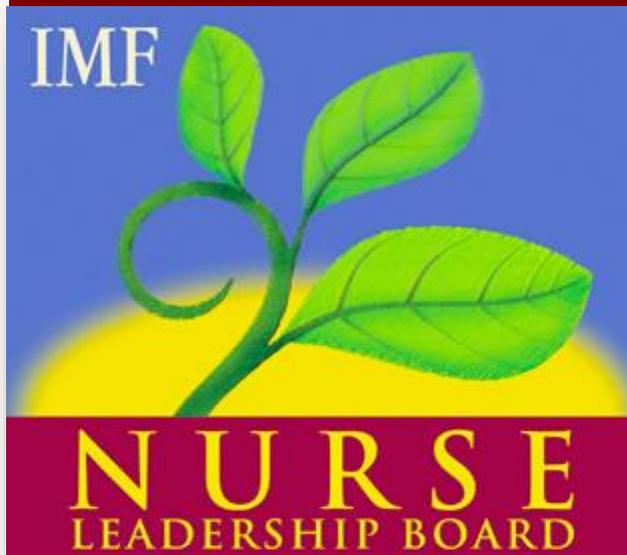




**Ciltacabtagene Autoleucel: Insights on Chimeric Antigen Receptor T-Cell Therapy Efficacy, Safety, and Management Approaches**

**Discussion with IMF Nurse Leadership Board**

**July 27, 2021  
Virtual Advisory Board**





## **Table of Contents**

<b>2</b>	Overview
<b>2</b>	Introduction
<b>3</b>	CAR T-Cell Therapy in the MM Treatment Paradigm
<b>7</b>	Cilta-cel Clinical Studies
<b>11</b>	Education Needs of Patients and Providers
<b>12</b>	Closing Statements
<b>13</b>	References



## Overview

On July 27, 2021, members of the International Myeloma Foundation (IMF) Nurse Leadership Board (NLB) convened for a virtual advisory board meeting. The purpose of the meeting was to discuss the latest clinical data for ciltacabtagene autoleucl (cilta-cel), a novel B-cell maturation antigen (BCMA)-targeted chimeric antigen receptor T-cell (CAR T) therapy, in the treatment of patients with multiple myeloma (MM). Additional objectives of the meeting were to identify nursing-specific educational needs and data gaps, and to review patient management approaches for CAR T therapies.

The specific objectives of the discussion were to:

1. Gather insights on the impact of BCMA therapies on the MM landscape
2. Discuss safety management strategies for nursing education resources and identify nursing data gaps
3. Review and gather nursing feedback on BCMA data presented at the American Society of Clinical Oncology (ASCO)/European Hematology Association (EHA) 2021 meetings

## Introduction

Multiple myeloma (MM) is a relatively rare malignancy of plasma cells that accumulate in the bone marrow, with an estimated 34,920 new cases and 12,410 deaths in 2021 in the United States.<sup>1,2</sup> [SEER

## Myeloma Statistics 2021/p1/Box1

[Kumar 2021/pMS-2/col1/para1/ln1-3]

The abnormal clonal plasma cell proliferation can lead to low blood counts, bone and calcium complications, kidney damage, and higher susceptibility to infections.<sup>3</sup> [ACS 2018/What is Multiple Myeloma/p2-3]

The median age of patients at MM diagnosis is 69, with the most frequent diagnosis of MM in patients aged 65–74.<sup>2</sup> [SEER Myeloma Statistics 2021/p4/Box2] MM is more common in men than women, in African Americans (AAs), with a 3-fold higher incidence rates for those aged <50 years for AAs than their White counterparts and a younger mean age at diagnosis.<sup>2,4</sup> [SEER Myeloma Statistics 2021/p4/Box1] [Waxman 2010/p1/Abstract]

The 5-year relative survival for patients with MM is 55.6%, a survival rate that has doubled over the last 2 decades, in large part due to advancements in the diagnosis, treatment, and management of these patients.<sup>2,5</sup> [SEER Myeloma Statistics 2021/p2/Box1] [Rajkumar 2016/p1/Abstract] The therapeutic landscape of MM has undergone a rapid expansion in recent years, with the introduction of multiple agents with novel mechanisms, including monoclonal antibodies (mAbs), immunomodulatory drugs (IMiDs), and cellular therapies, and combinations thereof. Additional promising drugs are in the development pipeline.<sup>6</sup> [Caers 2020/p1/para2] Despite these improvements, MM management remains

challenging, as relapse and disease progression are nearly inevitable even after achievement of a complete remission, and most patients have multiple relapses.<sup>7</sup>

