Moderna Oncology Event

June 1, 2026

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Forward-looking statements

This presentation contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995, as amended, including statements regarding: mRNA's potential in cancer care and the potential of personalized treatments; the mechanism of action of intismeran; the potentail to generate a significant translational clinical dataset; intismeran's clinical development program, including ongoing clinical trials; the ability of intismeran in combination with pembrolizumab to demonstrate sustained improvement in RFS and DMFS compared with pembrolizumab alone; the encouraging trend in overall survival compared with pembrolizumab alone; the tolerability and safety profile of intismeran in combination with pembrolizumab; and the potential long-term benefit of intismeran. In some cases, forward-looking statements can be identified by terminology such as “will,” “may,” “should,” “could,” “expects,” “intends,” “plans,” “aims,” “anticipates,” “believes,” “estimates,” “predicts,” “potential,” “continue,” or the negative of these terms or other comparable terminology, although not all forward-looking statements contain these words. The forward-looking statements in this presentation are neither promises nor guarantees, and you should not place undue reliance on these forward-looking statements because they involve known and unknown risks, uncertainties, and other factors, many of which are beyond Moderna’s control and which could cause actual results to differ materially from those expressed or implied by these forward-looking statements. These risks, uncertainties, and other factors include, among others, those risks and uncertainties described under the heading “Risk Factors” in Moderna’s Annual Report on Form 10-K for the fiscal year ended December 31, 2025, filed with the U.S. Securities and Exchange Commission (SEC), and in subsequent filings made by Moderna with the SEC, which are available on the SEC’s website at www.sec.gov. Except as required by law, Moderna disclaims any intention or responsibility for updating or revising any forward-looking statements contained in this presentation in the event of new information, future developments or otherwise. These forward-looking statements are based on Moderna’s current expectations and speak only as of the date of this presentation.

Agenda

Intismeran overview	**David Berman, MD, PhD** Chief Development Officer, Moderna
Intismeran neoantigen selection and mechanism foundations	**Michelle Brown, MD** Vice President, Portfolio Lead, Oncology, Moderna
Individualized neoantigen therapy intismeran autogene plus pembrolizumab in resected melanoma: 5-year update of the Phase 2 KEYNOTE-942 study	**Matteo S. Carlino, MBBS, PhD, FRACP** Medical Oncologist, Melanoma Institute Australia, The University of Sydney
Intismeran autogene to induce de novo neoantigen-specific T cells as adjuvant therapy in melanoma	**Ryan Sullivan, MD** Director, Cutaneous Medical Oncology, Mass General Brigham Cancer Institute
Conclusion	**David Berman, MD, PhD** Chief Development Officer, Moderna
Q&A	

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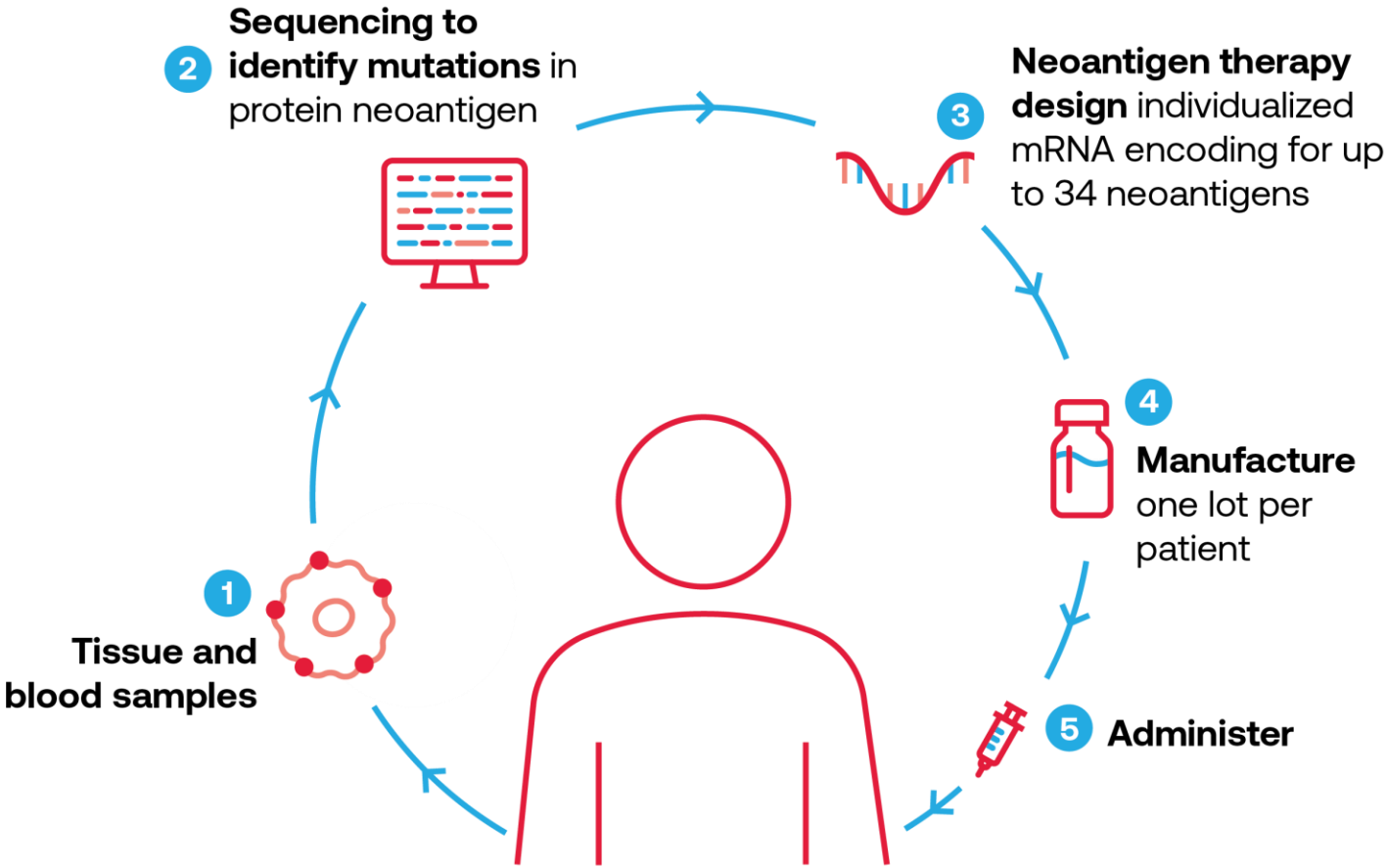
Intismeran overview

David Berman, MD, PhD
Chief Development Officer, Moderna

Intismeran autogene is the most advanced individualized neoantigen therapy in development



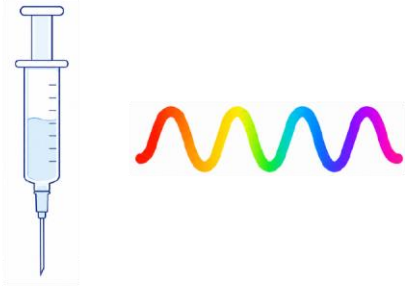
Intismeran is an investigational lipid encapsulated messenger ribonucleic acid (mRNA)-based **individualized neoantigen therapy**

It consists of an **mRNA that encodes neoantigens designed specifically to each individual patient's tumor** mutanome and human leukocyte antigen (HLA) type

A stepwise experimental framework for intismeran

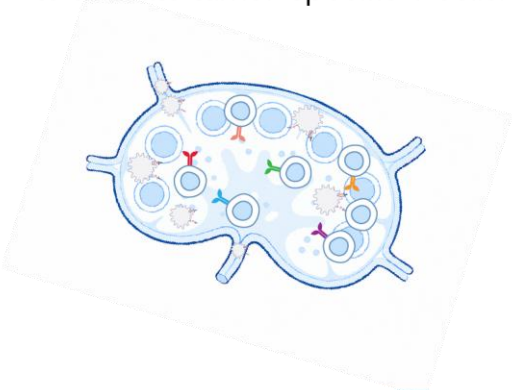
Intismeran drug product

Intismeran adminstered with KEYTRUDA™



Lymph node

Intismeran is taken up by antigen-presenting cells, which then present neoantigens in lymph nodes to activate tumor-specific T cells.



MEASUREMENT
Activated T-cells

METRIC
CD4 versus CD8 T cell

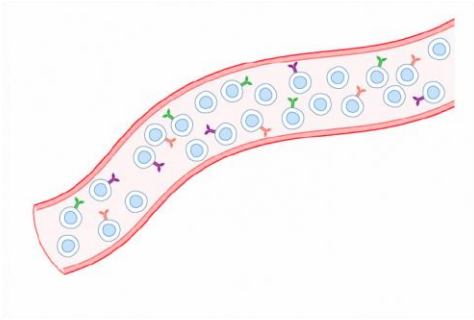
Neoantigen-specific T cells

Activation state (41BB, CD69, CD107)

Functional state (IFN, Granzyme)

Blood

Novel T-cells in blood



MEASUREMENT
Number of novel T-cells

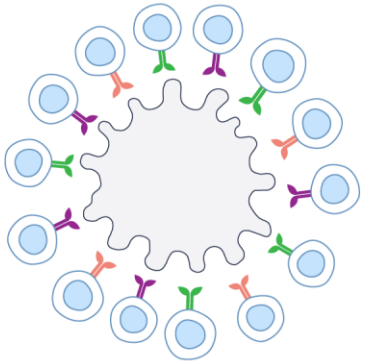
METRIC
Degree of T cell clonality (Shannon clonality*)

Novel T-cell frequency**

Unique novel T-cell clonotypes***

Tumor

Neoantigen-specific T cell clones attack the tumor



MEASUREMENT
Efficacy

METRIC
Recurrance-free survival

Distant metastasis-free survival

*Ranges from 1 (highest clonality) to 0 (highest diversity). Higher clonality can indicate a more focused immune response; **Total number of novel T cell clones divided by total T cells; ***Number of novel T cells clonotypes

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Unmet need still exists in the adjuvant setting

Estimated recurrence rate with adjuvant checkpoint inhibitors

Bladder cancer (MIUC)	**~64%** recurrence rate at 5 years[1]
Melanoma	**~50%** recurrence rate at 7 years[2]
Lung cancer	**~48%** recurrence rate at 4 years[3]
Renal cancer	**~39%** recurrence rate at 5 years[4]
Gastric/ GEJ cancer	**~33%** event rate at 2 years**[5]
Pancreatic cancer	**~74%** recurrence rate at 5 years with FOLFIRINOX*[6]

*No Phase 3 data from checkpoint inhibitor; **Event rate as EFS is the endpoint in the peri-operative setting.

1. Galsky, Matthew D., et al. "Adjuvant Nivolumab versus Placebo for High-Risk Muscle-Invasive Urothelial Carcinoma: 5-Year Efficacy and ctDNA Results from CheckMate 274." *Annals of Oncology*, vol. 37, no. 1, 2026, pp. 69–78 , 2. Eggermont AMM, Kicinski M, Blank CU, et al. Seven-year analysis of adjuvant pembrolizumab versus placebo in stage III melanoma in the EORTC1325/KEYNOTE-054 trial. *Eur J Cancer*. 2024;211:114327. doi:10.1016/j.ejca.2024.114327, 3. Merck & Co., Inc. KEYNOTE-091: Clinical Trial Results & Study Design. KEYTRUDA® (pembrolizumab) HCP website. Accessed May 27, 2026, 4. Klaassen Z. ASCO 2025: Five-year follow-up results from the phase 3 KEYNOTE-564 study of adjuvant pembrolizumab for the treatment of clear cell RCC. *UroToday*. Published during the American Society of Clinical Oncology 2025 Annual Meeting, May 30-June 3, 2025. Accessed May 27, 2026., 5. Janjigian, Yelena Y., et al. "Perioperative Durvalumab in Gastric and Gastroesophageal Junction Cancer." *New England Journal of Medicine*, vol. 393, no. 3, 16 July 2025, pp. 217–230, 6. Conroy, Thierry, et al. "Five-Year Outcomes of FOLFIRINOX vs Gemcitabine as Adjuvant Therapy for Pancreatic Cancer: A Randomized Clinical Trial." *JAMA Oncology*, vol. 8, no. 11, 2022, pp. 1571–1578

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Intismeran development initially focused in IO-sensitive tumors

IO-sensitive tumors

Late-stage trials Phase 2 and 3

Rationale: Tumors that are validated as IO-sensitive

Earliest stages

- Stage 1 non-small cell lung cancer (NSCLC)
- Non-muscle invasive bladder cancer (NMIBC)

Adjuvant

- Melanoma
- NSCLC
- Renal cell carcinoma (RCC)
- Muscle invasive bladder cancer (MIBC)

