Transition of Care Across the CAR T-Cell Therapy Continuum: Implications and Best Practices for the Clinical Team

Discussions with Physicians and the International Myeloma Foundation Nurse Leadership Board

Physician Roundtable
August 28, 2022

and

International Myeloma Foundation Nurse Leadership Board Roundtable
September 16, 2022

INTERNATIONAL MYELOMA FOUNDATION

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Overview

Chimeric antigen receptor T-cell (CAR T) therapy is an innovative and highly effective immunotherapy for patients with relapsed/refractory multiple myeloma (RRMM). However, significant challenges with the application of CAR T therapy in routine practice must be addressed to actualize the promise of this novel multiple myeloma (MM) treatment modality. The International Myeloma Foundation (IMF) convened 2 roundtables, involving hematology/oncology physicians and the IMF Nurse Leadership Board (NLB), on August 28 and September 16 of 2022, respectively. In these roundtables, discussions focused on best practices for ensuring care continuity across the CAR T therapy continuum. Major challenges and possible solutions were discussed to identify strategies for facilitating the patient journey and access to CAR T therapy, improving communication between referring centers and CAR T centers (CTCs), and optimizing post-CAR T therapy patient management in the community practice setting.

The specific objectives were to:

1. Review the landscape of triple-class RRMM and the current CAR T-cell therapies available
2. Outline the different targets and approaches for CAR T-cell therapies and their potential future clinical significance
3. Discuss the patient journey during CAR T-cell therapy
4. Discuss the interaction between CAR T therapy centers and referring physicians
5. Outline the post-infusion monitoring approach to reincorporate patients into community care

Importantly, the focus of the discussion was on the patient perspective and the transition of care (objectives 3–5), rather than on the clinical data for CAR T therapy in RRMM.

Introduction

MM accounted for 176,404 new diagnoses and 117,077 deaths worldwide in 2020.[1] In the United States alone, MM was the second most common hematologic malignancy and was projected to account for 34,470 new diagnoses and 12,640 deaths in 2022.[2,3] Despite significant improvements in the survival of patients with MM, in part due to advances in MM therapeutics, relapse and disease progression are inevitable, with each additional line of therapy (LOT) yielding diminishing returns—ie, responses are less durable and the depth of response decreases, which ultimately limits survival gains.[4–6] Moreover, the proportion of patients receiving treatment decreases with increasing LOTs, with an attrition rate ranging from 14%–50% per LOT and only 1%–22% of patients receiving a fifth LOT.[5-7] These data underscore the

importance of optimizing the treatment of patients upfront and/or at an earlier LOT, to ensure that patients receive the most effective options earlier in their disease course.

Among patients with RRMM, those who develop disease that is refractory to multiple standard classes of drugs have a significantly worse prognosis, as there are fewer treatment options for heavily pretreated patients with aggressive RRMM.[8–10] For instance, the median overall survival (mOS) for patients refractory to immunomodulatory imide drugs (IMiDs) and proteasome inhibitors (PIs) is 6.7–11.5 months (referred to as double-class refractory),[10] while the mOS for those with MM refractory to PIs (bortezomib and carfilzomib), IMiDs (pomalidomide and lenalidomide), and anti-CD38 monoclonal antibody (mAb) therapy (daratumumab) is 5.6 months (referred to as triple-class refractory).[9] For patients with late relapses (>3 prior therapies), such as in patients with triple-class refractory disease, guidelines currently include bendamustine-based regimens, and high-dose or fractionated chemotherapy as therapeutic options.[11] In addition, the US FDA-approved B-cell maturation agent (BCMA)-targeted antibody-drug conjugate belantamab mafodotin, the CAR T therapies idecabtagene vicleucel (ide-cel) and ciltacabtagene autoleucel (cilta-cel) are options for patients with RRMM after ≥4 prior therapies, including an anti-CD38 mAb, a PI, and an IMiD.[11] Selinexor with dexamethasone is the primary option for patients with penta-refractory RRMM (refractory to ≥2 PIs, ≥2 IMiDs, and an anti-CD38 mAb).[11]

CAR T Therapy in MM: Progress and Challenges

Of the available approaches for heavily pretreated RRMM, the 2 BCMA-targeted FDA-approved CAR T therapies have yielded remarkable and unprecedented clinical activity, with overall response rates (ORRs) of 73% (33% complete or stringent complete response [CR or sCR, respectively]) and 97.9% (80.4% sCR) with ide-cel and cilta-cel, respectively.[12,13,14] The main attributes of ide-cel and cilta-cel are shown in **Figure 1;** key data from the phase 2 KarMMa study of ide-cel and the phase 1b/2 CARTITUDE-1 study of cilta-cel, based on which these agents gained regulatory approval in RRMM, respectively, are summarized in **Table 1**.

Both the physicians and the NLB commented on the “striking” and “impressive” response rates with ide-cel and cilta-cel, especially in the heavily pretreated clinical study populations, and expressed enthusiasm for the transformative and revolutionary potential of these CAR T therapies in the management of RRMM. However, the significant challenges with and barriers to the widespread use of CAR T therapy in routine clinical practice, and the opportunities for further improvements at key waypoints along the CAR T continuum, were recognized in both roundtables. Challenges associated with the routine use of CAR T in MM practice include:

- **Access**—substantial logistical challenges exist due to lengthy CAR T manufacturing times, risk of manufacturing failure, and limited manufacturing slots, limited access due to care location or socioeconomic factors, and cost-related hurdles [13,15]
- **Care coordination and transition back to community care**—educational needs/knowledge deficits regarding CAR T therapy among non-CAR T specialists, toxicity concerns, and resource limitations in the community[13,15]

At the physician and NLB roundtables, manufacturing capacity and consistency, lymphodepletion protocols and timing, and optimal maintenance therapy after CAR T therapy were noted as aspects of CAR T therapy that need further improvement.

Data from other clinical studies of ide-cel, cilta-cel, and non-BCMA CAR T therapies directed at novel MM-specific targets continues to evolve, and the portfolio of CAR T options for MM is expected to expand.[13] However, the promise demonstrated by these therapies in clinical studies can only be fully actualized in clinical practice if the barriers to access and application of CAR T are addressed. To this end, the roundtables focused on identifying optimal approaches for ensuring continuity of care for patients with MM eligible for/receiving CAR T therapy, throughout their therapeutic journey— starting with potential eligibility/referral for CAR T therapy and their first interaction with the CTC care team, progressing to initiation of CAR T therapy at a CTC, then continuing to post-CAR T patient management and continuation of care in community practice.

Overview of the Patient Journey

The RRMM Patient Journey to CAR T Therapy

Traditionally, delivery of CAR T therapy has occurred predominantly either at large academic centers or CTCs and/or in the outpatient context as part of recent clinical studies.[15] However, with the availability of an increasing number of commercial guideline-recommended CAR T therapies, there is a greater interest in developing an outpatient model for CAR T delivery, care coordination, and care continuation in community oncology practice.[15] Currently, there are no robust models or guidelines for optimizing CAR T delivery in the outpatient or community oncology settings for patients with RRMM. Moreover, slow intake processes at CTCs can serve as a barrier to the timely referral of patients for CAR T therapy by community hematology/oncology practices.[16]

Most CTCs are implementing CAR T therapy primarily as an inpatient procedure, with a stepwise approach to transitioning to an outpatient process in the future, per the physicians and NLB. Some components of CAR T therapy can be managed/delivered in the outpatient setting (eg, bridging therapy), by leveraging existing infrastructures, processes, and

provider/MM patient familiarity with outpatient bone marrow transplant (BMT); however, CAR T therapy requires substantial support and extended time commitments, which can be challenging for patients as well as their care partners.

