ASSOCIATION OF COMMUNITY CANCER CENTERS

IMMUNO-ONCOLOGY INSTITUTE

Essentials for Identifying Patients

Part of the Bringing CAR T-Cell Therapy to Community Oncology Series

Chimeric antigen receptor (CAR) T-cell therapy is quickly emerging as a promising new treatment for hematologic malignancies. Like its more broadly used predecessor, immune checkpoint inhibitors, CAR T-cell therapy has the ability to shrink and even eradicate tumors found in patients with acute lymphocytic leukemia, non-Hodgkins lymphoma, and most recently, multiple myeloma. Nationwide, cancer programs are looking to join more than 100 institutions already delivering CAR T-cell therapy. Moreover, in addition to the six currently approved CAR T-cell therapy products,[1] providers anticipate the U.S. Food and Drug Administration (FDA) to approve 10 to 20 new gene therapy products annually by 2025.[2]

Yet, within community-based oncology care settings, barriers persist that preclude CAR T-cell therapy from being readily available; these barriers include limited infrastructure and resources, high costs of products, inadequate reimbursement, and challenges associated with the management of treatment-related adverse events, such as cytokine release syndrome and immune effector cell-associated neurotoxicity syndrome. To overcome these barriers to be able to offer eligible patients CAR T-cell therapy, community oncologists have established referral networks with FDA-certified treatment centers that are equipped to handle these complex therapies with the necessary multidisciplinary teams, patient care requirements, and infrastructure.

As the demand for CAR T-cell therapy continues to grow, it has become more important than ever for oncology providers and community-based cancer programs to understand how to identify patients who could potentially qualify for this therapy. While the patient eligibility process can be grueling, providers who have been successful in identifying, referring, and treating patients have three key factors in common:

- They use a multidisciplinary committee to identify and select patients
- They implement a three-pronged assessment that considers clinical, financial, and logistical requirements to determine eligibility
- They offer comprehensive patient and caregiver education to ensure seamless continuity of care.

As part of its educational initiative, *Bringing CAR T-cell Therapies to Community Oncology*, the Association of Community Cancer Centers (ACCC) shares these essentials for identifying patients who may benefit from CAR T-cell therapy.

The Multidisciplinary Committee

At the core of a successful CAR T-cell therapy program is a multidisciplinary committee for patient identification and selection. Due to numerous complexities about CAR T-cell therapy, including clinical concerns surrounding risks for

treatment-related adverse events, evaluation of the efficacy and safety of products, steep costs for products, billing and reimbursement requirements, and substantial logistical considerations, a multidisciplinary selection committee should be in place. This committee should be representative of the many departments within the institution involved in initial referral, patient selection, enrollment, ordering of products, cell collection, processing, bridging therapy, infusion, post-infusion care, and outcomes tracking, as well as the multitude of administrative and financial workflows related to CAR T-cell therapy.

Committee members should include physician representatives from oncology, hematopoietic cell transplantation, leukemia, lymphoma, or other clinical specialties, and physicians should be authorized to prescribe CAR products and manage CAR T-cell therapy patients. The committee should also include nursing leadership, pathologists, pharmacists, apheresis and transfusion medicine specialists, financial navigators, social workers, and other hospital administration members.[3] Revenue cycle specialists are also recommended for care value assessment and coverage investigation.

In a 2018 survey of cancer institutions authorized for CAR T-cell therapy conducted by the American Society for Blood and Marrow Transplantation, 31 of 52 surveyed institutions (60 percent) indicated using an institutional (i.e., multidisciplinary) committee for clinical data review and approval for each patient being considered for CAR T-cell therapy. While the type of committees ranged from hematopoietic stem cell transplantation, immunotherapy or cell therapy, administration or high-cost drug, pharmacy and therapeutics, or breakthrough therapy committees, 72 percent of institutions confirmed that a pharmacist representative was essential to establishing practice standards for the cellular therapy service or was a part of the review committee.[4]

Patient Eligibility & Selection

Once the multidisciplinary committee is in place, the rigorous eligibility process for patient selection can take place. Pre-screening and evaluation for CAR T-cell therapy is extensive, as demand for this therapy is high and eligibility criteria is complex. The multidisciplinary committee should assess patients for treatment eligibility based on a three-pronged process that gauges clinical indication and disease burden, physiological stability, and care coordination requirements. This includes a comprehensive clinical evaluation, a financial assessment including pre-authorization, and a logistics assessment to determine availability of appropriate caregiver support, patient resources, and potential travel and lodging requirements.

