MCM Tampa Bay Edition: January 2024
Fostering Multidisciplinary Care in the Era of Complex Cancer Treatments

Neoantigen Vaccines for Melanoma:
Déjà Vu All Over Again?

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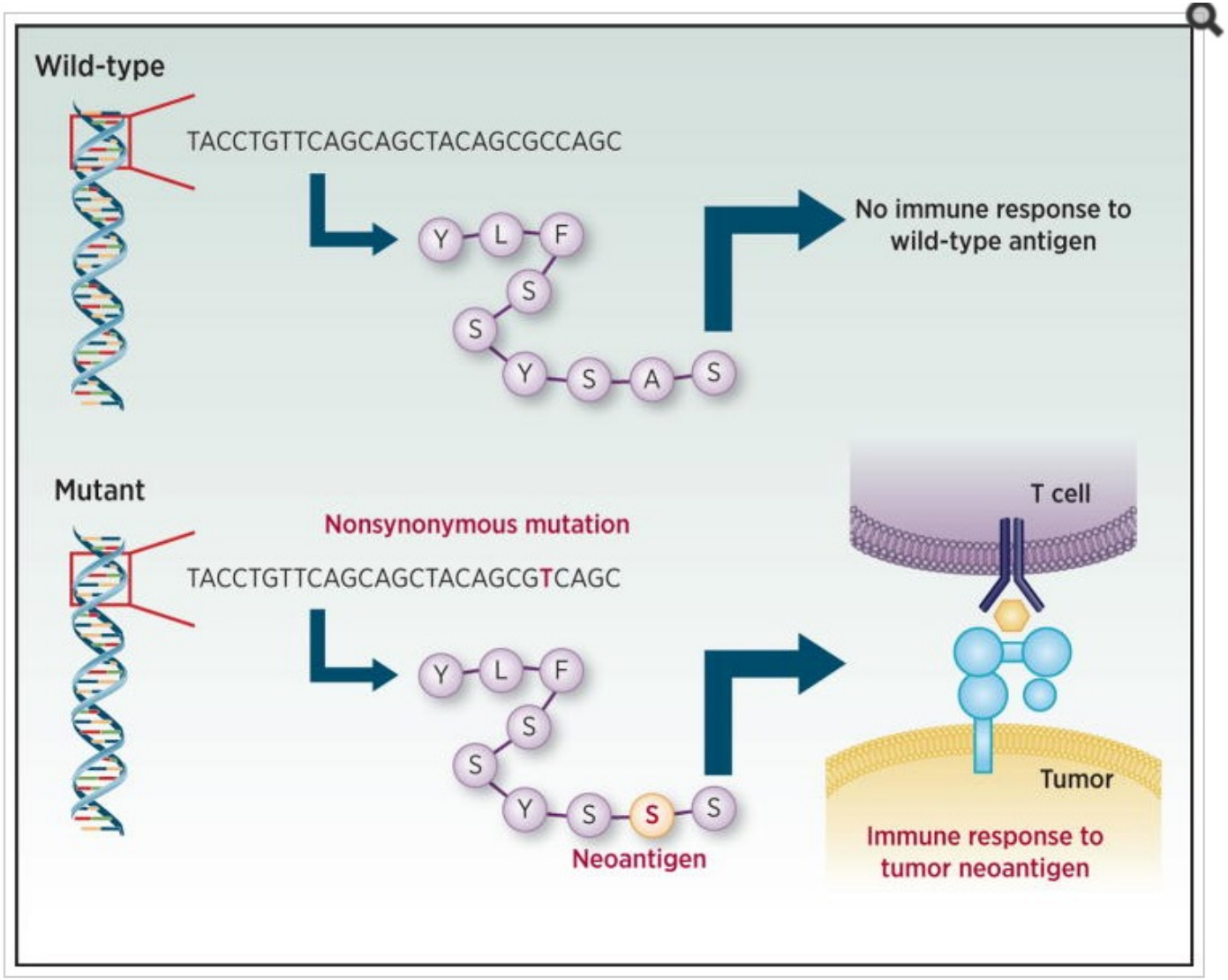
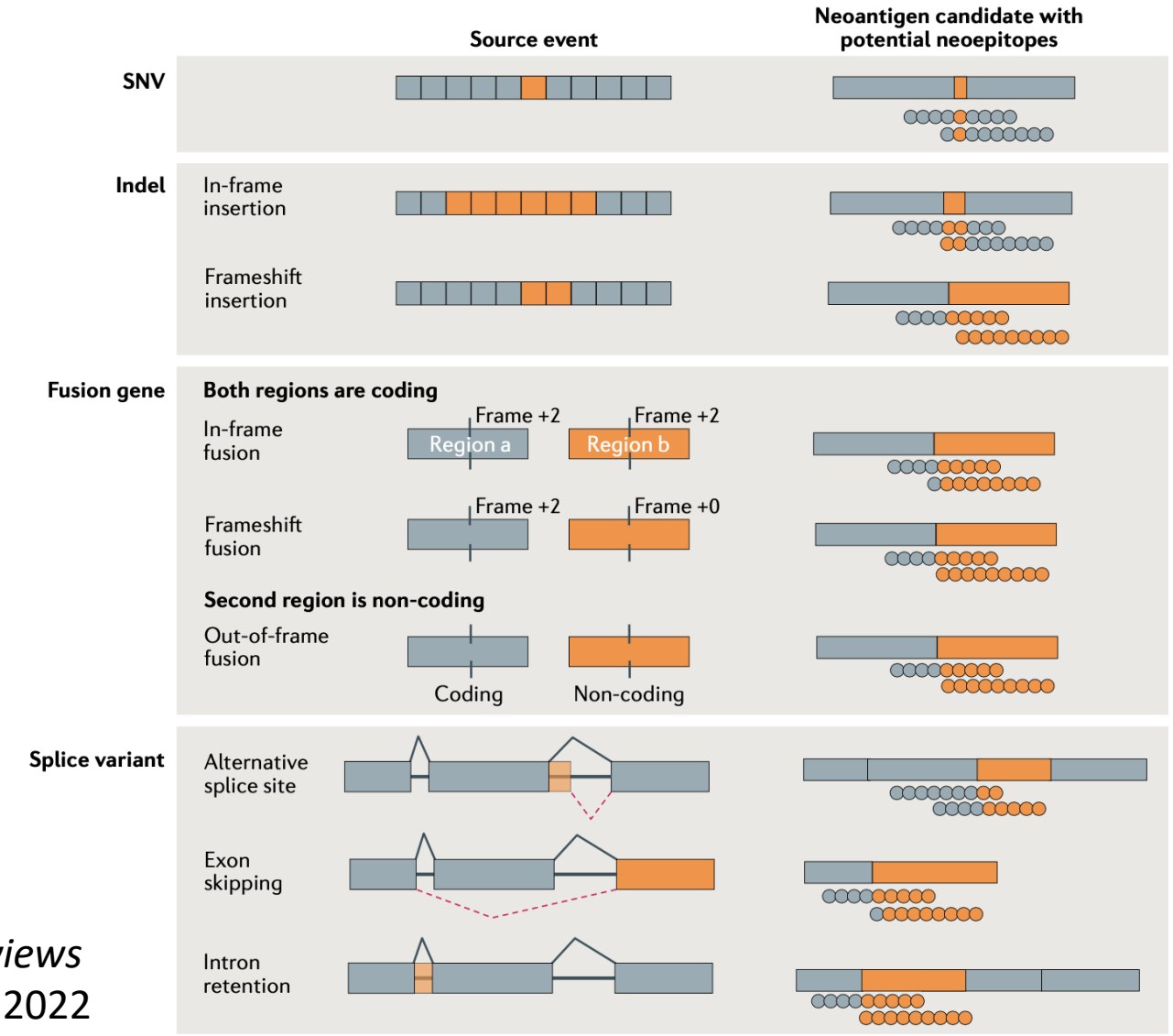
What are neoantigens? They are <u>usually</u> generated by mutations within tumors, not present in normal tissue



Clin Cancer Res. 2016 Dec 1; 22(23): 5642–5650.

Not all neoantigens are single nucleotide variants!



Lang F et al. *Nature Reviews Drug Discovery.* 21:261 2022

What is the direct clinical evidence that neoantigens are tumor rejection antigens in humans?

