

# OncoVantage

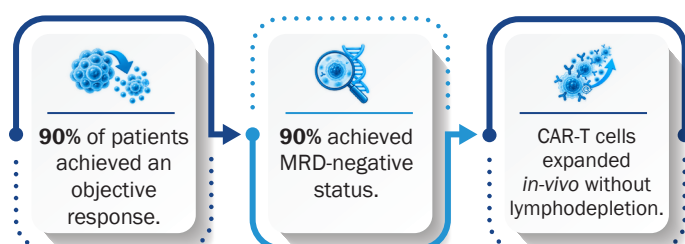
Insights into global breakthroughs in cell-based therapies

IN VIVO BCMA CAR-T | KRAS VACCINE | PD-1/VEGF BISPECIFIC | EARLY PANCREATIC DETECTION

## First-in-Human Data for a Single-Infusion *In Vivo* BCMA CAR-T (IAS0206) Show 90% Response in Heavily Pretreated Myeloma, Without Chemotherapy Conditioning

IAS0206 is an *in vivo* BCMA-targeted CAR-T therapy evaluated in a Phase 1 study involving 10 heavily pretreated relapsed/refractory multiple myeloma patients. A single IV infusion generated functional CAR-T cells without apheresis, ex vivo manufacturing, or lymphodepleting chemotherapy. CAR-T cells expanded *in vivo* and persisted for up to six months. The overall response rate and MRD-negativity rate were both 90%, reaching 100% in the high-dose cohort. No dose-limiting toxicities, ICANS, or treatment-related deaths occurred. CRS was grade 2 or lower. Follow-up remains limited, requiring further evaluation of response durability and optimal dosing.

### IAS0206: Promising Efficacy with Simplified CAR-T Therapy



### Clinical Implications

- **Response:** The objective response rate was 90% (9/10), including three stringent complete responses, and the MRD-negativity rate was 90%. Both reached 100% in the high-dose cohort.
- **Expansion:** CAR-positive cells expanded without lymphodepletion, peaked between days 12 and 21, and most remained detectable beyond 60 days and up to six months.
- **Safety:** No dose-limiting toxicities, ICANS or treatment-related deaths. CRS was grade 1 in seven patients and grade 2 in one, and two patients had none. Two patients had grade 3 or higher viral infections due to low immunoglobulin levels and recovered with IVIG.

### Why It Matters

- Conventional CAR-T is limited by manufacturing time, cost and conditioning chemotherapy. An off-the-shelf infusion could widen access and, as the developers suggest, eventually be tested earlier in the treatment course.
- It follows other *in-vivo* CAR-T programs reporting early data this year, including KLN-1010 in myeloma and LB2501 in lymphoma.

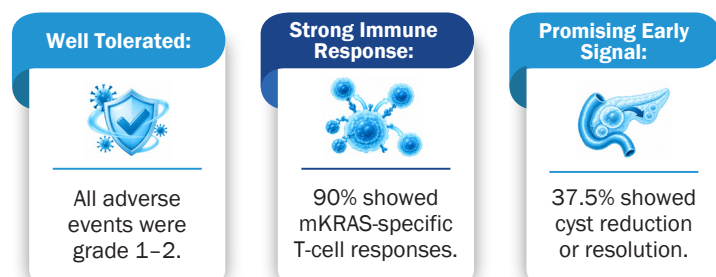
Reference: Yan W, Zou H, Wang Q, et al. First-in-Human Clinical Proof-of-Concept of IAS0206, 2026 IMS Annual Meeting. Oral LBA-11

## Phase I Trial of a Mutant KRAS Peptide Vaccine (mKRAS-VAX) Shows Safety and Durable T-Cell Responses in People at High Risk of Pancreatic Cancer

Pancreatic ductal adenocarcinoma (PDAC) arises from precursor lesions over a decade or more, which offers a window for interception in high-risk individuals. However, current surveillance detects only a minority of precursors. Mutant KRAS (mKRAS) is present in most PDACs and their precursors, making it an appealing target for immune-based interception.

A phase I, first-in-human study tested mKRAS-VAX, a peptide vaccine targeting six common KRAS mutations (G12D, G12V, G12R, G12C, G12A and G13D). The trial enrolled 20 individuals with hereditary PDAC predisposition and a radiographic pancreatic abnormality, typically a small cyst consistent with an IPMN (NCT05013216, Cohort A). The primary aims were to assess safety, immunogenicity and T cell persistence. Participants received the vaccine four times over 13 weeks.

### mKRAS-VAX Shows Promising Immune Response in High-Risk Individuals



### Clinical Implications

- **Safety:** All adverse events were grade 1-2, and no high-grade events were reported in otherwise healthy, high-risk individuals.
- **Immune response:** Vaccination elicited a significant mKRAS-specific T-cell response in 18 of 20 participants (90%).
- **Durability:** Longitudinal TCR sequencing showed persistence of vaccine-induced mKRAS-specific clonotypes for up to 2 years.
- **Early clinical signal:** Over a median follow-up of 16.5 months, no participants developed PDAC. In an exploratory analysis, 37.5% of vaccinated individuals had cyst reduction or resolution, compared with 6.8% in an unvaccinated cohort with similar characteristics.

### Why It Matters

- Current surveillance detects only a minority of precursor lesions, so an approach that acts on the precancerous stage addresses a real gap.
- This is the first report of safety and immunogenicity for a neoantigen vaccine targeting mKRAS in the precancer setting for PDAC.

