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ASCO 2026:

Key Takeaways from the American Society of Clinical Oncology Annual Meeting for Cell and Gene Therapies

Cell and gene therapy (CGT) updates at ASCO 2026 showed continued progress across hematologic malignancies and solid tumors, with an emphasis on improving durability and reducing barriers to treatment. Across CGT and other advanced therapies, the data reflected a field that is becoming more clinically specialized and increasingly focused on how these treatments are delivered in practice. This report focuses on three key themes from ASCO 2026: CAR-T optimization and sequencing, personalized neoantigen therapy, and emerging solid tumor cell therapy platforms in melanoma.

CAR-T Therapy Moves Toward Broader, More Flexible Delivery

The CAR-T presentations at ASCO 2026 pointed to clear progress for the field. They included promising data around in-vivo delivery, strong efficacy in patients with high unmet need, reinforcement of CAR-T first treatment sequencing, and emerging evidence supporting safe and effective delivery across a broader range of care settings.

KLN-1010 was one of the more notable early-stage updates because it provided initial clinical evidence that a BCMA-directed CAR-T response may be achievable through in vivo delivery. In the ongoing first-in-human phase 1 inMMyCAR study, 18 patients with relapsed/refractory multiple myeloma were treated with KLN-1010.[1] Patients had clinically challenging disease, with a median of 3.5 prior lines of therapy, and many with high-risk cytogenetics, extramedullary disease (EMD), and triple-class refractory disease. Despite short median follow-up of 2.8 months, early efficacy signals were encouraging: the overall response rate was 100%, and all 14 minimal residual disease (MRD)-evaluable patients achieved MRD-negative bone marrow responses at 10^-5 or deeper. The safety profile also supported continued development, with CRS limited to grade 1-2 events, one grade 3 ICANS and no delayed neurotoxicity. While the dataset remains small and follow-up is early, KLN-1010 could represent an important step toward a more scalable CAR-T delivery model, with the potential to preserve the depth of response associated with BCMA-directed CAR-T therapy while reducing the logistical burden of ex vivo manufacturing and lymphodepleting chemotherapy.

Other CAR-T updates reinforced the movement of established platforms into patient groups with limited treatment options. In CASSIOPEIA/COG AALL1721, tisagenlecleucel was evaluated earlier in the treatment course for pediatric and

young adult patients with high-risk B-cell acute lymphoblastic leukemia (B-ALL) who remained MRD-positive after frontline consolidation, a population historically associated with poor outcomes and unclear optimal management.[2] The study met its 4-year overall survival (OS) primary endpoint, with an estimated 4-year OS of 85%; estimated 5-year disease-free survival (DFS) was 64% without censoring and 62% with censoring for new therapy or stem cell transplant (SCT). Separately, an exploratory analysis of the FELIX study evaluated obecabtagene autoleucel (obe-cel) in adult relapsed/refractory (R/R) B-ALL with EMD.[3] Although outcomes were numerically better in patients without EMD, obe-cel demonstrated activity in the EMD cohort, with an overall response rate (ORR) of 59% overall and 71% among patients with EMD and <5% marrow blasts at lymphodepletion. These findings are especially important because patients with B-ALL and active EMD have limited treatment options and remain a population with substantial unmet need.

Sequencing was also a focus at this year's ASCO, as panelists and experts discussed how to best manage the order of care between CAR-T and bispecific antibodies in relapsed/refractory multiple myeloma. In a retrospective analysis of patients who received both therapies, investigators compared CAR-T followed by a bispecific versus a bispecific followed by CAR-T.[4] After propensity matching, each cohort included 112 patients, and outcomes favored CAR-T first. Median OS was 5.0 years with CAR-T first versus 3.1 years with bispecific first, and 5-year OS was 50% versus 25%, respectively. In adjusted Cox regression, CAR-T-first sequencing was associated with lower 5-year mortality (hazard ratio 0.57, 95% CI 0.34-0.95). Clinically, this supports the rationale that earlier CAR-T use may preserve T-cell fitness and maintain bispecific therapy as a later option. Notably, the CAR-T–first cohort included 72% of patients treated with idecabtagene vicleucel while 86% of patients in the bispecific-first cohort were treated with ciltacabtagene autoleucel. This imbalance is important when interpreting the results, because the survival signal favoring CAR-T first was observed despite differences in CAR-T product distribution across the two groups. While these findings remain retrospective and will need continued evaluation as clinical data evolve, they are consistent with expert guidance, including the International Myeloma Working Group (IMWG) recommendations, that when patients are eligible for both BCMA CAR-T and a T-cell engager, CAR-T is generally preferred first.[5]

