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ASCO 2025

Key Takeaways from the American Society of Clinical Oncology Annual Meeting

Each year, the American Society of Clinical Oncology (ASCO) Annual Meeting brings together global leaders in cancer care to spotlight the most impactful advances in research and treatment. This year's gathering offered a broad and deeply informative view into the evolving landscape of cell and gene therapy (CGT).

At InspiroGene by McKesson, we came away from this year's meeting energized by the depth of innovation and collaboration on display. From early-phase trials to long-term follow-up data, the presentations demonstrated the promise of cellular immunotherapy as a durable and potentially curative approach for patients with otherwise limited treatment options, particularly for complex diseases such as solid tumor and hematological cancers. Just as importantly, discussions around access, safety, and scalability served as a reminder that scientific progress must be paired with strategies for broader implementation.

In the sections that follow, we share our key takeaways from ASCO 2025, reflecting on the progress, challenges, and emerging directions that are shaping the future of CGT in cancer care.

Advances and Challenges in Cell Therapy for Solid Tumors

Solid tumors present a distinct set of challenges and complexities, including a lack of uniformly expressed tumor surface antigens, highly hostile and immunosuppressive tumor microenvironments, and barriers to efficient tumor trafficking and infiltration. [1] However, there have been encouraging advancements as the field explores novel target antigens and innovative mechanisms of action. The rapid evolution of cell therapy for solid tumor indications, such as tumor-infiltrating lymphocyte (TIL) therapy, chimeric antigen receptor (CAR) T-cell therapy, and T-cell receptor-engineered (TCR) therapy, is generating increasing excitement as new data emerge on safety, efficacy, and expanding applicability.

Spotlight: TIL Therapy

Notably, the approval of Amtagvi (lifileucel) in 2024, a TIL therapy for advanced melanoma, marked an important milestone. Pivotal trial data demonstrated response rates exceeding 30% in refractory metastatic melanoma patients with many achieving durable responses. Encouragingly, early-phase data are also emerging for TIL therapies in other solid tumor types, including non-small cell lung cancer and gastrointestinal cancers, demonstrating durable outcomes and highlighting the need for larger randomized controlled trials.

When discussing TIL therapy outcomes at the conference, panelists emphasized the significance of earlier intervention in the disease course, with new data suggesting that patients treated sooner may experience higher response rates and better

outcomes. Panel discussions also placed strong emphasis on patient selection. Many candidates struggle to make it through the time-intensive manufacturing process and the availability of surgically resectable tumor remains as a limiting factor. In institutional experience, real-world application of TIL highlighted both the logistical complexity and the importance of careful triage to maximize success.

Spotlight: CAR T Therapy

CAR T therapies targeting solid tumors continue to focus on identifying cell surface antigens that are highly expressed on tumor cells while minimally expressed on normal healthy tissues. Novel targets such as Claudin-6, Claudin-18.2, glypican-2 (GPC2), GD2, and HER2 are under active investigation. Claudin 18.2-targeted CAR T-cells in particular have demonstrated exceptional response rates of nearly 40% in advanced gastric and gastroesophageal junction cancers, with a manageable toxicity profile primarily consisting of low-grade cytokine release syndrome (CRS) and minimal mucosal injury.[2] Additionally, primary results from the Phase II trial of satricabtagene autoleucel (satri-cel) demonstrated significantly improved median progression-free survival (PFS) compared to physician's choice treatment.[3] Safety was manageable, with CRS in 95.5% of patients (primarily grade 1–2) and no cases of immune effector cell-associated neurotoxicity syndrome (ICANS). These early results suggest that carefully selected antigens may allow CAR T therapy to overcome some of the most formidable challenges in solid tumor treatment.

This year's meeting also featured a prominent spotlight on CAR T-cell therapies for glioblastoma, one of the most common and aggressive forms of brain cancer, highlighting a new wave of research aimed at adapting cell-based treatments to the brain's unique tumor environment. One notable example was the readout from a first-in-human Phase I trial that evaluated intracerebroventricular delivery of a bivalent CAR T-cell therapy in recurrent glioblastoma.[4] Delivering CAR T cells directly into the cerebrospinal fluid mitigates trafficking limitations and improves local bioavailability. Additionally, the dual-antigen targeting construct may help overcome antigen escape, which is a major cause of therapeutic resistance in glioblastoma multiforme (GBM). While durability remains a challenge, this trial is a promising example of next-generation immunotherapy, demonstrating early signs of activity despite the unique challenges of solid tumors.