In their discussions on facilitating the patient journey to CAR T therapy, physicians and the NLB described some of the creative and innovative approaches that have been employed in their institutions/CTCs to:

- Leverage existing infrastructure—for example, by routing financial clearance via BMT teams/team members and utilizing lodging assistance available via the BMT programs for patients receiving CAR T therapy
- Conduct outreach efforts to establish and maintain relationships with regional community practices—such as conducting community clinics, collaborating with local churches to educate residents in the CTC catchment area, and inviting community physicians to multidisciplinary tumor board (MTB) meetings at the CTC
- Streamline patient identification, referral, and intake for CAR T therapy—for example, by establishing internal teams/coordinators to vet, inform, and manage CAR T therapy referrals and waiting lists

The Critical Role of Multimodal Communication Between CTCs and Community Physicians in the RRMM Patient Journey

One of the most challenging aspects of managing patients with RRMM is the heterogeneity and complexity of this population—in terms of the diversity, number, and responses to prior therapeutic regimens as well as the disease course; this complexity is encapsulated by the lack of consensus regarding standard-of-care regimens/algorithms applicable for this population.[5,8,17–19] Therefore, consideration of the needs and optimal therapeutic options for individual patients is fundamental to personalizing their treatment.

The treatment approach should focus on the patient with RRMM, rather than choosing therapy solely based on the CAR T referral. The objective of this approach is to ensure that the entire spectrum of therapeutic options and/or clinical trials is available to patients, based on their individual needs and disease profiles.

The physicians and NLB noted that initiating and maintaining relationships and developing multifaceted ways of routine communication with community physicians and practices are both helpful and important for optimizing CAR T therapy delivery to patients with RRMM. Communication and outreach strategies may include — CTC-mediated outreach to large hospitals or medical centers in the geographic region to educate their staff about CAR T;

providing opportunities for other large medical centers to participate in the CAR T program at the CTC (e.g., opening up the weekly new MM patient or MTB meetings to clinicians in community practice); engaging satellite sites where clinical trials are co-located; sharing the contact information for CAR T providers with referring physicians; and conducting community clinics.

Physician Perspective of the Patient Journey to CAR T

"[One of the] most difficult things I've ever done in my career is to deal with CAR T cells. The reality is that we have incredibly limited mileage in understanding how [the CAR T delivery process] works. I think we all need to learn how to establish the systems [to optimize CAR T delivery to patients with MM]." — Physician

Overall, CAR T therapy was described as "still relatively new to MM practice," with commercial products becoming available only in the past couple of years and most CTCs currently managing 2–4 patients receiving CAR T therapy per month. Therefore, the composition of the clinical care teams that manage the referral, eligibility screening, and initial consultation for patients entering the CAR T pipeline within the CTC are specific to each institution and their existing resource structures. For instance, while some CTCs have established a specific CAR T coordinator (a registered nurse), who manages CAR T referrals, other institutions rely on Nurse Navigators (NNs) to conduct the initial triage to identify patients eligible to enter the CAR T pipeline at the CTC. At 1 CTC, the physician noted that 2 Advanced Practice Providers (APPs) within their New Patient Access Group assess the eligibility of referred patients for clinical trials and/or CAR T. Prior experience with BMT practice in hematology/oncology and involvement with CAR T clinical trials was noted as an advantage in advancing CAR T application in their practice. Conversely, translating CAR T therapy into routine practice was more challenging for physicians without transplant experience. Indeed, several physicians noted leveraging the existing BMT infrastructure at their CTCs to facilitate different parts of the patient journey—such as patient triage, screening, and/or financial/insurance clearance. The goal of the "triage" process is not only to identify patients who may benefit from CAR T therapy and prioritize them on the CAR T waitlist but also to expedite their entry, and ultimately, receipt of CAR T therapy.

The physicians noted that the majority (approximately 80%) of patients receiving CAR T therapy in their care are either patients from within their practice or are referred to their practice from within the local area (150-mile radius), by community physicians with whom they have an established relationship. One physician indicated providing CAR T therapy for patients referred from up to 350 miles away. Given the limited availability of manufacturing slots for commercial CAR T products, established patients of practice collaborators are often prioritized.

If there is a CAR T referral from farther away or from community practices that do not have established relationships with the CTC, it is often routed through the CTC faculty or new patient coordinators. The request is then directed to NNs, before eventually being assessed by CAR T specialists. For patients who enter the CAR T pipeline in this manner, the CTC must find an "extra" CAR T slot, if available. Although telehealth/virtual visits may facilitate the first consultation with patients in farther locations, telehealth options may be limited to in-state or regional patients due to physician licensing restrictions.

The importance of setting expectations for the patient, from the very first consult at CTC was highlighted by physicians. According to a physician, this first visit "should be seen as an investment," to ensure that the patient is aware of all their options. The first visit can also help allay patient dejection and mitigate inappropriate demand for CAR T, in case CAR T is not the optimal option for the patient, especially for self-referrals for CAR T.

NLB Perspective of the Patient Journey to CAR T

Overall, the perspective of the NLB on the patient journey, referral process and source, and patient entry into the CAR T pipeline mirrored that of the physicians. A Nurse Leader noted, for example, that in addition to having a CAR T program with specific CAR T coordinators, their CTC has also established a dedicated CAR T service line to serve as a central point of contact for all stakeholders. A Nurse Leader also mentioned that differences in the approved indications for CAR T across world regions may preclude intake of internationally referred patients—ide-cel and cilta-cel are approved for use in patients with RRMM after 3 LOTs in the EU, for instance, while they are approved after 4 LOTs in the US.[20–23]

NLB members noted that having nurses as coordinators not just for CAR T therapy but also for following individual patients throughout their MM care journey, including clinical trials, is a key element for ensuring continuity of care. The NLB discussions also highlighted how different clinical care team members—BMT coordinators, APPs, and the MM nursing team—facilitate different parts of the CAR T patient journey, with BMT coordinators often tasked with financial clearance/insurance authorization and APPs or nurses taking over once the patient has entered the CAR T pipeline.

Summary of Recommendations for Optimizing CAR T Therapy Patient Intake

Key recommendations for optimizing the intake of patients and facilitating their entry into the CAR T pipeline at a CTC are summarized in **Figure 2**. The care team members and their responsibilities in vetting and managing patients who are referred to the CTC for CAR T therapy are outlined in **Table 2**.

Identifying the Ideal Patient for CAR T therapy

Principles of Patient Selection for CAR T Therapy

At present, as stated previously, in the US both CAR T agents approved for MM are indicated for patients with RRMM after ≥4 prior therapies, including an anti-CD38 mAb, a PI, and an IMiD.[20,21] However, both physicians and nurses noted that they anticipate CAR T therapies to be used earlier in the patient's disease course in the future. Given the high demand for CAR T therapies and limited access, primarily due to limited manufacturing slots, optimizing patient selection for CAR T therapy is a critical factor for optimizing its use in clinical practice. Patient selection is likely to be even more important as additional therapies, especially BCMA-targeted bispecific antibodies, enter the therapeutic space.[24] [

"I would say that my pendulum has moved. When these agents were first FDA-approved, every patient we treated [with CAR T] was on their last leg. I think that in some ways, the shortage [of CAR T spots] has been helpful to figure out who would really benefit from [CAR T] the most. [The patients] who are earlier in their journey of myeloma, but who are out of the conventional therapies, are likely to obtain long-term responses." — Physician

Physicians and the NLB identified some key features of their ideal patient for CAR T-cell therapy in addition to the criteria specified in the FDA-approved indications: RRMM that is progressing slowly enough that the patient can survive the duration of the manufacturing process; overall health status needs to be stable enough for the patient to survive the waiting period, manufacturing times, and withstand toxicities associated with CAR T therapy; T cell health needs to be adequate for manufacturing success; and disease that is refractory but was responsive to treatment.

