

Read Before You Remove

A personalised mRNA vaccine for melanoma, the closure rule of the vacuum.net, and the alternative already in hand

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This essay is a reading of published trials through a theory. It is not treatment advice. A patient with melanoma decides with an oncologist.

1. What was found

The question was simple. Does the vacuum.net theory offer an alternative way to treat high-risk melanoma, beside the personalised mRNA vaccine that made the news on 24 October 2026? And if so, which?

The answer is yes, with a precise limit. The theory does not supply a new substance. It supplies an ordering rule, and that rule points to three moves.

1. **Read before you remove.** Give immunotherapy while the tumour is still in the body, and operate afterwards. The tumour then serves as its own vaccine, made in place, for every patient whose tumour is still in the body, with no sequencing and no factory. This move is already tested. In cross-trial comparison its effect is of the same size as the vaccine's, and larger with two checkpoint drugs. In the Netherlands it has been the preferred treatment for resectable stage III melanoma since October 2025.
2. **Read what is shared, not what changes.** Aim at features that every melanoma carries, not at the mutations that differ from patient to patient. One drug then serves everyone. The evidence here is mixed: one clear success, one modest result, one miss.
3. **Set the zero locally.** Change the body's tolerance only where the tumour sits, instead of everywhere. The evidence is partial and open.

The theory also made five predictions about the vaccine trial before its detailed data were read. Two came true, one partly, one could not be scored, and one was not blind. None was a sharp test. That is reported in Section 5, plainly.

The strongest result is the first move. A theory built far from biology arrives, by its own rule, at the treatment order that the best recent trials have just established. That is a correspondence, not a proof. It is still worth having.

2. The occasion

On 24 October 2026 WIRED reported the phase 3 trial INTerpath-001. Merck and Moderna tested a personalised mRNA vaccine, intismeran autogene, in 1,137 people whose high-risk melanoma had been completely removed. Two thirds received the vaccine plus pembrolizumab, a checkpoint drug. One third received pembrolizumab alone.

The detailed results were presented at the ESMO congress in Madrid as late-breaking abstract LBA1. After a median follow-up of 24.6 months, the vaccine reduced the risk of recurrence or death by 42 percent (hazard ratio 0.58). Two years on, 82.2 percent of vaccinated patients were free of recurrence, against

70.0 percent without the vaccine. Distant spread fell by 38 percent (hazard ratio 0.62). Overall survival did not yet differ significantly (hazard ratio 0.77, $p = 0.33$).

These are real gains. They are reported as the first positive phase 3 result for an mRNA cancer therapy.

The article also contained errors. It said the scientists chose “up to three” molecular targets per patient. The vaccine encodes up to 34, and 91 percent of patients received all 34. It said the vaccine was awaiting FDA approval. No filing had been confirmed by 25 October. It said a pancreatic cancer vaccine had greatly improved survival. That was a phase 1 study of 16 patients, without a control group.

The article ended on the real problem, in the words of the melanoma researcher Marisol Soengas: the vaccine is literally bespoke. Each dose is made for one person from one tumour. The trial adds detail to that problem. The median time to the first vaccine dose was 64 days. And 302 of 1,749 screened patients, 17.3 percent, were excluded because their tumour sample was not good enough to build a vaccine from.

That is the question this essay puts to the theory. Is there a road to the same effect that does not need a factory per patient?

3. The theory, in full

The essay must stand on its own, so the theory comes first. It fits in a few paragraphs.

One strand. The vacuum.net theory describes everything that lasts as one strand that crosses itself. Picture a fishing net. The net is a single cord. Where the cord crosses itself there is a crossing. Between crossings lie the open meshes. A stretch of cord that returns to where it started, in step, is a winding.

One register. At a crossing the cord passes over, passes under, or does not cross. The theory writes these as +1, −1 and 0. Such a three-valued digit is a *trit*. Counting with trits is called balanced ternary.

One rule. Three crossings in a row form a *window*. A window is *closed* when its three trits add up to a multiple of three. The single selection rule of the theory, its axiom N2, says: what closes stays; what does not close passes its tension on to its neighbours.

Two kinds of closure. Of the 27 possible windows exactly 9 close. This is a proven theorem, not a choice. Moreover, a window closes if and only if its three trits are all equal or all different. The three all-equal windows are the form of a crystal: they hold and do not turn. The six all-different windows are the form of living matter: their content keeps changing while their closure holds. A seam between the two kinds is always open, and carries tension.