Beyond glioblastoma, the Phase Ib TRAVERSE study, researching the allogeneic anti-CD70 CAR T-cell therapy ALLO-316, showed encouraging results in heavily pretreated advanced or metastatic clear cell renal cell carcinoma (RCC).[5] A key differentiator of ALLO-316 is its off-the-shelf, donor-derived design, enabling rapid treatment initiation and enhanced expansion via depletion of host CD70+ T cells, promoting engraftment and supporting its promise as a scalable cell therapy for RCC and potentially other CD70-positive tumors.

Spotlight: TCR Therapy

Another area of particularly rapid progress has been TCR therapies. Unlike CAR T cells, which are limited to recognizing extracellular surface antigens, TCR T-cells are capable of recognizing intracellular antigens presented via major histocompatibility complex (MHC) molecules. This approach enables access to a broader array of tumor-specific targets, as intracellular antigens presented via MHC far outnumber the tumor-specific proteins available on the cell surface.

TCR therapies targeting cancer-testis antigens (CTAs) have demonstrated meaningful and durable responses in sarcomas. Tecelra (afamitresgene autoleucel), the first FDA-approved TCR therapy for synovial sarcoma, targets MAGE-A4 and has shown a 39% response rate and a median duration of response of 12 months in clinical trials. Outcomes were especially positive in patients with high antigen expression, low disease burden, and in those who did not need bridging therapy, highlighting the importance of early referral and careful patient selection.

Overall, the steady progress in TIL, CAR T, and TCR platforms reflects meaningful scientific advancement and increasing clinical potential. As new targets are identified and novel mechanisms

of action are explored, cellular therapies are well-positioned to play an expanding role in the management of solid tumors, offering hope for patient populations with limited existing treatment options. However, scaling these therapies beyond clinical trials to commercial availability will require specialized infrastructure, trained teams, and deep institutional expertise to manage unique safety needs and manufacturing complexities.

Emerging Data in Cellular Immunotherapy for Hematologic Diseases

With several encouraging advances in the solid tumor space, attention at ASCO 2025 also focused on hematologic disorders, where CAR T-cell therapies continue to expand their reach and improve long-term outcomes. Several abstracts this year highlighted important progress with novel dual-targeted constructs such as Kite-363, BCMA-targeted therapies like NXC-201, and extended follow-up data for Carvykti (ciltacabtagene autoleucel) in multiple myeloma. Together, these studies reinforce the field's evolving focus on optimizing efficacy, safety, and durability of response in patients with blood cancers and other hematologic disorders.

Long-term follow-up from the CARTITUDE-1 trial highlights the potential for durable remissions with Carvykti (ciltacabtagene autoleucel) in heavily pretreated relapsed/refractory (r/r) multiple myeloma. [6] In a setting where median progression-free survival is historically less than 6 months and overall survival is around 1 year, 33% of patients remained progression-free after a single infusion for at least 5 years, and median overall survival reached 60.7 months after a median follow-up of 61.3 months. Additionally, long-term safety data revealed no new neurological toxicities or new cases of Parkinsonism or cranial nerve palsy. These findings support Carvykti's transformative and curative potential in r/r multiple myeloma.

Additionally, in a Phase I study, KITE-363, a bicistronic autologous CD19/CD20-targeted CAR T-cell therapy, demonstrated high response rates and manageable safety in r/r large B-cell lymphoma (LBCL). [7] With strong in vivo expansion and a median vein-to-vein time of 27 days, KITE-363 shows promise as a next-generation CAR T-cell option in r/r LBCL. Another study of note is the Phase Ib/II NEXICART-2 trial of NXC-201, a BCMA-directed autologous CAR T-cell therapy, which showed rapid, deep, and durable responses in all patients with heavily pre-treated r/r AL amyloidosis and a manageable safety profile.[8] As the first CAR T therapy reported for r/r AL amyloidosis, NXC-201 could offer a breakthrough for this rare and difficult-to-treat disease.