Although CAR T therapy is generally applied in younger patients, with some CTCs using 75 years as the upper age limit,[24] physicians noted that neither advanced age nor renal insufficiency precludes CAR T therapy. No formal renal impairment studies of ide-cel or cilta-cel have been conducted and the KarMMa and CARTITUDE-1 studies enrolled patients with adequate renal function (defined as creatinine clearance [CrCl] ≥45 mL/min in KarMMa and >45 mL/min in CARTITUDE).[20,21,25–26] However, pharmacokinetics of CAR-positive T cells administered in CARTITUDE-1 was not affected by mild renal dysfunction (60 mL/min ≤ CrCL <90 mL/min).[26] Available data from a post-hoc analysis (excluding patients with estimated glomerular filtration rate <30 mL/min/1.73 m^2) and a small study (7 patients with RRMM and renal impairment) showed that CAR T therapy yielded responses in patients with RRMM who had impaired kidney function.[25,27,28] Available clinical study and real-world data also support the clinical activity of CAR T therapy in older (≥65 years) patients with MM.[12,29]

In describing patients who may not be ideal candidates for CAR T therapy, similar factors were identified in both roundtables. These included previous lymphodepleting regimens, such as

bendamustine regimens, that may lead to T cell exhaustion; poorly controlled disease despite the use of bridging therapy; and prior use of BCMA-directed therapies.

One physician with significant CAR T therapy experience noted avoiding the use of alkylators prior to CAR T therapy or allowing for a washout period after alkylator-based therapy before leukapheresis for T cell collection in patients selected for CAR T therapy.

Beyond the available clinical trial data, approved indications, and clinical judgment, there are currently no validated scoring systems to facilitate patient selection for CAR T therapy from a waiting list. One Nurse Leader noted the use of a color-coded CAR T waiting list for categorizing the urgency of the patient's need, based on their health status (Charlson comorbidity index), insurance authorization, and response/remission on current therapy. In this regard, recent work presented at the 2022 International Myeloma Society Annual Meeting on a proposed clinical factor scoring system for CAR T patient selection in RRMM was discussed at both roundtables.[30] This scoring system for estimating a patient's need for CAR T therapy and the potential benefit is based on 6 key criteria: penta-refractory disease, recent aggressive relapse with extramedullary disease and significant tumor burden, bridging therapy requiring salvage chemotherapy, lack of effective therapeutic options or clinical trials with a life expectancy <1 year, not in remission with clinically active or extramedullary relapse, and clinically stable with life expectancy long enough to receive future CAR T therapy.[30] With the increased uptake of CAR T therapy in routine practice and expansion of the MM CAR T therapy options, scoring systems will likely not only help allow for optimal patient selection but also equitable access to CAR T therapy.

Available data indicate persistent geographical and racial/ethnic disparities in MM care, including access to CAR T clinical studies.[31–33] Physicians noted that improving their understanding of the socioeconomic and demographic distribution within their region can facilitate access and promote equity. They described creative ways for reaching communities not captured using conventional methods, such as outreach to churches and using virtual methods for contacting and raising awareness.

Coordination of Care

Optimal Care Coordination: Challenges and Barriers

The delivery of CAR T therapy is a complex and multistage process, requiring significant collaboration and care coordination across settings and throughout the therapeutic continuum (**Figure 3**). Coordination between the CTC and the referring physician/community oncology practice was identified as one of the most significant challenges by physicians and the NLB. As mentioned before, CTCs rely on existing relationships and multimodal channels of

communication with physicians, hospitals, and regional oncology centers to facilitate care coordination. However, keeping track of MM patients was identified as a substantial challenge, especially when certain aspects of care may be handled outside the CTC—such as pre-CAR T assessments, MM treatments, and evaluations conducted before the first CTC consult, and bridging therapy (if provided outside the CTC). Staffing shortages, even at CTCs and especially among nursing staff, were also noted to "tax resources" and add to the challenge of ensuring coordinated care for patients receiving CAR T therapy. Nurse Leaders shared the different strategies in use at their CTCs to navigate these shortages, including allocating additional responsibilities to BMT or CAR T nurses and leveraging telehealth options and electronic communication methods, when feasible/appropriate.

"I think we all have [staffing] shortages. The myeloma nurses are taking care of [the CAR T processes], but it is a big stressor for them on top of the other stressors and tasks they have. Keeping track of [CAR T] patients is a lot of work." — Nurse Leader

One of the key steps in the CAR T process is bridging therapy—treatments administered between apheresis and the initiation of lymphodepleting chemotherapy, to control disease progression during the waiting time prior to CAR T cell infusion.[34] Physicians and Nurse Leaders reported that bridging therapy needed to be individualized based on the patient's prior exposure and disease status. At both meetings, the potential for bridging therapy in community practice was acknowledged, depending on the comfort level of the community provider, the travel distance for the patient, and whether an all-oral regimen may be an option.

Overall, the bridging therapy considerations outlined at the 2 roundtables were commensurate with recommendations in published literature—all treatments can be considered except for anti-BCMA therapies; nearly all patients would be candidates for bridging therapy, exceptions may include patients with stable or slowly progressing MM after leukapheresis.[34]

The roles and responsibilities of care team members along the patient's CAR T therapy journey are outlined in **Table 2**.

Physician Perspective on Care Coordination

Patients receiving CAR T therapy should be seen as shared patients.

Maintaining communication with community physicians/primary oncologists, especially in cases where there is no prior relationship between the CTC and the practice or in geographically distant or outlying areas, is a substantial challenge. For instance, several physicians noted that information on laboratory assessments, other clinical evaluations, and any interventions the

patient received while waiting for CAR T therapy is not always communicated clearly or accurately with the CTC team. Moreover, once CAR T therapy is completed and the patient has returned to community practice for routine care, physicians noted that significant collaboration and communication between the CTC and the community oncology practices are needed to track trends in changes for key clinical assessments.

Physicians identified different approaches that they/their CTCs have adopted to manage these challenges. For instance, while some CTCs have opted to accept laboratory results generated outside the CTC, others have opted to restrict assessments to solely CTC-associated labs. They also described using multimodal communication methods such as including their/key CTC team members' mobile numbers or email addresses on the discharge summary provided to the patient and shared with the community physician.

The perspective shared by several physicians indicated that if CTCs take primary responsibility for the patient receiving CAR T therapy, and support, inform, and collaborate with community physicians to manage the patient, this may ease the burden on community practices (which may also be resource-limited) and increase their comfort with CAR T therapy.

"[The CTC physicians/center] have to take responsibility for these patients throughout the continuum [of CAR T therapy]." — Physician

NLB Perspective on Care Coordination

"Early referral is the best referral so that all patients can get on the CAR T waitlist and avail of CAR T /other optimal treatments when they need it." — Nurse Leader

Nurse Leaders emphasized the importance of early referral of patients who may be eligible for CAR T therapy to the CTC, because:

- The referral process takes time, up to 8 weeks in some cases
- Patients potentially eligible for CAR T therapy may be lost to the process, due to disease progression or death, during the waiting period for completion of the CAR T referral review or therapy initiation
- Early referral allows for sufficient time to plan for subsequent CAR T therapy (eg, washout period from prior T cell-depleting treatments, insurance authorization, etc)
- Patients who are referred early can avail of the CTC/MM expertise and therapeutic options
- Early referral also allows for the time to establish relationships and communication between stakeholders (patient/care partner, referring physician, CTC team) and facilitate the patient journey to and after CAR T/RRMM therapy

The importance of educating community physicians on CAR T therapy was identified as an area of critical need by several Nurse Leaders. Some key areas with educational needs include:

- The CAR T process timeline and supportive care, in terms of both clinical needs and care partners
- Tenets of an ideal CAR T referral
  - Referral of heavily pretreated patients
  - Referral focused on identifying strategic solutions (not focused on CAR T therapy alone) for the RRMM patient that incorporate optimal therapies and clinical trial options
  - Early referral, at the second or third LOT, to allow sufficient time for the patient to be integrated into CTC practice

Nurse Leaders noted that bridging therapy can often be administered in the community, especially with all-oral regimens, with adequate monitoring and support from the CTC team. Exceptions may include cases where the recommended therapy requires hospitalization for infusion or aggressive management. Also, community physicians may prefer to have patients with aggressive or more advanced disease treated and followed at the CTCs.

Summary of Best Practices and Recommendations for Care Coordination

Best practices, tools, and recommendations from the physicians and the NLB for facilitating care continuity and enabling consistent and clear communication with the referring physician/community oncology practice for their patients receiving CAR T therapy throughout the CAR T process are summarized in **Table 3**.