Cancer Immunotherapy Based on Mutation-Specific CD4+ T Cells in a Patient with Epithelial Cancer

Eric Tran,[1] Simon Turcotte,[1]* Alena Gros,[1] Paul F. Robbins,[1] Yong-Chen Lu,[1] Mark E. Dudley,[1]† John R. Wunderlich,[1] Robert P. Somerville,[1] Katherine Hogan,[1] Christian S. Hinrichs,[1] Maria R. Parkhurst,[1] James C. Yang,[1] Steven A. Rosenberg[1]‡

Limited evidence exists that humans mount a mutation-specific T cell response to epithelial cancers. We used a whole-exomic-sequencing-based approach to demonstrate that tumor-infiltrating lymphocytes (TIL) from a patient with metastatic cholangiocarcinoma contained CD4+ T helper 1 (T_H1) cells recognizing a mutation in erbb2 interacting protein (ERBB2IP) expressed by the cancer. After adoptive transfer of TIL containing about 25% mutation-specific polyfunctional T_H1 cells, the patient achieved a decrease in target lesions with prolonged stabilization of disease. Upon disease progression, the patient was retreated with a >95% pure population of mutation-reactive T_H1 cells and again experienced tumor regression. These results provide evidence that a CD4+ T cell response against a mutated antigen can be harnessed to mediate regression of a metastatic epithelial cancer.

Tran E et al. *Science* 344:641 2014

The evolution of neoantigen vaccines

LETTER

doi:10.1038/nature22991

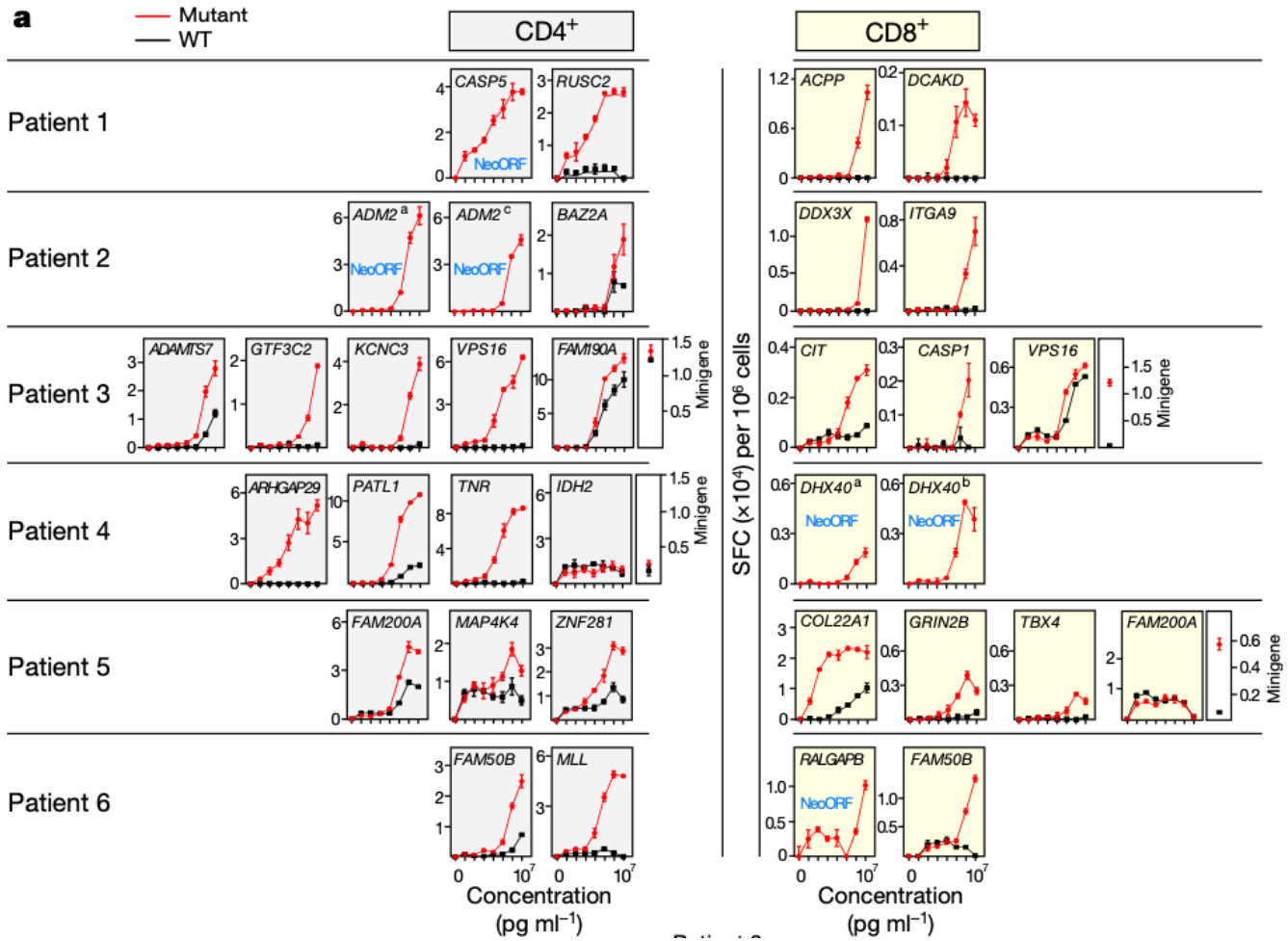
An immunogenic personal neoantigen vaccine for patients with melanoma

Patrick A. Ott[1,2,3]*, Zhuting Hu[1]*, Derin B. Keskin[1,3,4], Sachet A. Shukla[1,4], Jing Sun[1], David J. Bozym[1], Wandi Zhang[1], Adrienne Luoma[5], Anita Giobbie-Hurder[6], Lauren Peter[7,8], Christina Chen[1], Oriol Olive[1], Todd A. Carter[4], Shuqiang Li[4], David J. Lieb[4], Thomas Eisenhaure[4], Evisa Gjini[9], Jonathan Stevens[10], William J. Lane[10], Indu Javeri[11], Kaliappanadar Nellaiappan[11], Andres M. Salazar[12], Heather Daley[1], Michael Seaman[7], Elizabeth I. Buchbinder[1,2,3], Charles H. Yoon[3,13], Maegan Harden[4], Niall Lennon[4], Stacey Gabriel[4], Scott J. Rodig[9,10], Dan H. Barouch[3,7,8], Jon C. Aster[3,10], Gad Getz[3,4,14], Kai Wucherpfennig[3,5], Donna Neuberg[6], Jerome Ritz[1,2,3], Eric S. Lander[3,4], Edward F. Fritsch[1,4]†, Nir Hacohen[3,4,15] & Catherine J. Wu[1,2,3,4]

8 patients NED at baseline, 4 remained NED at median of 25 months; 2 recurrent patients had a CR with PEMBRO

Ott P et al. *Nature* 547: 217 2017

Vaccine-induced T cells discriminate mutated vs wild-type antigens and detect endogenously processed and presented peptides



Ott P et al. *Nature* 547: 217 2017

Strong selectivity for MT vs WT peptides

LETTER

doi:10.1038/nature23003

Personalized RNA mutanome vaccines mobilize poly-specific therapeutic immunity against cancer

