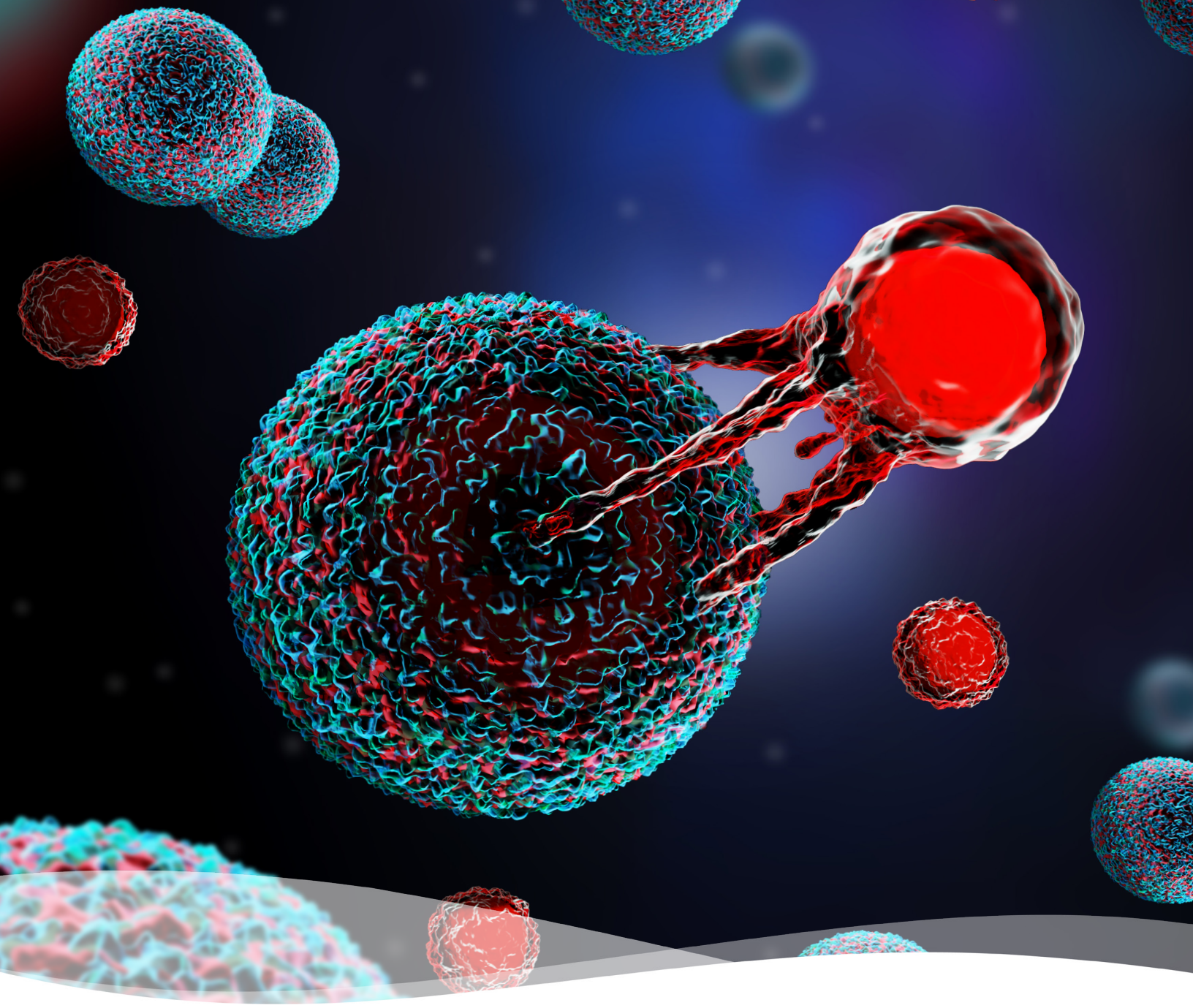


The Evolving Role of CAR T-Cell Therapy in Multiple Myeloma

Based on Insights from Leading Multiple Myeloma Experts

INTERNATIONAL MYELOMA FOUNDATION

OVERVIEW

The introduction of B-cell maturation antigen (BCMA) directed chimeric antigen receptor T-cell (CAR-T) therapy has represented a major advance in the treatment of multiple myeloma. Clinical studies have demonstrated the ability of these personalized cellular therapies to induce deep and durable responses following a single treatment administration, prompting their integration into earlier lines of therapy and reshaping treatment paradigms.[1,2,3]

The first BCMA-directed CAR-T therapy, ABECMA® (idecabtagene vicleucel; ide-cel), received U.S. Food and Drug Administration (FDA) approval in March 2021 for adults with relapsed or refractory multiple myeloma after four or more prior lines of therapy. [4,5]

CARVYKTI® (ciltacabtagene autoleucel; cilta-cel) followed in February 2022 with the same initial indication. [6,7] In April 2024, both therapies received expanded FDA approvals for use in earlier lines of treatment based on positive phase 3 clinical trial results.