Patient Monitoring and Long-Term Care

Toxicities Associated with CAR T Therapy

Management of short- and long-term toxicities associated with CAR T therapies, characterized by cytokine release syndrome (CRS) and immune effector cell-associated neurologic syndrome (ICANS)/neurotoxicities, is challenging.[13] CRS was common among patients treated with ide-cel (84%) or cilta-cel (94.8%) in the KarMMa and CARTITUDE-1 studies, respectively; however, most CRS events in both studies were grade 1 or 2 and were resolved/manageable with supportive care and tocilizumab.[12,14,35] Neurotoxicity, though less common than CRS with ide-cel (18%, all ≤grade 3) and cilta-cel (21%, 10% ≥ grade 3), is another toxicity of concern.[12,35,36] Other toxicities to consider in routine practice include cytopenias, including B-cell aplasia, hypogammaglobulinemia associated with the need for infection prophylaxis, and hemophagocytic lymphohistiocytosis.[36] Data on long-term and late toxicities for CAR T therapy in RRMM are currently limited; however, prolonged/delayed cytopenias and risk of infections

and associated complications are not uncommon and need to be mitigated/managed; recommendations for managing short- and long-term toxicities are included in the product labels for the CAR T products (summarized in **Table 4**) and recent publications.[20,21,36,37]

Management of CAR T-Associated Toxicities in Coordination with Community Oncology Practice/Providers

Patients are typically managed at the CTC until 30 days after CAR T infusion, which includes the monitoring period for short-term/early-onset toxicities. Patients often remain at the CTC until neurotoxicities, if any, are resolved. Although physicians and the NLB acknowledged the importance of educating community physicians about late toxicities, they reported that late neurotoxicities have been rare in their experience, with some instances of movement-related neurotoxicities such as twitching or tremors.

Post-treatment monitoring practices at the CTCs include some standard assessments such as bone marrow (BM) biopsies and positron emission tomography (PET), with these procedures included in the CAR T therapy cost estimates. However, the exact type and timing of the assessments varied by practice/CTC. For instance, a physician with significant CAR T therapy experience indicated BM biopsies and PET scans prior to leukapheresis and at day 30. For patients deemed to be at high risk of toxicities, longer follow-up (for up to 100 days) at the CTC may be warranted. While some CTCs include PET assessments at day 60 after CAR T infusion, others may not, for patients without PET-positive disease at the first assessment.

Overall, the long-term care practices for CAR T patients after they return to the community also varied across CTCs and depended on the patient's recovery/progress after the CAR T therapy and the comfort level of the patient/care partner/community physician with returning to the community. The patient's preference is also a primary decision driver of the timing of their return to the community.

A physician discussed using the post-transplant model for monitoring and assessments: weekly follow-ups for the first month, monthly follow-ups until 3 months, and consults once every 3 months and as needed, thereafter. Both physicians and Nurse Leaders noted that the occurrence and timing of disease relapse would also dictate how follow-up schedules and any subsequent therapies are coordinated between the CTCs and the referring physicians.

Patients and their care partners should be educated about monitoring CRS and neurotoxicities and informed of the generally mild and reversible nature of these toxicities. Establishing trust with the patient is critical to optimal toxicity management.

In the NLB roundtable, the CARTOX app was discussed as an important resource that can assist clinicians with accurate and timely grading and treatment of CAR T-associated toxicities. The CARTOX app, developed at the MD Anderson Cancer Center and free to download and use on different mobile devices/platforms, incorporates the American Society for Transplantation and Cellular Therapy (ASTCT) recommendations for grading CAR T-related toxicities and is based on CAR T toxicity management guidelines published by researchers at the MD Anderson CARTOX Program.[38–41] The application also provides guidance on key interventions, including antiviral, antibiotic, and antifungal prophylaxis, such as with acyclovir, levofloxacin, and fluconazole.[36]

Nurse Leaders also indicated that patients receiving CAR T therapy are typically managed for the first 30 days at the CTC. Patients who are still transfusion-dependent or who may require more frequent laboratory assessments (>once per week) will continue to receive care at the CTC. Vaccinations and their schedules mirror that of post-transplant patients, with the standard practice of re-vaccinating patients past 30 days of CAR T infusion. While the post-CAR T vaccinations are managed by community physicians, the process may be handled at the CTC instead, depending on the comfort level of the community physicians. Nurses at the CTCs are also the key educators of patients and guide appropriate prophylactics and vaccinations.

If there are infectious complications or late neurotoxicities seen 30 days after CAR T therapy, the patient and the community physicians are informed that the patient must schedule a follow-up at the CTC. A fact sheet or summary on ICANS, neurotoxicities, and other late toxicities of concern, indicating the signs and symptoms to watch out for and if/when the patient needs to contact/follow up with the CTC team is shared with the community physicians at discharge. Patients would also be provided with a wallet card (example shown in **Figure 3**) that includes the contact information of the CAR T physician, to share with providers in case of emergency department (ED) visits/hospitalization.[37] Addition of a banner on the patient's EPIC/electronic health record, indicating that they are a CAR T therapy recipient, was also noted as a way to inform community hospitals/EDs.

An important message to share with community physicians/primary oncologists: CRS is common, mostly grade 1 or 2, occurs soon after CAR T therapy, and can be resolved in most cases with supportive care.

Stakeholder Responsibilities

Role of the Manufacturer

At both roundtables, clinicians expressed the need for enhanced communication from CAR T-cell manufacturers with the CTC, pertaining to the availability and timing of CAR T

manufacturing spots as well as the status of CAR T cells along the manufacturing process and shipping.

A CAR T-specific support line available throughout the day was identified by several physicians as a key manufacturer-mediated resource for assisting community physicians with any CAR T therapy-related concerns or questions.

Lodging and logistical assistance to support patients with their residential and transportation arrangements near the CTC during the immediate follow-up period was mentioned as another resource challenge by physicians. Some physicians noted that manufacturers may be able to participate in programs for supporting patients with their lodging/travel needs during CAR T therapy. At some CTCs, lodging arrangements for CAR T patients and their care partners may use the same resources made available to patients receiving BMTs.

Physicians and Nurse Leaders also pointed to the significant educational need for both clinicians and patients/care partners as an area where manufacturers can play an important supporting role.

Role of the Patient and their Care Partners

The importance of engaging and educating patients on the CAR T therapy process and journey and the commitment in terms of time, treatment steps, and support from care partners was emphasized at both roundtables. Physicians shared that an educational initiative, developed by patient-focused organizations such as the IMF, may also be helpful in this regard. Nurse Leaders indicated that the CTC team should ensure that patients have engaged their care partners and their support throughout the CAR T therapy process to optimize patient outcomes.

Closing Statements

There is an expanding portfolio and increasing demand for CAR T-cell therapy for patients with RRMM and currently approved CAR T therapies have yielded remarkable response rates in heavily pretreated RRMM patients. However, there is a substantial need to educate clinicians, including non-CAR T specialists at academic centers and community physicians/primary oncologists, on best practices for patient management prior to, during, and after CAR T therapy. Education for community physicians also needs to focus on CAR T-specific toxicities, such as ICANS/neurotoxicities, as non-CAR T specialists may not be familiar with the manifestations of these toxicities. Education and candid communication with patients on the CAR T therapeutic journey, perhaps spearheaded by patient-focused organizations and/or including the perspective of CAR T recipients, are also needed to improve the understanding of MM patients. The development and implementation of communication channels between the CTC team and

the community physicians using multiple methods is another critical area that needs improvement.

The enthusiasm for and expectations of CAR T therapies, with approved agents thus far yielding unprecedented responses in patients with highly refractory MM, remain high among both healthcare providers and patients. Moreover, this innovative immunotherapy for MM is anticipated to be introduced to patients earlier in their myeloma journey. There is also an increasing appreciation of the need to improve coordination across care settings and for expanding outpatient/community-based delivery of CAR T therapy.[42,43] [This would enable genuine improvements in access and equity in CAR T therapy delivery for MM patients, and ultimately, continued progress in improving outcomes for MM patients. Indeed, several clinical trials, such as the CARTITUDE-2/4/5/6 studies of cilta-cel, are assessing CAR T therapies in different MM patient populations and outpatient settings.[43,44] Efforts to streamline communications between referring physicians and the CTC team, as well as augment resources and staffing across care settings need to be strengthened to make seamless outpatient CAR T therapy delivery a reality in routine clinical care of patients with MM.

