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Oncology therapeutics

Program Pack

Intismeran autogene (mRNA-4157)

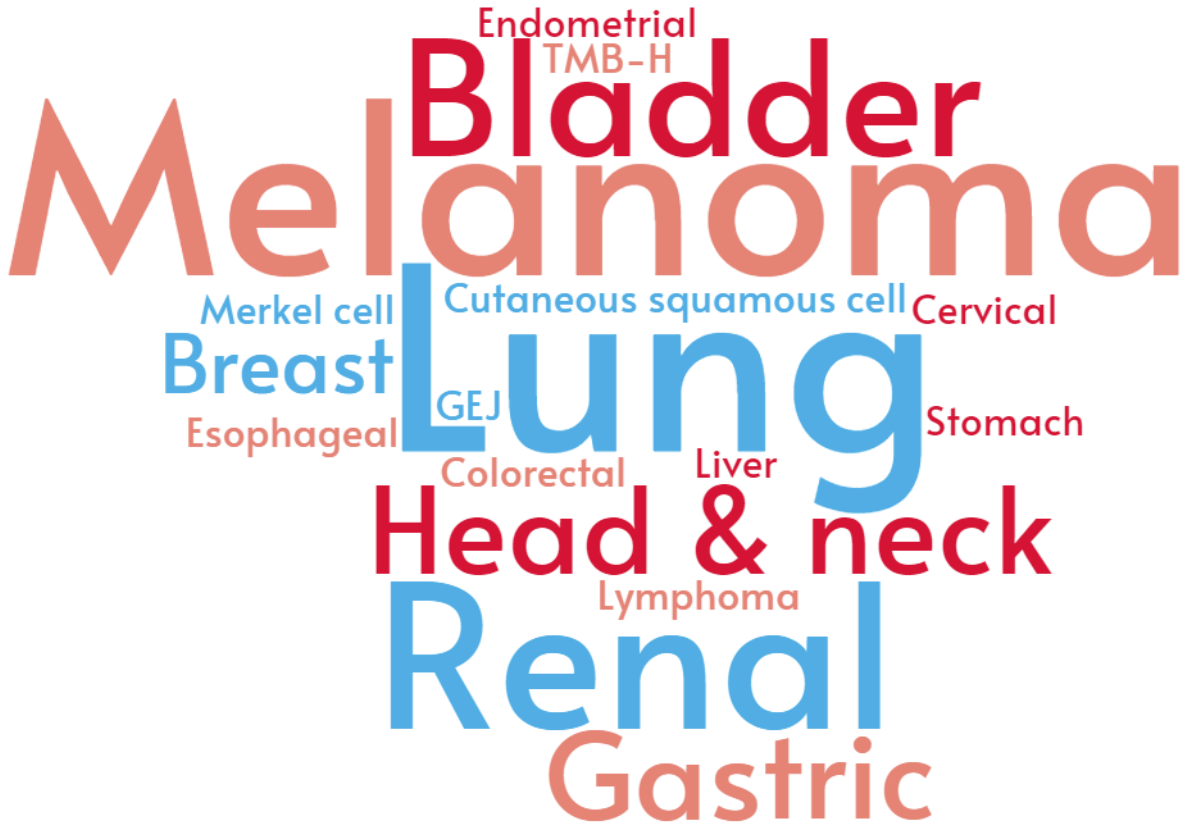
Common characteristics for therapeutic development in the oncology franchise

Elicit specific T-cell responses

Robust safety data on delivery mechanism

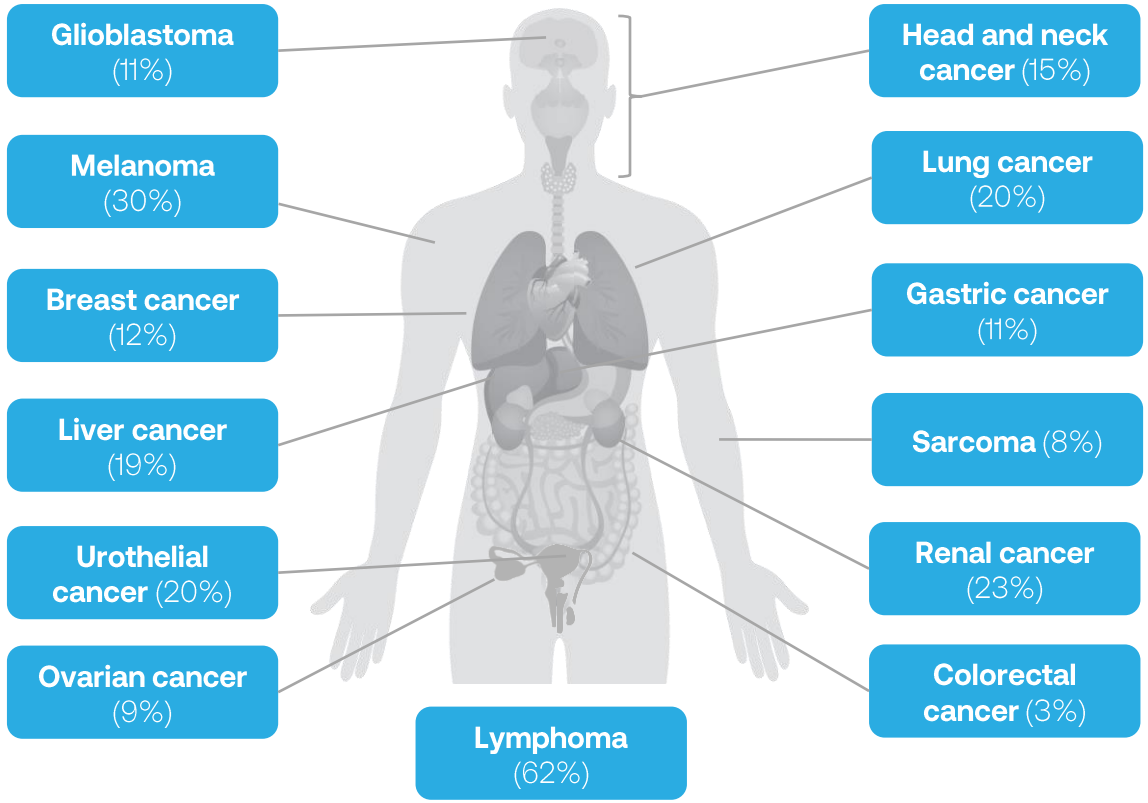
Low-grade, self-limited safety profile distinct from traditional oncology therapies

Non-specific therapies like checkpoint inhibitors set the standard for immuno-oncology treatment



Despite success with checkpoint inhibitors, unmet medical need exists

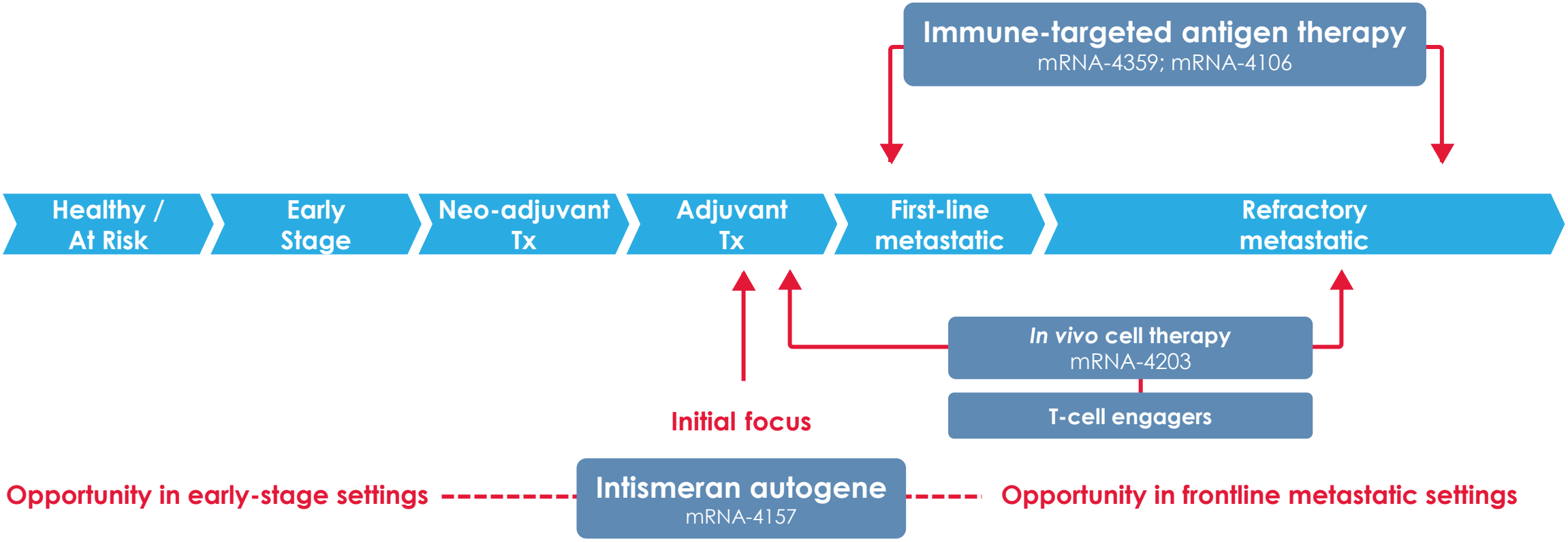
Anti-PD-L1/PD-1 response rates among various tumor types[1]



Response rates to ICIs typically range from 10% to 30% depending on the tumor type[1-3]

1. Zhao B, et al. *Ther Adv Med Oncol.* 2020;12:1–22; 2. Sun JY, et al. *Biomark Res.* 2020;8:35; 3. Zhang T, et al. *Oncotarget.* 2016;7(45):73068–73079.

Advancing a vision to treat patients across all stages of cancer



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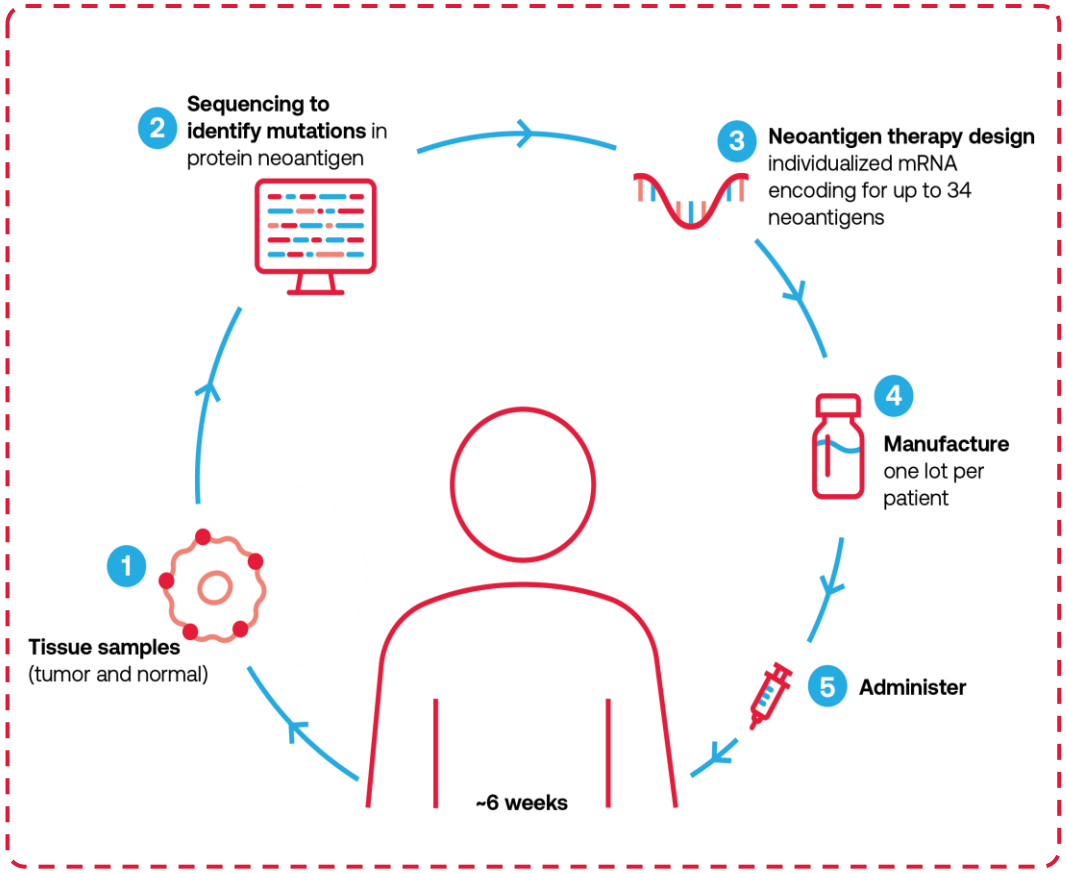
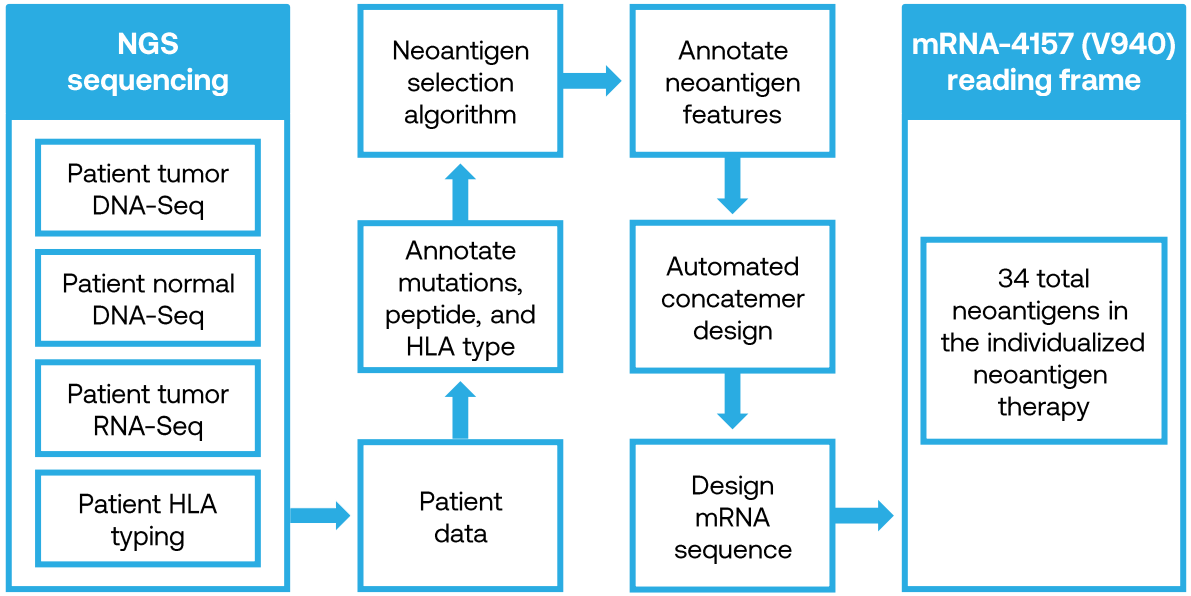
mRNA-4157 (V940): An Individualized Neoantigen Therapy (INT)