Appropriate patient candidates should:

- Have a disease type and tumor burden that will benefit from CAR T-cell therapy
- Meet the label indications for the product
- Have the minimum physical functionality to undergo therapy and cope with potential cytokine release syndrome post-infusion (i.e., meet reasonable renal, cardiac, and pulmonary function requirements)
- Have a dedicated caregiver
- Have the capability to stay within a 2-hour/30-mile radius of the treatment facility for a duration of one month
- Have health insurance coverage or other financing available for treatment (pre-authorization must be obtained prior to clinical evaluation).

Clinical Evaluation

Clinical evaluations should gauge and assess the level of disease control, disease location, metastasis, and current treatment status (e.g., currently undergoing chemotherapy). The multidisciplinary committee should assess patient history, activity level, performance status, and organ function to determine if the patient will have the ability to handle the rigors of CAR T-cell therapy and tolerate potential adverse effects. Baseline laboratory studies and a complete clinical workup should also be conducted at this stage.[5] (see Figure 1).

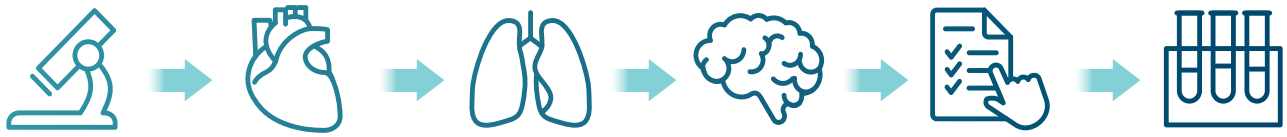
Clinical workup should also include involvement of social workers, who can gauge the patient and caregiver's emotional and psychological well-being to undertake the CAR T-cell process.

Financial Assessment & Pre-Authorization

Like other types of medical testing, the patient intake process requires a robust administrative team working in tandem with financial navigators and insurance and benefits specialists to secure eligibility. However, this is where the similarities end.

Since CAR T-cell therapy carries a hefty price tag, ensuring that patients have the necessary health insurance coverage or self-pay/financing available for treatment is a substantial consideration for patient eligibility. Financial navigators

Figure 1. Recommended Clinical Workup



Confirmatory biopsy of disease *(if not recently completed)*

Echocardiogram for cardiac evaluation

Pulmonary function tests

Magnetic resonance imaging of brain

Baseline neurologic assessment

Laboratory studies*

*Laboratory studies (e.g., C-reactive protein, ferritin, lactate dehydrogenase, complete blood count with differential, comprehensive metabolic panel, coagulation panel, etc.)

should work to investigate a patient's insurance coverage, seek pre-authorization, and determine eligibility for other financial assistance or support programs that could aid with associated out-of-pocket expenses, including relocation, transportation, and lodging expenses. For example, foundations, like the Leukemia and Lymphoma Society, and most CAR T-cell manufacturers offer travel assistance to eligible patients.[6]

Although CAR T-cell therapy may be covered by most commercial payers, single-case insurance agreements can help shorten the time to approval. Delays in financial approval can negatively impact a patient's eligibility to undergo planned therapy, therefore, pre-authorization and/or financial clearance which considers patient disease status, treatment timeline, patient relocation expenses, and other factors that may impact costs must be obtained as part of the patient eligibility process.

While total treatment costs and reimbursement rates can be impacted significantly by single-case insurance agreements and other considerations, the American Society of Clinical Oncology estimates the average price for a single CAR T-cell infusion to be more than $370,000 (without accompanying services and follow up care)[7] and real-world costs for a single patient are estimated to be between $500,000 to $1 million dollars.[8] Associated direct costs may include imaging studies, biopsies, ICU admission costs, and hospital stays, while indirect costs could include travel and lodging expenses for patients who must relocate for significant periods of time for treatment and follow-up care.

