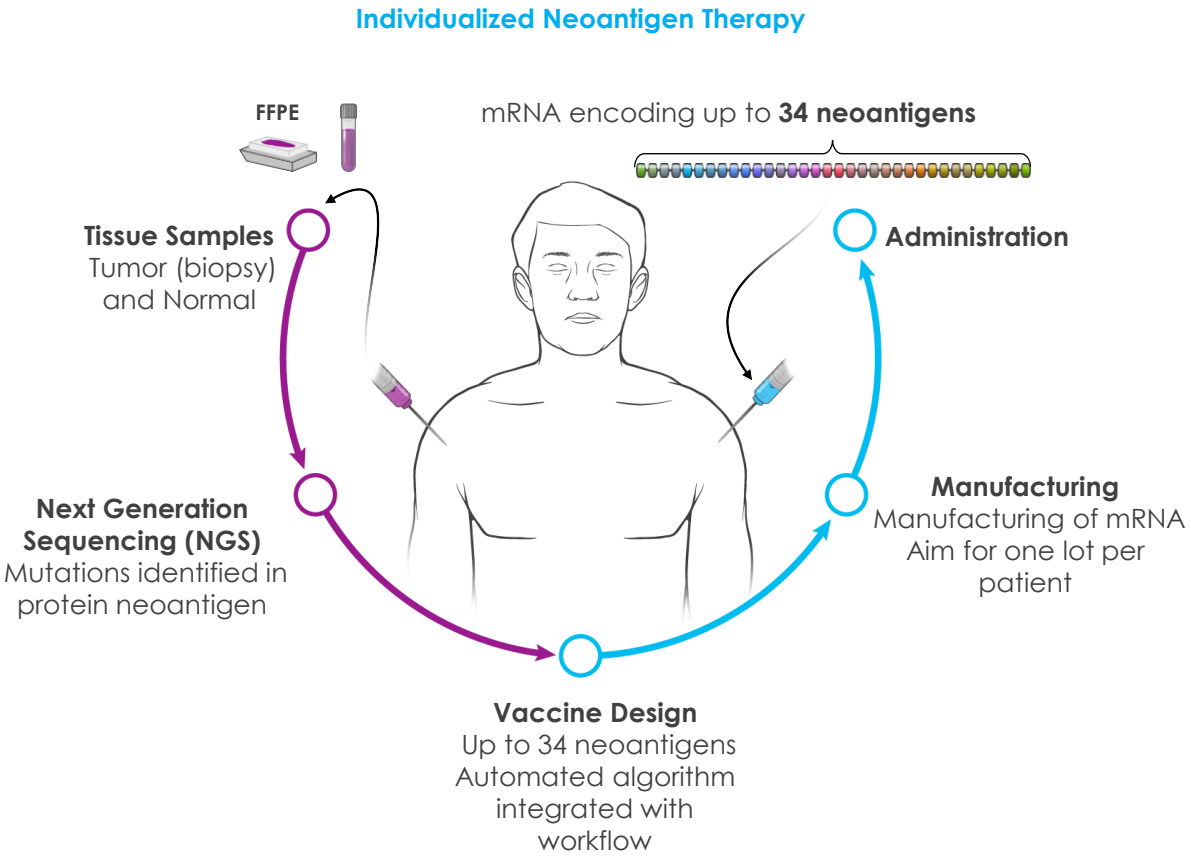
Individualized Neoantigen Therapy (INT) (mRNA-4157)

Last updated: May 4th, 2023

Modality	Program	ID #	Preclinical development	Phase 1	Phase 2	Phase 3	Commercial	Moderna rights
Systemic secreted & cell surface therapeutics	Relaxin *Heart failure*	mRNA-0184						Worldwide
	PD-L1 *Autoimmune hepatitis*	mRNA-6981						Worldwide
Cancer vaccines & therapeutics	Individualized neoantigen therapy (INT)	mRNA-4157						50-50 global profit sharing with **Merck**
	KRAS vaccine	mRNA-5671						Worldwide
	Checkpoint vaccine	mRNA-4359						Worldwide
Intratumoral Immuno-oncology	OX40L/IL-23/IL-36γ (Triplet) *Solid tumors/lymphoma*	mRNA-2752						Worldwide
	IL-12 *Solid tumors*	MEDI1191						Worldwide
Localized regenerative therapeutics	VEGF-A *Myocardial ischemia*	AZD8601						Worldwide
	Propionic acidemia (PA)	mRNA-3927						Worldwide
	Methylmalonic acidemia (MMA)	mRNA-3705						Worldwide
Systemic intracellular therapeutics	Glycogen storage disease type 1a (GSD1a)	mRNA-3745						Worldwide
	Ornithine transcarbamylase deficiency (OTC)	mRNA-3139						Worldwide
	Phenylketonuria (PKU)	mRNA-3283						Worldwide
Inhaled pulmonary therapeutics	Crigler-Najjar syndrome type 1 (CN-1)	mRNA-3351						Provided to **ILCM** free of charge
	Cystic fibrosis (CF)	VX-522						**Vertex** to pay milestones and royalties

Individualized Neoantigen Therapy (INT) (mRNA-4157)

