awareness: Increase awareness and education among patients and healthcare providers
2. Poverty: Identify patients at high risk of adverse outcomes due to socioeconomic adversity and develop initiatives to improve access and survival
3. Racial and ethnic inequity: Improve equity in access and outcomes for all cell therapy recipients

To support knowledge-sharing, the Awareness Committee established the Regional Physician Exchange Program, to give transplant and hematology or oncology physicians a platform to share experiences, insights and challenges.[111]

In 2023, the Poverty Committee commissioned a survey of all 50 US states to understand Medicaid coverage for CAR T-cell therapy and HCT. The findings revealed substantial geographical variation in coverage and eligibility criteria.[112] In response, ASTCT and NMPD are creating clinical guidelines on CT and HCT for state Medicaid offices to reference and liaising with state programs to align their coverage with current clinical standards.[110]

Further details available in the Appendix.

5.2.3. Delays between referral and commencement of treatment

The time between initial referral and receiving CAR T-cell therapy varies across geographies, and some patients may become ineligible for treatment during this time. In a survey of 129 treating physicians across seven countries (Australia, Canada, France, Germany, Italy, Spain and the UK), the percentage stating that it took two months or more from initial referral to commencement of treatment ranged from 37% in Canada to 83% in the UK.[6]

Delays during this period can be caused by a range of factors, including treatment center capacity limitations, manufacturing timelines and delays. For instance, limited capacity at the CAR T-cell therapy center was reported by 40% of HCPs in the US (n=73) and 58% of HCPs in the UK (n=52) as a barrier to treatment for non-Hodgkin lymphoma (NHL) patients,[9] particularly as CAR T-cell therapy is primarily delivered in an inpatient setting.

Resources at treatment centers may become further constrained as more CAR T-cell therapies become commercially available. The need to expand apheresis capacity has recently been raised in Parliament in the UK.[113] Similarly, a review in Spain revealed that workforce capacity (e.g., hematologists and nurses) and beds are going to be key when the demand for CAR T-cell therapy increases.[114] A lack of available apheresis capacity is a bottleneck that could also become more acute in the future. In response, Spain has established apheresis-only centers to expand capacity within the healthcare system.[115]

Manufacturing timelines and delays are also a contributing factor. An analysis of data from the JULIET trial reported that 52 out of 167 patients with LBCL did not receive CAR T-cell therapy for reasons including death and dropouts due to manufacturing delays.[116] In multiple myeloma, real-world patient access to CAR T-cell therapy remains challenging owing to supply chain considerations impacting manufacturing.[117] Advances in manufacturing, including greater use of automation and rapid manufacturing protocols will help to improve manufacturing capacity limitations and may also positively impact product efficacy.[118]

> “System readiness and capacity comes through clearly as a persistent challenge in delivering CAR T-cell therapies. There are innovative and effective ways to build capacity within the system, and there is more we can do to plan effectively for current and future demand for CAR T-cell therapies.”

Professor John Gribben

Barts Cancer Institute London; European Hematology Association

CASE STUDY

Building capacity beyond CAR T treatment centers in France

Health system capacity is an important factor in the delivery of CAR T-cell therapy. For example, treatment centers need enough intensive care beds to manage potential treatment-related adverse events and apheresis units must be able to keep up with demand for CAR T-cell therapy to prevent any delays in treatment.[6]

As indications for CAR T-cell therapy are expected to expand, it is important to carefully plan capacity to manage the pressures on healthcare systems and ensure eligible patients can access treatment. In France, several CAR T treatment centers have found and built on capacity elsewhere in the system.[6] For example:

- Collaboration with the French Blood Collection Association (EFS) has developed apheresis capacity beyond the CAR T-cell therapy treatment centers.[6]
- Specialized rehabilitation centers offer patient monitoring and accommodation following CAR T-cell therapy infusion, which has helped release hospital beds at treatment centers in Montpellier and Lyon.[6]
- The Centre Hospitalier Universitaire de Montpellier has lowered their average patient hospital stay by three days by shifting lymphodepletion (temporarily depleting a person's T-cell numbers before CAR T-cell therapy) to an outpatient setting.[6] Similarly, Toulouse University Hospital and West Onco-Occitanie cancer network have outsourced lymphodepleting chemotherapy to their referring centers (n=163). This approach reduced hospital stays from a median of 20 to 14 days.[119]

Further details available in the Appendix.

Underpinning all our advocacy as the CAR T Vision Steering Committee is the belief that CAR T-cell therapies will continue to evolve and mature, guided by robust collaboration and pioneering innovations emerging from projects like T2EVOLVE. Together, we are committed to accelerating progress, driven by a passionate, talented research community dedicated to transforming patient outcomes."

Professor Dr. Michael Hudecek

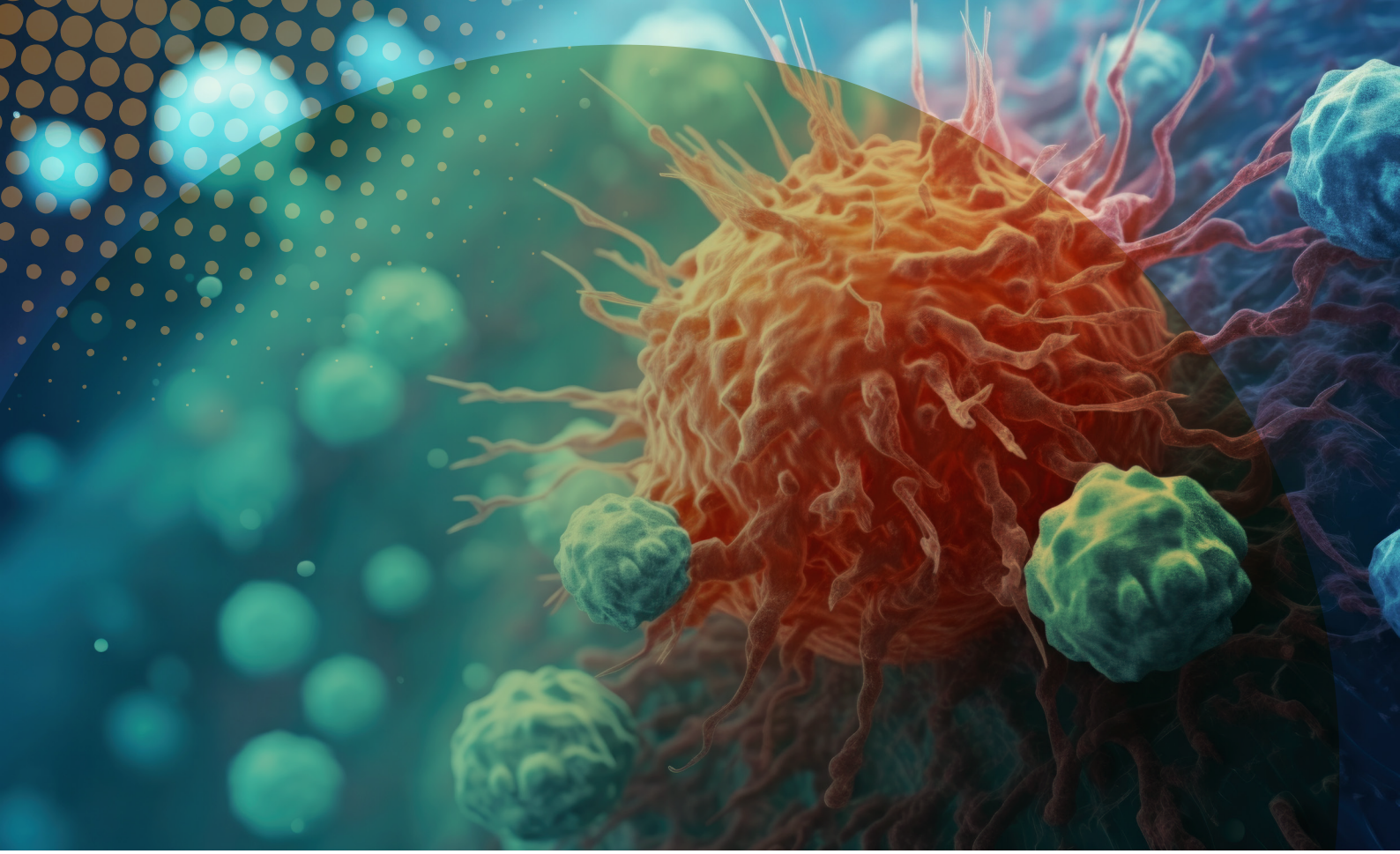
Universitätsklinikum Würzburg, Germany and
T2EVOLVE IMI Consortium

Overall, there are signs of progress in reducing the time between referral and receiving CAR T-cell therapy. A recent assessment of the Sarah Cannon Transplant and Cellular Therapy Network (SCTCTN) found that in the US, median time from consultation to CAR T-cell infusion declined from 207 to 108 days between 2018 and 2022. But even here, 41% of referred patients were unable to access CAR T-cell therapy due to disease progression or poor health.[120] Time is of the essence with CAR T-cell therapy, and there is work still to do.

One element that the CAR T Vision Steering Committee really wanted to get across is a sense of urgency – the urgent need for policy and system change to improve patient access to CAR T-cell therapies, but also urgency in getting patients from referral to treatment centers to ensure they can get the most out of their treatment."