Several presentations also addressed the practical realities of CAR-T delivery, including where treatment can be safely and effectively administered. One particularly relevant analysis compared outcomes for patients with large B-cell lymphoma treated at Foundation for the Accreditation of Cellular Therapy (FACT)-accredited versus non-FACT centers.[6] Overall, baseline characteristics and key outcomes were largely similar across groups, including CRS, ICANS, infections, time to next treatment, inpatient utilization, and length of stay. Although FACT centers had somewhat higher outpatient and ICU visit rates, the analysis did not show a clear clinical advantage associated with FACT accreditation itself. While the study has limitations, including its retrospective design and smaller non-FACT cohort, the findings suggest that CAR-T can be delivered safely in appropriately trained and prepared non-FACT accredited treatment settings.

Advanced Therapy Spotlight: Personalized Neoantigen Immunotherapies

Moving beyond CAR-T, ASCO 2026 also highlighted other individualized immune-based treatment strategies that are beginning to reshape how advanced therapies are delivered. Because many tumor mutations are patient-specific, personalized neoantigen immunotherapies are developed from each

patient's tumor tissue and somatic mutation profile, with the goal of generating or expanding T-cell responses against multiple neoantigens unique to that patient's cancer.[7] Experts contrasted this with shared neoantigen vaccines, which offer practical advantages such as off-the-shelf manufacturing and immediate availability, but require patient selection based on mutation profile matching and may apply to only a subset of patients.[8]

Two neoantigen immunotherapy platforms were highlighted as examples of how this field is progressing.[8] Autogene cevumeran is an intravenous personalized mRNA therapy formulated in a lipoplex and designed to encode up to 20 neoantigens. Early studies in pancreatic ductal adenocarcinoma have shown induction of T-cell responses when combined with anti–PD-L1 therapy and adjuvant chemotherapy. Intismeran autogene, by contrast, is an individualized mRNA neoantigen therapy delivered intramuscularly in a lipid nanoparticle and designed to encode up to 34 neoantigens. The 5-year phase 2 KEYNOTE-942 update in resected high-risk melanoma showed durable benefit for intismeran plus pembrolizumab versus pembrolizumab alone, including a 49% reduction in risk of recurrence or death and a 59% reduction in risk of distant metastasis or death, with a manageable safety profile and no new safety signals.[9] While phase 3 data are still needed, these findings keep individualized neoantigen therapy as one of the more closely watched advanced immunotherapy strategies moving forward.

Emerging Cell Therapies Aim to Expand Solid Tumor Treatment Options

Additional cell therapy data highlighted efforts to make solid tumor treatment more effective and less burdensome for patients and treatment centers.

OBX-115 was a notable tumor-infiltrating lymphocyte (TIL) update in advanced melanoma after progression on immune checkpoint inhibitors.[10] Unlike conventional TIL therapy, OBX-115 is engineered to express regulatable membrane-bound IL-15, controlled through oral acetazolamide, which is intended to support TIL expansion and persistence without high-dose IL-2. In the Agni-01 phase 1/2 study, 15 patients were treated at the recommended phase 2 dose; most had difficult-to-treat disease, including prior anti–PD-1 combination exposure. Early efficacy was strong, with an ORR of 67%, including 2 complete responses, and tumor reduction in 80% of patients. The regimen may also address some practical limitations of TIL therapy: it used low-dose lymphodepletion, eliminated the need for toxic IL-2, and allowed tumor procurement via core needle biopsy instead of surgical resection. Safety was manageable, with low rates of grade ≥3 non-hematologic toxicity, no ICANS, and no treatment-related mortality. Although follow-up remains early, OBX-115 offers a potentially more scalable and tolerable TIL approach for patients with checkpoint-refractory melanoma.

Anzutresgene autoleucel (anzu-cel) added to the solid tumor cell therapy discussion by showing how TCR-engineered T cells may broaden the reach of cell therapy beyond conventional surface-antigen targets.[11] Unlike CAR-T therapies, which typically recognize cell-surface antigens, TCR-based therapies can target intracellular tumor antigens presented on human leukocyte antigen (HLA), potentially expanding the range of actionable cancer targets. Anzu-cel is a one-time autologous TCR T-cell therapy targeting PRAME presented on HLA-A*02:01, with PRAME expression reported across multiple tumor types, including cutaneous, uveal, and mucosal melanoma. In the phase 1 melanoma efficacy population, patients had high-risk disease features, including prior immune checkpoint inhibitor exposure in 82% and liver metastases

