

VDS Annual Meeting
October 2026

Melanoma update 2026

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The University
of North Carolina
at Chapel Hill

Topics to be covered



- Screening and Early Detection
- Systemic therapy
 - Advanced Disease
 - Adjuvant therapy and Imaging
 - Neoadjuvant therapy
- Intralesional therapy
- GEP

Population Skin Cancer Screening: Does It Reduce Melanoma Mortality?



Research question: *Since Germany introduced population-based skin screening in 2008, has melanoma mortality declined more than in neighboring countries without screening?*

**ECOLOGIC COMPARATIVE-EFFECTIVENESS STUDY •
POPULATION DATA, NOT AN RCT**

79.1M

Germans across 15 federal states

164.8M

Residents of 9 neighboring countries

2009–2022

14-year melanoma mortality trend
analyzed

~32%

2-year screening participation rate (age
35+)

No Mortality Difference Between Germany and Neighboring Countries



Hübner J, Schumann L, Eisemann N, Katalinic A, Beckhaus J. JAMA Dermatol. 2026;162(8):775-779.

GERMANY
-1.8%/yr

Pooled APC, 95% CI -2.3 to -1.4

Population-based screening since 2008 — 15 states, 79.1M residents

P = .42

NOT SIGNIFICANT

9 NEIGHBORING COUNTRIES
-2.2%/yr

Pooled APC, 95% CI -2.8 to -1.6

No population-based screening — 9 countries, 164.8M residents

Consistent Null Result Across Both Pre and Post IO Treatment Eras

Subperiod	Germany (SCS)	Neighboring Countries
2009–2013 (pre targeted/IO era)	+1.1%/yr	+1.0%/yr
2013–2022 (targeted & IO therapy era)	-2.7%/yr	-2.8%/yr

Limitation: Possible Contamination in controls? the Euromelanoma campaign offers free skin checks across many neighboring countries, which could narrow the true gap.

Screening asymptomatic patients: Who benefits?



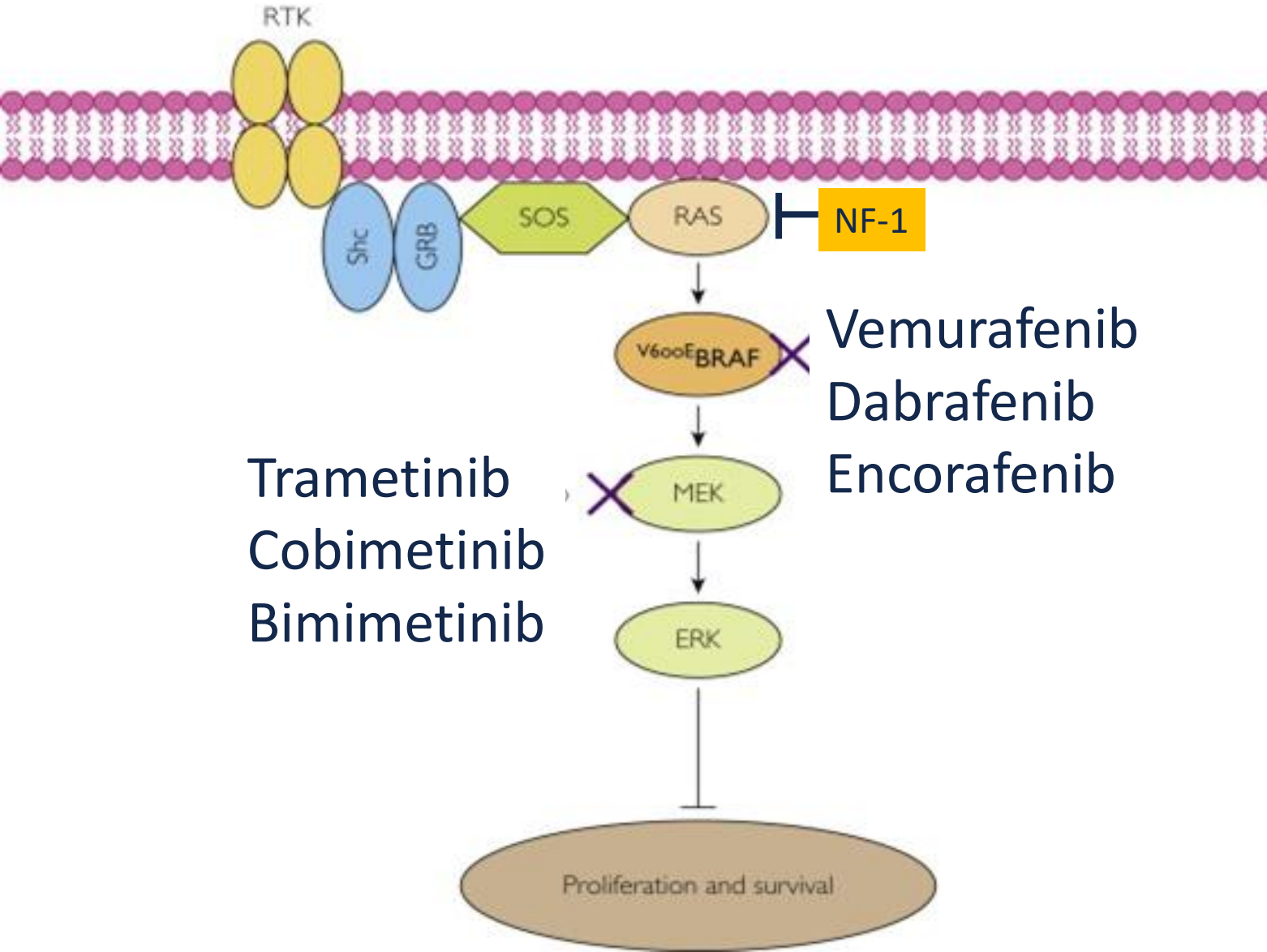
- **Design:** cross-sectional survey, Emory dermatology
Cohort: 1074 new patients with no LOC presenting for a general skin cancer screening exam; mean age 50.3 years, 59.9% female; 186 +PMH skin ca
- **Yield:** 131 patients (12.2%), 146 biopsies
 - 38 skin cancer: 22 BCC, 9 SCC, 6 MM (4 in situ)
- **Risk concentration:** 37/38 cancers in skin phototypes I–III; only 3 in age <50 (no MM)
- **Takeaway:** Simple triage on age, phototype and prior skin-cancer history would concentrate screening on far higher-yield patients

Subgroup	Number needed to examine
All patients	33
Age $\leq$ 50 years	181
Age $\geq$ 70 years	7
Prior skin cancer	12
No prior skin cancer	52



Systemic Therapies

BRAF / MEK Inhibitors

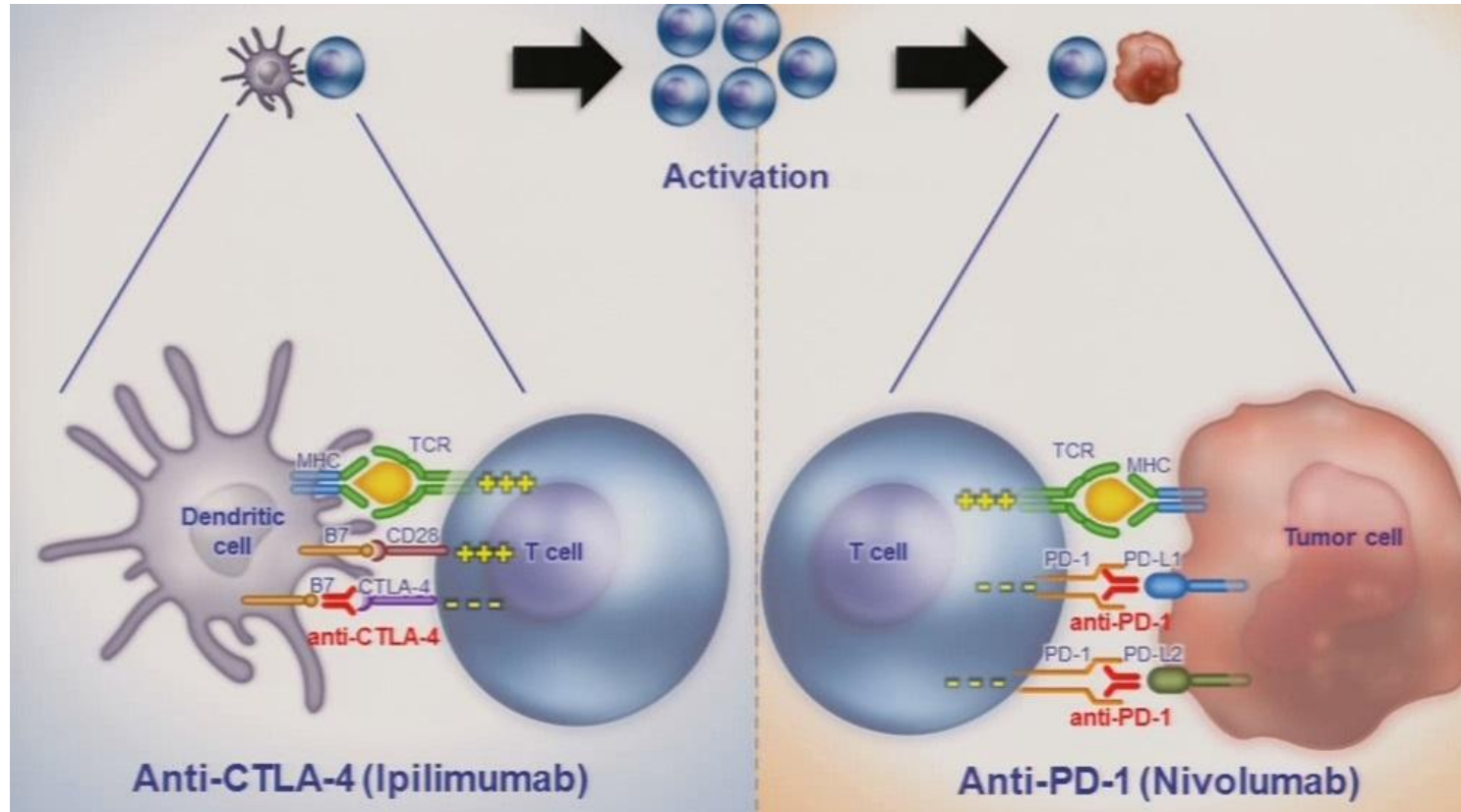


Given as combination therapy:

- Dabrafenib / trametinib,
- Vemurafenib / cobimetinib
- Encorafenib / binimetinib

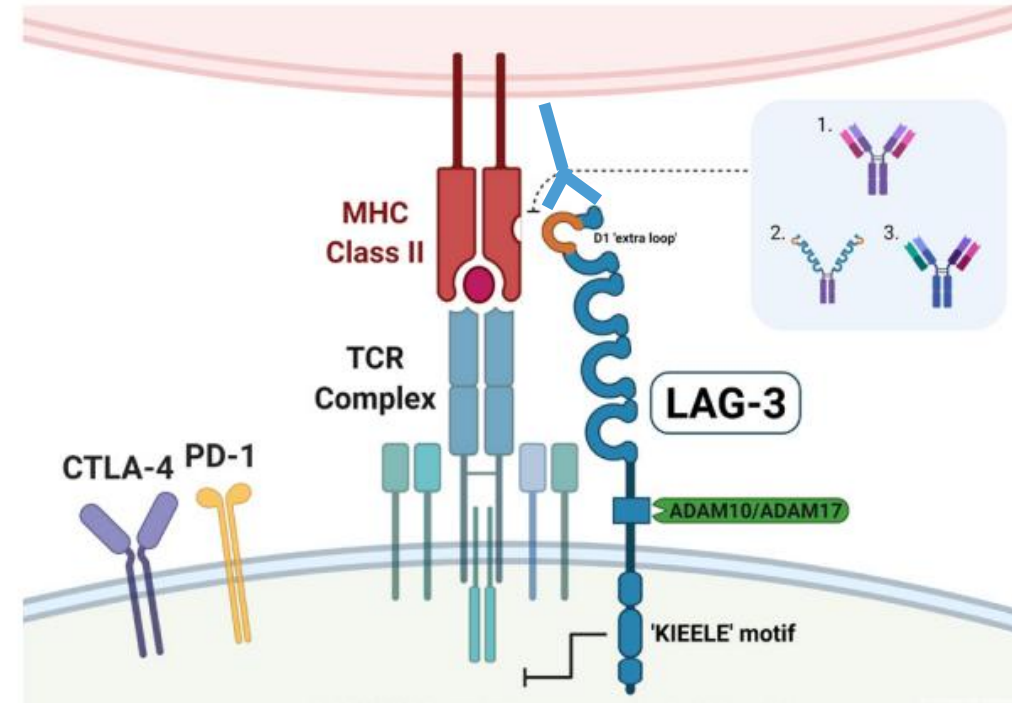
ONLY effective in melanoma that carries BRAF V600 mutation

Immune Checkpoint Inhibitors



Central T cell tolerance
Blocked by anti-CTLA4
(ipilimumab)

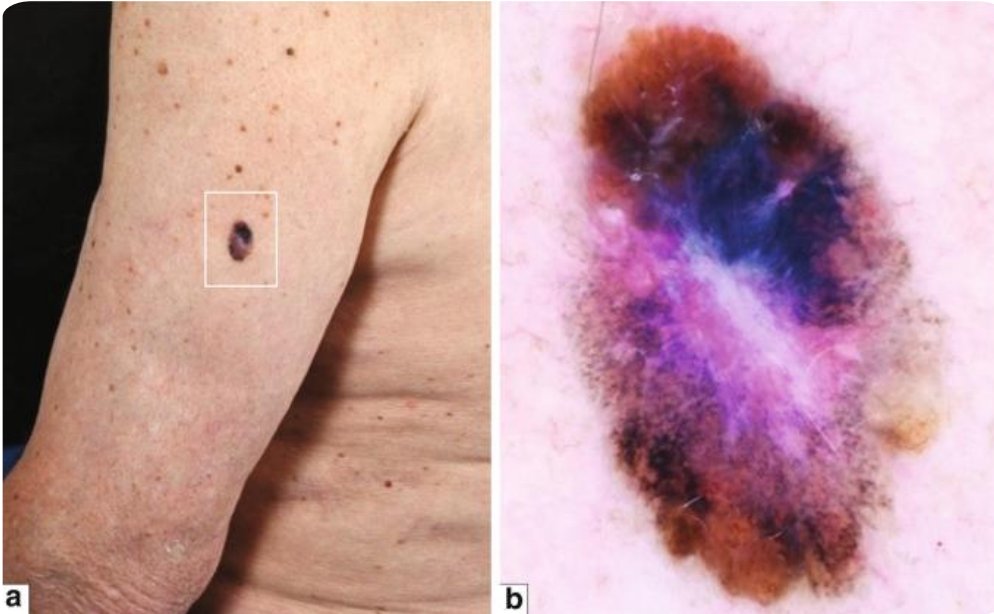
Peripheral T cell tolerance
Blocked by inhibitors of PD-1
(Pembrolizumab, Nivolumab) or
PD-L1 (atezolizumab)



Peripheral T cell tolerance
Blocking of LAG-3 (Relatlimab)

