SunAct

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OncoVantage

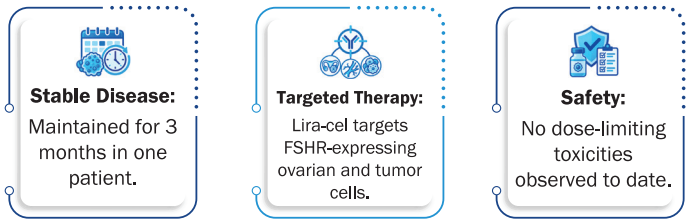
Insights into global breakthroughs in cell-based therapies

FSHR CAR-T | *IN VIVO* CAR-NK ENGINEERING | URINE cfRNA | TRE-515 + KRAS INHIBITORS

FSHR-Directed CAR T-Cell Therapy: Stable Disease Observed in Recurrent Ovarian Cancer in Phase 1 Dose-Escalation Trial

Liraltagene autoleucel (lira-cel) is an autologous CAR T-cell therapy targeting the follicle-stimulating hormone receptor (FSHR), which is expressed on ovarian cells, tumor vasculature, and certain cancer cells, with limited expression in healthy tissues. In the ongoing Phase 1 dose-escalation trial (NCT05316129) involving adult women with recurrent ovarian cancer who have progressed after at least two prior therapies, one patient achieved stable disease lasting 3 months, **representing the first reported case of stable disease in the trial.** The patient received lira-cel at a dose of 1×10^7 CAR-positive cells/kg, following lymphodepletion, in the fifth dose cohort, the highest dose level evaluated to date. Stable disease was observed 90 days after treatment. Additionally, multiple patients have survived for more than 1 year after treatment, including one who survived beyond 2 years. No dose-limiting toxicities have been observed in any patient treated to date.

FSHR-Directed CAR T-Cell Therapy in Ovarian Cancer



Clinical Implications

- Suggests that higher dose levels of lira-cel may produce clinical activity in recurrent ovarian cancer.
- Supports FSHR as a CAR T target in a solid tumor setting where options are limited after recurrence.
- Targeting both tumor cells and tumor vasculature, with limited expression in healthy tissue, may support a favorable safety profile.
- The absence of dose-limiting toxicities across dose cohorts supports continued dose escalation.

Why It Matters

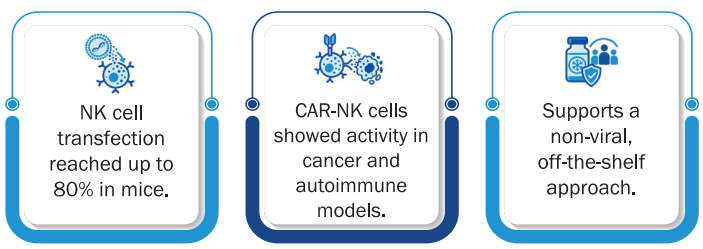
- Solid tumors, including ovarian cancer, have been difficult to treat with CAR T therapy, so any signal of disease control is notable.
- Survival beyond 1 to 2 years in some heavily pre-treated patients is an encouraging early sign of durability.
- This is early-phase data from a small dose-escalation study.

Reference: ClinicalTrials.gov, NCT05316129; clinical update, 5 October 2026. Trial record.

In vivo engineering of CAR natural killer cells for immunotherapy using ligand-directed lipid nanoparticles