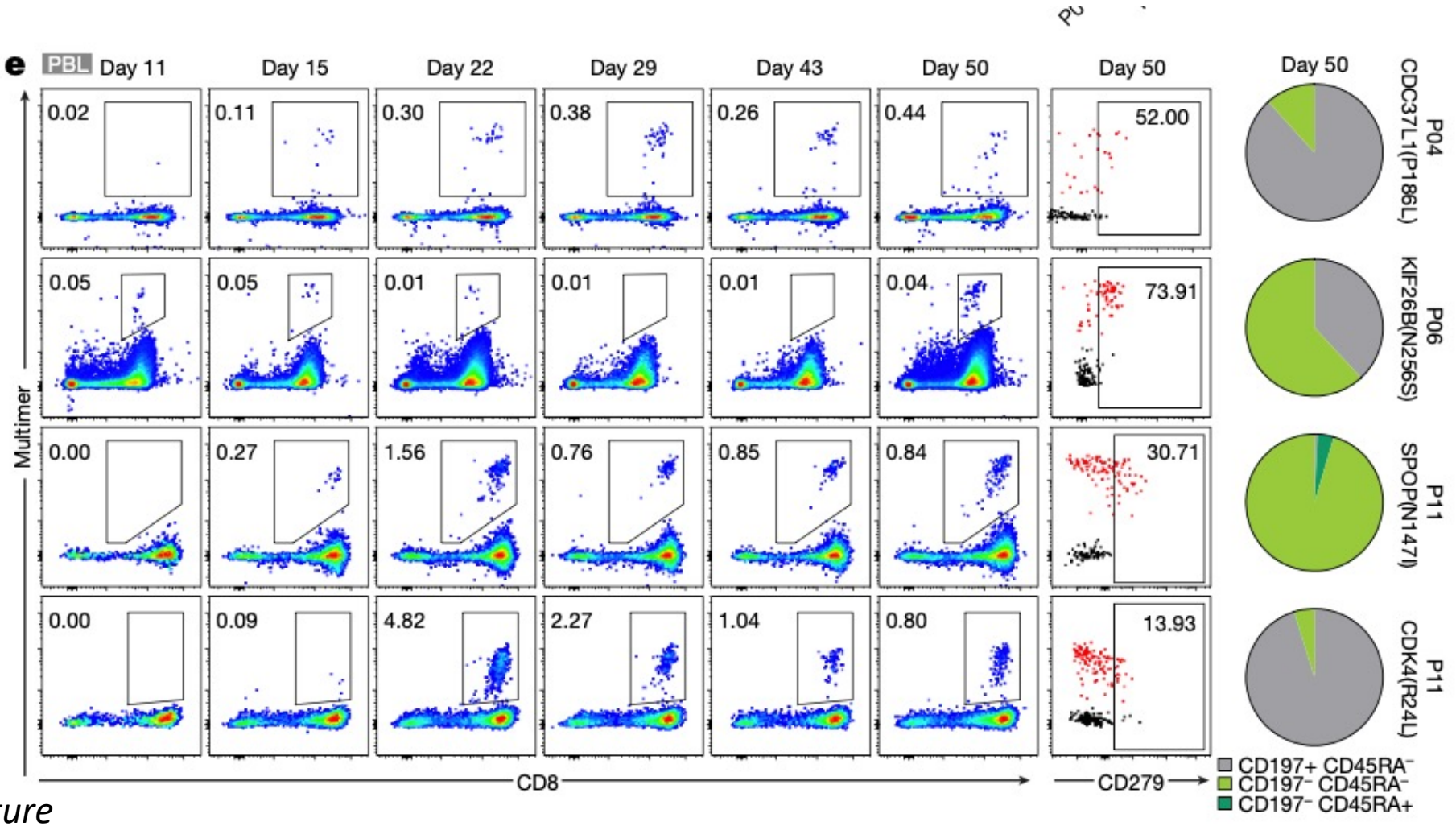
Ugur Sahin[1,2,3], Evelyna Derhovanessian[1], Matthias Miller[1], Björn-Philipp Kloke[1], Petra Simon[1], Martin Löwer[2], Valesca Bukur[1,2], Arbel D. Tadmor[2], Ulrich Luxemburger[1], Barbara Schrörs[2], Tana Omokoko[1], Mathias Vormehr[1,3], Christian Albrecht[2], Anna Paruzynski[1], Andreas N. Kuhn[1], Janina Buck[1], Sandra Heesch[1], Katharina H. Schreeb[1], Felicitas Müller[1], Inga Ortseifer[1], Isabel Vogler[1], Eva Godehardt[1], Sebastian Attig[2,3], Richard Rae[2], Andrea Breitkreuz[1], Claudia Tolliver[1], Martin Suchan[2], Goran Martic[2], Alexander Hohberger[3], Patrick Sorn[2], Jan Diekmann[1], Janko Ciesla[4], Olga Waksmann[4], Alexandra-Kemmer Brück[1], Meike Witt[1], Martina Zillgen[1], Andree Rothermel[2], Barbara Kasemann[2], David Langer[1], Stefanie Bolte[1], Mustafa Diken[1,2], Sebastian Kreiter[1,2], Romina Nemecek[5], Christoffer Gebhardt[6,7], Stephan Grabbe[3], Christoph Höller[5], Jochen Utikal[6,7], Christoph Huber[1,2,3], Carmen Loquai[3]* & Özlem Türeci[8]*

13 patients, 102 days median prep time

Sahin U et al *Nature*
547:222. 2017

Rapid expansion of neo-epitope- specific T cells with central and effector memory phenotypes by vaccination.

8/13 patients were NED, 5 had metastases; 2 responses seen of 5



Some responses occurred by 2-4 weeks

Sahin U et al *Nature* 547:222. 2017

nature medicine

ARTICLES

https://doi.org/10.1038/s41591-020-01206-4

Check for updates

Personal neoantigen vaccines induce persistent memory T cell responses and epitope spreading in patients with melanoma

Zhuting Hu[1,20], Donna E. Leet[1,2,20], Rosa L. Allesøe[3,20], Giacomo Oliveira[1], Shuqiang Li[4,5], Adrienne M. Luoma[6], Jinyan Liu[7], Juliet Forman[1,4,5], Teddy Huang[5], J. Bryan Iorgulescu[1,2,8], Rebecca Holden[9], Siranush Sarkizova[4], Satyen H. Gohil[1,4,10], Robert A. Redd[11], Jing Sun[1], Liudmila Elagina[4], Anita Giobbie-Hurder[11], Wandi Zhang[1], Lauren Peter[7], Zoe Ciantra[12], Scott Rodig[8,12], Oriol Olive[1], Keerthi Shetty[1], Jason Pyrdol[6], Mohamed Uduman[11,12], Patrick C. Lee[1,2], Pavan Bachireddy[1,2,4,13], Elizabeth I. Buchbinder[1,2,13], Charles H. Yoon[2,14], Donna Neuberg[11], Bradley L. Pentelute[4,9,15], Nir Hacohen[2,4,16], Kenneth J. Livak[1,5], Sachet A. Shukla[1,4,5], Lars Rønn Olsen[17,18], Dan H. Barouch[2,7,19], Kai W. Wucherpfennig[2,6], Edward F. Fritsch[1,4], Derin B. Keskin[1,4,5], Catherine J. Wu[1,2,4,13,21] and Patrick A. Ott[1,2,4,13,21] ✉

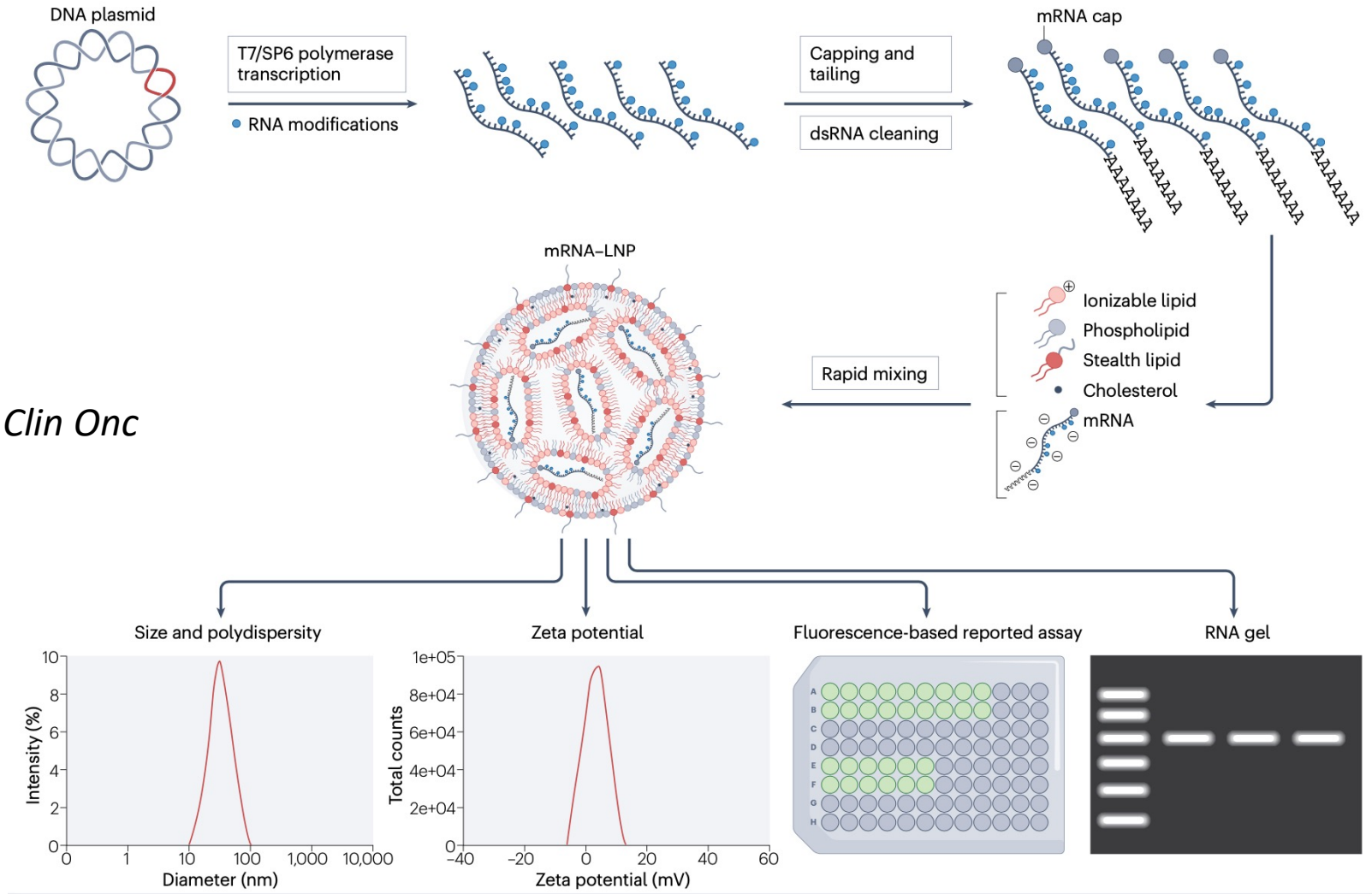
5 of 8 patients relapsed after vaccination

Hu Z et al *Nat Med* 27:515 2021

What were the hurdles to overcome with mRNA vaccines?