[Chim 2018/p1/Intro/para1] The management of relapsed/refractory MM (R/RMM) is a significant clinical challenge, as each additional line of therapy (LOT) is associated with progressively shorter durations of remission or response, and ultimately shorter survival.<sup>7,8</sup> [Chim 2018/p1/Intro/para1] [Braunlin 2021/p2/Abstract] Indeed, the prognosis for patients with MM that relapses or is refractory to the 3 major classes of agents credited with outcome improvements—proteasome inhibitors (PIs), IMiDs, and mAbs—is poor.<sup>9</sup> [Mikhael 2020/p2/col1/para2] The median overall survival (OS) for patients with IMiD and PI double-class refractory disease was 6.7–11.5 months,<sup>10</sup> [Usmani 2016/p3/col2/para2] while patients with MM refractory to PIs (bortezomib and carfilzomib), IMiD (pomalidomide and lenalidomide), and anti-CD38 mAb (daratumumab) had a median OS of less than 6 months (5.6 months).<sup>11</sup> [Gandhi 2019/p2/ para3] Therefore, there is an urgent unmet need for novel therapies that can improve outcomes for patients with R/RMM following multiple lines of treatment with the current mainstays of anti-myeloma therapies.

A relatively new immunotherapy approach, using genetically modified T-cells harboring chimeric antigen receptors that target myeloma cell-specific antigens, has

emerged as a key option for treatment of recurrent disease.<sup>12</sup> [Padda 2021/p1/Intro and Background/para1; Review/para1] In March 2021, the US Food and Drug Administration (FDA) granted approval to the CAR T therapy targeting the B-cell maturation antigen (BCMA) idecabtagene vicleucel (ide-cel) for treatment of R/RMM that recurs following ≥4 prior lines of therapy.<sup>13</sup> [FDA 2021/p1] Additional CAR T therapies, including cilta-cel, are currently in various phases of clinical development.<sup>14</sup> [Su 2021/p3/Table 1; p5/Table 2]

The IMF NLB’s discussions focused on the position of CAR T therapy in the MM treatment paradigm, the latest data for cilta-cel from the CARTITUDE-1 and -2 studies, a case study-based discussion of considerations around outpatient/inpatient administration of CAR T therapies, and approaches for coordinating and managing the toxicities and adverse events (AEs) associated with this therapy. The Board also discussed important aspects of patient communication, educational needs aimed at community practitioners and other providers, and key questions/data gaps surrounding the optimal use of cilta-cel, pending FDA approval, for patients with R/RMM.

## **CAR T Therapy in the MM Treatment Paradigm**

IMF NLB Perspective on CAR T Therapy in MM

While CAR T therapies have been in use for treatment of leukemia and lymphoma subtypes since the first approval of this type of therapy in 2017,<sup>15</sup> [AACR 2017/p1] this therapeutic approach is still in its infancy in MM, with the first commercial approval this year. Given the remarkable outcomes with CAR T therapy in acute lymphocytic leukemia and lymphomas, often considered a “one and done” curative option for some patients, the Board noted that there are high expectations and eager anticipation around CAR T therapy in myeloma, from both patient and provider perspectives. The NLB perceived CAR T therapy as a great additional option for patients with multiply relapsed disease, as this is an area of significant unmet clinical need in MM. They also noted, however, that it is important to engage and communicate with patients to set reasonable expectations around outcomes for this new option in R/RMM.