Dr. Anna Sureda

Clinical Hematologist, Professor and Cell Therapy Researcher;
CAR T Vision Steering Committee Co-Chair



Vision Goal

Expand resources and capacity to deliver CAR T-cell therapy

It is vital that we find ways to relieve the bottlenecks that can cause delays in referrals and treatment. In building and expanding capacity to bring treatment closer to home, we need to see that:

- Decentralized care delivery models – with the infrastructure and capital necessary to deliver care in accordance with quality and safety standards – are in place to bring care closer to people's homes
- Formalized processes and dedicated resources for coordination and communication between referral and treatment centers are in place, supporting eligibility assessment, referral and swift transfer of patients
- Manufacturer requirements for treating centers are harmonized to reduce duplication
- Qualification processes for treating centers are streamlined to maximize efficiency and reduce administrative burden, while maintaining quality and safety standards consistent with larger, integrated medical systems already administering CAR T-cell therapies
- Forecasting and demand planning processes are in place to support staff and expand health system capacity as more cell therapies are approved for further indications

5.3 Sustainable and innovative financing of treatment and care

5.3.1. Existing reimbursement frameworks limit access to CAR T-cell therapy

Significant work has been done to evolve HTA methods and models to enable broader assessments of the value of one-time, potentially transformative therapies that have a high upfront cost but demonstrate value over time.[121] Although there has been much discussion around utilizing different approaches for Advanced Therapy Medicinal Products (ATMPs) such as CAR T-cell therapies, most HTA bodies prefer to use a standardized approach for all health technologies.[122] Therefore, while some systems have demonstrated willingness to embrace CAR T-cell therapy, some reimbursement challenges remain.[123]

For some HTA bodies and payors, the limited clinical trial data, often derived from small, single-arm studies, has been cited as a limitation in determining their benefit and value.[124] In other systems, concerns have been raised regarding the ability of HTA methods and reimbursement models to accurately capture the long-term value of CAR T-cell therapies.[125,126,127] In one study of different models used by HTA bodies on the long-term benefits of CAR T-cell therapy in both young and older patients, the modelled benefit in terms of quality-adjusted life-years gained for young patients with ALL varied substantially by HTA agency. The study concluded that the high variability "suggests a need for alternative approaches to assess value for money".[128]

The uncertainty regarding the value of CAR T-cell therapy has led to significant disparity in HTA recommendations across different countries. An analysis of reimbursement decisions made by HTA bodies of the G7 countries and Australia for all 12 CAR T-cell indications approved in the US up to January 2024, revealed that the countries with the most recommendations for funding were France and Germany (11, 92%), followed by Japan with 9 (75%) indications, Italy and Canada, 8 (67%), with England (6, 50%) and Australia (4, 33%) with the fewest reimbursed indications.[129]

Payors and HTA bodies are major stakeholders and need to be a part of the conversation. As more complex and costly treatments come to market, typically through accelerated regulatory pathways, HTA methodologies will continue to evolve to determine the value of the treatments to patients and healthcare systems. We need to ensure we adopt a lifecycle approach to HTA, and introduce innovative reimbursement models to address uncertainties and support access to technologies like CAR T-cell therapies."

Brian O'Rourke

Independent healthcare advisor
and expert in the science and practice of HTA

Reimbursement frameworks need to evolve to reflect the added clinical and economic value of CAR T-cell therapy for patients and society. With increased demand and pressure on cancer services, CAR T-cell therapy offers a potential route to unlock efficiencies in care for some blood cancers; its potentially curative effect means that patients with high unmet need conditions could be treated successfully, decreasing need for supportive care and reducing the indirect societal costs of illness.[41]

Real-world evidence (RWE) is already playing a critical role in some jurisdictions in capturing the value of CAR T-cell therapies and informing reimbursement decisions. As innovative payment models for CAR T-cell therapy gain momentum, there are opportunities to maximize RWE including greater cross-country collaboration and use of RWE to manage long-term clinical and economic uncertainty, while supporting patient access to CAR T-cell therapy.

These measures, when added to future cost care reductions, expanded access and innovative financing partnerships, will contribute to the long-term sustainability of CAR T-cell therapy.

5.3.2. Delays between reimbursement and patient access

Even when national funding and reimbursement is approved, patient access can be hindered by additional layers of decision-making and administrative burden, for both patients and health systems. Often, there are additional exclusionary criteria and/or requests for further clinical information or assessments beyond the labeled indication. In Spain, approval is determined by a national multidisciplinary committee, who evaluate eligibility on a case-by-case basis.[130] In England, a National CAR T Clinical Panel (NCCP) meets to assess patient eligibility and prioritization.[107] Similarly, in the Netherlands, the Dutch CAR-T Tumorboard meets twice a week to discuss CAR-T eligibility and treatment strategies for referred patients.[80] Such approval processes can become highly burdensome for patients, bottlenecks for care, and disease progression during the evaluation process can mean people are no longer eligible for CAR T-cell therapy.[80]

In the US, measures such as prior authorization or step therapy protocols,[10] as well as 'single case agreement' (SCA), hinder access and result in delayed treatment.[131]

These measures often require patients to provide detailed medical justification from the treating HCP. It may include patients being subjected to additional tests and screenings to determine whether they meet an insurer's criteria for treatment.[132]

Unfortunately, there are cases where a patient's cancer has progressed while waiting for CAR T-cell therapy funding approval.[133]

5.3.3. Payor reimbursement does not always cover the full cost of CAR T-cell therapy and care

CAR T-cell therapy treatment centers often take on significant financial risk, as they may not be adequately compensated by insurers or payors to fully cover the treatment costs.

Across the European Union, there are differences in reimbursement schemes between the different Member States. In some countries, the associated costs of pre- and post-care are not reimbursed sufficiently.[91]

In the US, current reimbursement rates may leave some treatment centers with financial losses,[134] which could disincentivize them to offer CAR T-cell therapy as a treatment option.

Due to costs associated with hospitalization and patient management, it has been estimated that hospitals can lose upwards of $100,000 USD per patient when they provide CAR T-cell therapy to a patient with Medicare on an inpatient basis.[135] In addition, some insurers do not reimburse treatment centers until many months after patients have received treatment.[10] With treatment centers facing high financial risk of treating people with CAR T-cell therapy without a guarantee of payment, they may ultimately choose to limit or decline treatment. To facilitate patient access, it is important that insurers adapt their policies not only to cover the hospitals' costs of treatment and care but also align with evolving treatment paradigms for CAR T-cell therapy as its use expands across different indications.

Patients and caregivers are also often faced with high out-of-pocket costs for travel and accommodation in order to receive CAR T-cell therapy. Travel can be particularly costly and burdensome on patients and carers living in rural and remote communities, exacerbating inequities in patient access.[136] This can prevent some eligible patients from proceeding with therapy or put patients and their families in financial difficulties.

Vision Goal

Develop sustainable and innovative financing approaches to manage the costs of treatment and care

As more CAR T-cell therapies in different indications become available, it is essential that reimbursement and payor methodologies are able to keep pace with this innovation and that there are innovative and sustainable funding to cover the full cost of treatment and care in a timely way for all eligible CAR T-cell therapy patients. We must therefore work to ensure that:

- Economic models reflect that the upfront budget impact of CAR T-cell therapy can be mitigated in the long-term by reductions in healthcare spending
- Robust real-world data to support decision making on the clinical and economic value of CAR T-cell therapy is continually collected and utilized
- Innovative and sustainable contracting models ensure that patients have access to innovative treatments now and as more treatments become available
- Reimbursement for CAR T-cell therapy happens in a timely way to enable swift treatment, and covers the full cost of hospital treatment and care
- The long-term sustainability of CAR T-cell therapy is achieved by reductions in the total cost of care, expanded access and innovative financing partnerships

6. A call to action

This report provides the evidence base for why a CAR T Vision is needed, the challenges that it looks to solve, and the urgent action required to achieve it. It is a call to action for all stakeholders to unite with a single purpose to overcome the barriers that prevent eligible patients from having the opportunity for cure.

This is just the beginning.

We call on patient and caregiver organizations, HCPs, payors, HTA bodies, regulators, policymakers, legislators, and industry, to review this report and consider how you can contribute to joint efforts to ensure more eligible patients get access to CAR T-cell therapy in the next five years.

Building on this report, expert Working Groups will translate the Vision into local, measurable action, with measurement frameworks to track progress. Each Working Group will consist of Steering Committee members as well as additional ecosystem stakeholders and experts.

Creating a future where every eligible patient has the opportunity for cure with CAR T-cell therapy involves a complex ecosystem of partners, each with their own unique role to play in making the CAR T Vision a reality. To join the growing coalition of Vision endorsers and help inform future efforts, visit www.CARTVision.com or contact the Secretariat at visionforcart@incisivehealth.com for more information on how you can get involved.

It's time to seize the opportunity for cure.

CAR T VISION | It's Time for CAR T

Appendix

CASE STUDIES

Introduction

This case study compendium showcases real-world examples of implementable solutions to address three challenge areas to CAR T-cell therapy mentioned in the report:

- Awareness and understanding of CAR T-cell therapy
- Resources and capacity to deliver CAR T-cell therapy
- Sustainable and innovative financing approaches to manage the costs of treatment and care

PATIENT IDENTIFICATION AND REFERRAL

Spain: Supporting early identification and referral

Timely identification and referral are an important first step in the patient journey to CAR T-cell therapy. The delivery of CAR T-cell therapy is influenced by both clinical and system factors, which determine whether eligible patients are offered treatment. Recognizing this complexity, the Spanish Ministry of Health published a national Plan for the Approach to Advanced Therapies in the National Healthcare System in 2018.[86]

Building on the national policy environment, the IDEaL project (Identificación y Derivación Temprana de Pacientes con Linfoma Candidatos a Terapias CAR-T) was launched in 2024. Its aim was to analyze the CAR T-cell therapy landscape in Spain, and to develop guidance and recommendations to improve identification and referral for people living with lymphoma who are eligible for CAR T-cell therapy. The IDEaL project involved three leading professional societies (see below) and was sponsored by Gilead and Kite.[86]

- Sociedad Española de Hematología y Hemoterapia (SEHH – the Spanish Society of Hematology and Hemotherapy)
- Grupo Español de Linfoma y Trasplantes de Médula Ósea (GELTAMO – the Spanish Group for Lymphoma and Bone Marrow Transplants)
- Grupo Español de Trasplante Hematopoyético y Terapia Celular (GETH-TC – the Spanish Group for Hematopoietic Transplant and Cell Therapy)

The IDEaL project's CORE working group consisted of 9 hematology specialists, who developed practical recommendations and specific guidance for each type of lymphoma with a European Medicines Agency approved indication for CAR T-cell therapies.[86] The recommendations are based on working group insights and an online survey of 81 hematology specialists working in the National Healthcare Service (SNS). They are available online and free to use, supporting hematology specialists around Spain in determining eligibility for CAR T-cell therapy.[86]

US: Identifying patients who are eligible for CAR T-cell therapy

For CAR T-cell therapy, timely identification and referral are important first steps in helping eligible patients get the most out of treatment. However, HCPs, patients and caregivers may be unsure about whether to pursue this type of treatment. Delays in referral could lead to disease progression, making some people ineligible for CAR T-cell therapy.[8]

In 2024, the American Society for Transplantation and Cellular Therapy (ASTCT), the Association of American Cancer Institutes (AACI), and the Association of Community Cancer Care Centers (ACCC) launched the RECUR initiative – a multidisciplinary program that aims to empower oncologists, HCPs and patients with a strong understanding of the factors needed for successful CAR T-cell therapy.[84]

The three organizations took part in a roundtable to identify and prioritize the factors involved in CAR T-cell therapy eligibility and co-create a framework for rapid patient identification. The experts involved recognized that an effective framework for patient identification should include both clinical and non-clinical factors for eligibility. With a focus on large B cell lymphoma (LBCL), they created the RECUR framework to support rapid identification in community settings and referral to accredited treatment centers.[85]

If they **RECUR**, you should refer:[85]

1. **R**elapsed/refractory LBCL: Any person with relapsed or refractory LBCL should be referred for a consult with a CAR T-cell therapy specialist
2. **E**very age and comorbidity: Age and comorbidity should be evaluated on a case-by-case basis by a CAR T-cell therapy specialist
3. **C**aregiver support: Discuss the need for support and continuum of care throughout the patient journey
4. **U**rgency to recommend consult: Rapid identification and referral is important for people to undergo timely evaluation for CAR T-cell therapy
5. **R**eceive patients returning post-CAR T: Streamline communication across teams within the local network to optimize local care of patient's local teams to optimize care for people returning after CAR T-cell therapy

Building on the above, the RECUR initiative hosts educational programs, provides resources and acts as a platform for knowledge exchange to support HCPs and patients in navigating CAR T-cell therapy.[84] It is being disseminated amongst the professional bodies involved to ensure it is adopted as standard.