Key Takeaways
Currently approved BCMA-targeted CAR T therapies for patients with RRMM have yielded remarkable response rates
Logistical/manufacturing issues, toxicity concerns, and care coordination challenges can impede access to and delivery of CAR T therapy in routine clinical practice
To ensure continuity of care for patients eligible for/referred to/receiving CAR T therapy: • **Relationships and multimodal communication between the CTC and regional community oncology practices and hospital systems need to be established and maintained throughout the CAR T therapy continuum** • **Education around CAR T therapy, including the extended process and time commitments, and potential toxicities and management strategies should be provided to patients, their care partners, community physicians, and non-CAR T specialists at CTCs/large academic centers**
Manufacturers can facilitate improvements in the CAR T process by providing enhanced communication around the timing/availability of CAR T spots and the status of CAR T cells along the manufacturing process

Although there is significant demand, enthusiasm, and high expectations for CAR T therapy among patients and clinicians alike, it is important to consider the entire range of potential therapeutic options, including CAR T therapy, available to patients with RRMM, based on their individual profile and preferences

CAR T therapy options for patients with MM are expected to grow in the coming years; continued improvements focused on care coordination can help deliver CAR T therapy, helping to translate the striking clinical data into genuine access and improved outcomes for patients with MM

Acknowledgments: The IMF would like to thank the meeting attendees, authors, and Eubio for providing medical writing support for these roundtables, which were sponsored by Legend Biotech/Janssen.

The attendees of the Hematology/Oncology Physician Roundtable on August 28, 2022, were as follows:
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The attendees of the IMF NLB Roundtable on September 16, 2022, were as follows:
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Figures

Figure 1. Key Attributes of Approved CAR T Therapies for RRMM.

Shown are the schematic diagrams of the design of ide-cel and cilta-cel. Note that ide-cel contains 1 BCMA-binding domain, a murine extracellular scFv specific for recognizing BCMA, a human CD8a hinge domain, a transmembrane region, a T-cell cytoplasmic signaling domain (4-1BB), and a CD3ζ signaling domain.[37] Cilta-cel contains 2 BCMA-binding domains, thought to confer greater activity and lower immunogenicity, along with a CD8a hinge domain, a 4-1BB costimulatory domain, and a CD3z signaling domain.[43,45]

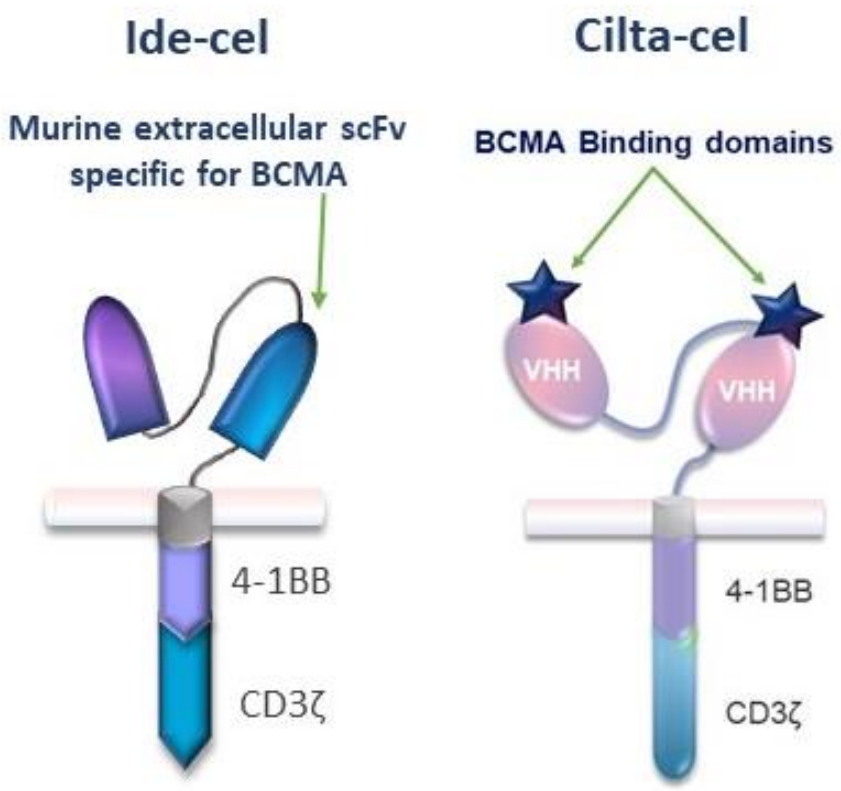

Figure 2. Summary of Recommendations and Best Practices for Optimizing CAR T Patient Intake.

APP, advanced practice provider; CAR T, chimeric antigen T cell receptor; CTC, CAR T therapy center; LOT, line of therapy; MM, multiple myeloma; MTB, multidisciplinary tumor board; NN, nurse navigator.

[a]Video presentations on the CAR T process that includes different members of the care team, such as pharmacists, APPs, and symptom management coordinators, can provide a detailed perspective on the timeline, resources, and steps involved in CAR T therapy. Some Nurse Leadership Board members also noted that videos that include the patient and caregiver perspective may be especially helpful to patients who may be eligible for CAR T therapy.

[b]Given the current limitations in the number of manufacturing spots for CAR T cells, consults with patients a few weeks in advance of therapy initiation can ensure that the patient is still eligible and/or wants to receive CAR T therapy. The advance consult can also ensure that manufacturing appointments can be utilized in a timely manner by the next patient on the waiting list, in case the patient becomes ineligible or opts out of the treatment.