The Board noted that, in community practice, many providers are still apprehensive and/or uncertain around this therapy and the strategies for managing patients on CAR T therapy. *“There’s still that apprehension and lack of knowledge that will prevent them from earlier referrals and referring their patients specifically to CAR T and [bone marrow transplant] BMT. How do I get them there? I can refer to the clinic, but how do I get them into the cellular therapy? There’s that knowledge gap there.”* – Nurse Leader

### Treatment Sequencing and Position of CAR T Therapy

CAR T therapy is currently approved only after 4 or more lines of therapy but is currently also in use in much later lines of therapy, even after 10 lines of therapy. While the Board felt that CAR T therapy might be applicable in earlier lines of treatment, the utility in earlier lines remains to be addressed in clinical studies. Nurse Leaders indicated that it may be prudent to consider CAR T therapy as an option after the fourth LOT, especially for patients with high-risk disease who may otherwise become ineligible or die due to advanced disease. With the recent expansion of therapeutic options for triple class-refractory myeloma—which now include selinexor, belantamab mafodotin, melphalan flufenamide, and ide-cel—and the anticipated approval of additional agents in this space, individualization of therapy based on patient-, disease-, and treatment-related factors is critical.<sup>16,17</sup> [Lee 2020/p14/Conclusions] [Josph 2021/p9/col2/para2] In the setting of multidrug-refractory disease, CAR T therapies have demonstrated significantly higher response rates compared to other currently available options,<sup>17-19</sup> which has established the therapeutic potential of this class of therapies in R/RMM. [Josph 2021/p2/col1/para2; p5/col2/para1; p9/col1/para4] [Rodigo-Otero 2021/p1/Abstract] [Jagannath 2021/p1/Abstract]

### CAR T Therapy Efficacy

The response rates to CAR T therapy, in patients with multiply relapsed MM, were

seen as promising compared to the rates with other available agents. For instance, the overall response rate (ORR) for patients with triple-class refractory MM treated with ide-cel in the KarMMa study was 76.6%, compared to 32.2% of a merged cohort of a similar population of patients treated with other available agents, according to a recent retrospective study.<sup>19</sup> [Jagannath 2021/p1/Abstract]

### Patient Selection and Referral

Despite the higher response rates, additional considerations were noted as being important in the therapeutic selection of CAR T therapy for individual patients with MM. These factors include patient fitness, comorbidities, preferences, caregiver perspectives, financial/insurance clearance, manufacturing turnaround time, willingness to accept side effects, and access to a specialty transplant/cellular therapy center. Other clinical considerations included the kinetics of the relapse and disease progression, and its impact on the ability to complete leukapheresis and CAR T cell manufacturing in a timely manner.

The availability of manufacturing appointments was noted as a potential barrier to uptake of CAR T therapy. Delayed ide-cel therapy initiation due to prolonged waiting for manufacturing appointments, rather than the limited leukapheresis access, was noted as a particularly “*frustrating*” concern by a Nurse Leader. The result of these delays is that some patients eligible for this therapy become

too ill from progressive disease and die before the CAR T infusion can be administered.

### CAR T Therapy Coordination

Critical components for ensuring uptake of CAR T therapy in eligible patients includes a long-term approach with multifaceted coordination and support, where patients anticipated to become eligible for CAR T therapy are identified earlier and referred for a cellular therapy consultation. The NLB indicated that Advanced Practice Providers (APPs) may play a key role in patient identification, as many have prior established relationships with patients who may have undergone stem cell transplant (SCT) and may be downstream CAR T therapy candidates. The existence or development of ongoing relationships and coordination with regional community oncologists may also facilitate and expedite patient identification, selection, and referral for CAR T therapy. Although Nurse Leaders acknowledged that patients are referred for CAR T therapy to their centers by community physicians in and outside their region, they also noted limited capacity to accept referrals. In some cases, the centers provide non-CAR T options that may not have been fully explored in community practice in lieu of CAR T therapy.

For post-CAR T therapy management of patients, protocols and guidelines for the follow-up assessments and procedures were identified as a necessity to ensure that patients receive appropriate supportive

care and achieve optimal outcomes, considering the anticipated addition of other CAR T therapies to the MM pipeline in the next few years.

### Bridging Therapy

Patients who are awaiting CAR T-cell infusion may need bridging therapy following T cell apheresis to reduce the tumor burden and/or stabilize disease. The initial clinical trials limited bridging therapy to approved agents and regimens to which many patients have had prior exposure. In the CRB-401 study of ide-cel, for instance, bridging therapy was given to 42% of the patients, mostly with dexamethasone, daratumumab, bortezomib or bendamustine.<sup>20</sup> [Raje 2019/p5/col1/para1] Currently, novel agents may be utilized for bridging therapy. Other bridging therapy options listed by the NLB included the BCMA-targeted bispecific agent belantamab mafodotin and the D-PACE (dexamethasone, cisplatin, doxorubicin, cyclophosphamide, and etoposide) chemotherapy regimen. Notably, in the KarMMa and CARTITUDE-1 studies, patients who received prior therapy with BCMA-targeted agents were excluded.<sup>19,21</sup> [Jagannath 2021/p2/col2/para1/ln1-2] [Berdeja 2021/p3/col1/para1/ln4-5] The choice of bridging therapy should be decided with input from both the institution administering the CAR T therapy and the referring oncologist.