ABECMA is currently indicated for adults with relapsed or refractory multiple myeloma after two or more prior lines of therapy, including an immunomodulatory agent (IMiD), a proteasome inhibitor, and an anti-CD38 monoclonal antibody. [8,9]

CARVYKTI is indicated for adults with relapsed or refractory multiple myeloma at first relapse following at least one prior line of therapy that included a proteasome inhibitor and an IMiD, and whose disease is refractory to lenalidomide. [10,11]

These expanded indications have accelerated the integration of CAR-T therapy into earlier treatment strategies and raised important questions regarding patient selection, treatment sequencing, timing of referral, toxicity management, and care coordination. [12]

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[1] Munshi NC, Anderson LD Jr, Shah N, et al. Idecabtagene Vicleucel in Relapsed and Refractory Multiple Myeloma. N Engl J Med. 2021;384:705-716. doi:10.1056/NEJMoa2024850. https://www.nejm.org/doi/full/10.1056/NEJMoa2024850

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[3] San-Miguel J, Dhakal B, Yong K, Spencer A, Anguille S, Mateos MV, et al. Cilta-cel or standard care in lenalidomide-refractory multiple myeloma. N Engl J Med. 2023;389(4):335-347. doi:10.1056/NEJMoa2303379.

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[5] Munshi NC, Anderson LD Jr, Shah N, et al. Idecabtagene Vicleucel in Relapsed and Refractory Multiple Myeloma. N Engl J Med. 2021;384:705-716. doi:10.1056/NEJMoa2024850. https://www.nejm.org/doi/full/10.1056/NEJMoa2024850

[6] February 28, 2022 Approval Letter - CARVYKTI

[7] Berdeja JG, Madduri D, Usmani SZ, Jakubowiak A, Agha M, Cohen AD, et al. Ciltacabtagene autoleucel, a B-cell maturation antigen-directed chimeric antigen receptor T-cell therapy in patients with relapsed or refractory multiple myeloma (CARTITUDE-1): a phase 1b/2 open-label study. Lancet. 2021;398(10297):314-324. doi:10.1016/S0140-6736(21)00933-8.

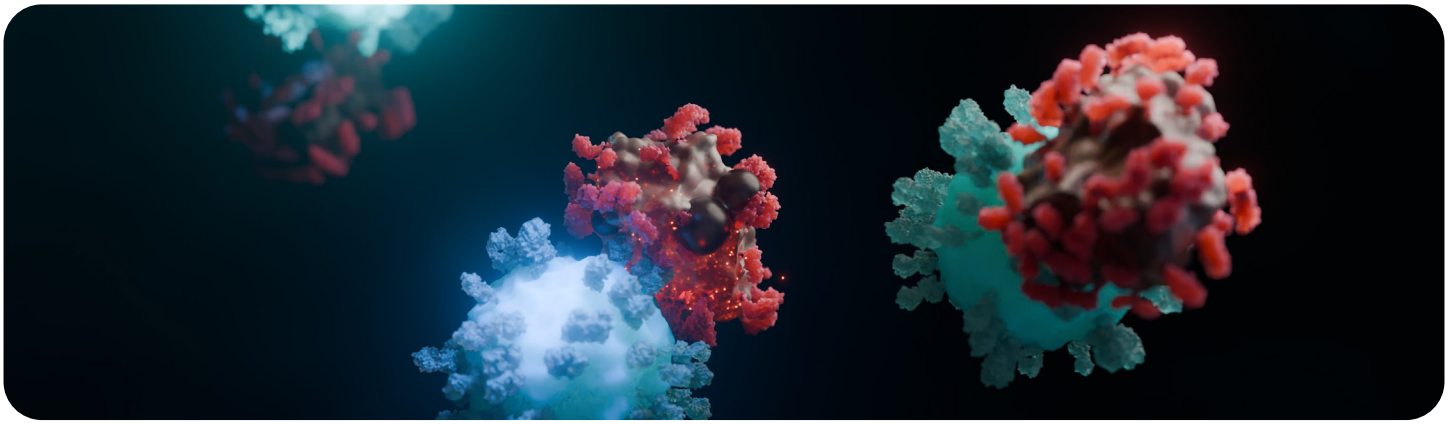
[8] Munshi NC, Anderson LD Jr, Shah N, et al. Idecabtagene Vicleucel in Relapsed and Refractory Multiple Myeloma. N Engl J Med. 2021;384:705-716. doi:10.1056/NEJMoa2024850.

[9] https://www.fda.gov/vaccines-blood-biologics/abecma

[10] https://www.fda.gov/vaccines-blood-biologics/cellular-gene-therapy-products/carvykti

[11] San-Miguel J, Dhakal B, Yong K, Spencer A, Anguille S, Mateos MV, et al. Cilta-cel or standard care in lenalidomide-refractory multiple myeloma. N Engl J Med. 2023;389(4):335-347. doi:10.1056/NEJMoa2303379.

[12] Hamadeh IS, Friend R, Mailankody S, Atrash S. Chimeric antigen receptor T-cells: a review on current status and future directions for relapsed/refractory multiple myeloma. Front Oncol. 2024;14:1455464. doi:10.3389/fonc.2024.1455464.



On June 10, 2026, the International Myeloma Foundation (IMF) convened a roundtable discussion of seven International Myeloma Working Group (IMWG) physician key opinion leaders and one nurse expert to examine the evolving role of CAR-T therapy in multiple myeloma.

The discussion explored emerging treatment paradigms, including sequencing strategies, earlier use of CAR-T and other novel therapies, bridging therapy, toxicity management, inpatient versus outpatient care models, and the evolving concept of "cure" in multiple myeloma. Participants also shared practical approaches to strengthening collaboration between academic and community practices to optimize care delivery and patient outcomes.