- Negatively charged phosphodiester backbone makes it hard to cross cell membranes
  - Lipid nanoparticle encasement to neutralize the RNA charge
- RNAses are ubiquitous and destroy RNA
  - Lipid nanoparticle encasement to protect the molecule
- RNA molecules elicit immune responses
  - Substitute N1-methylated pseudouridine for uridine to stabilize, increase protein production and decrease inflammatory reactivity via TLR7/8
  - N1-methylated pseudouridine also protects RNA from enzymatic degradation

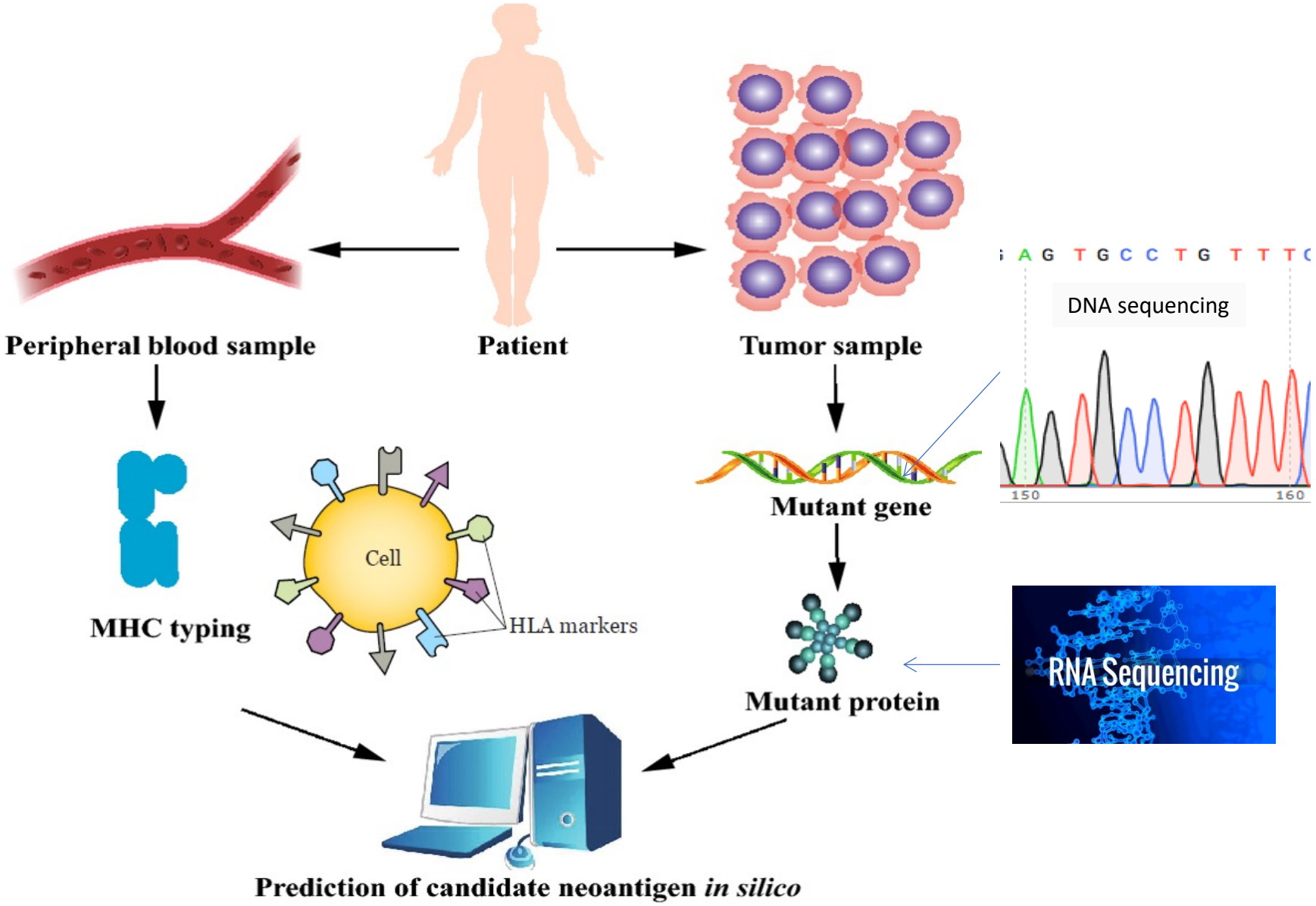
Generation of mRNA–vaccine lipid nanoparticles



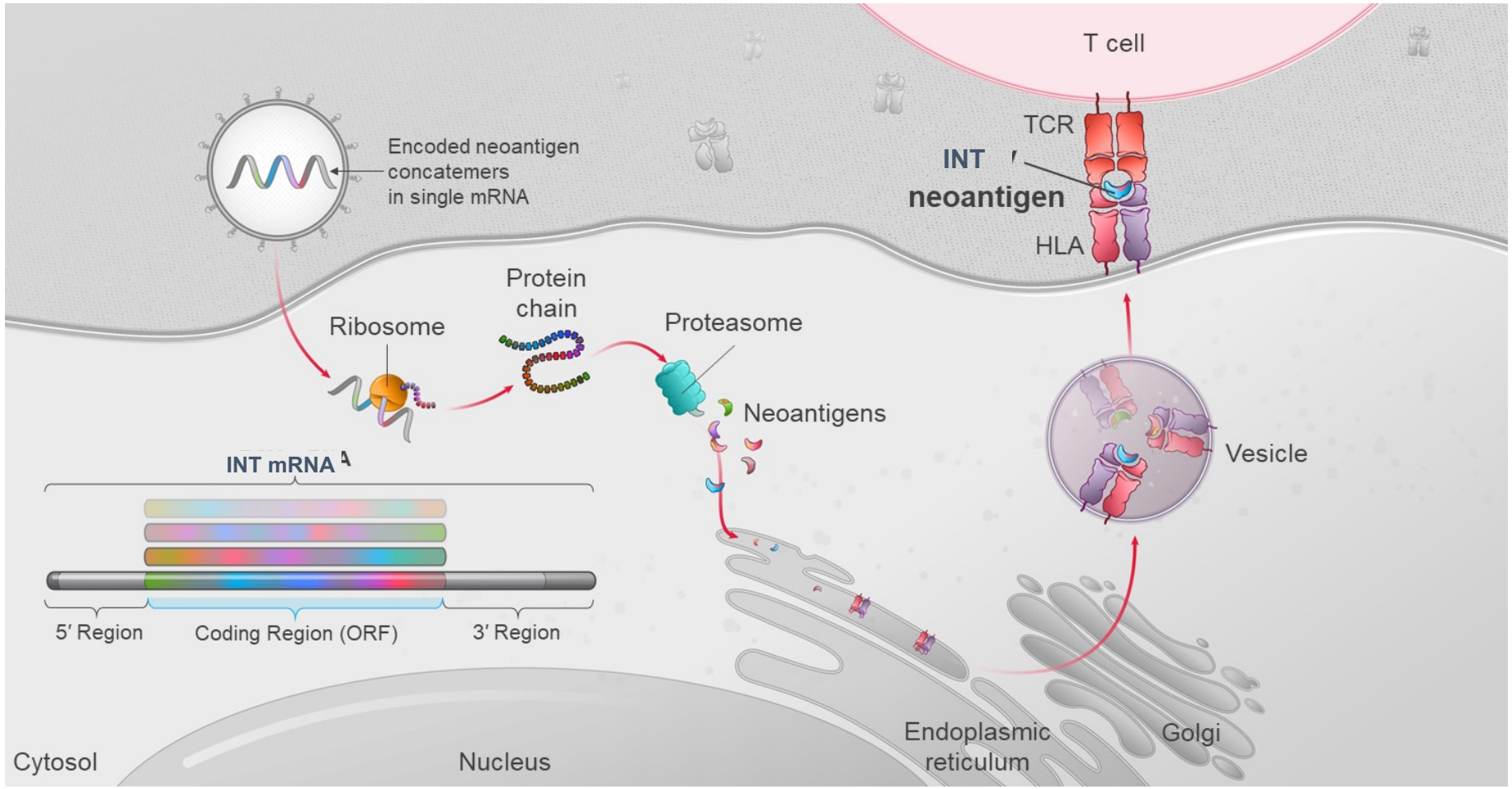
Kon E et al *Nat Rev Clin Onc* 20:739–754. 2023