### Management of CAR T Therapy-Related Toxicities

CAR T therapies are associated with a unique toxicity profile that includes cytokine release syndrome (CRS) and neurologic toxicities.<sup>22</sup> [Brudno 2019/p1/Abstract] CRS can manifest as fevers, hypotension, hypoxia, end-organ dysfunction, cytopenias, coagulopathy, and hemophagocytic lymphohistiocytosis.<sup>22</sup> [Brudno 2019/p1/Abstract] Neurologic toxicities are diverse and may include encephalopathy, cognitive deficits, dysphasia, seizure, and cerebral edema.<sup>22</sup> [Brudno 2019/p1/Abstract] Management of patients experiencing toxicities include supportive care measures such as volume resuscitation, vasopressors, transfusion support, growth factors, electrolyte repletion, IL-6 receptor antagonists such as tocilizumab, corticosteroids, and empiric broad spectrum antibiotic therapy in select patients.<sup>22</sup> [Brudno 2019/p10/para3; p8/para2/ln2-3 and ln17-18] Among the toxicities, the Board noted that cytopenia may be challenging for referral centers to manage, as such centers may not have a mechanisms in place for platelet or blood transfusions, if necessary. Once the patient is discharged from the specialty/tertiary center, it is essential to add a dedicated APP to the care team. An APP can manage outpatient/inpatient CAR T therapy recipients and communicate or coordinate follow-up procedures with the community physicians. Coordination of care may include the frequency and identity of various assessments and tests, the

spectrum of early and late side effects, and continued cytopenias. This team-based follow-up is an essential component for appropriate toxicity management.

## Cilta-cel Clinical Studies

### CARTITUDE-1 Study

The single-arm, open-label, phase 1b/2 CARTITUDE-1 study, conducted at 16 centers across the USA, evaluated the safety and clinical activity of cilta-cel in patients with R/RMM with poor prognosis.<sup>21</sup> [Berdeja 2021/p1/Abstract] Cilta-cel is a structurally differentiated CAR T-cell therapy that contains two BCMA-targeting single-domain antibodies, a CD3 $\zeta$  signaling domain, and a 4-1BB costimulatory domain (**Figure 1**). A total of 113 patients aged 18 or older, with an Eastern Cooperative Oncology Group (ECOG) performance status (PS) score of 0 or 1, who received  $\geq 3$  previous lines of therapy or were double-refractory to a PI and an IMiD, and had received a PI, an IMiD, and an anti-CD38 antibody, were enrolled in CARTITUDE-1. Updated data for a longer follow-up duration (median 18 months) from CARTITUDE-1 were presented at the ASCO 2021 Virtual Annual Meeting.<sup>23</sup> [Usmani ASCO2021 presentation; IMF NLB \_Cilta-cel.pdf/ slide 17] As of September 1, 2020, 97 patients with a median of 6 prior lines of therapy received a cilta-cel infusion at the recommended phase 2 dose of  $0.75 \times 10^6$  CAR-positive viable T cells per kg. Of these, 73 received bridging therapy.<sup>21</sup> [Berdeja

2021/p1/Abstract Findings] The median turnaround time for cilta-cel manufacture was 29 days (range, 23–64); notably, no treatment discontinuations occurred due to manufacturing failure.<sup>21</sup> [Berdeja 2021/p51/col1/Results/para3]

