CAR T-Cell Therapy: A Significant Advance for Patients With Hematologic Malignancies

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First approved in 2017, chimeric antigen receptor (CAR) T-cell therapy is a type of immunotherapy that has altered the way many hematologic malignancies are treated.[1] To date, 6 CAR T-cell therapies have been approved by the FDA for the treatment of blood cancers, including lymphomas, some forms of leukemia, and, most recently, multiple myeloma.[2] These therapies have produced remarkable responses in some patients for whom other treatments had stopped working, which has led to growing interest in the potential of CAR T-cell therapy beyond the particular blood cancers it is currently approved to treat. More than 600 active CAR T-cell therapy trials are currently ongoing worldwide.[3] Despite this significant clinical progress, access to CAR T-cell therapy raises several challenges, including but not limited to issues relating to geographic access, caregiving, and coverage and affordability.

How CAR T-Cell Therapies Are Administered[1]

Current CAR T-cell therapies are customized for each patient. T-cells are collected from the patient and re-engineered in a laboratory to produce proteins on their surface called chimeric antigen receptors, or "CARs," which recognize and bind to specific proteins, or antigens, on the surface of cancer cells. The revamped T-cells are "expanded" into the millions in the laboratory and then infused back into the patient. If the treatment progresses as planned, the CAR T-cells will continue to multiply in the patient's body and—guided by their engineered receptor—recognize and kill any cancer cells that harbor the target antigen on their surfaces.

Improving Access to CAR T-Cell Therapy in the Community Setting

CAR T-cell therapy is complex and, to date, has generally only been available at select treatment centers. Hence, distance to a treatment center may be a barrier for some patients. Nevertheless, most of the US population resides within a reasonable driving distance from a hematopoietic cell transplantation center. One study found that nearly half (46.7%) of the US population lives within 30 minutes of a transplant center and 65.9% to 77.1% of the population resides within a 60- or 90-minute travel time, respectively.[4] Additional concerns include whether these centers are certified to provide some of these therapies. For example, fewer than 100 centers were certified to give axicabtagene ciloleucel (Yescarta®) in the United States, as of 2020.[4]

Furthermore, FDA Risk Evaluation Mitigation Strategy programs for CAR T-cell therapies may require patients to remain within a specified travel time to the treatment center (between 30 minutes to 2 hours), restrict driving, and frequently require a caregiver to be present for 30 days post infusion. While these processes are critical for monitoring safety post infusion, these requirements can pose substantial challenges for patients and caregivers.[5]

Some cancer programs and practices with fewer resources are wary about offering CAR T-cell therapy, given the skills and infrastructure required to administer the treatment. Many smaller community cancer programs indicate that they prefer to refer patients who are (or may be) candidates for CAR T-cell therapy to larger cancer programs and academic medical centers. Some of the reasons for this hesitation include unfamiliarity with the therapy; inadequate reimbursement; insufficient infrastructure; and the potential for unfamiliar adverse events, such as life-threatening toxicities, to affect patients.[6]

The Association of Community Cancer Centers (ACCC) is helping community cancer programs and practices of various sizes to become educated about building their own CAR T-cell therapy programs. This requires an understanding of the operational infrastructure, such as care coordination and patient support, that is required for timely identification of patients who are good candidates for CAR T-cell therapy and improving referral relationships between noncertified and certified centers.[3,6] These educational projects are supported by Kite Pharma, Janssen Oncology, and Bristol Myers Squibb.

Coverage and Affordability Challenges

CAR T-cell therapy is costly. For example, the most recently approved CAR T-cell therapy costs more than $450,000.[2] This poses unique challenges for patients, caregivers, providers, and payers.

Many cancer programs and practices offer financial navigation services to patients to help them obtain available coverage and financial assistance. In fact, coverage is often a prerequisite before treatment can be initiated. For example, even Medicare beneficiaries may not be assured full coverage. If a traditional Medicare beneficiary does not have a supplemental plan (or is not covered by a Medicare Advantage plan), the significant cost-sharing under traditional Medicare (20%) may be prohibitive for patients and it may mean that some patients cannot afford their out-of-pocket

responsibility, thus deterring them from receiving the treatment.[7] Additionally, many insured patients face reimbursement restrictions. Approximately two-thirds of US health plans have restrictive coverage policies relating to cell and gene therapy, likely due to the high costs of treatment.[5] Treatment center and payer processes can add a week or more to CAR T-cell therapy timelines. These delays in treatment may may be detrimental for patients with active and rapidly progressing disease.

Innovative Payment Models

CAR T-cell therapies have the potential to save or significantly prolong many patients' lives. Yet the cost and reimbursement of these therapies pose some formidable challenges for the health care system. New payment models are emerging that seek to address patient mobility across payers over time and/or to create risk-sharing mechanisms whereby payments to the manufacturer are tied to certain treatment milestones. The following are some mechanisms that have been identified to help structure payments for cell and gene therapies:[8]

- ***Milestone-based contracts.*** Up-front payment with requirement for refund if certain milestones are not met. Generally, these contracts have a 1-year term.
- ***Multi-year milestone-based contracts.*** Performance-based agreement for the longer term with requirement for rebate if certain milestones are not met.
- ***Reinsurance.*** Insurance for insurance companies to reduce the impact of unexpected high costs for a patient or group of patients.
- ***Stop-loss insurance.*** A product that provides protection against unpredictable costs for a patient above a specified threshold. It is purchased by employers who have decided to self-fund their employee health plans.
- ***Risk pools.*** Federal or state government programs or coverage-specific insurance products in which a premium is set and paid for coverage of a defined treatment for a group of individuals, thereby creating cost predictability.
- ***Performance-based annuities.*** A multi-year payer-developer agreement in which the payer makes an up-front payment for part of the price of the therapy, as well as a commitment to further periodic payments as specific patient performance milestones or outcomes are met.
- ***Payment over time or installment financing.*** Paying for a treatment over multiple years rather than in one upfront payment.

Looking Forward

CAR T-cell therapies have ushered in a new era of treatment options for patients with certain hematologic malignancies and have saved the lives of many. Yet, these treatments raise logistical and financial challenges for many patients. It is, therefore, important to increase the number of cancer programs that offer these therapies, as well as to develop innovative payment mechanisms. ACCC will continue to work with its members and the broader provider, patient, caregiver, and stakeholder communities to provide educational background about—and help develop possible solutions to—some of the opportunities and challenges attendant to CAR T-cell therapies. OI

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