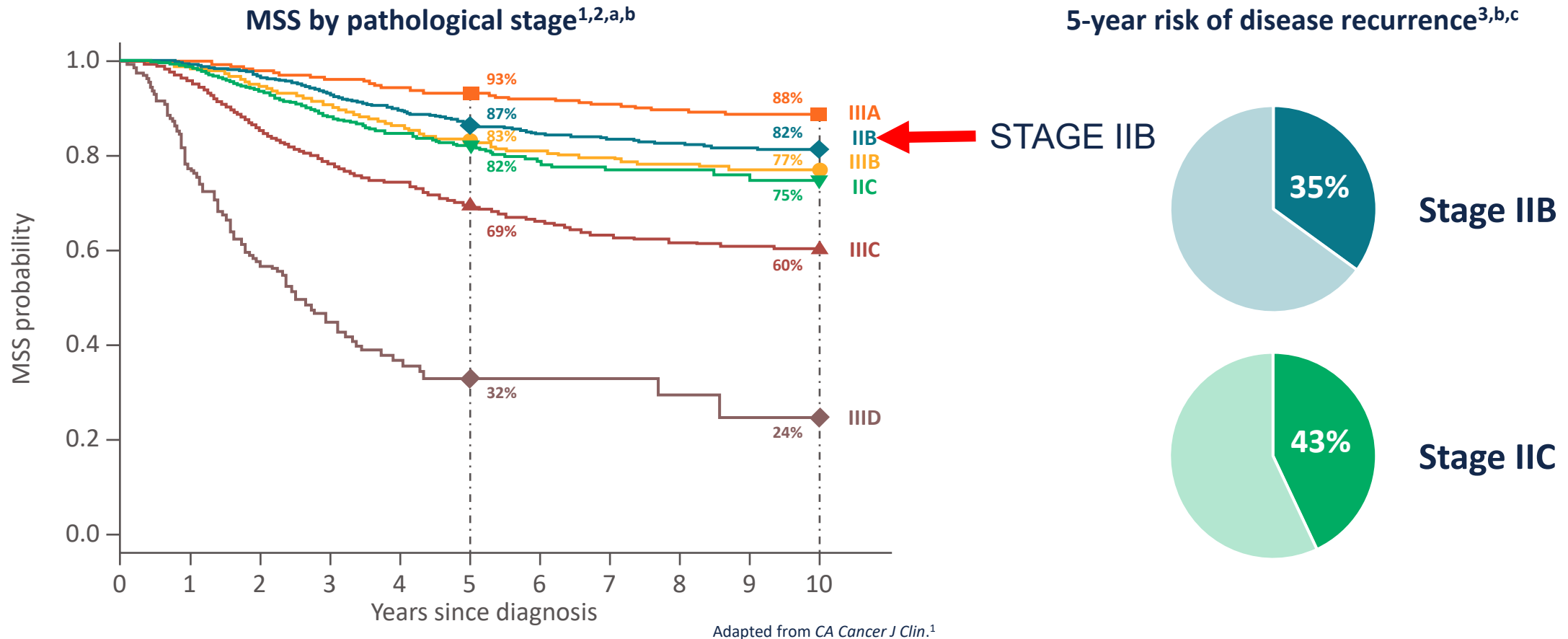
Adjuvant therapy

CASE 1:



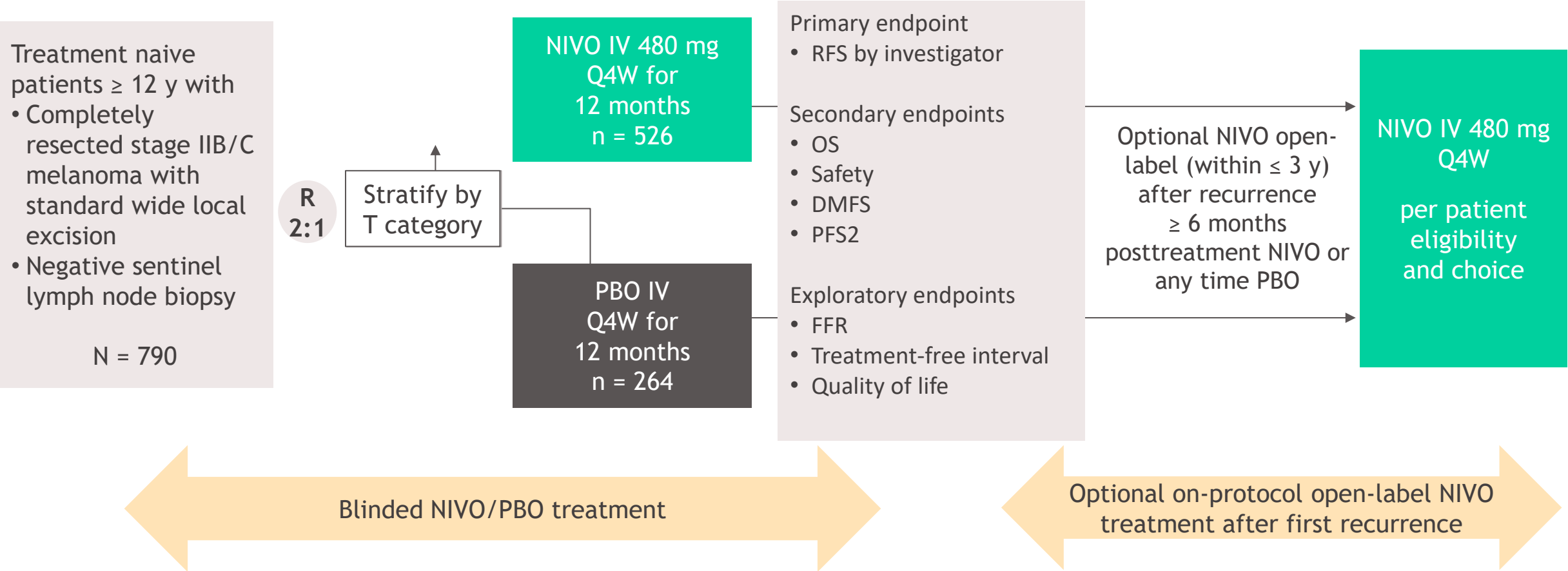
- 72-year-old female with 2.3mm deep, superficial spreading melanoma with ulceration and 3 mit/mm²
- WLE + SLNB were performed, and SLNB. 0/2 nodes involved and there was no residual melanoma.

Adjuvant treatment for stage II-III melanoma



^aMSS was calculated from the date of initial melanoma diagnosis. MSS survival rates represent the percentage of patients who have not died from melanoma in a defined time period. ^bBased on AJCC 8th edition. ^cConfirmatory cohort. AJCC, American Joint Committee on Cancer; Cancer Staging Manual; CMMR, Central Malignant Melanoma Registry; MSS, melanoma-specific survival; RFS, recurrence-free survival. 1. Gershenwald JE et al. *CA Cancer J Clin.* 2017;67:472–492. 2. NCI Dictionary. Disease-specific survival rate. Accessed February 2023. <https://www.cancer.gov/publications/dictionaries/cancer-terms/def/disease-specific-survival-rate> 3. Garbe C et al. *J Clin Oncol.* 2022;40:3741–3749. 4. Romano E et al. *J Clin Oncol.* 2010;28:3042–3047.

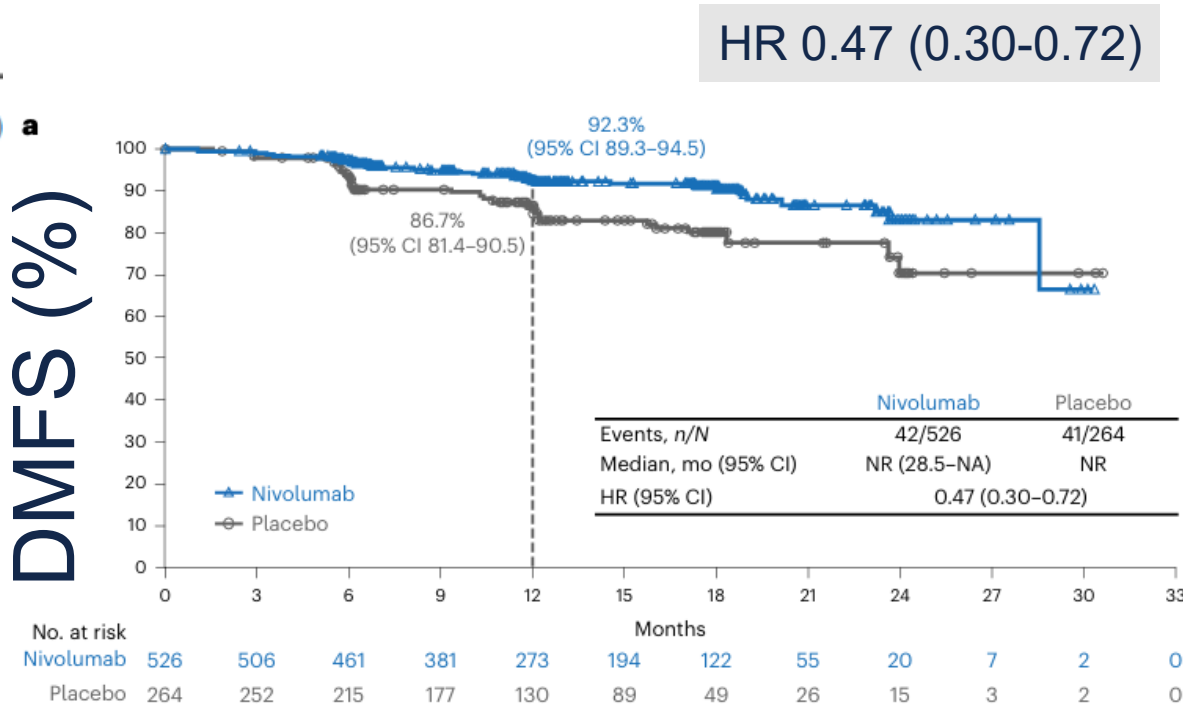
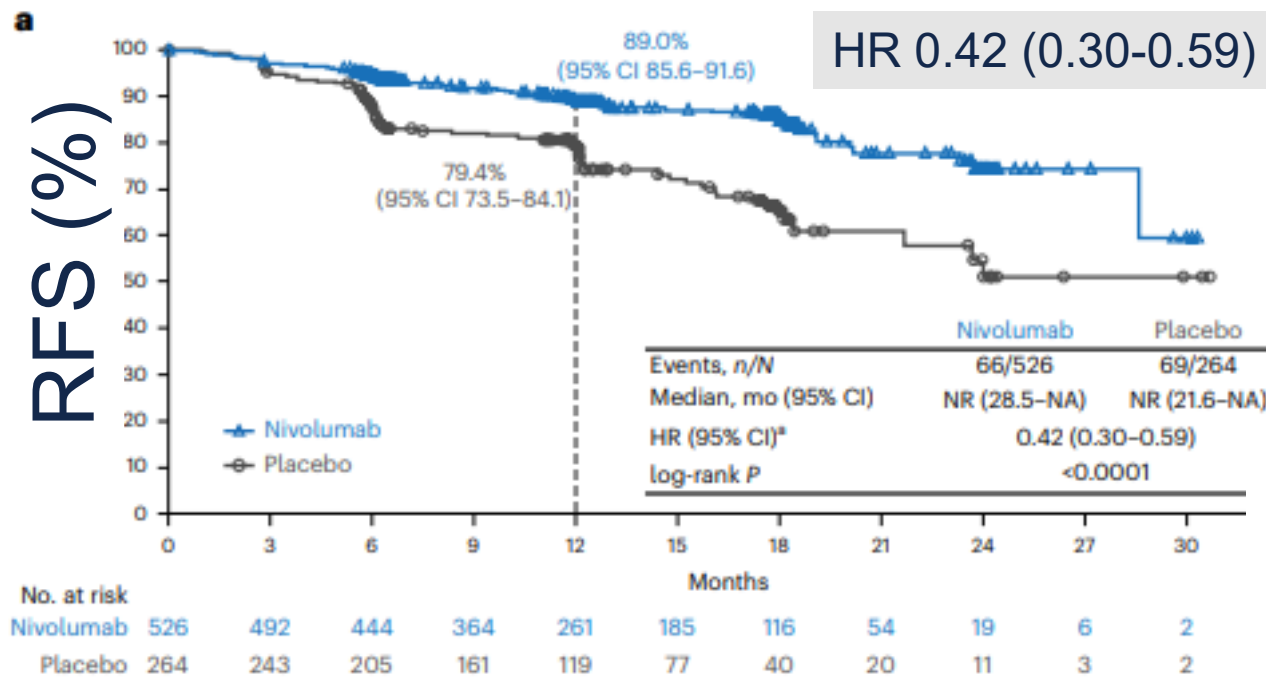
Adjuvant nivolumab in resected stage IIB/C melanoma: primary results from the randomized, phase 3 CheckMate 76K trial



DMFS, distant metastasis-free survival; FFR, freedom from relapse (with censoring patients who died from causes other than disease); NIVO, nivolumab; OS, overall survival; PBO, placebo; PFS2, progression-free survival through next-line therapy; RFS, recurrence-free survival. Adapted from Long GV et al. Oral presentation at Society for Melanoma Research (SMR); October 17–22, 2022; Edinburgh, Scotland.

Adjuvant nivolumab in resected stage IIB/C melanoma: primary results from the randomized, phase 3 CheckMate 76K trial

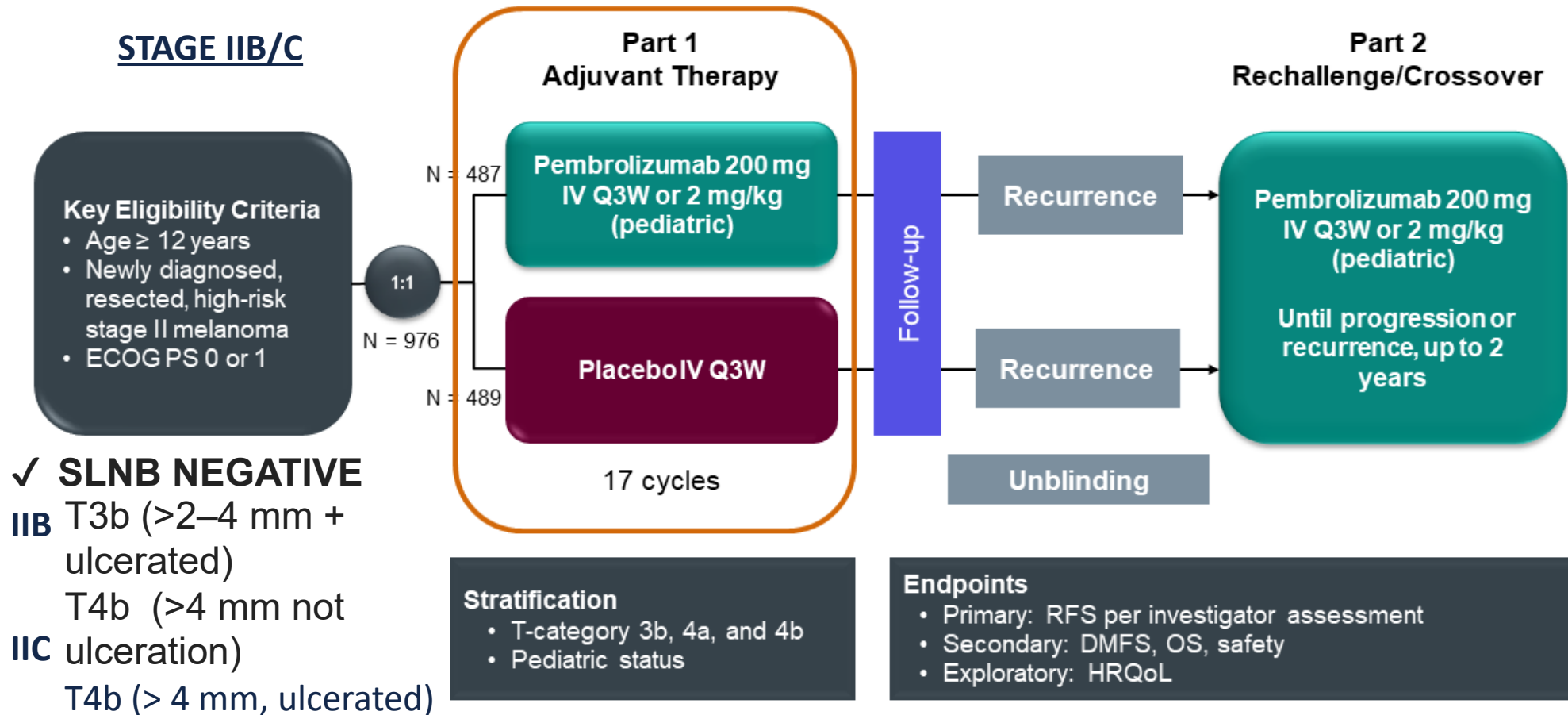
Nat Med. 2023 Nov;29(11):2835-2843.