Beyond reviewing current evidence and clinical experience, participants engaged in a forward-looking exchange that examined unresolved questions and future possibilities in myeloma care. Drawing on their collective expertise, they discussed where the field may be headed, considered the potential implications of emerging therapies and evolving treatment strategies, and explored important questions that are likely to shape the next generation of multiple myeloma management. While some topics reflected expert opinion in areas where evidence is still evolving, the discussion highlighted both current thinking and future directions for research and clinical practice.

THE DISCUSSION WAS GUIDED BY THE FOLLOWING OBJECTIVES:

- Assess evolving sequencing strategies in multiple myeloma, including optimal treatment initiation, management, and patient selection across therapies.
- Evaluate the role of CAR-T therapy and other novel therapies in earlier lines of treatment, including the implications of guideline updates and subgroup considerations.
- Examine current approaches to bridging therapy and treatment timing around CAR-T therapy, including induction, therapy holds, and considerations for T-cell fitness.
- Review best practices in toxicity management, including prevention, monitoring, and mitigation strategies based on real-world experience.
- Explore evolving definitions of "cure" in multiple myeloma and their relevance to clinical decision-making and patient expectations.
- Compare inpatient and outpatient care models and identify factors influencing site-of-care decisions and patient monitoring.
- Highlight strategies to strengthen collaboration between academic and community settings, including best practices for care coordination and shared learning.

INTRODUCTION

Multiple myeloma is a complex hematologic malignancy characterized by the uncontrolled proliferation of plasma cells and remains an incurable disease for most patients despite significant advances in treatment.[13] Over the past decade, advances in immunotherapy have expanded treatment options for patients with multiple myeloma, with BCMA emerging as a validated therapeutic target due to its high expression on malignant plasma cells.[14] BCMA-directed CAR-T therapies have demonstrated substantial clinical activity in patients with relapsed or refractory disease, including heavily pretreated populations with limited treatment options.[15]

With the expanding use of CAR-T therapy in earlier lines of treatment, determining the optimal role of cellular therapy within the broader treatment continuum has become an important clinical consideration.[16] The availability of multiple effective therapies, including novel immunotherapies and targeted agents, requires careful evaluation of sequencing strategies and patient-specific factors that may influence treatment selection and outcomes.[17,18] Considerations such as prior therapy exposure, disease burden, bridging approaches, and T-cell fitness may affect decisions regarding when CAR-T therapy should be introduced and how it should be integrated with other treatment modalities.[19]

Despite advances in CAR-T therapy, challenges remain in maximizing its clinical impact. Management of treatment-related toxicities, including cytokine release syndrome (CRS) and immune effector cell-associated neurotoxicity syndrome (ICANS), continues to evolve and improve as clinicians gain experience with these therapies.[20] In addition, increasing recognition of immune-mediated complications, such as enterocolitis, have highlighted the need for continued vigilance, early diagnosis, and refinement of management strategies.[21] Differences in care delivery models, including inpatient and outpatient approaches, also require consideration of institutional resources, monitoring capabilities, and multidisciplinary coordination.

The depth and durability of responses observed with CAR-T therapy have prompted ongoing discussions regarding long-term outcomes and the evolving concept of “cure” in multiple myeloma.[22,23] As the use of CAR-T therapy expands, collaboration across academic and community settings will be increasingly important to support consistent implementation of best practices, improve access, and optimize patient care.

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[13] Mohty M, Malard F, Facon T, et al. Toward a cure for multiple myeloma within a decade. Blood Cancer J. 2026;16:33. doi:10.1038/s41408-026-01461-7.

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[18] Costa LJ, Banerjee R, Mian H, et al. International Myeloma Working Group immunotherapy committee recommendation on sequencing immunotherapy for treatment of multiple myeloma. Leukemia. 2025;39:543-554. doi:10.1038/s41375-024-02482-6.

EVOLVING TREATMENT SEQUENCING AND PATIENT SELECTION

THE EVOLVING TREATMENT LANDSCAPE

To frame the discussion on future sequencing strategies, one expert reflected on the rapid evolution of the multiple myeloma treatment landscape. Initial enthusiasm for earlier use of CAR-T therapy was largely driven by the impressive outcomes reported in the CARTITUDE-1 and CARTITUDE-4 studies. More recently, emerging data from the MajesTEC-3 and MajesTEC-9 studies have further expanded the role of bispecific antibodies, contributing to an increasingly complex therapeutic landscape in which sequencing decisions continue to evolve.

Although current treatment guidelines recommend that all eligible patients discuss CAR-T therapy at first relapse, participants emphasized that optimal sequencing has become increasingly nuanced. Rather than applying a uniform treatment approach, experts described the importance of individualized, shared decision-making that balances efficacy, toxicity, patient preferences, logistical considerations, and the potential impact of prior therapies on future treatment options.

EARLIER INTEGRATION OF CAR-T THERAPY

Overall, participants favored integrating CAR-T earlier in the disease course rather than delaying treatment until patients become refractory to anti-CD38 therapy. Several experts noted that their own practice has evolved as longer-term clinical data have matured, with growing confidence that earlier use of CAR-T may provide the greatest benefit for appropriately selected patients. Many participants emphasized that discussions regarding BCMA-directed therapy should occur with all eligible patients at first relapse, with CAR-T representing their preferred option for most candidates.

There was broad agreement that patients with aggressive disease biology, including those with high-risk cytogenetics, primary refractory disease, or an anticipated short progression-free interval, should be prioritized for CAR-T at first relapse. For patients with standard-risk disease, participants supported a more individualized approach that incorporates disease characteristics alongside patient preferences, treatment goals, and quality-of-life considerations. It was noted, however, that the impressive outcomes with CAR T are not only seen in high risk patients, but even more so in standard risk patients.