The first randomized trial of a neoantigen vaccine to demonstrate clinical benefit

Screening and selection of candidate neoantigens



mRNA Neoantigen Vaccine: 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]

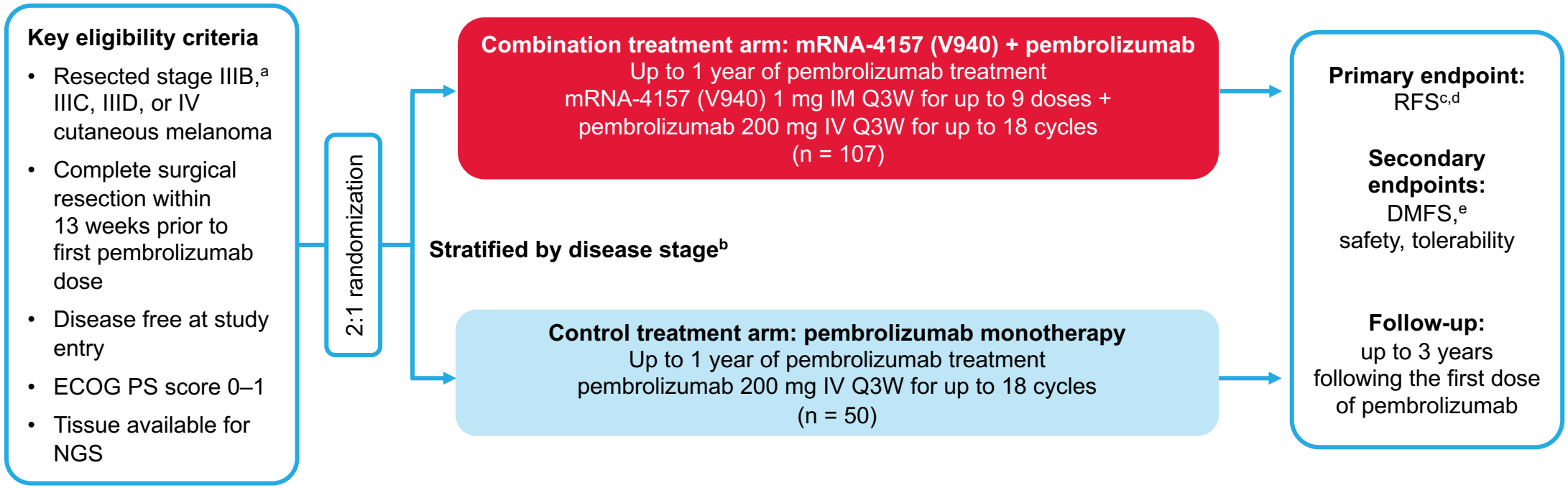
The modified mRNA **platform** was implemented for the COVID-19 vaccine (mRNA-1273), demonstrating its **utility and adaptability**[2]

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.

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

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



Designed with 80% power to detect an HR of 0.5 with ≥40 RFS events (with a 1-sided alpha of 0.1)
DMFS analysis was prespecified for testing following positive RFS in the ITT population[f]
Median follow-up[g]: 23 months for mRNA-4157 (V940) + pembrolizumab
24 months for pembrolizumab monotherapy

[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 ITT 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 was specified to occur when ≥51 RFS events were observe; [e]Investigator-assessed DMFS was defined as the time from first dose of pembrolizumab until the date of first distant recurrence or death from any cause; [f]The stratified log-rank test was used for comparison; [g]Time of database cutoff was November 14, 2022.
DMFS, disease metastasis-free survival; ECOG PS, Eastern Cooperative Oncology Group performance status; IM, intramuscular; ITT, intent-to-treat; IV, intravenous; mRNA, messenger RNA; NGS, next-generation sequencing; Q3W, every 3 weeks; RFS, recurrence-free survival.
Khattak A, et al. Previously presented at the American Association for Cancer Research® (AACR) Annual Meeting; April 14-19, 2023; Orlando, FL, USA. Oral presentation CT001 by Jeffrey Weber.

mRNA-4157-P201/KEYNOTE-942 Patient Demographics

Characteristic, n (%)	mRNA-4157 (V940) + pembrolizumab (n = 107)	pembrolizumab (n = 50)
Sex		
Male	70 (65.4)	31 (62.0)
Female	37 (34.6)	19 (38.0)
Age, years		
Mean (SD)	61.3 (13.50)	59.4 (14.25)
Median (range)	63 (26–83)	61.5 (24–89)
Age group		
<65 years	59 (55.1)	28 (56.0)
≥65 years	48 (44.9)	22 (44.0)
ECOG PS score[a]		
0	90 (84.1)	40 (80.0)
1	15 (14.0)	9 (18.0)
Stage[b]		
IIIC	89 (83.2)	42 (84.0)
IIID	2 (1.9)	2 (4.0)
IV	16 (15.0)	6 (12.0)
LDH, U/L		
Median (range)	189.5 (118–528)	185.5 (113–1180)
>ULN	5 (4.7)	3 (6.0)
Lymph node dissection	34 (31.8)	15 (30.0)
PD-L1 status		
Positive	**69 (64.5)**	**27 (54.0)**
Negative	**13 (12.1)**	**5 (10.0)**
Indeterminate[c]	**25 (23.4)**	**18 (36.0)**
***BRAF*[d]**		
V600K or V600E mutation	41 (38.3)	20 (40.0)
WT[e]	66 (61.7)	30 (60.0)
Tumor mutational burden[f]		
<10 mutations/Mb	**26 (24.3)**	**19 (38.0)**
≥10 mutations/Mb	**79 (73.8)**	**30 (60.0)**

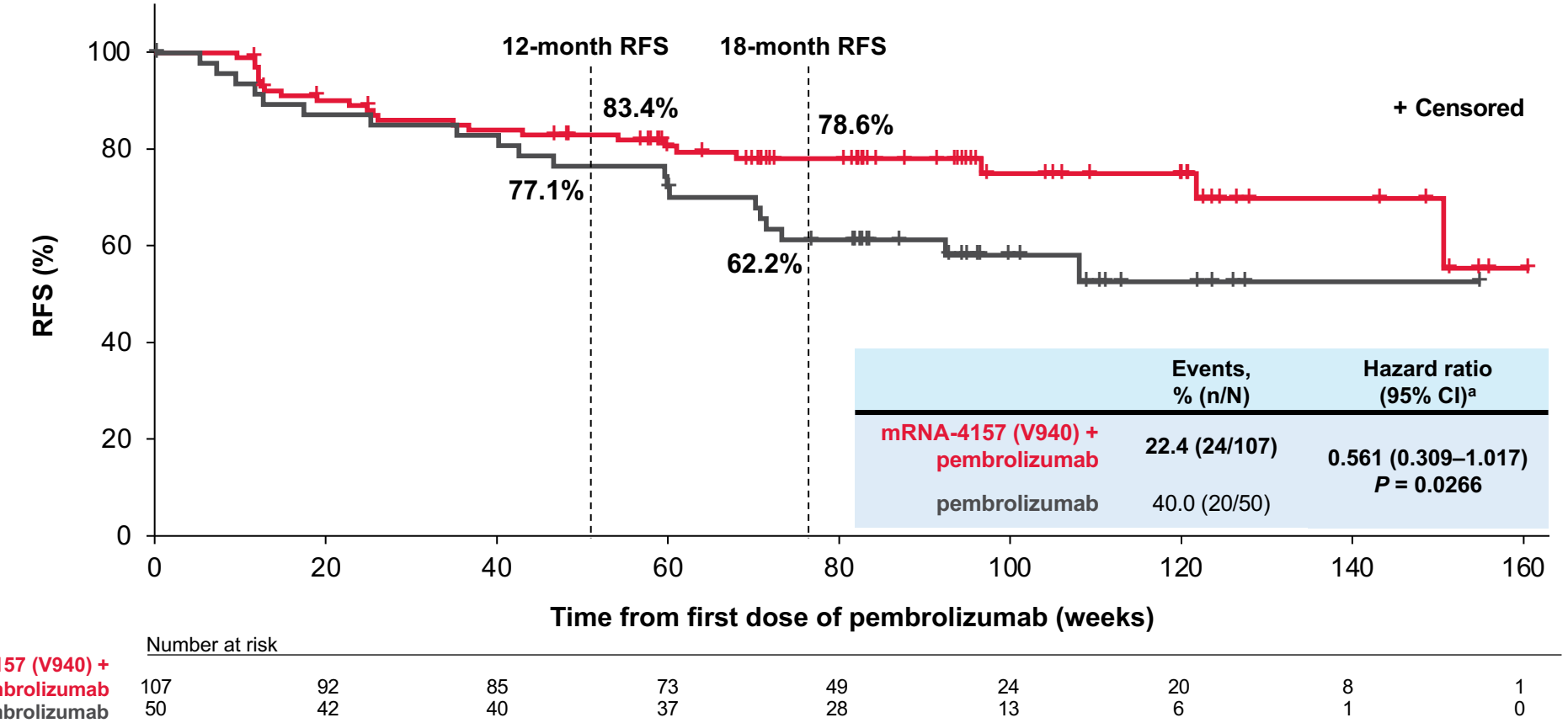
[a]Three patients were not treated and therefore had no baseline ECOG PS; [b]According to the 8th edition of the American Joint Committee on Cancer staging manual; [c]Patients for whom there was no sample to send for PD-L1 evaluation or for whom sample quality or quantity was too low to perform the assay; [d]*BRAF* status determined by whole exome sequencing on baseline tumor samples; [e]WT refers to position 600 on *BRAF* gene; [f]Available for 154 patients.
ECOG PS, Eastern Cooperative Oncology Group performance status; LDH, lactate dehydrogenase; mRNA, messenger RNA; PD-L1, programmed death ligand 1; ULN, upper limit of normal; WT, wild type.
Khattak A, et al. Previously presented at the American Society of Clinical Oncology (ASCO) Annual Meeting; June 2-6, 2023; Chicago, IL, USA. Oral presentation LBA9503.