Adjuvant Therapy for Stage IIB/IIC melanoma

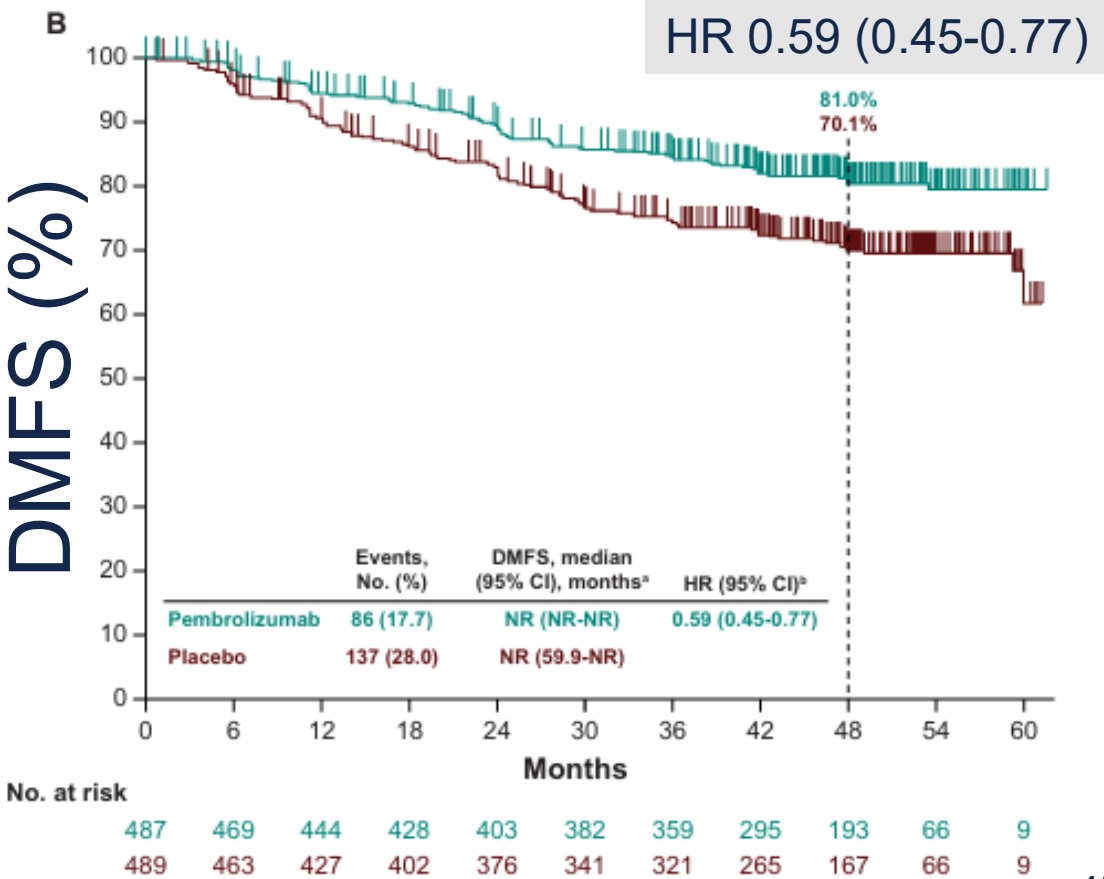
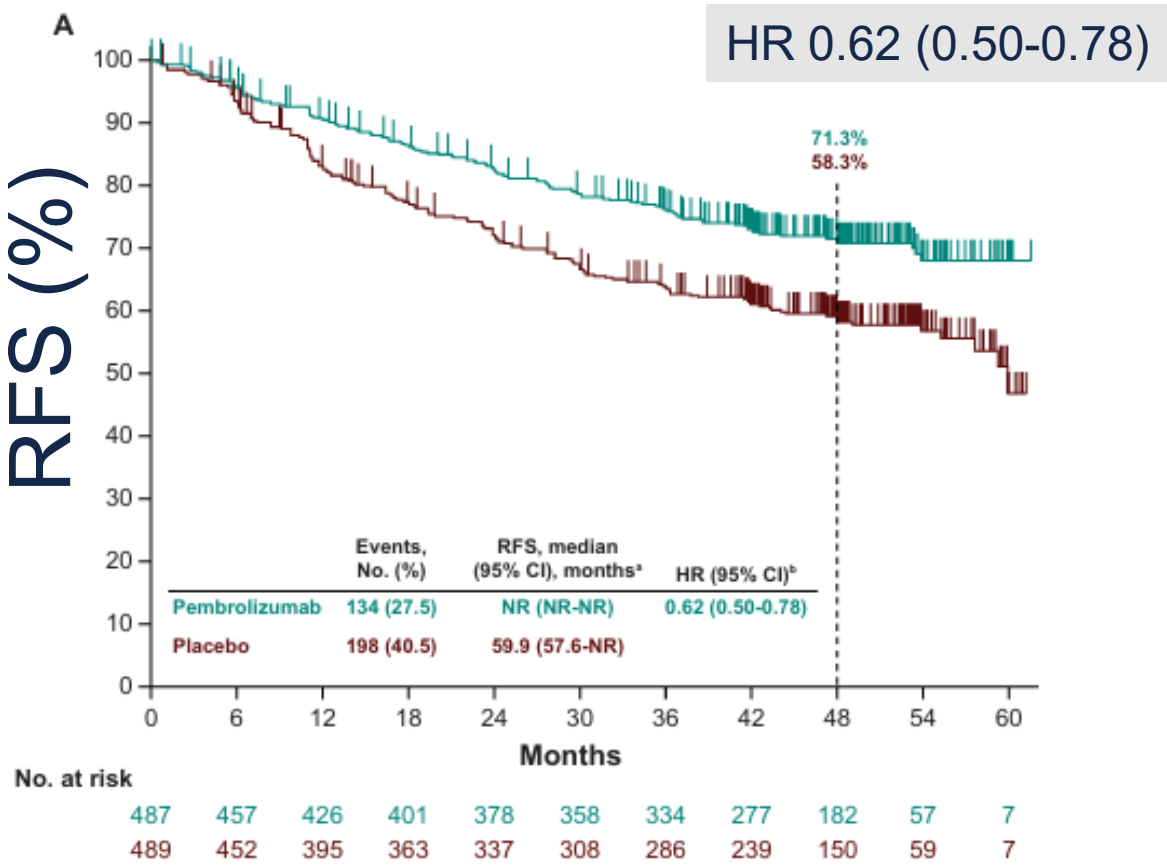
Luke KN716 ESMO 2021

KEYNOTE-716 Study Design (NCT03553836)

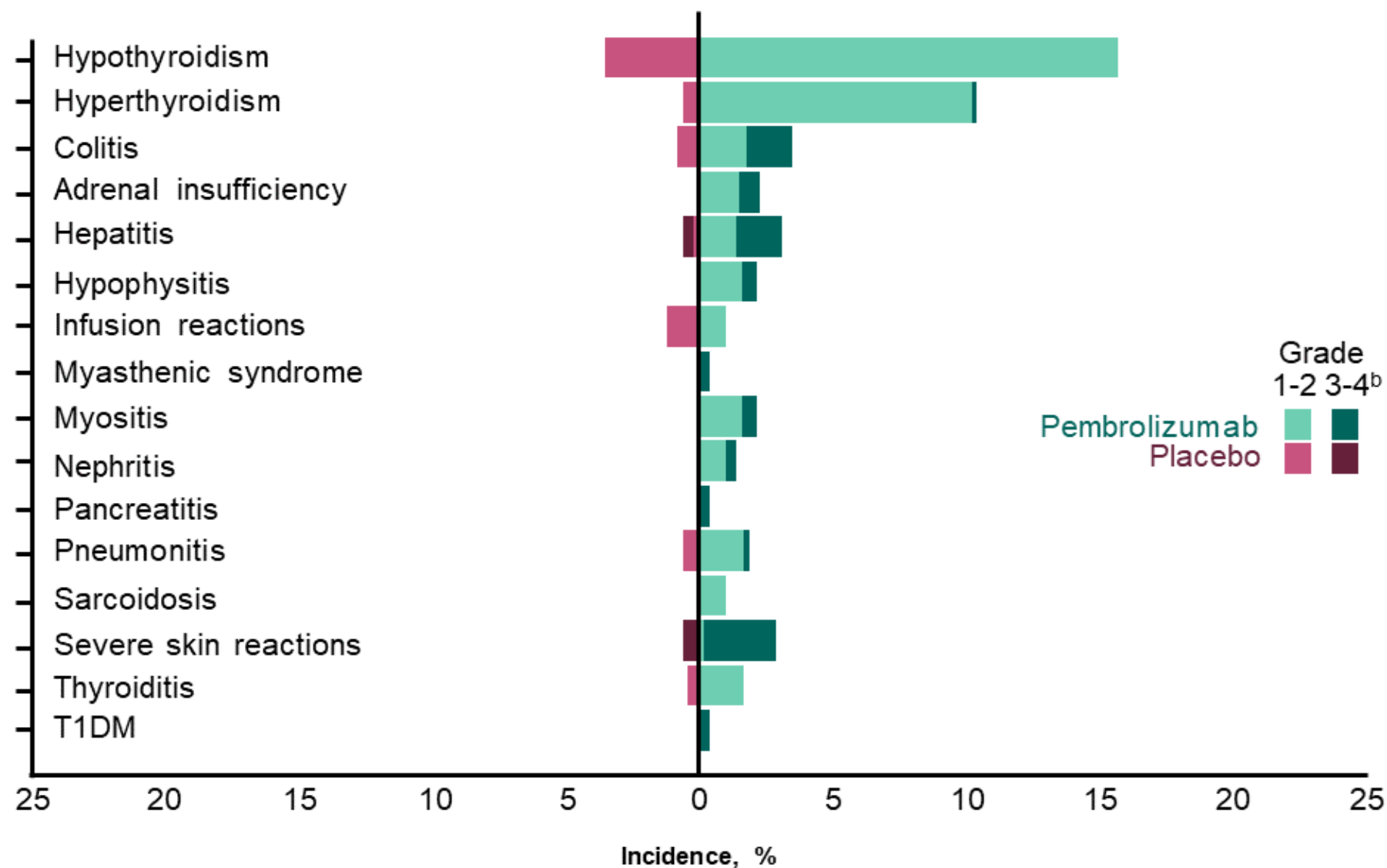


Pembrolizumab versus placebo as adjuvant therapy in resected stage IIB or IIC melanoma: Long-term follow-up, crossover, and rechallenge with pembrolizumab in the phase III KEYNOTE-716 study

Eur J Cancer. 2025 May 2;220:115381.



Adverse Events of Interest^a



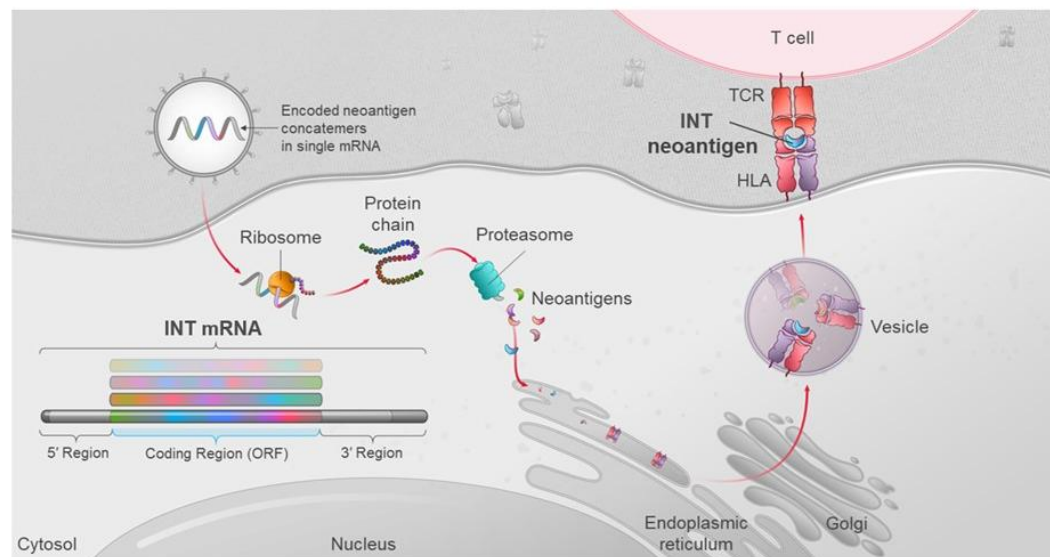
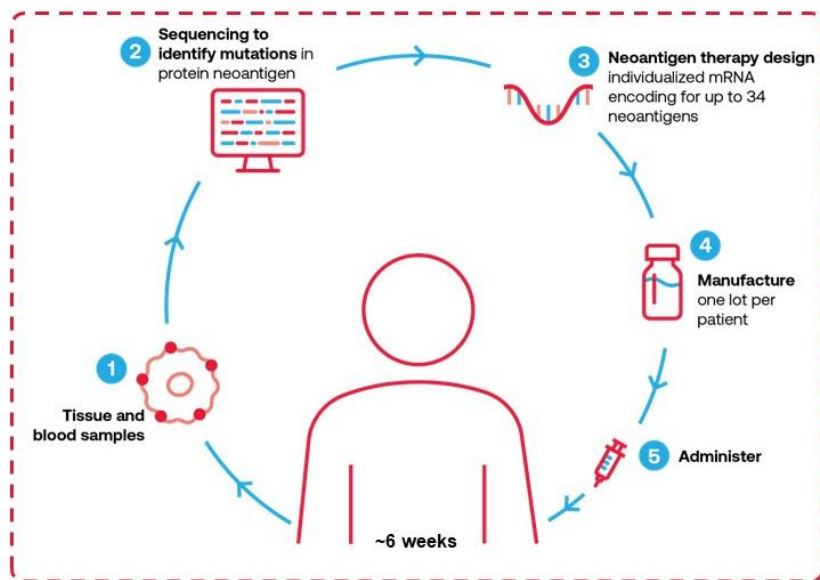
T1DM, Type 1 Diabetes Mellitus.

^aImmune-mediated AEs and infusion reactions occurring in at least 2 patients in decreasing incidence; ^bNo grade 5 events occurred in the pembrolizumab arm; Data cut-off: 04Dec2020.

Individualized mRNA Vaccine Against Melanoma: Intismeran Autogene

mRNA-4157 (V940) Mechanism of Action

- mRNA-4157 (V940) is **an individualized neoantigen therapy** designed to target an individual patient's unique tumor mutations and encodes up to 34 neoantigens^{1,2}
- 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 patients³⁻⁷

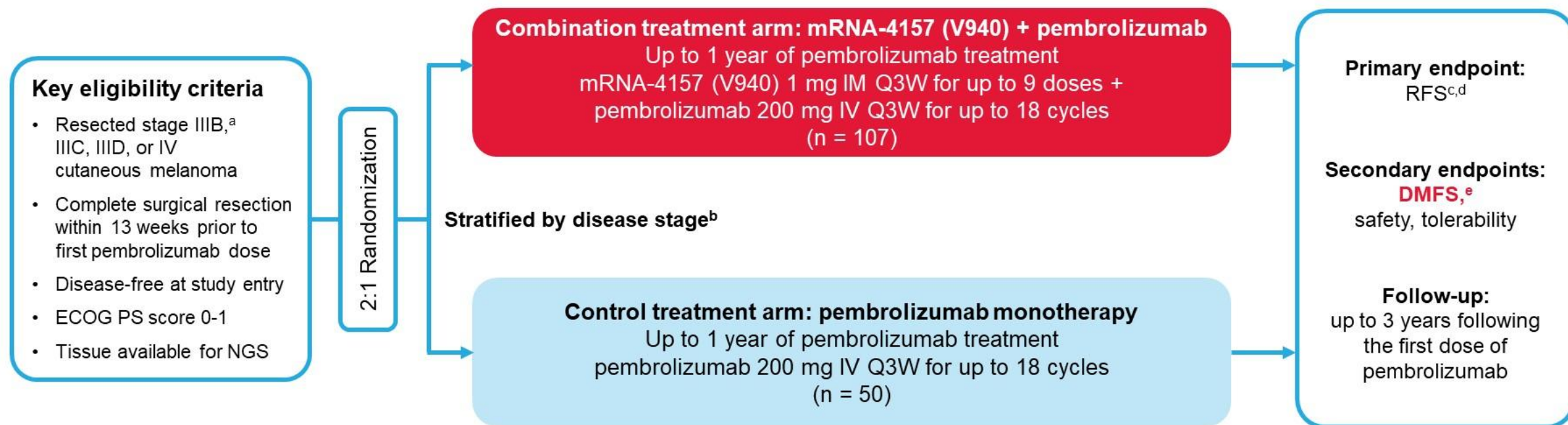


HLA, human leukocyte antigen; INT, individualized neoantigen therapy; ORF, open reading frame.

