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ASH 2025

Emerging Trends Accelerating the Promise of Cell and Gene Therapy

The 2025 American Society of Hematology (ASH) Annual Meeting & Exposition delivered a wave of clinical and scientific updates that put a spotlight on the rapid evolution of chimeric antigen receptor (CAR) T-cell therapy, next-generation platforms, and the expanding role of gene and gene-editing therapies. Multiple clinical updates addressed both the durability of currently approved CAR T products and the development of innovative platforms designed to enhance efficacy and improve feasibility of delivery. Presentations also highlighted the ongoing progress in gene therapy and gene editing for non-malignant hematologic disorders, with accumulating long-term data demonstrating durable clinical outcomes.

Collectively, the findings presented at ASH 2025 reinforced the pace of change in hematology, as cell and gene therapies continue to redefine treatment paradigms. In this summary, we break down our key takeaways and emerging themes from the conference shaping the future of cell and gene therapy.

Advancing the Next Generation of CAR T-Cell Therapy: Emerging Targets, Platforms and Clinical Strategies

Data presented at ASH highlight a rapidly evolving next-generation landscape of CAR T-cell therapy, featuring emerging targets and new clinical strategies designed to streamline access and delivery. Several alternative antigen targets, including CD70, CD79, and ROR1, are under active investigation and have demonstrated early encouraging activity in clinical settings where CD19-directed therapies may be limited.[1]

Additionally, dual- and tri-targeted CAR T-cell therapies, including CD19/CD20 and CD19/CD20/CD22 platforms, have been shown to mitigate antigen loss, with multiple programs increasingly advancing towards late-phase clinical trial evaluation.[1]

Beyond target selection, emerging CAR T platforms and manufacturing innovations are playing an increasingly critical role in improving treatment delivery, tolerability, and access.

Updated follow-up from the phase I study of KITE-363—a dual-targeted CD19/CD20 CAR T therapy in relapsed/refractory B-cell lymphoma—reinforced the durability of this platform, with a sustained overall response rate of 86% and manageable toxicity over extended follow-up.[2] In parallel, initial results for KITE-753, which incorporates the same dual-antigen design with a rapid manufacturing process, show encouraging early activity in CAR-naïve patients, highlighting the potential for this platform to deliver highly effective therapy with improved tolerability and streamlined patient accessibility.

In relapsed/refractory multiple myeloma, the dual–targeted BCMA/CD19 CAR T-cell therapy AZD0120 demonstrated a deep overall response rate of 96% alongside a favorable safety profile.[3] Importantly, AZD0120's ultra-fast manufacturing through the FasTCAR platform enabled a median vein-to-release time of 14 days, supporting reliable delivery even for heavily pretreated patients.

In line with the meeting's emphasis on enabling scalable CAR T solutions, ASH showcased first-in-human data for an in vivo CAR T-cell therapy that could meaningfully change how treatment is delivered.

A late-breaking abstract from ASH reported preliminary findings from the phase I inMMyCAR study evaluating KLN-1010, a novel in vivo therapy designed to generate anti-BCMA CAR T-cells directly within patients with relapsed or refractory multiple myeloma.[4] Unlike traditional ex vivo CAR T, KLN-1010 enables CAR T-cell treatment without lymphodepleting chemotherapy, simplifying treatment delivery and potentially expanding access. Early clinical results from the first four patients demonstrated robust CAR T-cell expansion, early MRD negativity, and a favorable safety profile, suggesting a potential path toward simpler and more accessible CAR T therapy.

Together, these developments signal rapid progress for the field, pointing to a future in which CAR T therapy becomes more precise and broadly accessible across diverse clinical settings.

Evolving Treatment Sequencing and Earlier Use of CAR T Across Hematologic Malignancies

ASH 2025 reinforced a clear shift in treatment sequencing, with CAR T therapy moving earlier across several hematologic malignancies.

In diffuse large B-cell lymphoma (DLBCL), the treatment paradigm is shifting from selecting patients based on transplant eligibility to assessing for CAR T eligibility, with second-line Yescarta (axicabtagene ciloleucel) and Breyanzi (lisocabtagene maraleucel) now preferred for primary refractory or early-relapsing disease when patients can be referred to a CAR T center.[5] In transplant-ineligible patients, who are typically older and have more comorbidities, second-line CAR T achieves high complete response rates and one-year progression-free survival (PFS) approaching 50%, representing a remarkable improvement in a population with historically poor outcomes.