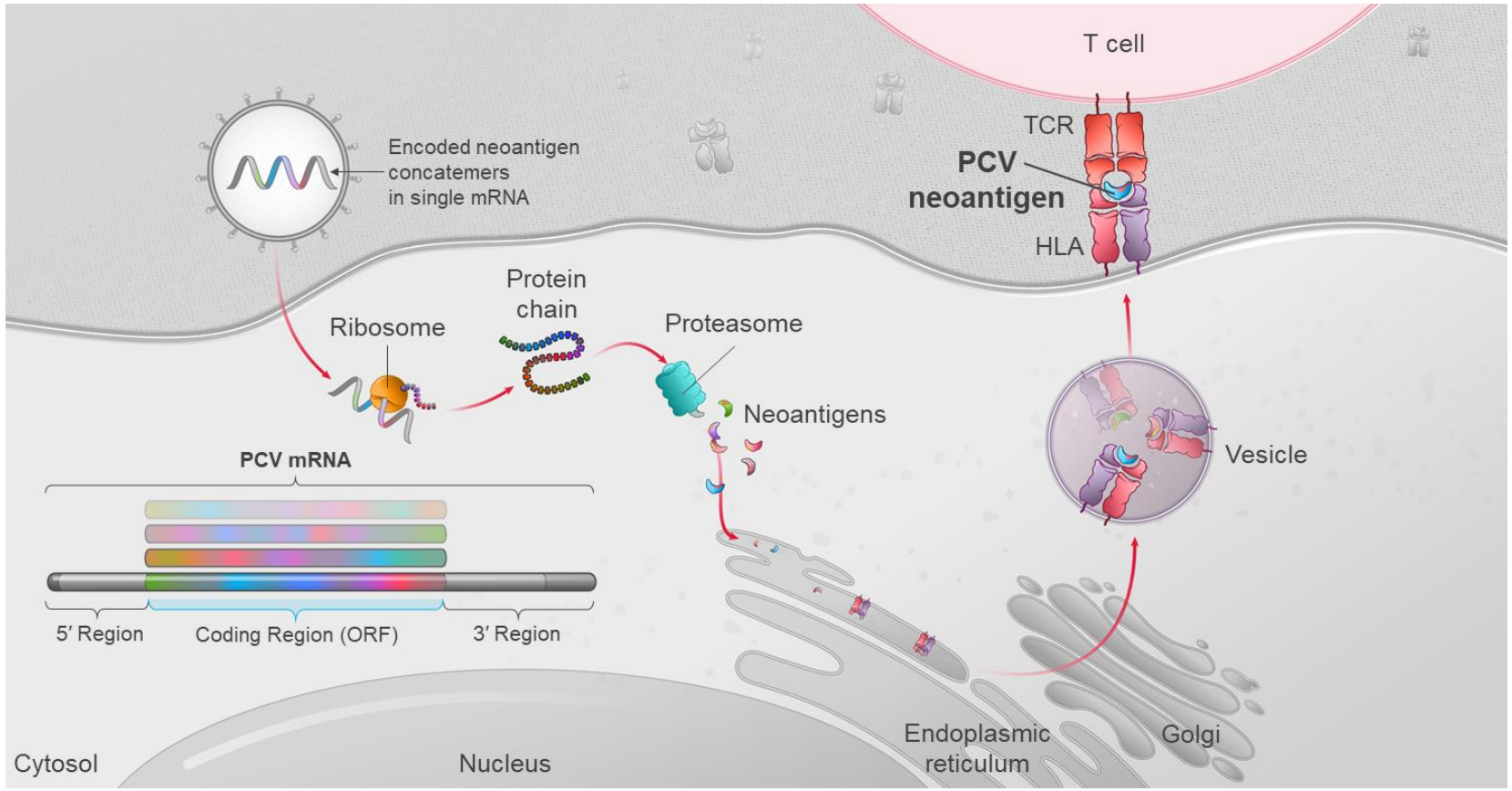
Our individualized neoantigen therapy designed to target an individual patient's unique tumor mutations and encodes up to 34 neoantigens





mRNA-4157 (V940) Mechanism of Action

Therapies targeting neoantigens can increase endogenous neoantigen T-cell responses and induce epitope spreading to novel antigens with the ability to drive antitumor responses and maintain memory with cytolytic properties, potentially producing long-term disease control for patients[1-5]



HLA, human leukocyte antigen; INT, individualized neoantigen therapy; ORF, open reading frame.

1. Wirth TC, Kühnel F. *Front Immunol.* 2017;8:1848. 2. Ott PA, et al. *Nature.* 2017;547:217-221. 3. Hu Z, et al. *Nat Med.* 2021;27:515-525. 4. Ott PA, et al. *Cell.* 2020;183:347-362. 5. Palmer CD, et al. *Nat Med.* 2022;28:1619-1629.

Oncology therapeutics portfolio

Expanding oncology portfolio with additional intismeran indication and new development candidates

Oncology therapeutics

Intismeran autogene
mRNA-4157

- **Adjuvant melanoma:** Phase 3 study fully enrolled
- **NSCLC:** in two adjuvant Phase 3 studies for those with and without prior neoadjuvant treatment
- **Adjuvant high-risk muscle invasive bladder cancer:** in randomized Phase 2 study
- **Adjuvant renal cell carcinoma**: in randomized Phase 2 study; fully enrolled
- **High-risk non-muscle invasive bladder cancer (HR NMIBC):** in randomized Phase 2 study

New study

In collaboration with Merck

Checkpoint AIM-T
mRNA-4359

- **First-line melanoma and first-line metastatic NSCLC:** in Phase 2 study

Newly prioritized

Early-stage oncology

Tumor-targeted antigen therapy

- mRNA-4106: dosed first patient in Phase 1 study

Cell therapy-enhancing antigen therapy

- mRNA-4203: IND open

Adjuvant melanoma Phase 3 (mRNA-4157 / V940) trial design

P303 was designed to test the immunogenicity and safety of an optimized composition of mRNA-1010

Randomized, double-blind placebo controlled, INT + pembrolizumab (KEYTRUDA®) vs. placebo + pembrolizumab (2:1) (INTerpath-001)

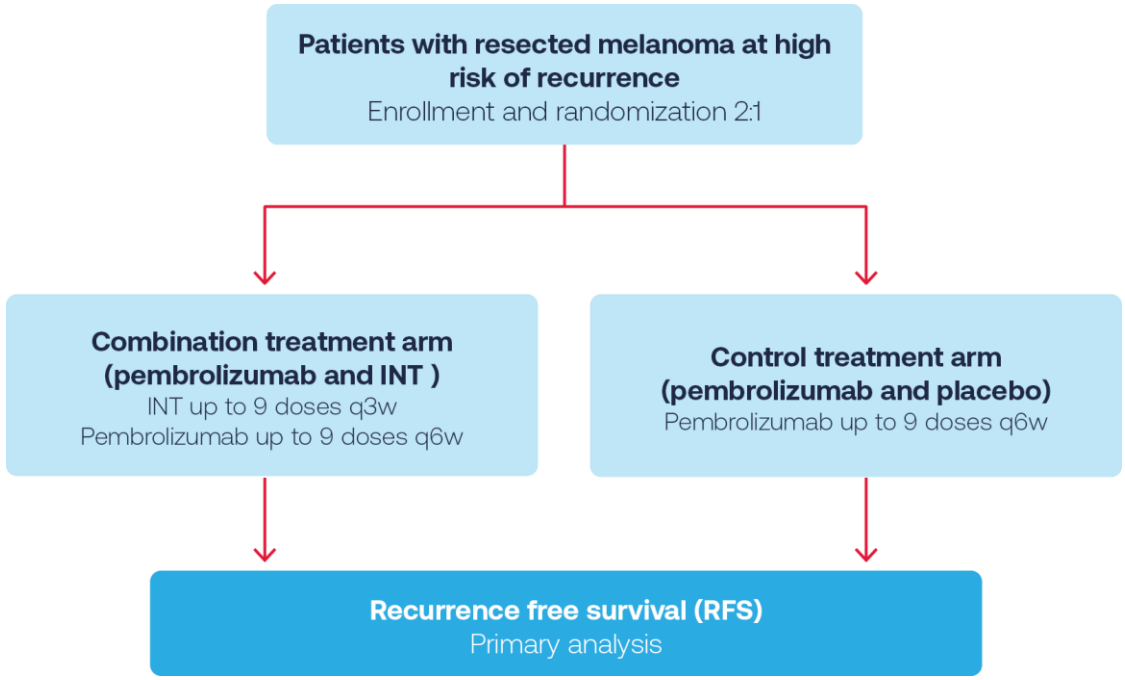
Resected melanoma patients: stage IIB or IIC, III, IV

Primary endpoint: recurrence free survival (RFS)

Secondary endpoints: Distant Metastasis-Free Survival (DMFS), Overall-Survival (OS)

Number of participants: ~1,089

Phase 3 trial is fully enrolled and accruing cases



NSCLC Phase 3 (mRNA-4157 / V940) trial design

Primary endpoint is disease free survival compared to pembrolizumab

Randomized, double-blind placebo and active comparator controlled, INT + pembrolizumab (KEYTRUDA®) vs. placebo + pembrolizumab (1:1) (INTerpath-002)

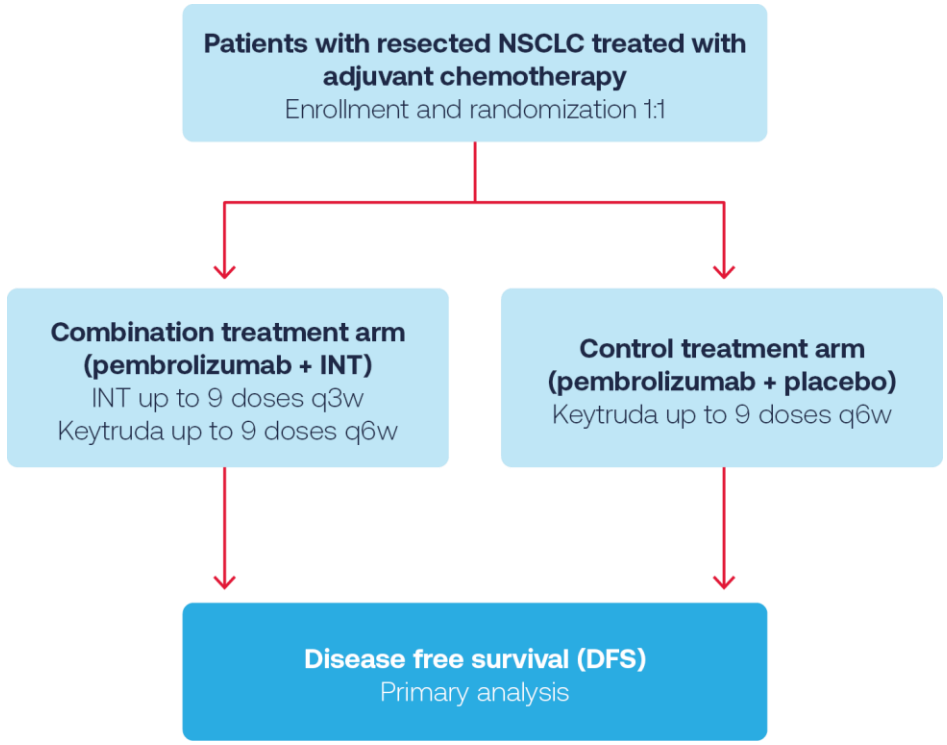
Resected non-small cell lung cancer (NSCLC) patients: stage II, IIIA, IIIB previously treated with adjuvant chemotherapy

Primary endpoint: disease free survival (DFS)

Secondary endpoints: Overall-Survival (OS), Distant Metastasis-Free Survival (DMFS), Safety, patient reported outcomes (PRO)