A preclinical study developed NK cell-targeted lipid nanoparticles (NtLNPs) incorporating engineered biparatopic NK cell ligands to enable receptor-specific uptake and mRNA delivery. The lead NtLNPs achieved up to 80% NK cell transfection in mice, with minimal off-target effects. Systemic administration of CAR-encoding mRNA generated CAR NK cells *in vivo*, demonstrating activity across healthy, autoimmune, solid tumor, and humanized hematologic malignancy models. In healthy mice, CD19-targeted CAR NK cells completely depleted circulating B cells, while CD3-targeted CAR NK cells eliminated nearly all autoreactive T cells in an autoimmune hepatitis model, highlighting their potential for treating T cell-driven autoimmune diseases. In solid tumor models, NtLNPs targeting the inhibitory checkpoint NKG2A enhanced antitumor efficacy by alleviating Qa-1b-mediated immunosuppression. Furthermore, NtLNPs optimized for human CAR NK cells induced tumor regression in two humanized hematologic malignancy models. These findings support the potential of targeted NtLNPs as a platform for systemic, *in vivo* CAR NK cell generation, although further studies are needed to establish clinical safety and efficacy.

***In Vivo* CAR-NK Cell Engineering with LNPs**



Clinical Implications

- Supports non-viral, *in vivo* cell engineering as an alternative to *ex vivo* CAR manufacturing.
- Offers an off-the-shelf approach that avoids patient cell collection and viral vector production.
- Extends the potential of CAR NK therapy beyond cancer to T cell-driven autoimmune disease.
- Provides a modular system in which the targeting ligand and CAR mRNA can be swapped to address new targets.

Why It Matters

- Demonstrates the integration of ligand engineering, mRNA technology and lipid nanoparticle delivery for *in vivo* immune cell programming.
- Addresses an underexplored area, as most *in vivo* LNP engineering has focused on T cells rather than NK cells.
- Represents a step toward simpler, scalable cell therapy, though the data are preclinical and clinical translation will require safety, dosing and durability studies.

Reference: Chen Y. *et.al.* 2026 In vivo engineering of CAR natural killer cells for immunotherapy using ligand-directed lipid nanoparticles. *Nat Biotechnol.* 2026 Oct 13.

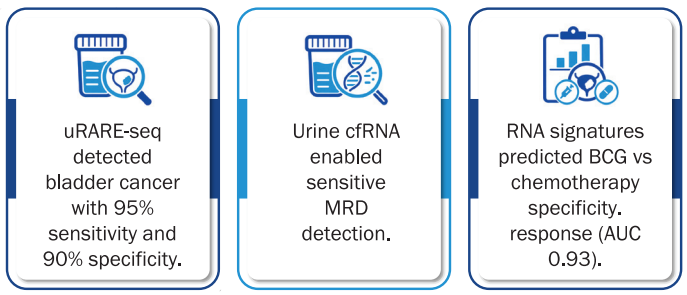
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Insights into global breakthroughs in cell-based therapies

Urine cell-free RNA for bladder cancer detection and treatment response prediction

Researchers developed uRARE-seq (urine random priming and affinity capture of cell-free RNA fragments for enrichment analysis by sequencing), a liquid biopsy method for profiling urine cell-free RNA (cfRNA), and evaluated it in 683 urine samples from patients with cancer and controls. The method identified transcripts originating from genitourinary tissues and tumour-derived transcripts in prostate, kidney and bladder cancers. It detected localized bladder cancer with 95% sensitivity at 90% specificity, outperforming urine cytology and a tumour-naive urine tumour-DNA assay in the reported comparisons, while remaining unaffected by field-effect mutations. uRARE-seq also enabled sensitive detection of minimal residual disease (MRD) and distinguished molecular responses following surgery from those after intravesical Bacillus Calmette–Guérin (BCG) therapy. Furthermore, pretreatment urine from BCG responders showed enrichment of T-cell and other immune signatures, whereas nonresponders exhibited higher proliferation-related gene expression. A treatment-response prediction model achieved an AUC of 0.93 for distinguishing likely responses to BCG versus chemotherapy, highlighting uRARE-seq's potential for non-invasive cancer detection, MRD monitoring and treatment-response prediction.