Safety Profile Reflects Individual Components With Infrequent Additional Clinically Significant AEs Over Pembrolizumab Alone

	mRNA-4157 (V940) + pembrolizumab (n = 104)		pembrolizumab (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 AEs[a]	**15 (14.4)**	**13 (12.5)**	**5 (10.0)**	**4 (8.0)**
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)	-	-
pembrolizumab 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

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.
AE, adverse event; mRNA, messenger RNA.
Khattak A, et al. Previously presented at the American Association for Cancer Research® (AACR) Annual Meeting; April 14-19, 2023; Orlando, FL, USA. Oral presentation CT001.

Primary Efficacy Endpoint: Recurrence-Free Survival

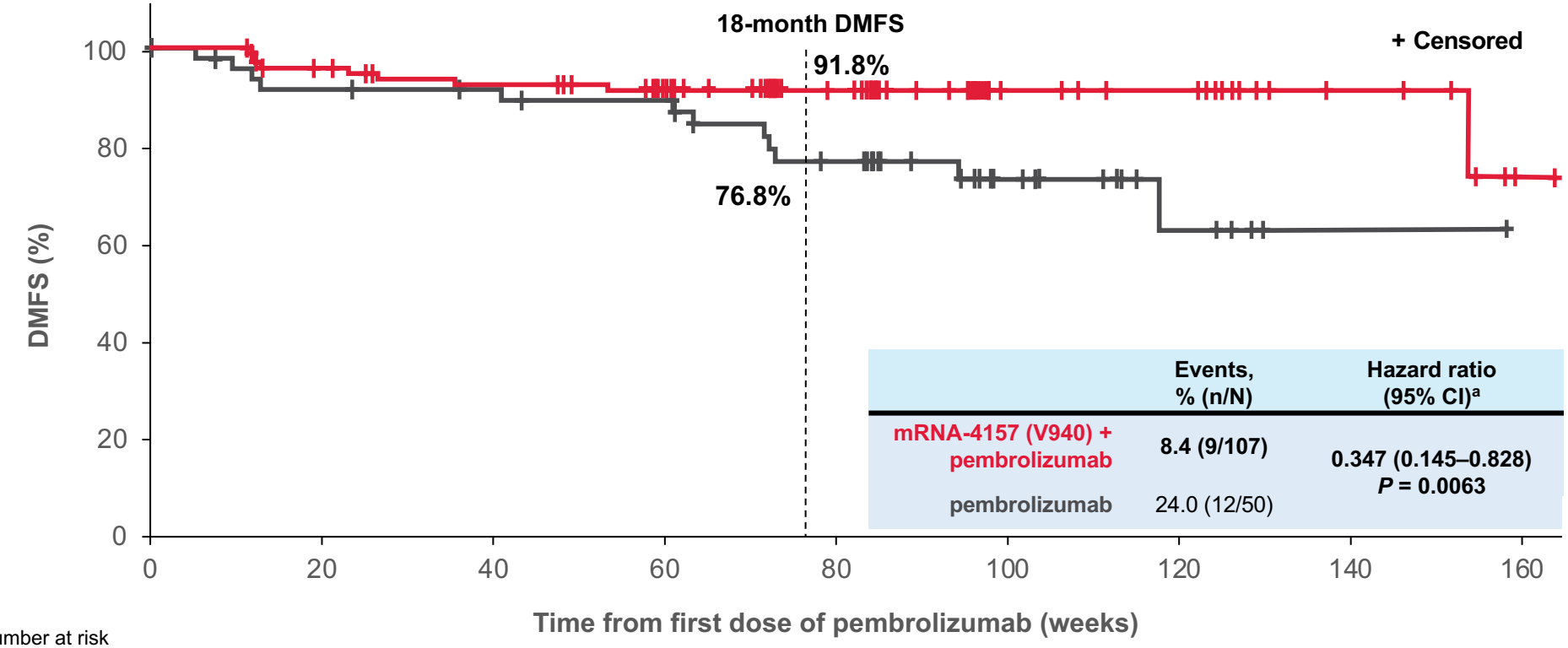


[a]The hazard ratio and 95% CI for mRNA-4157 (V940) plus pembrolizumab versus pembrolizumab alone are estimated using a Cox proportional hazards model with treatment group as a covariate, stratified by disease stage (stages IIIB or IIIC or IIID vs stage IV) used for randomization. The *P* value is based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

mRNA, messenger RNA; RFS, recurrence-free survival.

Khattak A, et al. Previously presented at the American Association for Cancer Research® (AACR) Annual Meeting; April 14-19, 2023; Orlando, FL, USA. Oral presentation CT001.

Secondary Efficacy Endpoint: Distant Metastasis-Free Survival



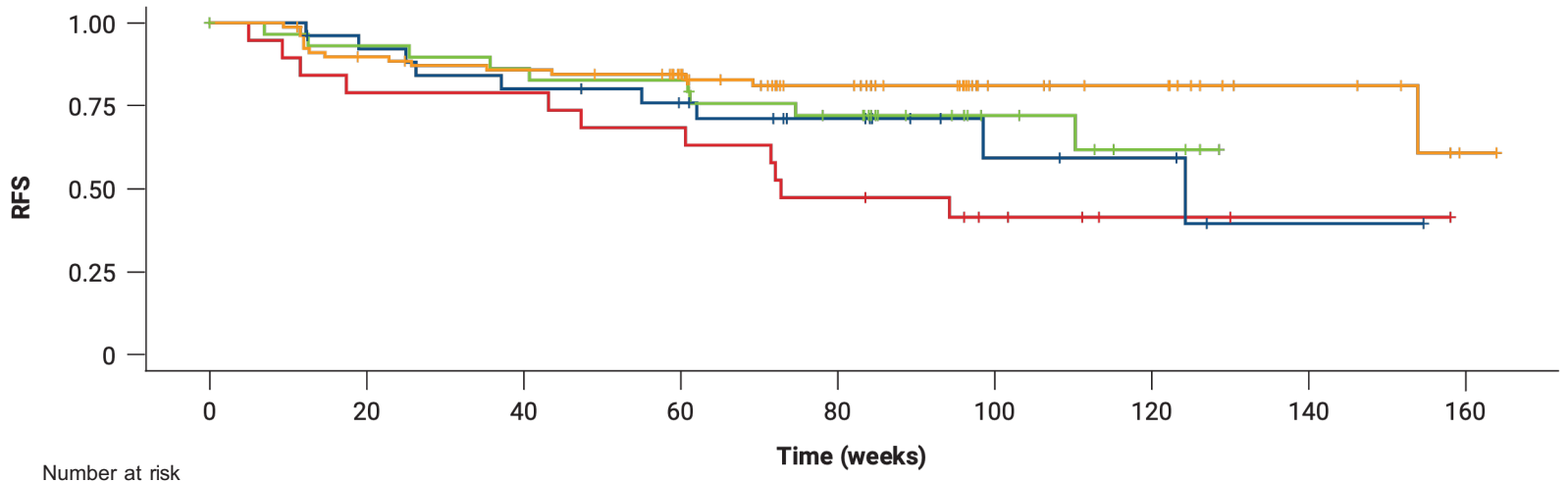
[a]The hazard ratio and 95% CI for mRNA-4157 (V940) plus pembrolizumab versus pembrolizumab alone are estimated using a Cox proportional hazards model with treatment group as a covariate, stratified by disease stage (stages IIIB or IIIC or IIID vs stage IV) used for randomization. The *P* value is based on a 1-sided log-rank test stratified by disease stage (stages IIIB or IIIC or IIID vs stage IV) used for randomization. At 18 months, the estimated DMFS rates were 91.8% (95% CI, 84.2-95.8) versus 76.8% (95% CI, 61.0-86.8) in the combination and monotherapy arms, respectively.

