SunAct

Volume 02
Issue 07

OncoVantage

Insights into global breakthroughs in cell-based therapies

TP53 TCR-T TRIAL | *IN VIVO* BCMA CAR-T | SOLID TUMOUR CAR-T | SPOT-MAS MCED TEST

The Phase 1 Trial Establishes Safety, Tolerability, and Early Efficacy of NT-175 TCR-T Cells Across TP53-Mutated Solid Tumours

A Phase I open-label dose-escalation study of **NT-175, an autologous CRISPR/Cas9-engineered T-cell receptor (eTCR-T)** therapy targeting the **TP53 R175H** neo-antigen, demonstrated manageable safety and encouraging anti-tumor activity in heavily pre-treated solid tumours.

Design, Safety & Efficacy: In the Phase I study **(NCT05877599),** HLA-A*02:01-positive patients with advanced/metastatic TP53 R175H-mutant solid tumours received NT-175, an autologous TCR-T therapy engineered using CRISPR/Cas9 to replace the endogenous TCRα with an HLA-A*02:01-restricted TP53 R175H-specific TCR while deleting TGFβR2 to overcome tumour micro-environment-mediated immunosuppression.

Following fludarabine/cyclophosphamide lymphodepletion, patients received a single NT-175 infusion plus subcutaneous recombinant IL-2. Among 21 treated patients (CRC n=10, PDAC n=6, breast cancer n=2, others n=3), **no dose-limiting toxicities or Grade 5 adverse events occurred.** CRS was observed **in 52.4% of patients (Grade ≥3: 9.5%)** and Grade 3 ICANS in one patient. **ORR was 47.6%, increasing to 53.8% at the highest dose level, with an 83% ORR in PDAC (5/6).**

The disease control rate was 66.7%, and engineered T cells showed dose-dependent expansion with persistence beyond 300 days, indicating durable engraftment.

Clinical Implications

- First clinical evidence supporting **CRISPR-engineered TP53-targeted TCR-T therapy in solid tumours.**
- Encouraging efficacy and manageable toxicity support continued clinical development.
- Durable T-cell persistence suggests potential for prolonged disease control after a single infusion.

Why It Matters

- TP53 is the most frequently mutated tumour suppressor gene, yet no approved TP53-targeted therapies exist.
- TGFβR2 knockout improves resistance to the immunosuppressive tumour micro-environment, representing a key advance over first-generation TCR therapies.
- These findings strengthen the potential of next-generation TCR-T therapies for multiple TP53-mutant solid tumours, particularly pancreatic cancer.

CRISPR TP53-Targeted TCR-T Shows Promise in Solid Tumours

Safety	No dose-limiting toxicities or Grade 5 adverse events.
Efficacy	ORR **47.6%,** rising to **53.8%** at the highest dose; **83% ORR** in pancreatic cancer.
Clinical Potential	First clinical evidence with **>300**-day T-cell persistence

Reference: Surana R, *et al*. 2026 ASCO Annual Meeting.

In Vivo BCMA CAR-T (KLN-1010): A Potential Paradigm Shift in Multiple Myeloma Treatment

KLN-1010 is a first-in-class *in vivo* CAR-T therapy designed to generate anti-BCMA CAR-T cells directly within the patient, offering a potential paradigm shift in the treatment of relapsed/refractory multiple myeloma.

Data, Safety & Efficacy: Updated Phase I **inMMyCAR** results (NCT07075185), evaluated **KLN-1010,** a modified lentiviral vector that generates fully human **anti-BCMA CAR-T cells directly** *in vivo,* eliminating the need for apheresis, *ex vivo* manufacturing, and lymphodepleting chemotherapy. Eligible patients had **relapsed/refractory multiple myeloma (RRMM)** with **≥3 prior therapies. Six patients** (61–72 years) were treated across two dose levels, with **5 exhibiting high-risk cytogenetics** and **1 presenting with extramedullary disease (EMD).**

All patients experienced treatment-emergent adverse events. **Infusion-related reactions** occurred in **3 patients,** resolving within **6–48 hours. Grade 2 cytokine release syndrome (CRS)** occurred in **4 patients** and was effectively managed with tocilizumab and corticosteroids. **No ICANS or delayed neurotoxicity** was reported. CAR-T cells persisted in peripheral blood for **up to 4 months,** exhibiting a predominantly **memory phenotype** by Month 3.

All six patients achieved MRD negativity by Month 1 (5 at 10^6 sensitivity) and 100% IMWG-defined responses, with responses deepening over time. The patient with **EMD achieved complete radiologic resolution,** and the first-treated patient maintained a durable response for >**10 months.**

Clinical Implications

- Demonstrates the feasibility of **direct *in vivo* generation of BCMA-targeted CAR-T** cells without apheresis, *ex vivo* manufacturing, or lymphodepleting chemotherapy.
- Achieved **100% ORR** and universal **MRD negativity,** supporting further clinical evaluation.
- Could substantially reduce **vein-to-vein time** and simplify CAR-T manufacturing and delivery.

Why It Matters

- Addresses key limitations of autologous CAR-T therapy, including **complex manufacturing, long production timelines, and logistical delays.**
- Represents a transformative *in vivo* **CAR-T** approach that could improve accessibility, scalability, and cost-effectiveness while maintaining the efficacy of CAR-T therapy.

In-Vivo CAR-T Therapy Shows Promising Activity in RRMM

Toxicity	Complete Responses	Simplified Therapy
No ICANS or delayed neurotoxicity.	100% ORR with universal MRD negativity.	*In-vivo* BCMA CAR-T generation.