Metastatic/ unresectable

- Melanoma
- Squamous NSCLC

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Future opportunity in tumors historically less sensitive to IO

IO-less sensitive tumors

Signal-seeking Phase 1 studies

Rationale: Exploring whether intismeran can work in tumors where IOs have historically been less effective

Earliest stages

Adjuvant

- Pancreatic cancer
- Gastric cancer

Metastatic/ unresectable

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Intismeran neoantigen selection and mechanism foundations

Michelle Brown, MD, PhD

Vice President, Portfolio Lead, Oncology, Moderna

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Next Generation Sequencing (NGS) has revolutionized personalized treatments, especially in oncology

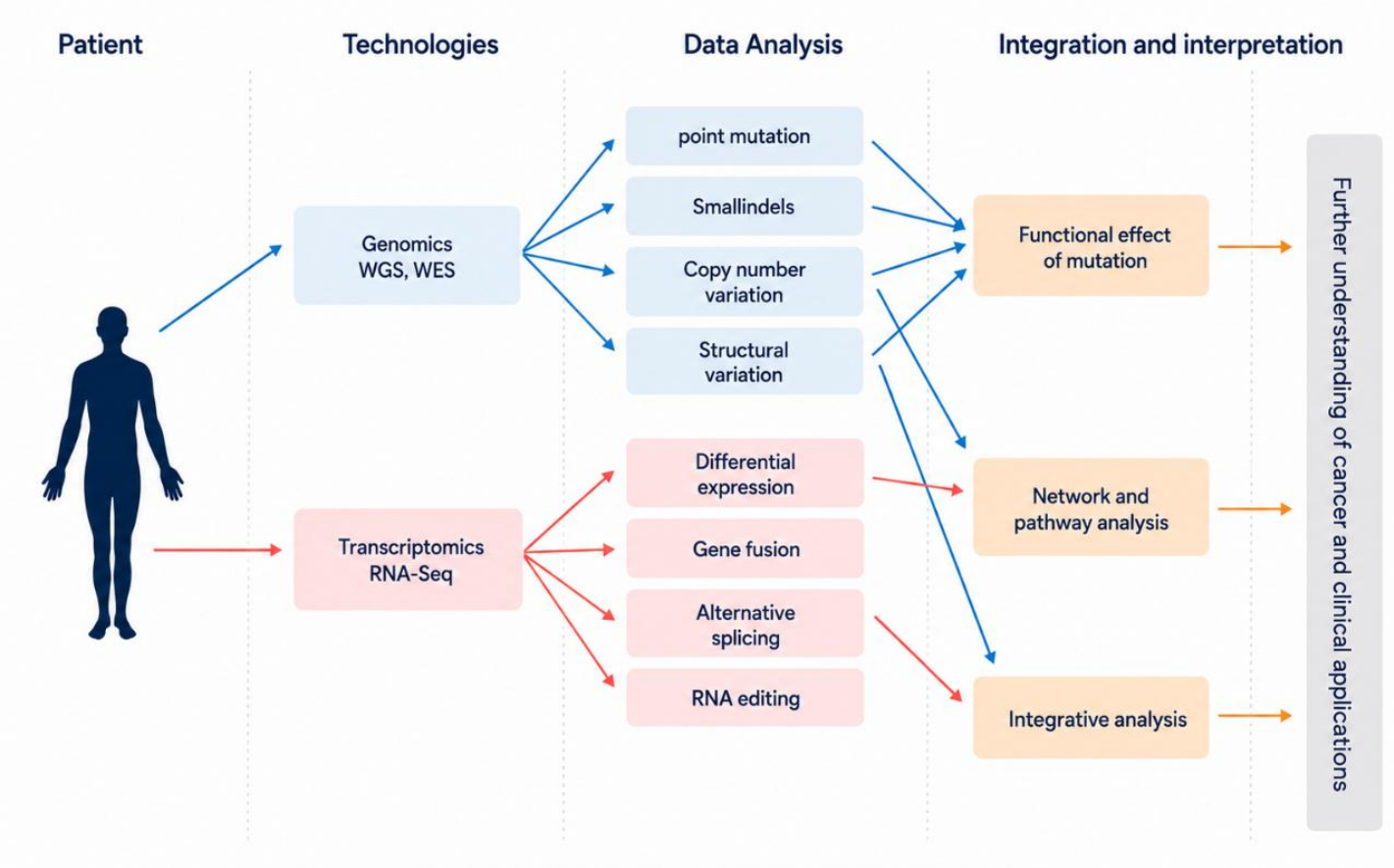
NGS technologies, including WGS and WES, have transformed our understanding of cancer.

NGS reveals a wide array of genomic alterations, including mutations, insertions, deletions, and structural changes.

Comparing tumor and normal genomes helps distinguish somatic cancer mutations from inherited germline variants.

RNA-Seq reveals gene expression, splicing variation, and RNA modifications.

Integrating these technologies with bioinformatics provides a detailed cancer genome view to inform personalized treatment.



Source: Shyr, D., Liu, Q. Next generation sequencing in cancer research and clinical application. *Biol Proced Online* **15**, 4 (2013). https://doi.org/10.1186/1480-9222-15-4

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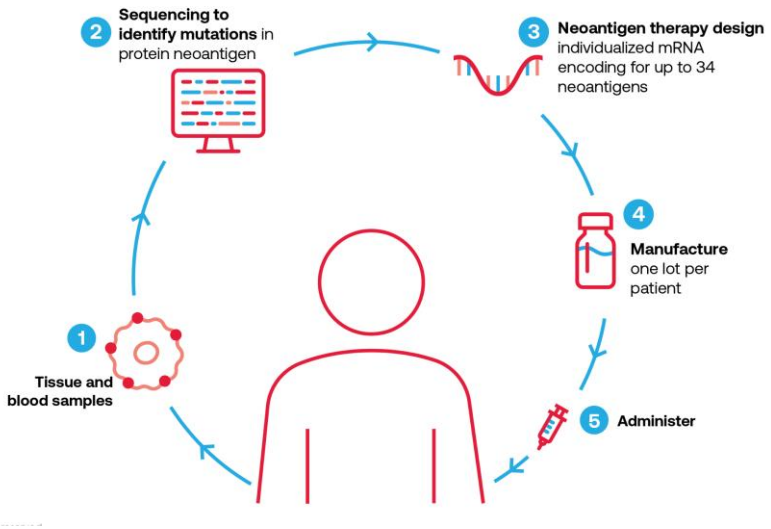
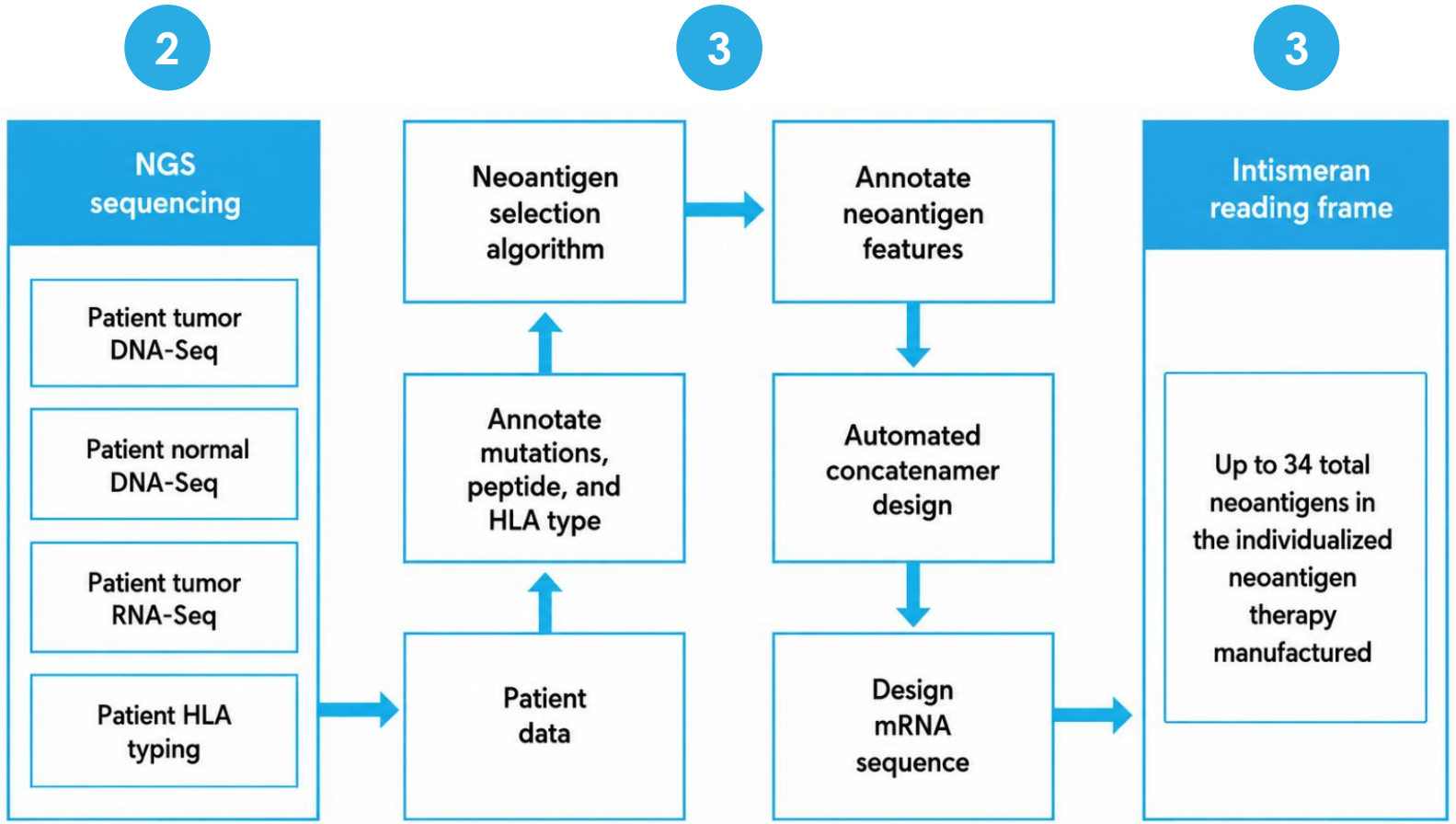
Deterministic machine learning algorithm for neoantigen selection

Objective:
Select neoantigens that induce de novo and increase endogenous T-cell responses





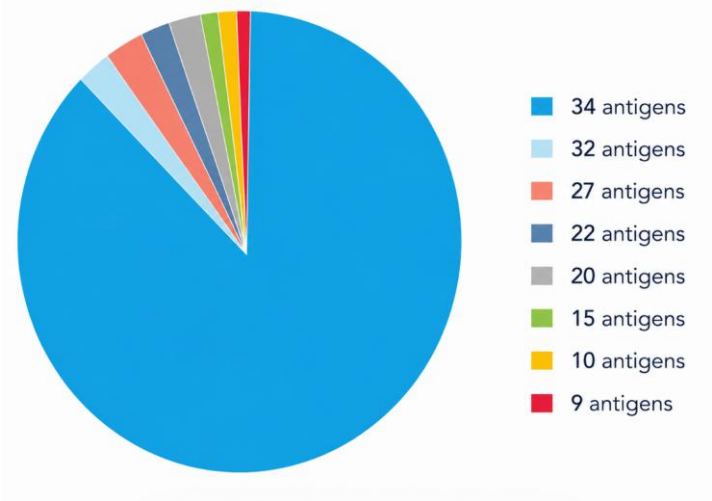
APC = antigen-presenting cell; CD = cluster of differentiation; INT = individualized neoantigen therapy; MHC = major histocompatibility complex; mRNA = messenger ribonucleic acid

1. Khattak A, et al. AACR 2023 (Abstract CT001).

In KEYNOTE-942, most melanoma patients received intismeran with the full 34 neoantigens with little to no overlap across neoantigens