Overall, while technical and logistical hurdles present challenges, ongoing innovation in cell design, delivery, and patient selection may significantly expand the impact of T-cell therapies in hematologic disorders.

Navigating Toxicities in Immunotherapy: Strategies for Safer Use

Immunotherapy toxicities were another key topic at ASCO 2025, offering critical insights into the evolving landscape of CAR T-cell therapy and its management.[9] A major focus was placed on the acute toxicities including CRS and ICANS that occur shortly after CAR T-cell infusion. These toxicities are largely cytokine-driven and tend to correlate with risk factors such as high tumor burden, patient comorbidities, and delays in therapy initiation. Management strategies have shifted in recent years, with growing emphasis on early intervention. The use of anti-IL-6 agents (e.g., tocilizumab), corticosteroids, and in some cases, prophylactic measures like dexamethasone or anakinra, is increasingly employed at earlier grades of toxicity to prevent escalation. Early referral, thoughtful patient selection, and CAR construct choice were consistently emphasized as key strategies to improving safety and outcomes.

Late toxicities are an increasingly important concern as patients transition back to the care of their local oncologist and live well beyond their initial CAR T-cell therapy. One key issue is prolonged cytopenias, defined as grade 3 or higher and lasting beyond 90 days, which occur in 10%

to 15% of patients. Infections are another major late toxicity concern and account for the highest incidence of post-treatment delayed adverse events, often occurring as late as nine months after infusion. Severe infections, defined as grade 3 or higher, affect 10% to 30% of patients and are the leading cause of non-relapse mortality in patients who have received CAR T-cell therapy. Notably, bispecific antibodies have been linked to higher infection rates compared to CAR T, which may be due to the need for their long-term chronic administration. To manage the risks of these late toxicities, ongoing collaboration between the CAR T center specialists and the primary oncologist is essential for effective long-term management.

Although less common, rare toxicities can be particularly devastating. Second primary malignancies are increasingly recognized with longer follow-up of patients after CAR T infusion. Proposed mechanisms include insertional mutagenesis from CAR transgene integration, inflammation-driven expansion of pre-leukemic clones, and immune dysregulation that may allow for solid tumorigenesis. While the absolute risk appears small and may not exceed that of standard of care therapies in controlled analyses, the potential clinical consequences are significant enough to warrant ongoing monitoring. Additionally, neurologic sequelae such as delayed Parkinsonian syndromes and cranial nerve palsies, particularly noted with certain BCMA-targeted products, highlight the need for detailed neurologic assessments and collaboration across multi-disciplinary specialists.

Altogether, experts emphasized that CAR T-cell therapy is not just an acute care intervention but requires longitudinal and multidisciplinary survivorship planning and monitoring. Toxicities may evolve long after infusion and require close coordination between CAR T treatment centers and community oncologists. Early identification, ongoing risk mitigation, and structured follow-up protocols are critical to maximizing the benefit and safety of these transformative therapies.

Next-Gen Cell Therapy: The Emerging Promise of NK Cell Therapies

At ASCO 2025, natural killer (NK) cells emerged as one of the most promising next-generation cell therapy platforms, with new data supporting their potential as effective, scalable, and safer alternatives to autologous CAR T-cell therapies.[10] NK cells offer several inherent advantages: they can be derived from allogeneic donors, do not cause graft-versus-host disease, and have innate antitumor activity that can be enhanced with engineered CAR constructs.

Unlike autologous CAR T, which faces access and scalability bottlenecks, NK cell therapies can be manufactured off-the-shelf and administered without the delays or infrastructure required for patient-specific therapies. NK cells tend to also have a favorable safety profile, with no severe CRS or neurotoxicity observed across multiple early-stage studies. However, limitations remain as NK cells typically have a limited *in vivo* lifespan in the absence of cytokine support, and selecting the optimal donor population for consistent and potent manufacturing is still an area of active investigation.

Early clinical trials have demonstrated high response rates even in heavily pretreated patients, with promising durability and minimal toxicity. Notably, the manufacturing cost of NK cell therapies appear to be significantly lower, with single-infusion production costs calculated at a fraction of the current CAR T-cell price points. Ultimately, NK cell therapies are well-positioned to address the access, scalability, and safety challenges facing traditional CAR T therapies.

