SunAct™

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OncoVantage

Insights into global breakthroughs in cell-based therapies

Welcome to the SunAct Cancer Research Insights Newsletter, your monthly update on global breakthroughs shaping the next generation of cancer and cell-based therapies.

In this issue, we explore pioneering advances in CGT/ACT therapy, advancement in detection methods, and regulatory fast-tracks that are accelerating access to life-changing treatments. Our goal is to keep clinicians and researchers informed about innovations redefining patient care worldwide.

In Vivo mRNA CAR-T Therapy Targeting Liver Cancer

Technology

Direct mRNA delivery via lipid nanoparticles enables in-body generation of CAR-T - cells targeting GPC3+ hepatocellular carcinoma, no cell harvesting, no lab expansion and just precision immunotherapy activated from within.

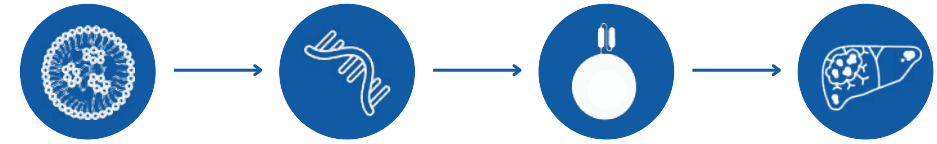
Clinical Impact

Delivers functional CAR T-cells without ex vivo cell manufacturing, enabling rapid deployment, reduced manufacturing burden, and targeted cytotoxicity against GPC3+ liver tumors, advancing accessibility in solid tumor immunotherapy.

Why This Matters

- Bypasses ex-vivo CAR-T production → treatment-ready within days, not weeks.
- Reduces attrition of patients who deteriorate while waiting for cell manufacturing.
- Opens the door to **CAR-T applicability in solid tumors,** where accessibility has been limited.
- LNP delivery allows **repeat dosing,** titration, and potentially improved safety control compared to persistent engineered cells.

Process Flow: MT-303 Treatment Journey



Lipid Nanoparticle (LNP) Delivery → CAR - encoding mRNA Transfection → In Situ CAR-T - cell Generation → GPC3 - Positive HCC Targeting

Take Home Point

"Off-the-shelf" in-body–generated CAR-T could become a realistic option for GPC3+ HCC—and eventually other solid tumors—reshaping referral pathways, eligibility timing, and sequencing of systemic therapies.

Next-generation, CRISPR/Cas9-edited, TIL Therapy for the Treatment of Solid Tumors

Technology

Novel CRISPR/Cas9-edited Tumor-Infiltrating Lymphocytes (TILs) with enhanced cytotoxicity, persistence, and resistance to immunosuppression within solid tumors have been developed. This dual-editing strategy reprograms TILs to achieve deeper tumor infiltration and superior anti-tumor activity.

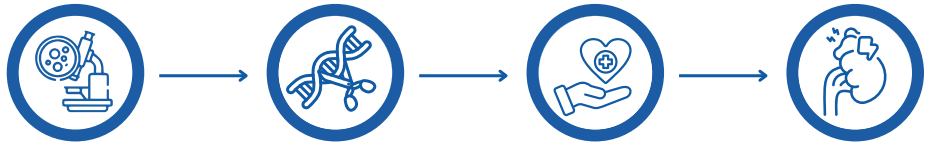
Clinical Impact

- **Improved Tumor Eradication:** Enhanced cytotoxicity and antigen-specific killing in solid tumors
- **Long-Term Therapeutic Activity:** Extended TIL survival supports enhanced anti-tumor activity
- **Wider Clinical Applicability:** Enables TIL therapy beyond melanoma, with applicability to multiple solid tumor types.

Why This Matters

- Dual CRISPR editing boosts cytotoxicity and infiltration → may translate into **higher response rates** in traditionally TIL-refractory solid tumors.
- Enhanced persistence → potential for **more durable remissions** with fewer re-infusions.
- Expands TIL therapy into **multiple tumor types,** potentially altering treatment sequencing and clinical trial referral patterns.

Process Flow: Tumor-Responsive TIL Engineering Strategy



Tumor Biopsy & TIL Isolation → CRISPR/Cas9 Gene Editing → Enhanced TIL Generation (eTIL) → Patient Infusion & Tumor Clearance

Take Home Point

Identify and refer patients with solid tumors earlier for trials using **CRISPR-optimized TILs,** as these engineered products may significantly elevate the therapeutic ceiling of adoptive cell therapy in solid malignancies.