Italy: Addressing regional disparities in access to CAR T-cell therapy

In Italy, access to CAR T-cell therapy is concentrated in a few regions, creating disparities for patients in underserved areas.[137] Challenges include uneven distribution of authorized treatment centers, shortages of specialist staff and fragmented referral pathways and reimbursement models.[137]

In 2022, The European House – Ambrosetti, Società Italiana di Leadership e Management in Medicina (SIMM), Gruppo Italiano per il Trapianto di Midollo Osseo (GITMO) launched the CAR-T Revolution initiative to assess the national access landscape and propose actions for more equitable and sustainable delivery of CAR T-cell therapies.[137]

Through expert consultation and policy analysis, the group identified key challenges and put forward recommendations to ensure sustainable future access, including:[137]

- Expanding and strengthening hub-and-spoke models to decentralize care delivery
- Establishing more efficient referral systems to streamline patient access
- Leveraging digital tools to support coordination among healthcare providers
- Introducing dedicated diagnosis related groups (DRGs) to standardize funding and reimbursement processes

The recommendations from this policy paper have been used to engage with policymakers and governments to advocate for increased CAR T-cell capacity and equity across regions in Italy.

US: Reducing disparities in access to cell therapy

Equitable access to cell therapy (CT) and hematopoietic cell transplantation (HCT) remains a challenge in the US due to sociodemographic factors, including race and poverty.[109] People from underserved groups often face greater obstacles in accessing these treatments.[109]

To help close these gaps, the American Society for Transplantation and Cellular Therapy (ASTCT) and the National Marrow Donor Program (NMDP) created the ACCESS Initiative in 2022. The initiative aims to reduce barriers to CT and HCT and ensure equal access to care and outcomes for all patients in need, through changes in practice and policy.[110]

The ACCESS initiative formed three multi-stakeholder committees to drive the program:[109]

1. Awareness: Increase awareness and education among patients and healthcare providers
2. Poverty: Identify patients at high risk of adverse outcomes due to socioeconomic adversity and develop initiatives to improve access and survival
3. Racial and ethnic inequity: Improve equity in access and outcomes for all cell therapy recipients, regardless of their race or ethnicity

To support knowledge-sharing, the Awareness Committee established the **Regional Physician Exchange Program**, to give transplant and hematology or oncology physicians a platform to share experiences, insights and challenges.[111] Peer-to-peer learning is a useful tool for physicians to observe best practices and stay updated on the evolving CT and HCT landscape.

In 2023, the Poverty Committee commissioned a survey of all 50 US states to understand

Medicaid coverage for CAR T-cell therapy and HCT. The findings revealed substantial geographical variation in coverage and eligibility criteria,[112] contributing to the inequalities in access to these treatments. In response, ASTCT and NMPD are creating clinical guidelines on CT and HCT for state Medicaid offices to reference, and liaising with state programs to align their coverage with current clinical standards.[110]

HEALTHCARE SYSTEM CAPACITY AND INFRASTRUCTURE

France: Building capacity beyond CAR T-cell therapy treatment centers

Health system capacity is an important factor in the delivery of CAR T-cell therapy. For example, treatment centers need enough intensive care beds to manage potential treatment-related adverse events and apheresis units must be able to keep up with demand for CAR T-cell therapy to prevent any delays in treatment.[6]

As indications for CAR T-cell therapy expand, it is important to carefully plan capacity to manage the pressures on healthcare systems and ensure patients can access treatment. In France, several CAR T treatment centers have found and built on capacity elsewhere in the system.[6] For example:

- Collaboration with the French Blood Collection Association (EFS) has developed apheresis capacity beyond the CAR T treatment centers.[6]
- Specialized rehabilitation centers offer patient monitoring and accommodation following CAR T infusion, which has helped release hospital beds at treatment centers in Montpellier and Lyon.[6]
- The Centre Hospitalier Universitaire de Montpellier has lowered their average patient hospital stay by 3 days by shifting lymphodepletion (temporarily depleting a person's T-cell numbers before CAR T-cell therapy) to an outpatient setting.[6] Similarly, Toulouse University Hospital and West Onco-Occitanie cancer network have outsourced lymphodepleting chemotherapy to their referring centers. This approach reduced hospital stays from a median of 20 to 14 days.[119]

US: Expanding CAR T-cell delivery through satellite models

Access to CAR T-cell therapy is often concentrated in large academic centers in cities, creating logistical barriers for patients who must travel to access treatment.[70]

To address this, the University of Pennsylvania (UPenn) developed a satellite expansion model to deliver CAR T-cell therapy through a network of affiliated and non-affiliated community hospitals.[138] UPenn manages key functions such as reimbursement strategy, adverse event management training, and education on the CAR T-cell care pathway for these satellite sites.[138] This model enables the community hospitals to operate independently while adhering to a shared framework of standards and protocols.

It has helped extend CAR T-cell therapy access to community hospitals to provide treatment and care closer to people's homes.

US: Supporting community oncology to deliver CAR T-cell therapies

Smaller community cancer programs may refer patients to larger centers for CAR T-cell therapies because of unfamiliarity with the treatment, inadequate reimbursement and infrastructure challenges.[71] As a result, access to CAR T-cell therapy is still concentrated in large academic medical centers, creating logistical challenges for patients in rural or underserved areas.[70]

In 2021, the Association of Cancer Care Centers (ACCC) launched the Bringing CAR T-cell Therapies to Community Oncology initiative to help community cancer programs and practices obtain the education and tools they need to offer CAR T-cell therapy locally.[71]

As part of this initiative, the ACCC shares effective practices on overcoming logistical and financial hurdles, and highlights tips on the operational infrastructure needed for a successful CAR T-cell therapy program.[71] This is delivered through a series of webinars and resources to help physicians identify patient candidates for CAR T-cell therapy and coordinate their care.[72]

By bridging knowledge and infrastructure gaps between academic and community settings, the ACCC initiative is helping to decentralize access to CAR T-cell therapy. Thus, helping more patients receive treatment closer to home and reducing barriers in access while maintaining high standards of quality and safety.

POLICY AND REGULATORY SUPPORT

Austria: Expanding equitable access to CAR T-cell therapy

Although CAR T-cell therapy has been available in Austria since 2019, access remained limited, with only a small proportion of eligible patients receiving treatment by 2021.[139] Identified barriers included restrictive patient selection criteria, suboptimal referral pathways, and limitations in funding and infrastructure.[139]

To address these challenges, a national policy initiative was launched by stakeholders from clinical, academic, and policy communities. The group conducted multi-stakeholder roundtable discussions which brought together clinicians, payors, and policymakers to discuss systemic barriers to access and propose actionable reforms.

The discussions resulted in the publication of a report with recommendations aimed at improving access to CAR T-cell therapy in Austria.[139] These included strengthening communication between referring and CAR T centers, setting up a CAR T-cell therapy registry and coordinating funding decisions through an independent national supervisory board.[139]

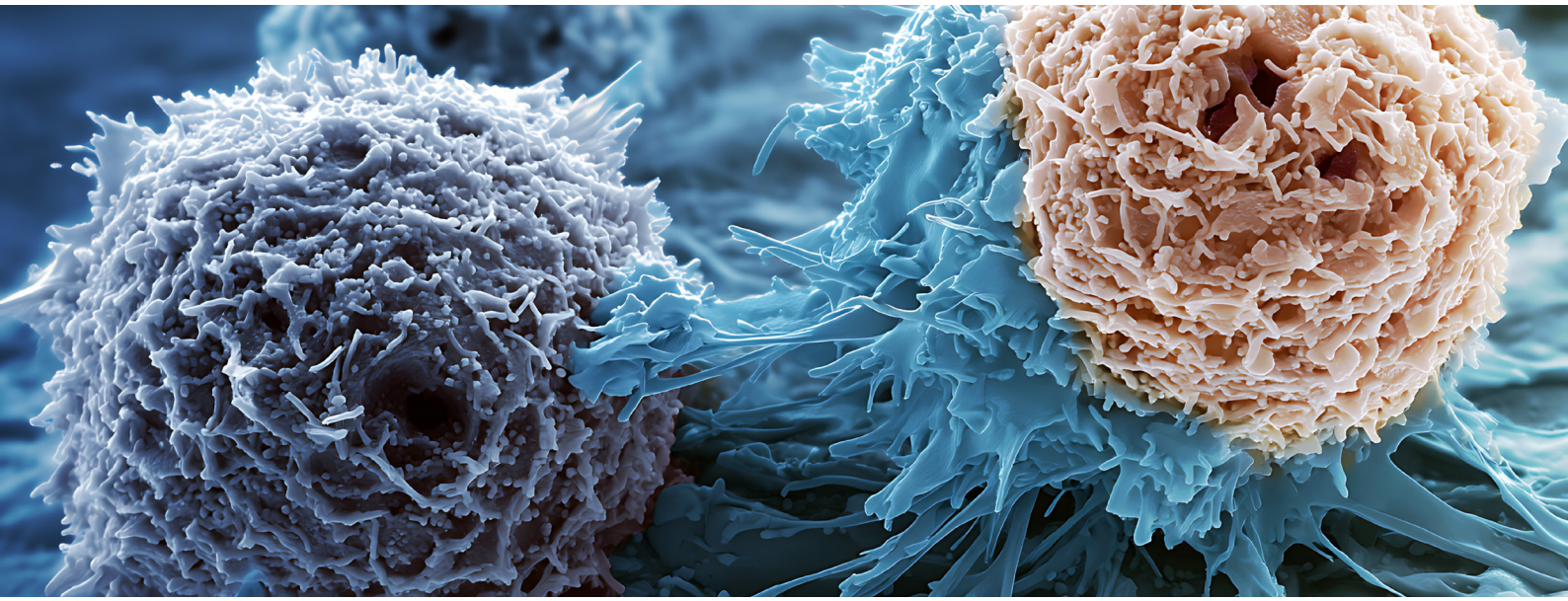
These proposals informed broader policy discussions and were cited in key forums including presentations at the EHA and ASH congresses and the annual meeting of the Austrian Hematology and Oncology Association (ÖCHO). As a result of these collaborative efforts, increased uptake of CAR T-cell therapy has been reported.