### Efficacy

The ORR per independent review was 97% (95% confidence interval [CI], 91–99), with 67% achieving stringent complete response (sCR). The median time to first response was 1 month (range, 1–9), and median time to complete response (CR) or better was 2 months (range, 1–15). Responses deepened over time, and median duration of response (mDOR) was not reached. Of the 57 patients evaluable for minimal residual disease (MRD) assessment, 93% were MRD-negative at  $10^{-5}$ . Median progression-free survival (PFS) was not reached; 12-month PFS and OS were 77% (95% CI, 66–84) and 89% (80–94), respectively.<sup>23</sup> [Usmani ASCO2021/p4/Results] At a longer median follow-up of 18 months, the ORR was 98%, with an 80% sCR and 92% MRD-negativity at  $10^{-5}$  in evaluable patients. The 18-month PFS and OS were 66% and 81%, respectively. [IMF NLB Cilta-cel/Slide20]

### Safety

Overall, no new safety signals were noted with the longer follow-up. Grade 3/4 hematologic AEs that occurred in  $\geq 20\%$  patients included neutropenia (95%), anemia (68%), leukopenia (61%), thrombocytopenia (60%), and lymphopenia

(50%). CRS occurred in 95% of patients, with grade 3/4 CRS in 4%; median time to onset of CRS was 7 days (range, 1–12), and median duration was 4 days (range, 1–14, excluding 1 patient with a prolonged 97-day CRS duration). CRS resolved in all but 1 patient with grade 5 CRS/hemophagocytic lymphohistiocytosis. Neurotoxicity occurred in 24% of patients, with grade 3/4 CAR T-associated neurotoxicity occurring in 10% of patients. Of the 21 study deaths, 6 were treatment-related as assessed by the investigator. [Usmani ASCO2021 presentation; IMF NLB \_Cilta-cel.pdf/ Footnote c/slide 13] In patients who experienced movement and neurocognitive treatment-emergent neurotoxicity, 2 or more of these risk factors were present: high tumor burden, grade  $\geq 2$  CRS, immune effector cell-associated neurotoxicity syndrome (ICANS), and high CAR T-cell expansion and persistence. Patient management strategies used to address these risk factors included early and aggressive treatment of CRS and ICANS and implementation of handwriting assessments and extended monitoring to capture subtler manifestations of neurotoxicity. Moreover, enhanced bridging therapy was allowed in the trial to reduce tumor burden, following a protocol amendment. With the implementation of these mitigation strategies in new and ongoing cilta-cel studies, 150 additional patients have been dosed with a significant reduction of movement and neurocognitive TEAEs observed, from 5% in CARTITUDE-1

to <1% in subsequent patients dosed across the CARTITUDE program.

### CARTITUDE-2 Study

CARTITUDE-2 is a multicohort, phase 2 study assessing cilta-cel safety and efficacy in various clinical settings for patients with MM and exploring suitability of outpatient administration.<sup>24</sup> [Agha ASCO2021/p2/Background] Preliminary data for CARTITUDE-2 cohort A, consisting of patients with progressive lenalidomide-refractory MM after 1–3 prior lines of therapy, including a PI and an IMiD, without prior exposure to BCMA-targeting agents, were reported at the ASCO 2021 Virtual Annual Meeting.<sup>24</sup> As of the Feb 2021 data cutoff, with a median follow-up of 5.8 months (range, 2.5–9.8), 20 patients received a single cilta-cel infusion at a target dose of  $0.75 \times 10^6$  CAR-positive viable T cells per kg, of whom 1 patient received therapy in an outpatient setting. Patients had received a median of 2 prior lines of therapy (range, 1–3), and all patients were exposed to PI, IMiD, and dexamethasone; 95% had exposure to alkylating agents, and 65% to daratumumab. Notably, 40% had triple-refractory disease. [Agha ASCO2021/p2/Methods]

### Efficacy

The ORR was 95% (95% CI, 75–100), with 75% (95% CI, 51–91) achieving sCR/CR, and 85% (95% CI, 62–97) achieving very good partial response (VGPR) or better. The median time to first response was 1.0 month (0.7–3.3) and the median time to

best response was 1.9 months (0.9–5.1). All evaluable patients at the data cut-off were MRD negative; mDOR had not been reached. [[Agha ASCO2021/p2/Results](#)]