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[19] Lin Y, Qiu L, Usmani S, et al. Consensus guidelines and recommendations for the management and response assessment of chimeric antigen receptor T-cell therapy in clinical practice for relapsed and refractory multiple myeloma: a report from the International Myeloma Working Group Immunotherapy Committee. Lancet Oncol. 2024;25:e374-e387.

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Throughout the discussion, participants emphasized that sequencing decisions extend beyond comparative efficacy. In their experience, treatment selection should also account for the practical realities associated with each therapeutic approach, including care partner requirements, recovery time, supportive care needs, and anticipated treatment-free intervals. In addition to presenting CAR-T as simply a "one-and-done" therapy, experts described framing discussions around the complete treatment journey. This approach helps patients develop realistic expectations and make informed decisions that align with their individual priorities.

EMERGING CHALLENGES IN TREATMENT SEQUENCING

Participants acknowledged that emerging data supporting fixed-duration bispecific antibody therapy have added further complexity to treatment sequencing. While these findings have increased confidence in the use of bispecific antibodies earlier in the disease course, most participants continued to favor CAR-T as the preferred initial BCMA-directed therapy for eligible patients whenever feasible. At the same time, participants recognized that sequencing strategies will likely continue to evolve as additional efficacy, durability, and long-term safety data become available.

REAL-WORLD CONSIDERATIONS FOR TREATMENT SELECTION

Although clinical efficacy remains a primary consideration, participants emphasized that optimal sequencing is not always achievable in routine practice. Language barriers, limited health literacy, insufficient care partner support, socioeconomic challenges, geographical location, and access to specialized treatment centers frequently influence treatment selection. In these circumstances, several experts noted that bispecific antibody therapy may represent the more practical option, particularly for patients who may have difficulty recognizing or reporting treatment-related toxicities or completing the intensive monitoring required following CAR-T therapy.

REFERRAL PATTERNS AND PATIENT PERCEPTIONS

Participants also discussed how the expanding availability of outpatient BCMA-directed therapies may influence referral patterns. As more community oncology practices gain experience administering bispecific antibodies, some experts anticipated that fewer patients may be referred to academic centers for CAR-T evaluation. Several participants emphasized the importance of maintaining timely referrals and multidisciplinary collaboration to ensure that all eligible patients are informed about the full range of available treatment options before sequencing decisions are made.

Experts further observed that concerns regarding CAR-T-associated neurotoxicity, particularly Parkinsonism, continue to shape patient perceptions despite advances in toxicity prevention, monitoring, and management. Participants noted that public perception has not kept pace with the evolving safety profile of CAR-T therapy and emphasized the need for continued patient education to address misconceptions, communicate current evidence, and support informed shared decision-making.

OPTIMIZING CAR-T OUTCOMES: SAFETY, DISEASE BURDEN, AND BRIDGING STRATEGIES

LONG-TERM SAFETY CONSIDERATIONS

The experts discussed the growing recognition of secondary myeloid malignancies following treatment, including myelodysplastic syndromes (MDS) and acute myeloid leukemia (AML). While some experts noted an increasing number of cases observed after CAR-T therapy, others cautioned that these findings may reflect characteristics of an older, heavily pretreated academic referral population rather than the direct effect of CAR-T itself. Several centers have begun incorporating clonal hematopoiesis of indeterminate potential (CHIP) and myeloid mutation testing into treatment planning for selected patients to better understand baseline risk and inform clinical decision-making.

REDUCING DISEASE BURDEN BEFORE CAR-T INFUSION

There was broad agreement that reducing disease burden before CAR-T infusion has become an essential component of contemporary practice. In contrast to earlier clinical trial designs that often prioritized proceeding directly to CAR-T, experts described a shift toward more strategic use of holding and bridging therapy to improve patient readiness and optimize outcomes. The rationale has expanded beyond disease control alone to include improving tolerability, reducing treatment-related toxicities, and potentially enhancing long-term efficacy.

The experts consistently emphasized that achieving the lowest possible disease burden before CAR-T should be a goal whenever feasible. Lower disease burden was associated with reduced toxicity, including neurotoxicity such as Parkinsonism, and several experts believed that deeper disease control before infusion may also contribute to improved efficacy and longer progression-free survival.

As one expert noted, *"You should have zero disease if you can do it."* Another emphasized, *"It's definitely a safety issue, but it's an efficacy issue too. There's a huge difference when patients go into CAR-T with very low disease burden."*

EVOLVING BRIDGING STRATEGIES

There was agreement that proactive holding and bridging strategies play an increasingly important role in preparing patients for CAR-T therapy, although the optimal approach remains an area of ongoing discussion. The group also discussed emerging approaches being explored as bridging strategies at some centers. Several experts favored combination regimens designed to achieve rapid and effective disease control before infusion while maintaining patient fitness for cellular therapy, whereas others described increasing use of talquetamab as a bridging strategy.

At the same time, experts emphasized the importance of carefully balancing disease reduction with the potential for treatment-related toxicities that could affect recovery, timing, or readiness for CAR-T. Some experts expressed caution regarding prolonged treatment-related toxicities associated with certain bridging approaches that may complicate recovery following CAR-T. These discussions highlighted the need for individualized bridging strategies that consider disease burden, urgency of treatment, patient fitness, and the goal of optimizing outcomes following cellular therapy.