The majority of patients had 34 neoantigens successfully identified and included

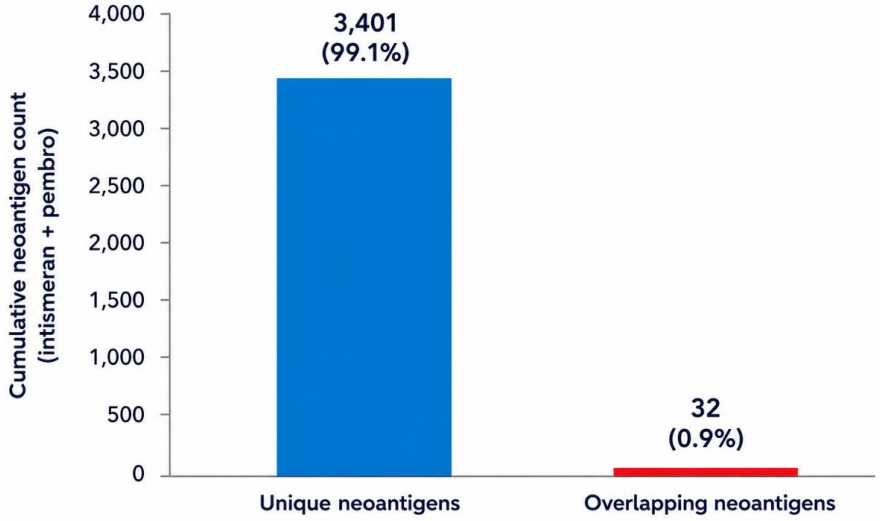
91% of patients in the combination arm had 34 targetable neoantigens included in their intismeran



Khattak A, et al. AACR 2023 (Abstract CT001), published as table Lancet Article Appendix https://doi.org/10.1016/ S0140-6736(23)02268-7

Low overlap of neoantigens across patients

99.1% of neoantigens were unique

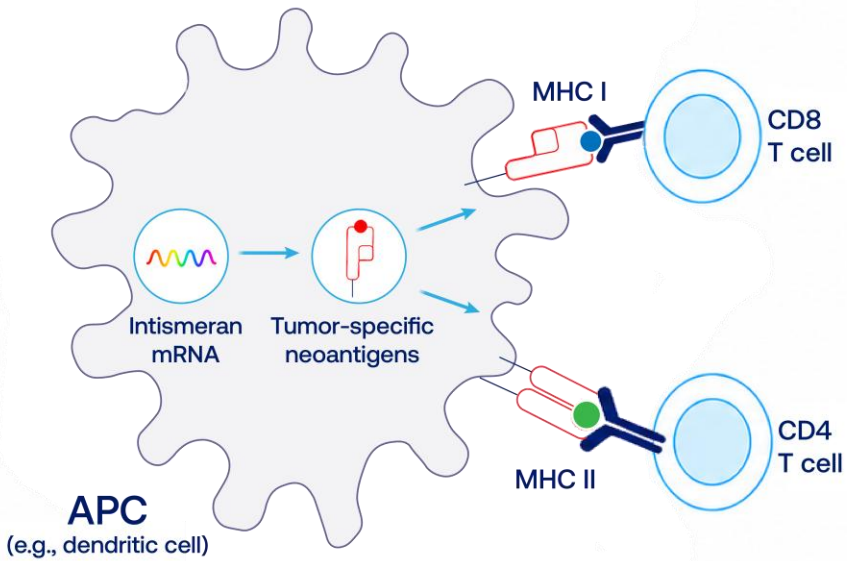


Sullivan et al 2025 SMR Poster Presentation

Intismeran autogene's proposed mechanism of action

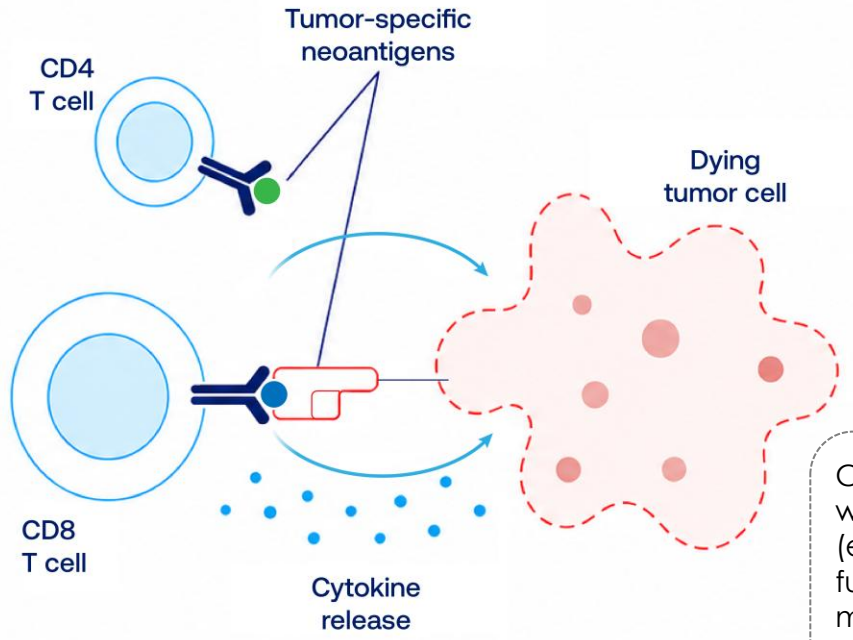
T-CELL ACTIVATION

APCs naturally process intismeran, then present tumor-specific neoantigens, generating *de novo* and activating pre-existing T-cell clones



TUMOR DESTRUCTION

Neoantigen-specific T cells recognize and attack tumor cells.



Combination of intismeran with checkpoint inhibitors (e.g. pembrolizumab) may further enhance immune-mediated tumor cell destruction

APC = antigen-presenting cell; CD = cluster of differentiation; MHC = major histocompatibility complex; mRNA = messenger ribonucleic acid

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The intismeran program has the potential to generate a significant translational clinical dataset to drive learnings

Large-scale longitudinal biospecimen collection across multi-study, multi-tumor portfolio

Tumor samples

Genomic foundation for intismeran design & tumor biology

Mandatory
Baseline tumor in all studies

Optional
Upon recurrence or progression biopsy to understand mechanisms of resistance

~5,000+
enrolled patients
across studies*

Blood samples

For genomic baseline & intismeran biological activity

Mandatory
Baseline sample in all studies

Planned analysis on available study samples

- **ctDNA** to monitor disease
- **T cell immunogenicity** to assess immune activation profile
- **TCR-Seq** to define clonality & track immune responses

NGS, Next Generation Sequencing; **ctDNA**, Circulating tumor DNA; **PBMC**, Peripheral blood mononuclear cells; **PD**, Progressive disease

*Enrolled patients for studies that are completed and projected per protocol for those that are still ongoing

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Intismeran's clinical development program

Partnered with Merck

	Ph 1	Ph 2	Ph 3	Commercial	Treatment in investigational arm: **intismeran +**
ADJUVANT					
Melanoma					pembrolizumab
NSCLC					pembrolizumab
NSCLC non-pCR post-neoadjuvant					pembrolizumab
Stage 1 NSCLC					Arm 1: monotherapy Arm 2: pembrolizumab subcutaneous
Renal cell carcinoma (RCC)					pembrolizumab
Bladder cancer (MIBC)					pembrolizumab
Bladder cancer (NMIBC)					Bacillus Calmette-Guérin
METASTATIC					
First-line melanoma					pembrolizumab
First-line squamous NSCLC					pembrolizumab + chemotherapy
EARLY AND ADVANCED CANCERS					
Solid tumors					standard of care

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REPRISE: ASCO 2026 PRESENTATION

Individualized neoantigen therapy intismeran autogene + pembrolizumab in resected melanoma: 5-year update of the Phase 2 KEYNOTE-942 study

Matteo S. Carlino, MBBS, Ph.D., FRACP

Medical Oncologist, Melanoma Institute Australia, The University of Sydney

Matteo S. Carlino,[1,a] Adnan Khattak,[2,a] Tarek Meniawy,[3] George Ansstas,[4] Matthew H. Taylor,[5] Kevin B. Kim,[6] Meredith McKean,[7] Georgina V. Long,[8] Ryan J. Sullivan,[9] Mark Faries,[10] Thuy T. Tran,[11] C. Lance Cowey,[12] Andrew Pecora,[13] Theresa Medina,[14] Victoria Atkinson,[15] Clemens Krepler,[16] Thomas Jemielita,[16] Huzhang Mao,[17] Mariana Faria-Urbina,[17] Janice M. Mehnert[18]

[1]Westmead and Blacktown Hospitals, Melanoma Institute Australia, and The University of Sydney, Sydney, NSW, Australia; [2]One Clinical Research, Hollywood Private Hospital and Edith Cowan University, Perth, WA, Australia; [3]Saint John of God Subiaco Hospital, Subiaco, WA, Australia; [4]Washington University School of Medicine, St. Louis, MO, USA; [5]Earle A. Chiles Research Institute, Providence Cancer Institute, Portland, OR, USA; [6]California Pacific Medical Center Research Institute, San Francisco, CA, USA; [7]Sarah Cannon Research Institute, Nashville, TN, USA; [8]Melanoma Institute Australia, The University of Sydney, and Royal North Shore and Mater Hospitals, Sydney, NSW, Australia; [9]Massachusetts General Hospital, Harvard Medical School, Boston, MA, USA; [10]The Angeles Clinic and Research Institute, a Cedars-Sinai affiliate, Los Angeles, CA, USA; [11]Smilow Cancer Center at Yale New Haven Hospital, New Haven, CT, USA; [12]Texas Oncology PA, Dallas, TX, USA; [13]Hackensack University Medical Center, Hackensack, NJ, USA; [14]University of Colorado Cancer Center, Aurora, CO, USA; [15]Princess Alexandra Hospital, Brisbane, QLD, Australia; [16]Merck & Co., Inc., Rahway, NJ, USA; [17]Moderna, Inc., Cambridge, MA, USA; [18]Laura and Isaac Perlmutter Cancer Center at NYU Langone Health, New York, NY, USA

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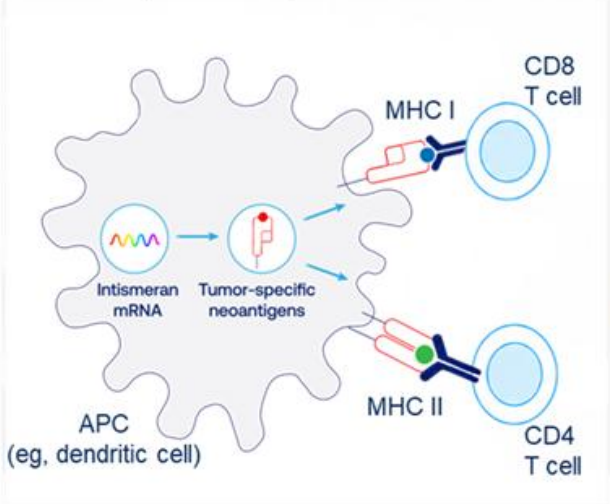
Key findings

- At **5 years of planned follow-up** analysis from the phase 2 KEYNOTE-942 study, intismeran plus pembrolizumab demonstrated durable treatment benefits vs pembrolizumab alone in patients with resected high-risk melanoma
  - There was a **49% reduction in risk of recurrence or death, a 59% reduction of distant metastasis or death**, and trend towards improved overall survival with intismeran plus pembrolizumab versus pembrolizumab alone
- The data continues to demonstrate a **favorable safety profile** of intismeran in combination with pembrolizumab
- Intismeran plus pembrolizumab compared to pembrolizumab alone **increased T-cell clonality** and enhanced the generation of novel T-cell clones
  - A trend towards **higher novel clone generation** was associated with reduced recurrence in patients receiving intismeran plus pembrolizumab

Intismeran autogene proposed mechanism of action

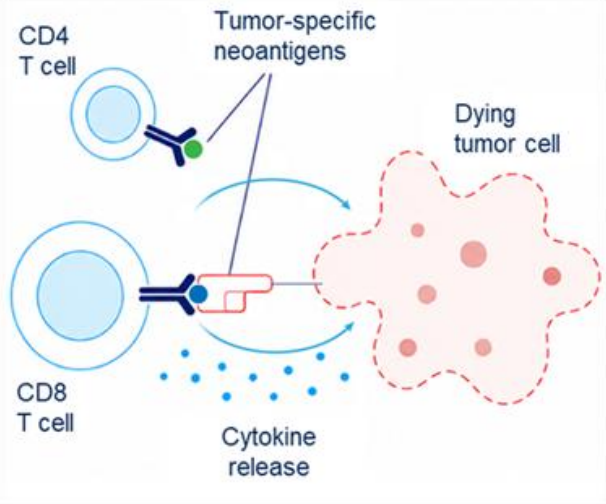
T-CELL ACTIVATION

APCs naturally process intismeran, then present tumor-specific neoantigens, generating de novo and activating pre-existing T-cell clones



TUMOR DESTRUCTION

Neoantigen-specific T-cells recognize and attack tumor cells



- Neoantigen-targeted therapies can **strengthen existing** and **create new** T-cell responses[1]
- **Intismeran autogene (intismeran)** is an mRNA-based individualized neoantigen therapy designed to **enhance endogenous antitumor T-cell responses** by targeting patient-specific tumor mutations[2]
- Combining intismeran with an immune checkpoint inhibitor may **enhance tumor destruction and support durable T-cell responses**

APC, antigen-presenting cell; CD, cluster of differentiation; MHC, major histocompatibility complex.