### *Safety*

The most common hematologic AEs (in ≥20% patients) were neutropenia (95%; grade 3/4, 90%), thrombocytopenia (80%; grade 3/4, 35%), anemia (65%; grade 3/4, 40%), lymphopenia (60%; grade 3/4, 55%), and leukopenia (55%; all grade 3/4). CRS occurred in 85% of patients, with 10% of these patients experiencing CRS of grade 3/4. Median time to CRS onset was 7 days (5–9), with a median duration of 3.5 days (2–11). CAR T-cell neurotoxicity occurred in 20% of patients (all grade 1/2). Three patients had ICANS (1=grade 1, and 2=grade 2), with a median time to onset of 8 days (7–11) and median duration of 2 days (1–2). Grade 2 facial paralysis occurred in 1 patient, with time to onset of 29 days and a duration of 51 days. The safety profile in the patient who received therapy in the outpatient setting was manageable. [[Agha ASCO2021/p2 and p3/Results](#)]

### *Perception of IMF NLB of CARTITUDE-1 and CARTITUDE-2 Studies*

*“Over two-thirds of patients had over five lines of therapy. I can’t even think of any other treatment that would have these kinds of results.” – Nurse Leader*

Overall, the NLB found that the CARTITUDE-1 ORR data showed remarkable efficacy for cilta-cel, especially in the heavily pre-

treated population enrolled in the study; of which 42.3% were penta-refractory and 83.5% were penta-drug exposed, and with 23.7% of participants having high-risk cytogenetic profiles. [[IMF NLB Cilta-cel/Slide14](#)] The Board also noted that the therapy appeared well-tolerated overall.

*“I think the data is obviously pretty impressive, and it’s very significant, especially with the overall survival, PFS, duration of response that hasn’t even been reached.” – Nurse Leader*

The ORR and the scaling of the response was considered superior to currently available options for this patient population. The comparable response rates across subgroups, including those with extramedullary disease (EMD), was especially encouraging, given that EMD is especially challenging to manage. EMD is characterized by the MM cells forming tumors outside of the bone marrow and it has been reported to occur in 6% to 37% of patients with MM. However, there is no standard treatment for R/RMM with EMD. EMD is associated with aggressive disease and a poor prognosis, with shorter OS and PFS than patients with MM but without EMD.<sup>25</sup>[[Sevcikova 2019/p1/col1/Intro/para2; p2/col1/Incidence/para3; p3/col2/Prognosis/para5](#)]

Given this remarkable efficacy, the Board felt that cilta-cel safety and efficacy in earlier lines of treatment would be of great interest, to maximize the potential benefit

in patients. CARTITUDE-2 assessed cilta-cel earlier in the treatment continuum, with patients in cohort A only required to be lenalidomide-refractory. While the overall impression was that the safety profile and response rates in CARTITUDE-2 were promising, the NLB cautioned that the data are yet to mature, and the depth and duration of response need to be confirmed with a longer follow up.

In the coming years, the number of patients exposed to frontline triplet and quadruplet combination regimens, with disease progression even after subsequent SCT, are likely to increase. Patients with disease progression following these treatments will have multidrug-refractory disease after their first LOT and will then have limited options. The availability of CAR T therapy as a new option, offered in an earlier LOT, would be important for such patients.

#### Clinical Data and Nursing-Specific Gaps

As mentioned above, additional mature data from CARTITUDE-2 and other studies are needed to address the utility of cilta-cel in earlier lines of treatment. The efficacy of cilta-cel in patients with prior exposure to BCMA-targeted therapies is currently not known and needs to be addressed as more BCMA-directed agents enter the MM treatment space. The comparability of clinical trial results with real-world evidence, not only for therapeutic efficacy but also for manufacturing ease and timeliness, would further clarify the position of cilta-cel in the R/RMM

treatment paradigm. Special considerations for patients who may have inadequate renal function or renal insufficiency, such as optimal choice or dosing of bridging therapy, may need to be explored in further studies.

The possibility of collecting T cells prior to stem cell mobilization and evaluating viability duration of stored T cells to be used later for CAR T cell manufacture was raised as an interesting avenue for exploration. However, this strategy may be limited due to costs associated with this approach and manufacturing, the specific party responsible for bearing the costs of the procedures involved, and the uncertainty of whether/when the patient will receive the CAR T product.

#### Non-clinical Concerns

Logistical concerns and timely availability of leukapheresis and cilta-cel manufacturing positions were listed as the major non-clinical concerns. Most members of the Board did not report experience with bacterial contamination or poor T cell expansion as significant barriers to CAR T manufacture. While outpatient administration is a possibility with cilta-cel, most NLB members reported either admitting patients for CAR T therapy or admitting them following the infusion. The paucity of inpatient beds and staff shortages add to the complexity of managing patients across care settings.