EARLIER REFERRAL ENABLES GREATER FLEXIBILITY

There was strong agreement that identifying patients earlier in relapse and initiating referral for CAR-T evaluation before disease acceleration are critical components of optimizing outcomes. Early referral allows clinicians to individualize treatment timing, maintain disease control with interim therapy when needed, and coordinate CAR-T around patient goals without compromising therapeutic options. Experts emphasized that early CAR-T referral expands treatment options by creating greater flexibility in how and when cellular therapy is incorporated into the treatment course. Rather than requiring immediate treatment initiation at a time of clinical urgency, early planning allows time for appropriate patient selection, T-cell collection, bridging therapy, and coordination of care. As one expert noted, *"One of the biggest advantages of CAR-T is the flexibility. Patients don't have to move immediately; they can be ready when the timing is right."*

Another expert highlighted the importance of recognizing patients with slower biochemical progression before they develop more advanced disease: *"We're trying to identify those slow biochemical progressors early, collect their cells, and then bridge them appropriately."* The group also emphasized that timely referral can facilitate efficient cell collection, with one expert noting, *"You can often get patients to apheresis within a week or ten days if you start planning early."*

EVOLVING CAR-T SUPPORTIVE CARE MODELS AND TOXICITY MANAGEMENT

TRANSITION TOWARD OUTPATIENT CAR-T MODELS

There was broad agreement that the increasing use of outpatient CAR-T administration is reshaping supportive care practices and requiring a more proactive approach to toxicity monitoring and management. While inpatient management remains appropriate for selected patients, several experts described actively transitioning toward outpatient CAR-T programs supported by remote monitoring, standardized toxicity management pathways, and early intervention protocols.

Experts emphasized that successful outpatient delivery requires identifying patients at risk for complications before symptoms become clinically significant. As one expert noted, *"We're trying to move to a total outpatient CAR-T model."* However, the group stressed that expanding outpatient care must be accompanied by safeguards designed to maintain patient safety, including rapid recognition of complications and clear protocols for intervention. One expert described the goal of developing systems in which emergency departments can appropriately recognize and manage low-grade CRS, allowing patients to receive timely treatment without automatic admission.

Several centers have incorporated remote monitoring technologies, including wearable devices, to detect early physiologic changes that may precede clinical deterioration. Experts described these approaches as an opportunity to further personalize monitoring and intervene earlier during the post-infusion period. One expert observed that *"There is no treatment in myeloma that we use today the same way it was first introduced,"* a sentiment that resonated across the discussion. The experts agreed that supportive care continues to evolve alongside CAR-T therapy and anticipated that ongoing clinical experience will lead to further refinements in toxicity prevention, outpatient management, and overall safety, ultimately expanding access while maintaining high-quality care.

EVOLVING APPROACHES TO CRS PREVENTION AND TOCILIZUMAB USE

Experts agreed that CRS has become an increasingly manageable complication of CAR-T therapy, although approaches to prophylactic tocilizumab (Toci) remain variable across institutions. Some centers reserve Toci for patients demonstrating early laboratory or clinical indicators of inflammation, whereas others have incorporated prophylactic Toci into outpatient CAR-T protocols.

Several experts reported favorable experiences with prophylactic Toci strategies, including lower CRS rates, fewer urgent interventions, shorter hospital stays, and smoother outpatient management. One expert summarized this perspective by noting, *"If we're treating patients completely outpatient, they receive prophylactic Toci."* Other centers continue to individualize Toci use based on inflammatory markers, clinical changes, or institutional protocols. Differences in practice were attributed not only to clinical philosophy but also to operational considerations, including reimbursement challenges.

MOVING BEYOND CRS: EARLY IDENTIFICATION OF IMMUNE ACTIVATION AND NEUROTOXICITY RISK

Several experts described a shift in focus from CRS management alone toward identifying early immune activation patterns that may predict more serious neurologic complications. One institution reported adopting an absolute lymphocyte count (ALC)-guided dexamethasone strategy, with frequent reassessment and escalation when lymphocyte counts continued to rise. The goal of this approach is not simply to manage CRS, but to potentially reduce the risk of delayed neurotoxicity, including Parkinsonism.

As one expert explained, *"It's not a 'fire-and-forget' approach. We monitor ALC sometimes twice a day and escalate steroids if the counts continue to rise."* Other experts emphasized that approaches remain institution-specific and that additional prospective data are needed to determine the optimal strategy for preventing delayed neurologic complications.

DISEASE BURDEN AS A POTENTIAL MODIFIER OF NEUROLOGIC RISK

Experts discussed the possibility that improved disease control before CAR-T may be contributing to the declining incidence of Parkinsonism observed in current practice. Several attributed this trend to earlier referral, more effective bridging strategies, and lower disease burden at the time of infusion. However, the group acknowledged that current evidence remains largely observational and that the relationship between disease burden, immune activation, and neurologic toxicity requires further investigation.

One expert summarized this evolving understanding by stating, *"Better bridging and lower disease burden seem to be making a real difference."* Participants noted that continued study will be important to determine whether these strategies can reliably reduce the risk of delayed neurologic complications.

CONTINUED VIGILANCE FOR IEC-ASSOCIATED COLITIS

Experts agreed that awareness of immune effector cell-associated colitis (IEC-associated colitis) has increased substantially, leading to earlier evaluation and treatment of gastrointestinal symptoms following CAR-T therapy. At the same time, they acknowledged that heightened clinical vigilance has made the true incidence and risk factors more difficult to define.