Designed to target an individual patient's unique tumor mutations



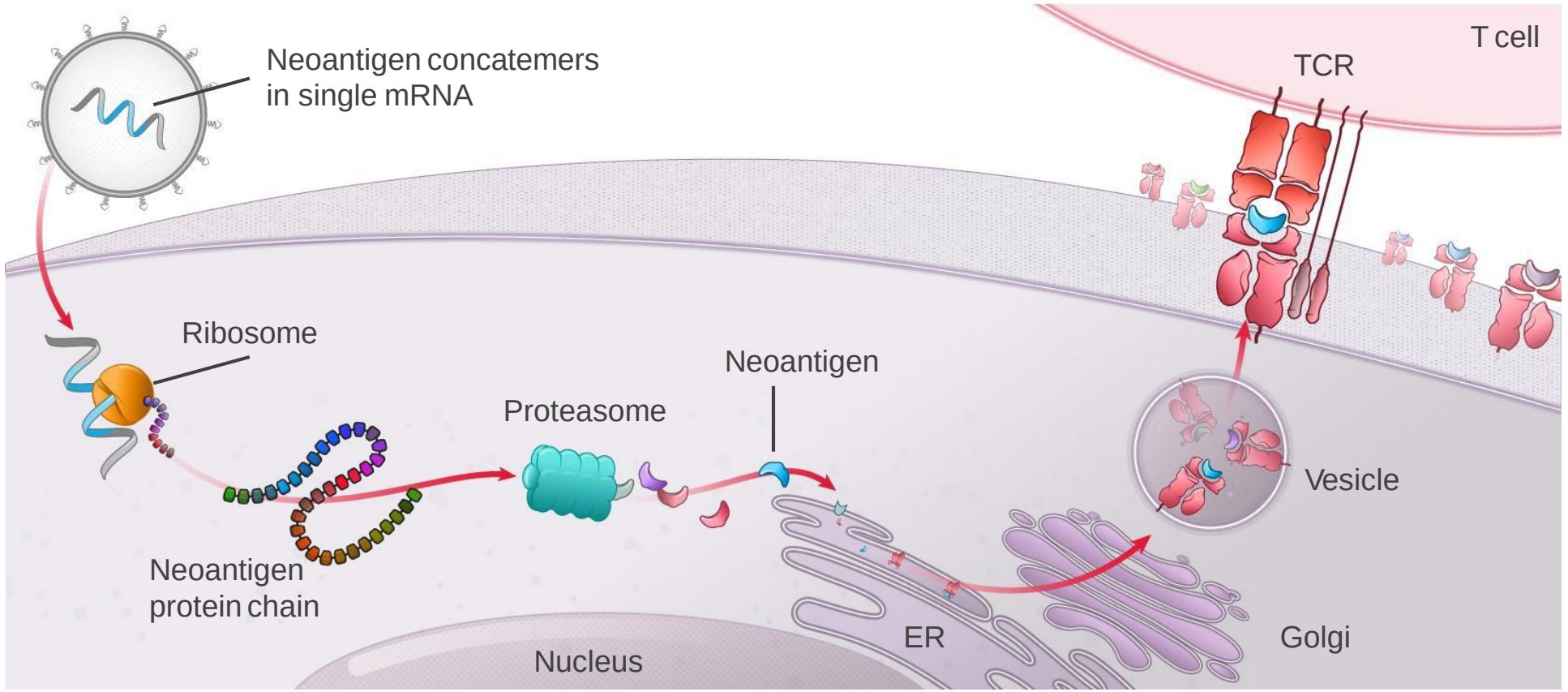
Personalized drug design

Rapid turnaround times

Needle-to-needle in just **weeks**

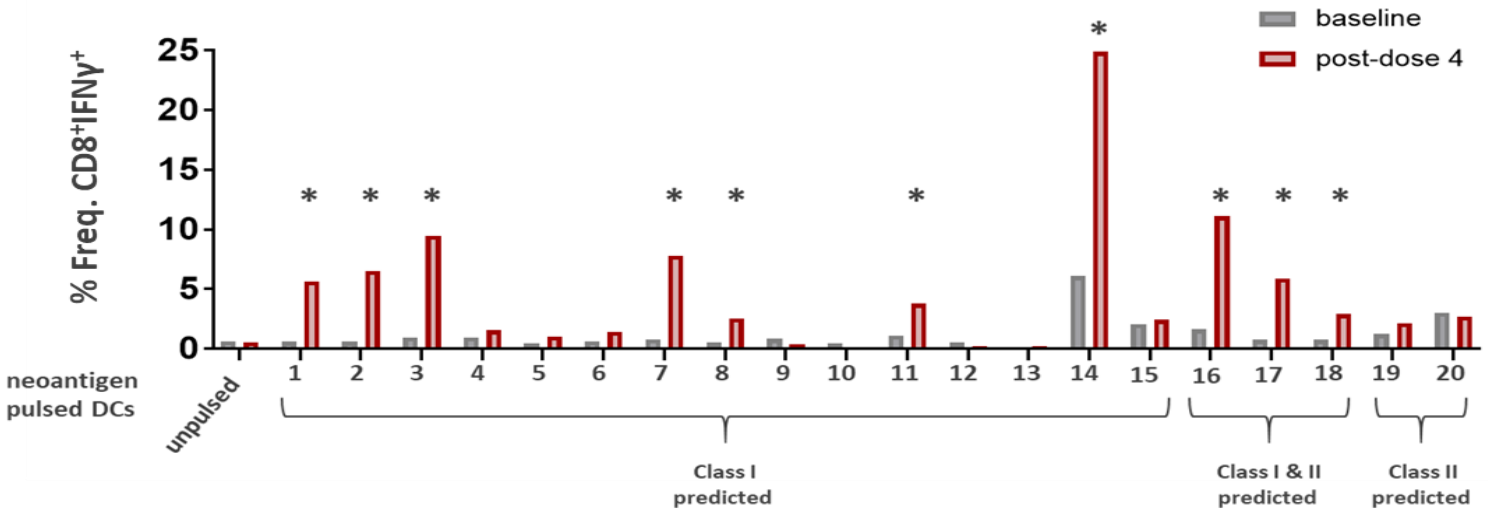
INT (mRNA-4157) elicits T cells required for curative cancer therapy

Designed to target an individual patient's unique tumor mutations



Phase 1 study demonstrates PCV (now known as INT) induces CD8 T-cell proliferation against selected neoantigens incorporated in vaccine

Previously shared at ASCO 2019



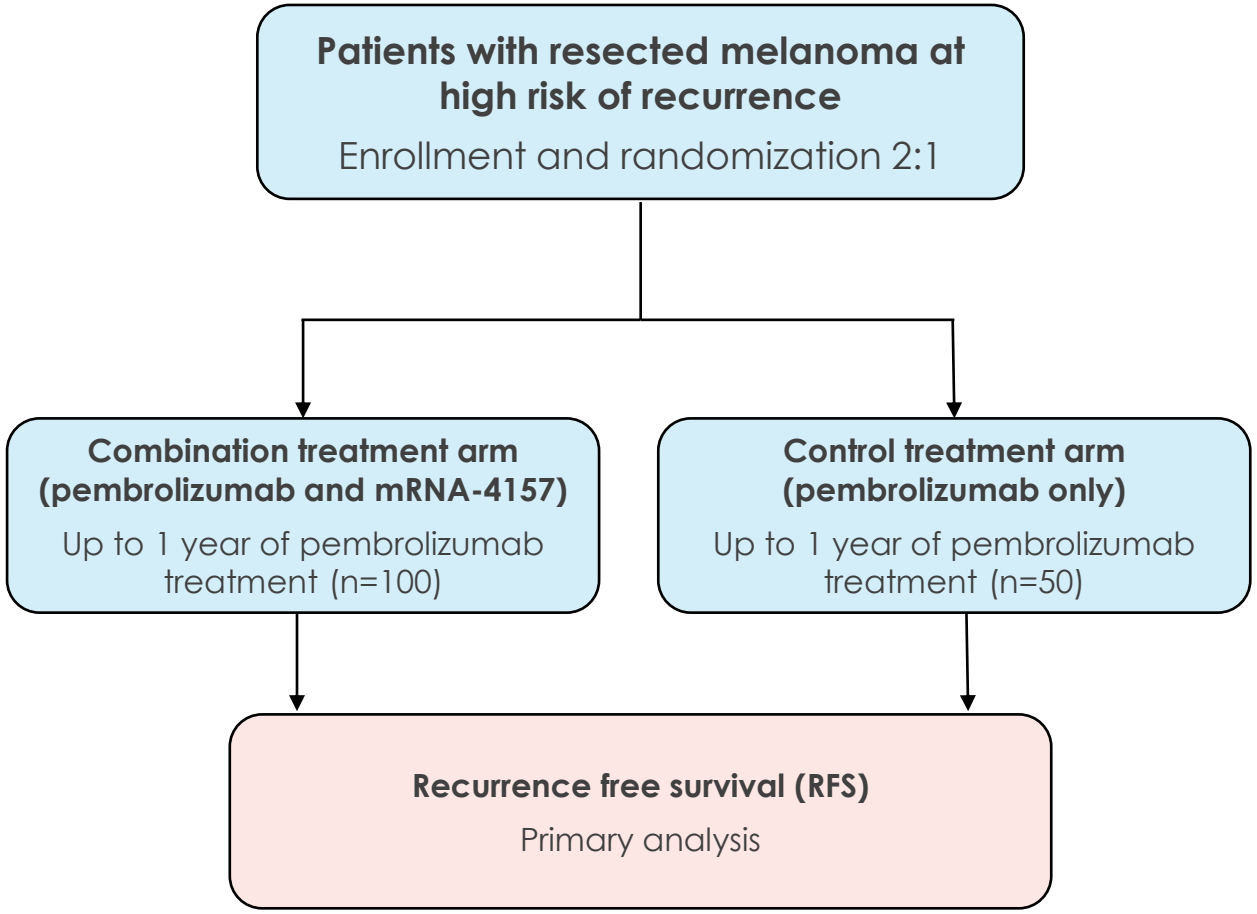
CD8 T cell responses to individual neoantigens were measured in in vitro stimulated (IVS, expanded) T cells
Flow cytometry plots show increases in % freq. of CD8 cells producing IFNγ 7d post 4th vaccine dose to multiple neoantigens
** Is greater than 3x increased in neoantigen specific CD8 T-cells post vaccination*

- **Greater than 3x increases in neoantigen specific CD8 T-cells were detected post 4th dose vaccination against 10 out of 18 class I targeted neoantigens**
- All positive CD8 T-cell responses post vaccination were to **neoantigens with high predicted binding affinity of < 500 nm**

Moderna 2019 ASCO presentation

PCV (now known as INT) (mRNA-4157) Phase 2 trial results announced in 4Q22

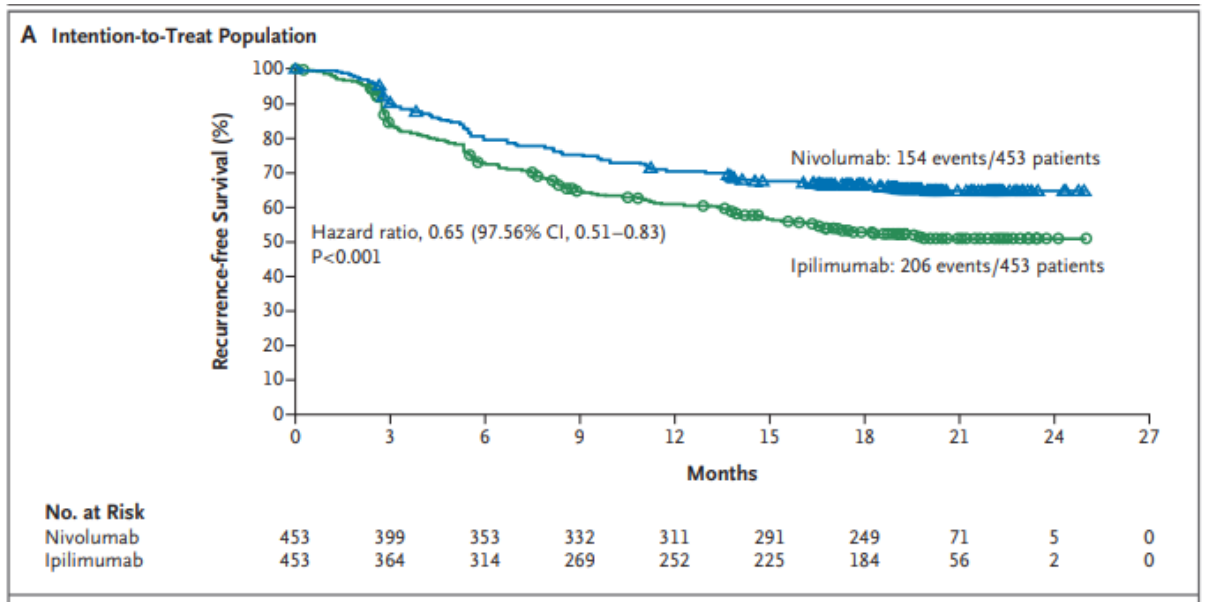
Primary endpoint is recurrence free survival compared to pembrolizumab