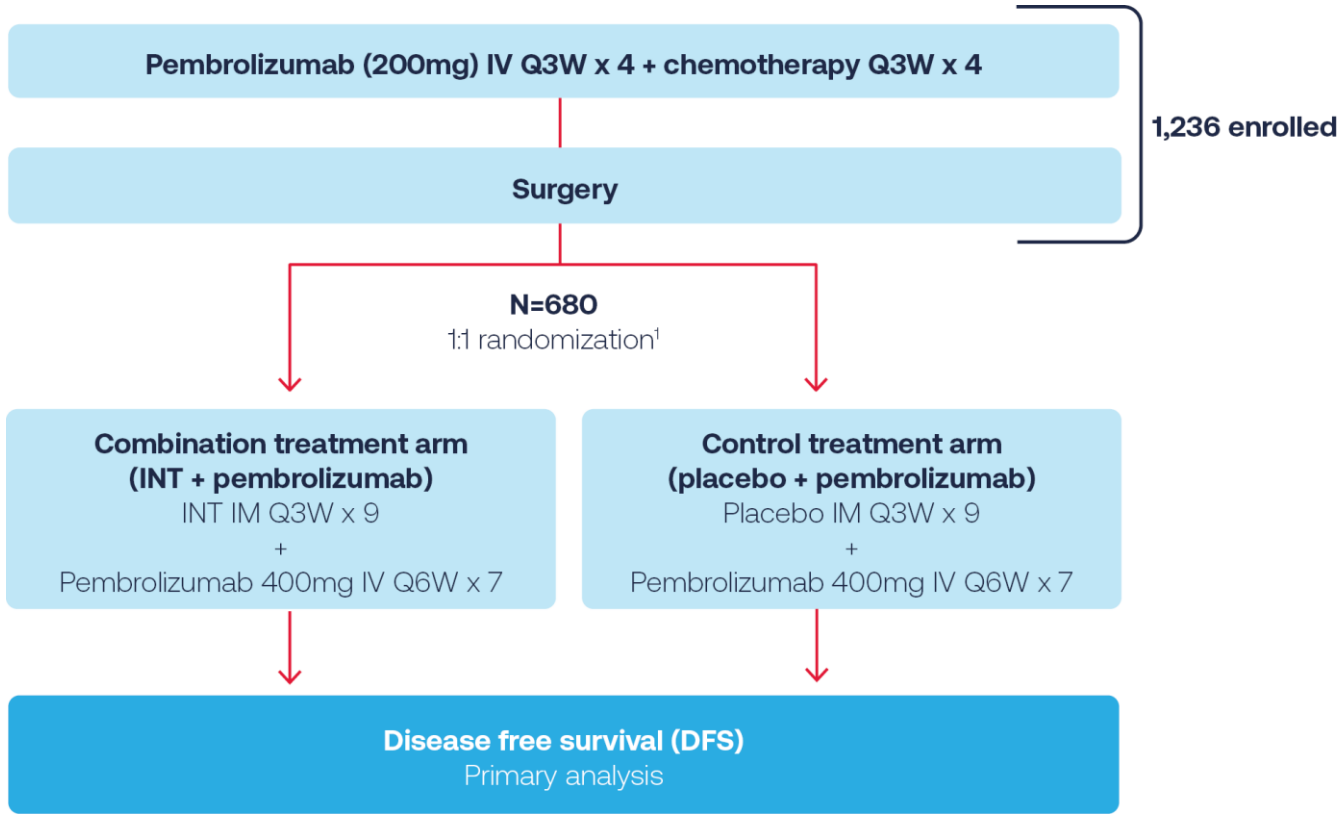
Number of participants: ~868

Currently enrolling



NCT05933577

Phase 3 trial evaluating adjuvant mRNA-4157 (V940) in combination with pembrolizumab after neoadjuvant pembrolizumab and chemotherapy in patients with certain types of NSCLC



NCT05933577

1. **Eligibility for randomization:** No pCR by local testing; Completed (R0-R1) surgery; No disease re-baseline image; Participants previously treated outside the study with neoadjuvant pembrolizumab and platinum-based chemotherapy and who successfully completed surgery with surgical tumor tissue sample are eligible

Randomized double-blind placebo-controlled study of adjuvant pembrolizumab with or without individualized neoantigen therapy (INT) for patients not achieving PCR after receiving neoadjuvant pembrolizumab + chemotherapy followed by surgery

Stage 2-3b NSCLC patients able to undergo surgery without EGFR mutation

Primary endpoint: disease-free survival (DFS)

Secondary endpoints include: Distant Metastasis-Free Survival (DMFS), Overall-Survival (OS)

Number of participants: ~680

In collaboration with Merck

Adjuvant high risk muscle invasive bladder cancer (mRNA-4157 / V940) trial design

Phase 2, randomized, double-blind, placebo and active-comparator controlled clinical study (INTerpath-005)

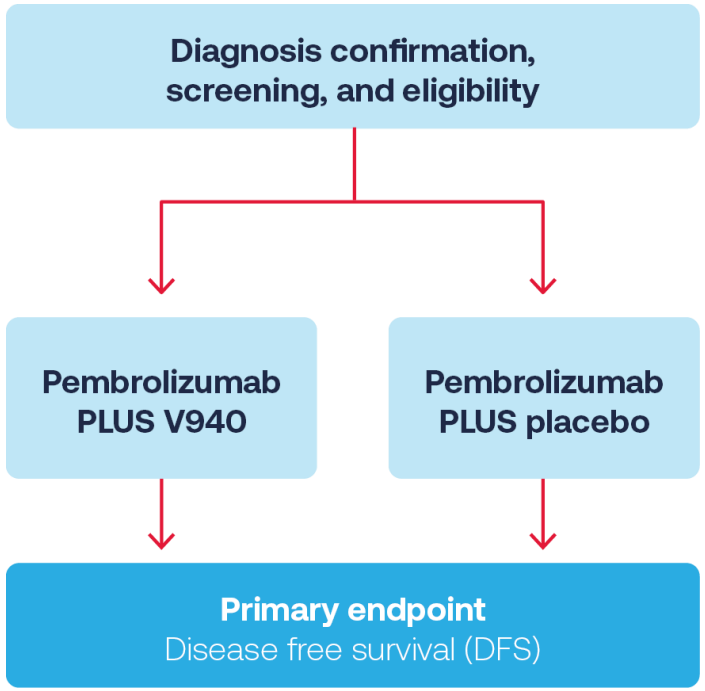
Patients with high-risk muscle invasive urothelial cancer (MIUC), dominant histology of urothelial cancer (UC) and high-risk pathologic disease after radical resection

Primary endpoint: disease free survival (DFS)

Secondary endpoints: Overall survival (OS), distant metastasis-free survival (DMFS), number of participants who experience an adverse event (AE), number of participants who discontinue study treatment due to an AE

Number of participants: 200

Currently enrolling



NCT06305767

Adjuvant renal cell carcinoma (mRNA-4157 / V940) trial design

Phase 2, randomized, double-blind, clinical study (INTerpath-004)

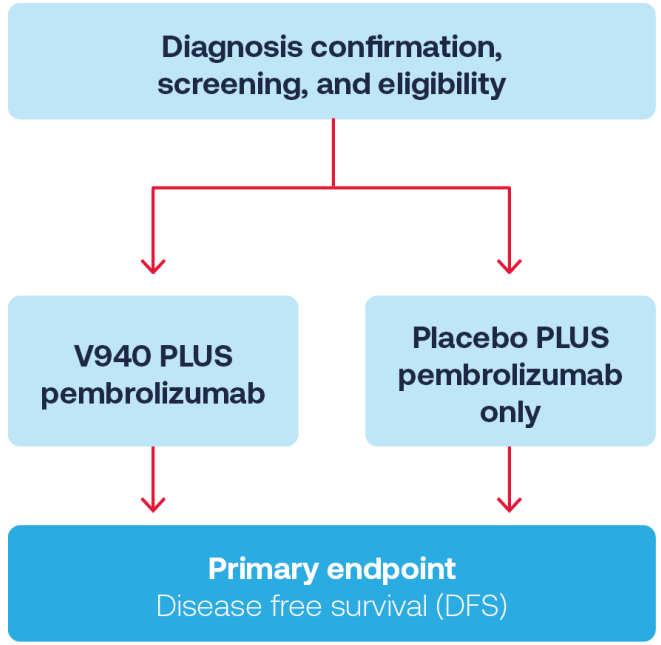
Patients with histologically or cytologically confirmed diagnosis of RCC with clear cell or papillary histology and intermediate-high-risk, high-risk, or M1 no evidence of disease (NED) RCC

Primary endpoint: disease free survival (DFS)

Secondary endpoints: Overall survival (OS), distant metastasis-free survival (DMFS), percentage of participants who experience an adverse event (AE), percentage of participants who discontinue study treatment due to an AE

Number of participants: 272

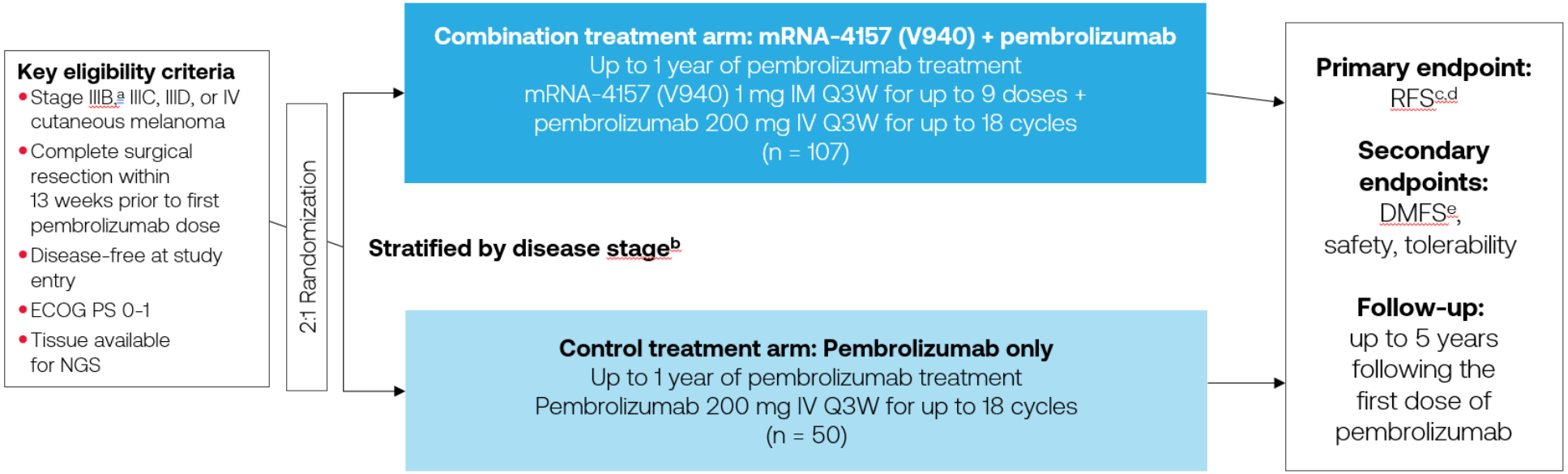
Currently enrolling



NCT06307431

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

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



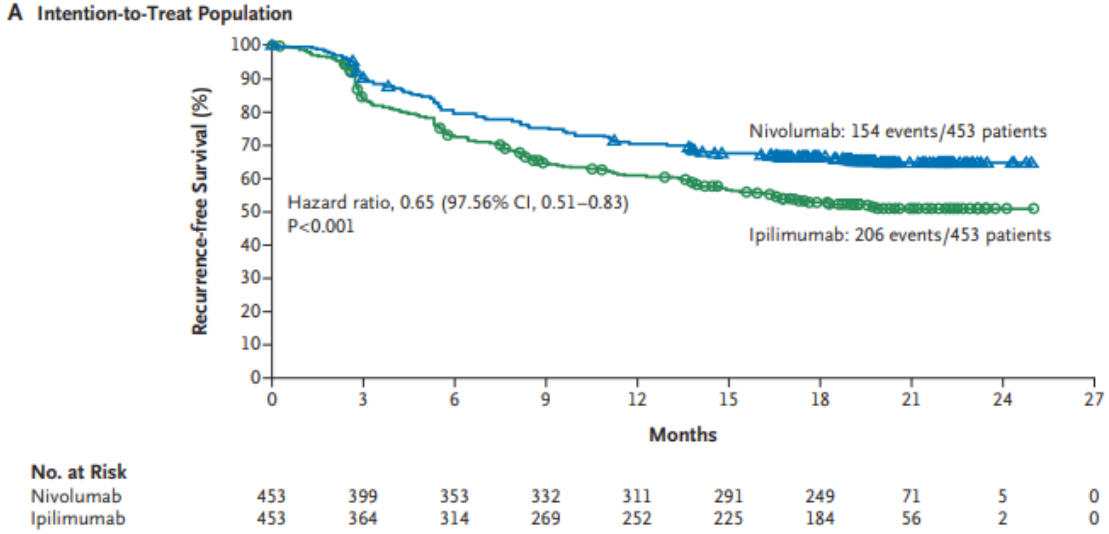
Designed with 80% power to detect an HR of 0.5 with ≥40 RFS events (with a 1-sided alpha of 0.1)
DMFS analysis was prespecified for testing following positive RFS in the ITT population[f]
Median follow-up: 23 months for mRNA-4157 (V940) + pembrolizumab
24 months for pembrolizumab only
Time of database cutoff was November 14, 2022