1. Burris HA, et al. *J Clin Oncol*. 2019;37(suppl 15). Abstract 2523. 2. Zhong S, et al. *Cancer Res*. 80(suppl 16). Abstract 6539. 3. Wirth TC, Kühnel F. *Front Immunol*. 2017;8:1848. 4. Ott PA, et al. *Nature*. 2017;547:217-221. 5. Hu Z, et al. *Nat Med*. 2021;27:515-525. 6. Ott PA, et al. *Cell*. 2020;183:347-362. 7. Palmer CD, et al. *Nat Med*. 2022;28:1619-1629.

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

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



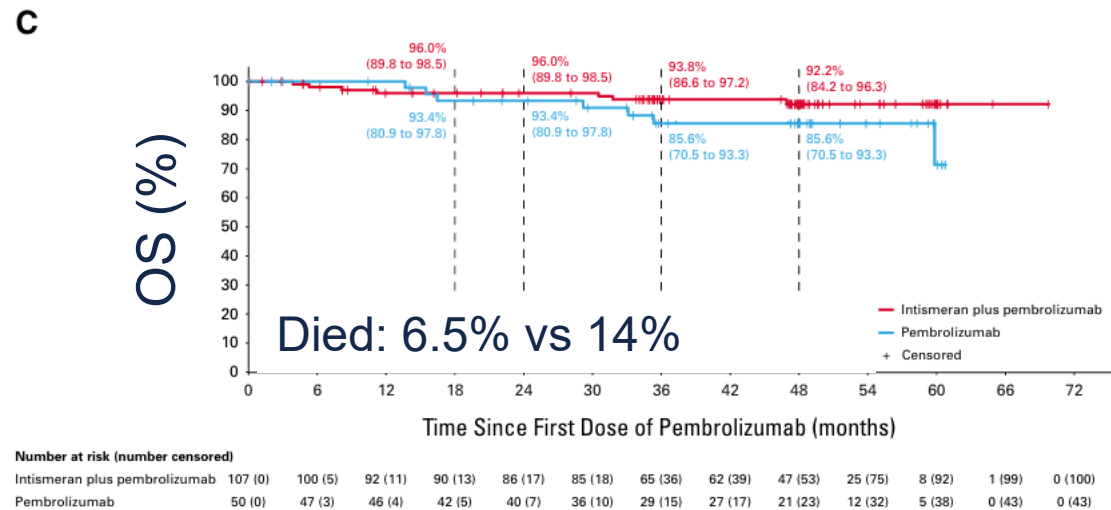
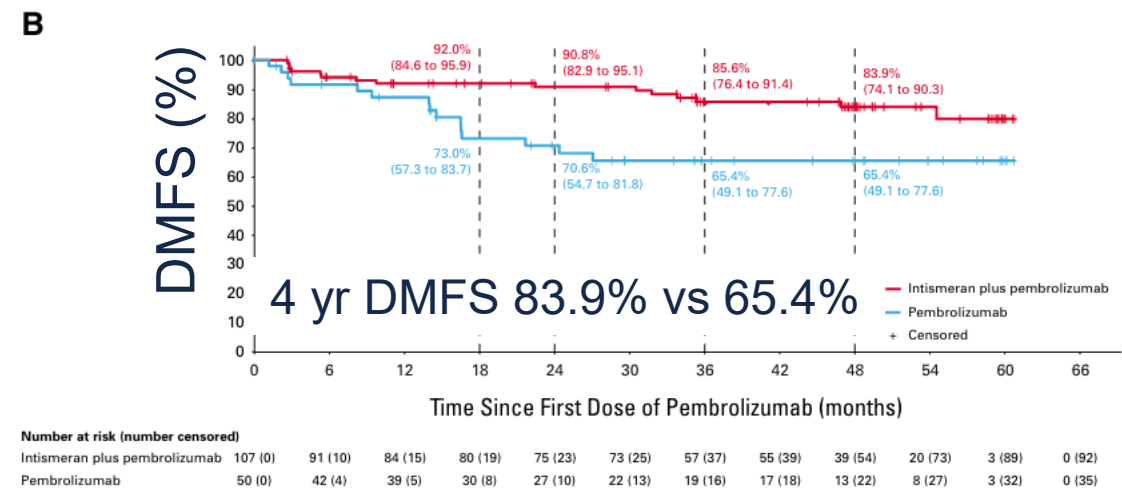
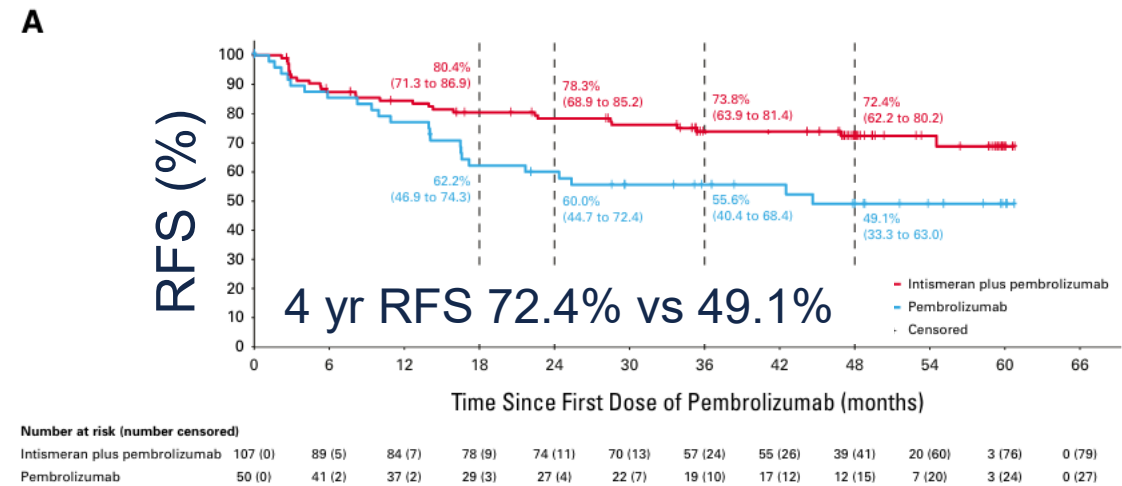
Designed with 80% power to detect an HR of 0.5 with ≥ 40 RFS events (with a 1-sided alpha of 0.1)

DMFS analysis was prespecified for testing following positive RFS in the ITT population^f

Median follow-up^g: 23 months for mRNA-4157 (V940) + pembrolizumab
24 months for pembrolizumab monotherapy

^aPatients with stage IIIB disease were eligible only if relapse occurred within 3 months of prior surgery of curative intent. ^bAccording to the 8th edition of the American Joint Committee on Cancer Staging Manual. ^cThe 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. ^dThe 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 observed. ^eInvestigator-assessed DMFS was defined as the time from first dose of pembrolizumab until the date of first distant recurrence or death from any cause. ^fThe stratified log-rank test was used for comparison. ^gTime of database cutoff was November 14, 2022.

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



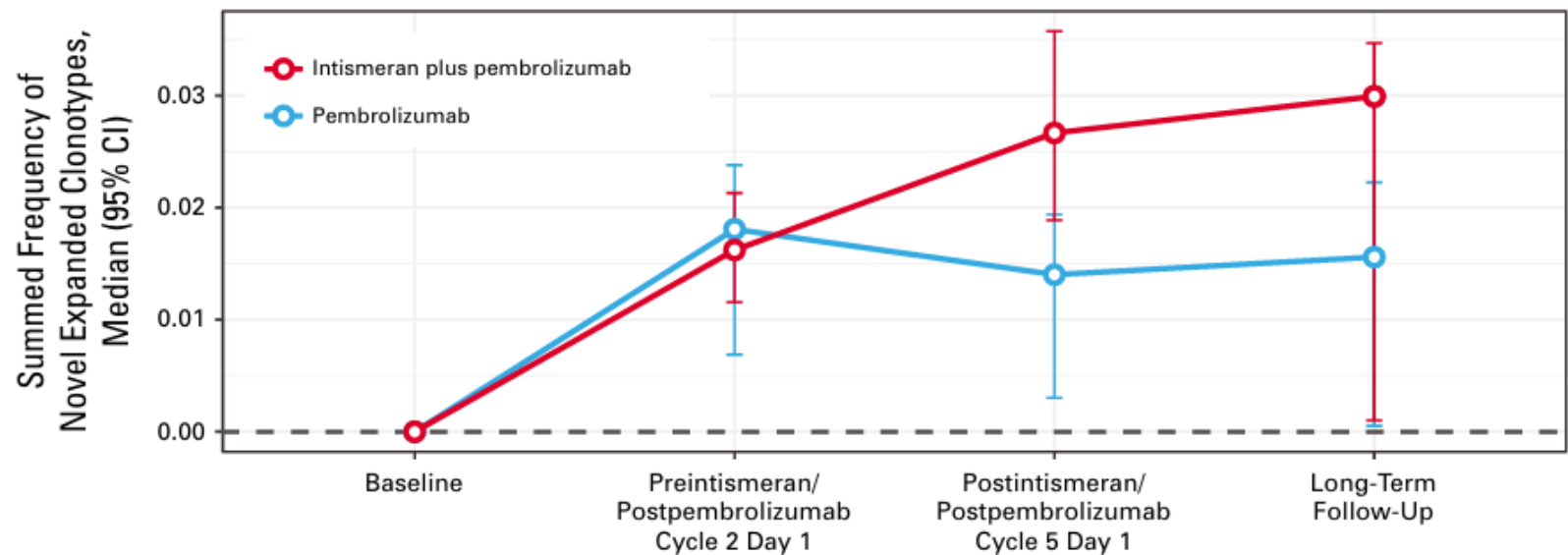
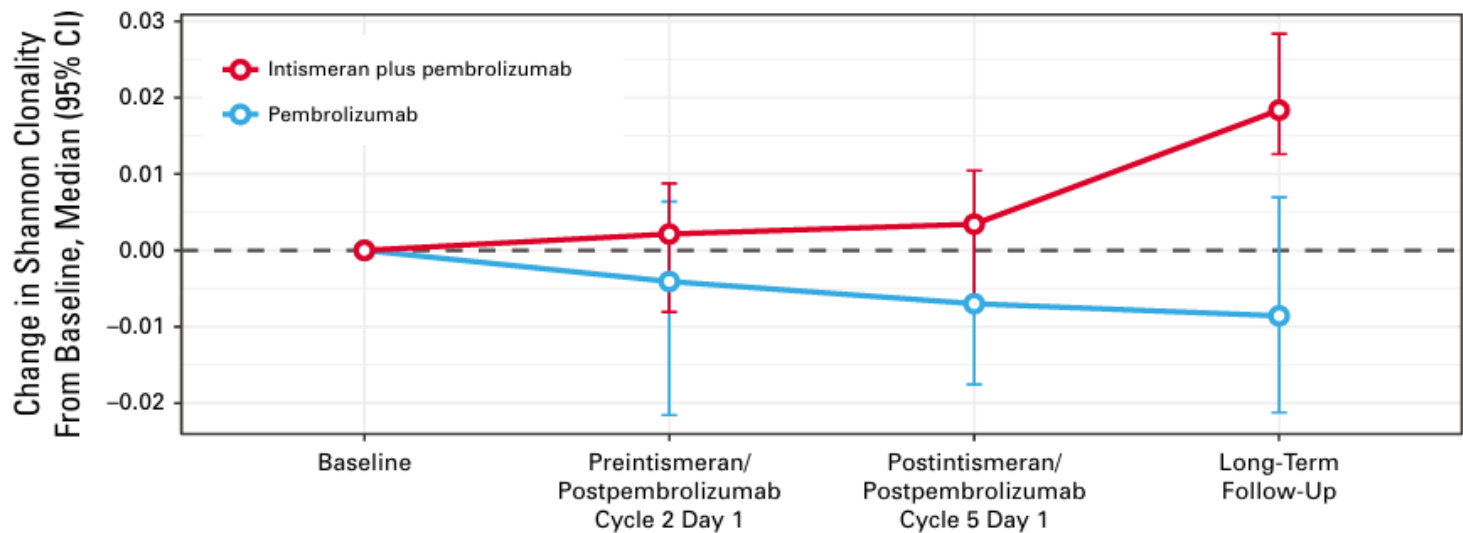
HR (95% CI)

RFS = 0.510 (0.294 to 0.887)

DMFS = 0.411 (0.200 to 0.843)

OS = 0.471 (0.165 to 1.345) (NS)

Increased clonality and a higher magnitude of novel clonotypes observed with intismeran + pembrolizumab



MODERNA CANCER VACCINE STOPS MELANOMA RETURNING

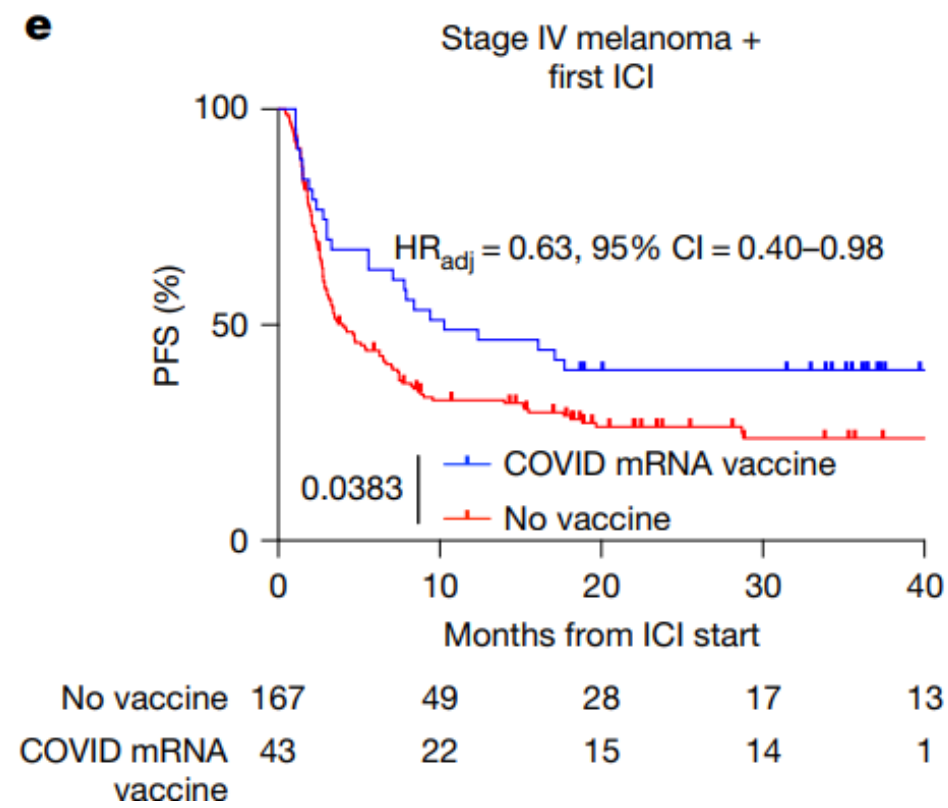
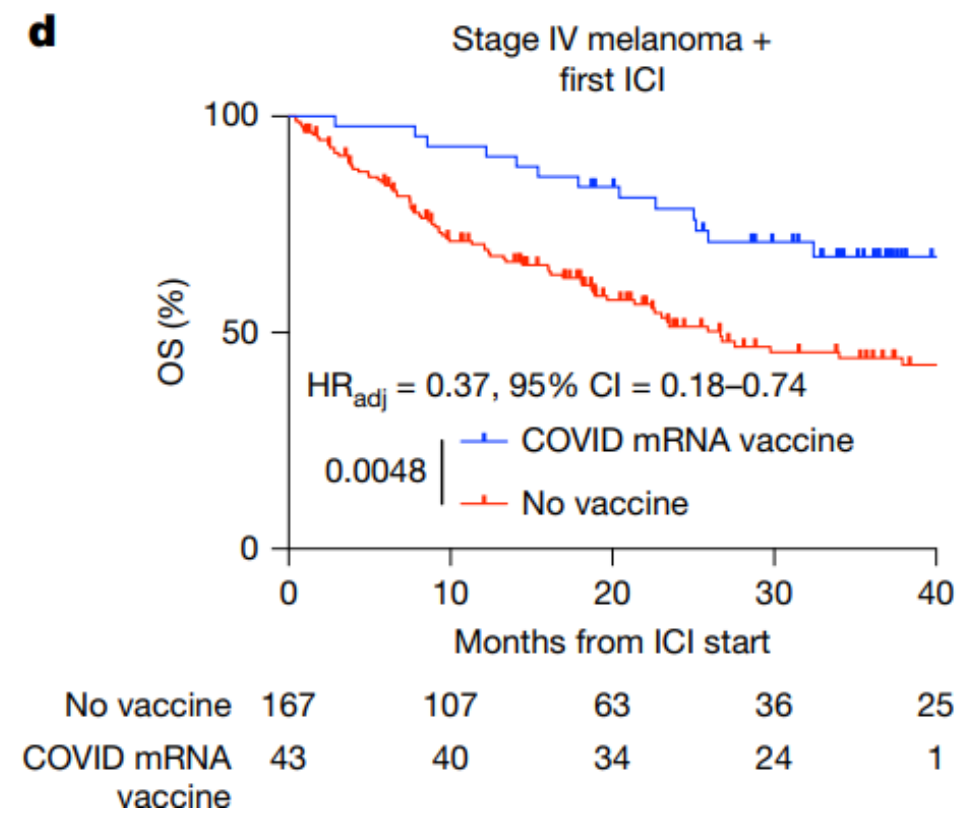
Promising trial results suggest that cancer vaccines work and could be used to target other tumours.