Germany: Creating a supportive policy environment for gene and cell therapies

National and regional policies, strategies and guidance have an important role in supporting the life sciences. They can boost inward investment, drive economic growth, advance research and development and help improve access to medicines.[140]

In 2022, the German Federal Ministry of Education and Research (BMBF) commissioned the Berlin Institute of Health (BIH) to coordinate the development of a National Strategy for Gene and Cell Therapies (GCTs). The initiative drew from eight expert working groups, with 150 stakeholders from across different sectors. The resulting paper was handed to the German Federal Government in December 2023 to guide the negotiation and finalization of a National GCT Strategy.[141]

The strategy paper highlights eight "fields of action" to cement Germany's position as a global leader in GCTs. Each field is presented with strategic objectives and proposed measures to implement (see below).[141] This initiative is effective because it is expert-led, patient-centric and proposes actionable recommendations at every stage of the CAR T-cell therapy journey (spanning topics like such as Research and Development (R&D) and regulation, as well as public awareness and patient support).



Field of Action	Example objective and/or measures[141]
Connecting and supporting stakeholders	Objective to strengthen national GCT networks, with a proposed measure of creating a "CGT network map" to provide a structured overview of relevant stakeholders.
Training and strengthening of skills in the area of GCT	Objective to develop training and professional development programs for junior and senior professionals.
Technology transfer	Objective to improve the conditions for the early recognition and realization of innovative potential of scientific findings, with proposed measure to establish a product development unit focused on GCT that can train, advise and support institutions.
Standards, regulations and regulatory framework	Objective to defragment and standardize competencies and processes in clinical R&D of GCT, and proposed measure to coordinate regulatory procedures and approvals through a central point (the Paul Ehrlich Institute).
Expansion of quality and capacities Good Manufacturing Practice	Objective to increase efficiency and accelerate processes in manufacturing, with proposed measure to create a central national production facility for critical starting materials for GCT.
R&D	Objective to improve the structural conditions for technology transfer research and development, with proposed measure to establish flexible funding formats with short lead-in times to cover unmet needs.
Market authorization and transition to healthcare provision	Objective to create flexible care and reimbursement models in the application of GCT, with a proposed measure to maintain the necessary flexibility in the benefit assessment and pricing in the German AMNOG process.
Interaction with society	Object to inform society about GCT by providing reliable and target group-specific information, with a proposed measure to establish a central web-based point of contract for quality-checked information.

UK: Leveraging the power of cross-center collaboration

Delivering innovative therapies often involves new ways of working for healthcare systems, including the National Healthcare Service (NHS) in the UK.[142] CAR T-cell therapy is delivered by select treatment centers, which are formally evaluated and accredited. Standards are set by the Joint Accreditation Committee (JACIE) in Europe for consistent quality and safety.[101]

The UK's Advanced Therapy Treatment Centre (ATTC) network was set up in 2018, connecting centers delivering Advanced Therapy Medicinal Products (ATMPs) in the UK,[142] including CAR T-cell therapies. It was set up with government funding from Innovate UK, which is an agency that supports companies in growing through the development and commercialization of new products and services.[143] The network includes four specialist hubs (see below),[142] which meet regularly and collaborate across topics such as clinical trials, training and education, patient and public involvement and engagement, patient recruitment and data collection.[144]

- Innovate Manchester Advanced Therapy Centre Hub (iMATCH)
- London Advanced Therapies Advanced Therapy Treatment Centre (LAT-ATTC)
- Midlands-Wales Advanced Therapy Treatment Centre (MW-ATTC)
- Northern Alliance Advanced Therapies Treatment Centre (NA-ATTC)[142]

Since its launch, the ATTC network has developed and shared knowledge and practices to support the NHS in delivering advanced therapies.[142] This has helped make the UK a more attractive place for life sciences investment.[142] It successfully increased patient access to ATMPs through clinical trial support and improvements to supply chain and logistics.[145] With new funding received in 2024, the network will expand its activities across:[145]

- Equity of access to transformative therapies
- Healthcare system readiness for ATMP clinical trials
- Improved ATMP workforce efficiency
- The UK's attractiveness to sponsors launching ATMP clinical trials
- Economic growth in priority locations in the UK
- Societal benefits from patients treated with ATMPs
- The number of ATMPs approved for use by the NHS

HARMONIZING ONBOARDING PROCESSES AND ACCREDITATION STANDARDS

Europe: Driving coordinated European action on cellular therapy access

In 2020, the European Hematology Association (EHA) and the European Society for Blood and Marrow Transplantation (EBMT) founded the GoCART Coalition - a European group of patient representatives, HCPs, pharmaceutical companies, regulators and medical organizations working together to promote patient access to novel cellular therapies.[146]

The GoCART Coalition is organized around five key pillars: data harmonization, standards of care, education and training, policy and advocacy and scientific excellence.[147]

Recognizing that there is significant overlap between different manufacturers on their requirements for site qualification processes, the standards of care group launched an expert-led working group to reduce the inspection workload for centers, while protecting product quality and patient safety.[148] The group consisted of industry representatives, researchers, clinicians, nurses and JACIE colleagues.[103] Through this, they were able to launch a new initiative which would allow centers holding JACIE accreditation to opt for a reduced or remote audit focused on product-specific requirements for cell therapies (subject to market authorization holders' agreement and obligations). This is the case for centers undergoing inspections with Bristol Myers Squibb, Janssen, Gilead and Kite and Novartis.[103]

The education and training working group has also launched an initiative with industry partners and national country representatives to develop a CAR T-cell therapy passport to harmonize training requirements and educational materials for HCPs.[65] As part of this, they are consolidating a core training program consistent with JACIE accreditation requirements, with passports tailored to each HCP role.[65]

US: Streamlining onboarding processes for CAR T-cell treatment centers

The US Food and Drug Administration (FDA) mandates product-specific education and training to ensure the safe use of CAR T-cell therapies.[104] This is delivered through the Risk Evaluation Mitigation Strategies (REMS) program, which involves manufacturers evaluating and monitoring treatment sites to ensure compliance.[104] As the number of approved CAR T-cell therapies increases, treatment centers will face a growing inspection burden involving qualification, ongoing auditing and reporting.

The American Society for Transplantation and Cellular Therapy (ASTCT) launched the 80/20 Initiative to streamline the onboarding and operational processes for clinical centers administering cell therapies.[98] Recognizing that approximately 80% of the requirements for clinical site onboarding and ongoing operations are common across different manufacturers, the initiative aims to standardize procedures to improve efficiency and cost-effectiveness.[98]

The 80/20 Task Force convened multi-stakeholder workshops to identify and prioritize common challenges in the onboarding and maintenance of operations at treatment sites, and ways to streamline the process.[98,104] The workshops brought together over 60 stakeholders, including clinicians, regulators, accrediting bodies and manufacturers.[98,104] In the second workshop, they identified key measures that would help simplify the qualification process, minimize duplication of efforts and ensure consistent safety standards across CAR T-cell centers:[104]

- Conducting training programs led by treatment centers and/or professional societies to replace manufacturers' product training
- Reporting standardized data points into a central, accessible repository for tracking of safety trends and identification of new signals
- Enabling accrediting bodies to attest to programs' quality and ongoing compliance with field safety expectations to replace initial manufacturer evaluation and ongoing REMS audit

The Task Force's recommendations were shared with the FDA at the Cell Therapy Liaison Meeting and in multiple professional society meetings and public forums with regulators, manufacturers, and FDA representatives.[104] Recently, the FDA scaled back several of the features of existing CAR T-cell therapy REMS programs redundant to standard clinical practice, including requirements related to manufacturer-created training, product-specific testing of trained staff and data reporting to manufacturers.[104]

By implementing these strategies, the "80/20 Initiative" aims to find efficiencies in the inspection process for treatment centers and facilitate broader and more equitable access to CAR T-cell therapies.

US: Reviewing clinical accreditation standards to ensure patient access

The Foundation for the Accreditation of Cellular Therapy (FACT) has announced the formation of a 'Community CAR T Working Group' (working group) to discuss and propose clinical accreditation standards for community-based providers of CAR T cell therapies.[149]

The working group builds on discussions around the multiple, complex challenges surrounding eligible patient access to these innovative therapies. Comprised primarily of community-based physicians currently administering—or preparing to administer—CAR-T cell therapies, the working group also includes leaders from academic medical centers, representatives of relevant professional societies and members of FACT headquarters.[149]

This effort will operate in association with the development of the upcoming third edition of the FACT Standards for Immune Effector Cells, scheduled for release later this year,[149] with the expected output being to guide physicians toward the development and maintenance of quality- and safety-focused infrastructure and systems closer to the homes and workplaces of eligible patients.[149]

FUNDING AND REIMBURSEMENT

Europe: Developing HTA models to capture the value of CAR T-cell therapies

One persistent challenge for CAR T-cell therapies is that traditional HTA models are often not fit-for-purpose to capture the characteristics of CAR T-cell therapy (e.g., as a one-time treatment).[133,150] T2EVOLVE is a consortium working to accelerate the process of developing CAR T-cell therapy in the European Union (EU) to support patient access to this type of technology, while providing guidance on costs and implementation for EU healthcare systems.[151]

In collaboration with the ASCERTAIN and JOIN4ATMP projects, T2EVOLVE are working on value-based, flexible assessment and reimbursement approaches that can capture the long-term patient benefit and support sustainable innovation for CAR T-cell therapies.[152] JOIN4ATMP has a dedicated work program focused on value assessment, pricing and reimbursement schemes for CAR T-cell therapy. Its aim is to use real-world data to map hurdles in the commercial uptake of Advanced Therapy Medicinal Products (ATMPs), including CAR T-cell therapies.[153] The initiative (currently ongoing) seeks to propose ways for manufacturers to improve their interactions with HTA bodies throughout the R&D process and propose alternative pricing and reimbursement schemes.[153]

Italy: Enabling rapid funding decisions

In Italy, funding for CAR T-cell therapy and associated care must be approved by regional authorities.[154] For patients referred to treatment centers outside of their home region, approvals must be obtained from authorities in the referring and receiving region, with costs ultimately billed to the patient's home region.[154] This process is time-consuming and can lead to delays, which can negatively impact patient eligibility and outcomes.[154]

In Lombardy, regional authorities promise funding decisions within 24 hours and cover procedure costs for out-of-region patients at regional CAR T-cell therapy centers if the home region refuses payment.[154] While not every region will have adequate resources to take this approach, it helps to minimize treatment delays and facilitate access to CAR T-cell therapy for patients, regardless of their region of residence.