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

RFS of pembrolizumab control arm in P201 consistent with historical studies Checkmate-238 and Keynote-054

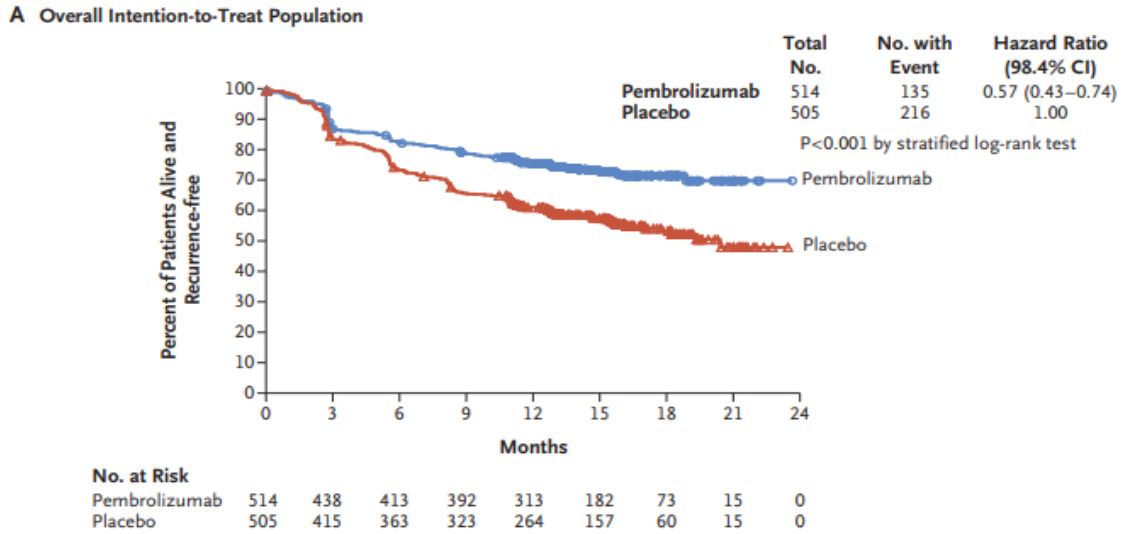
Increasing confidence in the treatment effect observed with the INT + pembro combination over pembro monotherapy

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



Primary RFS analysis in the ITT Population, Minimum follow-up 18mo

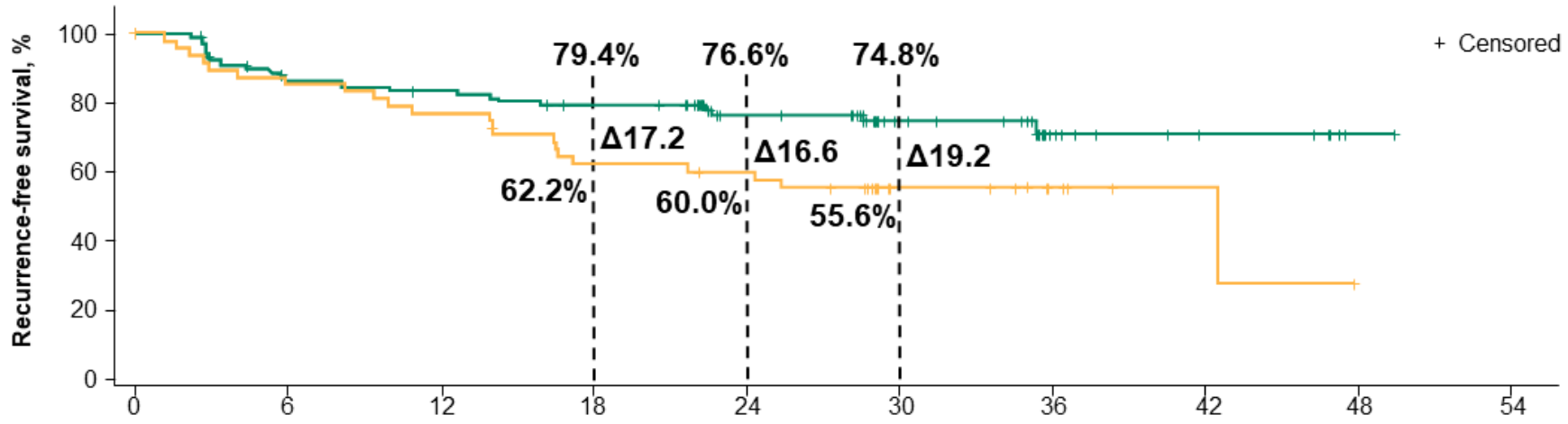
Keynote-054 — 12mo RFS: 75.4% vs 61.0%



Primary RFS analysis in the ITT Population, Median f/u 15mo

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

Sustained improvement of RFS primary efficacy endpoint



Patients at risk										
mRNA-4157 (V940) + pembrolizumab	107	87	83	77	52	29	12	6	1	0
Pembrolizumab	50	41	37	29	27	10	5	2	0	0

	Median (95% CI), months	Events, % (n/N)	Hazard ratio (95% CI)[a]
mRNA-4157 (V940) + pembrolizumab	NE	23.4 (25/107)	0.510 (0.288–0.906) *P* = 0.019[b]
pembrolizumab	42.51 (16.59–NE)	44.0 (22/50)	

[a]The hazard ratio and 95% CI for mRNA-4157 (V940) + pembrolizumab versus pembrolizumab were 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 2-sided log-rank test stratified by disease stage (stages IIIB or IIIC or IIID vs stage IV) used for randomization; [b]Formal hypothesis testing of RFS was performed using November 2022 data cut. *P* value reported above used the November 2023 data cut; it's nominal and not for formal hypothesis testing. NE, not estimable.

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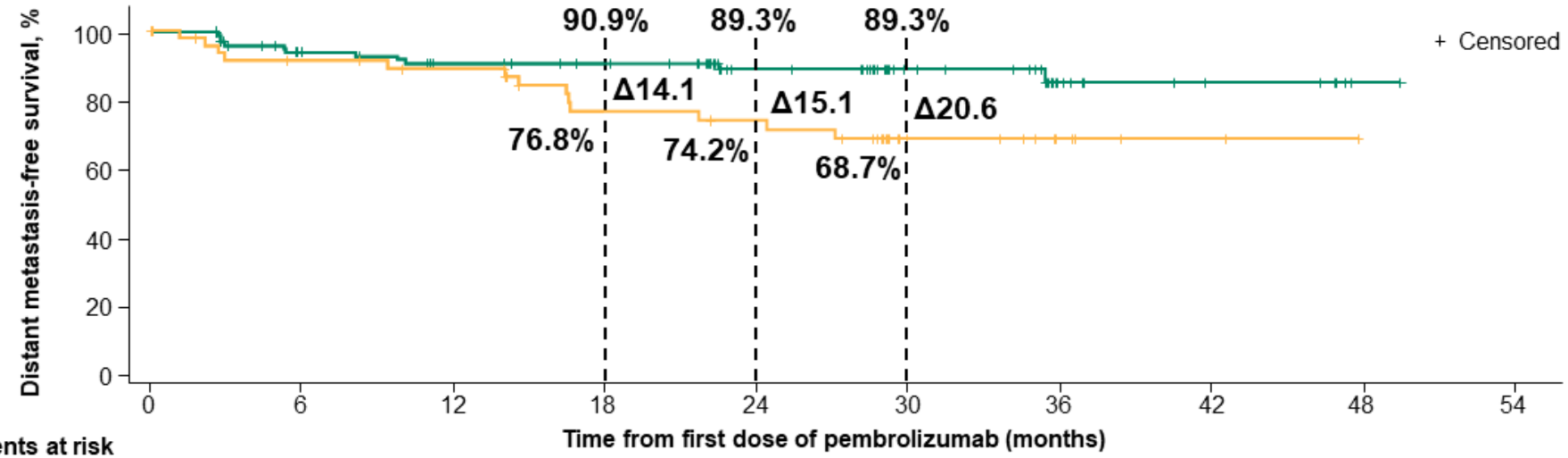
Sustained improvement of DMFS secondary endpoint



Patients at risk										
mRNA-4157 (V940) + pembrolizumab	107	89	82	78	52	30	12	6	1	0
Pembrolizumab	50	42	39	30	27	10	5	2	0	0

	Median (95% CI), months	Events, % (n/N)	Hazard ratio (95% CI)[a]
mRNA-4157 (V940) + pembrolizumab	NE	10.3 (11/107)	0.384 (0.172–0.858) *P* = 0.015[b]
Pembrolizumab	NE	26.0 (13/50)	

[a]The hazard ratio and 95% CI for mRNA-4157 (V940) plus pembrolizumab versus pembrolizumab were 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 2-sided log-rank test stratified by disease stage (stages IIIB or IIIC or IIID vs stage IV) used for randomization; [b]Formal hypothesis testing of DMFS was performed using November 2022 data cut. *P* value reported above used the November 2023 data cut; it's nominal and not for formal hypothesis testing.

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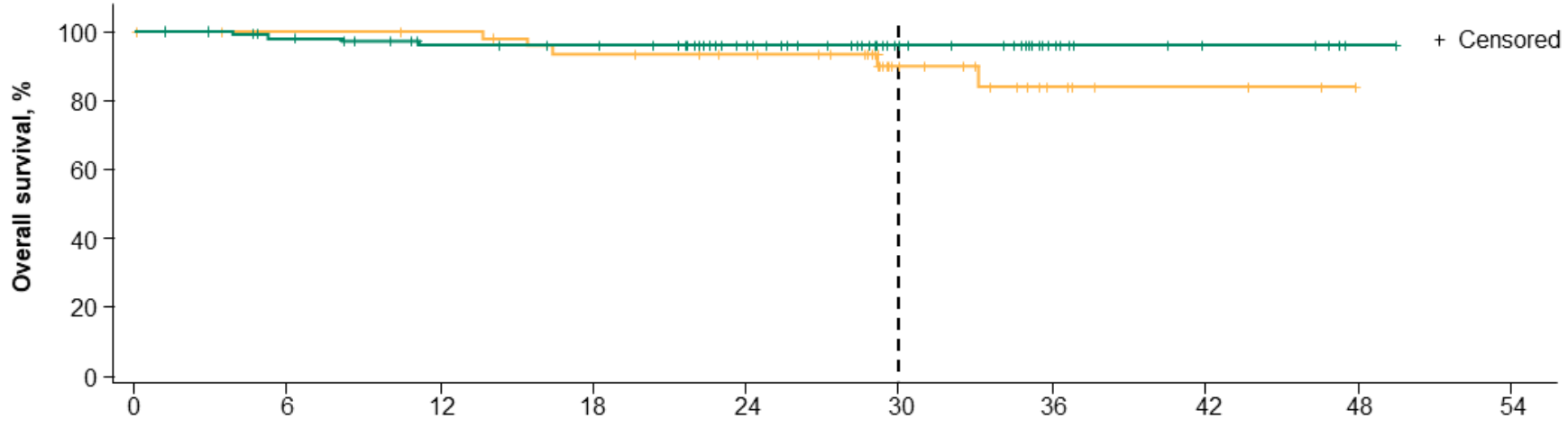
Overall survival shows encouraging trend with mRNA-4157 (V940) + pembrolizumab



Patients at risk										
mRNA-4157 (V940) + pembrolizumab	107	100	92	90	65	35	14	6	1	0
Pembrolizumab	50	48	47	43	40	18	7	3	0	0

	Median (95% CI), Months	Events, % (n/N)	Hazard ratio (95% CI)[a]
mRNA-4157 (V940) + pembrolizumab	NE	3.7 (4/107)	0.425 (0.114–1.584)
Pembrolizumab	NE	10.0 (5/50)	

[a]The hazard ratio and 95% CI for mRNA-4157 (V940) plus pembrolizumab versus pembrolizumab were 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.