While bispecifics and antibody-drug conjugate (ADC) chemotherapy combinations are emerging as new off-the-shelf alternatives, experts reinforced that current evidence still supports prioritizing CAR T when feasible, with bispecifics and novel combinations serving as the preferred strategy after CAR T failure.[5] This approach is further supported by long-term follow-up from CAR T trials demonstrating durable remission in patients.

In multiple myeloma, sequencing has become increasingly complex as the use of immunotherapies, such as BCMA-targeted CAR T-cells, bispecific antibodies, and ADCs, continues to rapidly expand.[6] Data presented at ASH support the use of BCMA-directed CAR T earlier in the disease course, particularly given evidence that CAR T efficacy may be diminished following previous BCMA-directed therapy. Long-term follow-up from CARTITUDE-4 reinforced the durability of Carvykti (ciltacabtagene autoleucel) when used in earlier relapse, alongside the added benefit of a meaningful treatment-free interval that can improve patients' quality of life. Experts also highlighted how bispecific antibodies retain activity after CAR T, particularly when switching targets from BCMA to GPRC5D, supporting their role later in the treatment journey.

As novel immunotherapies continue to mature and move earlier in the disease course, optimal sequencing will remain a rapidly evolving area, and today›s data favor early use of CAR T to maximize depth and durability of response.

Sustained Efficacy and Survival with CAR T-Cell Therapy in Long-Term Follow-Up

Multiple long-term datasets presented continued to strengthen the case for CAR T therapy as transformative and potentially curative.

Five-year follow-up from the phase II ELARA trial showed durable benefit with Kymriah (tisagenlecleucel) in relapsed/refractory follicular

lymphoma, with a median PFS of 53 months.[7] Complete responders experienced especially sustained benefit, with 61% in response at 57 months post-treatment. Overall, more than 75% of patients were alive at 5 years, indicating meaningful long-term survival benefit.

Similarly, updated long-term results from the phase III CARTITUDE-4 demonstrated exceptionally durable outcomes with Carvykti in standard-risk relapsed/refractory multiple myeloma.[8] With a 30-month PFS of 81% and OS of 87%, these findings support the possibility of a "cure" for these patients. Importantly, when comparing survival outcomes of CARTITUDE-4 vs CARTITUDE-1 in this patient population, earlier use of Carvykti was shown to deliver higher rates of survival.

Altogether, the durable survival outcomes and low progression rates offer renewed optimism that CAR T therapy may meaningfully redefine long-term expectations for patients.

Navigating Care Pathways in CAR T-Cell Therapy: Key Considerations for Referral, Coordination, and Long-term Care

Experts at ASH stressed the importance of community and academic partnerships to enable effective CAR T treatment. As CAR T-cell therapy is still more commonly administered at academic centers, early referral, efficient coordination, and clearly defined roles across the treatment continuum are critical.[1]

When a patient appears to meet U.S. FDA label indications, experts at ASH recommended avoiding pre-screening delays by referring patients early and allowing the treating center to initiate eligibility assessment and insurance authorization as soon as possible.

Additionally, key shared responsibilities between referring and treating physicians are disease monitoring and any required bridging or salvage therapy. Panelists stressed that the importance of comprehensive education of both patients and caregivers is critical, particularly given the risks of cytokine release syndrome and neurotoxicity in the first two weeks. Just as important is the ongoing follow-up and long-term management of adverse events as patients transition back to the care of their local community oncologists. Ultimately, successful treatment relies on continuous communication, shared clinical judgment, and a mutual understanding of the logistical and patient/caregiver requirements to ensure timely access and safe delivery of treatment.

Gene Therapy and Gene Editing: Durable Outcomes Beyond Oncology

ASH 2025 also highlighted continued progress in gene therapy for non-malignant hematologic disorders.

Gene therapy for hemophilia B emerged as a meaningful area of progress, with Hemgenix (etranacogene dezaparvovec) representing an important advancement in long-term hemophilia management.[9] In the five-year follow-up of the HOPE 3 phase III trial, Hemgenix demonstrated durable FIX expression and sustained clinical benefit, including a 96% reduction in mean annualized consumption of exogenous FIX, markedly reduced bleeding rates, and a favorable safety profile.