Unlike CRS and some neurologic complications, IEC-associated colitis currently lacks a validated prevention and treatment strategy. The unpredictability of this toxicity remains an important area of concern as CAR-T use expands.

TOWARD BIOMARKER-GUIDED SUPPORTIVE CARE

The experts highlighted differences in approaches to monitoring and responding to laboratory abnormalities following CAR-T therapy. Some centers rely primarily on clinical symptoms to guide intervention, whereas others proactively monitor inflammatory markers, lymphocyte kinetics, and other biomarkers to identify patients at risk before symptoms emerge.

The group discussed the potential for increasingly individualized, biomarker-guided supportive care models as an important component of future CAR-T programs. These approaches may allow clinicians to better tailor monitoring intensity and interventions based on each patient's evolving risk profile.

ADVANCING PATIENT COMMUNICATION AND SUPPORTIVE CARE BEST PRACTICES

COMMUNICATING THE RISKS AND BENEFITS OF CAR-T

There was broad agreement that IEC-associated colitis and Parkinsonism-like syndromes represent two of the most challenging toxicities to discuss with patients considering CAR-T therapy. Although these events are uncommon, experts emphasized that their potential severity warrants thoughtful and transparent conversations as part of shared decision-making.

At the same time, the experts cautioned against allowing rare toxicities to disproportionately influence treatment decisions. Several noted that patient perceptions are often shaped by highly visible stories shared through social media and online patient communities, which may not reflect the current incidence of these complications or recent advances in supportive care. As one expert observed, *"I don't want to minimize the risk, but I also don't want it to become the centerpiece of the conversation."*

The discussion emphasized the importance of providing balanced education that acknowledges potential risks while placing them in the context of expected benefits, evolving toxicity management strategies, and improving clinical outcomes. Experts also expressed optimism that continued advances in supportive care may further reduce the incidence of these uncommon but serious complications over time.

BUILDING CONSENSUS ON SUPPORTIVE CARE BEST PRACTICES

There was agreement that supportive care for CAR-T continues to evolve rapidly, with many institutions independently developing innovative approaches to toxicity prevention and management. Strategies discussed throughout the roundtable included prophylactic Toci, ALC-guided monitoring, earlier intervention for immune activation, and more proactive bridging therapy.

Despite encouraging institutional experiences, experts emphasized that many current practices remain based on single-center experience rather than prospective evidence. As one expert noted, ***"These are still largely institutional experiences—we need prospective validation."*** The group highlighted the importance of multicenter collaboration and prospective clinical research to determine which supportive care strategies most effectively reduce toxicity, improve patient outcomes, and warrant broader adoption across treatment centers.

THE EVOLVING CONCEPT OF CURE IN MULTIPLE MYELOMA

Participants engaged in a forward-looking discussion about whether advances in cellular therapy and other immune-based approaches are bringing the field closer to achieving a functional cure for some patients with multiple myeloma. While acknowledging that cure remains an aspirational goal, experts described a growing shift in thinking from continuous disease control toward the possibility of sustained, treatment-free remission in carefully selected patients.

FRONTLINE CAR-T MAY REDEFINE FUNCTIONAL CURE

Participants agreed that the most compelling evidence supporting a functional cure is likely to emerge from frontline CAR-T studies rather than from later-line treatment. Several experts predicted that, if the CARTITUDE-5 study demonstrates favorable long-term efficacy and safety, CAR-T could become the preferred frontline therapy, fundamentally reshaping treatment paradigms and future sequencing discussions. Participants noted that earlier intervention, before extensive disease evolution and treatment resistance, may provide the greatest opportunity to achieve deep, durable remissions that could ultimately redefine expectations for long-term outcomes.

LONG-TERM FOLLOW-UP WILL BE ESSENTIAL

Experts emphasized that establishing a functional cure will require substantially longer follow-up than is currently available from most clinical trials. Several participants expressed concern that long-term outcome collection often diminishes once primary study endpoints have been achieved, limiting opportunities to evaluate sustained MRD negativity, durable treatment-free remissions, and the potential for prolonged disease control without additional therapy. Participants stressed that extended follow-up will be critical to determining whether these deep responses translate into meaningful long-term benefit.

DURABLE TREATMENT-FREE REMISSION MAY EXTEND BEYOND CAR-T

Although participants generally agreed that CAR-T currently provides the strongest evidence supporting prolonged treatment-free remission, several highlighted emerging data suggesting that some patients treated with fixed-duration bispecific antibody therapy may also achieve sustained MRD-negative remissions after treatment discontinuation. While recognizing that available follow-up remains limited, participants viewed these findings as encouraging and agreed that ongoing studies will help determine whether durable outcomes following bispecific antibody therapy ultimately approach those observed with CAR-T.

Participants noted that these discussions reflect an evolving view of treatment success in multiple myeloma. Beyond depth of response alone, experts emphasized the importance of evaluating the durability of remission, the potential to discontinue therapy, and the ability to achieve meaningful periods without disease progression or ongoing treatment. As new clinical data mature, these factors will become increasingly important in determining whether emerging therapies can redefine expectations for long-term outcomes in multiple myeloma.