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Liquid Biopsy in Lymphoma: Tracking CAR-T Response

Technology

Blood-based liquid biopsy monitors circulating tumor DNA (ctDNA) to assess CAR-T therapy effectiveness in lymphomas like DLBCL and follicular lymphoma. It detects minimal residual disease (MRD) and CAR-T persistence without tissue samples, using genomic and epigenomic markers, delivering results in ~7 days.

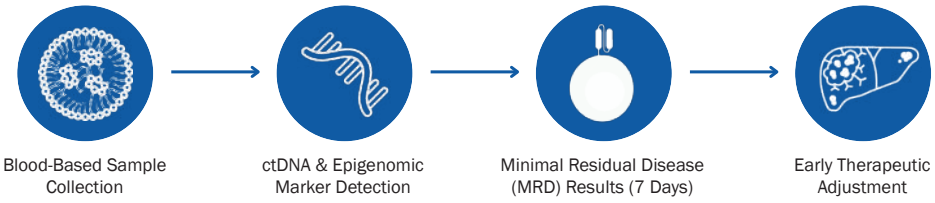
Clinical Impact

Recent 2025 data (Clinical Lymphoma Myeloma & Leukemia, August 2025; ASGCT 2025) shows MRD in 89% of cases and predicts progression-free survival with 85% accuracy, spotting relapse 3–6 months before imaging. Early intervention based on these insights may boost outcomes by 20–30%, with integration into CAR-T protocols underway (NCT05588094, targeting 2026).

Why This Matters

- Monitoring CAR-T persistence genomically/epigenomically provides **actionable real-time response assessment.**
- Integration into CAR-T follow-up algorithms is already underway → oncologists should expect **MRD-guided post–CAR-T management** to become standard.

Process Flow: Real-Time CAR T Response Monitoring in blood cancers



Take Home Point

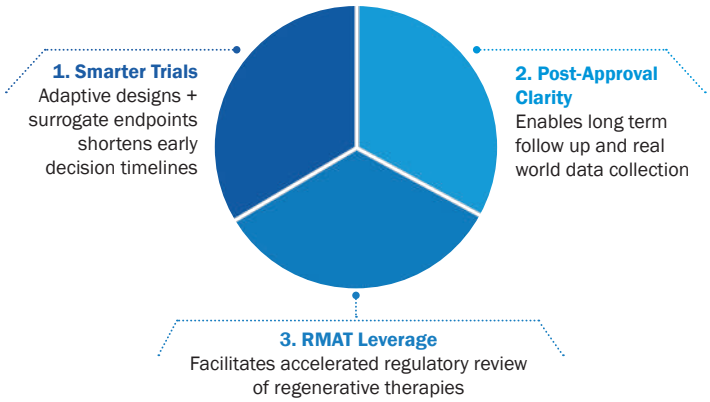
Plan to incorporate **serial ctDNA MRD testing** into lymphoma CAR-T follow-up to stratify relapse risk early and personalize post-infusion management.

Fast-Track CGT: FDA's Blueprint for Speed & Impact

Regulatory initiatives emphasise adaptive trial designs, clearer post-approval frameworks and priority pathways to streamline CGT development.

Key Regulatory Accelerators

- **Smarter Trials:** Adaptive designs and surrogate endpoints shorten timelines.
- **Post-Approval Clarity:** Enables long-term follow-up and real-world data collection.
- **RMAT Leverage:** Facilitates accelerated regulatory review of regenerative therapies.



Clinical Impact

These frameworks cut CGT development time by up to 50%, bringing rare disease therapies to patients faster, with smarter trials and real-world data.

Why This Matters

- Adaptive designs + surrogate endpoints → **quicker trial readouts** and earlier patient access.
- Clearer post-approval expectations → more **real-world monitoring** and long-term follow-up responsibilities for treating clinicians.
- RMAT and priority pathways → **accelerated review** for innovative CGTs, especially in rare and hard-to-treat cancers.

Take Home Point

Prepare for **more rapid adoption** of early-approved CGTs and ensure systems are in place for vigilant post-marketing surveillance and timely referral to adaptive trials.