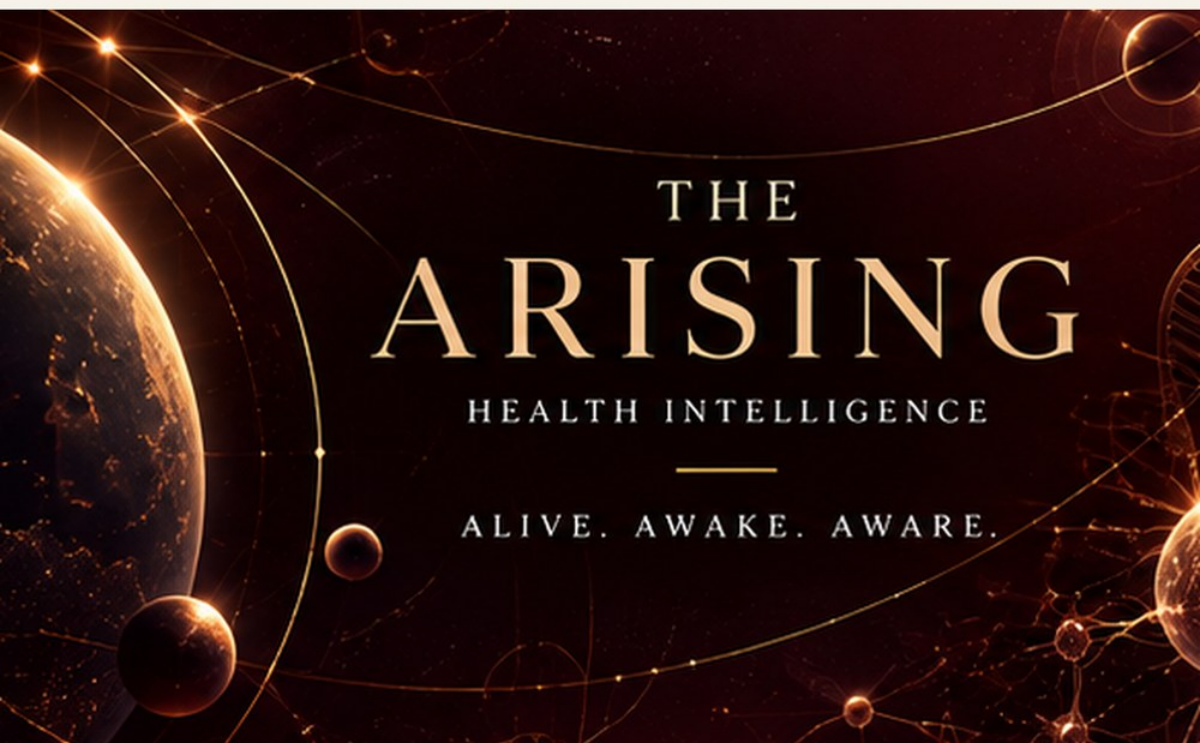
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FRONTIERS / 04

When Medicines Become Instructions

Personalized cancer vaccines, recurrence, and what five-year follow-up adds.



Alive. Awake. Aware.

John Griffin, MD / Arising Health

READING EDITION / OCTOBER 25, 2026

How to read this companion

Original randomized phase 2b report and descriptive five-year update checked at record/abstract level October 25, 2026. This booklet does not establish current approval or availability for an individual patient.

Evidence is attached to the question it answers. Human clinical effects, observational associations, animal experiments, cellular measurements and computational proposals are kept distinct. This reading copy is not individual medical advice.

In this booklet

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03 Reading the long follow-up without enlarging it

Follow the evidence

Each chapter identifies the sources supporting its factual claims. Direct primary-source links and review limitations appear in the reference section. Study dates are retained even when older work provides context for a newer story.

01 / A cancer vaccine written for one tumor

Evidence for this chapter: 1, 2. Source details and direct links appear at the end.

A personalized cancer vaccine begins with a specific ambition: help the immune system recognize features of this person's tumor. It is not a general vaccine against every cancer, and its success in one setting cannot establish success in another.

The KEYNOTE-942 program tested an individualized mRNA neoantigen therapy, now called intismeran autogene, alongside pembrolizumab after complete resection of high-risk melanoma. The original phase 2b trial randomized 157 patients: 107 to combination treatment and 50 to pembrolizumab alone.

The initial comparison

At the original analysis, estimated 18-month recurrence-free survival was 79% with the combination and 62% with pembrolizumab alone–an absolute difference of 17 percentage points at that time point. The hazard-ratio confidence interval crossed one, and the reported two-sided p-value was 0.053. Those details belong beside the favorable point estimate.