1. Gainor JF, et al. *Cancer Discov*. 2024;14(11):2209-2223. 2. Weber JS, et al. *Lancet*. 2024;403(10427):632-644.

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Background

- Despite PD-1 based adjuvant therapy, ~40%–50% of patients with high-risk melanoma experience recurrence, including progression to distant metastatic disease[1]
  - Improving DMFS by delaying/preventing metastasis is clinically meaningful, and can precede improvement in overall survival[2,3]
- To date, no randomized controlled trial evaluating adjuvant immunotherapy in stage III melanoma has demonstrated significantly improved outcomes with a combination regimen vs anti–PD-1 monotherapy
- In the primary analysis and 3-year supportive analysis of the phase 2 KEYNOTE-942 study, patients with completely resected, high-risk, stage IIIB–IV cutaneous melanoma had prolonged RFS and DMFS with intismeran plus pembrolizumab vs pembrolizumab alone[4,5]

Objective:

Assess the efficacy and safety of intismeran plus pembrolizumab and evaluate the combination's effects on T-cell receptor dynamics after 5 years of median planned follow-up (median [range], 60.3 [50.5–76.4] months)

DMFS, distant metastasis-free survival; RFS, recurrence-free survival.

1. Eggermont AMM, et al. *NEJM Evid.* 2022;1(11):EVIDoa2200214. 2. Eggermont AMM, et al. *Eur J Cancer.* 2019;119:1-10. 3. Eggermont AM, et al. *Eur J Cancer.* 2024;211:114327. 4. Weber JS, et al. *Lancet.* 2024;403(10427):632-644. 5. Carlino MS, et al. *JCO Oncol Adv.* 2026;3(1):e2500008

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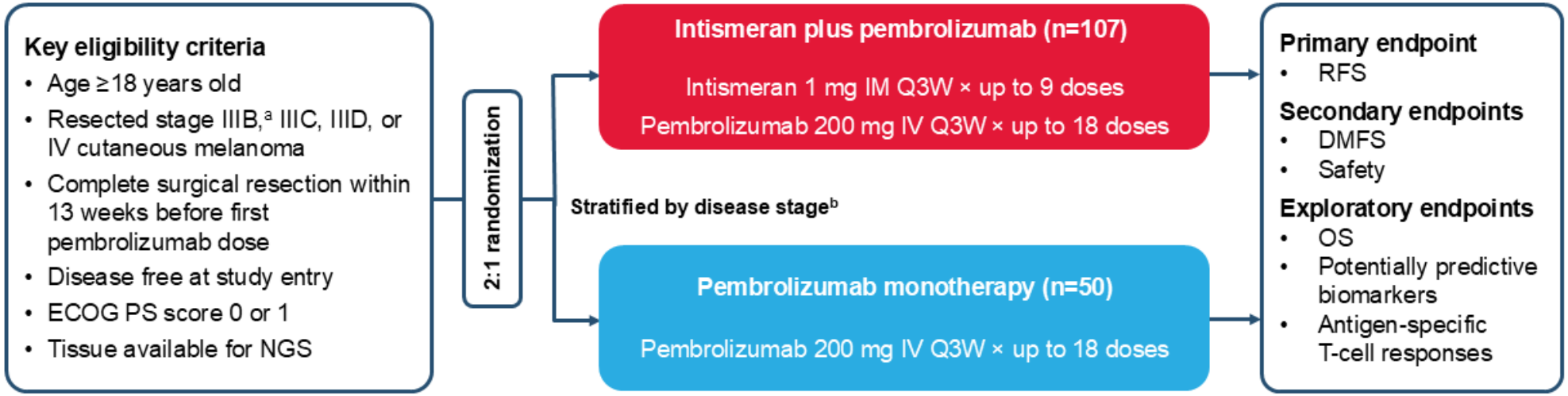
KEYNOTE-942 (NCT03897881) study design

Randomized, phase 2, open-label study of adjuvant therapy in patients with completely resected melanoma at high risk of recurrence



The 5-year analysis was conducted after the last enrolled patient had ≥4 years of planned follow-up (data cutoff: December 15, 2025); no α was assigned to this long-term follow-up analysis

IM, intramuscular; NGS, next-generation sequencing; TCR, T-cell receptor.
[a]Patients with stage IIIB disease were eligible if relapse occurred within 3 mo of prior surgery of curative intent. [b]According to the American Joint Committee on Cancer Staging Manual 8th edition.

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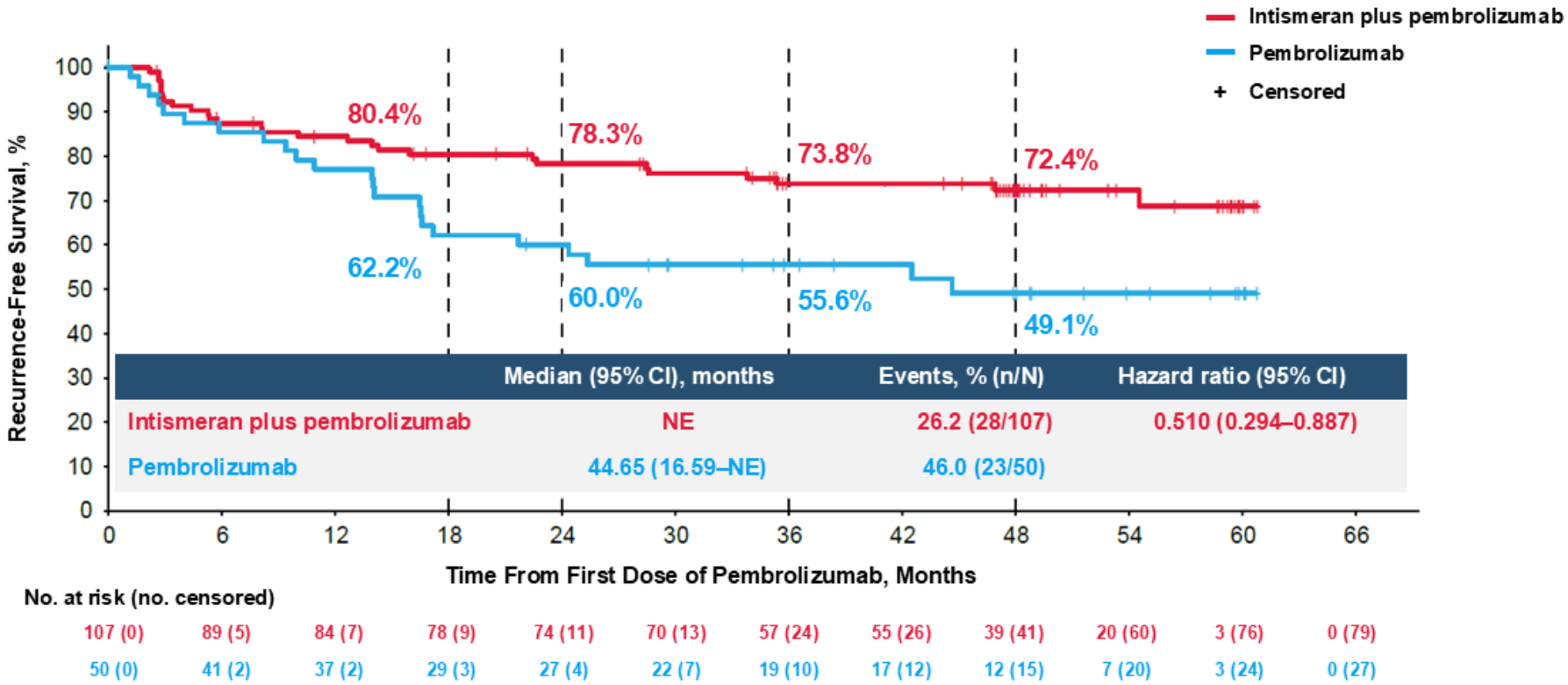
Durable benefit in RFS (primary endpoint)



	Median (95% CI), months	Events, % (n/N)	Hazard ratio (95% CI)
Intismeran plus pembrolizumab	NE	26.2 (28/107)	0.510 (0.294–0.887)
Pembrolizumab	44.65 (16.59–NE)	46.0 (23/50)	

NE, not estimable.

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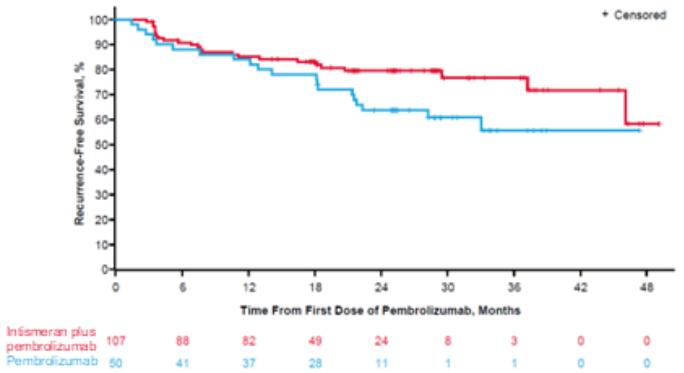
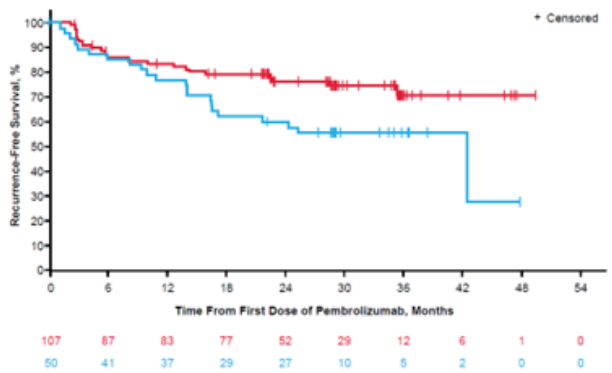
Consistent and durable RFS benefit across primary, 3-year, and 5-year analyses

Primary Analysis: Nov 14, 2022[1]



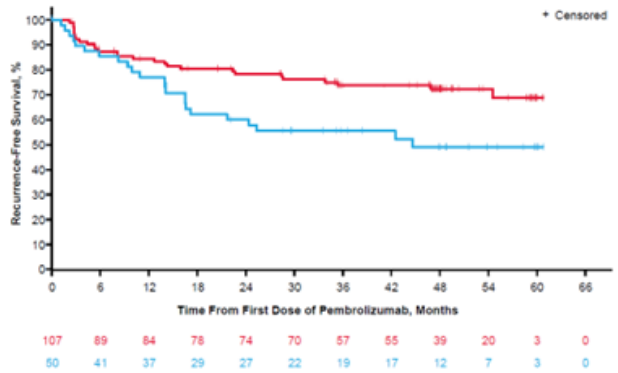
	Events, % (n/N)	Hazard Ratio (95% CI)
Intismeran plus pembrolizumab	22.4 (24/107)	0.561 (0.309–1.017) $P = 0.0266^b$
Pembrolizumab	40.0 (20/50)	

3-Year Analysis: Nov 3, 2023[2]



	Events, % (n/N)	Hazard Ratio (95% CI)
Intismeran plus pembrolizumab	23.4 (25/107)	0.510 (0.288–0.906)
Pembrolizumab	44.0 (22/50)	

5-Year Analysis: Dec 15, 2025



	Events, % (n/N)	Hazard Ratio (95% CI)
Intismeran plus pembrolizumab	26.2 (28/107)	0.510 (0.294–0.887)
Pembrolizumab	46.0 (23/50)	

[a]Formal hypothesis testing of RFS (overall one-sided α=0.10) was performed at primary analysis (Nov 2022 data cut).