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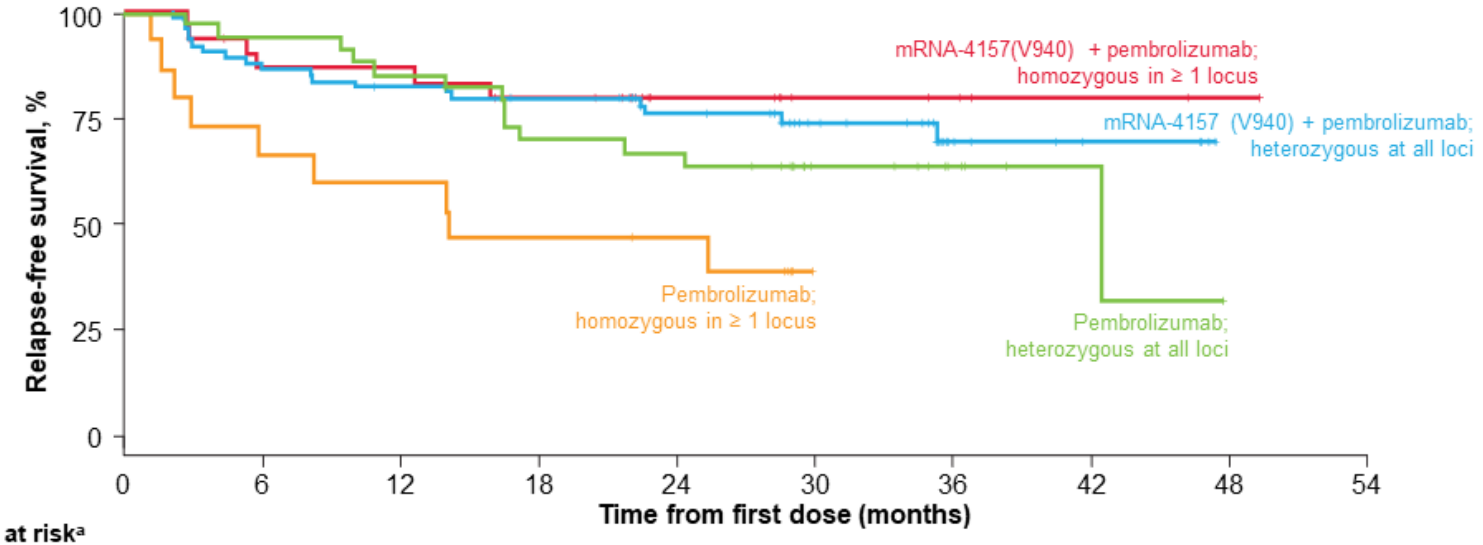
Biomarker analyses suggest mRNA-4157 (V940) + pembrolizumab may benefit a broad patient population

- HLA class I plays a key role in CD8 T cell immunosurveillance
- HLA diversity has been linked with differential immune responses to infection and autoimmune diseases
- No significant associations between individual HLA alleles and RFS were observed for mRNA-4157 + pembrolizumab



Patients at risk[a]

mRNA-4157 (V940) + pembrolizumab; heterozygous at all loci[b]	74	62	58	55	42	24	8	4	0	0
mRNA-4157(V940) + pembrolizumab; homozygous in ≥ 1 locus[c]	31	25	25	22	10	5	4	2	1	0
Pembrolizumab; heterozygous at all loci[b]	34	31	28	22	21	10	5	2	0	0
Pembrolizumab; homozygous in ≥ 1 locus[c]	15	10	9	7	6	0	0	0	0	0

The benefit of mRNA-4157 (V940) + pembrolizumab continued to be observed irrespective of PD-L1, TMB, and ctDNA status,[d] as presented previously

Note: In a large dataset, HLA diversity has not been shown as a determinant of response to pembrolizumab.[1]
[a]Analyses are based on subpopulation with HLA data (n = 154) and excluded 3 patients who did not receive treatment in either arm; [b]HLA heterozygous: heterozygous at all HLA-A/B/C loci; [c]HLA homozygous: homozygous at ≥ 1 locus of HLA-A, HLA-B, and HLA-C; [d]Supportive analysis RFS HR (95% CI) for mRNA-4157 + pembrolizumab versus pembrolizumab in TMB-high: 0.564 (0.253–1.258); TMB-non-high: 0.571 (0.245–1.331); PD-L1-positive: 0.471 (0.226–0.979); PD-L1-negative: 0.147 (0.034–0.630); and ctDNA-negative: 0.207 (0.091–0.470) subgroups; ctDNA-positive HR was not estimable. CD, cluster of differentiation; ctDNA, circulating tumor DNA; HLA, human leukocyte antigen; PD-L1, programmed death ligand 1; TMB, tumor mutational burden.
1. Chhibber A, et al. *Immunity* 2022;55:56-64.e4.

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3-year safety follow-up on safety demonstrates a manageable profile consistent with the primary analysis

	mRNA-4157 (V940) + pembrolizumab (n = 104)		Pembrolizumab (n = 50)	
Event, n (%)	**Any grade**	**Grade ≥ 3**	**Any grade**	**Grade ≥ 3**
Any AE	104 (**100%**)	36 (**34.6%**)	46 (**92.0%**)	18 (**36.0%**)
Any treatment-related AE	104 (**100%**)	26 (**25.0%**)	41 (**82.0%**)	10 (**20.0%**)
Serious AE[a]	15 (**14.4%**)		5 (**10.0%**)	
Immune-related AE[b]	39 (**37.5%**)	11 (**10.6%**)	18 (**36%**)	7 (**14.0%**)

mRNA-4157 (V940) + pembrolizumab (n = 104), n (%)	Grade 1	Grade 2	Grade 3	Grade 4/5	Total (n = 104)
Patients with mRNA-4157 (V940)–related AE[c]	**35 (33.7%)**	**51 (49.0%)**	**12 (11.5%)**	**0**	**98 (94.2%)**
Fatigue	40 (38.5%)	18 (17.3%)	5 (4.8%)	0	63 (60.6%)
Injection site pain	37 (35.6%)	22 (21.2%)	0	0	59 (56.7%)
Chills	48 (46.2%)	3 (2.9%)	0	0	51 (49.0%)
Pyrexia	34 (32.7%)	15 (14.4%)	1 (1.0%)	0	50 (48.1%)
Headache	20 (19.2%)	13 (12.5%)	0	0	33 (31.7%)
Injection site erythema	29 (27.9%)	4 (3.8%)	0	0	33 (31.7%)
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%)	5 (4.8%)	1 (1.0%)	0	22 (21.2%)

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 were not evaluated by toxicity grade; [b]Based on established list of pembrolizumab immune-related AEs (CMQ Pembrolizumab AEOSI); [c]mRNA-4157 (V940)–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. AE, adverse event; AEOSI, adverse event of special interest; CMQ, customized MedDRA queries.

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Conclusions

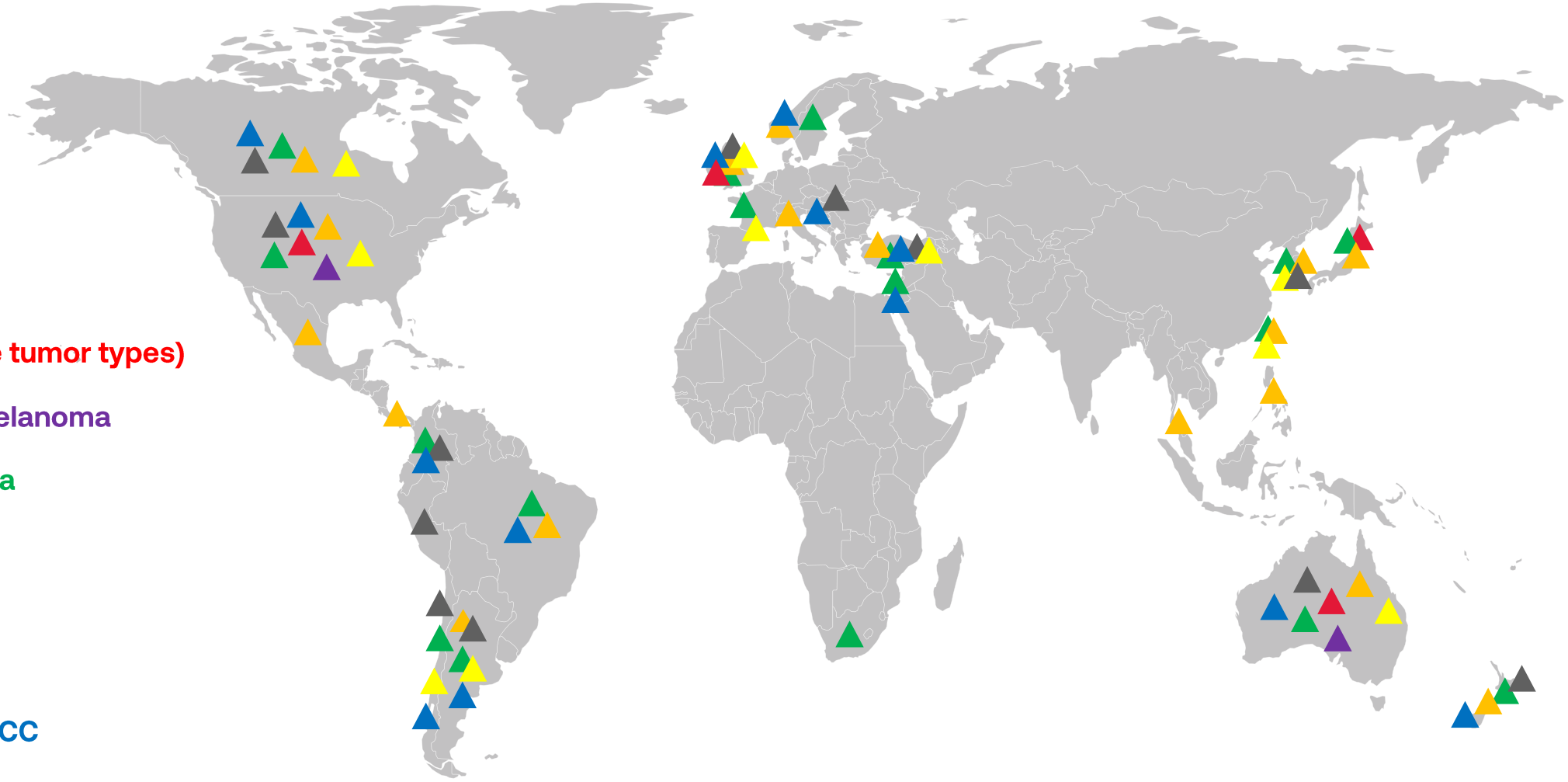
mRNA-4157 (V940) + pembrolizumab demonstrated a durable **clinically significant improvement in RFS & DMFS** compared with standard of care pembrolizumab in high-risk resected melanoma, with a **49% reduction in the risk of recurrence or death** and a **62% reduction of distant recurrence or death** with 3 years of follow-up

3-year exploratory endpoint showed an **encouraging trend in overall survival** with the combination versus pembrolizumab monotherapy

mRNA-4157 (V940) + pembrolizumab has a **manageable safety profile** without potentiation of immune-related AEs compared with pembrolizumab monotherapy

Translational analyses suggest mRNA-4157 (V940) + pembrolizumab may benefit a **broad patient** population **irrespective of the status of PD-L1, TMB, ctDNA, and HLA heterozygosity**

Merck's and Moderna's global INT program has expanded to more than 45 countries



P101 – Phase 1 (multiple tumor types)

P201 – Ph2 adjuvant melanoma

Ph3 adjuvant melanoma

Ph3 adjuvant NSCLC

Ph2 adjuvant RCC

Ph2 adjuvant MIBC

Ph2/3 peri-adjuvant cSCC

Intismeran Adjuvant Melanoma Summary

Clinical Results and Experience (Phase 2)

- mRNA-4157 (V940) + pembrolizumab demonstrated a durable **clinically significant improvement in RFS & DMFS** at 3 years follow-up compared to standard of care pembrolizumab in high-risk resected melanoma:
  - 49% reduction (HR 0.51) in the risk of recurrence or death (RFS)
  - 62% reduction (HR 0.38) of distant recurrence or death (DMFS)
- 3-year exploratory endpoint showed **encouraging trend in overall survival (OS)**

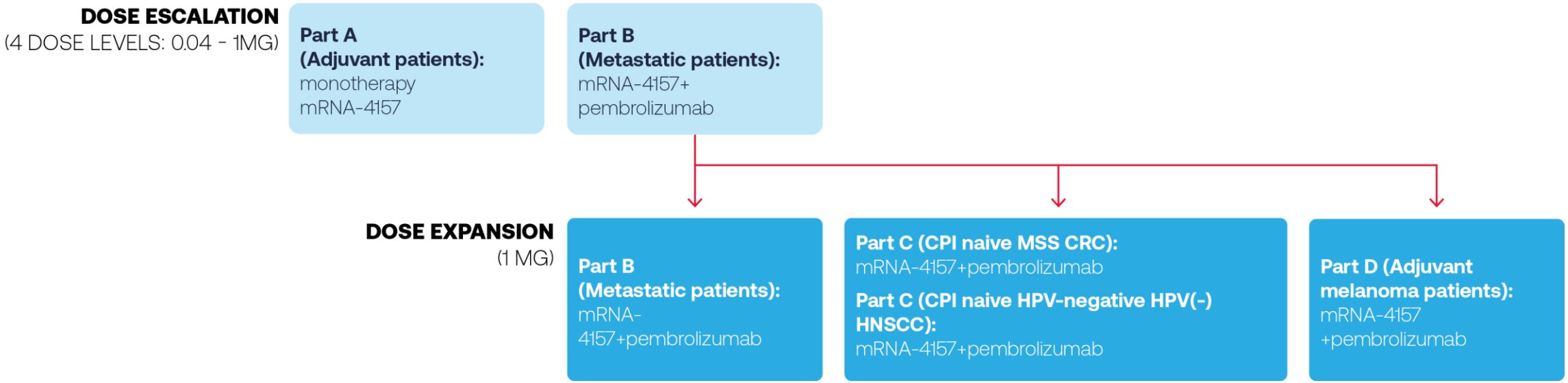
Safety (Phase 2)

- Showed a manageable safety profile without potentiation of immune-related AEs compared with pembrolizumab monotherapy

Next steps

- Expecting to share 5-year data for Phase 2 study, and executing on Phase 3 study

mRNA-4157-P101/KEYNOTE-603 Phase 1 study provided data on multiple tumor types



Part A histologies (adjuvant)