TALKING ABOUT CURE

There was broad agreement that advances in myeloma therapy have brought the field to a point where meaningful discussions about cure are now possible. At the same time, experts expressed differing opinions regarding whether current evidence justifies using the term in routine clinical practice. While the unprecedented durability of responses achieved with newer therapies has fueled optimism, many cautioned against equating prolonged treatment-free remission with certainty that an individual patient has been cured.

Several experts expressed concern that the proposed definition of cure, which requires sustained treatment-free remission with serial MRD assessments and negative imaging over five years, could unintentionally create unrealistic expectations for patients. As one expert observed, *"We don't know if they are cured... Today, if I treat someone, am I going to cure them? Maybe yes, maybe no."*

The discussion also highlighted the biologic complexity of multiple myeloma. Experts noted that plasma cells are inherently long-lived and that late relapses continue to occur, even after many years of remission. Although one participant humorously suggested that *"The definition of cure is when your oncologist shakes your hand and says, 'I don't need to see you anymore,'"* the group agreed that multiple myeloma has not yet reached that point.

ESTABLISHING A RESEARCH DEFINITION

Despite reservations about using the term "cure" in routine practice, there was strong agreement that the field requires a standardized definition to advance clinical research and regulatory science. Experts emphasized that every curable malignancy has required objective criteria that could be incorporated into clinical trials, long-term outcomes research, and discussions with regulatory agencies.

The group emphasized that the proposed definition should be viewed as a research endpoint representing the probability of sustained remission rather than a guarantee that an individual patient has been cured. Experts also recognized that any definition adopted today will continue to evolve as therapies improve and longer-term follow-up becomes available. As one expert noted, *"For cure to become a surrogate endpoint, you have to define it. That's how it's been done for every other cancer."*

COMMUNICATING THE CONCEPT OF CURE

Experts agreed that discussions about cure require careful communication to balance optimism with realistic expectations. Although the possibility of cure has generated considerable excitement within the myeloma community, there was concern that patients may interpret research definitions as assurances of permanent remission.

Several experts advocated framing these conversations around "measured hope," acknowledging the remarkable durability now being achieved while recognizing that late relapses remain possible. As one expert explained, *"I'm comfortable using the word cure with patients—but with measured hope."* The discussion underscored the importance of helping patients understand that the concept of cure continues to evolve and that individual outcomes remain difficult to predict.

DEVELOPING A PRACTICAL AND MEANINGFUL DEFINITION

There was agreement that any future definition of cure must be practical enough to implement beyond the clinical trial setting. Experts questioned whether serial MRD assessments and repeated bone marrow biopsies over five years could realistically be incorporated into routine clinical practice, particularly in community settings. While acknowledging these operational challenges, the group viewed the current proposal as an important starting point that can be refined as experience grows and monitoring strategies continue to evolve.

REDEFINING TREATMENT SUCCESS

The discussion also highlighted how conversations about cure are beginning to reshape broader treatment goals in multiple myeloma. Rather than assuming that patients will require continuous therapy indefinitely, experts described an emerging shift toward pursuing durable treatment-free remission whenever possible and considering whether therapy can be safely discontinued in selected patients. The experts also emphasized that treatment success should be defined not only by traditional clinical endpoints such as progression-free survival and MRD negativity, but also by outcomes that matter most to patients, including quality of life, symptom burden, and freedom from ongoing therapy. These discussions reflected an increasingly patient-centered approach to evaluating long-term outcomes and therapeutic success.

PERSONALIZED RISK MODELS

There was broad agreement that the biologic heterogeneity of multiple myeloma makes it unlikely that a single definition of cure will apply equally to every patient. Experts anticipated that advances in disease biology, molecular profiling, and risk stratification will help identify distinct patient populations, including those most likely to achieve prolonged treatment-free remission and those whose disease may be best managed through long-term control.

The discussion also acknowledged that some patients may experience decades of excellent disease control without ever meeting strict MRD-based definitions of cure. As understanding of disease biology continues to advance, experts suggested that increasingly personalized risk models may provide a more meaningful framework for estimating an individual patient's likelihood of sustained remission and guiding long-term treatment decisions.

STRENGTHENING ACADEMIC–COMMUNITY PARTNERSHIPS TO EXPAND ACCESS TO CAR-T

BUILDING INTEGRATED MODELS OF CARE

There was broad agreement that successful integration of CAR-T and bispecific therapies into community practice depends on strong, bidirectional partnerships between academic centers and community oncologists. As these therapies move closer to the community, experts emphasized that collaborative care models will be essential to ensure timely referrals, maintain continuity of care, and support patients throughout treatment and recovery.

Although direct physician accessibility remains highly valued, the experts agreed that long-term success cannot depend solely on individual relationships. As one expert noted, *"Accessibility is a huge thing... But as volumes increase, there's only so much one physician can do. We need better systems, so it doesn't all depend on one doctor."*

BUILDING SUSTAINABLE INFRASTRUCTURE

There was consensus that expanding access to advanced therapies will require dedicated infrastructure capable of supporting patients as they transition between academic and community settings.

Experts highlighted nurse navigators, telemedicine, satellite clinics, electronic consultations, coordinated communication pathways, and shared-care models as important components of sustainable care delivery.

While physicians provide specialized expertise and facilitate access to advanced therapies, the group emphasized that multidisciplinary systems are needed to coordinate ongoing care, monitor for delayed toxicities, ensure supportive care measures such as intravenous immunoglobulin (IVIG) administration, and maintain communication across treatment settings. Several experts also described successful outreach programs in which academic teams provide education within community practices and support initial administration of newer therapies, helping to build confidence and strengthen long-term collaboration.