Four further axioms. N1: there is one strand, and every distinction is a place where it touches itself. N3, memory: at every crossing the first passage fixes the orientation, and later passages are read relative to it; order matters. N4, context: what looks like a constant is a function of the local state. N5, scale: the same rules hold at every depth, and what does not close at one scale becomes material for the next.

The test in a body. Apply the rule to a living body. The body carries a reading layer, the immune system, that tests every form it meets. There are three outcomes. +1: the form fits, and stays. −1: it does not fit, and is taken apart. 0:

it is not read, and simply remains.

The zero outcome is essential. The body must not attack the gut wall at every meal, the eye, or a child in the womb, who is half foreign. So it carries official zero-tokens that switch local reading off. Physicians call them checkpoints; PD-1 is one. Without them the body attacks itself. With them it has a blind spot.

Cancer in one sentence. Read this way, a tumour is the remainder of a selection. For years every abnormal cell that did not carry a zero-token was read and removed. Every cell that did carry one remained. What a surgeon cuts out is that remainder.

What the two drugs do. Pembrolizumab removes the zero-token. It does so everywhere, which is why its side effects resemble autoimmunity. The mRNA vaccine adds words for the test to read: up to 34 fragments of the patient's own mutated proteins.

4. What the rule says about the vaccine

Now apply the theorem on the two kinds of closure.

A melanoma is living matter. Its windows are of the mixed kind. Their content changes while their closure holds. The mutations a vaccine is built from are content. They differ between patients, and they drift within one patient over time.

So a vaccine built from mutations reads the part of the tumour that changes. That is why it must be made per person, why it takes nine weeks, and why one patient in six could not get one. The cost follows from what is read, not from the mRNA technology.

The rule suggests three other things to read.

The remainder itself, in place (axiom N3). Order matters. If the tumour is removed first and the immune system is trained afterwards, the trainer needs a copy of the tumour: a sample, a sequence, a factory. If the zero is lifted first, while the tumour is still there, the immune system reads the original. The tumour then is its own vaccine, complete and current, and it needs no manufacture.

What every melanoma shares. A melanoma descends from a pigment cell. It keeps features of that lineage, and often carries proteins that many melanomas share. Reading those is reading the closure, not the content. One product could serve many patients.

The local zero (axiom N4). A zero-token is a function of the local state, not a fixed property of the body. That suggests lifting it only at the tumour, not everywhere.

5. The experiment

The work followed the Respondent-Judge Protocol. A respondent fixed predictions in writing before the detailed trial data were looked up. The file was locked with a cryptographic hash at 11:16 UTC on 25 October 2026 (SHA-256 beginning e7d5f06b). A separate judge then verified the hash, found the data on its own, and scored each prediction.

The predictions, with their failure criteria:

- **P1.** The vaccine's relative benefit is about the same at every stage of

disease.

- **P2.** The benefit does not rise steadily with the number of mutations in the tumour.
- **P3.** The survival curves do not separate in the first three months, and separate after that.
- **P4.** Overall survival is not yet significant at this interim analysis.
- **P5.** Reading the tumour in place gives a relative benefit at least as large as adding the bespoke vaccine after removal. This one was known to be not blind.

6. Evaluation and adjustment

	Verdict	Evidence
P1	Hit, coarse	Hazard ratio 0.60 in the lower-risk group, 0.57 in the higher-risk group. Only two pooled groups are public.
P2	Not decidable	No phase 3 data on mutation load are public. The phase 2b trial fits the prediction (0.65 against 0.59), but cannot score it.
P3	Partial	No early separation: hazard ratio 0.99 over months 0–6. But the benefit appears only after month 6 (0.42), not after month 3.
P4	Hit	Overall survival hazard ratio 0.77, $p = 0.33$.
P5	Hit, not blind	Neoadjuvant pembrolizumab (SWOG S1801): 0.58. Neoadjuvant ipilimumab plus nivolumab (NADINA): 0.32, later 0.40. Vaccine: 0.58.

The verdict must be honest. P1 and P4 were hits, but P4 was what any oncologist would have expected. P3 failed on its timing. Its first half held for a reason the theory did not need: the vaccine simply starts nine weeks late. None of the blind predictions discriminated sharply between this theory and ordinary immunology.