Urine cfRNA in Bladder Cancer Detection & Response



Clinical Implications

- Noninvasive urine cfRNA profiling could improve detection and molecular characterization of bladder cancer and potentially other genitourinary malignancies.
- Sensitive detection of minimal residual disease may support post-treatment monitoring and earlier identification of recurrence.
- Pretreatment urine from complete responders to BCG was enriched for T cell and other immune signatures, whereas nonresponders showed higher expression of proliferation-related genes.
- In pretreatment urine from 114 patients, this difference enabled a biomarker predicting response to BCG versus chemotherapy (AUC 0.93) that was strongly associated with recurrence risk.

Why It Matters

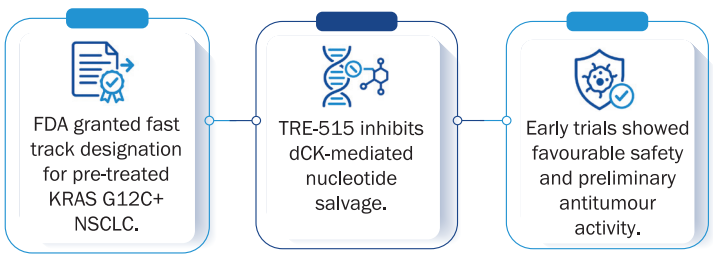
- Field-effect mutations in normal-appearing urothelium can confound urine tumour DNA assays, and RNA-based profiling was unaffected by them.
- Enrichment of T cell signatures in BCG responders suggests a pre-existing anti-tumour immune response, whereas high proliferation signatures mark tumours less likely to respond.
- Transcriptomic profiling adds information on tumour biology and immune state that DNA mutation analysis alone cannot provide, supporting treatment selection between BCG and chemotherapy.

Reference: Liu, *et al*. Urine cell-free RNA for bladder cancer detection and treatment response prediction. *Nat Med* (2026).

FDA Grants Fast Track Designation to TRE-515 Plus KRAS Inhibitors in Pre-treated KRAS G12C+ NSCLC

The FDA has granted Fast Track designation to TRE-515 in combination with KRAS inhibitors for patients with KRAS G12C mutation-positive non-small cell lung cancer (NSCLC) previously treated with an anti-PD-(L)1 antibody and platinum-based chemotherapy. TRE-515 is a first-in-class oral small-molecule inhibitor of deoxycytidine kinase (dCK), the rate-limiting enzyme in the nucleoside salvage pathway and the only dCK inhibitor currently in clinical development. KRAS inhibitor-treated tumours may increase their reliance on this pathway to maintain nucleotide availability under therapeutic stress. Preclinical PET imaging demonstrated persistent dCK activity following KRAS inhibition, which was subsequently blocked by TRE-515. TRE-515 has also demonstrated favourable safety and preliminary antitumour activity in an ongoing first-in-human trial.

TRE-515 Plus KRAS Inhibitors in NSCLC



Clinical Implications

- Metabolic resistance targeting: dCK inhibition may disrupt compensatory nucleotide salvage that supports tumour-cell survival during KRAS inhibition.
- Rational combination strategy: Simultaneous inhibition of oncogenic signalling and nucleotide metabolism may enhance antitumour activity and improve response durability.
- Pharmacodynamic monitoring: dCK-targeted PET imaging may help evaluate salvage-pathway activity and target engagement during treatment.

Why It Matters

- Targets metabolic plasticity: Tumour cells can adapt nucleotide metabolism to sustain DNA synthesis and repair under therapeutic stress.
- Exploits a metabolic vulnerability: Blocking dCK may restrict the use of salvaged deoxynucleosides when KRAS signalling is inhibited.
- Addresses acquired resistance: This complementary strategy may help overcome incomplete responses and relapse associated with KRAS G12C inhibitors, although clinical benefit remains to be established.

Reference: TRE-515 FDA Fast Track designation announcement, October 2026.

At SunAct, we remain dedicated to tracking and sharing global advances that continue to redefine the landscape of cellular therapy and oncology. Stay tuned for our next edition as we uncover more breakthroughs and emerging trends shaping the future of cancer research.

Disclaimer: This newsletter is intended for healthcare professionals and researchers. Information is for educational purposes only.