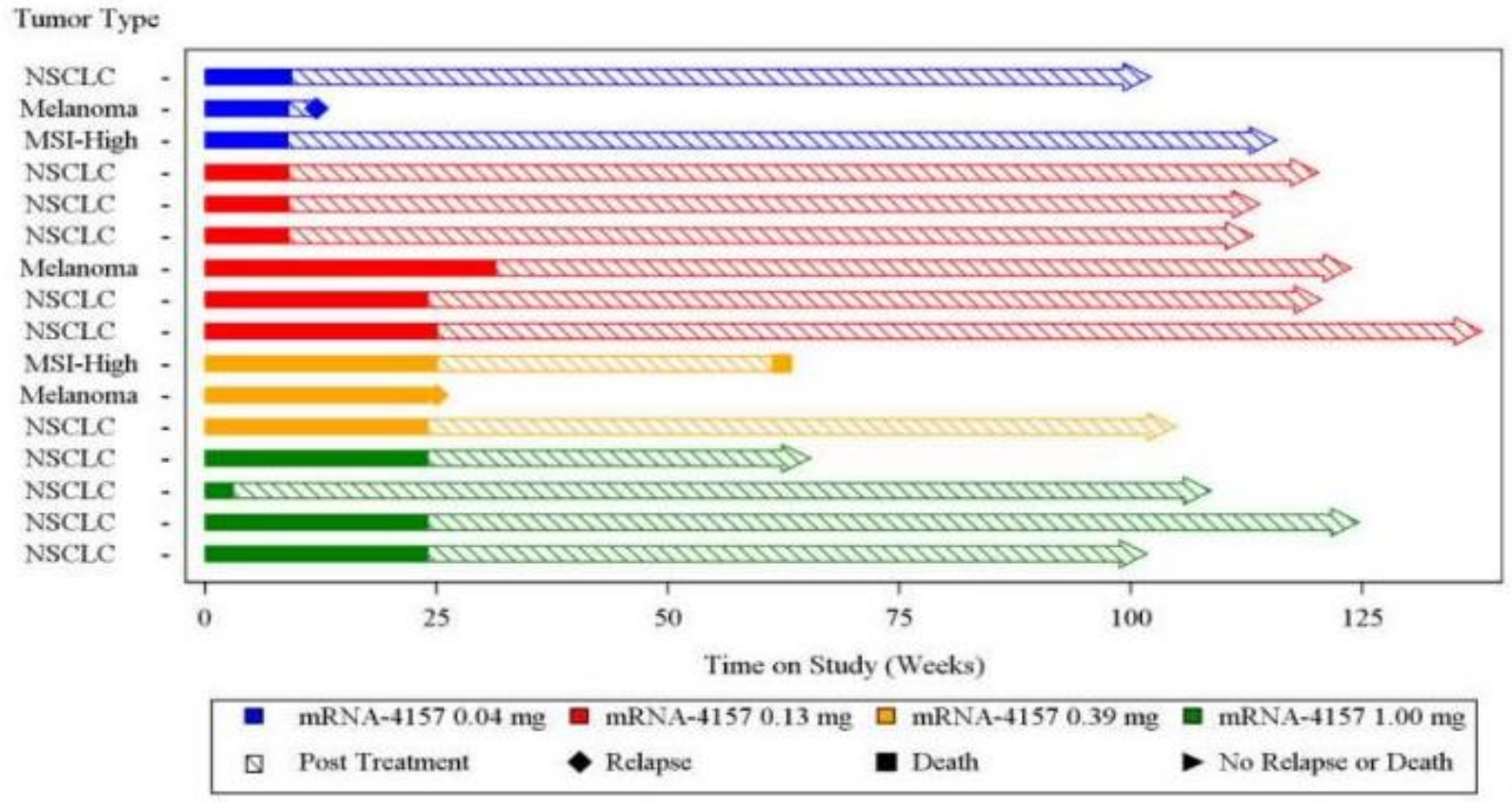
- Melanoma
- MSI High/MMR Deficient
  - Colorectal carcinoma
- Non-small cell lung cancer

Part B histologies (metastatic)

- TMB High Malignancies
- Bladder Urothelial carcinoma
- HNSCC
- Melanoma
- MSI High/MMR Deficient Malignancies
- Non-small cell lung cancer
- Small cell lung cancer

INT monotherapy in adjuvant suggests encouraging clinical activity in early disease setting

Part A: Adjuvant patients receiving mRNA-4157 monotherapy



Positive outcomes for patients treated with mRNA-4157 monotherapy

n= 11 early stage (1A-IIB) NSCLC patients showed potential benefit compared to historical studies, aligned with Ph2 melanoma results

NSCLC Ph1 Data and adjuvant Phase 3 summary

Non-small cell lung cancer (NSCLC) is one of the most common cancers in the world and remains an area of high unmet medical need with 5-year overall survival (OS) rates for patients with surgically treated NSCLC ranging from approximately 10% (Stage IIIB) to 65% (Stage I)

NSCLC can be regarded as a direct biological adjacency to melanoma, whereby increasing neoantigen presentation may produce clinically superior outcomes over checkpoint blockade alone

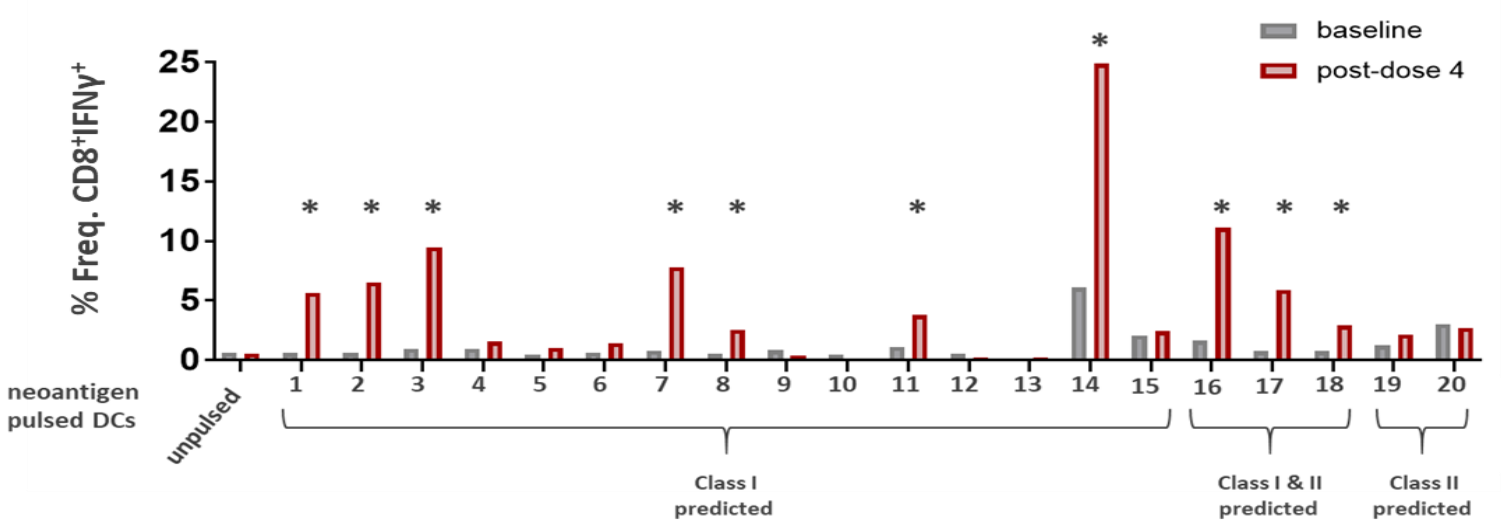
Treatment with mRNA-4157 monotherapy resulted in induction of T cell responses to selected INT neoantigens

11 of 11 participants with early-stage NSCLC treated with mRNA-4157 monotherapy remained recurrence event free throughout the Phase 1 study

Phase 3 study in adjuvant NSCLC is enrolling now

Phase 1 study demonstrates INT induces CD8 T-cell proliferation against selected neoantigens

Immunogenicity profile of an adjuvant NSCLC patient



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 treatment

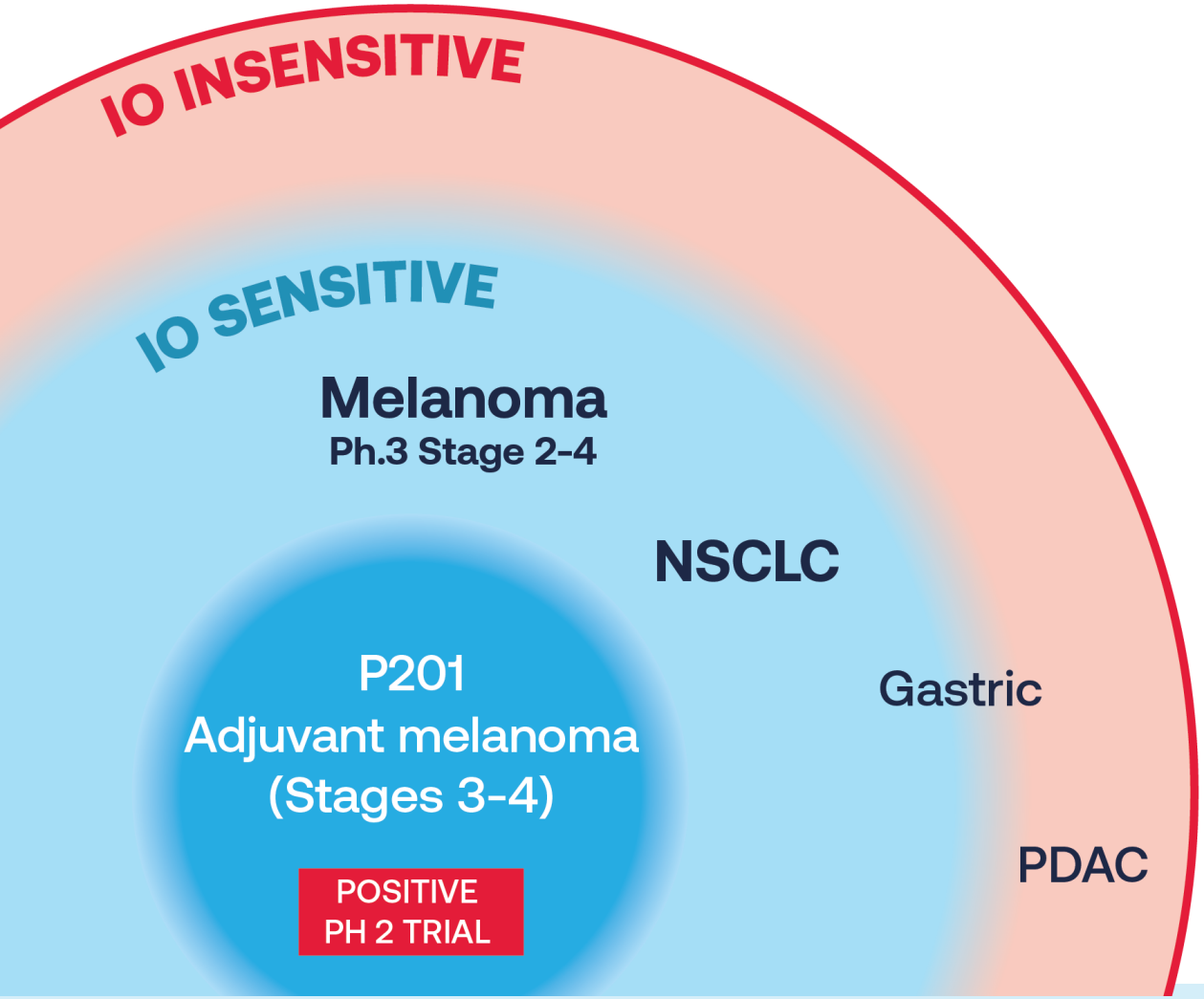
Previously shared at ASCO 2019

Greater than 3x increases in neoantigen specific CD8 T-cells were detected post 4th dose 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**

Burris H.A., et al. Presented at the American Society of Clinical Oncology(ASCO) Annual Meeting; May 31-June 4, 2019; Chicago, IL, USA. Abstract 93