One adjustment follows. The delay in P3 is larger than the manufacturing delay alone. Months 0 to 6 show no measurable effect, though most patients had their first dose by month 2 to 3. Reading takes time after the words arrive. Future predictions from this theory should allow a reading time of about three months after the first dose, not zero.

P5 carries the weight of this essay. It must be read with care. The trials differ in endpoint, in comparator and in patients. S1801 and NADINA enrolled people with tumour that could still be seen and felt; S1801 also included resectable stage IV. INTERpath-001 also enrolled stage IIB and IIC, where only the primary skin tumour had been removed. Cross-trial comparison is suggestive, never decisive.

With that caution, the picture is still clear. Reading the tumour in place matches the vaccine's effect with pembrolizumab alone. With two checkpoint drugs it exceeds it, though part of that gain comes from the second drug. The Dutch melanoma guideline drew the practical conclusion on 9 October 2025: for

resectable stage III melanoma, treatment before surgery is preferred.

7. The alternative

The answer to the research question can now be stated.

Move 1 — read before you remove. For melanoma that can still be found in the lymph nodes, give the checkpoint drug before the operation. The tumour does the work of the vaccine. No sample needs to qualify for manufacture, no sequence needs to be read, and no dose needs to be made. Status: *corresponded*, and guideline-preferred in the Netherlands for resectable stage III. The theory did not discover it. It arrives at it by its own rule.

Move 2 — read what is shared. For patients who have no tumour left to read in place, the bespoke vaccine remains one route. The other is a product aimed at what melanomas share. The evidence is uneven. Tebentafusp, aimed at the pigment-cell protein gp100, reduced the risk of death by 49 percent in uveal melanoma of the eye. BNT111, built on four shared melanoma proteins, gave a response rate of 18.1 percent with cemiplimab, against 13.6 percent for cemiplimab alone. IO102-IO103, aimed at two shared immune-escape proteins, narrowly missed its phase 3 goal (hazard ratio 0.77, $p = 0.056$). Status: *open*.

Move 3 — set the zero locally. Treat the tumour where it lies, so that it opens to reading without lifting the body's tolerance everywhere. The first approved example is T-VEC, a modified virus injected into the tumour. In its main trial durable responses rose from 2.1 to 16.3 percent. Before surgery, in a phase 2 trial, it lowered the risk of death with a hazard ratio of 0.54, measured with a wide 80 percent confidence interval; survival was not the trial's primary endpoint. Status: *open*.

Upstream of all three. Fewer remainders mean fewer recurrences. In the Nambour trial in Australia, daily sunscreen halved new melanomas, 11 against 22. Among Australians aged 15 to 24, melanoma incidence now falls by about 5 to 7 percent a year. Those studies do not prove the cause. Status: *corresponded*.

8. One prediction for the next trial

A theory must say something before the data arrive. Here is one, fixed with this essay.

The rule says that once the tumour has been read in place, the reading has happened. A bespoke vaccine added afterwards supplies words the immune system already has.

Hypothesis H-1. In patients who receive neoadjuvant immunotherapy and still have no viable tumour left at surgery, adding a bespoke neoantigen vaccine afterwards will give a hazard ratio for recurrence of 0.80 or higher. In patients with substantial viable tumour left at surgery, it will give 0.65 or lower.

Failure. The prediction fails if the vaccine's benefit is equal in both groups, or larger in the first.

This is checkable. It costs nothing to state. And it turns the theory's reading into a claim that a trial can refute.

9. What the theory does not do

The theory supplied no dose, no molecule and no number. Every figure in this

essay comes from the trials. The theory's own ledger says the same: where it counts closures it holds; where it must fix a size, it has not yet done better than chance.

Its contribution is narrower and real. It asks of every treatment one question: does the chain close at the point of need? For a bespoke vaccine, the chain runs from tumour to sequencer to factory and back, in nine weeks. For treatment before surgery, the chain closes inside the patient.

Annotated references

Long, G. V. et al. (2026). INTERpath-001: intismeran autogene plus pembrolizumab versus pembrolizumab in resected high-risk melanoma. ESMO Congress 2026, LBA1. Reported by OncLive and CancerNetwork, 24-25 October 2026. <https://www.onclive.com/view/adjuvant-intismeran-autogene-plus-pembrolizumab-improves-rfs-and-dmfs-in-melanoma> *Why read?* The trial that prompted this essay, with the piecewise hazard ratios used in Section 6. *Reading advice:* the full paper is due in the *New England Journal of Medicine* on 11 November 2026; read its subgroup tables first.

