SunAct

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OncoVantage

Insights into global breakthroughs in cell-based therapies

MULTI-ANTIGEN T-CELL I KRAS PEPTIDE VACCINE I NON-INVASIVE BIOPSY (OSCC) I AFAMI-CEL APPROVAL

Phase I Trial Demonstrates Safety and Early Clinical Activity of Multi-Antigen T-Cell Therapy in Pediatric CNS Tumors

The Phase I ReMIND trial (NCT03652545) demonstrated the safety and feasibility of autologous, non-engineered T cells targeting WT1, PRAME, and survivin in children with high-risk CNS tumours. In this open-label, dose- escalation study, 51 pediatric patients with newly diagnosed DIPG or relapsed/recurrent non-brainstem CNS tumours received repeated IV infusions (MTD: **8 × 107 cells/m²**). Treatment was generally well tolerated, with fatigue and headache as the most common adverse events; two patients developed treatment-related tumour swelling, and one Grade 5 dose-limiting toxicity occurred. Median overall survival was **13.7 months** in DIPG, with durable disease-free survival observed in three patients, including one complete response.

Clinical Implications

- Demonstrates the feasibility and safety of multi-antigen-targeting, non-genetically engineered T-cell therapy for pediatric CNS tumours.
- Simultaneous targeting of WT1, PRAME, and survivin may reduce the risk of tumour antigen escape, a common mechanism of treatment resistance.
- Provides evidence that systemically administered antigen-specific T cells can persist *in-vivo* and generate durable immune responses without genetic engineering.
- Establishes an optimal dose for future clinical studies and supports further evaluation in larger efficacy trials.

ReMIND Trial Shows Promising Results in Pediatric CNS Tumours

13.7-Month Survival

Median overall survival achieved in patients with DIPG.

Durable Benefit

Long-term disease-free survival.

Triple-Antigen Targeting

WT1, PRAME, and survivin targeted simultaneously.

Why It Matters

- Pediatric CNS tumours are the leading cause of cancer death in children, with very limited options for recurrent or high-grade disease.
- This approach uses autologous, non-engineered T cells targeting multiple intracellular antigens, simplifying manufacturing versus CAR-T/TCR-T.
- Targeting WT1, PRAME, and survivin, broadly expressed across pediatric brain tumours reduces immune escape versus single-antigen therapies.
- A durable complete response and long-term disease-free survival in three patients signal promise for multi-antigen T-cell therapy, warranting further development.

Reference: Gomez S, *et al., Nat Med* 32, 2481–2493 (2026).

Mutant KRAS Peptide Vaccine Combined with Dual Checkpoint Blockade Shows Promising Immune Responses in MSS Metastatic Colorectal Cancer

A Phase I, **single-arm clinical trial (NCT04117087)** evaluated mKRAS-VAX, a pooled peptide vaccine targeting six common KRAS mutations, in combination with the dual immune checkpoint inhibitors **nivolumab and ipilimumab** in 13 patients with previously treated mismatch repair-proficient/microsatellite stable (MMRp/MSS) metastatic colorectal cancer (mCRC). MSS colorectal cancer is largely unresponsive to immune checkpoint inhibitors alone, making it a challenging disease to treat with immunotherapy. The study met its primary endpoints of safety and immunogenicity, with all vaccine-related adverse events limited to Grade 1–2, and no increase in severe immune-related toxicities beyond those expected with dual checkpoint blockade. The vaccine induced **KRAS-specific T-cell responses in 75% (8/12)** of biomarker-evaluable patients by direct *ex-vivo* IFN-γ ELISpot and in 100% of patients following *in-vitro* expansion, demonstrating robust activation of mutation-specific antitumor immunity.

Clinical Implications

- **mKRAS-VAX** was safe and induced robust KRAS-specific T-cell responses when combined with nivolumab and ipilimumab in MMRp/MSS metastatic colorectal cancer.
- The study provides proof-of-concept that **personalized neoantigen vaccines** can overcome the poor immunogenicity of MSS colorectal cancer.
- Combining **therapeutic cancer vaccines with checkpoint inhibitors** enhances T-cell responses against KRAS mutations.
- The findings establish a foundation for combining **KRAS vaccines** with TCR-T, CAR-T, and bispecific T-cell engagers.

mKRAS-VAX Advances Precision Immunotherapy

Cold Tumours Activated
Generated KRAS-specific immune responses in MSS mCRC.

Neoantigen Vaccine Validated
Demonstrated clinical immunogenicity of mKRAS-VAX.

Checkpoint Response Enhanced
Strengthened T-cell immunity with dual ICIs.

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Why It Matters

- Approximately 95% of metastatic colorectal cancers are MMRp/MSS, limiting the efficacy of checkpoint inhibitors.
- KRAS mutations occur in ~40% of colorectal cancers, making them a major oncogenic driver.
- Targeting shared KRAS neoantigens can induce functional antitumor T-cell responses in immunologically "cold" tumors.
- Neoantigen-based cancer vaccines represent a promising precision immunotherapy for patients with limited treatment options.