Grade 3 or worse treatment-related adverse events occurred in 25% versus 18%. A promising recurrence result does not eliminate the additional treatment burden or the need to judge safety in a larger population.

What five years adds

The September 2026 follow-up reported a recurrence-or-death hazard ratio of 0.510 and a distant-metastasis-or-death hazard ratio of 0.411, both with confidence intervals below one. These five-year analyses were descriptive; they extend the picture but should not be presented as a new independent randomized trial.

The overall-survival estimate remained uncertain: its confidence interval crossed one. This is therefore not proof of an established

survival advantage. The same 157-patient trial also cannot settle effectiveness across every cancer type or clinical setting.

Why the platform matters

The strategy turns an individual tumor's molecular information into a therapeutic design. The scientific challenge extends beyond identifying a plausible target: manufacturing, immune recognition, delivery, treatment timing and durable clinical benefit must all work together.

For readers, the appropriate conclusion is specific. This randomized melanoma program provides encouraging evidence about recurrence-related outcomes in a defined postoperative population. It does not establish a general preventive vaccine for healthy people.

The original October 16 archive relied on a business-news report. This reading version instead anchors the story in the primary trial and its published follow-up, separating the 2024 initial report from the 2026 update. That change makes the promise more useful: it gives us an identifiable experiment to follow, rather than an ambition to believe.

02 / Personalized does not mean proven for everyone

Evidence for this chapter: 2. Source details and direct links appear at the end.

The therapy studied in KEYNOTE-942 uses an individualized neoantigen approach. The intent is to direct an immune response toward features of a particular patient's cancer. The clinical evidence in this companion concerns the combination with pembrolizumab after resection of high-risk melanoma.

It does not establish that the same strategy prevents every cancer, treats every stage of melanoma, or works equally well without pembrolizumab. A platform can support many future applications, but each clinical use has its own evidence requirements.

The original trial randomized 157 patients: 107 to the combination and 50 to pembrolizumab alone. This unequal allocation and modest sample should remain visible when interpreting both benefit and toxicity. Randomization strengthens the comparison; it does not make a small phase 2b study the final answer.

In the initial report, grade 3 or worse treatment-related adverse events occurred in 25% of the combination group and 18% of the monotherapy group. The seven-percentage-point difference is part of the clinical account, even though many reported adverse events were less severe. No mRNA-4157-related grade 4 or 5 events were reported in that analysis. These observations are not equivalent to a claim that the intervention has no serious risks.

03 / Reading the long follow-up without enlarging it

Evidence for this chapter: 1. Source details and direct links appear at the end.

The five-year update is valuable because durability matters in an adjuvant cancer treatment. Preventing or delaying a recurrence over a meaningful interval can be important to patients even before every survival question is settled.

The analysis remained descriptive. The reported hazard ratio for recurrence or death was 0.510, with a 95% confidence interval of 0.294 to 0.887. The distant-metastasis-free survival estimate also favored combination treatment. These are time-to-event relative measures, not the percentage of patients cured.

Overall survival had a favorable point estimate, but its confidence interval extended from 0.165 to 1.345. That interval is compatible with substantially different effects and includes no benefit. The appropriate headline is therefore not that longer overall survival has been established.

The update described no new safety signals. This means the investigators did not identify a newly emerging pattern in the

reported follow-up; it does not erase known adverse events or establish universal safety.

For a future report, look for confirmatory randomized evidence, absolute event risks over specified time horizons, detailed harms, patient eligibility and evidence about implementation. Manufacturing speed and access matter, but this trial cannot answer every delivery question. The scientific advance and the practical work of making it useful belong in the same conversation.

Sources & review scope

1. Intismeran Autogene Plus Pembrolizumab Versus Pembrolizumab Alone in High-Risk Resected Melanoma: 5-Year Update of KEYNOTE-942
September 10, 2026 journal issue
Descriptive long-term follow-up of randomized phase 2b trial
PubMed · PMID 42223134
Primary record and complete abstract checked October 25, 2026; full-text/supplement appraisal not completed in this pass.

2. Individualised neoantigen therapy mRNA-4157 (V940) plus pembrolizumab versus pembrolizumab monotherapy: KEYNOTE-942
February 17, 2024 journal issue
Open-label randomized phase 2b trial
PubMed · PMID 38246194
Primary record and complete abstract checked October 25, 2026; full-text/supplement appraisal not completed in this pass.

Illustrations are conceptual editorial art, not photographs of study results or anatomical diagrams. The Horizon and supporting celestial themes are reused from the approved Arising visual collection.