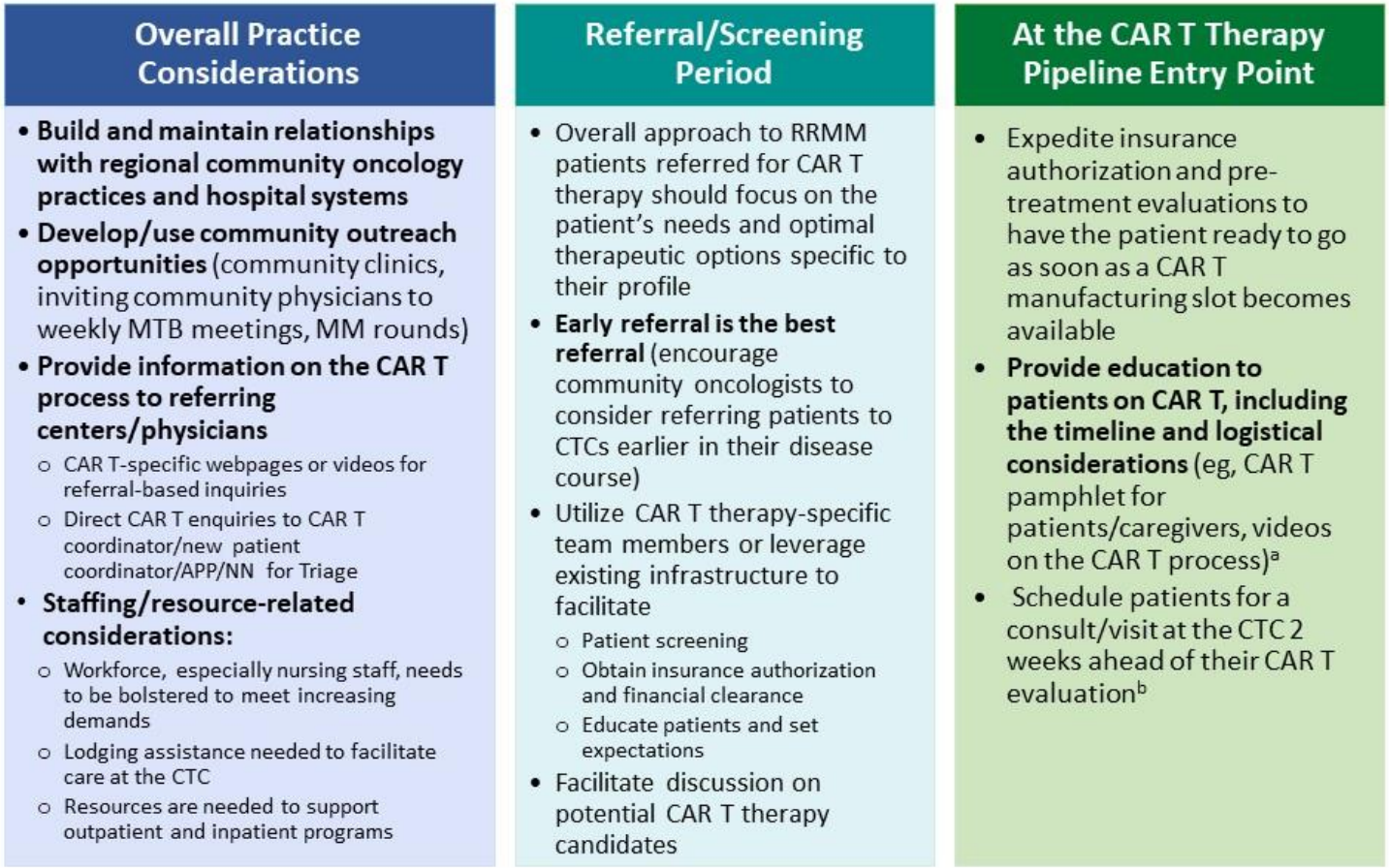

Figure 3. Overview of the Patient Journey Along the CAR T Therapy Continuum.

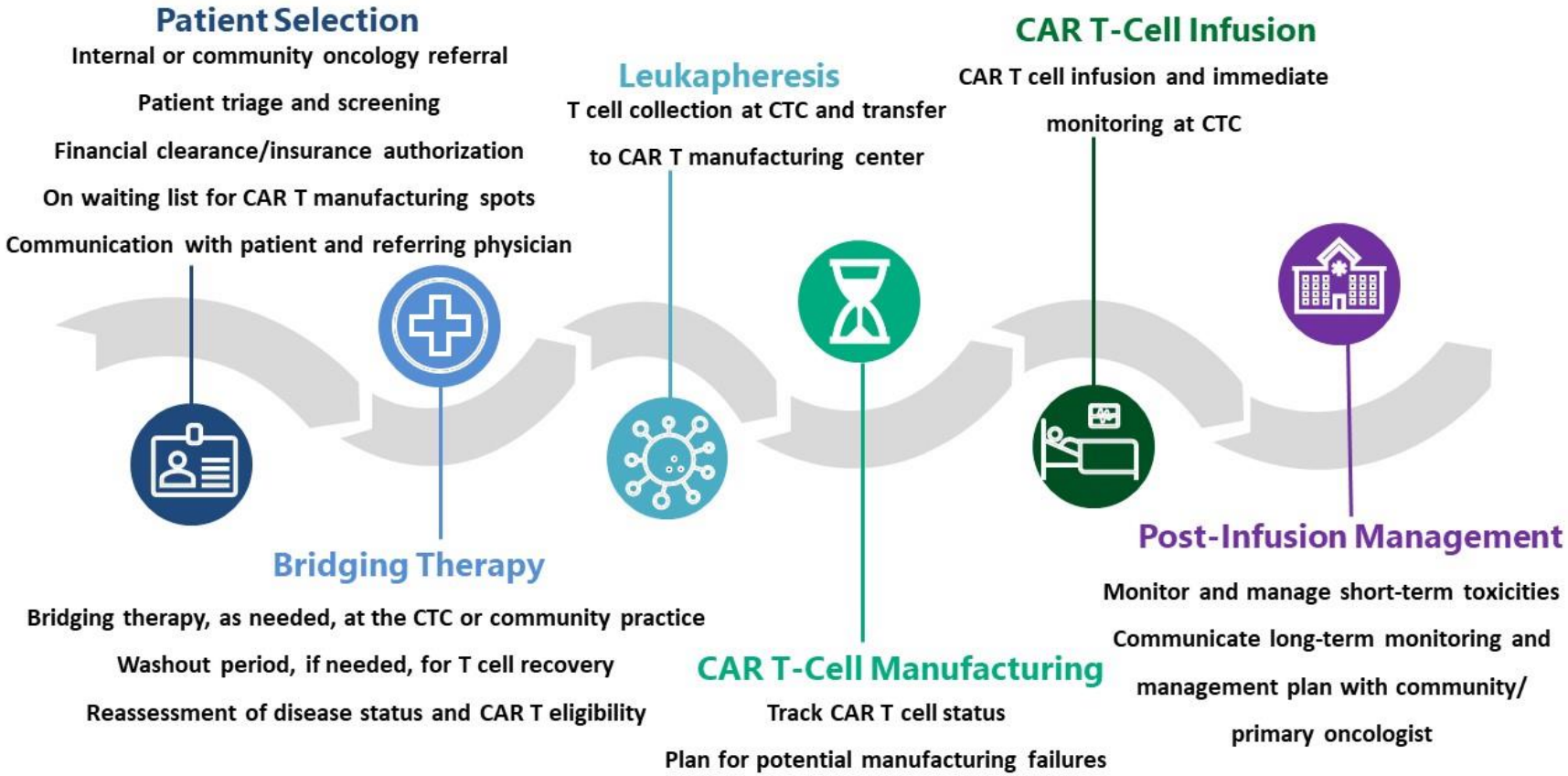

Figure 3. Example of Patient Wallet Card.

Shown are the front (top panel) and back (bottom panel) of the Patient Wallet Card that all patients treated with ide-cel (ABECMA™) receive. A similar card is provided to all patients who receive cilta-cel (CARVYKTI™). The Wallet Card should be carried by patients who have recived CAR T therapy to remind them of the signs and symptoms of CRS and neurological toxicities that require immediate medical attention. The Patient Wallet Card can be shared by the patients with any healthcare provider to inform them of the patient's receipt of CAR T cells and when to contact the patient's oncologist.

Information for Patient

ABECMA may cause side effects that are life-threatening and can lead to death.

Call your healthcare provider or get emergency help right away if you get any of the following:

- Difficulty breathing
- Fever (100.4°F/38°C or higher)
- Chills/shivering
- Confusion
- Dizziness or lightheadedness
- Shaking or twitching (tremor)
- Fast or irregular heartbeat
- Severe fatigue
- Severe nausea, vomiting, or diarrhea

Bristol Myers Squibb™

Abecma (idecabtogene vicleucel)

Patient Wallet Card

Have this card with you at all times. Show it to any doctor who sees you and when you go to the hospital.

- Tell any healthcare provider who sees you that you are being treated with ABECMA®.
- For at least 4 weeks after receiving ABECMA, you should plan to stay within 2 hours of the location where you received treatment.
- Refrain from driving or operating heavy or potentially dangerous machines until at least 8 weeks after ABECMA administration.

Name of ABECMA Treating Oncologist

Office Phone Number

After-hours Phone Number

Hospital Name (for Management of ABECMA Side Effects)

Date of ABECMA Infusion

03/21 US-REMS-ABM190003

www.AbecmaREMS.com

Information for the Healthcare Provider

This patient has received ABECMA CAR T cell therapy, a BCMA-directed genetically modified autologous T cell immunotherapy.

Following treatment with ABECMA, cytokine release syndrome (CRS) or neurologic toxicities may occur, which may be fatal or life-threatening. CRS may involve any organ system.

Contact Patient's Oncologist Immediately for Further Information and in the Following Situations:

- The administration of steroids or cytotoxic medications.
- If the patient has a serious infection.
- Any planned invasive procedure(s) for the patient.

