SUMMARY OF RESEARCH

INTerpath-001: Phase 3 Study of the mRNA-Based Individualized Neoantigen Therapy (INT) Intismeran Autogene plus Pembrolizumab vs Pembrolizumab Alone for Adjuvant Treatment of Resected Stage IIB–IV Melanoma

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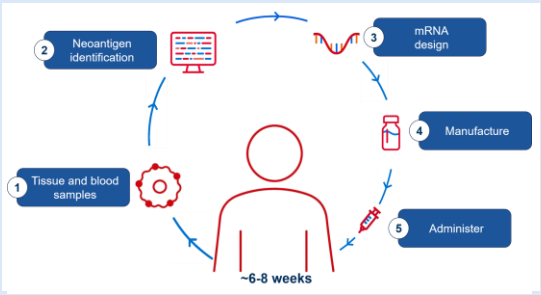
What is cutaneous melanoma?

Cutaneous melanoma is a type of cancer that starts in melanocytes in the skin. For many people, melanoma can be removed by surgery. To help prevent melanoma from recurring after surgery, physicians may prescribe adjuvant therapy with pembrolizumab or nivolumab. However, many patients experience recurrence despite adjuvant therapy.

What is intismeran autogene?

Intismeran is a new type of treatment called individualized neoantigen therapy (INT). It is designed specifically for each patient based on unique mutations in their cancer that give rise to markers called neoantigens.

Intismeran consists of mRNA enclosed in tiny fat particles called lipid nanoparticles. The mRNA carries instructions for making up to 34 neoantigens, which help activate T cells, a type of immune cell, to recognize and attack cancer cells.



Who took part in the study?

Patients were adults (median age 61 years) from 157 sites across 5 continents with

- ✓ Cutaneous melanoma of stage IIB, IIC, III, or IV that was removed by surgery
- ✓ Tumor samples suitable for next-generation sequencing and intismeran generation
- ✓ Eastern Cooperative Oncology Group performance status score of 0 or 1

Patients could not have

- × Received prior systemic anticancer therapy
- × Evidence of melanoma recurrence or metastasis since their most recent surgery

How was the study conducted?

Randomized, double-blind, active- and placebo-controlled, phase 3 study

1137 patients randomized 2:1

- **757** to **intismeran** 1 mg given intramuscularly every 3 weeks **+ pembrolizumab** 400 mg given intravenously every 6 weeks
- **380** to **placebo** given intramuscularly every 3 weeks **+ pembrolizumab** 400 mg given intravenously every 6 weeks

- Up to 9 doses of intismeran and 9 cycles of pembrolizumab
- Pembrolizumab, which is a standard of care, was started at randomization for all patients
- Intismeran was started upon availability to the site, no earlier than cycle 1, day 22 and no later than cycle 4, day 1
- Placebo start was randomly delayed to keep treatment assignments unknown

Median study follow-up for current analysis (Study ongoing)

24.6 months

Median time to first intismeran dose

~9 weeks

What were the main efficacy findings of the study?

Primary end point: Recurrence-free survival (RFS)

Intismeran + pembrolizumab significantly **improved RFS** compared with **placebo + pembrolizumab**

42% reduction in **risk of recurrence or death** with **intismeran + pembrolizumab**



Patients **alive and without recurrence 24 months** after randomization

Secondary end point: Distant metastasis-free survival (DMFS)

Intismeran + pembrolizumab significantly **improved DMFS** compared with **placebo + pembrolizumab**

38% reduction in **risk of distant metastasis or death** with **intismeran + pembrolizumab**



Patients **alive and without distant metastasis 24 months** after randomization

What were the main safety findings of the study?

For people in the intismeran + pembrolizumab group*:

- **98%** had at least 1 adverse event
- **24%** had at least 1 grade 3–5 adverse event
- **17%** discontinued treatment due to an adverse event
- **1%** died because of an adverse event

For people in the placebo + pembrolizumab group*:

- **96%** had at least 1 adverse event
- **20%** had at least 1 grade 3–5 adverse event
- **9%** discontinued treatment due to an adverse event
- **0%** died because of an adverse event

The **3 most common adverse events** in patients treated with **intismeran + pembrolizumab** were **fever**, **injection site pain**, and **fatigue**. The **3 most common adverse events** in patients treated with **placebo + pembrolizumab** were **fatigue**, **diarrhea**, and **pruritus (i.e., itchy skin).**.

5 of 8 patients who **died because of an adverse event** died **before the first dose of intismeran**. **No patients died** from **adverse events caused by intismeran**. **2 of 8** patients **died** from **adverse events caused by pembrolizumab**; these patients died before the first dose of intismeran.

*Includes people who received any study treatment.

What do the study results mean?

People with cutaneous melanoma treated with intismeran + pembrolizumab lived longer without recurrence and lived longer without distant metastasis that people treated with pembrolizumab alone. Most of the adverse events experienced by patients in the intismeran + pembrolizumab group were low grade and managed without treatment discontinuation.

Who sponsored this study?

This study was paid for by Merck Sharp & Dohme LLC, a subsidiary of Merck & Co., Inc., Rahway, NJ, USA (+1-888-577-8839; www.msd.com) and Moderna, Inc., Cambridge, MA, USA (+1-866-663-3762; https://www.modernatx.com/.
The sponsor thanks all the people who took part in this study.



For more information on this study, please visit:
https://clinicaltrials.gov/study/NCT05933577
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