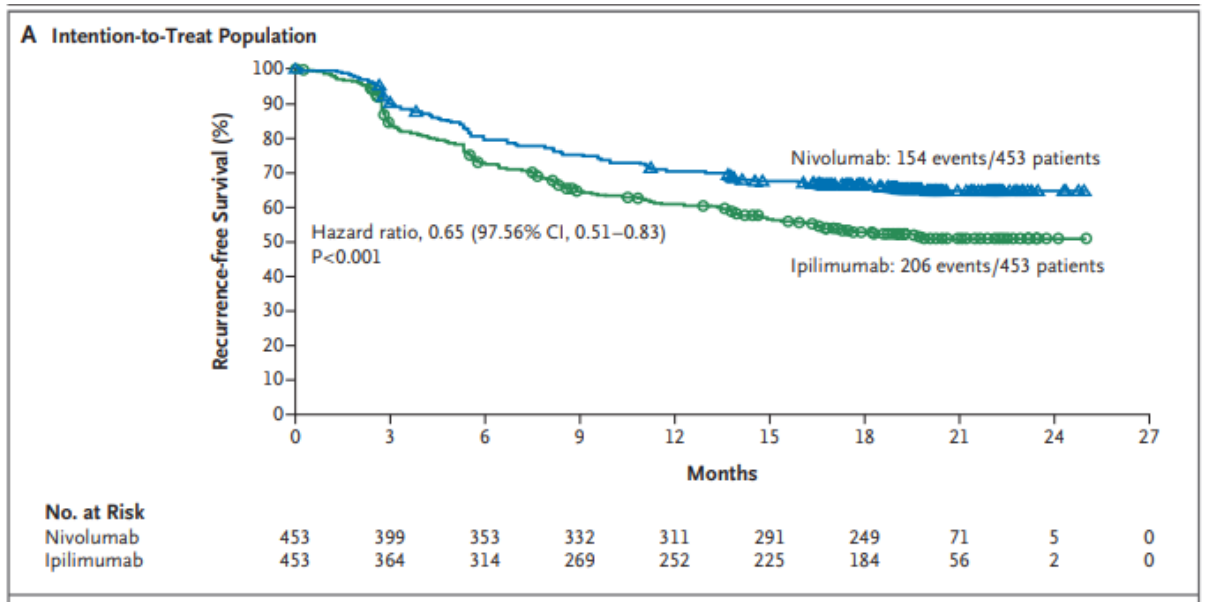
Potential INT indications



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

Checkmate-238

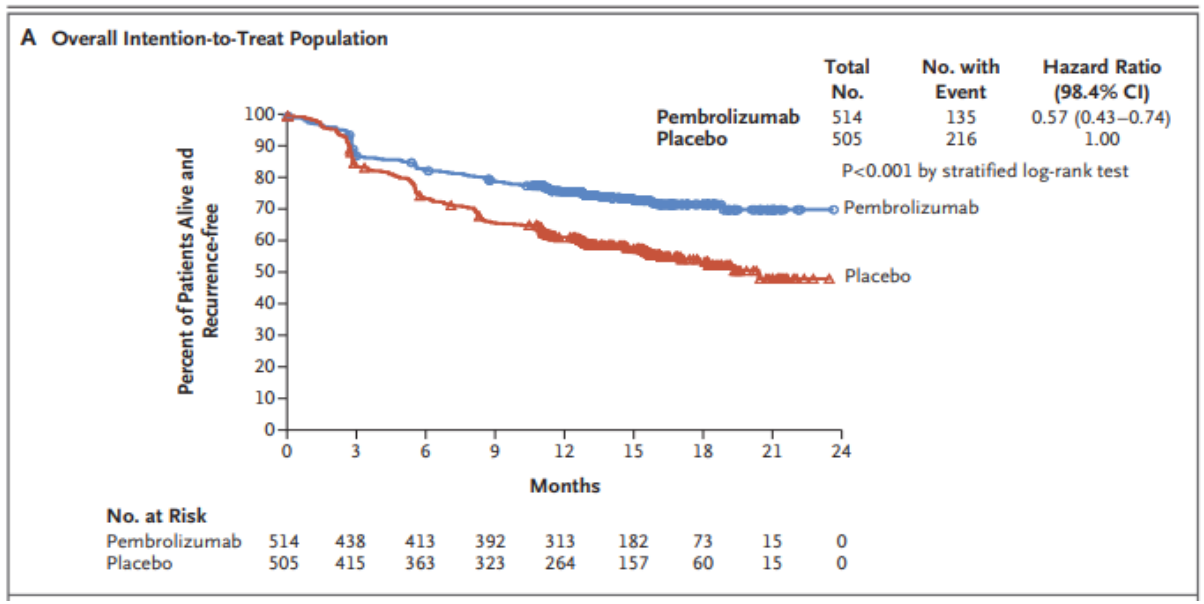
12mo RFS: 70.5% vs. 60.8%



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

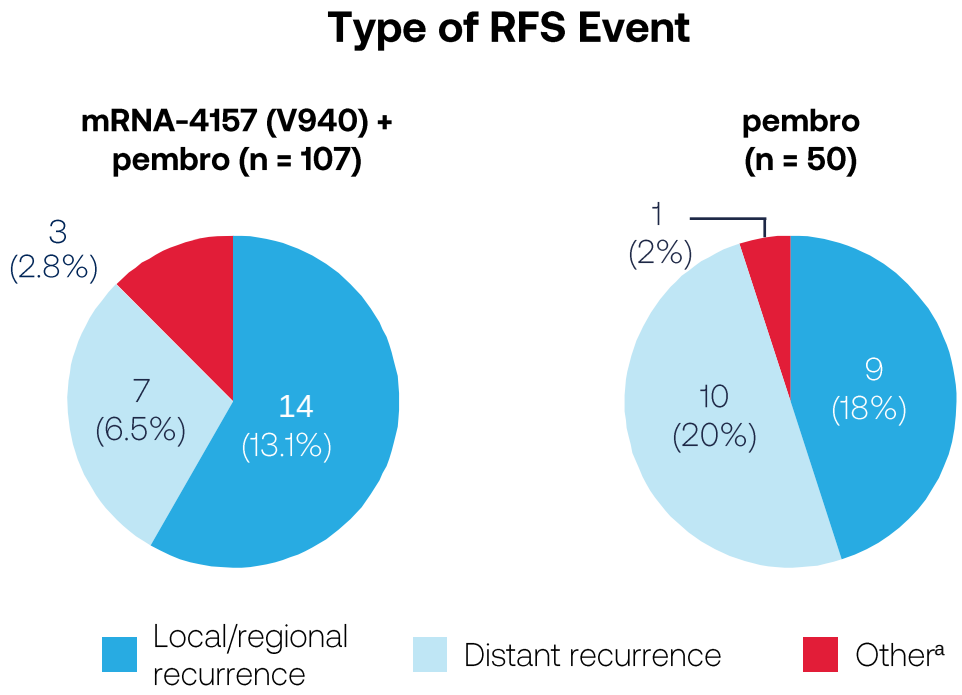
mRNA-4157-P201/KEYNOTE-942 Patient Demographics

Characteristic, n (%)	mRNA-4157 (V940) + pembro (n = 107)	Pembro (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)
Range (median)	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]		
Stage IIIC	89 (83.2)	42 (84.0)
Stage IIID	2 (1.9)	2 (4.0)
Stage 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)
Indeterminant[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 WES on baseline tumor samples. [e]WT refers to position 600 on BRAF gene. [f]Available for 154 patients. WES, whole exome sequencing; WT, wild type.

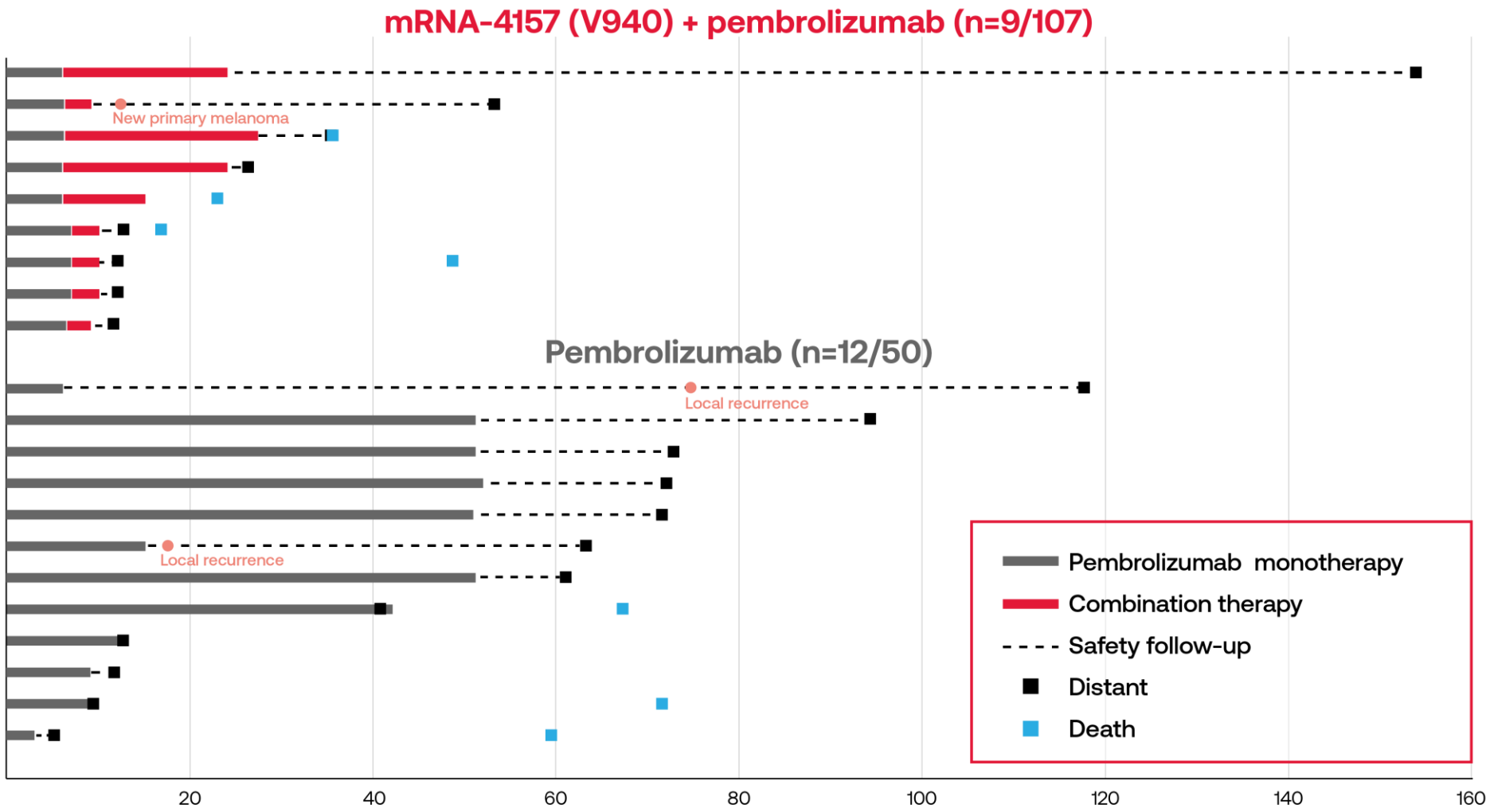
Recurrence Type and Distant Recurrence Location

24/107 (22.4%) patients in the mRNA-4157 (V940) + pembro arm versus 20/50 (40.0%) in the pembro monotherapy arm experienced an RFS event



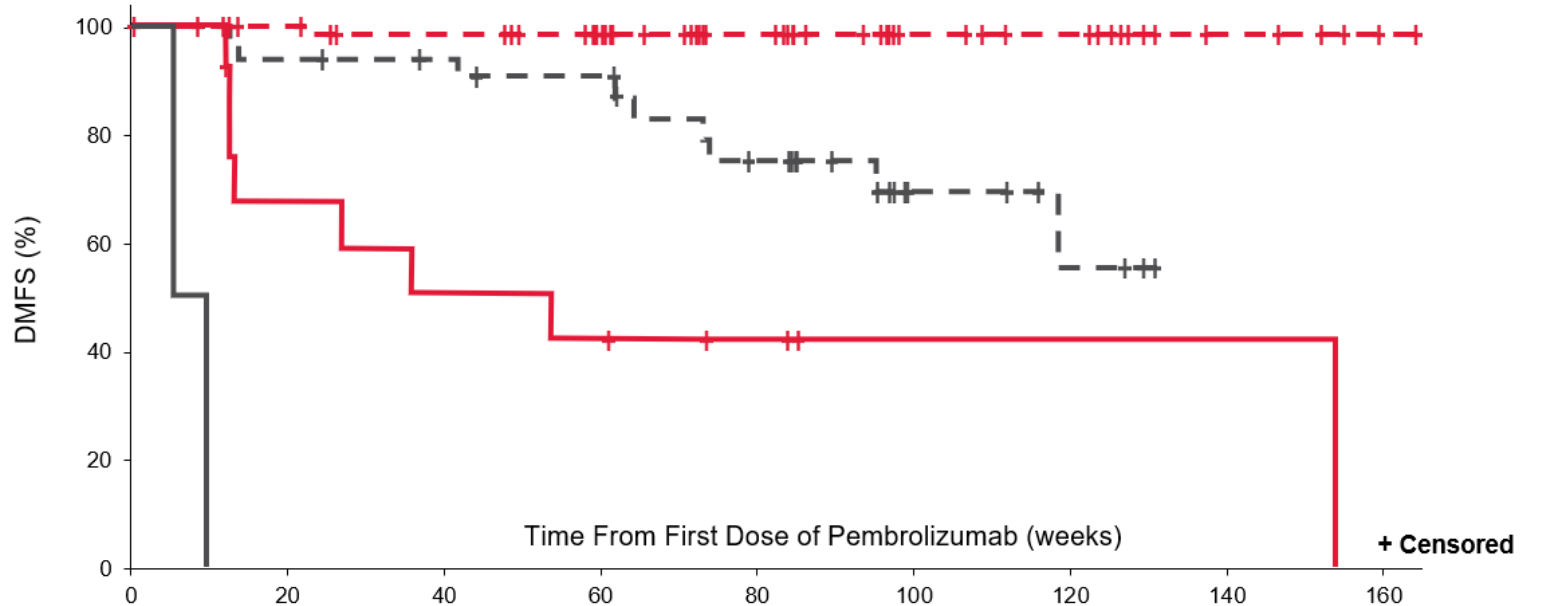
	mRNA-4157 (V940) + pembro (n = 107)	pembro (n = 50)
Patients with distant recurrence (with or without prior recurrence) or death, n (%)	**9 (8.4)**	**12 (24.0)**
Site of distant recurrence, n (%)		
Lymph node	2 (1.9)	4 (8.0)
Lung	2 (1.9)	4 (8.0)
Liver	3 (2.8)	1 (2.0)
Bone	1 (0.9)	2 (4.0)
Brain	1 (0.9)	3 (6.0)
Skin	0	4 (8.0)
Colon	1 (0.9)	1 (2.0)
Spleen	0	1 (2.0)
Soft tissue	1 (0.9)	0
Other site	2 (1.9)	1 (2.0)
Death not due to melanoma	1 (0.9)[b]	0

Longitudinal Pattern of DMFS Events During and After Treatment Completion



Reasons for death were disease progression (n = 2), unrelated AE (n = 1, without distant recurrence, from sepsis), and unknown (n = 1) in the mRNA-4157 (V940) + pembrolizumab arm and disease progression (n = 3) in the pembrolizumab monotherapy arm.