#### Management of Adverse Events

Overall, the toxicity profile for cilta-cel was aligned with expectations for CAR T therapies. As more CAR T therapies enter the clinical space and are integrated into practice, providers are likely to gain familiarity and confidence in managing CAR T-associated toxicities.

Prolonged cytopenia, can be a challenging toxicity for community physicians to manage, due to the need for more frequent monitoring and lack of transfusion resources.

The grade and frequency of neurotoxicities with cilta-cel were generally considered to be manageable with corticosteroids or early introduction of tocilizumab to manage CRS-driven neurologic AEs. The absence of new neurocognitive/movement TEAEs with the patient management strategies—enhanced bridging therapy to reduce tumor burden, early and aggressive treatment of CRS and ICANS, and handwriting assessments and extended monitoring—in the CARTITUDE studies were described as *“reassuring.”* Neurotoxicity can be a significant concern for patients and caregivers. Providers need training concerning monitoring and managing subtler manifestations of neurotoxicity, such as the implementation of handwriting and cognitive assessments.

### **Education Needs of Patients and Providers**

*“Education will be key for all providers, whether it be at the academic institutions or community based, focusing—I always think*

*that the best way to funnel information is through patients.” – Nurse Leader*

#### **Patient Educational Needs**

A MM diagnosis can be overwhelming for patients and their caregivers. There has been considerable excitement and anticipation around CAR T therapies in hematologic malignancies, which is likely to be mirrored upon cilta-cel approval. Nurses need to be armed with specific resources to communicate all aspects of care prior to, during, and after discharge following CAR T therapy and to also set patient expectations regarding therapeutic efficacy. At the time of discharge and return to community practice, patients should be provided information and guidance on expected early/late toxicities, follow-up assessments and care, supportive care measures, and indicators for emergency department or inpatient admittance. The same materials should also be shared with the patient’s community physician to ensure care coordination and optimal treatment outcomes.

#### **Provider Educational Needs**

Providers also need education concerning the efficacy and safety of CAR T therapy, expected early/late toxicities, best practices for identifying and referring eligible patients for CAR T therapy, and optimal strategies for mitigating and managing adverse reactions. As CAR T-cell therapy is an emerging therapy, many clinicians may be unfamiliar with how to manage CAR T-cell toxicities. This is especially the case in

community hospitals or rural settings, where providers may not manage many MM patients, or they are unlikely to be using investigational agents such as cilta-cel. Protocols, algorithms, and guidelines need to be established to ensure streamlined procedures for patient care coordination across care settings, whether inpatient/outpatient, within academic/specialty/tertiary centers or community practice.

### Closing Statements

FDA approval of cilta-cel will provide opportunities to improve standard-of-care practices for patients with MM who have been exposed to several lines of therapy that ultimately failed.

Cilta-cel represents a promising new cellular immunotherapy for patients with R/RMM, especially in multidrug-exposed/-refractory patients. However, CAR-T therapy is still a new entrant into the MM treatment landscape; therefore, complexities and expectations surrounding therapy coordination and management of toxicities and follow-up care can be challenging. As

with other CAR T therapies currently in use for MM, logistical concerns, and establishment of streamlined protocols for coordinating inpatient and outpatient care across care settings, will need special attention to ensure that this therapy is commercially available and accessible to all eligible patients. In addition, the potential to combine other agents, such as bispecific therapies, with CAR T therapies to prolong and deepen responses in patients with MM warrants further exploration.

Given the increased interest in the use of CAR T-cell therapy for patients with R/RMM and the remarkable response rate for cilta-cel, all providers who interact with patients across the CAR T-cell therapy continuum require education and training in best practices for patient management prior to, during, and after CAR T therapy. This is essential to ensure the best clinical outcomes for patients. Nurses must continue to provide the necessary education to properly inform patients and caregivers about this treatment option and its toxicities and to set patient and caregiver expectations for therapeutic efficacy.

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The attendees were as follows:

**Donna Catamero** (co-chair, Mount Sinai Hospital)

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Figure 1. Ciltacabtagene Autoleucel [IMF NLB Cilta-cel/slide12]