Caregiver & Logistical Needs Assessment

CAR T-therapy is a process that requires meticulous logistical considerations for optimal care and outcomes. Navigators, social workers, or dedicated cellular therapy coordinators (depending on the institution's framework) should conduct a thorough review of the patient's logistical needs to assess potential barriers to care and determine where (in what care setting) the various stages of CAR T-cell will be delivered.

During the bridging, lymphodepletion, infusion, and post-infusion stages, patients may be required to stay within a 2-hour/30-mile radius of the treatment facility, sometimes for extended periods of time. For patients living in remote areas, this may mean additional costs for travel and lodgings that should be considered when evaluating a patient's financial readiness.

Caregivers, who may be family members, friends, or other individuals, should be assessed to ensure they can satisfy the requirements needed for optimal care. Caregiver assessments should ensure that caregivers are:

- At least 18 years of age and able to drive
- Able to stay with patient 24 hours a day during any outpatient stages
- Able to transport patient to appointments and participate in care team meetings
- Able to manage patient medication and administration
- Responsible for practicing safe, off-site chemotherapy precautions
- Responsible for cleaning and cooking during care stages
- Responsible for knowing when to call and who to call on the medical team for emergencies

Patient Education

Fundamental to the patient identification and eligibility process is patient education. For every stage of the CAR T-cell therapy process, patients and their caregivers should be educated on the risks, benefits, processes, and key considerations, and informed consent must be obtained. Conversations may be led by navigators, social workers, or dedicated cellular therapy coordinators, who guide patients through each stage of the therapy process and manage communications across all stakeholders (e.g., CAR T-cell product manufacturers, physicians, multidisciplinary care team members, apheresis specialists, insurance providers).

During the consultation stage, when detailed patient history is gathered and baseline laboratory studies are conducted, patients should be instructed to bring all diagnostic scans and pathology reports for evaluation. Navigators, social workers, or designated care team members should guide patients through all financial, logistical, and caregiver requirements. Social workers can also assist in patient education to provide emotional, psychological, and financial support as needed. Patient and caregiver education should also include details on the proposed treatment plans, as well as the roles of the referring, treatment, and community providers.

In preparation for the leukapheresis stage, patient and caregiver education should include information focused on the leukapheresis process, including potential side effects (e.g., fatigue, cytopenia [low blood cell counts], hypocalcemia [low calcium levels], cardiovascular events).[9]

As manufacturing of CAR T-cells takes at least two to eight weeks (depending on the manufacturer), patients and caregivers should be educated on bridging therapies that may be given to control disease, debulk tumors, and maintain performance status.[5] Patients and caregivers who receive bridging therapy at a referring center but will transition to a treatment center for infusion should be guided on the role the referring center will continue to play during infusion and subsequent stages.

Caregiver requirements during the lymphodepletion stage are complex. Patients and caregivers should understand that during chemotherapy in ambulatory settings, caregiver support may be required 24 hours a day and patients will need to be located within a 2-hour/30-mile radius of the treatment facility during this stage. Caregivers should be educated on expectations during this stage.

Finally, comprehensive patient and caregiver education on infusion, post-infusion, and long-term follow-up care is recommended. Patients should be made aware of signs and symptoms of cytokine release syndrome and neurologic toxicity, as well as delayed complications of therapy which could include prolonged cytopenias, increased risk of infection, or delayed neurologic toxicities, such as tremors and poor short-term memory.[5]

Community Readiness

As the reach and widespread use of CAR T-cell therapy expands, community oncology programs and providers can utilize referral networks with certified treatment facilities to effectively overcome barriers to offer CAR T-cell therapy to eligible patients in their care. Understanding the critical components for patient identification, and training and educating multidisciplinary care teams who need to be involved in selection processes on eligibility guidelines and expectations, can better prepare communities for utilization of these advanced therapies nationwide.

This educational project is sponsored by Bristol Myers Squibb, Janssen Oncology, and Legend Biotech.