US: Advocating for adequate reimbursement for hospitals delivering CAR T-cell therapy

Delivering CAR T-cell therapies is a complex process, which may not be reflected in local reimbursement policies. For treatment centers in the US, Medicare reimbursement did not cover the full cost of delivering CAR T-cell therapy under existing payment models.[155]

The US CAR T Working Group was set up to advocate for policy change to improve patient access to CAR T-cell therapy. It includes over 20 patient advocacy organizations (including Lymphoma Research Foundation), the Association of Cancer Care Centers, the American Society for Transplantation and Cellular Therapy, industry associations (including Alliance for Regenerative Medicine) and biopharmaceutical companies (including Gilead and Kite, Bristol Myers Squibb and Johnson & Johnson).

Through coordinated advocacy, the working group successfully engaged with the Centers for Medicare & Medicaid Services to advocate for the creation of a new Medicare Severity Diagnosis Related Group (MS-DRG) specifically for CAR T-cell therapy.[156] The revised MS-DRG more appropriately compensates hospitals for the costs associated with administering the therapy.[156]

This change in reimbursement policy has helped increase access to CAR T-cell therapy for Medicare beneficiaries and encourages more hospitals to provide the treatment to eligible patients.

PATIENT SUPPORT AND INFORMATION

Europe: Creating a digital hub for patients and caregivers

T2EVOLVE is a consortium working to accelerate the process of developing CAR T-cell therapy in the European Union (EU) to support patient access to this type of technology, while providing guidance on costs and implementation for EU healthcare systems.[151]

As part of their program, the consortium is developing a central digital hub for patients and caregivers, co-created with leading European patient advocacy groups and clinicians involved in CAR T-cell therapy. This will build on their existing patient hub, containing patient information resources co-created with Working Group of Patients and Caregivers (WGPC), EuroGCT, Acute Leukemia Advocate Network (ALAN), Myeloma Patients Europe (MPE) and Lymphoma Coalition.[157] This additional platform aims to provide accessible, multilingual educational resources, practical guidance, and support tools to empower patients and caregivers, thus enhancing patients' understanding of their CAR T-cell therapy journey.[157]

References

[1] National Cancer Institute. CAR T-cell therapy. Available online: https://www.cancer.gov/publications/dictionaries/cancer-terms/def/car-t-cell-therapy

[2] Abramson J, Palomba ML, Gordon LI, et al. Five-Year Survival of Patients (pts) from Transcend NHL 001 (TRANSCEND) Supports Curative Potential of Lisocabtagene Maraleucel (liso-cel) in Relapsed or Refractory (R/R) Large B-Cell Lymphoma (LBCL). Blood. 2024;144(1):3125. https://doi.org/10.1182/blood-2024-200204.

[3] Neelapu SS, Jacobson CA, Ghobadi A, et al. Five-year follow-up of ZUMA-1 supports the curative potential of axicabtagene ciloleucel in refractory large B-cell lymphoma. Blood. 2023 May 11;141(19):2307-2315. doi: 10.1182/blood.2022018893.

[4] Rives S, Maude S, Hiramatsu H, et al. S112: Tisagenlecleucel in pediatric and young adult patients (PTS) with relapsed/refractory (R/R) b-cell acute lymphoblastic leukemia (B-ALL): Final analysis from the ELIANA study. HemaSphere. 2022.6:13-14. DOI: 10.1097/01.HS9.0000843344.19780.98

[5] Xu J, Wang BY, Yu SH, et al. Long-term remission and survival in patients with relapsed or refractory multiple myeloma after treatment with LCAR-B38M CAR T cells: 5-year follow-up of the LEGEND-2 trial. J Hematol Oncol. 2024;17(1):23. Published 2024 Apr 24. doi:10.1186/s13045-024-01530-z

[6] IQVIA. Achieving CAR T-cell Therapy Health System Readiness. 2025. Available online: https://www.iqvia.com/insights/the-iqvia-institute/reports-and-publications/reports/achieving-car-t-cell-therapy-health-system-readiness

[7] Kaltwasser J. Investigators set sights on optimizing CAR T-cell therapy in lymphoma. OncLive. 2022. Available online: https://www.onclive.com/view/investigators-set-sights-on-optimizing-car-t-cell-therapy-in-lymphoma

[8] Hoffmann MS, Hunter BD, Cobb PW, Varela JC, Munoz J. Overcoming Barriers to Referral for Chimeric Antigen Receptor T Cell Therapy in Patients with Relapsed/Refractory Diffuse Large B Cell Lymphoma. Transplant Cell Ther. 2023 Jul;29(7):440-448. doi: 10.1016/j.jtct.2023.04.003. Epub 2023 Apr 7. PMID: 37031747.

[9] Sureda A, Adam SE, Yang S, et al. Logistical challenges of CAR T-cell therapy in non-Hodgkin lymphoma: a survey of healthcare professionals. Future Oncol. 2024;20(36):2855-2868. doi: 10.1080/14796694.2024.2393566. Epub 2024 Sep 13. PMID: 39268892; PMCID: PMC11572306.

[10] Kamal-Bahl S, Puckett JT, Bagchi I, Miller-Sonet E, Huntington SF. Barriers and solutions to improve access for chimeric antigen receptor therapies. Immunotherapy. Published online May 27, 2022. doi:10.2217/imt-2022-0037

[11] Nze C, Flowers CR. Barriers to accessing cellular therapy for patients receiving care in community practices. Hematology Am Soc Hematol Educ Program. 2023;2023(1):382-385. doi:10.1182/hematology.2023000518

[12] MD Anderson Center. T cells, B cells and the immune system. 2021. Available online: https://www.mdanderson.org/cancerwise/t-cells--b-cells-and-the-immune-system.h00-159465579.html

[13] American Cancer Society. CAR T-cell Therapy and Its Side Effects. 2024. Available online: https://www.cancer.org/cancer/managing-cancer/treatment-types/immunotherapy/car-t-cell1.html

[14] FDA. FDA approves tisagenlecleucel for B-cell ALL and tocilizumab for cytokine release syndrome. 2017. Available online: https://www.fda.gov/drugs/resources-information-approved-drugs/fda-approves-tisagenlecleucel-b-cell-all-and-tocilizumab-cytokine-release-syndrome

[15] FDA. FDA approves axicabtagene ciloleucel for large B-cell lymphoma. 2017. Available online: https://www.fda.gov/drugs/resources-information-approved-drugs/fda-approves-axicabtagene-ciloleucel-large-b-cell-lymphoma

[16] FDA Package Insert- tisagenlecleucel. 2024. Available online: https://www.novartis.com/usen/sites/novartis_us/files/kymriah.pdf

[17] FDA Package Insert- axicabtagene ciloleucel. 2024. Available online: https://www.fda.gov/media/108377/download

[18] FDA Package Insert- brexucabtagene autoleucel. 2024. Available online: https://www.fda.gov/media/140409/download

[19] FDA Package Insert- lisocabtagene maraleucel. 2024. Available online: https://www.fda.gov/media/145711/download

[20] FDA Package Insert- idecabtagene vicleucel. 2025. Available online: https://packageinserts.bms.com/pi/pi_abecma.pdf

[21] FDA Package Insert- ciltacabtagene autoleucel. 2024. Available online: https://www.fda.gov/media/156560/download

[22] FDA Package Insert- obecabtagene autoleucel. 2024. Available online: https://www.fda.gov/media/183463/download

[23] EMA Summary of product Characteristics-axicabtagene ciloleucel. 2024. Available online: https://www.ema.europa.eu/en/documents/product-information/yescarta-epar-product-information_en.pdf

[24] EMA Summary of product Characteristics-tisagenlecleucel. 2024. Available online: https://www.ema.europa.eu/en/documents/product-information/kymriah-epar-product-information_en.pdf

[25] EMA Summary of product Characteristics-brexucabtagene autoleucel. 2025. Available online: https://www.ema.europa.eu/en/documents/product-information/tecartus-epar-product-information_en.pdf

[26] EMA Summary of product Characteristics-lisocabtagene maraleucel. 2024. Available online: https://www.ema.europa.eu/en/documents/product-information/breyanzi-epar-product-information_en.pdf

[27] EMA Summary of product Characteristics- Idecabtagene vicleucel. 2024. Available online: https://www.ema.europa.eu/en/documents/product-information/abecma-epar-product-information_en.pdf

[28] EMA Summary of product Characteristics- ciltacabtagene autoleucel. 2024. Available online: https://ec.europa.eu/health/documents/community-register/2022/20220525155688/anx_155688_en.pdf

[29] MHRA Summary of Product Characteristics. axicabtagene ciloleucel. 2024. Available online: https://www.medicines.org.uk/emc/product/9439/smpc

[30] MHRA Summary of Product Characteristics. tisagenlecleucel. 2024. Available online: https://mhraproducts4853.blob.core.windows.net/docs/77ca601287e4511f589db473fffbf9e91885b5c2

[31] MHRA Summary of Product Characteristics. lisocabtagene maraleucel. 2024. Available online: https://mhraproducts4853.blob.core.windows.net/docs/2c68e01fa042193dc39c81d76e2e9164e83b87e6

[32] MHRA Summary of Product Characteristics. brexucabtagene autoleucel. 2025. Available online: https://mhraproducts4853.blob.core.windows.net/docs/491a85cb9078bb88925ff650439e5e249f313453

[33] MHRA Summary of Product Characteristics. Idecabtagene vicleucel. 2024. Available online: https://mhraproducts4853.blob.core.windows.net/docs/20575242e44b0d5f7b12bbb409c576fa2a76b7d4

[34] MHRA Summary of Product Characteristics. ciltacabtagene autoleucel. 2024. Available online: https://mhraproducts4853.blob.core.windows.net/docs/b346f6dc8ac277fa852342d572b4cda794a32030

[35] National Cancer Institute. CAR T Cells: Engineering Patients' Immune Cells to Treat Their Cancers. 2025. Available online: https://www.cancer.gov/about-cancer/treatment/research/car-t-cells

[36] Odstrcil MS, Lee CJ, Sobieski C, Weisdorf D, Couriel D. Access to CAR T-cell therapy: Focus on diversity, equity and inclusion. Blood Rev. 2024;63:101136. doi:10.1016/j.blre.2023.101136

[37] Wang V, Gauthier M, Decot V, Reppel L, Bensoussan D. Systematic Review on CAR-T Cell Clinical Trials Up to 2022: Academic Center Input. Cancers (Basel). 2023;15(4):1003. Published 2023 Feb 4. doi:10.3390/cancers15041003

[38] Li YR, Lyu Z, Chen Y, Fang Y, Yang L. Frontiers in CAR-T cell therapy for autoimmune diseases. Trends Pharmacol Sci. 2024;45(9):839-857. doi:10.1016/j.tips.2024.07.005