Merck and Moderna Announce Phase 3 INTerpath-001 Trial of Intismeran Autogene Plus KEYTRUDA® Met Endpoints of Recurrence-Free Survival (RFS) and Distant Metastasis-Free Survival (DMFS) in Patients With Completely Resected Stage IIB-IV Melanoma

“At a pre-specified interim analysis, intismeran in combination with KEYTRUDA as adjuvant therapy demonstrated statistically significant and clinically meaningful improvements in RFS and DMFS compared to KEYTRUDA alone for patients with completely resected stage IIB, IIC, III or IV cutaneous melanoma who had not undergone prior treatment with systemic therapy. In accordance with the trial protocol, the study will continue in order to evaluate other key secondary endpoints, including overall survival (OS).”

Personalized vaccine response? Or just mRNA vaccine effect?

Receipt of SARS-CoV-2 mRNA vaccines within 100 days of initiating ICI is associated with significantly improved median and three-year overall survival in multiple large retrospective cohorts



TRIM: whole-body imaging in melanoma follow-up



Physical examinations and whole-body imaging versus physical examinations alone during follow-up after radical surgery of stage IIB–C and III cutaneous malignant melanoma (TRIM): an interim analysis of a multicentre, randomised, phase 3 trial in Sweden

Ladjevardi, Naeser, Dyrke, Papantoniou, Olofsson Bagge, Elander, Ingvar, et al.

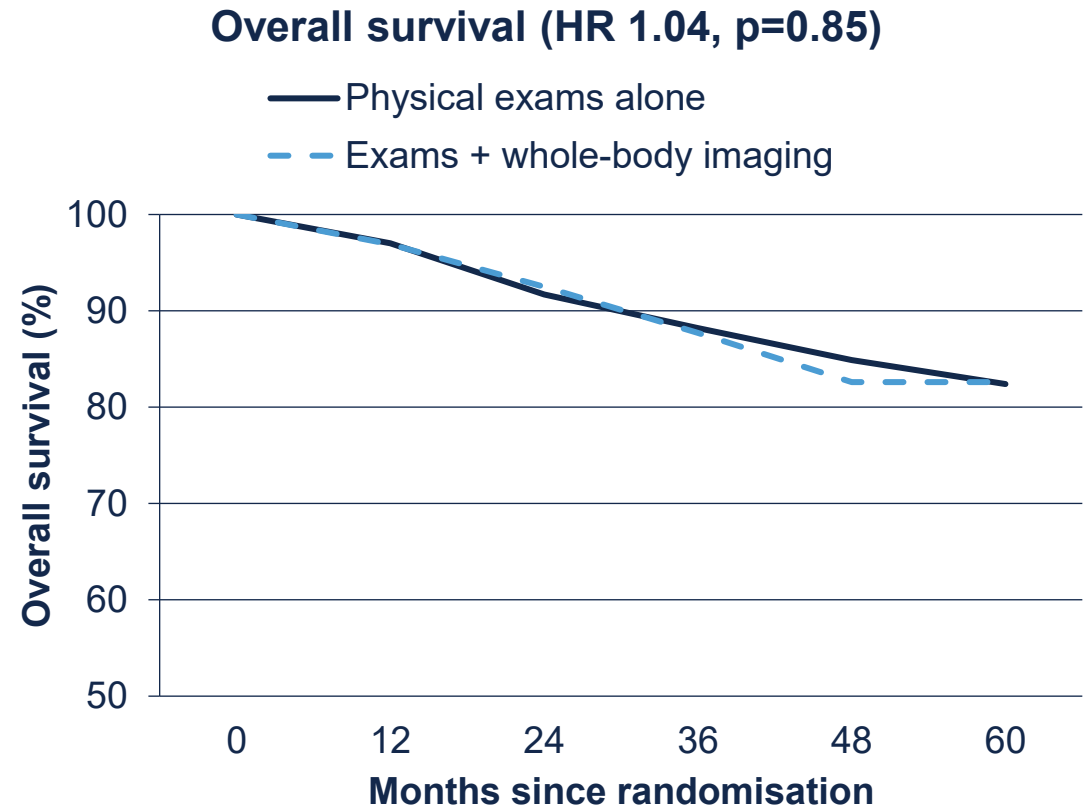
Lancet Oncol 2025;26:1501–10

- **Question:** does adding routine whole-body imaging to clinical follow-up after radical melanoma surgery improve survival?
- **Design:** multicentre, randomised, phase 3 trial in Sweden - interim analysis of the first 983 participants
- **Population:** radically resected stage IIB–C and III cutaneous malignant melanoma
- **Standard arm (n=498):** physical examinations alone for 3 years, plus ultrasound of the sentinel node basin
- **Imaging arm (n=485):** examinations plus whole-body CT or FDG-PET-CT at baseline, 6, 12, 24 and 36 mo
- **Endpoint:** 5-year OS (final analysis); median follow-up so far 33.6 months, enrolment continues toward 1300

TRIM interim results: no survival benefit from imaging



- **Overall survival:** 88.2% vs 87.7% at 3 years; HR 1.04 (95% CI 0.71–1.51), $p=0.85$; 53 vs 54 deaths
- **Distant metastasis-free:** 81.6% vs 79.3%; HR 1.20 (0.89–1.64), $p=0.24$
- **Relapse-free:** 69.3% vs 67.1%; HR 1.10 (0.86–1.39), $p=0.45$; 159 (32%) vs 177 (36%) relapses
- **Locoregional relapse-free:** 84.3% vs 84.1%; HR 0.97 (0.70–1.36), $p=0.86$
- **CT vs FDG-PET-CT:** no significant difference in any outcome
- **Earlier radiographic detection of recurrence did not improve survival at this interim point; follow-up is short and the trial continues to its 5-year OS endpoint**

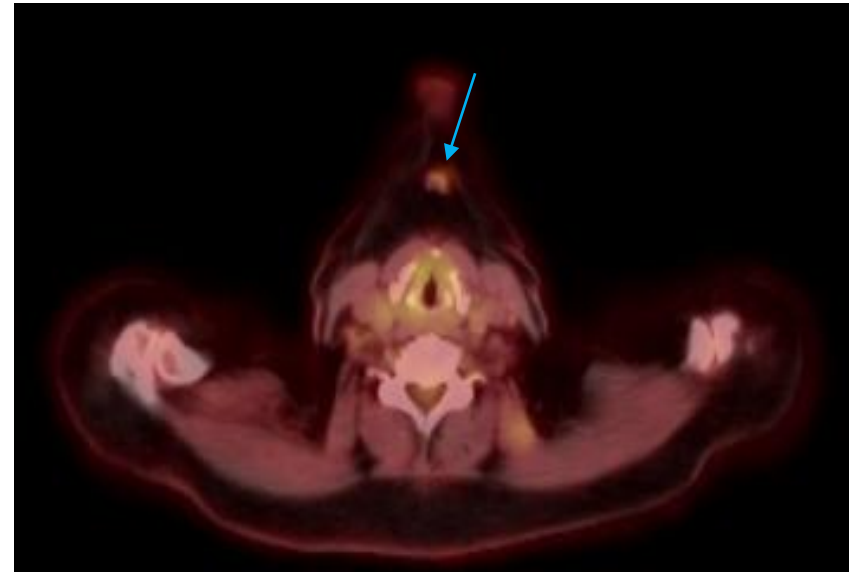


Neoadjuvant therapy

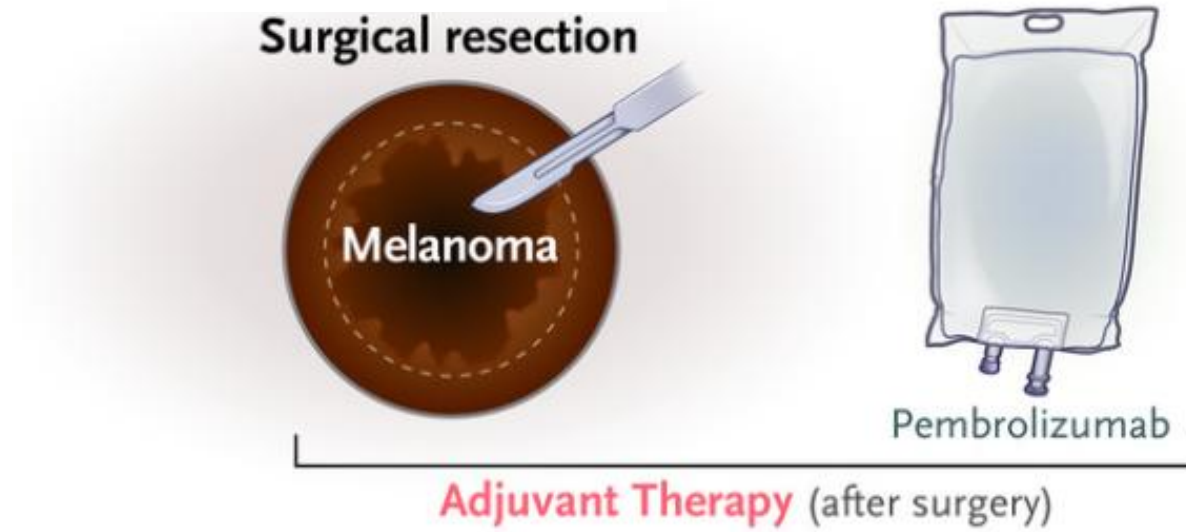
CASE 2:



- 76-year-old with a lesion on the right cheek: biopsied.
 - 3.1mm deep
 - Ulcerated
 - 4 mit/mm²

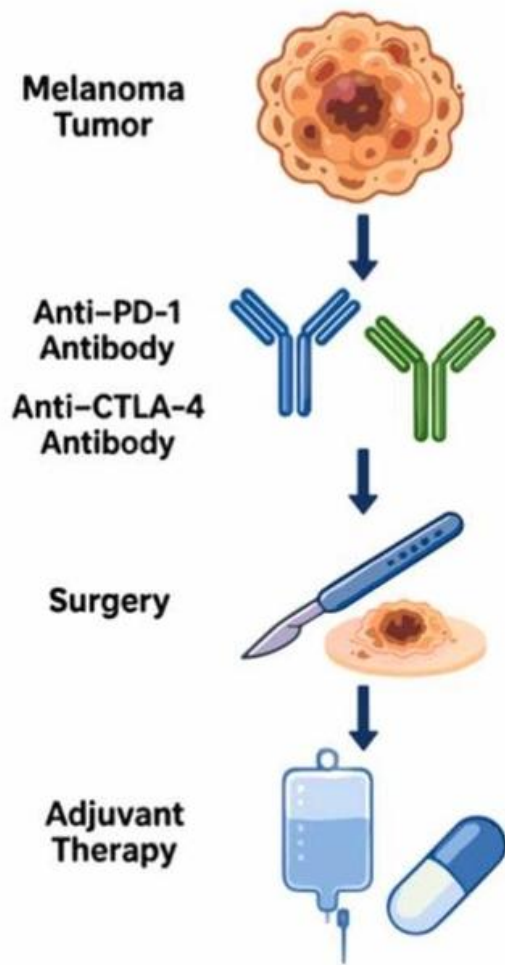


Palpable submandibular node on initial exam



N Engl J Med. 2023 Mar 2;388(9):813-823.

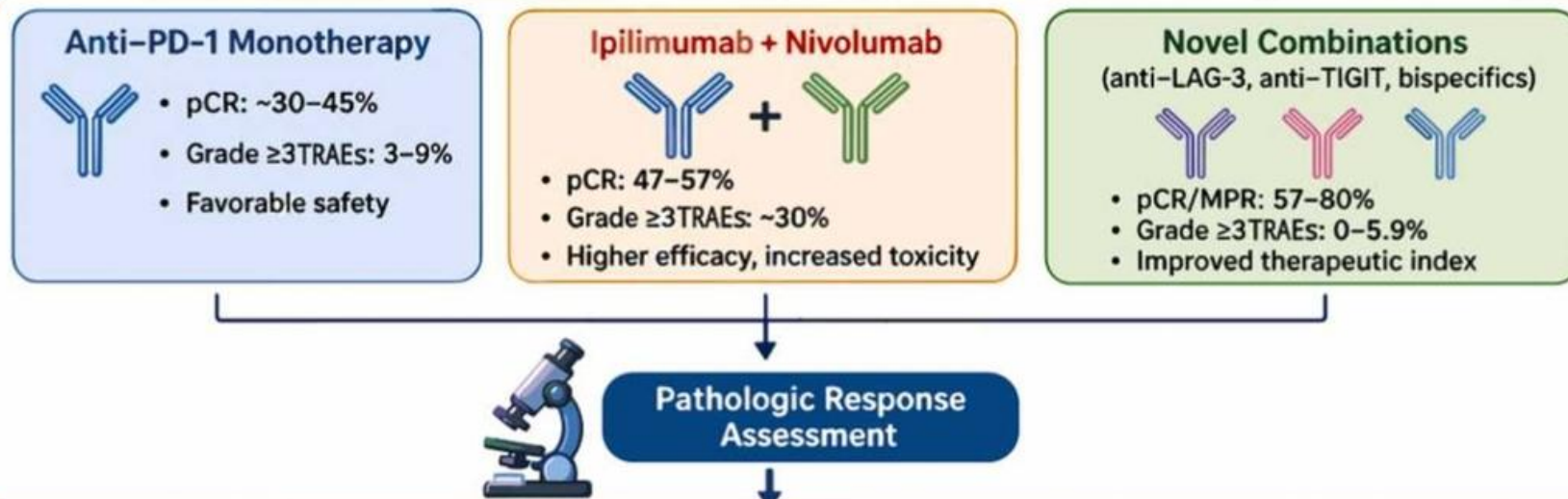
1 NEOADJUVANT IMMUNOTHERAPY PARADIGM IN MELANOMA



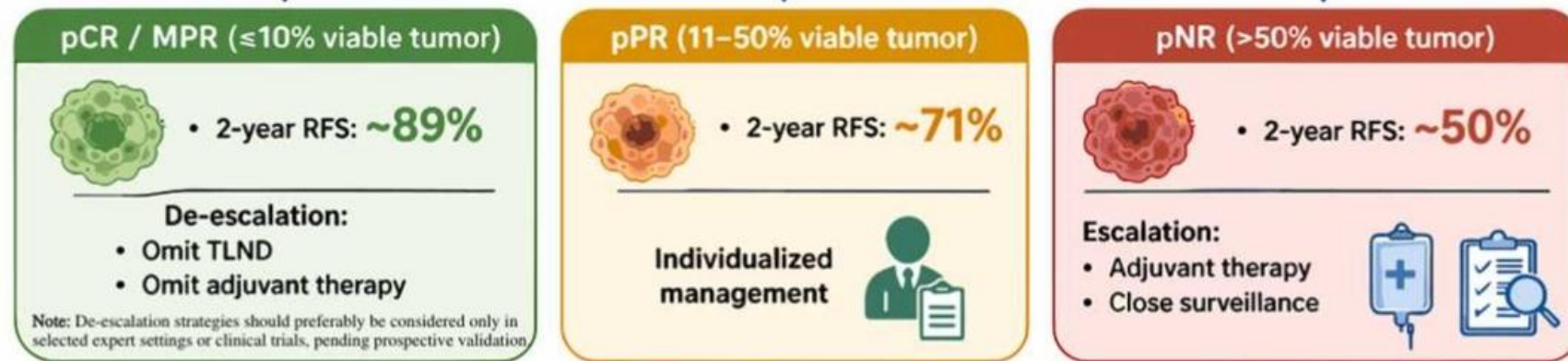
NADINA Trial
12-month EFS:
83.7% vs 57.2%
(Ipi 1/ Nivo 3)