- Randomized, placebo controlled, INT + pembrolizumab (KEYTRUDA®) vs. pembrolizumab alone (2:1)
- Resected melanoma patients - high recurrence risk
- Primary endpoint = recurrence free survival (RFS)
- Trial was fully enrolled (~150 participants) in September '21: Data announced in 4Q22
- Merck exercised option to jointly develop and commercialize mRNA-4157

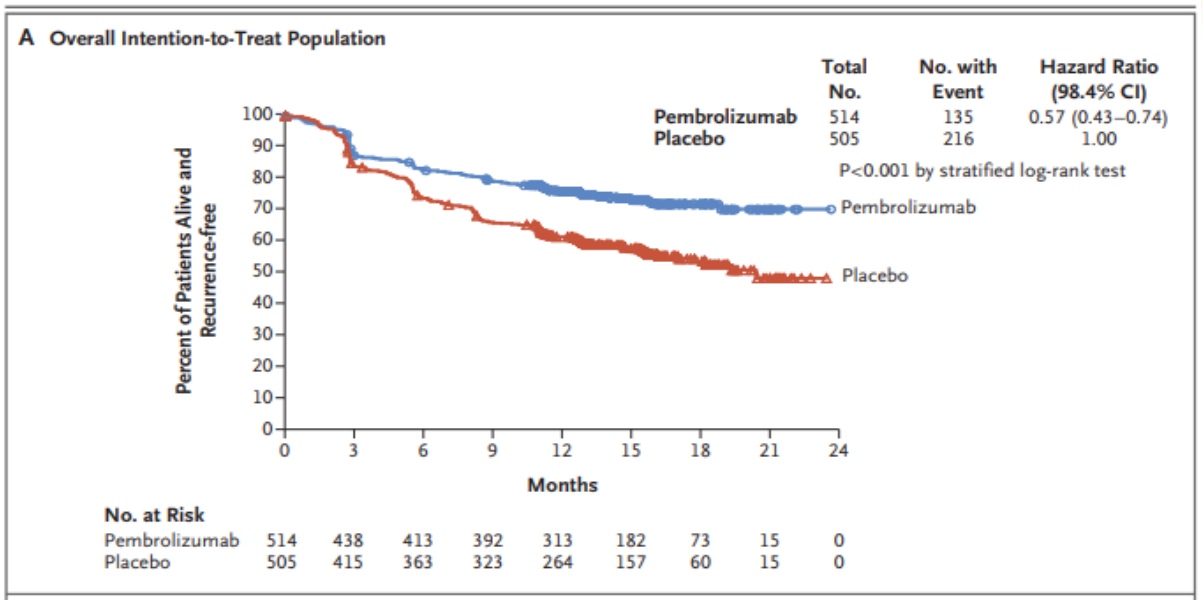
Previous studies in resected melanoma population: Kaplan-Meier curves for Checkmate-238 and Keynote-054

Checkmate-238 12mo RFS: 70.5% vs. 60.8%



Primary RFS analysis in the ITT Population

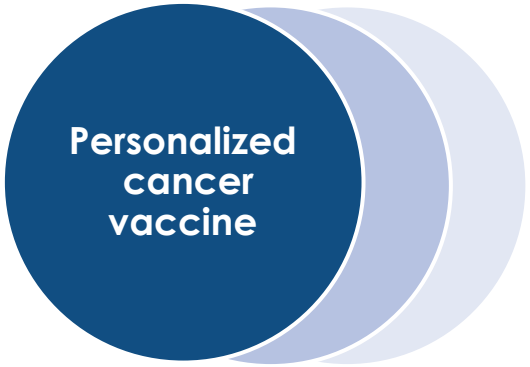
Keynote-054 12mo RFS: 75.4% vs 61.0%



Primary RFS analysis in the ITT Population

1. Checkmate-238:A Phase 3, Randomized, Double-blind Study of Adjuvant Immunotherapy With Nivolumab Versus Ipilimumab After Complete Resection of Stage IIIb/c or Stage IV Melanoma in Subjects Who Are at High Risk for Recurrence Weber, Jeffery et al., The New England Journal of Medicine (2017), https://www.nejm.org/doi/full/10.1056/nejmoa1709030
2. Keynote 054: Adjuvant Immunotherapy With Anti-PD-1 Monoclonal Antibody Pembrolizumab (MK-3475) Versus Placebo After Complete Resection of High-risk Stage III Melanoma: A Randomized, Double- Blind Phase Trial of the EORTC Melanoma Group. Eggermont, Alexander et al., The New England Journal of Medicine (2018), https://doi.org/10.1056/NEJMoa1802357

mRNA personalized cancer vaccine in combination with Keytruda met primary efficacy endpoint in Phase 2 study



1. mRNA-4157/V940 in combination with KEYTRUDA **reduced the risk** of **recurrence or death by 44% (HR=0.56 [95% CI, 0.31-1.08]; one-sided p value=0.0266)** compared with KEYTRUDA alone

2. Results are **the first demonstration of efficacy for an investigational mRNA cancer treatment** in a randomized clinical trial

3. Companies plan to discuss results with regulatory authorities and **initiate a Phase 3 study in melanoma in 2023 and rapidly expand to additional tumor types**

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A Personalized Cancer Vaccine, mRNA-4157 (V940), Combined With Pembrolizumab Versus Pembrolizumab Alone in Patients With Resected High-risk Melanoma: Efficacy and Safety Results From the Randomized, Open-label Phase 2 mRNA-4157-P201/KEYNOTE-942 Trial

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Sponsored by Moderna, Inc., in collaboration with Merck Sharp & Dohme LLC, a subsidiary of Merck & Co., Inc., Rahway, NJ, USA.

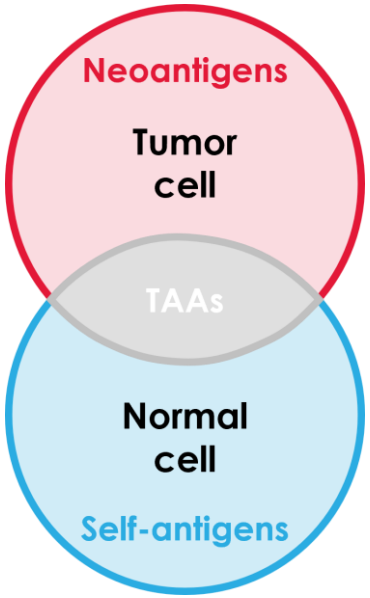
Disclosure Information: Jeffrey S. Weber

I have the following relevant financial relationships to disclose:

- I consult for and have received less than $10,000 per annum from Merck, Genentech, AstraZeneca, GSK, Novartis, Nektar, Celldex, Incyte, Biond, Moderna, ImCheck, Sellas, Evaxion, Pfizer, Regeneron, and EMD Serono and received $10-$25,000 from BMS for membership on advisory boards
- I hold equity in Biond, Evaxion, OncoC4, and Instil Bio
- I am on scientific advisory boards for CytomX, Incyte, ImCheck, Biond, Sellas, Instil Bio, OncoC4, and NexImmune and am remunerated between $10,000-$50,000
- I am not a member of any speaker's bureau
- NYU, but not myself personally, received research support from BMS, Merck, GSK, Moderna, Pfizer, Novartis, and AstraZeneca
- Moffitt Cancer Center filed a patent on an ipilimumab biomarker and on TIL preparation that I am named on, and Biodesix filed a PD-1 patent that I was named on; I receive less than $6000 annually in royalties

Neoantigen-based Therapies May Overcome Limitations of Previous Failed Cancer Vaccine Approaches