Scientific Breakthroughs Bring Increased Complexity

The CGT landscape is advancing at a pace that would have been difficult to imagine even a few years ago. ASCO 2025 reinforced the growing momentum in CGT, from first-in-human trials to durable long-term outcomes demonstration.

We saw both new breakthroughs and continued evolution of earlier innovations, demonstrating the real potential of these therapies to advance the treatment paradigm for patients with cancer.

But progress comes with complexity. Access, infrastructure, long-term follow-up, and affordability remain pressing challenges. As more therapies advance from trials into practice, collaboration across stakeholders will be essential to ensure these breakthroughs translate into real-world benefit.

We leave ASCO inspired by the scientific advances yet mindful of the complexity and effort that is still necessary to make these groundbreaking therapies more accessible. Encouragingly, new manufacturing technologies and process innovations, such as decentralized hubs and closed-loop automation, alongside the growing shift toward outpatient and community-based CAR T delivery, offer promising ways to increase access and reduce logistical barriers in the CGT value chain. The path forward involves a coordinated ecosystem that can support new science and greater capacity while ensuring that CGT delivers on its promise for all patients.

1. American Society of Clinical Oncology. CAR T-Cell Therapy and T-Cell Receptor Therapy for Solid Tumors. Presented at: ASCO 2025 Annual Meeting. May 30 – June 3, 2025.; Chicago, IL.
2. Qi C, Liu C, Gong J, Liu D, et al. Claudin18.2-specific CAR T cells in gastrointestinal cancers: phase 1 trial final results. Nat Med. 2024 Aug;30(8):2224-2234.
3. Qi C, Liu C, Pehng Z, et al. Claudin18.2-specific CAR T cells (Satri-cel) versus treatment of physician's choice (TPC) for previously treated advanced gastric or gastroesophageal junction cancer (G/GEJC): Primary results from a randomized, open-label, phase II trial (CT041-ST-01). Presented at: ASCO 2025 Annual Meeting. May 30 – June 3, 2025.; Chicago, IL. Abstract #4003.
4. Bagley SJ, Binder ZA, Fraietta JA, et al. A phase 1 study of intracerebroventricular (ICV) delivery of bivalent chimeric antigen receptor (CAR) T-cells targeting EGFR and IL13Ra2 in patients with recurrent glioblastoma (rGBM). Presented at: ASCO 2025 Annual Meeting. May 30 – June 3, 2025.; Chicago, IL. Abstract #102.
5. Srour S, Chahoud J, Drakaki A, et al. ALLO-316 in advanced clear cell renal cell carcinoma (ccRCC): Updated results from the phase 1 TRAVERSE study. Presented at: ASCO 2025 Annual Meeting. May 30 – June 3, 2025.; Chicago, IL. Abstract #4508.
6. Jagannath S, Martin TG, Lin Y, et al. Long-Term (≥5-Year) Remission and Survival After Treatment With Ciltacabtagene Autoleucel in CARTITUDE-1 Patients With Relapsed/Refractory Multiple Myeloma. J Clin Oncol. 2025 Jun 3:JCO2500760. doi: 10.1200/JCO-25-00760.
7. Dahiya S, Ulrickson M, Topp M, et al. A phase 1 study of KITE-363 anti-CD19/CD20 chimeric antigen receptor (CAR) T-cell therapy in patients (pts) with relapsed/refractory (R/R) B-cell lymphoma (BCL). Presented at: ASCO 2025 Annual Meeting. May 30 – June 3, 2025.; Chicago, IL. Abstract #7003.
8. Landau H, Hughes C, Rosenberg A, et al. Safety and efficacy data from Nexicart-2, the first US trial of CAR-T in R/R light chain (AL) amyloidosis, Nxc-201. Presented at: ASCO 2025 Annual Meeting. May 30 – June 3, 2025.; Chicago, IL. Abstract #7508.
9. American Society of Clinical Oncology. Toxicities of Immunotherapies Including CAR T-Cell Therapy. Presented at: ASCO 2025 Annual Meeting. May 30 – June 3, 2025.; Chicago, IL.
10. American Society of Clinical Oncology. Beyond CAR-T and CRISPR: The Promise of Natural Killer Cells. Presented at: ASCO 2025 Annual Meeting. May 30 – June 3, 2025.; Chicago, IL.