DMFS, disease metastasis-free survival; mRNA, messenger RNA.

Khattak A, et al. Previously presented at the American Society of Clinical Oncology (ASCO) Annual Meeting; June 2-6, 2023; Chicago, IL, USA. Oral presentation LBA9503.

RFS Improved With mRNA-4157 and Pembrolizumab Irrespective of TMB Status

RFS by treatment arm stratified by TMB-high and non–TMB-high subgroups



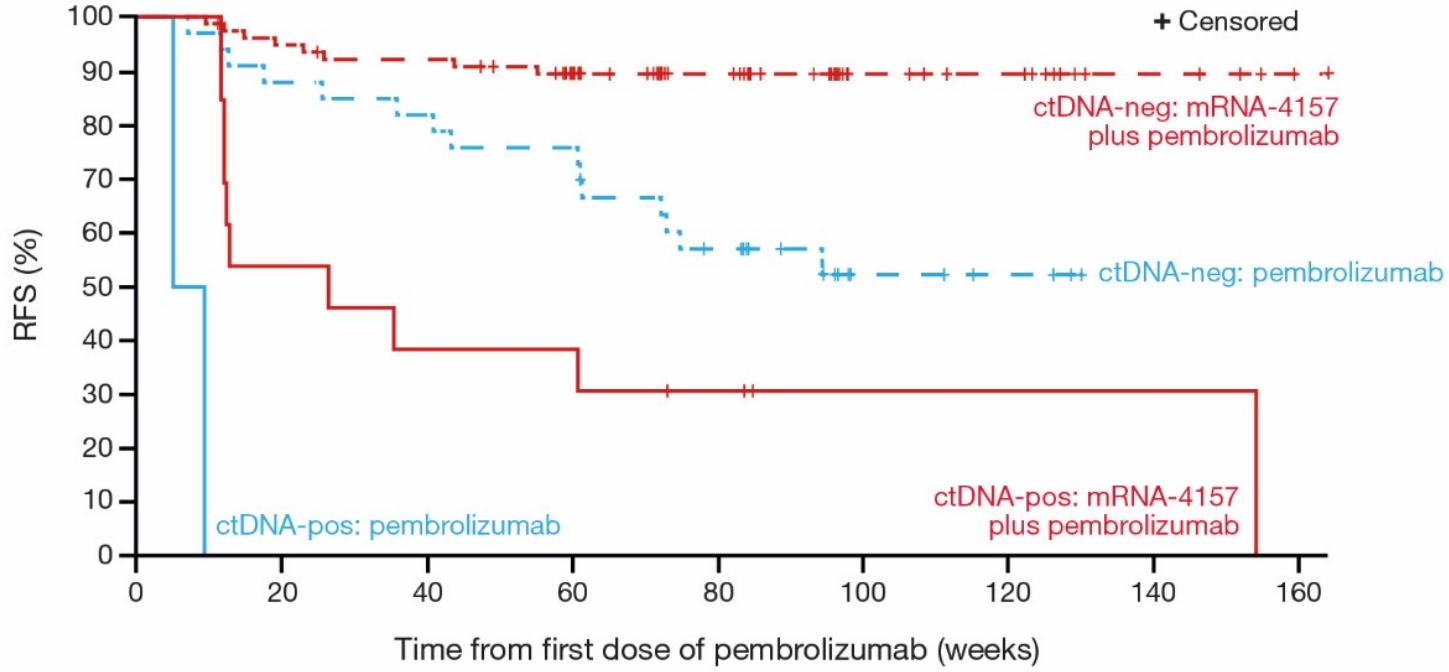
Number at risk									
Non–TMB-high: pembrolizumab	19	15	15	13	9	5	2	1	0
Non–TMB-high: mRNA-4157 (V940) + pembrolizumab	26	23	20	17	12	5	4	1	0
TMB-high: pembrolizumab	30	27	25	24	19	8	4	0	0
TMB-high: mRNA-4157 (V940) + pembrolizumab	79	69	65	56	37	19	16	7	1

	mRNA-4157 (V940) + pembrolizumab versus pembrolizumab Hazard ratio (95% CI)	mRNA-4157 (V940) + pembrolizumab Events, n/N (%)	pembrolizumab Events, n/N (%)
TMB-high	0.652 (0.284–1.494)	15/79 (19.0)	9/30 (30.0)
non-TMB-high	0.586 (0.243–1.415)	9/26 (34.6)	11/19 (57.9)

	TMB-high versus non–TMB-high Hazard ratio (95% CI)	TMB-high Events, n/N (%)	Non–TMB-high Events, n/N (%)
mRNA-4157 (V940) + pembrolizumab	0.536 (0.234–1.225)	15/79 (19.0)	9/26 (34.6)
pembrolizumab	0.482 (0.199–1.166)	9/30 (30.0)	11/19 (57.9)

Hazard ratios and 95% CIs were calculated based on a stratified Cox proportional hazards model.
mRNA, messenger RNA; RFS, recurrence-free survival; TMB, tumor mutational burden.
Sullivan RJ, et al. Previously presented at the American Association for Cancer Research® (AACR) Annual Meeting; April 14-19, 2023; Orlando, FL, USA. Poster presentation CT224.

RFS is Improved in Patients With a ctDNA-negative or positive Result at Baseline Who Received Combination Therapy



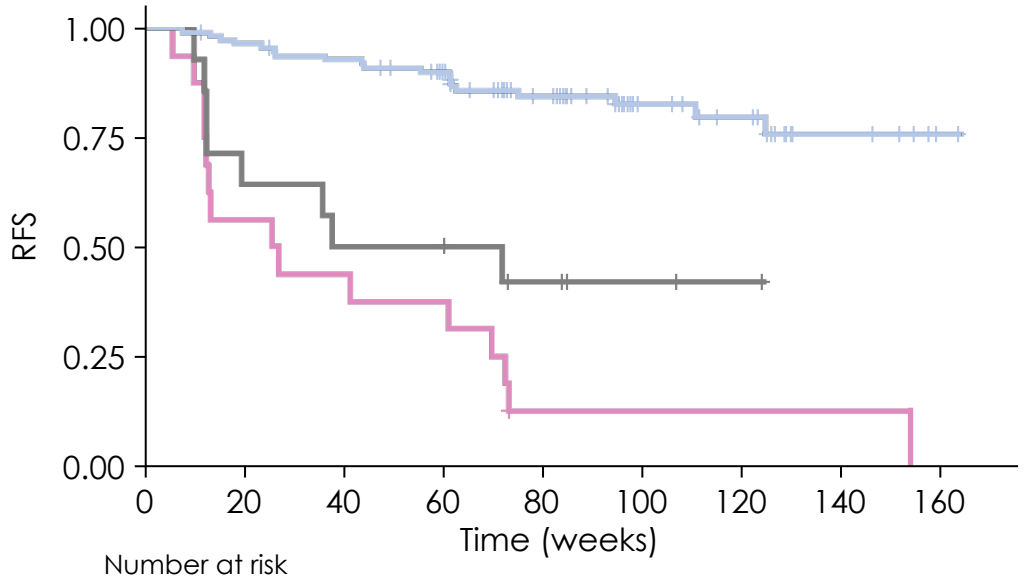
Number at risk									
ctDNA-neg: mRNA-4157 plus pembrolizumab	77	72	69	57	38	18	15	6	1
ctDNA-neg: pembrolizumab	33	29	27	25	17	6	4	0	0
ctDNA-pos: mRNA-4157 plus pembrolizumab	13	7	5	5	3	1	1	1	0
ctDNA-pos: pembrolizumab	2	0	0	0	0	0	0	0	0

	mRNA-4157 (V940) + pembrolizumab versus pembrolizumab Hazard ratio (95% CI)	mRNA-4157 (V940) + pembrolizumab Events, n/N (%)	pembrolizumab Events, n/N (%)
ctDNA-pos	NE	10/13 (76.9)	2/2 (100)
ctDNA-neg	0.225 (0.095–0.531)	8/77 (10.4)	15/33 (45.5)

Hazard ratios and 95% CIs were calculated based on a stratified Cox proportional hazards model.
ctDNA, circulating tumor DNA; mRNA, messenger RNA; NE, not evaluable; neg, negative; pos, positive; RFS, recurrence-free survival.
Carlino MS, et al. Previously presented at the American Society of Clinical Oncology (ASCO) Annual Meeting; June 2-6, 2023; Chicago, IL, USA. Poster presentation LBA9515.