1. Weber JS, et al. *Lancet*. 2024;403(10427):632-644. 2. Carlino MS, et al. *JCO Oncol Adv*. 2026;3(1):e2500008

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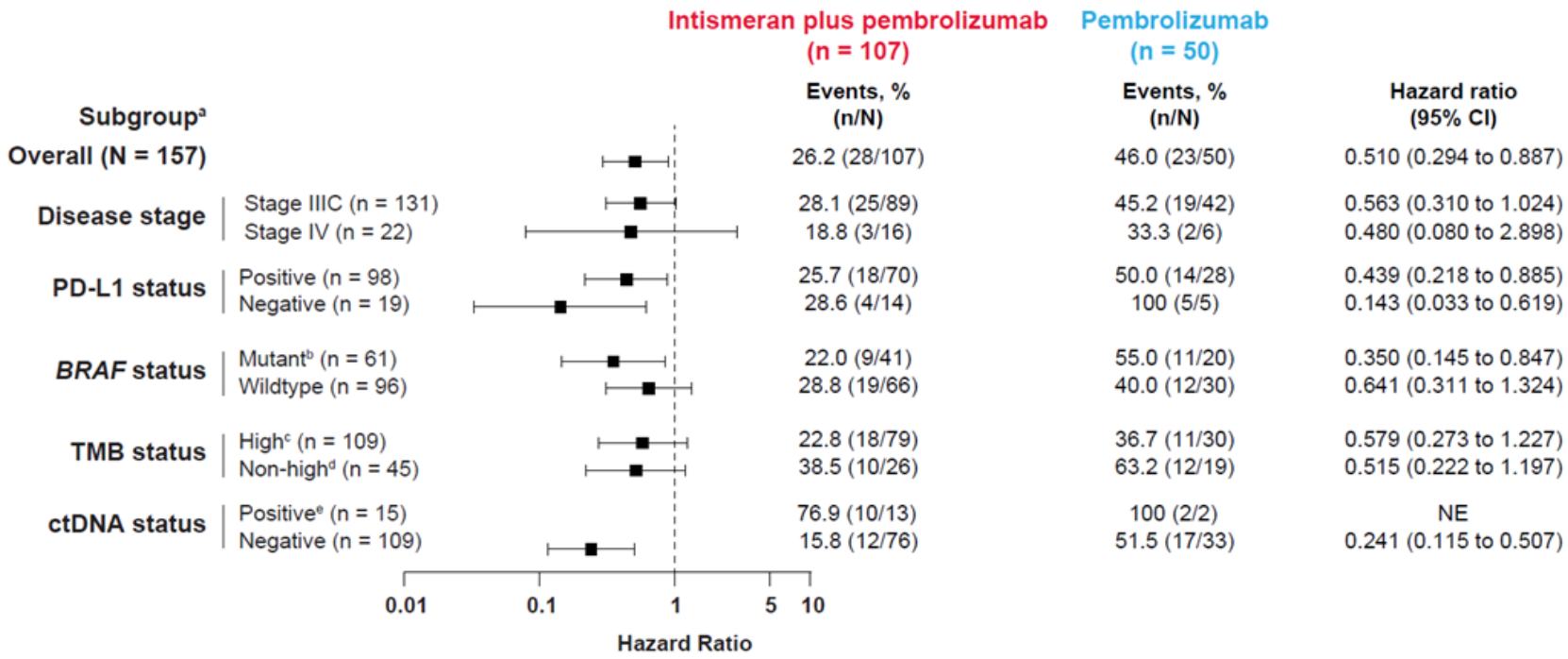
Subgroup analyses indicate RFS benefit is maintained across a broad patient population



[a]RFS in the overall population was estimated by a stratified Cox proportional hazards model; an unstratified analysis was used for subgroup analyses. [b]V600K or V600E mutation. [c]≥175 mutations/exome; [d]<175 mutations/exome. [e]Hazard ratio for the ctDNA-positive subgroup was NE as all patients in the pembrolizumab had a recurrence event. Subgroups were defined as previously described.[1]

1. Weber JS, et al. *Lancet*. 2024;403(10427):632-644

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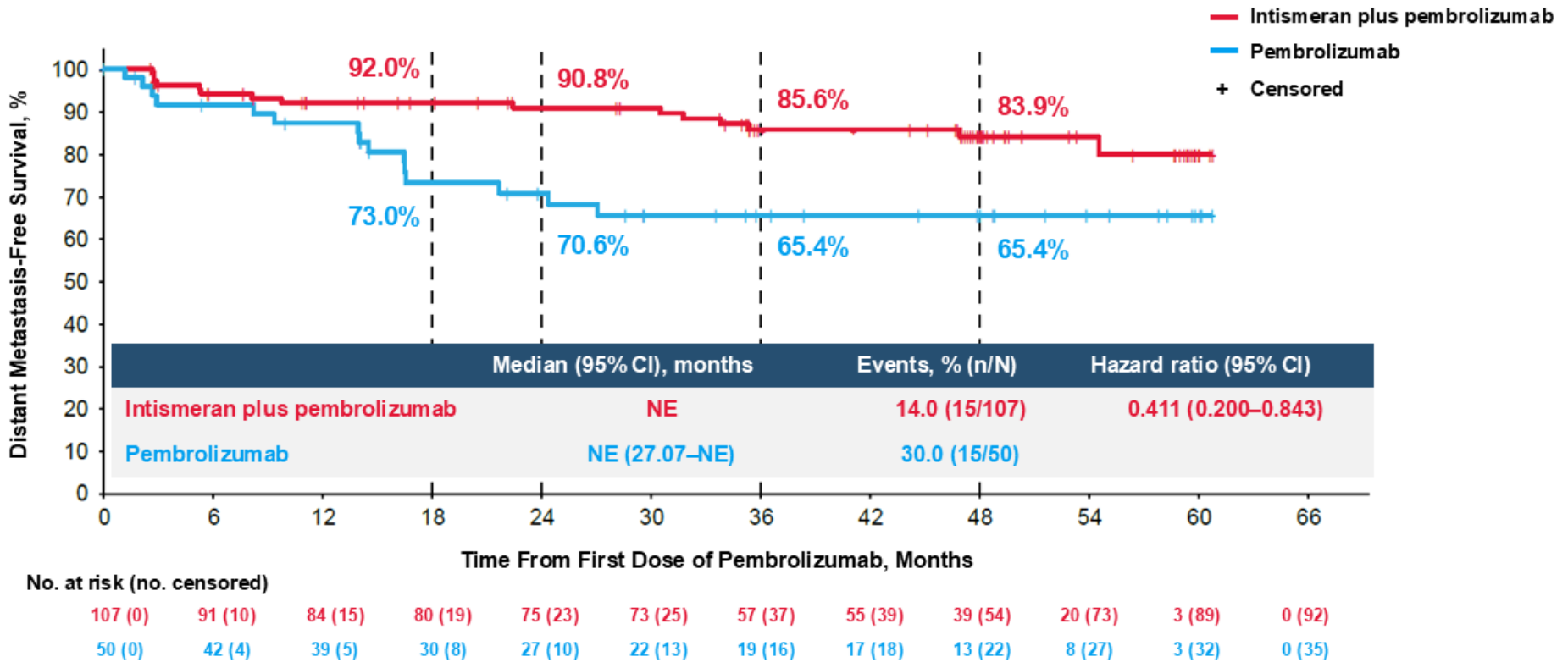
Durable benefit in DMFS (secondary endpoint)



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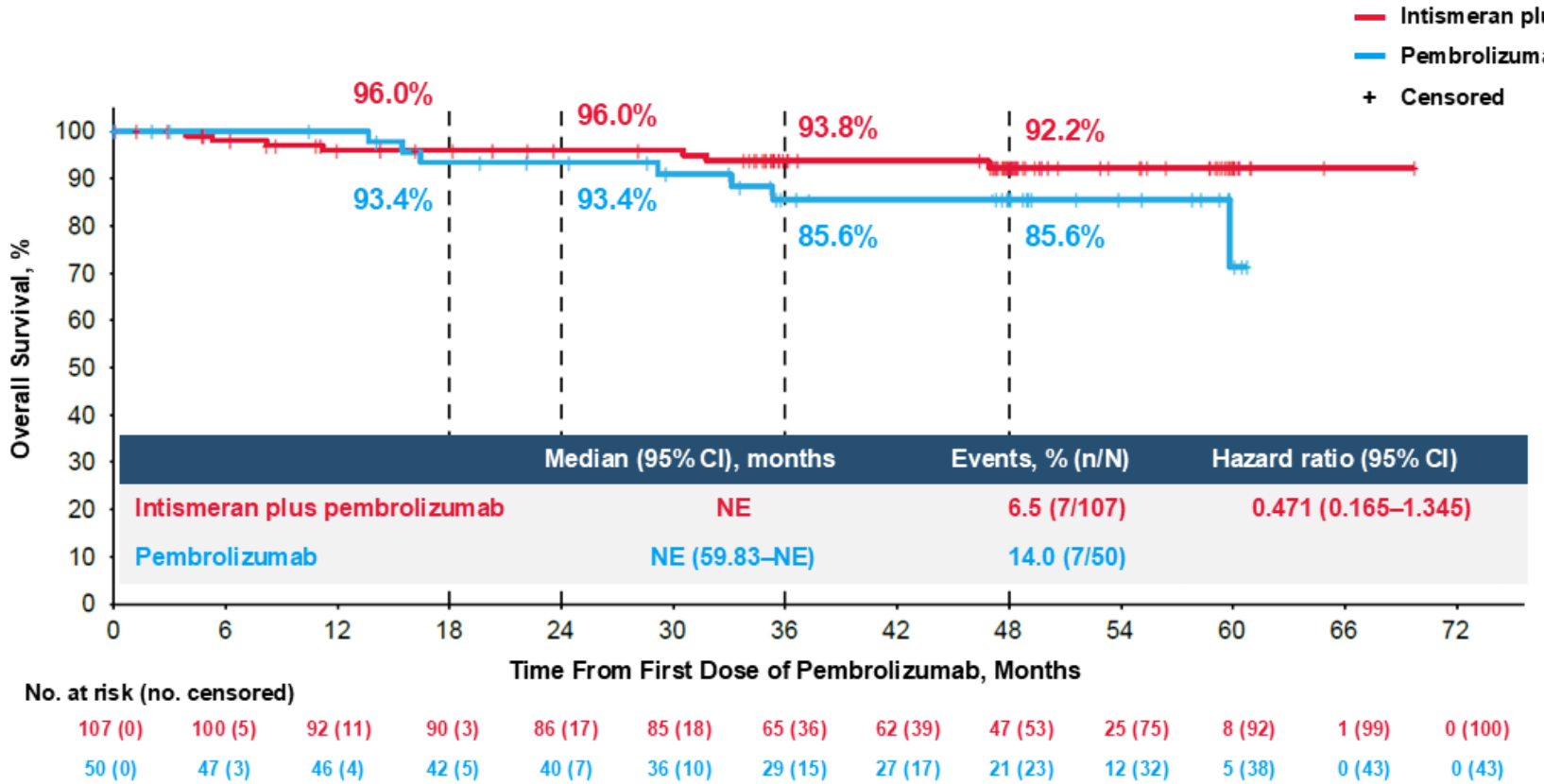
Overall survival shows an encouraging trend, but data remain immature



	Median (95% CI), months	Events, % (n/N)	Hazard ratio (95% CI)
Intismeran plus pembrolizumab	NE	6.5 (7/107)	0.471 (0.165–1.345)
Pembrolizumab	NE (59.83–NE)	14.0 (7/50)	

No. at risk (no. censored)

107 (0)	100 (5)	92 (11)	90 (3)	86 (17)	85 (18)	65 (36)	62 (39)	47 (53)	25 (75)	8 (92)	1 (99)	0 (100)
50 (0)	47 (3)	46 (4)	42 (5)	40 (7)	36 (10)	29 (15)	27 (17)	21 (23)	12 (32)	5 (38)	0 (43)	0 (43)

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At 5-year follow-up, established safety profile was maintained with no new safety signals

	Intismeran + Pembrolizumab (n=104)		Pembrolizumab (n=50)	
Event, n (%)	**Any grade**	**Grade ≥3**	**Any grade**	**Grade ≥3**
Any AE	104 (100)	35 (33.7)	47 (94.0)	15 (30.0)
Any treatment-related AE	104 (100)	26 (25.0)	42 (84.0)	7 (14.0)
Serious AE	14 (13.5)	13 (12.5)	5 (10.0)	4 (8.0)
Immune-mediated AEs[a]	38 (36.5)	11 (10.6)	19 (38.0)	6 (12.0)

Intismeran + pembrolizumab (n=104), n (%)	Grade 1	Grade 2	Grade 3	Grade 4/5	Total (n=104)
Patients with intismeran-related AE[b]	33 (31.7)	54 (51.9)	11 (10.6)	0	98 (94.2)
Fatigue	39 (37.5)	18 (17.3)	5 (4.8)	0	62 (59.6)
Injection site pain	37 (35.6)	25 (24.0)	0	0	62 (59.6)
Chills	49 (47.1)	4 (3.8)	0	0	53 (51.0)
Pyrexia	35 (33.7)	15 (14.4)	1 (1.0)	0	51 (49.0)
Injection site erythema	28 (26.9)	5 (4.8)	0	0	33 (31.7)
Headache	19 (18.3)	13 (12.5)	0	0	32 (30.8)
Influenza-like illness	21 (20.2)	10 (9.6)	0	0	31 (29.8)
Nausea	23 (22.1)	3 (2.9)	0	0	26 (25.0)
Myalgia	16 (15.4)	6 (5.8)	1 (1.0)	0	23 (22.1)

AE, adverse event; AEOSI, adverse event of special interest; CMQ, customized MedDRA queries.
Safety was analyzed in all randomized patients with ≥1 treatment dose. AEs were monitored throughout the study through 100 days after last intismeran dose and 30 days after last pembrolizumab dose (90 days for serious AEs). All patients completed study treatment before primary analysis (2022). Grading per NCI CTCAE v5.0. [a]Based on established list of pembrolizumab immune-related AEs (CMQ Pembrolizumab AEOSI); [b]Intismeran-related AEs included events attributed by investigators to intismeran alone and to both intismeran and pembrolizumab.