Reference: Ho, P. J. *et. al.,* (2026). Journal of Clinical Oncology, 44(16_suppl), 7509.

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Satri-cel Receives NMPA Approval: World's First CAR T-Cell Therapy for Solid Tumours

China's National Medical Products Administration (NMPA) approved **satricabtagene autoleucel or Satri-cel,** an autologous humanized Claudin18.2 CAR T-cell therapy, for patients with Claudin18.2-positive, HER2-negative advanced gastric/gastroesophageal junction adenocarcinoma (G/GEJA) who have failed at least two prior lines of therapy **becoming the world's first approved CAR T-cell therapy for solid tumours.**

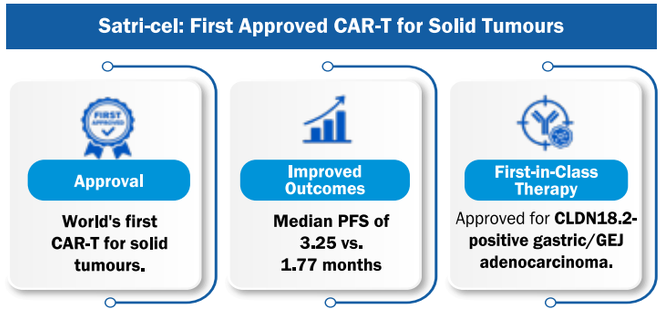
Supporting its approval, the pivotal Phase 2 CT041-ST-01 trial enrolled 1,566 screened patients with CLDN18.2-positive advanced gastric or GEJ cancer, randomizing 104 patients to satri-cel and 52 to physician's choice of therapy (nivolumab, paclitaxel, docetaxel, irinotecan, or rivoceranib). Median PFS was 3.25 months with satri-cel versus 1.77 months with standard treatments. Median overall survival trended longer with satri-cel (7.9 vs. 5.5 months), though this difference did not reach statistical significance.

Clinical Implications

- Provides a first-in-class, approved cellular therapy option for heavily pre-treated CLDN18.2-positive gastric/GEJ adenocarcinoma.
- Validates CLDN18.2 as an actionable, tumour-selective CAR-T target with limited normal-tissue expression.
- Establishes proof-of-concept that CAR-T can achieve meaningful efficacy in solid tumours, a setting where the modality has historically underperformed relative to hematologic malignancies.

Why It Matters

- Advanced gastric/GEJ cancer carries a poor prognosis after progression on standard therapies, with few effective options in the third-line setting.
- CLDN18.2 is frequently expressed in gastric and gastroesophageal junction adenocarcinomas, representing a substantial addressable patient population.
- This approval breaks a long-standing barrier for CAR-T in solid tumours, potentially catalysing further investment and trial activity in CLDN18.2-directed and other solid-tumour CAR-T programs.



Reference: Qi C, Liu C, *et al.* NMPA approval announced by CARsgen Therapeutics, June 22, 2026.

SPOT-MAS Multi-Cancer Early Detection Test Shows Real-World Accuracy Across Asian Populations

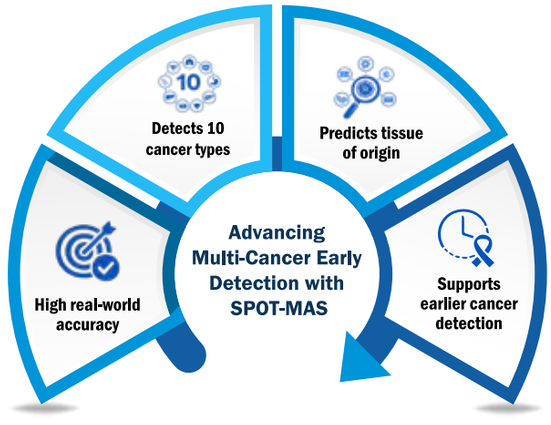
Study, Performance & Clinical Utility: SPOT-MAS is a multimodal **cell-free DNA (cfDNA)** test for **multi-cancer early detection (MCED)** that analyzes **methylomics, fragmentomics, copy number alterations, and end-motif profiles,** integrating these signals using machine learning to detect **10 cancer types.** A large retrospective real-world study evaluated **84,145 asymptomatic individuals** across **Vietnam, Thailand, Indonesia, the Philippines, Malaysia, and Singapore,** with **22,597 participants** meeting ≥12-month follow-up criteria. SPOT-MAS identified **64 confirmed precancer/cancer cases** (0.4% positivity rate) and accurately predicted the **tissue of origin in 79.7%** of cases, including **stomach, liver, and nasopharyngeal cancers,** for which routine screening is unavailable. Among **22,503 negative results, 99.51% were true negatives. The assay achieved 79.0% sensitivity, 99.9% specificity, 68.1% positive predictive value**, and 99.9% negative predictive value, consistent with findings from the earlier **K-DETEK** trial. Based on this data, the **FDA granted SPOT-MAS Breakthrough Device Designation in May 2026.**

Clinical Implications

- Demonstrates robust real-world performance of a **multimodal cfDNA MCED assay** in routine clinical practice.
- Detects cancers lacking established screening programs while accurately predicting tissue of origin to guide diagnostic work-up.
- Confirms reproducibility of results beyond controlled clinical trials.

Why It Matters

- Represents the **largest real-world MCED study in Asian populations,** addressing a major evidence gap.
- Provides a scalable strategy for earlier cancer detection in regions where screening programs are limited.
- Supports broader adoption of **liquid biopsy-based population screening,** particularly in low- and middle-income countries.



Reference: Nguyen DLH, *et. al.,* J Clin Oncol. 2026;44(19_suppl):14.