- Whole-exome sequencing (WES) has identified neoantigens/tumor-specific antigens, which are mutated proteins expressed due to somatic mutations, posttranslational modifications, or oncogenic viral proteins[1]
- Individualized neoantigen approaches can increase endogenous neoantigen T-cell responses and induce epitope spreading[2-5]



NeoVax[2,3]
Trial design: Phase 1
Results: Safe, feasible, and capable of eliciting strong T-cell responses

NEO-PV-01[4]
Trial design: Phase 1b
Results: Safe, capable of eliciting T-cell responses and epitope spread to novel antigens

samRNA[5]
Trial design: Phase 1
Results: Safe, feasible, and induced long-lasting neoantigen-specific CD8 T-cell responses

MAGE-A3[6]
Trial design: Randomized, phase 3
Results: No increase in DFS vs placebo

GM2-KLH[7]
Trial design: Randomized, intergroup trial
Results: HDI improved RFS and OS over GM2-KLH

gp100[8]
Trial design: Randomized, phase 3
Results: No difference in OS between ipilimumab alone or with gp100

DFS, disease-free survival; GM2, GM2 conjugated to keyhole limpet hemocyanin and administered with QS-21; gp100, glycoprotein 100; HDI, high-dose interferon alfa-2b; OS, overall survival; RFS, relapse-free survival; samRNA, self-amplifying messenger RNA; TAA, tumor-associated antigen.

1. Peng M, et al. *Mol Cancer*. 2019:18(1):128. 2. Ott PA, et al. *Nature*. 2017;547(7662):217-221. 3. Hu Z, et al. *Nat Med*. 2021;27(3):515-525. 4. Ott PA, et al. *Cell*. 2020;183(2):347-362.e24. 5. Palmer CD, et al. *Nat Med*. 2022;28(8):1619-1629. 6. Vansteenkiste JF, et al. *Lancet Oncol*. 2016;17(6):822-835. 7. Kirkwood JM, et al. *J Clin Oncol*. 2001;19(9):2370-2380. 8. Hodi FS, et al. *N Engl J Med*. 2010;363(8):711-723.

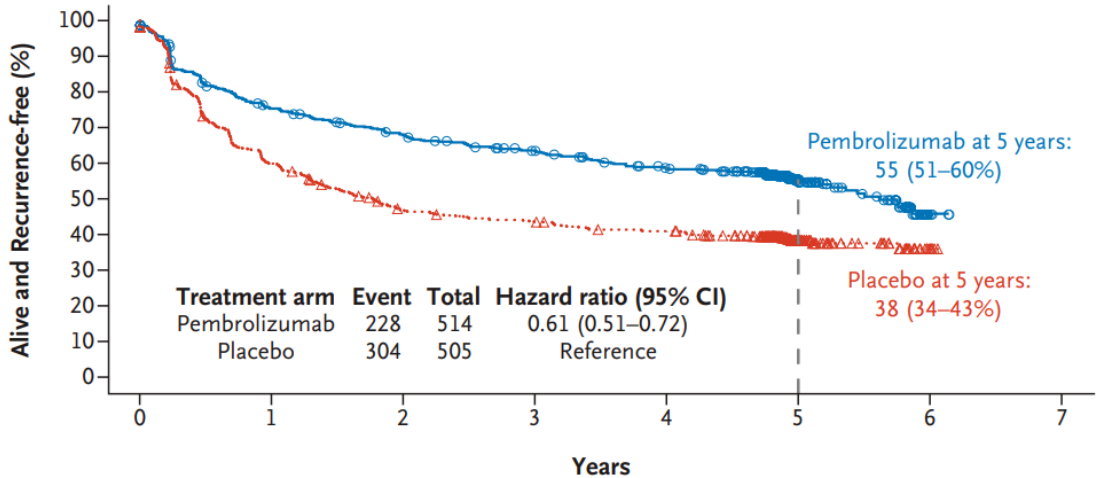
Immune Checkpoint Inhibitors Are Standard of Care Adjuvant Treatment for High-risk Resected Melanoma[1]

The **KEYNOTE-054** study showed sustained RFS improvement with adjuvant pembrolizumab versus placebo, with **5-year RFS rates** of 55.4% versus 38.3%[2,3]

4-year analysis of the **CHECKMATE-238** study showed RFS rates of 51.7% for nivolumab versus 41.2% for ipilimumab[4]; median RFS is 5 years

However, these analyses suggest an **unmet clinical need with high relapse rates** even with effective adjuvant melanoma therapy

KEYNOTE-054

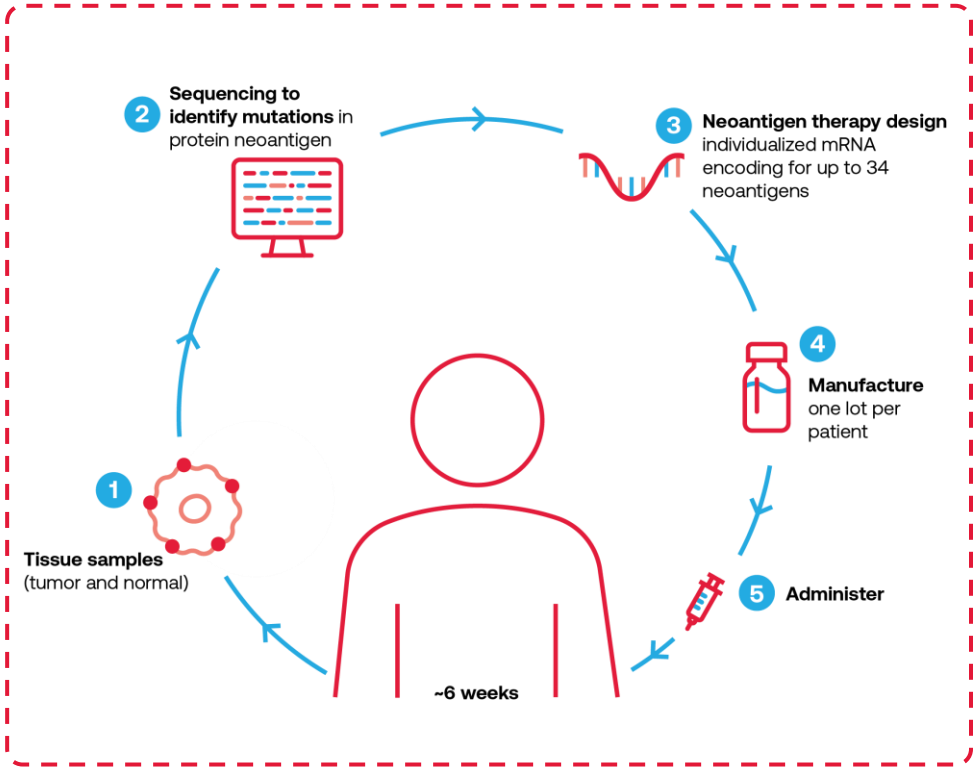


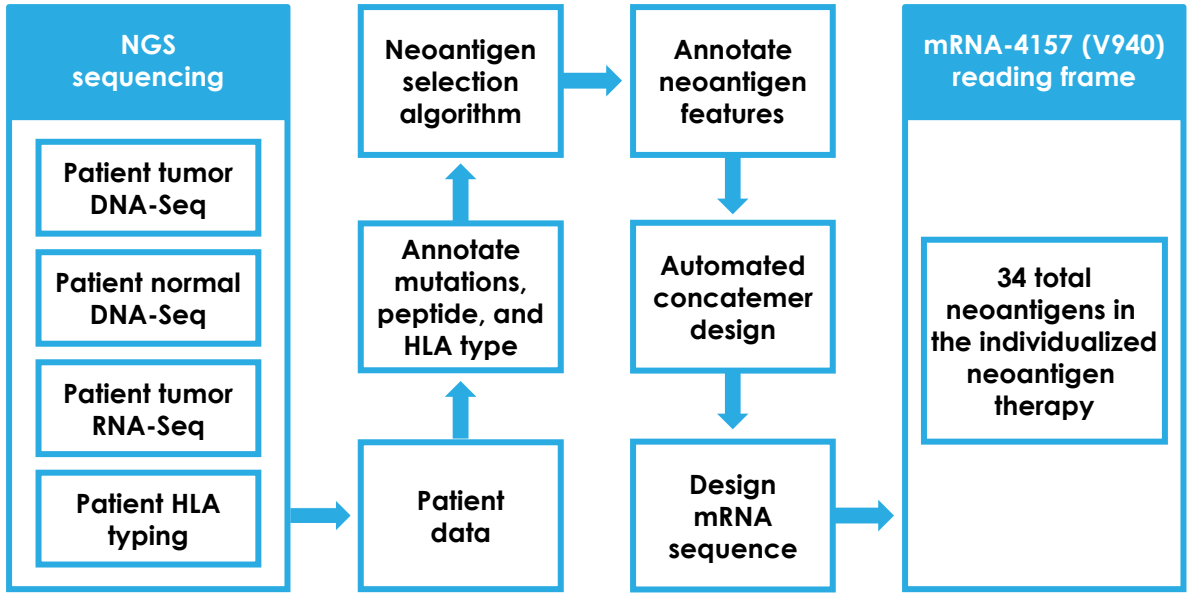
CI, confidence interval; RFS, recurrence-free survival.