[39] Haghikia A, Schett G, Mougiakakos D. B cell-targeting chimeric antigen receptor T cells as an emerging therapy in neuroimmunological diseases. Lancet Neurol. 2024;23(6):615-624. doi:10.1016/S1474-4422(24)00140-6

[40] Mao Y, Liao Q, Zhu Y, et al. Efficacy and safety of novel multifunctional M10 CAR-T cells in HIV-1-infected patients: a phase I, multicenter, single-arm, open-label study. Cell Discov. 2024;10(1):49. Published 2024 May 14. doi:10.1038/s41421-024-00658-z

[41] Cappell KM, Kochenderfer JN. Long-term outcomes following CAR T cell therapy: what we know so far. Nat Rev Clin Oncol. 2023;20(6):359-371. doi:10.1038/s41571-023-00754-1

[42] Children's Hospital of Philadelphia. Emily Whitehead, First Pediatric Patient to Receive CAR T-Cell Therapy, Celebrates Cure 10 Years Later. 2022. Available online: https://www.chop.edu/news/emily-whitehead-first-pediatric-patient-receive-car-t-cell-therapy-celebrates-cure-10-years

[43] Jaeger U, Bishop MR, Salles G. Myc Expression and Tumor-Infiltrating T Cells Are Associated with Response in Patients (Pts) with Relapsed/Refractory Diffuse Large B-Cell Lymphoma (r/r DLBCL) Treated with Tisagenlecleucel in the Juliet Trial. Poster #1194. Presented at the 62nd American Society of Hematology Annual Meeting & Exposition; December 5-8, 2020.

[44] Westin JR, Oluwole OO, Kersten MJ, et al. Survival with Axicabtagene Ciloleucel in Large B-Cell Lymphoma. N Engl J Med. 2023;389(2):148-157. doi:10.1056/NEJMoa2301665

[45] Kamdar M, Solomon SR, Arnason J, et al. Lisocabtagene maraleucel (liso-cel) vs standard of care (SOC) with salvage chemotherapy (CT) followed by autologous stem cell transplantation (ASCT) as second-line (2L) treatment in patients (pt) with R/R large B-cell lymphoma (LBCL): 3-year follow-up (FU) from the randomized, phase 3 TRANSFORM study. J Clin Oncol. 2024;42(suppl 16):7013.

[46] Mateos M-V, San-Miguel J, Dhakal, et al. Overall Survival (OS) With Ciltacabtagene Autoleucel (Cilta-cel) Versus Standard of Care (SoC) in Lenalidomide (Len)-Refractory Multiple Myeloma (MM): Phase 3 CARTITUDE-4 Study Update. Presented at: 2024 International Myeloma Society Annual Meeting; September 25-28, 2024; Rio de Janeiro, Brazil. Abstract OA – 65.

[47] Ailawadhi S, Arnulf B, Patel K, et al. Ide-cel vs standard regimens in triple-class-exposed relapsed and refractory multiple myeloma: updated KarMMa-3 analyses. Blood. 2024 Dec 5;144(23):2389-2401. doi: 10.1182/blood.2024024582. PMID: 39197072.

[48] National Cancer Institute. Trial Confirms CAR T-Cell Therapy Benefits People with Aggressive Lymphomas. July 10, 2023. Available online: https://www.cancer.gov/news-events/cancer-currents-blog/2023/large-b-cell-lymphoma-axi-cel-zuma-7-trial

[49] Chihara D, Liao L, Tkacz J, et al. Real-world experience of CAR T-cell therapy in older patients with relapsed/refractory diffuse large B-cell lymphoma. Blood. 2023;142(12):1047-1055. doi:10.1182/blood.2023020197

[50] Rojek AE, Ahmed N, Gomez Llobell M, et al. CAR T cell therapy in early relapsed/refractory large B-cell lymphoma: real world analysis from the cell therapy consortium. Abstract #4503. Presented at the 66th American Society of Hematology Annual Meeting & Exposition; December 7-10, 2024; San Diego, California.

[51] Strouse C, Farooq U, Shouval R et al. Predictors of Early Safety Outcomes with Axicabtagene Ciloleucel (axi-cel) in Patients with Relapsed or Refractory (R/R) Large B-Cell Lymphoma (LBCL). Blood. 2024;144 (Supplement 1):609. https://doi.org/10.1182/blood-2024-207976

[52] Mayo Clinic. Understanding CAR-T cell therapy and its potential side effects. 2023. Available online: https://cancerblog.mayoclinic.org/2023/08/31/understanding-car-t-cell-therapy-and-its-potential-side-effects/

[53] Cleveland Clinic. Top Myths About CAR T-Cell Therapy for Multiple Myeloma. 2025. Available online: https://consultqd.clevelandclinic.org/top-myths-about-car-t-cell-therapy-for-multiple-myeloma

[54] Sheykhhasan M, Manoochehri H, Dama P. Use of CAR T-cell for acute lymphoblastic leukemia (ALL) treatment: a review study. Cancer Gene Ther. 2022;29(8-9):1080-1096. doi:10.1038/s41417-021-00418-1

[55] Elsawy M, Chavez JC, Avivi I, et al. Patient-reported outcomes in ZUMA-7, a phase 3 study of axicabtagene ciloleucel in second-line large B-cell lymphoma. Blood. 2022;140(21):2248-2260. doi:10.1182/blood.2022015478

[56] Perthus A, Colin F, Charton E, et al. Remission after CAR T-cell therapy: Do lymphoma patients recover a normal life?. Hemasphere. 2024;8(5):e72. Published 2024 May 27. doi:10.1002/hem3.72

[57] Perales MA, McGuirk JP, Fesen MR, et al. Real-World Treatment Patterns of Large B-Cell Lymphoma Patients over Time in a Post-CAR T Approval Era. Transplant and Cell Ther. 2025;31(2):Supplement

[58] Kourelis T, Bansal R, Patel KK, et al: Ethical challenges with CAR T slot allocation with idecabtagene vicleucel manufacturing access. J Clin Oncol. 2022. 40(16):Supplement

[59] Canales Albendea MÁ, Canonico PL, Cartron G, et al. Comparative analysis of CAR T-cell therapy access for DLBCL patients: associated challenges and solutions in the four largest EU countries. Front Med (Lausanne). 2023;10:1128295. Published 2023 May 30. doi:10.3389/fmed.2023.1128295

[60] Buecklein VL, Ayuk FA, Holderried TAW, et al. Estimating the Impact on Survival of Not Receiving CAR T Therapy Despite Being Eligible in Relapsed or Refractory (R/R) Diffuse Large B-Cell Lymphoma (LBCL) Patients in Germany. 2024. [Poster Abstract #5037]. The 66th ASH Annual Meeting and Exposition, San Diego, California.

[61] Community Oncology Alliance. FACT Sheet: What is Community Oncology? Available online: https://communityoncology.org/wp-content/uploads/2017/08/What-is-Comm-Onc.pdf

[62] Gajra A, Jeune-Smith Y, Kish J, Yeh TC, Hime S, Feinberg B. Perceptions of community hematologists/oncologists on barriers to chimeric antigen receptor T-cell therapy for the treatment of diffuse large B-cell lymphoma. Immunotherapy. 2020;12(10):725-732. doi:10.2217/imt-2020-0118

[63] Levent A, Moseley A, Simons R, Adabra S. Barriers to CAR-T Therapy Adoption: Comparing Access in Academic and Community Settings in the US. Blood. 2024.144(1):5107. https://doi.org/10.1182/blood-2024-211499.

[64] Cliff ERS, Kelkar AH, Russler-Germain DA, et al. High Cost of Chimeric Antigen Receptor T-Cells: Challenges and Solutions. Am Soc Clin Oncol Educ Book. 2023;43:e397912. doi:10.1200/EDBK_397912

[65] GoCart Coalition. Education and training. Available online: https://thegocartcoalition.com/our-work/education-and-training/

[66] Zhang G, Davies GA, Lepic K, Balitsky AK. Development of an Electronic Learning Module for CAR-T Education in Canadian Hematology Residents. Blood. 2024. 144(1):3822. https://doi.org/10.1182/blood-2024-200444.

[67] European Hematology Association. 7th European CAR T-cell Meeting. Available online: https://ehaweb.org/meetings/previous-meetings/7th-european-car-t-cell-meeting

[68] VJHEMONC. Practical Considerations for CAR-T Therapy in Hematological Malignancies. Available online: https://www.vjhemonc.com/feature/practical-considerations-for-car-t-therapy-in-hematological-malignancies

[69] Gentile D, Jeune-Smith Y, Klink A, Feinberg B, Gajra A. Experiences with and Perceptions of CAR T-Cell Therapy for Multiple Myeloma Among Community-Based Hematologists/Oncologists. 2022. Value in Health. 25(7):S588.

[70] Snyder S, Albertson T, Garcia J, Gitlin M, Jun MP. Travel-Related Economic Burden of Chimeric Antigen Receptor T Cell Therapy Administration by Site of Care. Adv Ther. 2021;38(8):4541-4555. doi:10.1007/s12325-021-01839-y

[71] ACCC. Bringing CAR T-Cell Therapies to Community Oncology. Available online: https://www.accc-cancer.org/home/learn/precision-medicine/treatment/immunotherapy/car-t-cell-therapy/bringing-car-t-cell-therapies-to-community-oncology

[72] Targeted Oncology. 2021. Community Oncology Professionals Highlight Need for more Education on Immunotherapies. Available online: https://www.targetedonc.com/view/community-oncology-professionals-highlight-need-for-more-education-on-immunotherapies

[73] Leinemann V, Krutter S. 'The last bridge'- How patients experience the CAR T-cell therapy. A qualitative study. Eur J Oncol Nurs. 2024;68:102494. doi:10.1016/j.ejon.2023.102494

[74] Feldman J. Barriers to CAR T-Cell Therapy for LBCL Challenge Physicians and Patients. Targeted Oncology. 2023. Available online: https://www.targetedonc.com/view/barriers-to-car-t-cell-therapy-for-lbcl-challenge-physicians-and-patients

[75] Birch K, Snider JT, Chiu K, Baumgardner J, Wade SW, Shah G. Patient preferences for treatment in relapsed/refractory diffuse large B-cell lymphoma: a discrete choice experiment. Future Oncol. 2022;18(25):2791-2804. doi:10.2217/fon-2022-0421

[76] Johnson PC, Dhawale T, Newcomb RA, et al. Longitudinal patient-reported outcomes in patients receiving chimeric antigen receptor T-cell therapy. Blood Adv. 2023;7(14):3541-3550. doi:10.1182/bloodadvances.2022009117