Reference: Haldar SD, et al. Cancer Discovery, 2026. ClinicalTrials.gov: NCT05013216.

## FDA Grants Fast Track Designation to Ceslatamig, a PD-1/VEGF Bispecific Antibody, for Immunotherapy-Pretreated NSCLC

The U.S. Food and Drug Administration (FDA) has granted Fast Track Designation to ceslatamig (AI-081), an investigational PD-1/VEGF bispecific antibody. The designation applies to adults with advanced or metastatic non-small cell lung cancer (NSCLC) whose disease has progressed after PD-(L)1-targeted immunotherapy and platinum-based chemotherapy, given concurrently or sequentially. Ceslatamig is being evaluated in the global Phase 1/2 BiPAVE-001 program in the United States and China.

### Clinical Implications

- ▶ **Dual-pathway targeting:** Ceslatamig combines PD-1 checkpoint blockade with inhibition of VEGF-driven angiogenesis in a single molecule, addressing both immune suppression and tumor vascularization in the tumor microenvironment.
- ▶ **Engineering:** As reported, the antibody binds VEGF with more than 40-fold higher affinity than bevacizumab-based PD-1/VEGF bispecific candidates, and it is designed for cooperative binding in tumors enriched for PD-1 and VEGF. Fc-silencing modifications are intended to limit depletion of PD-1-positive effector T cells while preserving PD-1 blockade.
- ▶ **Expedited development:** Fast Track allows more frequent interaction with the FDA, rolling review of eligible portions of a future marketing application, and potential eligibility for priority review if the applicable criteria are later met.
- ▶ **Current status:** The ongoing BiPAVE-001 program is evaluating ceslatamig in advanced solid tumors, including NSCLC (US: NCT06635785; China: CTR20253261). The US study includes dose escalation and dose optimization with intravenous dosing every three weeks, and it is assessing safety, pharmacokinetics and preliminary antitumor activity while establishing the recommended Phase 2 dose.

**Reference:** FDA Fast Track Designation for Ceslatamig, an Investigational PD-1/VEGF Bispecific Antibody, September 16, 2026; ClinicalTrials.gov NCT06635785.

### Ceslatamig Targets PD-1 and VEGF in Advanced NSCLC



### Why It Matters

- ▶ Acquired resistance after immune checkpoint inhibitor and chemotherapy combinations is a central challenge in thoracic oncology, and treatment options in this setting are limited.
- ▶ The approach rests on the biological link between immune suppression and angiogenesis. VEGF can contribute to an immunosuppressive tumor microenvironment, while PD-1 blockade aims to restore antitumor T-cell activity.

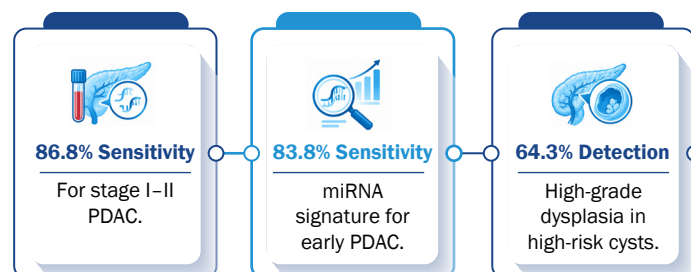
## Multicenter Prospective Study Shows PANXEON, a Blood-Based miRNA and CA19-9 Assay, Detects Early-Stage Pancreatic Cancer

An international, multicenter, prospective observational biomarker study of 1,785 individuals from four countries evaluated PANXEON (PANcreatic cancer eXosome Early detectionION). PANXEON is a composite score combining a 10-miRNA blood signature (hsa-miR-142-3p, miR-30c-5p, miR-335-5p, miR-340-5p, miR-200b-3p, miR-1260b, miR-145-3p, miR-145-5p, miR-429 and miR-200a-3p) with carbohydrate antigen 19-9 (CA19-9). The miRNA signature alone achieved an AUC of 88.6% in the testing cohort, with 83.8% sensitivity for early-stage pancreatic ductal adenocarcinoma (PDAC) and minimal cross-reactivity with other gastrointestinal cancers.

### Clinical Implications

- ▶ **Early-stage sensitivity:** Combined with CA19-9, the assay reached 86.8% sensitivity for stage I-II PDAC.
- ▶ **False-positive rates:** 3.2% in low-risk controls and 15.6% in high-risk controls in the testing cohort, which will shape how and in whom the test could be used.
- ▶ **Precancerous detection:** PANXEON detected high-grade dysplasia in 64.3% of individuals with high-risk pancreatic cysts, suggesting a role beyond detecting established cancer.
- ▶ **Possible disease monitoring:** In a small cohort of 19 individuals, miRNA signature levels fell during neoadjuvant chemotherapy and after surgery, and rose before disease recurrence. This is preliminary.

### PANXEON Shows Promise for Early Pancreatic Cancer Detection



### Why It Matters

- ▶ There is currently no clinically relevant blood-based assay for early-stage PDAC, a malignancy with poor outcomes that is usually diagnosed late.
- ▶ CA19-9 alone has limited value for early detection, so pairing it with an miRNA signature addresses a known gap.
- ▶ The findings support blood-based detection as a complement to existing strategies for high-risk populations.
- ▶ The authors state that the assay warrants further large-scale prospective studies. It is not yet a validated screening test, and it has not been shown to improve survival.

**Reference:** Xu, C., Mannucci, A., Han, H. et al. *Nature Medicine* (2026), ClinicalTrials.gov: NCT06388967.