1. Carlino, MS, et al. *Lancet.* 2021;398(10304):1002-1014. 2. Eggermont AMM, et al. *N Engl J Med*. 2018;378(19):1789-1801.
3. From New England Journal of Medicine Evidence, Eggermont AMM, et al., Five-Year Analysis of Adjuvant Pembrolizumab or Placebo in Stage III Melanoma. Volume No. 1(11). Copyright © 2022 Massachusetts Medical Society. Reprinted with permission from Massachusetts Medical Society. 4. Ascierto PA, et al. *Lancet Oncol.* 2020;21(11):1465-1477.

mRNA-4157 (V940): An Individualized Neoantigen Therapy (INT)

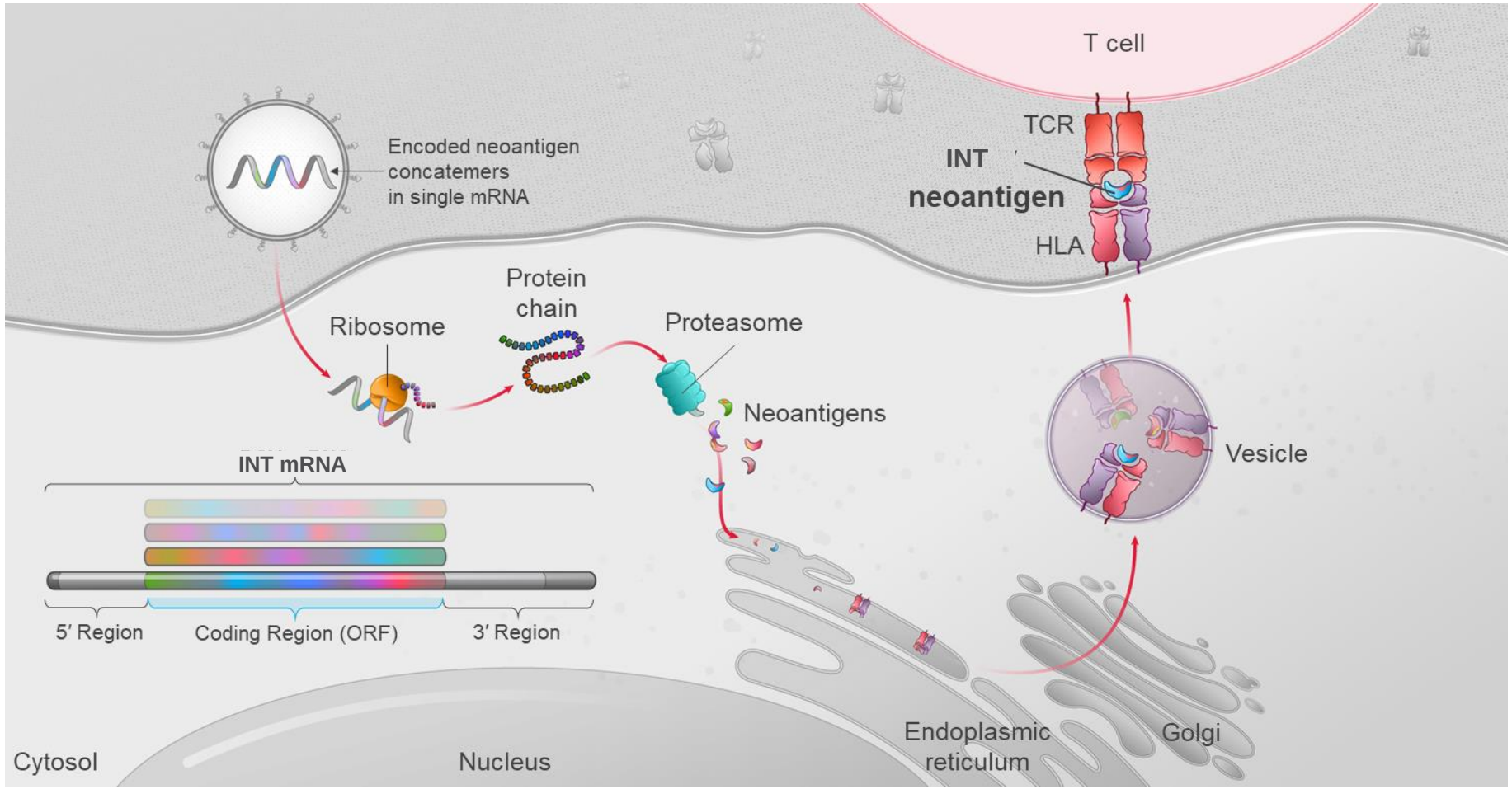
Designed to target an individual patient's unique tumor mutations through integrated manufacturing





DNA-Seq, DNA sequencing; HLA, human leukocyte antigen; mRNA, messenger RNA; NGS, next-generation sequencing; RNA-Seq, RNA sequencing.

mRNA-4157 (V940) Mechanism of Action



mRNA-4157 (V940) is a **customizable** individualized neoantigen therapy encoding up to 34 neoantigens

Targeting of neoantigens by T-cells has been demonstrated to **drive antitumor responses**[1]

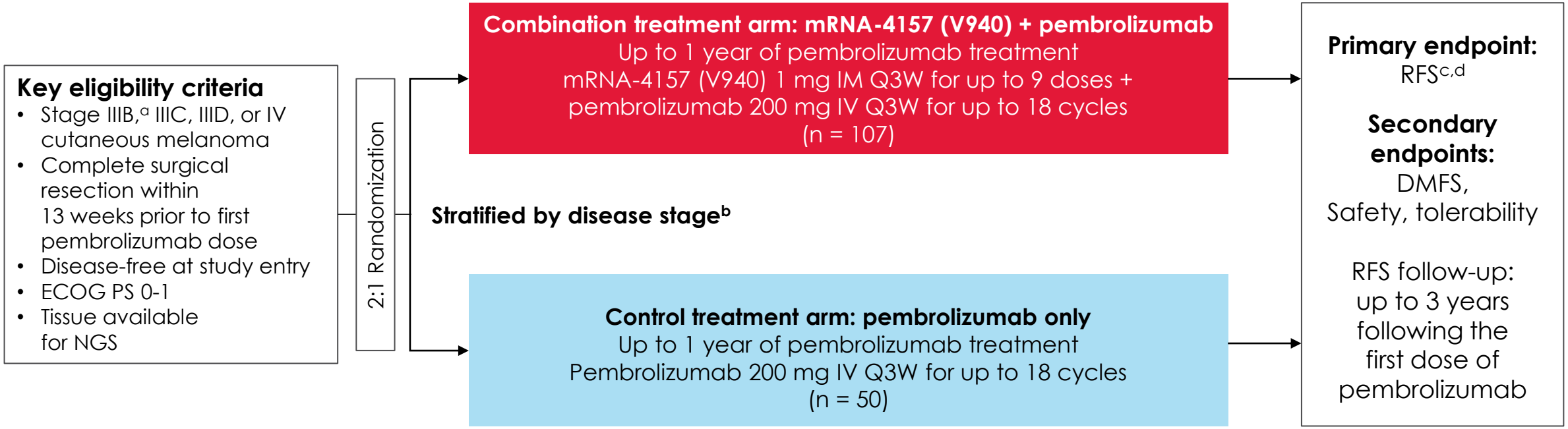
The modified mRNA **platform** was implemented for the COVID-19 vaccine (mRNA-1273), demonstrating its **utility and adaptability**[2]

HLA, human leukocyte antigen; mRNA, messenger RNA; ORF, open reading frame; PCV, personalized cancer vaccine; RFS, recurrence-free survival; TCR, T-cell receptor.