In pediatric patients aged 5–11 years with transfusion-dependent β-thalassemia (TDT) or sickle cell disease (SCD), updated data from the CLIMB trials showed complete and durable transfusion independence and freedom from severe vaso-occlusive crises following treatment with Casgevy (exagamglogene autotemcel).[10] These results support the value of earlier intervention before irreversible organ damage and potential expansion of treatment into younger patient populations.

Overall, these studies show promising options for patients to achieve long-term benefit with one-time therapies.

Conclusion

The data presented at the 2025 ASH Annual Meeting & Exposition showcased the continued development and expansion of cell and gene therapies across hematologic diseases. Ongoing innovation in product design and delivery platforms highlights efforts to improve efficacy and broaden access, while long-term follow-up

data demonstrate the value of these therapies earlier in the treatment course.

However, despite the scientific and clinical success observed in studies, significant challenges related to infrastructure, reimbursement, and variability in treatment and care pathways continue to limit timely access for patients. For InspiroGene by McKesson, the findings presented at ASH 2025 reinforce the importance of continued engagement and collaboration across commercialization and therapy delivery to enable greater access and optimized treatment outcomes for patients.

1. American Society of Hematology. Advancing Outcomes in Lymphoma Care: A Master Class on Integrating the CAR T-Cell Therapies into Clinical Practice. Presented at: ASH 2025 Annual Meeting & Exposition. December 6-9; Orlando, FL.
2. Dahiya S, Ulrickson M, Yared J, et al. A phase 1 study of KITE-753 or KITE-363 in patients with relapsed/refractory B-cell lymphoma: initial safety and preliminary efficacy of KITE-753 and updated results of KITE-363. Presented at: ASH 2025 Annual Meeting & Exposition. December 6-9; Orlando, FL. Abstract #265.
3. Richard S, Gaballa M, Gregory T. Safety and efficacy of AZD0120, a BCMA/CD19 dual-targeting CAR T-cell therapy, in relapsed/refractory multiple myeloma: Preliminary Results from the DURGA-1 Phase 1b/2 study. Presented at: ASH 2025 Annual Meeting & Exposition. December 6-9; Orlando, FL. Abstract #269.
4. Harrison S, Ho P, Lim S. Minimal residual disease (MRD)-negative outcomes following a novel, in vivo gene therapy generating anti–B-cell maturation antigen (BCMA) chimeric antigen receptor (CAR)-T cells in patients with relapsed and refractory multiple myeloma (RRMM): Preliminary results from inMMyCAR, the first-in-human phase 1 study of KLN-1010. Presented at: ASH 2025 Annual Meeting & Exposition. December 6-9; Orlando, FL. Abstract #LBA-1.
5. American Society of Hematology. Now Is the Time to Improve Outcomes in Diffuse Large B-Cell Lymphoma. Presented at: ASH 2025 Annual Meeting & Exposition. December 6-9; Orlando, FL.
6. American Society of Hematology. Treatment Refinement in Multiple Myeloma. Presented at: ASH 2025 Annual Meeting & Exposition. December 6-9; Orlando, FL.
7. Schuster S, Thieblemont C, Dickinson M, et al. Clinical outcomes of tisagenlecleucel in patients with relapsed/refractory follicular lymphoma (r/r FL): Phase 2 ELARA 5-year update. Presented at: ASH 2025 Annual Meeting & Exposition. December 6-9; Orlando, FL. Abstract #468.
8. Costa L, Oriol A, Dytfeld D, et al. Long-term progression-free survival benefit with ciltacabtagene autoleucel in standard-risk relapsed / refractory multiple myeloma. Presented at: ASH 2025 Annual Meeting & Exposition. December 6-9; Orlando, FL. Abstract #94.
9. Pipe S, Miesbach W, Recht M, et al. End-of-study analysis of the HOPE-B trial confirms the durable efficacy and safety of etranacogene dezaparvovec hemophilia b gene therapy over 5 years. Presented at: ASH 2025 Annual Meeting & Exposition. December 6-9; Orlando, FL. Abstract #538.
10. Frangoul H, Fuente J, Algeri M. First results of exagamglogene autotemcel in pediatric patients aged 5-11 years with transfusion-dependent β-thalassemia or sickle cell disease with recurrent severe vaso-occlusive crises. Presented at: ASH 2025 Annual Meeting & Exposition. December 6-9; Orlando, FL. Abstract #379.