SWOG S1801
2-year EFS:
72% vs 49%
(Pembro)

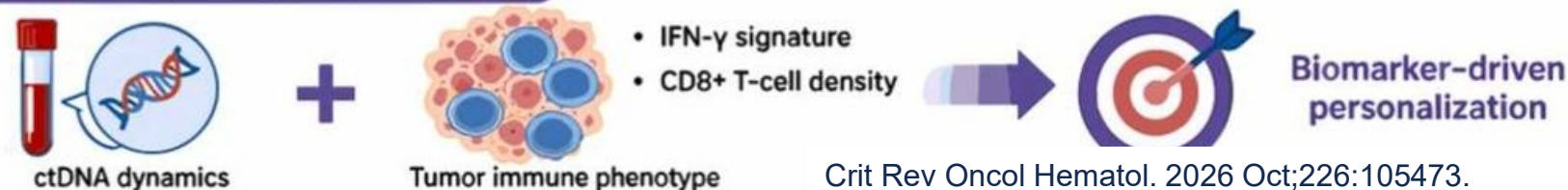
2 NEOADJUVANT IMMUNOTHERAPY REGIMENS: EFFICACY AND SAFETY



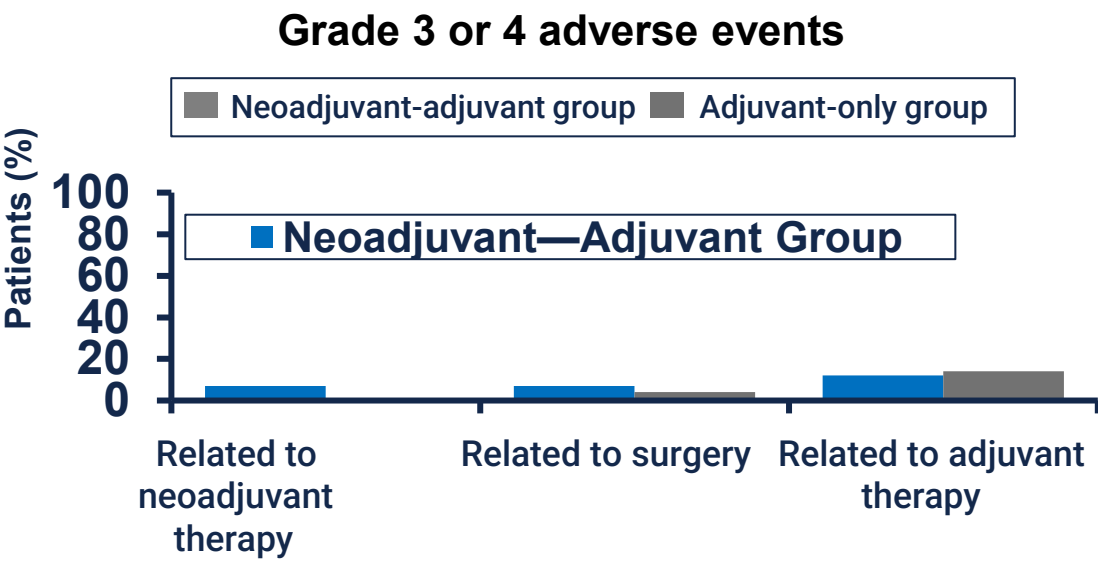
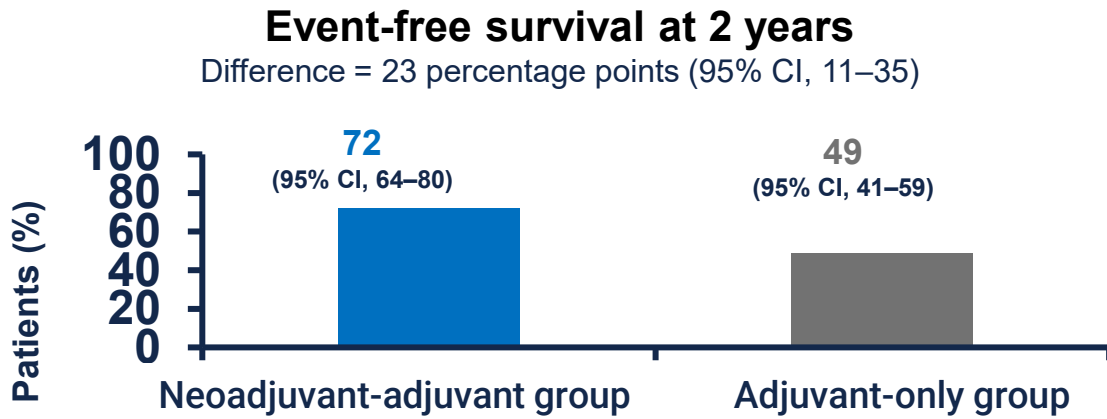
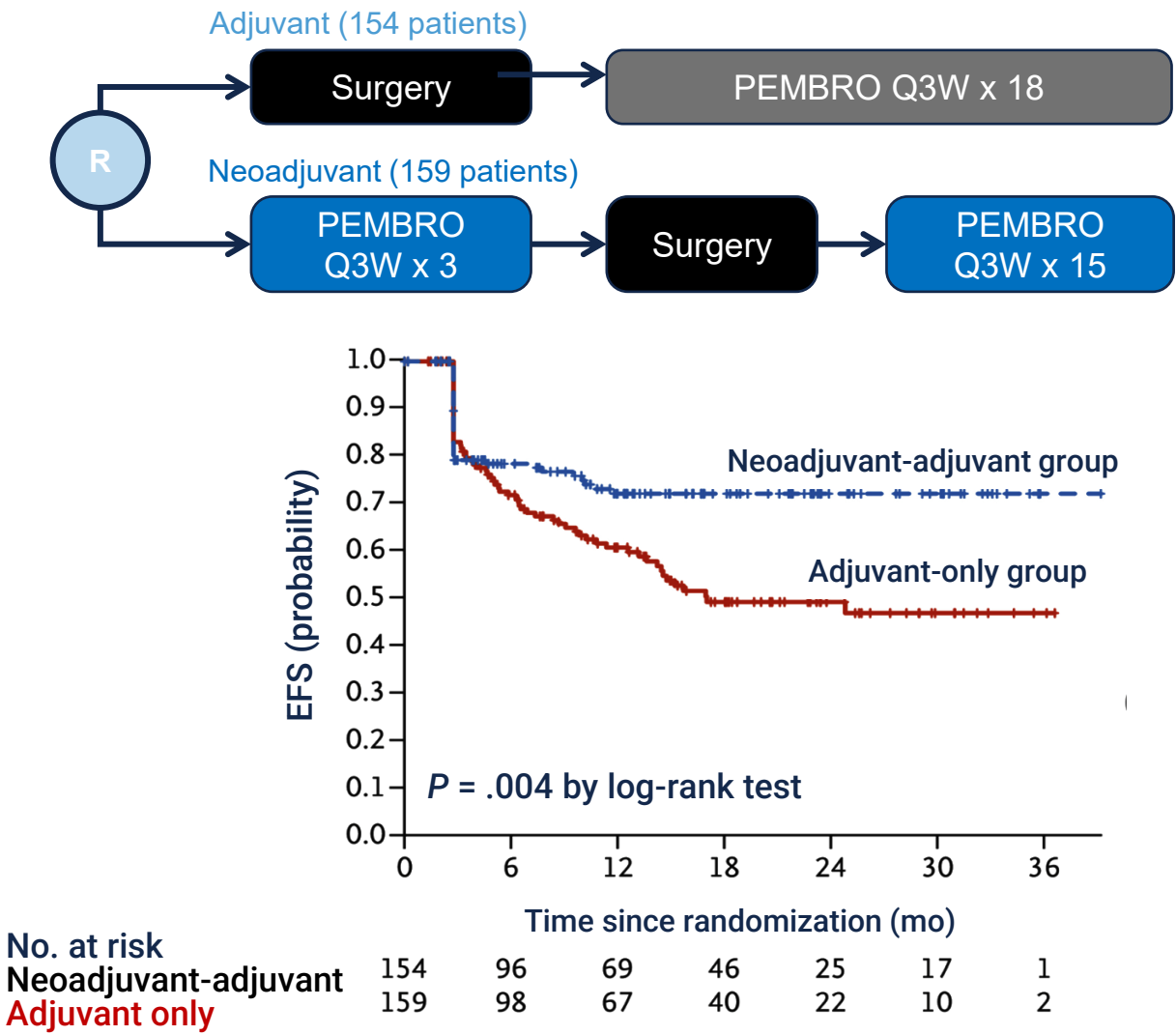
3 RESPONSE-ADAPTED MANAGEMENT (INMC CRITERIA)



4 FUTURE: BIOMARKER INTEGRATION



SWOG-S1801: Neoadjuvant + Adjuvant Pembrolizumab vs Adjuvant Pembrolizumab Alone in Resectable Stage III or IV Melanoma



SWOG S1512 (Cohort A): Neoadjuvant Pembrolizumab (Desmoplastic melanoma)

Resectable desmoplastic melanoma — Kendra, Bellasea, Ribas et al., Nat Cancer 2026 (NCT02775851)

Trial design

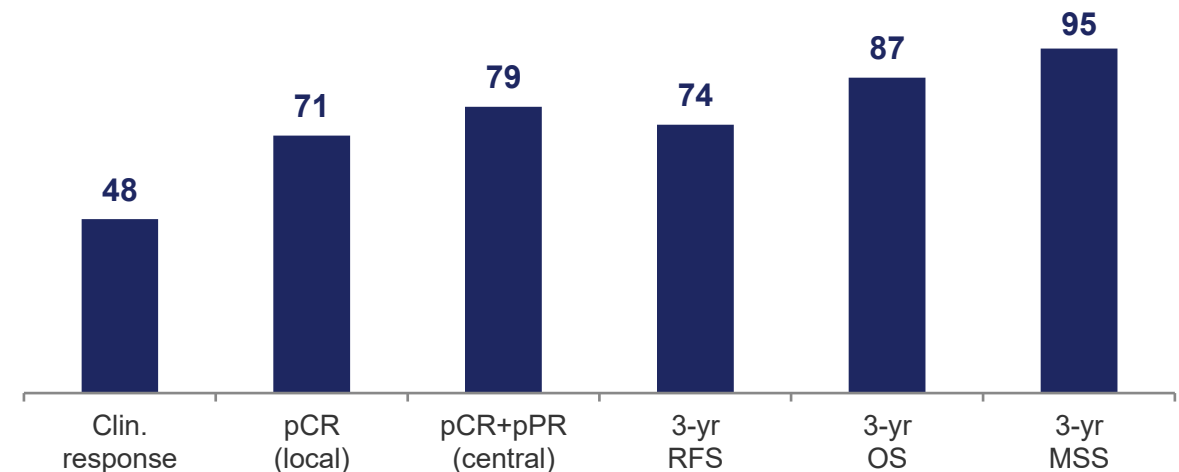
- Phase 2, single arm, n = 28, resectable desmoplastic melanoma, stages I–III
- 3 doses single-agent pembrolizumab 200 mg q3w → surgery at ~9 weeks (no adjuvant given)
- Rationale: desmoplastic melanoma has very high TMB (UV-driven, NF1-mutant)

Response & 3-year outcomes

71%

pathologic complete response rate

20/28 patients (95% CI 51–87%, $P < 0.001$) — primary endpoint met

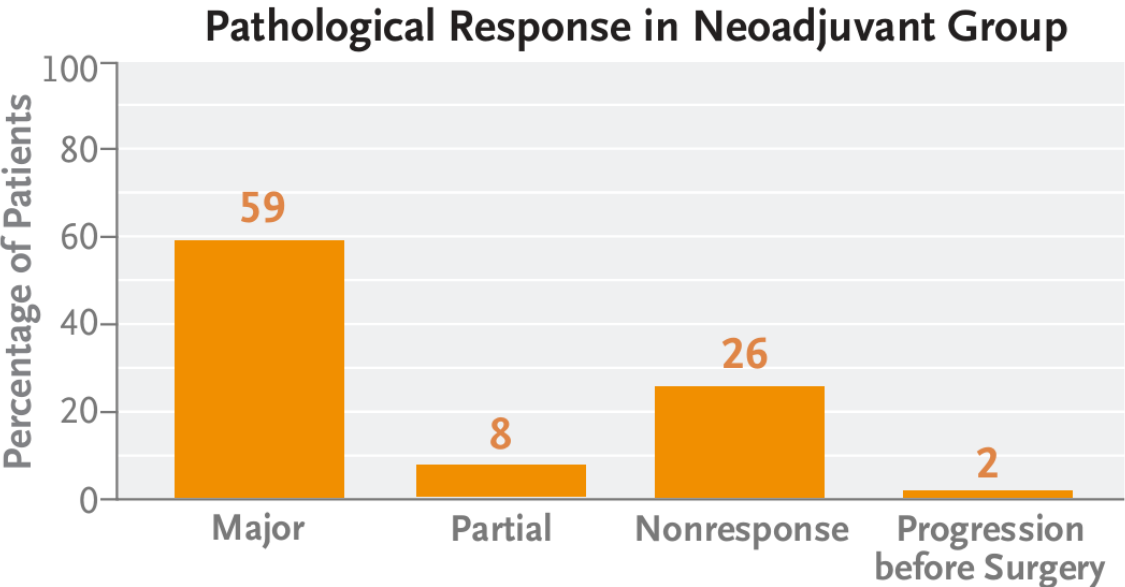
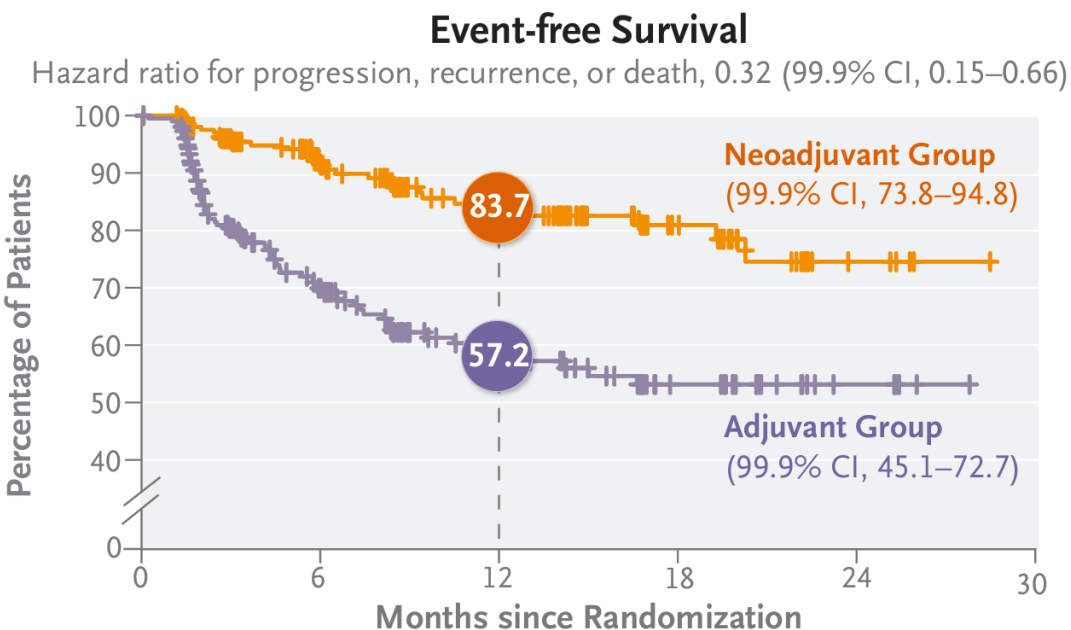
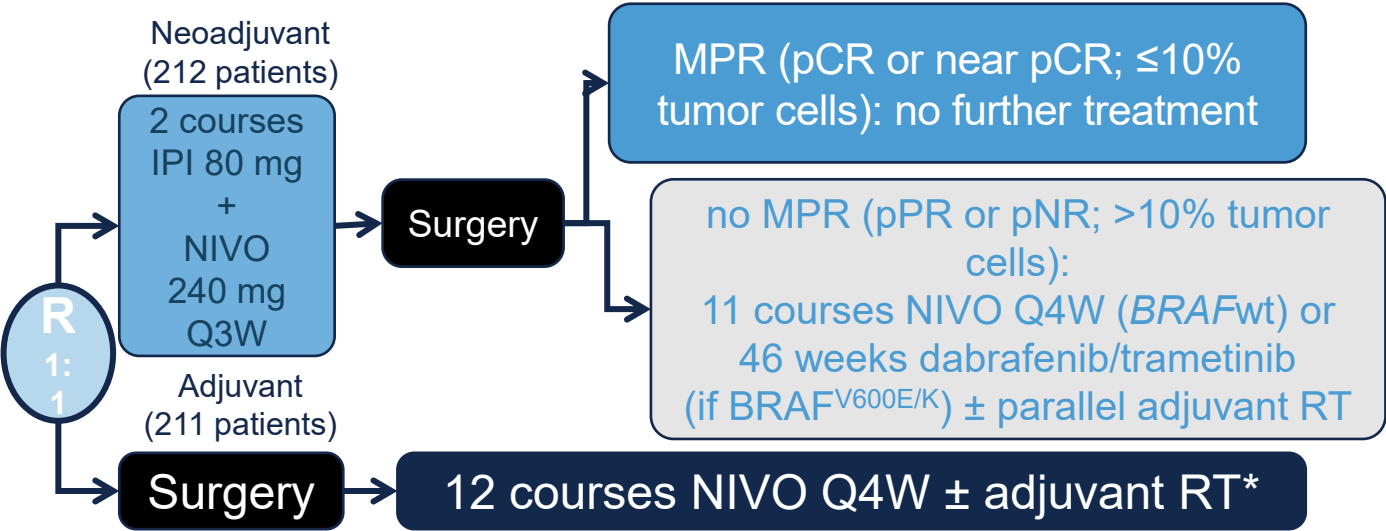