1. Wirth TC, Kühnel F. *Front Immunol*. 2017;8:1848. 2. Baden LR, et al. *N Engl J Med*. 2021;384(5):403-416.

mRNA-4157-P201/KEYNOTE-942 (NCT03897881) Study Design

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

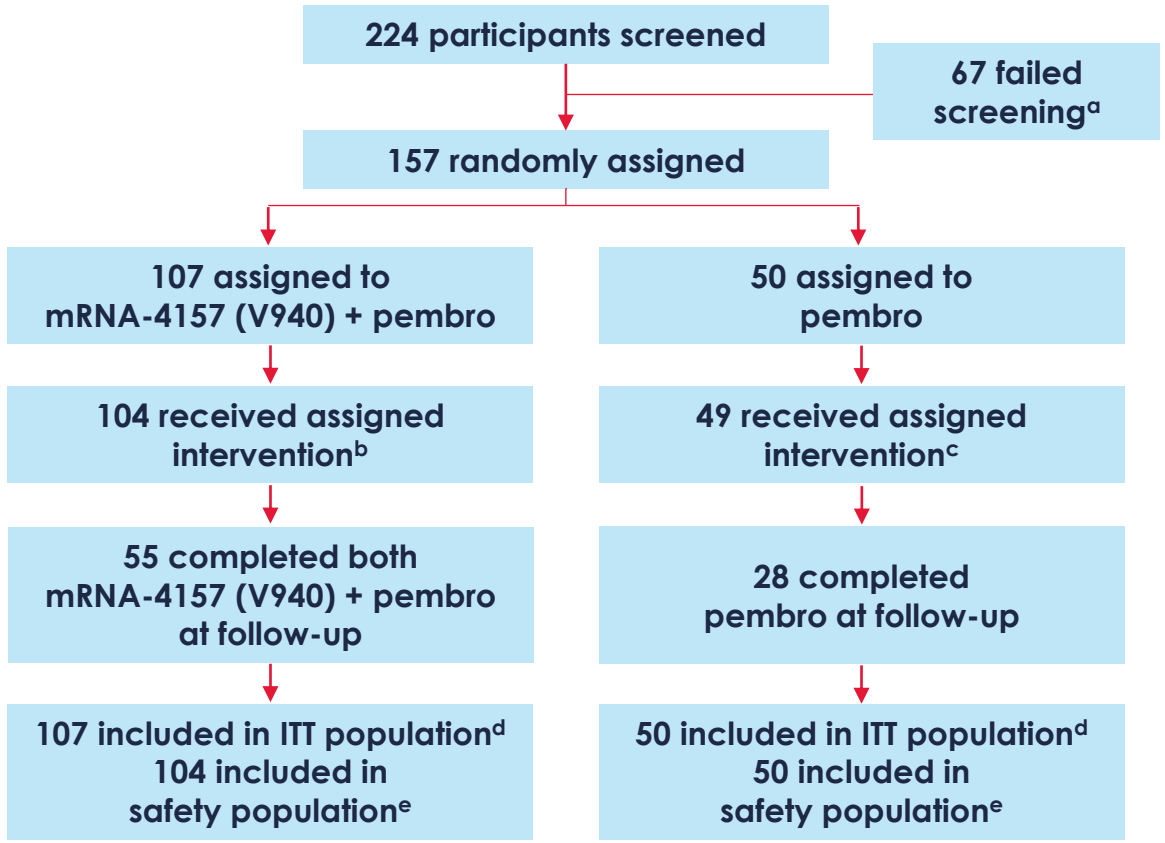


Designed with 80% power to detect an HR of 0.5 with ≥40 RFS events (with 1-sided alpha of 0.1)

Median follow-up[e]: 23 months for mRNA-4157 (V940) + pembrolizumab
24 months for pembrolizumab only

DMFS, distant metastasis-free survival; ECOG PS, Eastern Cooperative Oncology Group performance status; HR, hazard ratio; IM, intramuscular; IV, intravenous; mRNA, messenger RNA; NGS, next-generation sequencing; Q3W, every 3 weeks; RFS, recurrence-free survival.
[a]Patients with stage IIIB disease were eligible only if relapse occurred within 3 months of prior surgery of curative intent. [b]According to the 8th edition of the American Joint Committee on Cancer staging manual. [c]The primary endpoint was investigator-assessed RFS (defined as the time from first dose of pembrolizumab until the date of first recurrence [local, regional, or distant metastasis], a new primary melanoma, or death from any cause) in the intention-to-treat population. [d]The primary analysis for RFS was specified to occur after all patients completed ≥12 months on study and ≥40 RFS events were observed. Descriptive analysis specified to occur when ≥51 RFS events observed [e]Time of database cutoff was November 14, 2022.

Treatment Disposition



ITT, intention-to-treat; mRNA, messenger RNA; pembro, pembrolizumab.
[a]17 patients were not disease-free, 15 had inadequate tumor samples, 10 did not meet time requirements, 9 withdrew consent, 9 had incorrect stage, 4 had a history of other tumors, 2 had inadequate organ function, and 1 had a concurrent condition. [b]2 patients received no treatment because of a physician decision (n = 1) and ineligibility (n = 1), and 1 received only pembrolizumab because of inadequate tumor sample. [c]1 patient received no treatment because of withdrawal of consent. [d]The ITT population included all randomly assigned patients according to the intervention to which they were finally assigned. [e]The safety population included all randomly assigned patients who received ≥1 dose of treatment. The pembrolizumab safety group also included 1 patient who was randomized to the combination arm but only received pembrolizumab.

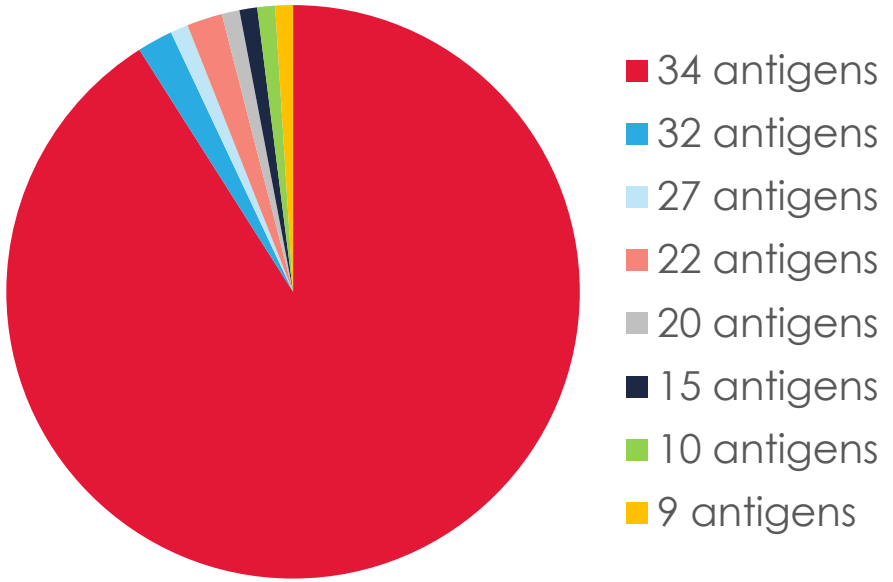
Individualized Neoantigen Therapy (INT) Characteristics

> 90% patients screened had tissue of sufficient quality/quantity for mRNA-4157 (V940) manufacture

mRNA-4157 (V940) was successfully prepared for > 99% patients in the combination arm

91% of patients in the combination arm had an INT with 34 neoantigens

The median number of neoantigens was 34 (range: 9-34)



Patient Demographics

	mRNA-4157 (V940) + pembro (n = 107)	pembro (n = 50)
Sex, n (%)		
Male	70 (65.4)	31 (62.0)
Female	37 (34.6)	19 (38.0)
Age		
Mean (SD)	61.3 (13.50)	59.4 (14.25)
Median (range)	63 (26-83)	61.5 (24-89)
Age group, n (%)		
<65 years	59 (55.1)	28 (56.0)
≥65 years	48 (44.9)	22 (44.0)
ECOG PS, n (%)[a]		
0	90 (84.1)	40 (80.0)
1	15 (14.0)	9 (18.0)
Stage, n (%)[b]		
Stage IIIC	89 (83.2)	42 (84.0)
Stage IIID	2 (1.9)	2 (4.0)
Stage IV	16 (15.0)	6 (12.0)

	mRNA-4157 (V940) + pembro (n = 107)	pembro (n = 50)
Number of prior cancer-related surgeries, n (%)		
1	41 (38.3)	24 (48.0)
2	36 (33.6)	18 (36.0)
≥3	30 (28.0)	8 (16.0)
LDH, U/L		
Median (range)	189.5 (118-528)	185.5 (113-1180)
>ULN, n (%)	5 (4.7)	3 (6.0)
PD-L1 status, n (%)		
Positive	69 (64.5)	27 (54.0)
Negative	13 (12.1)	5 (10.0)
Indeterminant[c]	25 (23.4)	18 (36.0)
Tumor mutational burden, n (%)[d]		
<10 mutations/Mb	**26 (24.3)**	**19 (38.0)**
≥10 mutations/Mb	**79 (73.8)**	**30 (60.0)**

ECOG PS, Eastern Cooperative Oncology Group performance status; LDH, lactate dehydrogenase; Mb, megabase; mRNA, messenger RNA; PD-L1, programmed death ligand-1; pembro, pembrolizumab; SD, standard deviation; ULN, upper limit of normal.