in 79%. Despite this, anzu-cel produced rapid responses, with a confirmed ORR of 56% across melanoma subtypes, including 50% in cutaneous melanoma and 67% in uveal melanoma. Across all melanoma patients, median PFS was 6.1 months and median OS was 16.2 months. Median time to best response was 1.4 months, and responses were durable, with median DOR of 14.6 months. Safety was described as predictable and manageable, with expected cytopenias from lymphodepletion, CRS in all patients but mostly grade 1/2, and low rates of ICANS. The update supports continued development of anzu-cel in melanoma, including the randomized phase 3 SUPRAME trial, and reinforces PRAME-directed TCR therapy as an important area to watch in solid tumors.

Cell therapy in melanoma is rapidly expanding and beginning to reshape treatment expectations for patients whose disease progresses after immune checkpoint blockade. The comparison in Table 1 below summarizes how current and emerging cellular therapies differ across mechanism, eligibility, outcomes, and durability in patients with previously treated advanced melanoma.

Table 1. Comparison of Current and Emerging Cell Therapies for Checkpoint-Refractory Advanced Melanoma[10,11,12,13,14]

	Amtagvi (Lifileucel)	OBX-115	Anzu-cel
Cell therapy type	Autologous TIL therapy	Engineered autologous TIL therapy	Engineered autologous TCR T-cell therapy
Targeting approach	Polyclonal TIL product with potential recognition of multiple tumor antigens	TIL product engineered with regulatable membrane-bound IL-15	PRAME-targeted TCR recognizing an intracellular antigen presented by HLA-A*02:01
HLA restriction	Not HLA restricted	Not HLA restricted	HLA-A*02:01 restricted
Cytokine support	IL-2 support	IL-2 sparing; acetazolamide-regulated membrane-bound IL-15	Low-dose subcutaneous IL-2
Observed response	Response rate ~32% in the registrational study	67% response rate in early data	56% confirmed ORR across melanoma subtypes; 50% in cutaneous melanoma and 67% in uveal melanoma
Durability	Most mature durability data with 31% of responses durable at 5 years	Early follow-up (median study follow-up of 4.3 months)	Median duration of response of 14.6 months across all melanoma subtypes.

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	Amtagvi (Lifileucel)	OBX-115	Anzu-cel
Safety considerations	Toxicity largely driven by lymphodepletion and high-dose IL-2; intensive monitoring and supportive care remain important	low-dose lymphodepletion, no IL-2; CRS occurred in 33%, with grade 3 CRS in 7%, and no ICANS or treatment-related mortality	Manageable but immune-effector toxicity remains relevant, including 100% CRS, with grade ≥ 3 CRS in 18%, ICANS in 12%, and HLH in 6%
Practical considerations	Approved option with established clinical experience	May reduce barriers through IL-2 avoidance and potential core needle biopsy procurement	Requires PRAME expression and HLA-A*02:01 eligibility

CRS = cytokine release syndrome; HLA = human leukocyte antigen; HLH = hemophagocytic lymphohistiocytosis; ICANS = immune effector cell–associated neurotoxicity syndrome; IL = interleukin; IL-2 = interleukin-2; IL-15 = interleukin-15; ORR = overall response rate; PRAME = preferentially expressed antigen in melanoma; TCR = T-cell receptor; TIL = tumor-infiltrating lymphocyte

Overall, the comparison suggests that melanoma cell therapy is moving toward more differentiated platforms of delivery. Lifileucel provides the most mature proof that TIL therapy can produce durable benefit in checkpoint-refractory melanoma, OBX-115 builds on the TIL concept with engineering intended to reduce treatment burden, and anzu-cel shows how TCR-directed therapy may reach intracellular targets such as PRAME, including in uveal melanoma. The next phase of development will likely depend not only on durability, toxicity management, and manufacturability, but also on how effectively developers work with treatment centers and other stakeholders to define patient selection and support broader implementation.

Conclusion

In summary, ASCO 2026 reinforced that cell and gene therapies are continuing to move in two directions at once: toward deeper clinical specialization and toward more practical delivery models. CAR-T updates focused on earlier use, optimized sequencing, in vivo delivery, and treatment-site flexibility, while neoantigen and solid tumor cell therapy data highlighted ongoing efforts to make immunotherapy more personalized and feasible to deliver. Across these updates, the next stage of progress will depend on whether promising efficacy can be sustained with longer follow-up, and whether manufacturers, treatment centers, and other stakeholders can translate increasingly complex therapies into scalable models of care.

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