Safety & genomics

- Grade 3 TRAEs in 2/28 (7%) — mucositis, immune-mediated colitis; no grade 4/5
- None of the 28 patients became surgically unresectable
- Median TMB 62.8 Mut/Mb — ~8× higher than cutaneous melanoma (7.55 Mut/Mb)
- NF1 mutations in 75% of tumors (predominantly loss-of-function), consistent with known biology

Highest reported pCR rate for neoadjuvant single-agent anti-PD-1 in any melanoma subtype — supports surgical de-escalation strategies

NADINA: Neoadjuvant “Flipped” NIVO3 + IPI1 Dose vs Adjuvant NIV in Resectable Stage III Melanoma



CONCLUSIONS

In patients with resectable, macroscopic stage III melanoma, neoadjuvant ipilimumab plus nivolumab prolonged event-free survival as compared with adjuvant nivolumab.

Baseline Biomarkers Predict Response & Outcome: Data from PRADO 5 yr update

IFN γ signature, tumor mutational burden (TMB), and PD-L1 expression — exploratory analysis

IFN γ signature

77% MPR rate, high vs **34%**
low

81% 5-yr EFS, high vs **54%**
low

P = 0.0039 (EFS)

TMB

78% MPR rate, high vs **35%**
low

75% 5-yr EFS, high vs **58%**
low

P = 0.10 (EFS, ns)

PD-L1 ($\geq 1\%$)

79% MPR rate, high vs **47%**
low

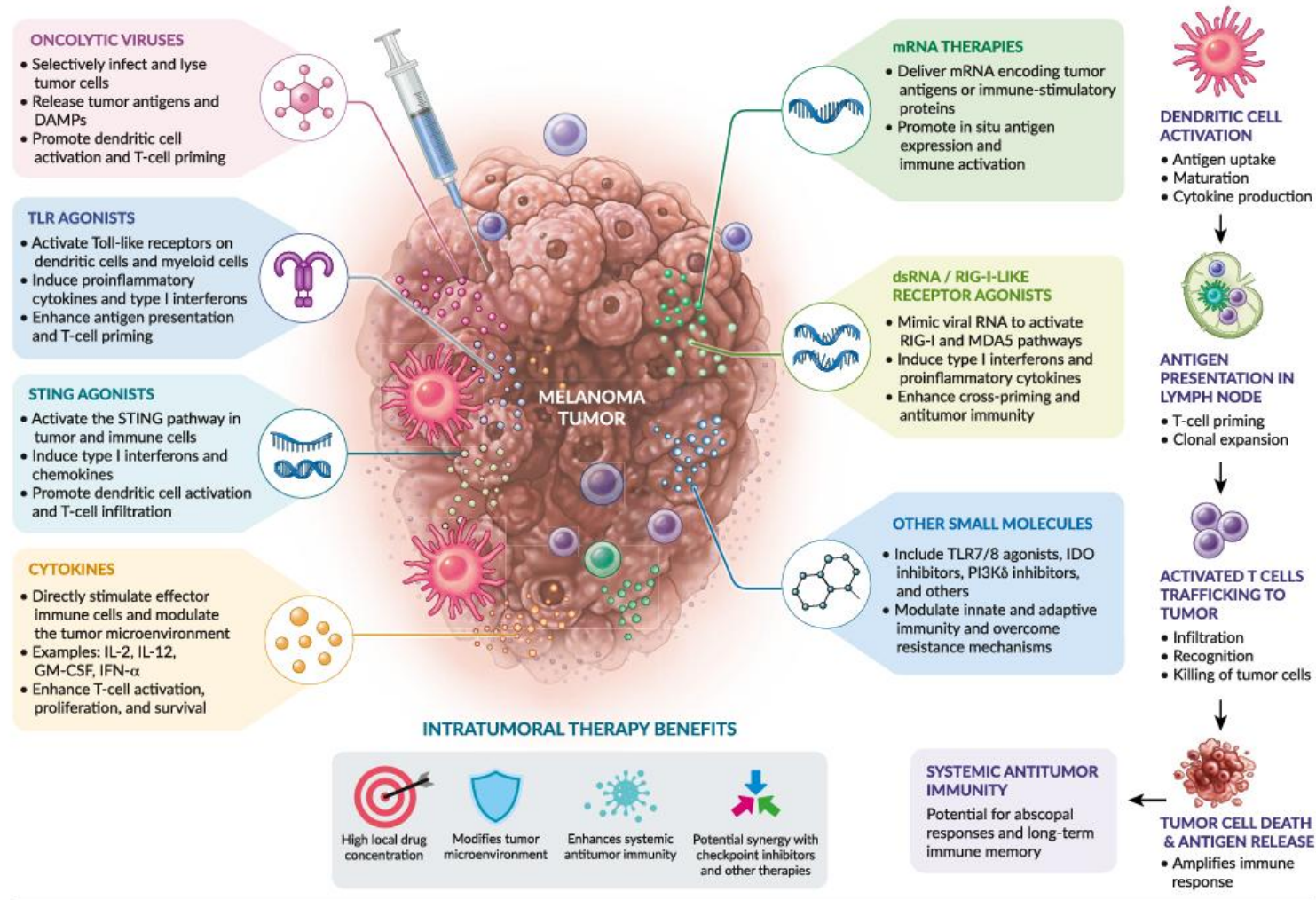
88% 5-yr EFS, high vs **60%**
low

P = 0.0036 (EFS)

Triple-high (high TMB + high IFN γ + PD-L1 $\geq 1\%$): 100% MPR, 100% 5-yr EFS (n = 11)

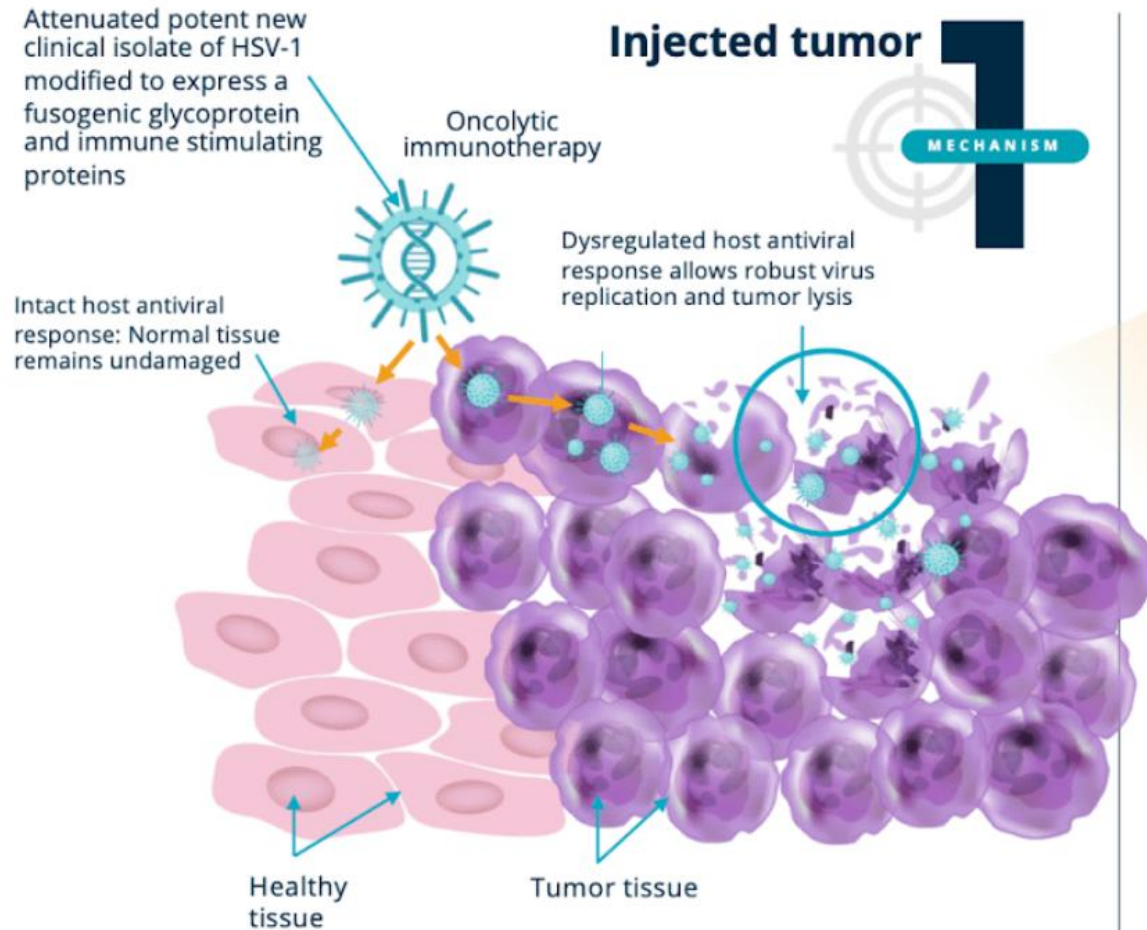
Triple-low: 18% MPR, 41% 5-yr EFS (n = 17)

Intratumoral therapies for melanoma



Abbreviations: DAMPs, damage-associated molecular patterns; IFN, interferon; IL, interleukin; mRNA, messenger RNA; TLR, Toll-like receptor; STING, stimulator of interferon genes; RIG-I, retinoic acid-inducible gene I; MDA5, melanoma differentiation-associated protein 5.

RP1 (vusolimogene oderparepvec)



- “Next Generation” oncolytic virus

Like T-vec, is HSV1 engineered with GM-CSF transgene

Added: GALV fusogenic glycoprotein to enhance syncytial lysis, immunogenic death

Engineered HSV US11 to be overexpressed to boost replication in tumor cells

RP1 Combined With Nivolumab in Advanced Anti-PD-1– Failed Melanoma (IGNYTE)

IGNYTE Study – Design & Outcomes

Phase 1/2, open-label, multicenter

 140 patients with unresectable/metastatic melanoma with confirmed progression on prior anti-PD-1 therapy

48.6% with Stage IV M1b/c/d disease

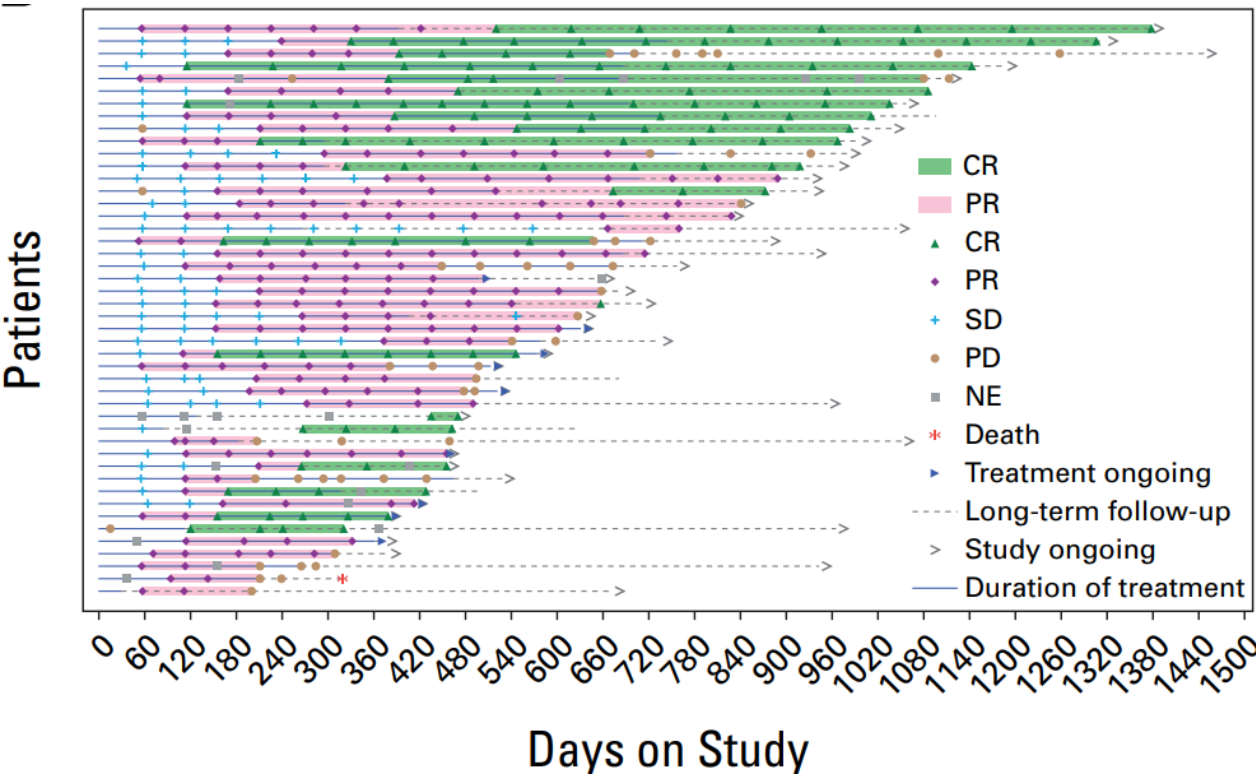
65.7% with primary anti-PD-1 resistance

56.4% were PD-L1 negative

46.4% had prior anti-CTLA-4 treatment

 Patients received intratumoral RP1 (up to 8 doses) in combination with nivolumab for up to 2 years.

RP1 Combined With Nivolumab in Advanced Anti-PD-1– Failed Melanoma (IGNYTE)



Median duration of response of 33.7 months, with a 2-year survival of 63.3%

All Patients (N = 140)	
BOR	
CR, No. (%)	21 (15.0)
PR, No. (%)	25 (17.9)
SD, No. (%)	31 (22.1)
PD, No. (%)	54 (38.6)
NE, No. (%)	9 (6.4)
ORR (95% CI)	32.9 (25.2 to 41.3)

- ✓ Higher response rate in PD1+ tumors
- ✓ Significant response in injected AND noninjected tumor
- ✓ Response in visceral tumors

PIVOTAL Phase III: Neoadjuvant Intralesional Daromun

L19IL2/L19TNF in resectable, locally advanced melanoma — Hauschild et al., J Clin Oncol 2026 (NCT02938299)

What is Daromun & why intralesional?