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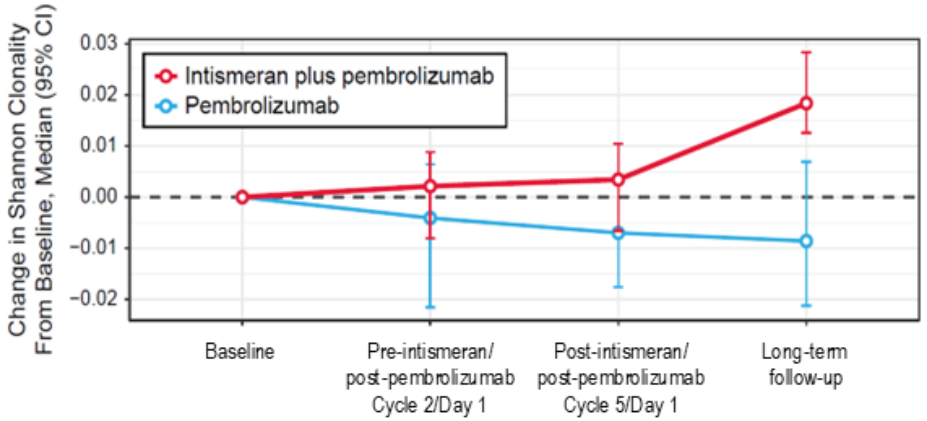
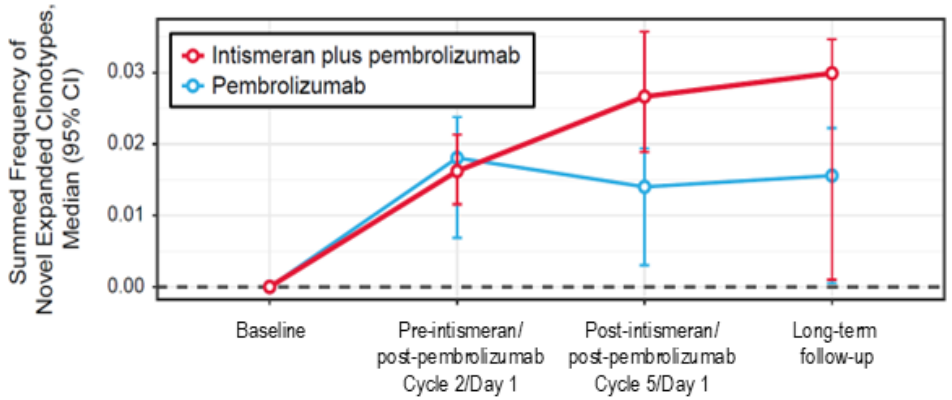
Intismeran plus pembrolizumab enhances T-cell clonal expansion and novel clone emergence

Combination therapy increased clonality, reflecting expansion of dominant T-cell clones



Intismeran plus pembrolizumab	n=78	n=69	n=73	n=56
Pembrolizumab	n=38	n=32	n=35	n=23

Combination therapy increased novel TCR clonotypes



Intismeran plus pembrolizumab	n=78	n=69	n=73	n=56
Pembrolizumab	n=38	n=32	n=35	n=23

Data are median (bootstrapped 95% CI). Whole blood TCR RNA sequencing at baseline, pre-intismeran/post-pembrolizumab (Cycle 2/Day 1), post-intismeran/post-pembrolizumab (Cycle 5/Day 1), and 30 days after the last pembrolizumab dose. Analyses used downsampled TCRβ chains normalized to 10,000 clones. Novel clones identified by absence at baseline. Differential clone abundance between baseline and on-treatment used 2-sample exact tests and *P* value adjusted for false discovery rates to identify novel-expanded clones.

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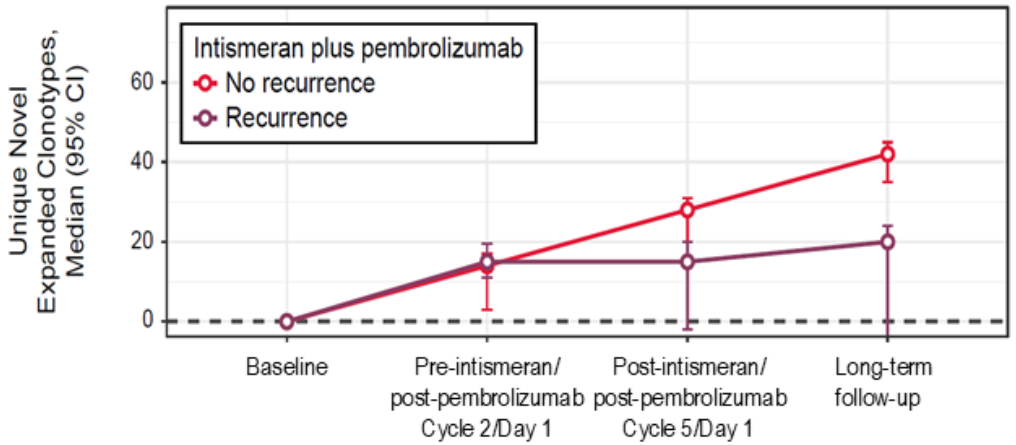
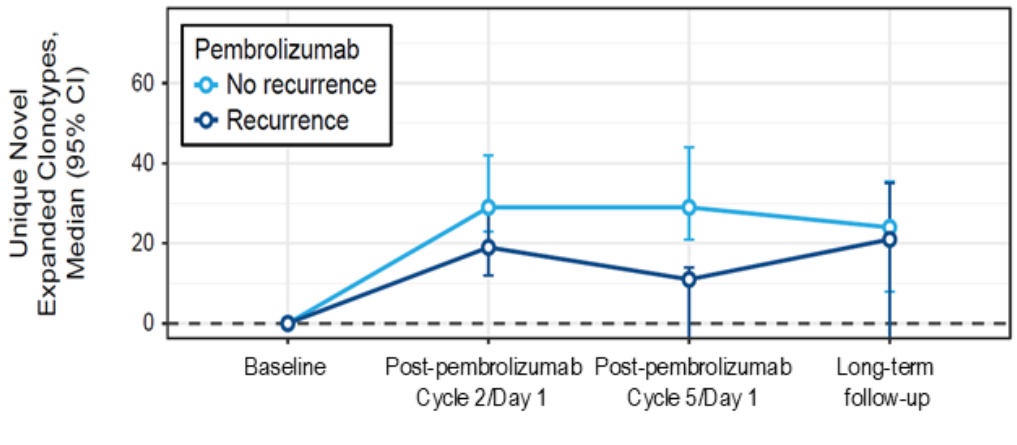
Greater novel clone expansion was associated with lower recurrence in the intismeran plus pembrolizumab arm

Intismeran Plus Pembrolizumab



No recurrence	n=57	n=49	n=54	n=43
Recurrence	n=21	n=20	n=19	n=13

Pembrolizumab



No recurrence	n=21	n=17	n=19	n=14
Recurrence	n=17	n=15	n=16	n=9

Data are shown as median and bootstrapped 95% CI. Whole blood TCR RNA sequencing at baseline, pre-intismeran/post-pembrolizumab (Cycle2/Day1), post-intismeran/post-pembrolizumab (Cycle5/Day1), and 30 days after the last pembrolizumab dose. Long-term follow-up data were collected at >170 days after last intismeran dose.

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Conclusions

- Intismeran plus pembrolizumab demonstrated **durable and clinically significant improvements in RFS and DMFS** vs standard-of-care pembrolizumab in high-risk resected melanoma at 5 years of follow-up
  - 49% reduction in risk of recurrence or death and 59% reduction in distant metastasis or death
  - Encouraging trend in overall survival
- Intismeran plus pembrolizumab maintained a **manageable safety profile** without potentiation of immune-related AEs vs pembrolizumab monotherapy
- Intismeran plus pembrolizumab generated **sustained novel T-cell clonotype expansion,** which was associated with lack of recurrence, supporting a durable immune surveillance mechanism
- Deep immune profiling established a **direct mechanistic link between these novel T-cell clonotypes and intismeran-encoded neoantigens** (*Sullivan, R et al; poster #9564*)
- Study limitations include the small sample size of this phase 2 study, immature overall survival results, and translational findings requiring validation in larger cohorts. **The phase 3 INTerpath-001 study (NCT05933577) of adjuvant melanoma is fully enrolled**; additional studies are ongoing across tumor types

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Plain Language Summary

- Intismeran is a cancer therapy that is personalized for each patient and is designed to help the body's immune system find and attack cancer cells
- In a study of people with high-risk melanoma, a serious type of skin cancer that has a high probability of coming back, intismeran was given in combination with pembrolizumab, another cancer medicine
- People who received both medicines were less likely to have their cancer come back than people who received pembrolizumab alone
- There were early signs that people who received both medicines may live longer, but more follow-up is needed to fully understand this
- Side effects were manageable, and most side effects linked to intismeran were mild or moderate
- The two medicines working together may help immune cells find and fight cancer cells

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We thank the patients, families, investigators, site staff, researchers, and collaborators who made this work possible.

We honor the memory of Dr. Jeffrey Weber, a lead investigator on this study and a giant in advancing melanoma treatment.

The following were members of the INT Research and Development Group:

George Ansstas, Victoria Atkinson, Elizabeth I. Buchbinder, Matteo S. Carlino, C. Lance Cowey, Mark Faries, Geoffrey T. Gibney, Omid Hamid, Julie Howle, Azim Khan, Adnan Khattak, Kevin B. Kim, Georgina V. Long, Jason J. Luke, Meredith McKean, Theresa Medina, Janice M. Mehnert, Tarek Meniawy, Meghan J. Mooradian, Andrew Pecora, Jennifer Segar, Montaser Shaheen, Ryan J. Sullivan, Matthew H. Taylor, Sajeve Thomas, Thuy T. Tran, Jeffrey S. Weber*, and Merck & Co., Inc., and Moderna, Inc. study teams.

**In memoriam*

Simultaneous publication: Khattak, A et al; *J Clin Oncol* https://ascopubs.org/doi/10.1200/JCO-26-00835

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Journal of Clinical Oncology®

Intismeran Autogene Plus Pembrolizumab Versus Pembrolizumab Alone in High-Risk Resected Melanoma: 5-Year Update of the Randomized Phase 2b KEYNOTE-942 Study

https://ascopubs.org/doi/10.1200/JCO-26-00835

Dr. Matteo S. Carlino

Listen to the accompanying podcast with Drs. Grant McArthur and Ash Gurumurthi linked from the article or at asco.org/podcasts

Join Dr. Grant McArthur for a Journal Club Discussion in JCO Central (S402a) on Monday, June 1, 2026, 4pm CDT

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REPRISE: ASCO 2026 POSTER PRESENTATION

Intismeran autogene induces *de novo* neoantigen-specific T cells as adjuvant therapy in melanoma

Ryan Sullivan, MD

Director, Cutaneous Medical Oncology,
Mass General Brigham Cancer Institute

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1. Massachusetts General Hospital, Harvard Medical School, Boston, MA, USA2. Westmead and Blacktown Hospitals, Melanoma Institute Australia, and The University of Sydney, Sydney, NSW, Australia 3. Hollywood Private Hospital & Edith Cowan University, Perth, WA, Australia 4. Melanoma Institute Australia, The University of Sydney, and Royal North Shore and Mater Hospitals, Sydney, NSW, Australia 5. Florida Cancer Specialists/Sarah Cannon Research Institute, Sarasota, FL, USA6. Duke University Medical Center, Durham, NC, USA 7. Moderna, Inc., Cambridge, MA, USA 8. Laura and Isaac Perlmutter Cancer Center at NYU Langone Health, New York, NY, USA

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Background

Intismeran autogene (intismeran), an mRNA-based individualized neoantigen therapy encoding up to 34 tumor neoantigens, was designed to enhance existing and induce de novo neoantigen-specific antitumor T-cell responses by targeting patient-specific tumor mutations.