[77] Park HJ, Jeong H, Yim HW, Kim NJ. Patient-reported outcomes of chimeric antigen receptor T-cell therapy in hematologic malignancies: a systematic review and meta-analysis. Sci Rep. 2024;14(1):25752. Published 2024 Oct 28. doi:10.1038/s41598-024-77210-2

[78] Abramson JS, Johnston PB, Kamdar M, et al. Health-related quality of life with lisocabtagene maraleucel vs standard of care in relapsed or refractory LBCL. Blood Adv. 2022;6(23):5969-5979. doi:10.1182/bloodadvances.2022008106

[79] Barata A, Dhawale T, Newcomb RA, et al. Quality of Life and Prognostic Awareness in Caregivers of Patients Receiving Chimeric Antigen Receptor T Cell Therapy [published correction appears in Transplant Cell Ther. 2025 Apr 3:S2666-6367(25)01065-6. doi: 10.1016/j.jtct.2025.03.002.]. Transplant Cell Ther. 2024;30(4):452.e1-452.e11. doi:10.1016/j.jtct.2024.01.063

[80] Spanjaart AM, Pennings ERA, Mutsaers PGNJ, et al. The Dutch CAR-T Tumorboard Experience: Population-Based Real-World Data on Patients with Relapsed or Refractory Large B-Cell Lymphoma Referred for CD19-Directed CAR T-Cell Therapy in The Netherlands. Cancers (Basel). 2023;15(17):4334. Published 2023 Aug 30. doi:10.3390/cancers15174334

[81] Vic S, Lemoine J, Armand P, Lemonnier F, Houot R. Transplant-ineligible but chimeric antigen receptor T-cells eligible: a real and relevant population. Eur J Cancer. 2022;175:246-253. doi:10.1016/j.ejca.2022.08.019

[82] Johnson PC, Abramson JS. Patient selection for chimeric antigen receptor (CAR) T-cell therapy for aggressive B-cell non-Hodgkin lymphomas. Leuk Lymphoma. 2020;61(11):2561-2567. doi:10.1080/10428194.2020.1786563

[83] Davis JA, Dima D, Ahmed N, et al. Impact of Frailty on Outcomes after Chimeric Antigen Receptor T Cell Therapy for Patients with Relapsed/Refractory Multiple Myeloma. Transplant Cell Ther. 2024;30(3):298-305. doi:10.1016/j.jtct.2023.12.015

[84] ASTCT, AACI and AAC. ASTCT, AACI, and ACCC launched RECUR Initiative to Enhance Patient Access to CAR T Therapy. 2024. Available online: https://www.newswire.com/news/astct-aaci-and-accc-launch-recur-initiative-to-enhance-patient-access-22225939

[85] Riedell PA, Downs C, Boehmer L, et al. If They RECUR, You Should Refer: A Community Oncologist Patient ID Roundtable Summary. Transplant Cell Ther. 2024;30(1):14-16. doi:10.1016/j.jtct.2023.10.019

[86] Grupo de Trabajo CORE de Sociedad Española de Hematología y Hemoterapia. Guía de recomendaciones para la identificación y derivación temprana de pacientes con linfoma no Hodgkin de células B candidatos a terapias CAR-T. 2024. Available online: https://www.sehh.es/publicaciones/guias-recomendaciones

[87] Passweg JR, Baldomero H, Alexander T, et al. Utilization of hematopoietic cell transplantation and cellular therapy technology in Europe and associated Countries. Using the 2022 activity survey data to correlate with economic and demographic factors. A report from the EBMT. Bone Marrow Transplant. 2025;60(2):227-236. doi:10.1038/s41409-024-02459-0

[88] Goldfinger M, Shah N, Cooper DL. CAR T-Cell Therapy for Multiple Myeloma: Eliminating Disparities Through Accountability. Oncology Live. 2023.24(6)

[89] Ahmed N, Sun F, Teigland C, et al. Chimeric Antigen Receptor T-Cell Access in Patients with Relapsed/Refractory Large B-Cell Lymphoma: Association of Access with Social Determinants of Health and Travel Time to Treatment Centers. Transplant Cell Ther. 2024;30(7):714-725. doi:10.1016/j.jtct.2024.04.017

[90] Ahmed N, Wesson W, Lutfi F, et al. Optimizing the post-CAR T monitoring period in recipients of axicabtagene ciloleucel, tisagenlecleucel, and lisocabtagene maraleucel. Blood Adv. 2024;8(20):5346-5354. doi:10.1182/bloodadvances.2023012549

[91] European Cancer Patient Coalition. CAR-T Therapy White Paper. 2022. Available online: https://ecpc.org/wp-content/uploads/2022/11/White-Paper-CAR-T-therapy.pdf

[92] Kersten MJ, Oluwole OO, Speth K, et al. Incidence of Cytokine Release Syndrome and Neurological Events in Patients with Relapsed or Refractory Large B-Cell Lymphoma at and Beyond 2 Weeks Following Axicabtagene Ciloleucel Infusion. Transplant and Cell Ther. 2025;31(2):S230

[93] Snyder S, Chung KC, Jun MP, Gitlin M. Access to Chimeric Antigen Receptor T Cell Therapy for Diffuse Large B Cell Lymphoma. Adv Ther. 2021;38(9):4659-4674. doi:10.1007/s12325-021-01838-z

[94] Ahmed N, Shahzad M, Shippey E, et al. Socioeconomic and Racial Disparity in Chimeric Antigen Receptor T Cell Therapy Access. Transplant Cell Ther. 2022;28(7):358-364. doi:10.1016/j.jtct.2022.04.008

[95] Hoda D, Faber E Jr, Hunter B, et al: Considerations for optimal administration of chimeric antigen receptor (CAR) T-cell therapy programs: A multi-stakeholder qualitative analysis. Blood. 2021 Blood. 138(1):1932.

[96] Patel AR, Hsu H, Lau C, et al. Time to CAR T Infusion in Local Versus Distant Treatment Centers. Transplant and Cell Ther. 2025. 31(2):S340-S341

[97] Hansen DK, Liu YH, Ranjan S, et al. The Impact of Outpatient versus Inpatient Administration of CAR-T Therapies on Clinical, Economic, and Humanistic Outcomes in Patients with Hematological Cancer: A Systematic Literature Review. Cancers (Basel). 2023;15(24):5746. Published 2023 Dec 7. doi:10.3390/cancers15245746

[98] Nikiforow S, Frigault MJ, Frey NV, et al. Paving the Road for Chimeric Antigen Receptor T Cells: American Society for Transplantation and Cellular Therapy 80/20 Task Force Consensus on Challenges and Solutions to Improving Efficiency of Clinical Center Certification and Maintenance of Operations for Commercially Approved Immune Effector Cell Therapies. Transplant Cell Ther. 2023;29(4):228-239. doi:10.1016/j.jtct.2023.01.021

[99] Farinella JM, Brunstein CG. Health Care, Physics, and Finance: The Complex Equation of Outpatient CAR T-Cell Therapy. JCO Oncol Pract. Published online May 1, 2025. doi:10.1200/OP-25-00291

[100] Gatwood K, Mahmoudjafari Z, Baer B, et al. Outpatient CAR T-Cell Therapy as Standard of Care: Current Perspectives and Considerations. Clin Hematol Int. 2024;6(2):11-20. Published 2024 Apr 9. doi:10.46989/001c.115793

[101] EBMT. JACIE standards. 2025. Available online: https://www.ebmt.org/jacie

[102] Perica K, Curran KJ, Brentjens RJ, Giralt SA. Building a CAR Garage: Preparing for the Delivery of Commercial CAR T Cell Products at Memorial Sloan Kettering Cancer Center. Biol Blood Marrow Transplant. 2018;24(6):1135-1141. doi:10.1016/j.bbmt.2018.02.018

[103] GoCART Coalition. GoCART Coalition Provides Cell Therapy Treatment Centres Option to Reduce CAR T Therapy Site Qualification Burden by Leveraging JACIE Accreditation. 2022. Available online: https://thegocartcoalition.com/gocart-coalition-provides-cell-therapy-treatment-centres-option-to-reduce-car-t-therapy-site-qualification-burden-by-leveraging-jacie-accreditation/

[104] Locke FL, Mahmoudjafari Z, Kebriaei P, et al. Awakening from REMS: ASTCT 80/20 Ongoing Recommendations for Safe Use of Chimeric Antigen Receptor T Cells. Transplant Cell Ther. Published online February 13, 2025. doi:10.1016/j.jtct.2025.02.009

[105] Avalere Health. Cell and gene therapy in the Asia-Pacific region: rethinking ecosystems to enable access. 2024. Available online: https://avalerehealth.com/news/thought-leadership/cell-and-gene-therapy-in-the-asia-pacific-region-rethinking-ecosystems-to-enable-access/

[106] Gajra A, Jeune-Smith Y, Feinberg B. Barriers to Referral for Chimeric Antigen Receptor T Cell (CAR-T) Therapies Among U.S. Community Hematologists/Oncologists (cH/O). Blood. 2021.138(1):4010. https://doi.org/10.1182/blood-2021-151789.

[107] The ATTC Network. Future-proofi¬ng the UK CAR-T patient referral pathway. White Paper. 2023. Available online: https://www.theattcnetwork.co.uk/wp-content/uploads/2023/11/FINAL-Catapult-Collaborative-working-Project-final-report-1.pdf

[108] Dana-Farber Cancer Institute. Referrals and second opinions. Available online: https://www.danafarberbostonchildrens.org/medical-professionals/referrals-and-second-opinions

[109] Auletta JJ, Sandmaier BM, Jensen E, et al. The ASTCT-NMDP ACCESS Initiative: A Collaboration to Address and Sustain Equal Outcomes for All across the Hematopoietic Cell Transplantation and Cellular Therapy Ecosystem. Transplant Cell Ther. 2022;28(12):802-809. doi:10.1016/j.jtct.2022.09.020

[110] NMPD. ACCESS Initiative targets inequities in cell therapy. Available online: https://www.nmdp.org/what-we-do/research/access

[111] NMPD. NMPD Regional Physician Exchange. Available online: https://network.nmdp.org/training-education/catalog/nmdp-regional-physician-exchange

[112] Auletta JJ, Khera N, DeMartino P, et al. Assessing Medicaid Coverage for Hematopoietic Cell Transplantation and Chimeric Antigen Receptor T Cell Therapy: A Project from the American Society for Transplantation and Cellular Therapy and the National Marrow Donor Program ACCESS Initiative. Transplant Cell Ther. 2023;29(11):713-720. doi:10.1016/j.jtct.2023.08.007