Tables

Table 1. Summary of Key Data for Ide-cel and Cilta-cel in RRMM.[12,14,45,46]

	Ide-cel KarMMa; Phase 2 (n = 128)	Cilta-cel CARTITUDE-1; Phase 1b/2 (n = 97; Phase 1b, 29; Phase 2, 68)
Baseline Characteristics		
Target CAR T dose (cells)	450 million	0.75 million/kilogram
Median age (range)	61 years (33–78)	61 years (43–78)
Median prior lines (range)	6 (3–16)	6 (3–18)
Bridging therapy	87%	75%
R-ISS stage II/ III	86%	66%
Triple-refractory disease[a]	84%	88%
Penta-refractory disease[b]	26%	42%
High-risk cytogenetics[c]	35%	24%
Extramedullary disease[d]	40%	13%
Toxicity		
CRS (all; grades 3–4)	85% (6%)	95% (5%)
Median onset of CRS, duration	1 day, 5 days	7 days, 4 days
ICANS (all; grades 3–4)	19% (3%)	17% (2%)
Median onset of ICANS, duration	2 days, 3 days	8 days, 4 days
Infections (all; grade 3–4)	69% (22%)	59% (23%)
Grades 3–4 neutropenia >1 month	40%	30%
Grades 3–4 thrombocytopenia >1 month	48%	41%
Delayed neurotoxicity	–	12%
Efficacy		
ORR	**73%**	**97%**

sCR or CR	33%	sCR 78%
MRD negativity rate (10^-5)	33/119 (28%)	53/97 (58%)
Median PFS	**9.2 months (95% CI, 6.0–12.1)**	**24-month PFS: 60.5% (95% CI, 48.5–70.4)**
Median OS	**19.5 months (95% CI, 18.9–NR)**	**24-month OS: 74% (95% CI, 61.9–82.7)**
Median time to best response (range)	2.8 months (1.0–11.8)	2.6 month (1.0–6.1)
Median duration of response	11.1 months (95% CI, 9.1–11.3)	21.8 months (95% CI, 21.8 –NR)

Table adapted from Davis et al (2022).[46]

Cilta-cel, ciltacabtagene autoleucel; CR, complete response; CRS, cytokine release syndrome; ICANS, immune effector cell-associated neurotoxicity syndrome; Ide-cel, idecabtagene vicleucel; IMiD, immunimodulatory drug; mAb, monoclonal antibody; MRD, minimum residual disease; NR, not reached; ORR, overall response rate; OS, overall survival; PFS, progression-free survival; PI, proteasome inhibitor; sCR, stringent complete response.

[a]Refractory to ≥1 PIs, ≥1 IMiDs, and 1 anti-CD38 mAb.

[b]Refractory to ≥2 PIs, ≥2 IMiDs, and 1 anti-CD38 mAb.

[c]High-risk cytogenetic abnormalities included: del(17p), t(4;14), t(14;16).

[d]Extramedullary disease was defined as paraskeletal soft-tissue masses or soft-tissue masses spreading outside of the bone marrow.

Table 2. Members and Responsibilities of the Care Team at the CTC Involved in Managing CAR T Therapy Referrals.

Responsibility	Care Team Member (s)	Notes
Prior to CAR T Initiation		
Managing referrals for CAR T therapy made by community oncology practice	• Teams or care coordinators specific to CAR T therapy • APPs, NNs, RNP coordinators	• Can leverage existing infrastructure or teams, such as the BMT team, to facilitate the patient journey to CAR T therapy
Identifying patients eligible for CAR T therapy	• Initial triage by APPs, CAR T coordinators, or NNs • Eligibility and clinical need discussions during regular new patient/ MM patient/MTB meetings • Regional community physicians may be invited to present their patients to the MTB for CAR T consideration	• Scoring systems for patient selection for CAR T therapy are emerging, such as the recent clinical factor-based scoring system presented at the 2022 International Myeloma Society meeting[30]
Managing the CAR T therapy waitlist	• NNs, dedicated CAR T service line and coordinator	• Patients may be undergoing bridging therapy and/or completing other therapies while they await a CAR T manufacturing spot • Patients must be monitored regularly to assess their disease status and screened for CAR T eligibility • The waiting period can also be used to expedite financial clearance and insurance authorization for CAR T therapy
Patient education	• APPs, MM nurses	• Share educational videos/pamphlets, as applicable • Educational information delivered by patients who have received CAR T and their carers can be particularly useful • Patients need education about the extended process and timeline of events involved in CAR T therapy
Community provider education, engagement, and communication	• APPs, RNPs, CAR T physician team,	• Email blasts to regional/satellite clinical trial sites about CAR T spots/other clinical trials

	• Multimodal communication methods can be used	• Once a patient is assigned to a CAR T spot, information on the next steps (when to stop chemotherapy, bridging therapy options, timing, and location [CTC/community practice], etc) should be provided
Management of Patients on the CAR T Therapy Track		
Leukapheresis	• APP	• Provide patient education throughout the CAR T therapy process • Deliver targeted information personalized to the patient's schedule and place along the CAR T therapy continuum • Lymphodepletion can be delivered as an outpatient procedure • CAR T-cell infusion and immediate care typically requires 14 days of hospitalization to facilitate monitoring for CRS, ICANs, and other toxicities • Stay close by needed to facilitate weekly follow-up for the first month; generally, discharge to community after 30 days • Monthly follow-ups for the first 3 months after CAR T therapy, once per 3 months for the first year • The CARTOX app can be used to assist clinicians in identifying and grading CAR T-associated toxicities and obtain guidance on key interventions, such as antibiotic antifungal prophylaxis
Bridging therapy considerations	• CAR T coordinator and/or the CAR T physician's team	
Lymphodepletion	• CTC team	
T-cell Infusion	• CAR T team	
Immediate/short-term post-infusion monitoring		
Continuation of Care After CAR T Therapy		
Discharge letter and management plan	• APP	• Discharge summary travels with the patient and is shared with the community oncologist • EPIC (if applicable) discharge note should indicate the schedule of follow-ups

Long-term toxicity management plan	• APP	• Letter sent to community physician/primary oncologist on day 30 (typical day of return to the community) • Fact sheet on late toxicities (ICANs/neurotoxicities, infectious complications) and symptoms of concern that should prompt a follow-up at the CTC • The CARTOX app can be used to assist clinicians in identifying and grading CAR T-associated toxicities and obtain guidance on key interventions, such as antibiotic antifungal prophylaxis
Follow-up care	• CAR T nurse	• Important to follow up after discharge of patients who received CAR T therapy, such as with an annual "How are you" letter

APP, advanced practice provider; BMT, bone marrow transplant; CAR T, chimeric antigen T cell receptor; CTC, CAR T therapy center; CRS, cytokine release syndrome; ICANS, immune effector cell-associated neurotoxicity syndrome; LOT, line of therapy; MM, multiple myeloma; MTB, multidisciplinary tumor board; NN, nurse navigator; RNP, registered nurse practitioner.

Table 3. Best practices for Communicating with Community Oncologists/Practices Regarding Patients Receiving CAR-T to Facilitate Care Coordination.

	Tools and Resources for Facilitating Care Coordination
General resources	• CAR T-specific webpage for referral-based inquiries • Include information on CAR T therapy on the landing page for "Request for CAR T Appointments" • Establish and maintain ongoing multimodal (emails, community clinics, etc) communication with regional community physicians/hospitals/oncology practices and satellite clinical trial sites
Educational tools	• Educational tools, such as videos and documents, can be shared with referring physicians in regional community practice/hospitals on CAR T therapy, including the timeline of the process and key considerations along the therapeutic continuum • Inform community oncologists of the CTC's process for vetting and placing patients on the CAR T waiting list as soon as a CAR T referral is made to their centers • Patients and caregivers should also be provided information on CAR T therapy and the CAR T process • Patient education needs to be individualized based on their place along the CAR T therapy continuum and strategies to deliver targeted information can be adopted on the patient's personalized schedule ◦ For instance, a high-level overview of the therapeutic process and timeline is appropriate at the initial consult, and a more detailed summary and schedule for follow-up assessments and self-monitoring information for long-term toxicities can be shared when the patient returns to their primary oncologist/community practice for care
Resources to share with patients after CAR T therapy	• A standard template for a document can be useful for communicating important information regarding the patient receiving CAR T therapy. The template would have placeholders for: • A summary of the interventions, evaluations, and other assessments that were carried out at the CTC • Response monitoring information while the patient's care is continued in the community • Information on toxicities, if applicable, such as CRS, experienced by the patient • The exact details and timing of supportive measures that were employed, such as the date of the patient's last IVIG • Contact information for key contacts in the CTC clinical team managing the patient and coordinating with the community team, such as the Myeloma and CAR T specialists, nurse coordinators, and APPs