EDUCATION ACROSS THE CARE CONTINUUM

There was strong agreement that education must extend beyond myeloma specialists to include community oncologists, nurses, care partners, patients, and other healthcare professionals who may encounter patients receiving advanced therapies. Experts emphasized that educational efforts should encompass the entire myeloma treatment continuum, including frontline therapy, transplant timing, relapse management, and recognition of delayed toxicities associated with CAR-T and bispecific antibodies.

The group also highlighted the value of patient education as a means of improving care coordination. Empowering patients to understand their treatment options, recognize concerning symptoms, and seek timely referral may facilitate earlier intervention and more informed discussions with their healthcare teams.

BUILDING TRUST THROUGH COLLABORATION

Beyond education and infrastructure, experts repeatedly emphasized that trust remains the foundation of successful academic-community partnerships. Academic centers should reinforce that referrals are collaborative rather than competitive, with the shared goal of providing specialized treatment while allowing patients to return to their local oncology teams whenever appropriate.

Several experts noted that national networks of myeloma specialists have strengthened substantially over time, making it easier to connect patients with experienced centers while minimizing unnecessary travel. As one expert explained, ***"If someone calls me from another state asking if they need to travel to my center, I often tell them they don't. There is probably a myeloma expert closer to home."*** Collaboration should enable patients to receive specialized evaluation and treatment while spending as little time away from home as can be safely achieved. Building confidence among community oncologists to resume care after CAR-T was viewed as an important strategy for expanding access while maintaining continuity of care.

REDUCING BARRIERS WHILE MAINTAINING HIGH-QUALITY CARE

When discussing opportunities to improve access, there was broad agreement that reducing practical barriers could have a meaningful impact on timely referral and treatment. Experts identified travel assistance, lodging support, patient navigation, multilingual educational resources, and expanded financial assistance programs as important priorities. Several also noted that current eligibility criteria for many support programs, including income thresholds and mileage requirements, do not always reflect the realities faced by patients living in high-cost urban areas or geographically isolated regions.

At the same time, the experts emphasized that expanding access should not come at the expense of quality or patient safety. New CAR-T centers require sufficient patient volume, experienced multidisciplinary teams, and appropriate accreditation to safely manage complex toxicities. Similarly, proposals to decentralize aspects of CAR-T delivery, such as local apheresis, were viewed as promising but subject to significant regulatory and operational considerations that must be addressed before broader implementation.
Implementation strategies must be adapted to regional needs. Geographic distance, referral networks, healthcare infrastructure, transportation resources, and patient demographics vary considerably across urban and rural settings and across different regions of the country. As a result, the group agreed that expanding access to CAR-T will require flexible, locally tailored solutions rather than a single national model.

KEY TAKEAWAYS

The closing discussion reflected the forward-looking nature of the roundtable and reinforced many of the themes that emerged throughout the meeting. Drawing on their collective clinical experience and interpretation of the evolving evidence, these International Myeloma Working Group (IMWG) experts offered perspectives on where CAR-T therapy and the broader multiple myeloma treatment landscape may be headed. While many of the topics discussed represent areas of ongoing investigation rather than established standards of care, the conversation highlighted important considerations that are likely to influence future research, clinical practice, and patient care.

There was broad agreement that CAR-T therapy has fundamentally changed the treatment landscape in multiple myeloma and will play an increasingly important role as therapies move earlier in the disease course. At the same time, experts emphasized that realizing the full potential of CAR-T will require more than continued therapeutic innovation. Improving community education, expanding patient access, reducing logistical barriers, strengthening academic-community partnerships, and continuing to refine toxicity prevention and management were all viewed as essential to optimizing outcomes.

The discussion also reinforced the importance of addressing persistent patient concerns, particularly surrounding neurologic toxicities. Experts emphasized that educational efforts should communicate both the substantial benefits of CAR-T therapy and the current evidence regarding the incidence and management of serious adverse events. Providing balanced, evidence-based information was viewed as an important opportunity to reduce misconceptions, support informed shared decision-making, and improve patient confidence in these therapies.

Earlier referral to myeloma specialists and continued collaboration between academic centers and community oncology practices remained central priorities throughout the discussion. Experts agreed that patients should be evaluated for advanced therapies as early as appropriate while spending as little time away from home as can be safely achieved. They also recognized that successful implementation will require flexible care models that reflect regional differences in referral patterns, geography, healthcare infrastructure, and available resources rather than a single standardized approach.

Looking ahead, the experts expressed confidence that CAR-T therapy will continue to evolve through improvements in patient selection, toxicity management, supportive care, and delivery models. Many viewed this evolution as consistent with the historical trajectory of other transformative therapies in multiple myeloma, which have become safer and more effective over time as clinical experience has grown. Across many aspects of care, experts described a broader shift from reactive management toward proactive prevention through earlier referral, optimized bridging strategies, anticipatory toxicity monitoring, and coordinated multidisciplinary care.

The discussion also reflected a broader shift in how the field is thinking about long-term treatment goals. Advances in CAR-T therapy and other immune-based approaches have made it possible to consider concepts such as durable treatment-free remission and functional cure in ways that were unimaginable only a decade ago. Although many scientific and clinical questions remain, the experts expressed optimism that continued innovation, collaborative research, and thoughtful implementation will further improve outcomes and expand the number of patients who may ultimately achieve prolonged, meaningful remission.

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The attendees of the roundtable on June 10, 2026, were as follows:

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