DMFS by ctDNA Status at Baseline



Number at Risk

ctDNA-neg: mRNA-4157 (V940) + pembrolizumab	77	73	69	57	38	18	15	6	1
ctDNA-neg: pembrolizumab	33	30	28	26	18	7	4	0	0
ctDNA-pos: mRNA-4157 (V940) + pembrolizumab	13	8	6	5	3	1	1	1	0
ctDNA-pos: pembrolizumab	2	0	0	0	0	0	0	0	0

	mRNA-4157 (V940) + pembro vs pembro HR (95% CI)[a]	mRNA-4157 (V940) + pembro Events, % (n/N)	pembro Events, % (n/N)
ctDNA-neg	0.048 (0.006, 0.380)	1.3 (1/77)	27.3 (9/33)
ctDNA-pos	NE	61.5 (8/13)	100 (2/2)

See LBA9515 presented by Matteo S. Carlino on 03Jun

Minimal residual disease by circulating tumor DNA as a biomarker of recurrence free survival in resected high-risk melanoma patients treated with mRNA-4157 (V940), a personalized cancer vaccine, and pembrolizumab.

ctDNA was NE at baseline for 20.4% (32/157) patients from this study due to unavailability of the sample at baseline (mRNA-4157 (V940) + pembrolizumab, n = 15; pembrolizumab monotherapy, n = 14) or insufficient number of RaDaR® variants identified by WES (quality control flag: mRNA-4157 (V940) + pembrolizumab, n = 2; pembrolizumab monotherapy, n = 1). Results limited by small sample size and event number. ctDNA, circulating tumor DNA.

mRNA-4157-P201/KEYNOTE-942 Safety and Tolerability[1]

	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)**	**13 (12.5%)**	**5 (10.0)**	**4 (8.0%)**
mRNA-4157 (V940) 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

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 (V940), 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 pembrolizumab and mRNA-4157 (V940)..

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

mRNA-4157-P201/KEYNOTE-942 Safety and Tolerability

All-cause immune-mediated AEs	mRNA-4157 (V940) + pembro (n = 104)		pembro (n = 50)	
Event, n (%)	**Any grade**	**Grade ≥3[a]**	**Any grade**	**Grade ≥3[b]**
Any	**37 (35.6)**	**11 (10.6)**	**18 (36.0)**	**7 (14.0)**
Adrenal insufficiency	5 (4.8)	4 (3.8)	2 (4.0)	1 (2.0)
Colitis	6 (5.8)	3 (2.9)	2 (4.0)	0
Hepatitis	1 (1.0)	0	1 (2.0)	1 (2.0)
Hyperthyroidism	6 (5.8)	0	3 (6.0)	1 (2.0)
Hypophysitis	1 (1.0)	0	0	0
Hypothyroidism	21 (20.2)	0	8 (16.0)	0
Myositis	0	0	1 (2.0)	1 (2.0)
Nephritis	3 (2.9)	3 (2.9)	1 (2.0)	0
Pancreatitis	0	0	1 (2.0)	1 (2.0)
Pneumonitis	4 (3.8)	1 (1.0)	0	0
Sarcoidosis	0	0	1 (2.0)	0
Severe skin reaction	3 (2.9)	0	1 (2.0)	0
Thyroiditis	0	0	2 (4.0)	1 (2.0)
Type 1 diabetes mellitus	0	0	1 (2.0)	1 (2.0)
Uveitis	1 (1.0)	0	1 (2.0)	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]Includes grade 4 adrenal insufficiency and colitis (n = 1 each), attributed to pembro only and not mRNA-4157 (V940); no grade 5 events occurred. [b]No grade 4 or 5 events occurred.

Minimal Residual Disease by Circulating Tumor DNA as a Biomarker of Recurrence-free Survival in Resected High-risk Melanoma Patients Treated With mRNA-4157 (V940), a Personalized Cancer Vaccine, and Pembrolizumab

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Objectives and Methods

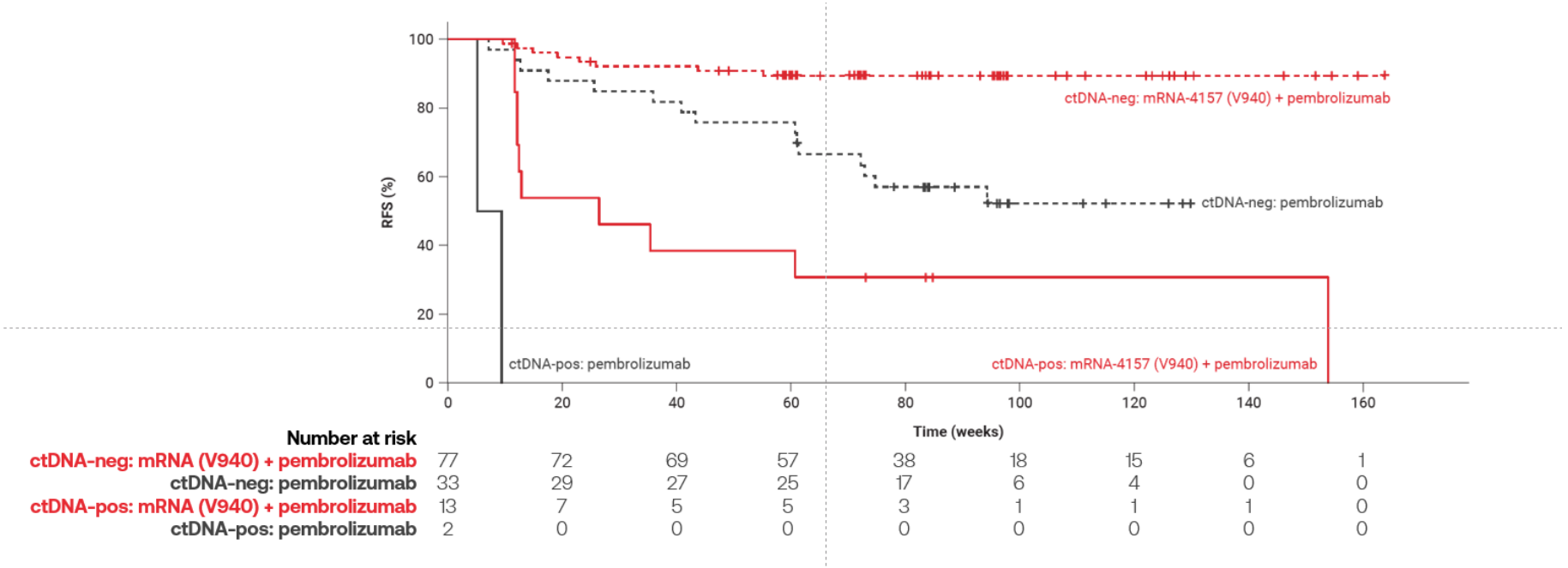
Objectives

- To assess the distribution of patients with minimal residual disease (MRD) at baseline across study arms
- To assess RFS (the primary study endpoint) in patient subgroups that are ctDNA-positive or ctDNA-negative at baseline
- To assess the prognostic value of ctDNA status at baseline

Methods

- ctDNA was assessed on baseline plasma samples using the personalized amplicon-based NGS NeoGenomics (RaDaR®) assay
  - Tumor core biopsies and matched whole blood samples were subjected to whole exome sequencing (WES) to identify up to 48 patient-specific somatic variants most suitable for MRD detection
  - ctDNA was not evaluable at baseline for 20.4% (32/157) of patients from this study due to unavailability of plasma sample at baseline or insufficient number of RaDaR® variants identified in WES data
- Tumor biomarker assessments were conducted on formalin-fixed paraffin-embedded tumor core biopsies as previously described13
- Association of ctDNA and tumor biomarkers with the primary study endpoint RFS were evaluated with Kaplan-Meier analyses and HR with 95% CI based on an unstratified Cox proportional hazards model
- The prognostic value of ctDNA and tumor biomarkers with respect to RFS was assessed by HRs (95% CIs) comparing ctDNA and biomarker subgroups, pooled from both treatment arms, and obtained from an unstratified Cox proportional hazards model that included biomarker group as a covariate

The combination of mRNA-4157 (V940) + pembrolizumab improved RFS in ctDNA-negative patients at baseline compared to pembrolizumab monotherapy

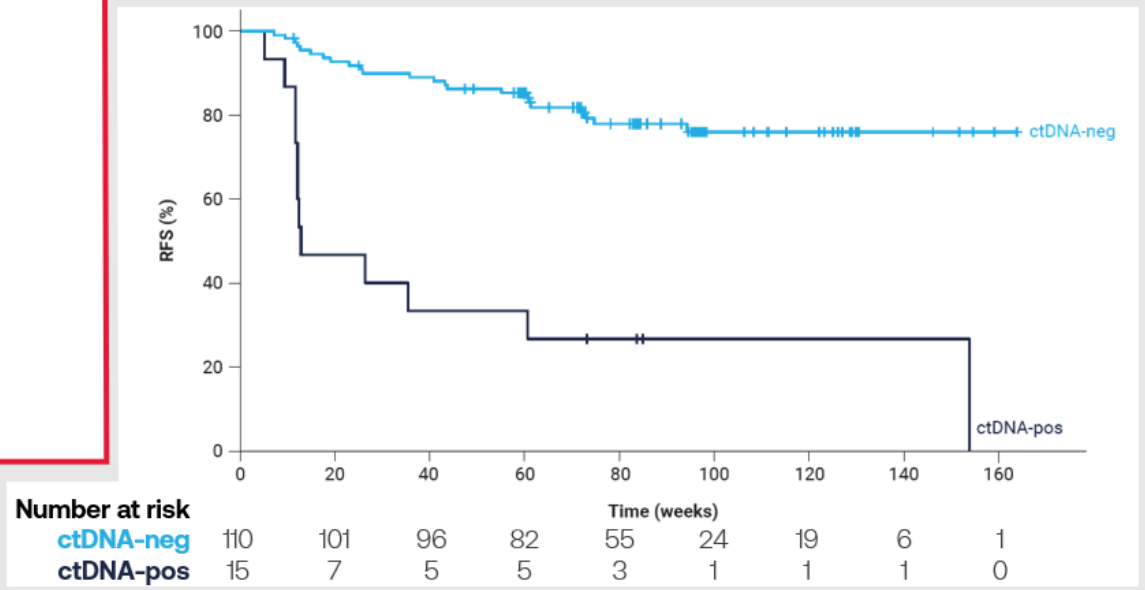


	mRNA-4157 (V940) + pembrolizumab vs pembrolizumab HR (95% CI)	mRNA-4157 (V940) + pembrolizumab Events, n/N (%)	pembrolizumab Events, n/N (%)
ctDNA-pos	NE	10/13 (76.9)	2/2 (100)
ctDNA-neg	0.225 (0.095, 0.531)	8/77 (10.4)	15/33 (45.5)

ctDNA, circulating tumor DNA; NE, non-evaluable; neg, negative; pos, positive.

Assessments of the association of various biomarkers with RFS across study arms suggested that ctDNA status at baseline had notable negative prognostic value

Distribution of ctDNA-positive and ctDNA-negative Patients Across Study Arms			
ctDNA, n (%)	**mRNA-4157 (V940) + pembrolizumab (n = 90)**	**Pembrolizumab (n = 35)**	**Total (n = 125)**
Positive	13 (14.4)	2 (5.7)	**15 (12.0)**
Negative	77 (85.6)	33 (94.3)	**110 (88.0)**



RFS HR (95% CI) Comparing Biomarker Subgroups in the Biomarker-evaluable Population			
ctDNA-neg vs ctDNA-pos	**TMB-high vs TMB–non-high**	**TIS-high vs TIS-low**	**PD-L1–pos vs PD-L1–neg**
0.149 (0.073, 0.306) n (110 vs 15)	0.476 (0.263, 0.862) n (109 vs 45)	0.452 (0.242, 0.844) n (77 vs 77)	0.661 (0.299, 1.46) n (96 vs 18)

CI, confidence interval; ctDNA, circulating tumor DNA; HR, hazard ratio; neg, negative; PD-L1, programmed death ligand-1; pos, positive; RFS, recurrence-free survival; TIS, tumor inflammation signature; TMB, tumor mutational burden.

Medical and scientific presentations

ASCO 2024 (3-year data)

https://s29.q4cdn.com/435878511/files/doc_presentations/2024/Jun/03/asco-2024-adjuvant-melanoma.pdf

AACR 2025 (TCR dynamics)

https://s29.q4cdn.com/435878511/files/doc_presentations/2025/Apr/27/KEYNOTE-942-TCR-dynamics-AACR-poster.pdf

SITC 2024 (Phase 1 trial designs – PDAC/Lung/Gastric)

https://s29.q4cdn.com/435878511/files/doc_presentations/2024/Nov/08/SITC-INT-Phase-1-Trial-Design.pdf

AACR 2024 (H&N clinical & translational data)

https://s29.q4cdn.com/435878511/files/doc_presentations/2024/Apr/08/12091203_aacr2024_baumann_poster_159-76x94-76_v22_final-61.pdf

ESMO 2023 (clinical data by biomarkers)

https://s29.q4cdn.com/435878511/files/doc_presentations/2023/Oct/23/esmo-2023.pdf

Additional presentations at 2023 ASCO & AACR

https://investors.modernatx.com/events-and-presentations/Scientific--Medical-Meetings/default.aspx

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; ongoing studies of mRNA-4157; plans to expand to additional tumor types; and the potential to treat patients across all stages of 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.