	• Discharge letter or summary sheet, indicating all the assessments, toxicity monitoring, interventions, and resolution details, provided to the patient and can be shared with the community physician/primary oncologist • A wallet card indicating that the patient is a CAR T-cell recipient that they may present with at their local hospital or ED • Patients should be educated on infectious complications and infection protection methods
Strategies/tools for facilitating continuity of care after CAR T therapy	• Fact sheet on ICANS, neutoxicities, and other potential late toxicities associated with CAR T therapy to be shared with community physician/referring oncologist listing symptoms of concern that should prompt them to call the CTC • It is important to educate the community physicians on CRS and neurotoxicities; "CRS and neurotoxicity associated with CAR T therapy is almost always reversible; however, the patient needs to be seen at the CTC if infectious complications or neurotoxicities of concern occur past 30 days after CAR T therapy" — *Physician* • Contact information for key personnel on the individual patient's clinical care team • Share the follow-up schedule and assessments with the community physician/primary oncologist; typically, the patient is hospitalized for 14 days following CAR T-cell infusion, followed by a weekly visit (with the APP or CAR T nurse) for the first month, after which they have a monthly follow-up for 3 months ad then once every 3 months • A banner can be added on the patient's EPIC chart identifying them as a CAR T-cell recipient to facilitate their management in case of ED visit or hospitalization in community setting

APP, advanced practice provider; CAR T, chimeric antigen T cell receptor; CRS, cytokine release syndrome; CTC, CAR T therapy center; ED, emergency department; ICANS; immune effector-associated neurologic syndrome; IVIG, intravenous immunoglobulin; LOT, line of therapy; MM, multiple myeloma; MTB, multidisciplinary tumor board; NN, nurse navigator.

Table 4. Summary of Monitoring Considerations for Ide-cel and Cilta-cel.[20,21]

	Monitoring Considerations	
	Ide-cel	**Cilta-cel**
General monitoring considerations	• Ide-cel must be administered at a REMS-certified healthcare facility (ie, CTC) • Monitor patients at least daily for 7 days following ide-cel infusion at the CTC for signs and symptoms of CRS and neurologic toxicities • Instruct patients to remain within proximity of the CTC for at least 4 weeks following infusion • Instruct patients to refrain from driving or hazardous activities for at least 8 weeks following infusion	• Cilta-cel must be administered at a CTC • Monitor patients at least daily for 10 days following cilta-cel infusion at the CTC for signs and symptoms of CRS and neurologic toxicities • Monitor periodically for 4 weeks for signs and symptoms of delayed neurologic toxicity • Instruct patients to remain within proximity of the CTC for at least 4 weeks following infusion • Instruct patients to refrain from driving or hazardous activities for at least 8 weeks following infusion
Adverse Events	**Monitoring Considerations for Ide-cel**	**Monitoring Considerations for Cilta-cel**
Cytokine Release Syndrome	• Most common CRS manifestations included pyrexia, hypotension, tachycardia, chills, hypoxia, fatigue, and headache • Ensure that a minimum of 2 doses of tocilizumab are available prior to infusion of ide-cel • Monitor patients at least daily for 7 days following ide-cel infusion at the CTC for signs and symptoms of CRS • Monitor patients for signs or symptoms of CRS for at least 4 weeks after infusion • At the first sign of CRS, treat with supportive care, tocilizumab and/or corticosteroids	• Most common manifestations of CRS included pyrexia, hypotension, increased AST, chills, increased ALT, and sinus tachycardia • Ensure that a minimum of 2 doses of tocilizumab are available prior to infusion of citla-cel • Monitor patients at least daily for 10 days following cilta-cel infusion at the CTC for signs and symptoms of CRS • Monitor patients for signs or symptoms of CRS for at least 4 weeks after infusion • At the first sign of CRS, immediately treat with supportive care, tocilizumab, or tocilizumab and corticosteroids
Neurotoxicity /ICANS	• Most frequent manifestations of neurotoxicity include encephalopathy, tremor, aphasia, and delirium • Monitor patients at least daily for 7 days following ide-cel infusion at the CTC for signs and symptoms of neurologic toxicities • Monitor patients for signs or symptoms of neurologic toxicities for at least 4 weeks after infusion and treat promptly	• Neurologic toxicities included ICANS and neurologic toxicity with signs and symptoms of parkinsonism, GBS, peripheral neuropathies, and cranial nerve palsies • ICANS manifestations included encephalopathy, aphasia, and headache • Monitor patients at least daily for 10 days following cita-cel infusion at the CTC for signs and symptoms of ICANS

	• Neurologic toxicity should be managed with supportive care and/or corticosteroids as needed	• Monitor patients for signs or symptoms of ICANS for at least 4 weeks after infusion and treat promptly • Neurotoxicity should be managed with supportive care and/or corticosteroids as needed • Monitor patients for signs and symptoms of parkinsonism that may be delayed in onset and managed with supportive care measures • Monitor for GBS and assess patients presenting with peripheral neuropathy for GBS; consider treatment of GBS with supportive care measures and in conjunction with immunoglobulins and plasma exchange, depending on GBS severity • Monitor patients for signs and symptoms of cranial nerve palsies; consider management with systemic corticosteroids, depending on the severity and progression of signs and symptoms
Hemophagocytic lymphohistiocytosis/ Macrophage activation syndrome	• HLH/MAS manifestations include hypotension, hypoxia, coagulopathy, multiple organ dysfunction, renal dysfunction, and cytopenia • HLH/MAS is a potentially life-threatening condition with a high mortality rate if not recognized early and treated • Treatment of HLH/MAS should be administered per institutional standards	
Infections	• Monitor patients for signs and symptoms of infection before and after infusion of ide-cel or cilta-cel and treat appropriately • Administer prophylactic, preemptive, and/or therapeutic antimicrobials according to standard institutional guidelines	
Prolonged and/or recurrent cytopenias	• Monitor blood counts prior to and after ide-cel or cilta-cel infusion • Manage cytopenia with myeloid growth factor and blood product transfusion support according to local institutional guidelines	
Hypogammaglobulinemia	• Monitor immunoglobulin levels after treatment with ide-cel or cilta-cel and administer IVIG for IgG <400 mg/dL • Manage per local institutional guidelines, including infection precautions and antibiotic or antiviral prophylaxis	

AE, Adverse event; ALT, alanine aminotransferase; AST, aspartate aminotransferase; CRS, cytokine release syndrome; CTC, CAR T therapy center; CMV, cytomegalovirus; GBS, Guillain-Barré Syndrome; HLH, hemophagocytic lymphohistiocytosis; ICANS, immune effector cell–associated neurotoxicity syndrome; IVIG, intravenous immunoglobulin; MAS, macrophage activation syndrome; REMS, Risk Evaluation and Mitigation Strategy.
Please refer to the product lables for complete information on monitoring and management procedures.[20,21]

Table 5. Improvements Focused on Stakeholder Responsibilities.

	Tools and Resources for Facilitating Care Coordination
Manufacturer	• Enhanced communication with the CTC around the manufacturing process and status of CAR T cells • Streamline communication methods to facilitate notifications to the CTC team regarding the timing and availability of CAR T cell manufacturing spots • Support educational initiatives for both clinicians and patients on CAR T therapy • CAR T-specific support line for assisting community physicians • Lodging and logistical assistance to support patients with their residential and transportation arrangements near the CTC during the immediate follow-up period
Patients and Their Care Partners	• Patients need education to understand the support requirements. They must also ensure that they have adequate and informed care partners to assist them on their CAR T therapy journey

CAR T, chimeric antigen T-cell receptor; CTC, CAR T therapy center.