González, F. (2026). "New mRNA Vaccine Reduces Risk of Melanoma Recurrence by Over 40 Percent." WIRED, 24 October 2026. *Why read?* The occasion. *Reading advice:* read it for the closing remark of Soengas on the bespoke vaccine; check its numbers of targets against the trial.

Weber, J. S. et al. (2024). Individualised neoantigen therapy mRNA-4157 (V940) plus pembrolizumab versus pembrolizumab monotherapy in resected melanoma (KEYNOTE-942). The Lancet 403:632-644. *Why read?* The phase 2b predecessor, with the mutation-load subgroup and the delayed separation of the curves.

Patel, S. P. et al. (2023). Neoadjuvant-adjuvant or adjuvant-only pembrolizumab in advanced melanoma (SWOG S1801). New England Journal of Medicine 388:813-823. *Why read?* The same drug, given before and after surgery rather than after only: two-year event-free survival 72 against 49 percent. The cleanest test of Move 1.

Blank, C. U. et al. (2024). Neoadjuvant nivolumab and ipilimumab in resectable stage III melanoma (NADINA). New England Journal of Medicine. DOI 10.1056/NEJMoa2402604. *Why read?* A phase 3 trial sponsored by the Netherlands Cancer Institute and co-sponsored by Melanoma Institute Australia. Twelve-month event-free survival 83.7 against 57.2 percent. *Reading advice:* read with the ESMO 2025 update (two-year 77.3 against 55.7 percent).

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Nathan, P. et al. (2021). Overall survival benefit with tebentafusp in metastatic uveal melanoma. New England Journal of Medicine 385:1196-1206. *Why read?* The clearest success of a shared, lineage target, reached with a T-cell receptor bispecific rather than a vaccine: one product for every eligible patient. *Reading advice:* note the restriction to one tissue type (HLA-A*02:01).

BNT111 phase 2 and IO102-IO103 phase 3 results, as reported by CancerNetwork (2025-2026). *Why read?* The modest and the missed results for shared-antigen vaccines. Together they keep Move 2 open.

Andtbacka, R. H. I. et al. (2015). Talimogene laherparepvec improves durable response rate in patients with advanced melanoma (OPTiM). *Journal of Clinical Oncology* 33:2780-2788. *Why read?* Treatment of the tumour where it lies. *Reading advice:* read with the five-year neoadjuvant T-VEC phase 2 data (ASCO Post, August 2023), and note the 80 percent confidence intervals.

Rohaan, M. W. et al. (2022). Tumor-infiltrating lymphocyte therapy or ipilimumab in advanced melanoma. *New England Journal of Medicine*. DOI 10.1056/NEJMoa2210233. *Why read?* The patient's own reading cells, grown and returned: progression-free survival hazard ratio 0.50. Personalised too, but without a mutation sequence. A useful contrast.

Green, A. C. et al. (2011). Reduced melanoma after regular sunscreen use (Nambour trial). *Journal of Clinical Oncology* 29:257-263; online 6 December 2010. *Why read?* The upstream move: 11 against 22 new melanomas in ten years. *Reading advice:* the 73 percent drop in invasive melanoma rests on 14 cases.

Konstapel, J. (2026). The Vacuum.Net Theory: Definition, Theorems and Tests. Version 4, 17 October 2026. <https://constable.blog/wp-content/uploads/vacuum-net-theory-v4.pdf> *Why read?* The axioms N1-N5 and the theorem on the two kinds of closure used in Section 3, with the theory's own ledger of tests passed and failed.

Konstapel, J. (2026). Where Illness Comes From, Completed. October 2026. <https://constable.blog/2026/10/20/where-illness-comes-from/> *Why read?* The reading of illness as a test with three outcomes, and of a tumour as the remainder of a selection. *Reading advice:* start with Part 0.

Konstapel, J. (2026). The Respondent-Judge Protocol. Version 1.0, 17 October 2026. <https://constable.blog/wp-content/uploads/respondent-judge-protocol.pdf> *Why read?* The method of Sections 5 and 6: predictions fixed and hashed before the data, scored by a separate judge.