Phase 1 KEYNOTE-603

What we learned:

- **100% of patients** had neoantigen-specific responses observed
- **29.8% of neoantigens** elicited immune responses
- **Both CD8+ and CD4+ neoantigen-specific T cell responses** were detected

Phase 2 KEYNOTE-942

What we learned:

- **Intismeran arm induced higher TCR clonality** and more novel T-cell clonotypes than control arm
- **Novel, expanded T cell clonotypes sustained** over study
- **Novel T cell clonotype expansion associated with efficacy** only in intismeran arm

Objectives

Link *de novo* T-cell clonotypes to intismeran-encoded neoantigens

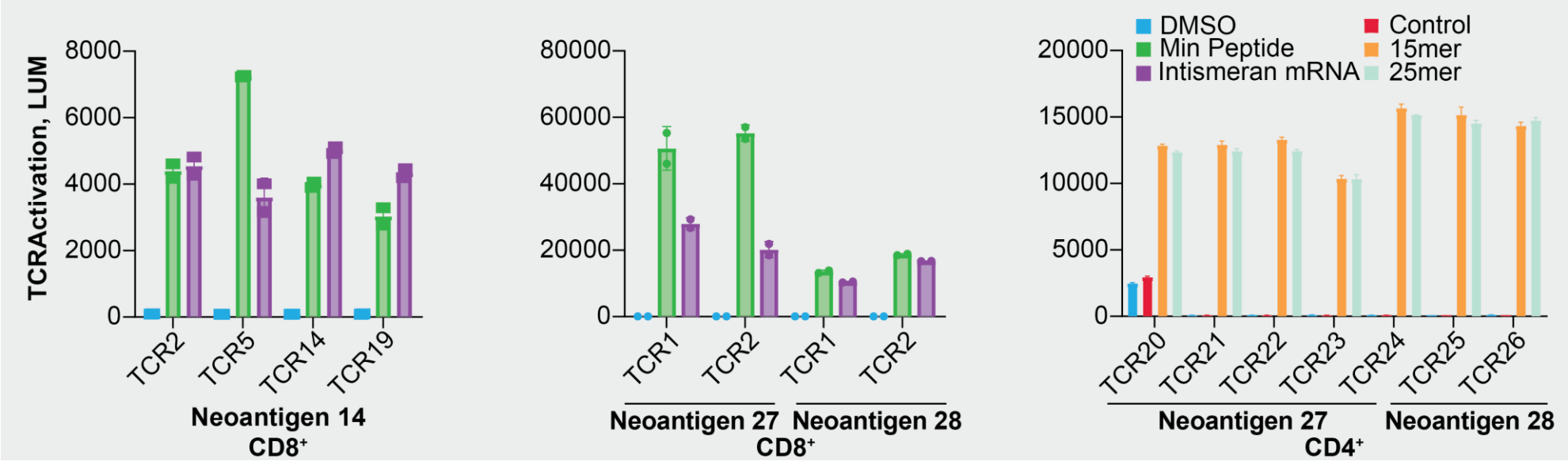
Characterize the resulting neoantigen-specific T-cell responses in patients receiving intismeran plus pembrolizumab

Functional validation that TCR clonotypes from blood recognize intismeran-encoded neoantigens

TCRs discovered from single cell TCR sequencing of blood enabled direct mapping of neoantigen-specific TCR clonotypes to individual intismeran-encoded neoantigens

- **Example of Patient #3**, putative neo-antigen specific T cells from blood tested *in vitro* for reactivity to 3 neo-antigens
- Prioritized high-frequency TCR clonotypes were functionally validated, with **all tested receptors confirmed to recognize their respective intismeran-encoded neoantigens**

Control: irrelevant peptide



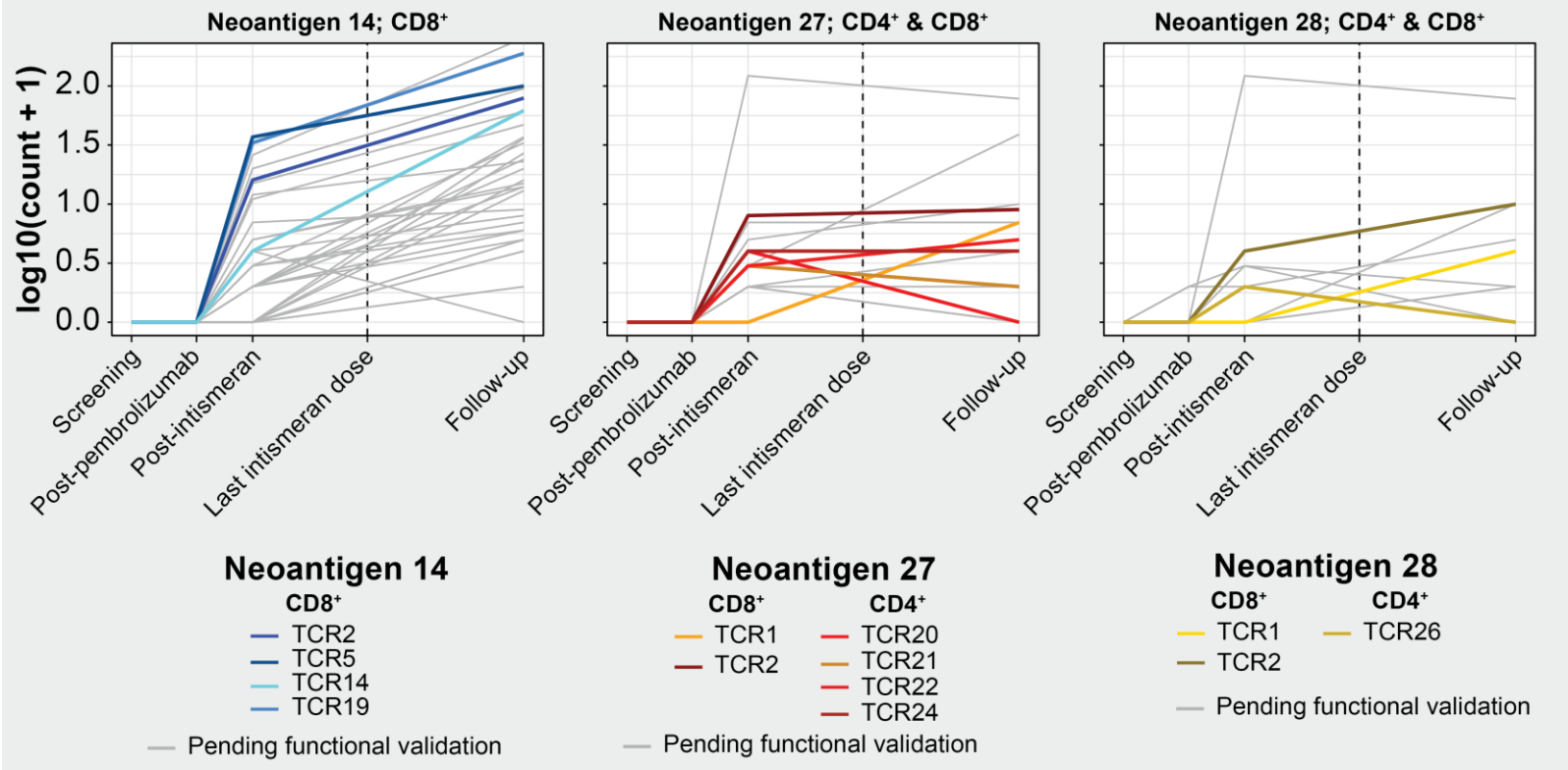
Methods: Activation-induced marker (AIM)-based enrichment of neoantigen-reactive CD4+/CD8+ T cells ex vivo or after in vitro expansion, followed by single-cell RNA/TCR sequencing, identified neoantigen-reactive TCRs. TCRs were expressed as mRNA in Jurkat NFAT-luciferase reporter cells and tested against neoantigen peptides or patient-specific intismeran mRNA cassettes presented by HLA-matched B-LCLs (n=3).

Validated neoantigen-specific T cells expand after intismeran and persist at least 6 months beyond last dose

In patient #3, intismeran neoantigen 14, 27 and 28 used to expand T cell *ex vivo* from blood

Dozens of different neoantigen-specific TCRs mapped to each neoantigen

Neoantigen-reactive T cells **expanded only after** interismeran and **sustained beyond last intismeran dose**



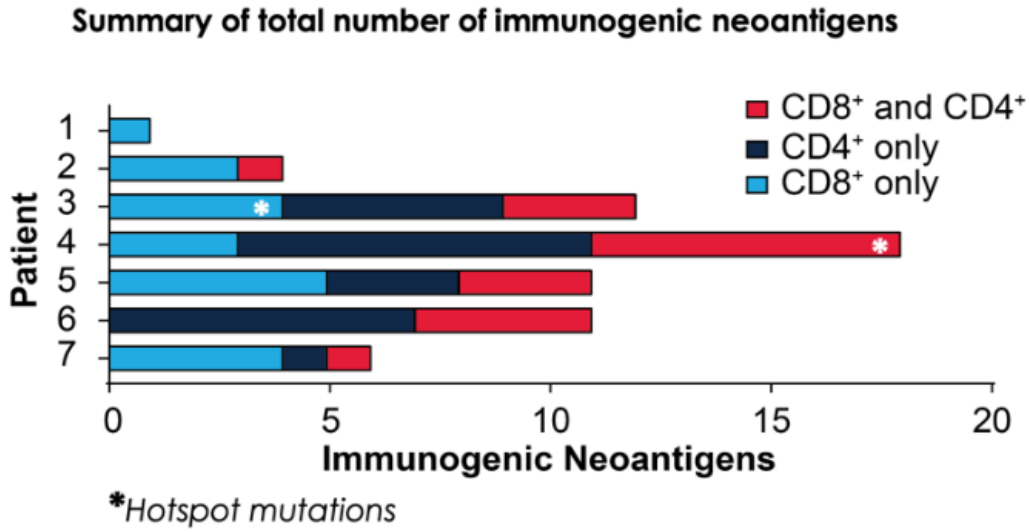
Method: AIM-based enrichment of CD4+ and CD8+ T cells *ex vivo* or after *in vitro* expansion; a >=5-cell threshold per clonotype(n=57 for neoantigen 14, n=38 for neoantigen 27, n=28 for neoantigen 28)

Intismeran induces neo-antigen specific CD8+ and CD4+ T-cells

Among the 34 intismeran-encoded neoantigens per patient, a range of 1-18 neoantigens were immunogenic, demonstrating **variable but substantial immunogenic potential**

Immunogenic neoantigens included hotspot mutations in BRAF and NRAS

Intismeran-encoded neoantigens elicited CD4+-only, CD8+-only, and combined CD4+/CD8+ T-cell responses, **demonstrating broad engagement of adaptive immunity**

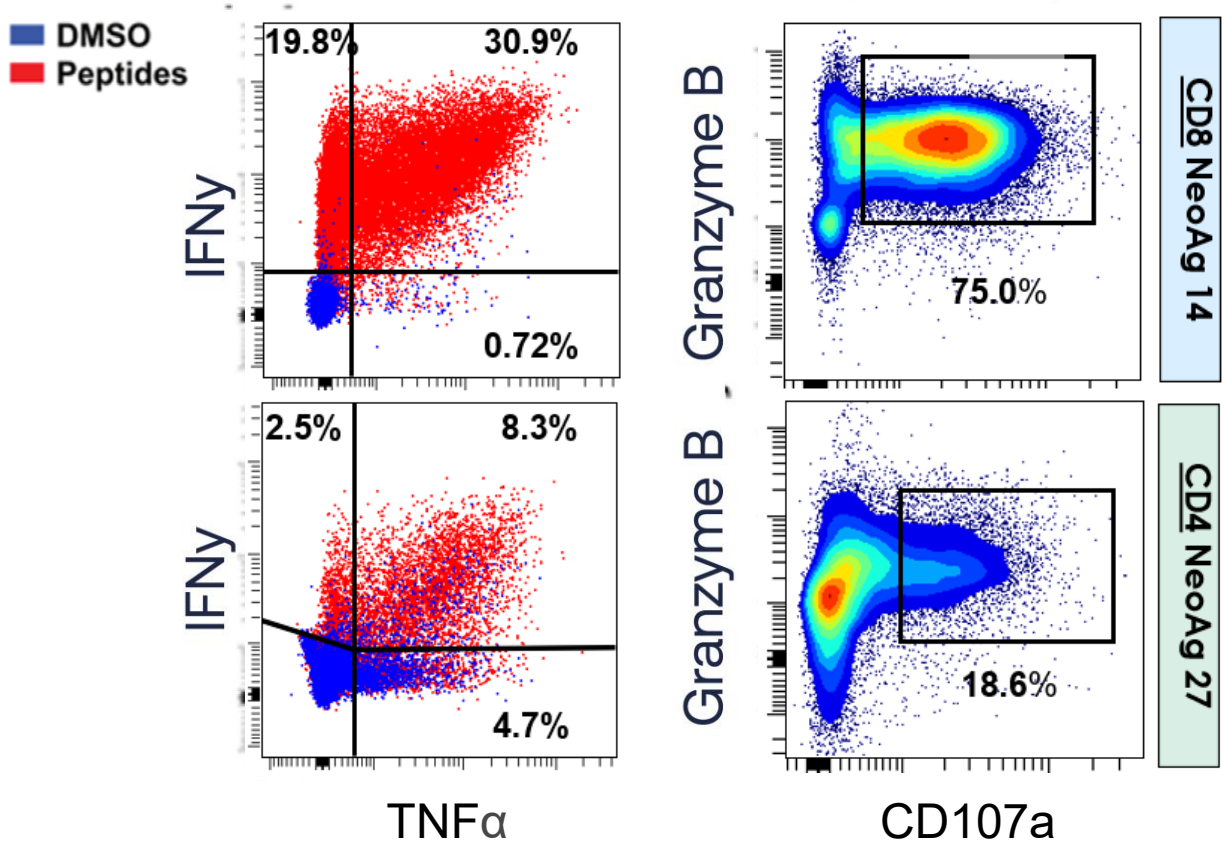


Methods:

- 7 patients with completely resected, high-risk melanoma who had received intismeran plus pembrolizumab treatment and had available peripheral leukapheresis samples from KEYNOTE-603 and KEYNOTE-942
- Leukapheresis performed at baseline and after 4 doses of intismeran therapy
- Immunogenicity (individual neoantigen-level) assessed by activation-induced marker (AIM) flow cytometry assay after 12-day expansion of T-cells

Intismeran-encoded neoantigens elicit polyfunctional and cytotoxic CD8+ and CD4+ T cells

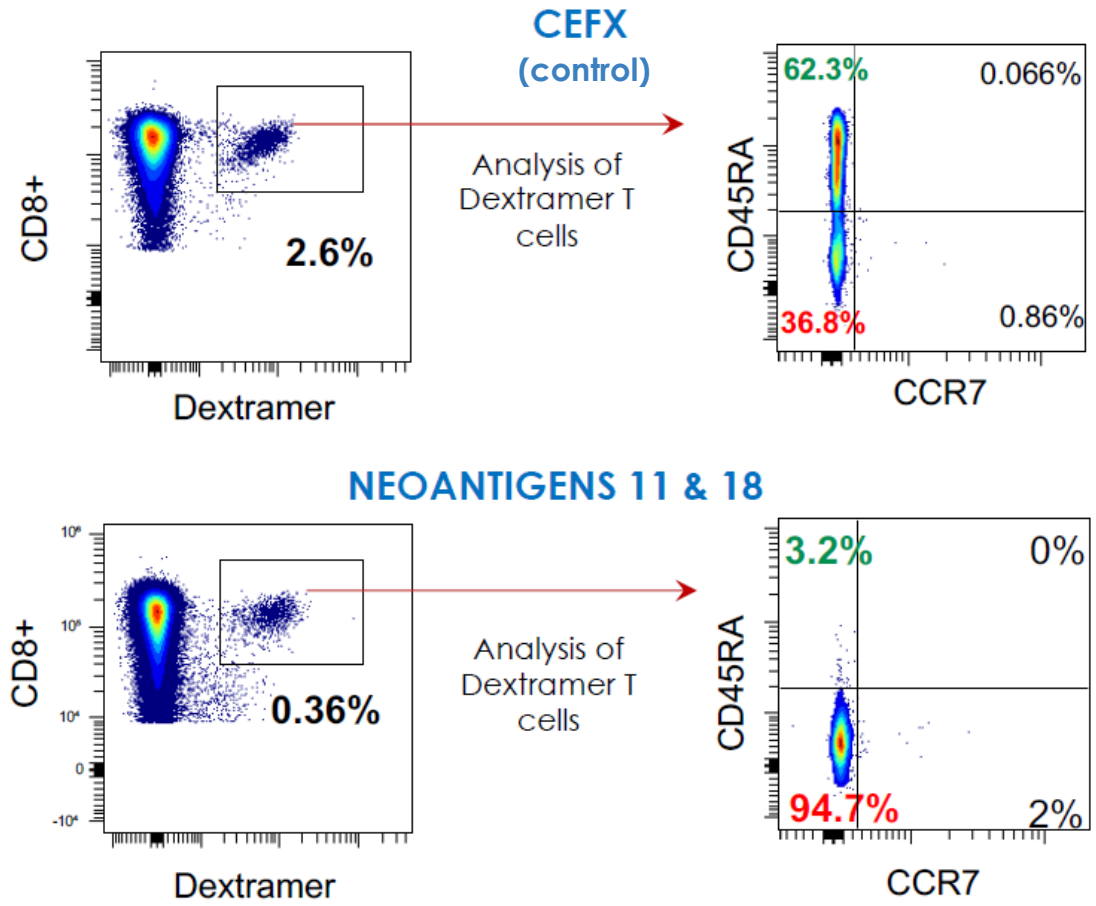
Intracellular cytokine staining (ICS) of AIM-enriched neoantigen-specific CD8+ and CD4+ T cells (Representative data from patient #3 of 5 analyzed)

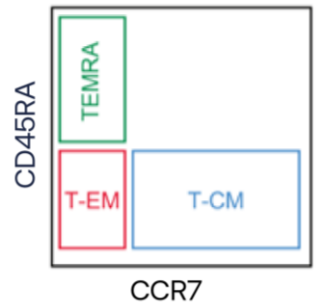


Neoantigen-reactive T cells expressed IFNy, TNFα, granzyme B and CD107a, consistent with polyfunctional cytotoxic effector function

Neoantigen-reactive CD8+ T cells are predominantly T-Effector Memory phenotype

Flow cytometry of neoantigen-specific T cells enriched by dextramer peptide-HLA multimer detection (Representative data from patient #2 of 3 analyzed)





TEMRA: Terminally differentiated, highly cytotoxic

T- Effector Memory (T-EM): Functionally active, positioned for rapid tumor surveillance, potentially peripheral tissue homing

T-Central Memory (T-CM): Lymphoid homing, high proliferative capacity

*CEFX positive control is a 176-peptide pool derived from common viral and bacterial pathogens, designed to stimulate CD4+ and CD8+ T cells across diverse HLA backgrounds.

Conclusions

Intismeran plus pembrolizumab induced **durable, de novo neoantigen-specific T-cell responses in patients with resected high-risk melanoma**

Neoantigen-specific TCR clonotypes from blood were **functionally validated and directly mapped to individual intismeran-encoded neoantigens**

Validated neoantigen-specific TCR clonotypes expanded during intismeran therapy and persisted beyond the last dose, demonstrating intismeran-driven T-cell remodeling

Intismeran-encoded neoantigens elicited broad CD4+ and CD8+ T-cell responses, including polyfunctional cytotoxic T cells with effector-memory characteristics

These findings **establish a direct mechanistic link between intismeran-encoded neoantigens and the emergence of de novo TCR clonotypes associated with improved clinical outcomes** in KEYNOTE-942

Conclusion

David Berman, M.D, PhD
Chief Development Officer, Moderna

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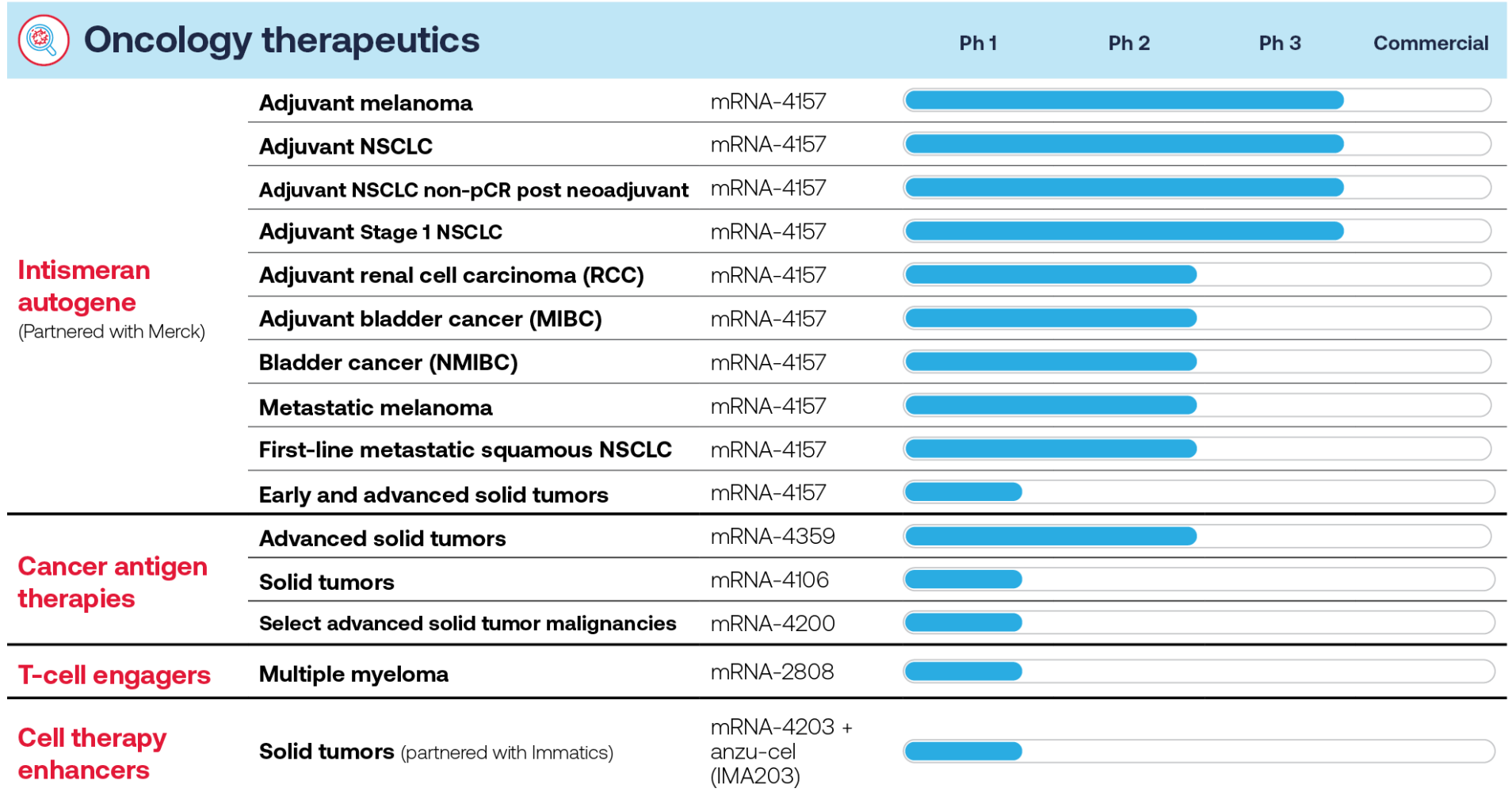
Moderna's broad oncology clinical pipeline



Intismeran autogene (Partnered with Merck)	**Adjuvant melanoma**	mRNA-4157	Ph 3
	Adjuvant NSCLC	mRNA-4157	Ph 3
	Adjuvant NSCLC non-pCR post neoadjuvant	mRNA-4157	Ph 3
	Adjuvant Stage 1 NSCLC	mRNA-4157	Ph 3
	Adjuvant renal cell carcinoma (RCC)	mRNA-4157	Ph 2
	Adjuvant bladder cancer (MIBC)	mRNA-4157	Ph 2
	Bladder cancer (NMIBC)	mRNA-4157	Ph 2
	Metastatic melanoma	mRNA-4157	Ph 2
	First-line metastatic squamous NSCLC	mRNA-4157	Ph 2
	Early and advanced solid tumors	mRNA-4157	Ph 1
Cancer antigen therapies	**Advanced solid tumors**	mRNA-4359	Ph 2
	Solid tumors	mRNA-4106	Ph 1
	Select advanced solid tumor malignancies	mRNA-4200	Ph 1
T-cell engagers	**Multiple myeloma**	mRNA-2808	Ph 1
Cell therapy enhancers	**Solid tumors** (partnered with Immatics)	mRNA-4203 + anzu-cel (IMA203)	Ph 1

Abbreviations: NSCLC, non-small cell lung cancer; RCC, renal cell carcinoma; MIBC, muscle-invasive bladder cancer; NMIBC, non-muscle invasive bladder cancer

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June 25, 2026

Moderna Science Day

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