Improved RFS and DMFS observed with favorable ctDNA longitudinal patterns

RFS by ctDNA longitudinal pattern

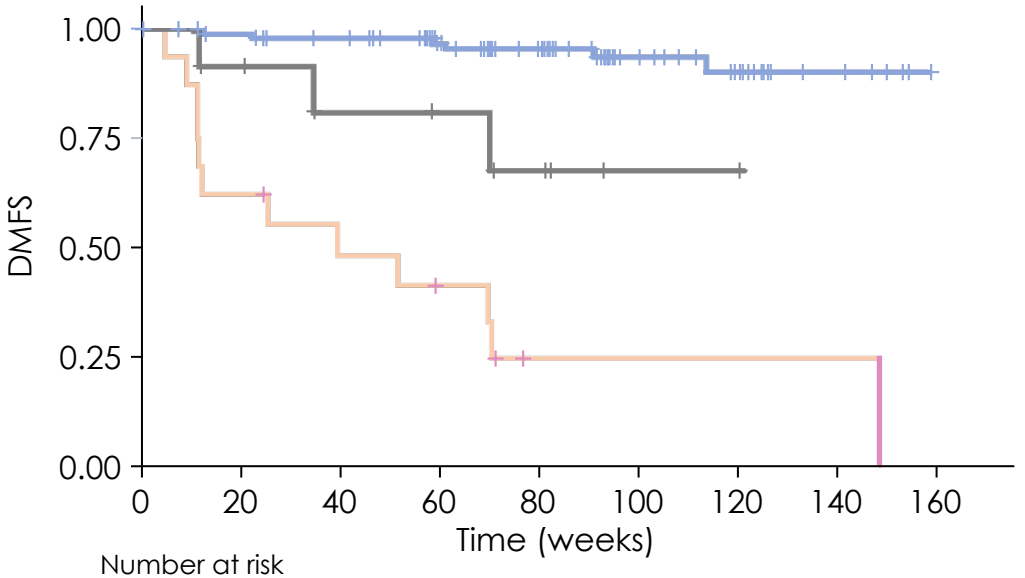


Number at risk

ctDNA negative	112	107	102	89	64	30	24	8	1
ctDNA positive MR	14	9	7	7	4	2	1	0	0
ctDNA positive MNR	16	9	7	6	1	1	1	1	0

	Events, n/N (%)	Hazard ratio (95% CI)
MR patterns	8/14 (57.1)	0.535 (0.224–1.278)
MNR patterns	15/16 (93.8)	

DMFS by ctDNA longitudinal pattern



Number at risk

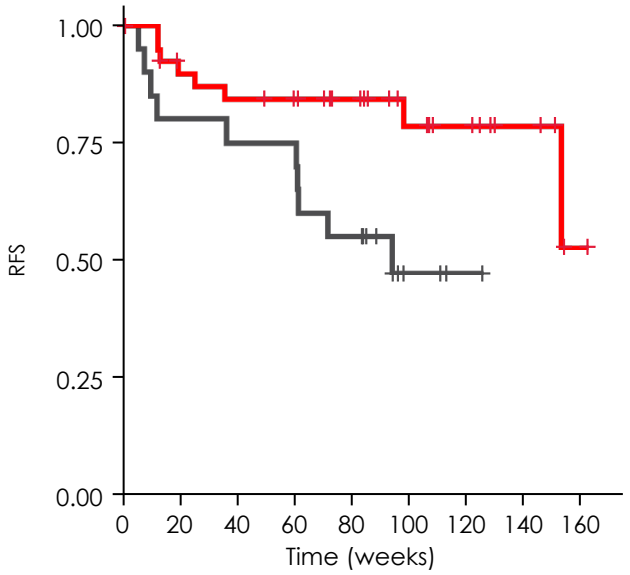
ctDNA negative	112	108	103	90	65	31	24	8	1
ctDNA positive MR	14	10	7	7	4	1	1	0	0
ctDNA positive MNR	16	10	8	6	1	1	1	1	0

	Events, n/N (%)	Hazard ratio (95% CI)
MR patterns	3/14 (21.4)	0.274 (0.076–0.984)
MNR patterns	12/16 (75.0)	

CI, confidence interval; ctDNA, circulating tumor DNA; DMFS, distant metastasis-free survival; MNR, molecular non-responder; MR, molecular responder; RFS, recurrence-free survival.

Improved RFS observed with mRNA-4157 (V940) plus pembrolizumab versus pembrolizumab monotherapy irrespective of BRAF status

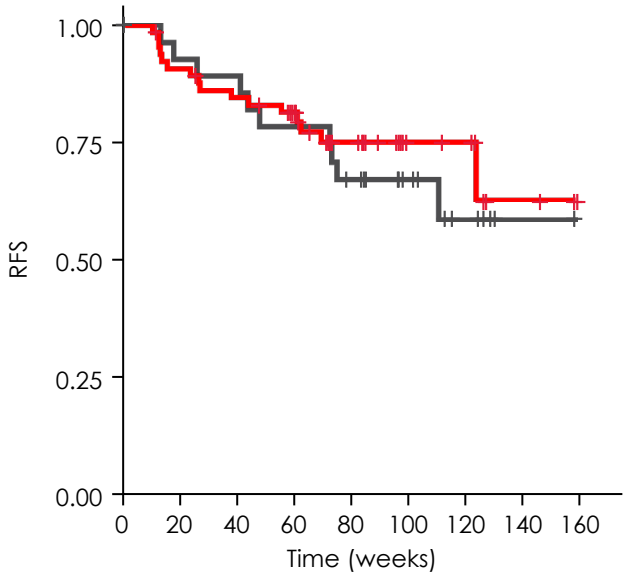
RFS in patients with BRAF MUT (n = 61, 38.9%)



Number at risk

mRNA-4157 + pembrolizumab	41	33	31	29	22	14	11	5	1
pembrolizumab	20	16	15	15	11	3	1	0	0

RFS in patients with BRAF WT (n = 96, 61.1%)



Number at risk

mRNA-4157 + pembrolizumab	66	59	54	44	27	10	9	3	0
pembrolizumab	30	26	25	22	17	10	15	1	0

	mRNA-4157 (V940) + pembrolizumab Events, n/N (%)	pembrolizumab Events, n/N (%)	mRNA-4157 (V940) + pembrolizumab versus pembrolizumab HR (95% CI)
V600K or V600E mutation	8/41 (19.5%)	10/20 (50.0%)	0.332 (0.13–0.85)
WT	16/66 (24.2%)	10/30 (33.3%)	0.808 (0.366–1.784)

- RFS improvement with the combination versus pembrolizumab monotherapy initially appears stronger in patients with BRAF MUT than in patients with BRAF WT
- In line with previous reports, pembrolizumab treatment effect is similar across BRAF WT and MUT subpopulations
- BRAF WT: combination arm had more patients with ctDNA positive results (12.1%) versus pembrolizumab monotherapy, which had no patients with ctDNA positive results

BRAF status determined by WES on baseline tumor samples. BRAF WT refers to position 600 on BRAF gene, BRAF MUT refers to V600K or V600E MUT.
BRAF, B-Raf proto-oncogene; CI, confidence interval; ctDNA, circulating DNA; HR, hazard ratio; mRNA, messenger RNA; MUT, mutation; NA, not applicable; RFS, recurrence-free survival; WT, wild type.

Conclusions for Keynote 942

- mRNA-4157-P201/KEYNOTE-942 is the first randomized trial to demonstrate improvement in RFS and DMFS with an individualized neoantigen therapy approach
- mRNA-4157 (V940) and pembrolizumab demonstrated a clinically significant improvement in RFS and DMFS compared with standard-of-care pembrolizumab in high-risk resected melanoma, with a 44% reduction in the risk of recurrence or death and a 65% reduction in the risk of distant metastasis or death with a median of 2 years of follow-up, considerably improved at 3 years of follow up with HR for RFS of 0.51 and two-side p of 0.019*
- Prolonged RFS was maintained in patients who received combination therapy regardless of TMB or ctDNA status at baseline; patients who were TMB high or who had a ctDNA-negative result at baseline had a greater RFS benefit compared with patients who were not TMB high or who had a ctDNA-positive result at baseline, respectively
- mRNA-4157 (V940) in combination with PEMBRO was well tolerated, without a substantial increase in clinically meaningful AEs compared with PEMBRO monotherapy
- mRNA-4157 (V940) in combination with pembrolizumab versus PEMBRO is in an ongoing phase III study in resected stages IIB/C/III/IV melanoma in over 1000 patients

*Moderna press release 12-14-23

AE, adverse event; ctDNA, circulating tumor DNA; DMFS, disease metastasis-free survival; mRNA, messenger RNA; RFS, recurrence-free survival; TMB, tumor mutational burden.

Conclusions:

"When you come to a fork in the road, take it"

Laurence Berra, 20th Century American Philosopher