[a]Three patients were not treated and therefore, had no baseline ECOG PS. [b]According to the 8th edition of the American Joint Committee on Cancer staging manual. [c]Patients for whom there was no sample to send for PD-L1 evaluation or for whom sample quality or quantity was too low to perform the assay. [d]Available for 154 patients

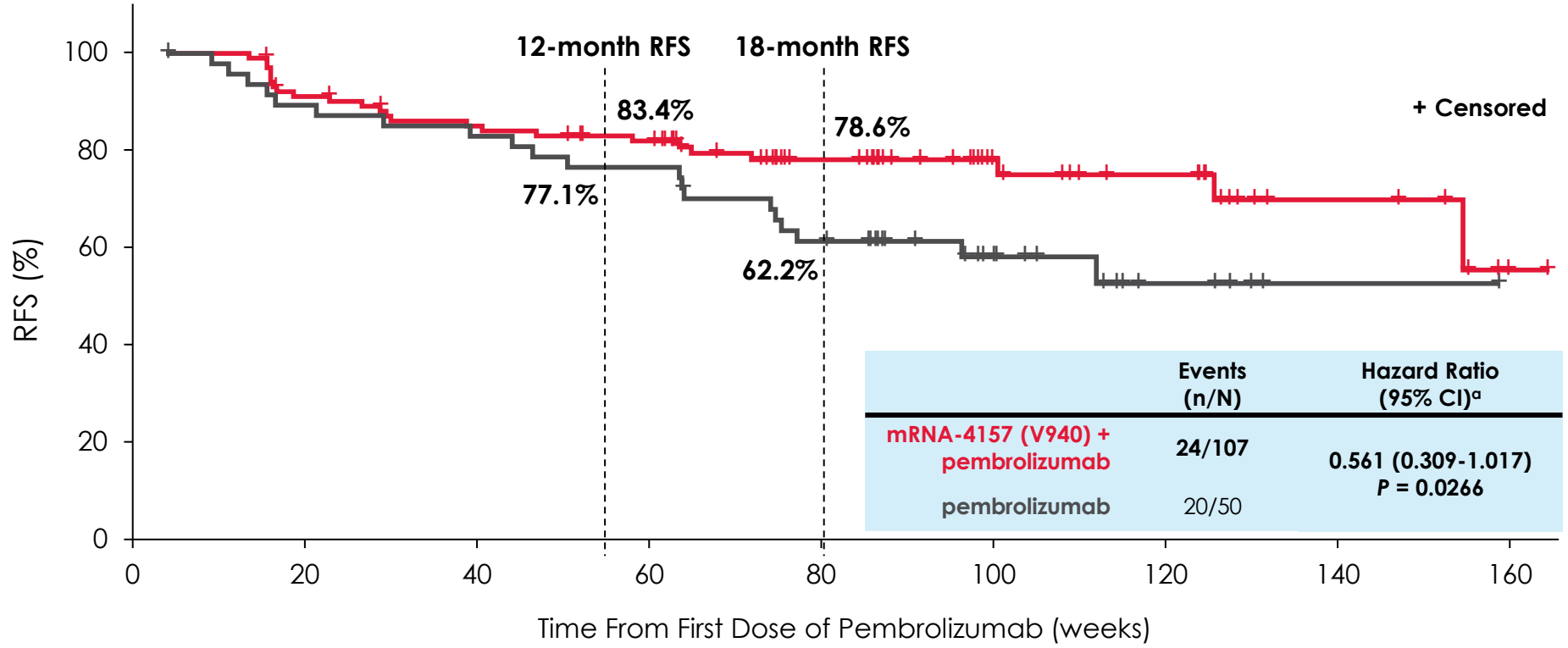
BRAF status was not available at the time of presentation but will be presented in the future.

Safety and Tolerability reflects individual components with infrequent additional clinically significant adverse events over pembro alone

	mRNA-4157 (V940) + pembro (n=104)		pembro (n=50)	
Event, n (%)	**Any grade**	**Grade ≥3**	**Any grade**	**Grade ≥3**
Any AE	104 (100.0)	36 (34.6)	47 (94.0)	18 (36.0)
Any treatment-related AE	104 (100.0)	26 (25.0)	41 (82.0)	9 (18.0)
Serious AE[a]	**15 (14.4)**		**5 (10.0)**	
Immune-mediated AEs	**37 (35.6)**	**11 (10.6)**	**18 (36.0)**	**7 (14.0)**
mRNA-4157 (V490) or combination-related AEs[b] occurring in >20% of patients				
Any	98 (94.2)	**12 (11.5)**	-	-
Fatigue	63 (60.6)	5 (4.8)	-	-
Injection site pain	58 (55.8)	0	-	-
Chills	52 (50.0)	0	-	-
Pyrexia	50 (48.1)	1 (1.0)	-	-
Headache	33 (31.7)	0	-	-
Injection site erythema	33 (31.7)	0	-	-
Influenza-like illness	32 (30.8)	0	-	-
Nausea	26 (25.0)	0	-	-
Myalgia	22 (21.2)	1 (1.0)	-	-
pembro or combination related AEs[c] occurring in >20% of patients				
Any	101 (97.1)	24 (23.1)	41 (82.0)	9 (18.0)
Fatigue	72 (69.2)	6 (5.8)	20 (40.0)	0
Diarrhea	31 (29.8)	2 (1.9)	5 (10.0)	0
Pruritus	30 (28.8)	0	10 (20.0)	0
Nausea	23 (22.1)	0	5 (10.0)	0
Chills	22 (21.2)	0	1 (2.0)	0
Pyrexia	22 (21.2)	0	0	0

AE, adverse event; mRNA, messenger RNA. Safety analyses were conducted in the safety population, which was defined as all randomly assigned patients who received ≥1 dose of treatment. Grading per National Cancer Institute Common Terminology Criteria for Adverse Events version 5.0. [a]Serious AEs included grade 1 fever, attributed to mRNA-4157, and grade 3 muscular weakness and grade 3 autoimmune nephritis, attributed to both mRNA-4157 (V940) and pembrolizumab. [b]mRNA-4157 (V940) treatment-related AEs included events attributed by the investigator to mRNA-4157 (V940) alone as well as events attributed to both mRNA-4157 (V940) and pembrolizumab. [c]AEs related to pembrolizumab include events attributed by the investigator to pembrolizumab alone and events attributed to both mRNA-4157 (V940) and pembrolizumab.

mRNA-4157 (V940) and pembrolizumab demonstrated an improvement in recurrence-free survival (RFS) vs pembrolizumab



	Events (n/N)	Hazard Ratio (95% CI)[a]
mRNA-4157 (V940) + pembrolizumab	24/107	0.561 (0.309-1.017) *P* = 0.0266
pembrolizumab	20/50	

Number at Risk

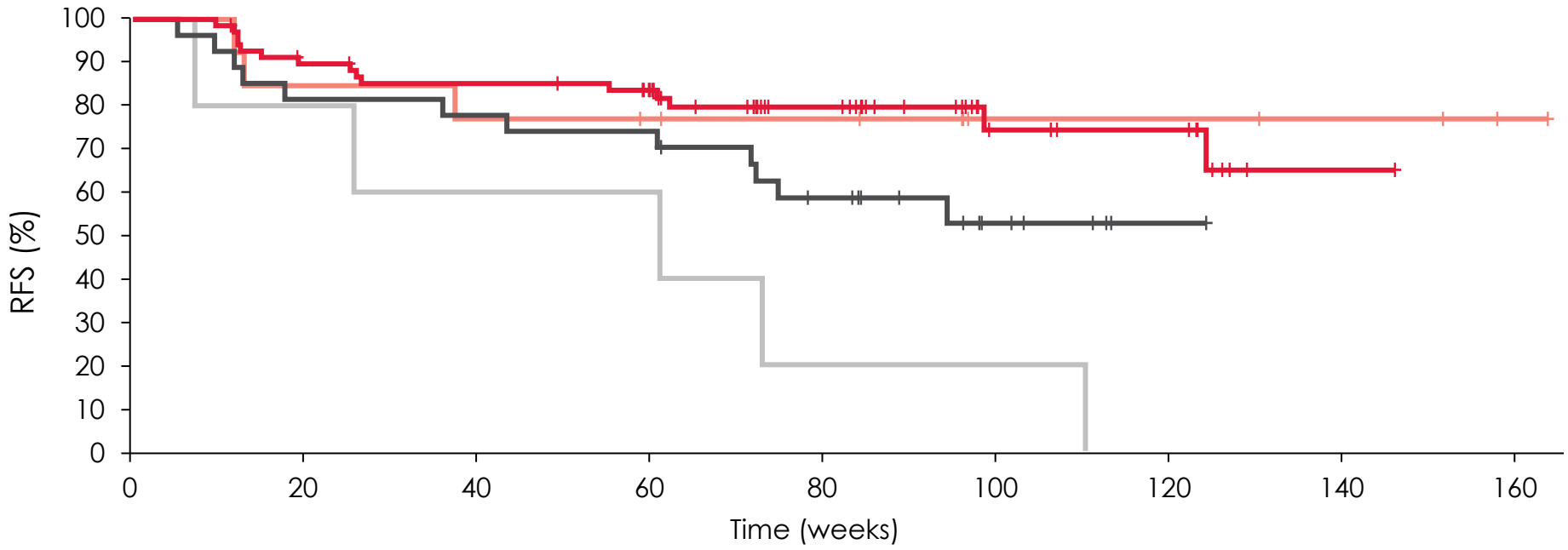
mRNA-4157 (V940) + pembrolizumab	107	92	85	73	49	24	20	8	1
pembrolizumab	50	42	40	37	28	13	6	1	0