Reference: Wang, H. *et al. Nat Commun* (2026).

Non-Invasive Brush Biopsy Test Enables Accurate Molecular Detection of Oral Squamous Cell Carcinoma

Researchers developed **qMIDSV3,** a rapid, non-invasive brush biopsy-based molecular assay for detecting oral squamous cell carcinoma (OSCC). Using a four-gene mRNA panel (INHBA, S100A16, YAP1, and POLR2A), it generates a molecular malignancy index to distinguish OSCC from oral potentially malignant disorders, with results available within **1 hour.** In a prospective study of **1,090 brush biopsy samples from 545 patients,** qMIDSV3 demonstrated excellent diagnostic performance, differentiating OSCC from oral leukoplakia and oral lichen planus with an **AUC of 0.975, 95.7% sensitivity, 95.1% specificity, 95.5% accuracy,** and low false-positive (4.9%) and false-negative (4.3%) rates.

Clinical Implications

- Validates **qMIDSV3** as a rapid, non-invasive molecular test for early OSCC detection.
- Delivers results within **1 hour,** enabling timely clinical decision-making and triage.
- Accurately stratifies the malignancy risk of oral potentially malignant disorders for earlier intervention.
- Supports point-of-care use through **room-temperature sample stability** and non-invasive brush biopsy.
- May reduce unnecessary scalpel biopsies in **>90% of low-risk OPMD patients,** lowering patient morbidity and healthcare burden.

qMIDSV3 Enables Accurate Non-Invasive OSCC Detection

Rapid Diagnosis
Results available within 1 hour for timely clinical decision-making.

High Diagnostic Accuracy
Achieved 95.7% sensitivity, 95.1% specificity, and 95.5% accuracy.

Non-Invasive Screening
Supports point-of-care testing while reducing unnecessary biopsies.

Why It Matters

- Oral squamous cell carcinoma accounts for ~90% of oral cancers, with survival closely tied to early diagnosis.
- Current diagnosis relies on invasive scalpel biopsy, often leading to unnecessary procedures, delayed diagnosis, and higher costs.
- As the largest validation study of a brush biopsy-based assay for OSCC, qMIDSV3 combines high diagnostic accuracy with rapid, non-invasive detection.
- qMIDSV3 enables point-of-care oral cancer screening, improving early diagnosis while reducing unnecessary biopsies and referrals.

Reference: Teh *et al. Biomarker Research* (2026) 14:76.

FDA Grants Full Approval to Afami-Cel for Advanced Synovial Sarcoma

FDA approved afamitresgene autoleucel (afami-cel), the first TCR-T therapy for a solid tumour, for adults with unresectable or metastatic **MAGE-A4-positive, HLA-A*02-positive synovial sarcoma** following prior chemotherapy. Afami-cel is an autologous TCR-T engineered to express a high-affinity TCR targeting **MAGE-A4 presented by HLA-A*02.** In the Phase II **SPEARHEAD-1** trial, it achieved a **43.8% ORR** (3.6% CR), **median DOR of 5.3 months, with 31.9% of responders maintaining responses for ≥24 months.** The safety profile was consistent with adoptive cell therapies, with manageable CRS, cytopenias, infections, fatigue, and no new safety signals.

Clinical Implications

- Becomes the first fully FDA-approved TCR-T cell therapy for a solid tumour.
- Provides a new treatment option for patients with advanced synovial sarcoma, a disease with limited effective therapies after chemotherapy.
- Clinically validates MAGE-A4 as an actionable intracellular antigen for engineered TCR therapies.
- Demonstrates that TCR-T therapy can achieve durable clinical responses in solid tumours, expanding adoptive cell therapy beyond hematologic malignancies.

Afami-Cel Marks a Milestone in Solid Tumour Immunotherapy

First Approved Solid Tumour TCR-T
First FDA-approved TCR-T therapy for advanced synovial sarcoma.

Durable Clinical Responses
43.8% ORR, with durable responses lasting ≥24 months.

Validates MAGE-A4 Targeting
Establishes MAGE-A4 as a clinically actionable TCR-T target.

Why It Matters

- Synovial sarcoma is a rare soft tissue sarcoma that primarily affects adolescents and young adults, with poor outcomes in metastatic disease.
- Unlike CAR-T cells, which recognize surface proteins, TCR-T cells can target intracellular tumour antigens presented by HLA molecules, greatly expanding the number of targetable cancer antigens.
- Represents a major milestone for adoptive T-cell therapy in solid tumours, reinforcing the clinical potential of biomarker-driven TCR-T therapies and paving the way for future engineered T-cell therapies targeting intracellular neoantigens.

Reference: SPEARHEAD-1; FDA Full Approval of Afamitresgene autoleucel (Afami-cel) for advanced synovial sarcoma (2026).

At SunAct, we remain dedicated to tracking and sharing global advances that contiune 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.