[113] Hansard. UK Parliament. NHS Hospitals: Apheresis. Volume 839: debated on Wednesday 9 October 2024. Available online: https://hansard.parliament.uk/lords/2024-10-09/debates/DFAAE3C2-F041-4330-9AC7-EE111D57FBD1/NHSHospitalsApheresis

[114] Solano C, Castro-Rebollo P, Pérez-Martínez A, et al. Quantifying the available capacity and resource needs for provision of CAR-T therapies in the National Health Service in Spain: a survey-based study. BMJ Open. 2023;13(7):e071371. Published 2023 Jul 25. doi:10.1136/bmjopen-2022-071371

[115] Coune P, Lenard A, Castañón H. Unlocking access to CAR-T in Europe: progress and growing pains. Pharmaceutical Market Europe. 2024. Available online: https://pme.pmlive.com/articles/ff2869a4-4429-11ef-8060-42010a800016

[116] Chen AJ, Zhang J, Agarwal A, Lakdawalla DN. Value of Reducing Wait Times for Chimeric Antigen Receptor T-Cell Treatment: Evidence From Randomized Controlled Trial Data on Tisagenlecleucel for Diffuse Large B-Cell Lymphoma. Value Health. 2022;25(8):1344-1351. doi:10.1016/j.jval.2022.02.007

[117] Kourelis T, Bansal R, Berdeja J, et al. Ethical Challenges with Multiple Myeloma BCMA Chimeric Antigen Receptor T Cell Slot Allocation: A Multi-Institution Experience. Transplant Cell Ther. 2023;29(4):255-258. doi:10.1016/j.jtct.2023.01.012

[118] Dias J, Garcia J, Agliardi G, Roddie C. CAR-T cell manufacturing landscape-Lessons from the past decade and considerations for early clinical development. Mol Ther Methods Clin Dev. 2024;32(2):101250. Published 2024 Apr 16. doi:10.1016/j.omtm.2024.101250

[119] Dumont A, Beziat G, Gadaud N et al. French Regional Experience of Pre-CAR-T Cells Lymphodepleting Chemotherapy Outsourced in the Patient's Referring Center. Blood. 2024. 144(S1): 7612. doi: 10.1182/blood-2024-201541

[120] Battiwalla M, Tees M, Flinn I, et al. Access barriers to anti-CD19+ CART therapy for NHL across a community transplant and cellular therapy network. Blood Adv. 2025;9(2):429-435. doi:10.1182/bloodadvances.2024014171

[121] Gye A, De Abreu Lourenco R, Goodall S. Different Models, Same Results: Considerations When Choosing Between Approaches to Model Cost Effectiveness of Chimeric-Antigen Receptor T-Cell Therapy Versus Standard of Care. Pharmacoeconomics. 2024;42(12):1359-1371. doi:10.1007/s40273-024-01430-7

[122] Drummond M, Ciani O, Fornaro G, et al. How are health technology assessment bodies responding to the assessment challenges posed by cell and gene therapy?. BMC Health Serv Res. 2023;23(1):484. Published 2023 May 13. doi:10.1186/s12913-023-09494-5

[123] Horgan D, Metspalu A, Ouillade MC, et al. Propelling Healthcare with Advanced Therapy Medicinal Products: A Policy Discussion. Biomed Hub. 2020;5(3):130-152. Published 2020 Dec 3. doi:10.1159/000511678

[124] Kowalska M, Koćwin A, Żyrekhttps J. Reimbursement of CAR-T cell therapies in Europe: Key challenges from precedents and lessons for the future. Presented at ISPOR Europe 2023. Available online: www.ispor.org/docs/default-source/euro2023/clement-francois2023reimbursement-of-car-t-cell-therapies-in-europe-key-challenges-from-precedents-and-lessons-for-future132523-pdf.pdf?sfvrsn=817579dc_0

[125] Gonçalves E. CAR-T cell therapies: patient access and affordability solutions. Future Sci OA. 2025;11(1):2483613. doi:10.1080/20565623.2025.2483613

[126] Alliance for Regenerative Medicine: Re: Comments to draft evidence report on anti B-cell maturation antigen CAR T-cell and antibody conjugate therapy for heavily pre-treated relapsed and refractory multiple myeloma. 2021. Available online: http://alliancerm.org/wp-content/uploads/2021/03/ARM-ICER-MM-response-to-draft-evidence-report-FINAL.pdf

[127] American Society for Transplantation and Cellular Therapy: Re: ICER "anti B-cell maturation antigen CAR T-cell and antibody drug conjugate therapy for heavily pre-treated relapsed and refractory multiple myeloma draft evidence report". Available online: https://icer.org/wp-content/uploads/2020/10/ICER_Multiple-Myeloma_Public-Comment-Folio-1.pdf

[128] Gye A, Goodall S, De Abreu Lourenco R. A Systematic Review of Health Technology Assessments of Chimeric Antigen Receptor T-Cell Therapies in Young Compared With Older Patients. Value Health. 2022;25(1):47-58. doi:10.1016/j.jval.2021.07.008

[129] Ge AY, Feldman WB, Kaiser MF, et al. Global Access to Chimeric Antigen Receptor (CAR) T-Cell Therapies: Health Technology Assessment (HTA) of CAR T in G7 Countries and Australia. Blood. 2024. 144(1):3659. https://doi.org/10.1182/blood-2024-208943.

[130] Litvinova Y, Merkur S, Allin S, et al. Availability and financing of CAR-T cell therapies: A cross-country comparative analysis. Health Policy. 2024;149:105153. doi:10.1016/j.healthpol.2024.105153

[131] Hu B, Vaidya R, Ahmed F, et al. Real-World Analysis of Barriers to Timely Administration of Chimeric Antigen Receptor T Cell (CAR T) Therapy in Diffuse Large B-cell Lymphoma. Transplant Cell Ther. 2024;30(11):1082.e1-1082.e10. doi:10.1016/j.jtct.2024.09.007

[132] Allen J, Berry D, Cook F, et al. Medicaid coverage practices for approved gene and cell therapies: Existing barriers and proposed policy solutions. Mol Ther Methods Clin Dev. 2023;29:513-521. Published 2023 May 16. doi:10.1016/j.omtm.2023.05.015

[133] Thornton Snider J, Brauer M, Kee R, et al. The potential impact of CAR T-cell treatment delays on society. Am J Manag Care. 2019 Aug;25(8):379-386. PMID: 31419095.

[134] ZS.com. CAR-T reimbursement in the US: ZS separates myths from reality. 2022, Available online: https://www.zs.com/insights/car-t-reimbursement-in-the-us-zs-separates-myth-from-reality

[135] Marwood Group. Navigating Provider Challenges to Growth of The CAR T-Cell Therapy Space. 2020, Available online: https://www.marwoodgroup.com/wp-content/uploads/2020/01/Marwood-Navigating-Provider-Challenges-to-Growth-of-The-CAR-T-Cell-Therapy-Space.pdf

[136] Shift Health. Enhancing Access to CAR T in the Canadian Healthcare System.2025. Available online: https://www.shifthealth.com/wp-content/uploads/2025/01/Policy-Brief_Enhancing-Access-to-CAR-T-in-the-Canadian-Healthcare-System.pdf

[137] Ambrosetti. 2024. Rivoluzione CAR-T. Proposte e azioni per un accesso equo e sostenibile alle terapie. Available online: https://www.ambrosetti.eu/en/search/?search=CAR+T

[138] McKesson. 2024 Cell and Gene Therapy Report: Advancing the Future of Medicine. Available online: https://inspirogene.com/wp-content/uploads/2024/10/McKesson-2024-CGT-Report.pdf

[139] Hopfinger G, Rupp B and Greil R. Barriers to patient access of CAR T cell therapies in Austria. Memo-Magazine of European Medical Oncology. 2023;16(1):79-90.

[140] EFPIA. A Competitiveness Strategy for European Life Sciences. 2024. Available online: https://efpia.eu/media/fzkbhzoe/a-competitiveness-strategy-for-european-life-sciences.pdf

[141] Covington. Germany prepares for new National Strategy for Gene and Cell Therapies. 2024. Available online: https://www.insideeulifesciences.com/2024/06/18/germany-prepares-new-national-strategy-for-gene-and-cell-therapies/

[142] The ATTC Network. About Us. 2024. Available online: https://www.theattcnetwork.co.uk/about

[143] UK Research and Innovation. Innovate UK. Available online: https://www.ukri.org/councils/innovate-uk/

[144] The ATTC Network. Network Activities. 2024. Available online: https://www.theattcnetwork.co.uk/about/network-activities

[145] The ATTC Network. Our Impact. 2024. Available online: https://www.theattcnetwork.co.uk/about/our-impact

[146] GoCART Coalition. About GoCART. Available online: https://thegocartcoalition.com/about-gocart/

[147] EBMT. Annual Report 2023. The GoCART Coalition in 2023. Available online: https://www.ebmt.org/annual-report-2023/gocart-coalition-2023

[148] GoCART Coalition. Standards of Care. Available online: https://thegocartcoalition.com/our-work/standards-of-care/

[149] FACT global. Press release: FACT convenes 'Community CAR T working group' to review and propose clinical accreditation standards. 2025. Available online: https://www.factglobal.org/education-and-resources/general/press-releases/202504-car-t-working-group/

[150] Mikhael J, Fowler J, Shah N. Chimeric Antigen Receptor T-Cell Therapies: Barriers and Solutions to Access. JCO Oncol Pract. 2022;18(12):800-807. doi:10.1200/OP.22.00315

[151] T2EVOLVE. Concept. Available online: https://t2evolve.com/concept/

[152] Information provided by T2EVOLVE representatives - personal communication

[153] Join4ATMP. Work Packages. Available online: https://join4atmp.eu/research/workpackage

[154] Jommi C, Bramanti S, Pani M, Ghirardini A, Santoro A. CAR T-Cell Therapies in Italy: Patient Access Barriers and Recommendations for Health System Solutions. Front Pharmacol. 2022;13:915342. Published 2022 Jun 23. doi:10.3389/fphar.2022.915342

[155] American Action Forum. 2020. A Path Forward for CAR-T Therapy Reimbursement Under the IPPS. Available online: https://www.americanactionforum.org/research/a-path-forward-for-car-t-therapy-reimbursement-under-the-ipps/

[156] CMS. Fiscal Year (FY) 2021. Medicare Hospital Inpatient Prospective Payment System (IPPS) and Long Term Acute Care Hospital (LTCH) Final Rule (CMS-1735-F). Available online: https://www.cms.gov/newsroom/fact-sheets/fiscal-year-fy-2021-medicare-hospital-inpatient-prospective-payment-system-ipps-and-long-term-acute-0

[157] T2EVOLVE. Patient Hub: What is CAR T-cell treatment? Available online: https://t2evolve.com/information-for-patients/what-is-car-t-cell-treatment/