CI, confidence interval; mRNA, messenger RNA; RFS, recurrence-free survival.

[a]The hazard ratio and 95% CI for mRNA-4157 (V940) plus pembrolizumab versus pembrolizumab is estimated using a Cox proportional hazards model with treatment group as a covariate, stratified by disease stage (stages IIIB or IIIC or IIID vs stage IV) used for randomization. The *P* value is based on a 1-sided log-rank test stratified by disease stage (stages IIIB or IIIC or IIID vs stage IV) used for randomization.

mRNA-4157 (V940) and pembrolizumab combination treatment demonstrated an improvement in RFS irrespective of PD-L1 status

RFS by treatment arm stratified by PD-L1–positive and PD-L1–negative subgroups



Number at Risk

PD-L1–neg: pembrolizumab	5	4	3	3	1	1	0	0	0
PD-L1–neg: mRNA-4157 (V940) + pembrolizumab	13	11	10	9	8	4	4	3	1
PD-L1–pos: pembrolizumab	27	22	21	20	14	6	1	0	0
PD-L1–pos: mRNA-4157 (V940) + pembrolizumab	69	60	56	48	29	13	11	2	0

mRNA, messenger RNA; neg, negative; PD-L1, programmed death ligand-1; pos, positive; RFS, recurrence-free survival.

Next Steps

Additional analyses to include **distant metastasis-free survival, treatment outcomes by *BRAF* status,** and **other translational analyses as well as RFS with ≥ 51 events**,

Longer follow-up with mRNA-4157-P201/KEYNOTE-942 to evaluate **durability**

A phase 3 study to confirm these results will be initiated in patients with high-risk resected melanoma **in 2023**

Expanded clinical studies to include **additional tumor types**, such as NSCLC

Session Title: Phase II Clinical Trials 2
Tuesday Apr 18, 2023
9:00 AM - 12:30 PM

"mRNA-4157, a personalized cancer vaccine, in combination with pembrolizumab, demonstrates trend for improved recurrence free survival compared to pembrolizumab alone in adjuvant melanoma patients across tumor mutational burden subgroups"

mRNA, messenger RNA; NSCLC, non-small cell lung cancer.

Conclusions

mRNA-4157 (V940) and pembrolizumab demonstrated a **clinically significant improvement in RFS** compared to standard of care pembrolizumab in high-risk resected melanoma, with a **44% reduction in the risk of recurrence or death** with 2 years of follow-up

mRNA-4157-P201/KEYNOTE-942 is the **first randomized trial** to **demonstrate improvement** in recurrence-free survival with **an individualized neoantigen vaccine approach**

mRNA-4157 (V940) in combination with pembrolizumab was **well-tolerated without increased** grade 3-4 immune mediated or serious AEs compared with pembrolizumab alone

mRNA-4157 (V940) in combination with pembrolizumab received **Breakthrough Therapy Designation** from FDA in February 2023 and **PRIME Designation** from EMA in April 2023

AE, adverse event; mRNA, messenger RNA; RFS, recurrence-free survival.

Acknowledgments

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- The patients and their families, along with all of the site staff
- The personnel at all of our vendors and collaborators
- The scientists, regulatory, operations, and manufacturing teams who discovered, improved, and enabled mRNA-4157 (V940)

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Thank you

Session Title: Phase II Clinical Trials 2
Tuesday Apr 18, 2023
9:00 AM - 12:30 PM

"mRNA-4157, a personalized cancer vaccine, in combination with pembrolizumab, demonstrates trend for improved recurrence free survival compared to pembrolizumab alone in adjuvant melanoma patients across tumor mutational burden subgroups"

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Abstract: Background

mRNA-4157, a personalized cancer vaccine, in combination with pembrolizumab, demonstrates trend for improved recurrence free survival compared to pembrolizumab alone in adjuvant melanoma patients across tumor mutational burden subgroups

Tumor immunogenicity provides a favorable landscape for inflammatory processes associated with clinical benefit to checkpoint inhibitors (ICI) and tumor mutational burden (TMB) has been shown to be an independent predictor of treatment outcomes in patients treated with ICI therapy.

Here we report analyses of baseline biopsies from the trial to explore the novel mechanism of action hypothesized to augment endogenous anti-tumor responses and generate immunity to additional tumor neoantigens.

Abstract: Methods

mRNA-4157, a personalized cancer vaccine, in combination with pembrolizumab, demonstrates trend for improved recurrence free survival compared to pembrolizumab alone in adjuvant melanoma patients across tumor mutational burden subgroups

Paraffin-embedded formalin-fixed baseline tumor core biopsies underwent whole exome sequencing (WES) and whole transcriptome sequencing.

According to the established WES genomic score for pembrolizumab, the TMB high threshold utilized for analysis was 175/exome (10 mutations/megabase per F1CDx).

The distribution of TMB expression in baseline tumor samples across study arms and their association with the primary RFS endpoint was evaluated.

The association with RFS of other markers of inflamed tumors, including those established for pembrolizumab (e.g. gene expression profile (GEP) and PD-L1 expression) was also assessed.

Abstract: Results

mRNA-4157, a personalized cancer vaccine, in combination with pembrolizumab, demonstrates trend for improved recurrence free survival compared to pembrolizumab alone in adjuvant melanoma patients across tumor mutational burden subgroups

The RFS benefit of mRNA-4157 and pembrolizumab combination compared to pembrolizumab monotherapy observed in the intention-to-treat population was maintained with a similar treatment effect magnitude across both high (HR = 0.65; 95% CI: 0.3, 1.5) and low (HR = 0.59; 95% CI: 0.3,1.4) TMB subpopulations.

In line with observations from historical data for pembrolizumab, improved RFS was observed in high TMB compared to low TMB patient subgroups in the pembrolizumab monotherapy arm. The trend for increased RFS benefit in the high TMB subpopulation was maintained in the mRNA-4157 and pembrolizumab study arm.

Additional subgroup analyses (e.g. GEP and PD-L1) were assessed and will be discussed.

Abstract: Conclusions

mRNA-4157, a personalized cancer vaccine, in combination with pembrolizumab, demonstrates trend for improved recurrence free survival compared to pembrolizumab alone in adjuvant melanoma patients across tumor mutational burden subgroups

Our results indicate that mRNA-4157 demonstrates improvements in RFS irrespective of TMB status when administered in combination with pembrolizumab compared to pembrolizumab monotherapy in patients with resected high-risk cutaneous melanoma.

The novel mechanism of action of mRNA-4157 may both deepen the activity of pembrolizumab and broaden the population of patients that can benefit from immune therapy. The association between TMB and mRNA-4157 treatment effect will be further explored in upcoming planned studies.

Thank you

Forward-looking statements

This presentation contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995, as amended, including regarding clinical studies and the ability of mRNA-4157 to target an individual patient's unique tumor mutations; the potential for neoantigen-based therapies to overcome limitations of previous failed cancer vaccine approaches; and plans to initiate a Phase 3 study of mRNA-4157 in adjuvant melanoma in 2023 and rapidly expand to additional tumor types, including non-small cell lung cancer. In some cases, forward-looking statements can be identified by terminology such as "may," "should," "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 those described in Moderna's most recent Annual Report on Form 10-K filed with the U.S. Securities and Exchange Commission (SEC) and in subsequent filings made by Moderna with 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 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 referenced on the first page.