REFERENCES

1. National Cancer Institute. CAR T Cells: Engineering Patients' Immune Cells to Treat Their Cancers. Updated March 10, 2022. Accessed December 6, 2022. https://www.cancer.gov/about-cancer/treatment/research/car-t-cells

2. May B. Barriers and solutions to expanding access to CAR T-cell therapy. Published August 9, 2020. December 6, 2022. https://dailynews.ascopubs.org/do/10.1200/ADN.20.200294/full/

3. Booth JP, Kusoski CL, Kennerly-Shah JM. The pharmacist's role in chimeric antigen receptor T cell therapy. *J Oncol Pharm Pract*. 2020;26(7):1725-1731. doi: 10.1177/1078155220948940

4. Mahmoudjafari Z, Hawks KG, Hsieh AA, et al. American Society for Blood and Marrow Transplantation pharmacy special interest group survey on chimeric antigen receptor T cell therapy administrative, logistic, and toxicity management practices in the United States. Biol *Blood Marrow Transplant*. 2019;25(1):26-33. doi: 10.1016/j.bbmt.2018.09.024.

5. Beaupierre A, Lundberg R, Marrero L, et al. Management across settings: an ambulatory and community perspective for patients undergoing CAR T-cell therapy in multiple care settings. *Clin J Oncol Nurs*. 2019;23(2):27-34. doi: 10.1188/19.CJON.S1.27-34.

6. The Leukemia & Lymphoma Society. Susan Lang pre CAR T-cell therapy travel assistance program. Accessed December 7, 2022. https://www.lls.org/support-resources/financial-support/susan-lang-pre-car-t-cell-therapy-travel-assistance-program

7. Association of Community Cancer Centers, ACCC Immuno-Oncology Institute. Bringing CAR T-cell therapies to community oncology. Published 2022. Accessed December 6, 2022. https://www.accc-cancer.org/docs/projects/bringing-car-t-cell-therapies-to-co/bringing-car-t-cell-therapies-to-co.pdf?sfvrsn=304cf153_0

8. Borgert R. Improving outcomes and mitigating costs associated with CAR T-cell therapy. *Am J Manag Care*. 2021;27(13 Suppl):S253-S261. doi: 10.37765/ajmc.2021.88737

9. Stenzinger M, Bonig H. Risks of leukapheresis and how to manage them—A non-systematic review. *Transfus Apher Sci*. 2018;57(5):628-634. https://doi.org/10.1016/j.transci.2018.09.008

10. CAR T-cell therapy requires complex patient navigation. Journal of Oncology Navigation and Survivorship. Published February 2019;10(2). Accessed December 6, 2022. https://www.jons-online.com/issues/2019/february-2019-vol-10-no-2/2252-car-t-cell-therapy-requires-complex-patient-navigation

11. Academy of Oncology Nurse & Patient Navigators. CAR T-cell therapy: implications for navigation practice. Published 2021. Accessed December 6, 2022. https://aonnonline.org/education/navigation-tools/car-t-cell-therapy-implications-for-navigation-practice

12. O'Rourke K. ASCO releases guideline on CAR T-cell therapy: A multidisciplinary team's recommendations help in the recognition, workup, evaluation, and management of the most common chimeric antigen receptor (CAR) T-cell-related toxicities. *Cancer*. 2022;128(3):429-430. doi: 10.1002/cncr.34080

13. Taylor L, Rodriguez ES, Reese A. Building a program: implications for infrastructure, nursing education, and training for CAR-T cell therapy. *Clin J Oncol Nurs*. 2019;23(2):20-26. doi: 10.1188/19.CJON.S1.20-26

14. Alexander M, Culos K, Roddy J. Chimeric antigen receptor T cell therapy: a comprehensive review of clinical efficacy, toxicity, and best practices for outpatient administration. *Transplant Cell Ther*. 2021;27(7):558-570. doi: 10.1016/j.jtct.2021.01.014.

This educational project is sponsored by Bristol Myers Squibb, Janssen Oncology, and Legend Biotech.

This publication is produced by the education project "*Bringing CAR T-Cell Therapies to Community Oncology*", which is part of the **ACCC Immuno-Oncology Institute**. Learn more at accc-cancer.org/CAR-T-Cell.

The Association of Community Cancer Centers (ACCC) is the leading education and advocacy organization for the cancer care community. For more information, visit accc-cancer.org.