- L19IL2 + L19TNF: two antibody-cytokine fusions targeting fibronectin (tumor neovasculature)
- IL-2 stimulates T cells; TNF is proinflammatory and vascular-disrupting — combined effect drives local tumor regression
- Injected intratumorally/intranodally → high local drug exposure, limited systemic toxicity
- Prior data: regression of both injected AND non-injected lesions

Local injection, systemic effect: designed to convert an immunologically “cold” tumor bed into a “hot” one before surgery, priming antitumor immunity

Study design

- Phase III, open-label, randomized 1:1; N = 256 (127 daromun+surgery vs 129 surgery-only)
- Eligibility: fully resectable stage III melanoma with ≥1 injectable skin/nodal lesion
- Daromun: weekly IL injection × up to 4 weeks → surgery
- 13% de novo diagnosed; 87% recurrent (after surgery ± RT ± systemic therapy, incl. prior ICI in ~21–25%)
- Primary endpoint: RFS (BICR); key secondary: DMFS, OS, safety; post hoc: EFS
- Updated analysis at median follow-up 36.8 months (cutoff Nov 28, 2025)

PIVOTAL: Efficacy, Safety & Clinical Implications

Updated results at 36.8-month median follow-up (ITT population, N = 256)

RFS (primary)

HR 0.55

95% CI 0.38–0.78 — P < .001

Median 23.8 vs 6.5 mo
(daromun vs surgery)

DMFS

HR 0.53

95% CI 0.33–0.83 — P = .005

Median 38.7 vs 14.0 mo
(daromun vs surgery)

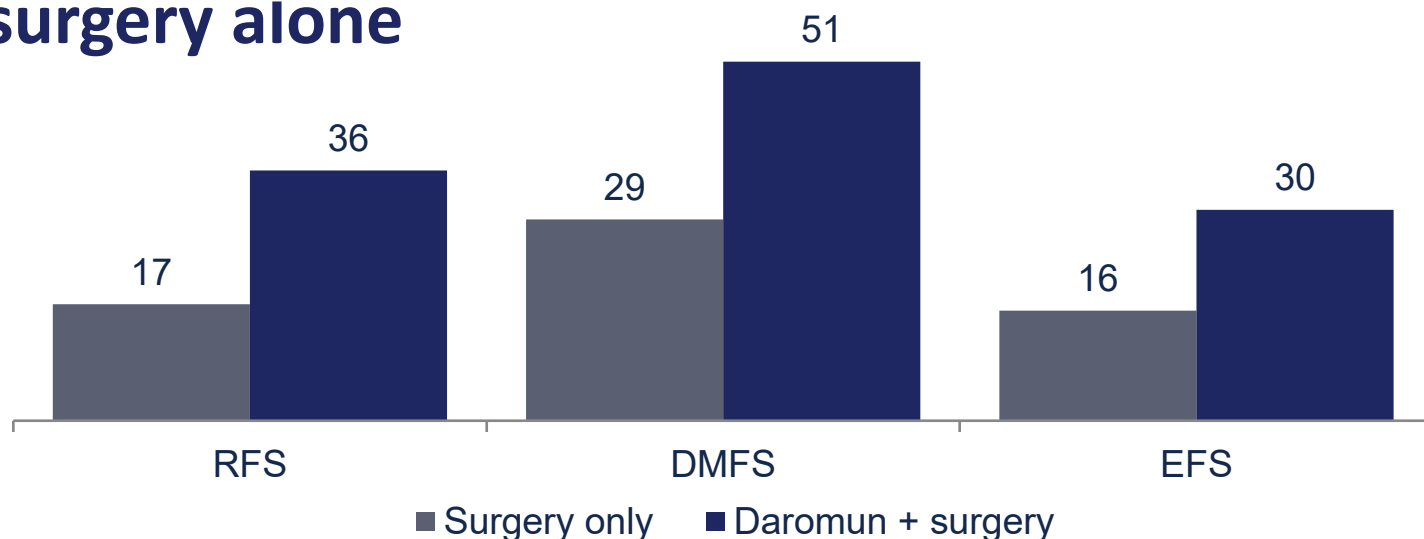
EFS (post hoc)

HR 0.71

95% CI 0.51–0.98 — P = .034

Median 16.1 vs 6.1 mo
(daromun vs surgery)

3-year outcome rates: daromun + surgery vs surgery alone



Safety

- Grade ≥3 TRAE: 28.7% (daromun) vs 7.3% (surgery only)
- **Most common: injection-site reaction (12.3%, grade 3)**
- No grade >3 TRAEs; no treatment-related deaths

Clinical implications

Benefit consistent regardless of prior ICI exposure — fills a gap for ICI-relapsed patients not covered by NADINA/S1801



Gene Expression Profiling

GEP in melanoma- prospective trials

Why does it matter?

- ✓ Major reason for exclusion from guidelines
- ✓ More objective data for guiding clinical decision making vs. less actionable “risk prediction”
- ✓ GEP tests are lab developed tests: No FDA oversight- we need to be the critical evaluators of the data!

3 trials

- MERLIN-001: Merlin for SLN reduction
- DECIDE: Decision Dx for SLN reduction
- Nivo-MELA: Melagenix to stratify patients for adjuvant therapy

Gene Expression Profile–Based Test to Predict Melanoma Sentinel Node Status

The MERLIN_001 Study

Tina J. Hieken, MD; Michael E. Egger, MD, MPH; Christina V. Angeles, MD; John R. Hyngstrom, MD; Erin E. Burke, MD, MS; Michael C. Lowe, MD; Georgia M. Beasley, MD; Edmund K. Bartlett, MD; Scott C. Bresler, MD, PhD; Kelly L. Harms, MD, PhD; Jonathan S. Zager, MD; Julia S. Lehman, MD; Nabil Wasif, MD, MPH; Sanjay P. Bagaria, MD; Kelly M. McMasters, MD, PhD; David A. Wada, MD; Prakash Pandalai, MD; Keith A. Delman, MD; Jay Lee, MD; Klaus J. Busam, MD; Jane L. Messina, MD; Vernon K. Sondak, MD

- ❖ Prospective study of patients with T1a HR – T3b melanoma who are candidates for SLNB
- ❖ All had CP-GEP testing and SLNB (blinded to the CP-GEP results)

Gene (protein)	Putative function(s)
<i>MLANA</i> (melanoma antigen recognized by t cells 1)	Melanosome biogenesis
<i>GDF15</i> (growth differentiation factor 15)	EMT, angiogenesis, metabolism
<i>CXCL8</i> (interleukin 8)	EMT, angiogenesis
<i>LOXL4</i> (lysyl oxidase homologue 4)	EMT, angiogenesis
<i>TGFBβ1</i> (transforming growth factor β receptor type 1)	EMT, angiogenesis
<i>ITGB3</i> (integrin β 3)	EMT, angiogenesis, cell adhesion & migration, blood coagulation
<i>PLAT</i> (tissue-type plasminogen activator)	EMT, blood coagulation
<i>SERPINE2</i> (glia-derived nexin)	EMT, blood coagulation

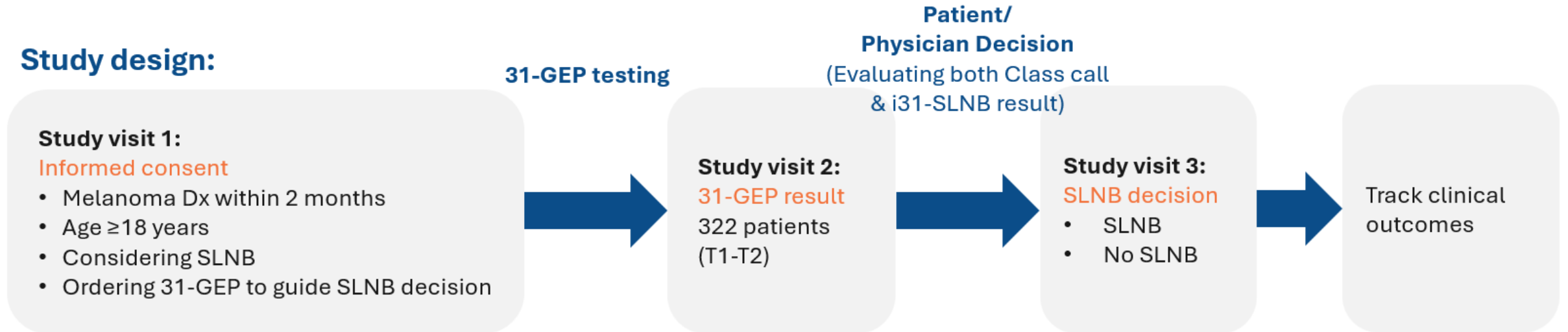
Abbreviations: CP-GEP, clinicopathologic gene expression profile; EMT, epithelial to mesenchymal transition.

Subset	No. (%)	% SLN positive	% Low risk		SLN positive (95% CI)	
					% Low risk	% High risk
Overall	1761 (100)	17.6	37.0	➔	7.1 (5.2-9.3)	23.8 (21.3-26.4)
T1	507 (28.8)	8.5	68.2		4.9 (2.9-7.8)	16.1 (10.8-22.8)
T1a	26 (1.5)	3.8	80.8	➔	0 (0-13.7)	20.0 (0.5-71.6)
T1b	481 (27.3)	8.7	67.6	➔	5.2 (3.1-8.2)	16.0 (10.6-22.7)
T2	897 (50.9)	16.1	32.9		9.2 (6.1-13.0)	19.4 (16.3-22.8)
T2a	706 (40.1)	15.0	36.8	➔	8.1 (5.1-12.1)	19.1 (15.5-23.0)
T2b	184 (10.4)	19.6	17.4	}	15.6 (5.3-32.8)	20.4 (14.3-27.7)
T3	357 (20.3)	34.5	2.8		20.0 (2.5-65.1)	34.9 (29.9-40.1)
T3a	198 (11.2)	33.3	4.0		12.5 (0.3-52.7)	34.2 (27.5-41.4)
T3b	159 (9.0)	35.8	1.3		50 (1.3-98.7)	35.7 (28.2-43.7)
Clinical stage IB	1187 (67.4)	12.5	49.3		6.5 (4.6-8.8)	18.3 (15.3-21.6)
Clinical stage II	548 (31.1)	29.4	8.2		17.8 (8.0-32.1)	30.4 (26.4-34.6)
Age <40 y	151 (8.6)	17.9	17.9		0 (0-12.8)	21.8 (14.9-30.1)
Age 40-64 y	778 (44.2)	20.8	35.2		8.4 (5.4-12.3)	27.6 (23.7-31.7)
Age ≥65 y	832 (47.2)	14.5	42.1		6.6 (4.2-9.7)	20.3 (16.8-24.2)

DECIDE prospective study

(DecisionDx-Melanoma Impact on Sentinel Lymph Node Biopsy Decisions and Clinical Outcomes)

Study design:



• Questions:

1. What % of patients with a low-risk (<5%/ class 1A) result decide *not* to get a SLNB?
2. In patients with a low/ high risk result who *do* get a SLNB, what % have a positive SLN?
3. What is the RFS/DMFS/OS in patients with a low-risk result who *do not* undergo SLNB?

The integrated 31-gene expression profile test identifies low-risk patients with cutaneous melanoma who can forego the SLNB procedure: results from a prospective, multicenter trial

Timothy Beard^a, J. Michael Guenther^b, Stanley P. Leong^c, Maki Yamamoto^d, Samuel Dierks^e, Brenda Sickle-Santanello^f, Andrew Ward^g, Mark Cripe^h, Parth Shahⁱ and Shawn Youngⁱ

(912 patients, SLN assessed in 430, not performed in 482 (esp T1a and T1b lesions))

T-stage, n (%)

T1a ^c	335 (36.7%)	T1a	26 (1.5)
T1b	330 (36.2%)	T1b	481 (27.3)
T2a	162 (17.8%)	T2a	706 (40.1)
T2b	24 (2.6%)	T2b	184 (10.4)
T3a	23 (2.5%)	T3a	198 (11.2)
T3b	16 (1.8%)	T3b	159 (9.0)
T4a	7 (0.8%)		
T4b	15 (1.6%)		

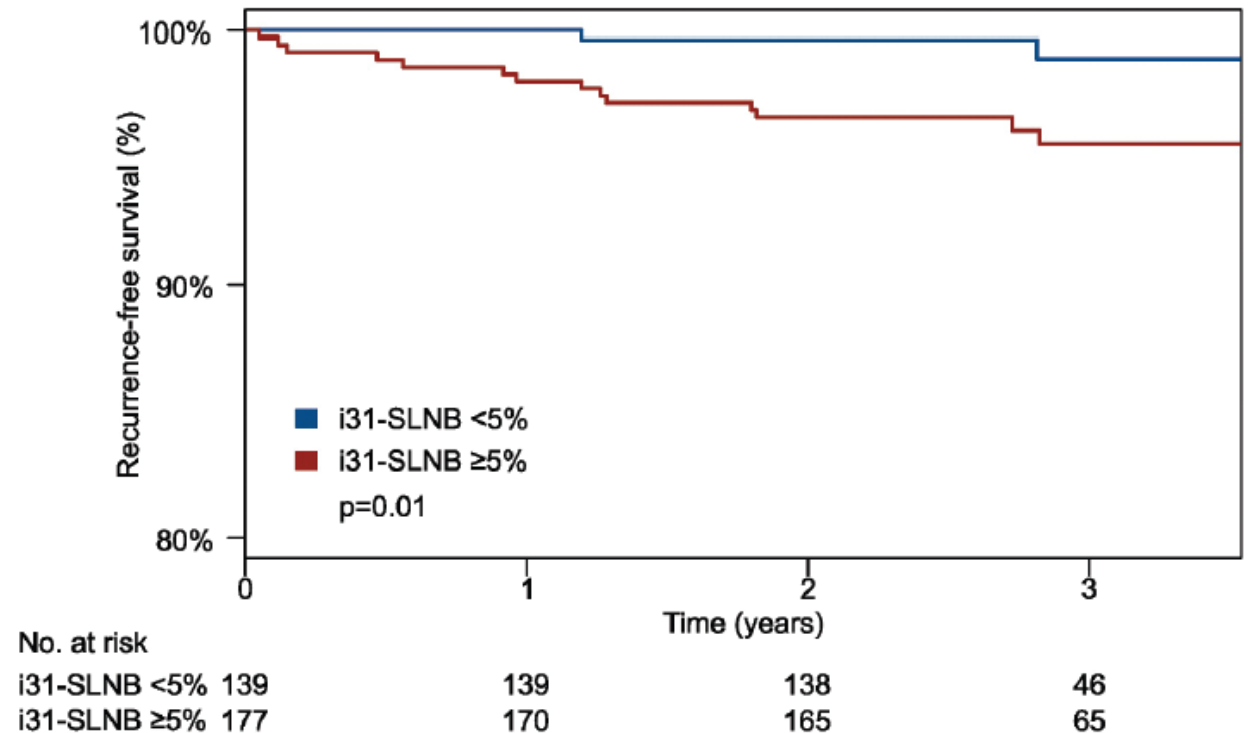
i31-SLNB predicted risk, n (%)

<5%	474 (52.0%)	(37% of tumors low risk in MERLIN)
5–10%	294 (32.2%)	
>10%	144 (15.8%)	

i31-SLNB predicted positivity risk		<5%	5–10%	>10%
T1 ^a -T4				
n (positive/all)		3/114	13/185	28/131
% (95% CI)		2.6% (0–5.8%)	7.0% (3.7–11.0%)	21.4% (14.7–28.7%)
T1 ^a -T2a				
n (positive/all)		2/111	11/176	12/72
% (95% CI)		1.8% (0–4.8%)	6.3% (2.9–10.2%)	16.7% (8.4–25.4%)



- 3/85 T2b-T4 patients has <5% risk of + SLN
- 1 of these had a + SLN
- So for T2b-T4 patients:
 - 3/85 (3.5%) has a low-risk score
 - Of whom 1/3 (33.3%) had a positive SLNB



The integrated 31-gene expression profile test identifies patients with T1b-T2a cutaneous melanoma who can safely avoid sentinel lymph node biopsy

Timothy Beard, MD¹, J. Michael Guenther, MD²; Stanley P. Leong, MD³, Maki Yamamoto, MD⁴, Andrew Ward, PhD⁵, Andrew Lewis, PhD⁶, Parth Shah, MD⁷, Shawn Young, MD⁷

¹Summit Medical Group, Bend OR, ²St Elizabeth Physicians General & Vascular Surgery, Edgewood, KY, ³California Pacific Medical Center and Research Institute, San Francisco, CA, ⁴School of Medicine, University of California-Irvine, Orange, CA, ⁵University of Tennessee Medical Center, Knoxville, TN, ⁶Castle Biosciences, Inc., Friendswood, TX, ⁷SurgOne Surgical Oncology, Boulder, CO

Table 1. Sentinel lymph node (SLN) positivity rates in T1-T4 (n=430) and T1b-T2a (n=275) SLN assessed patients.

T-category	i31-SLNB predicted <5%	i31-SLNB predicted 5-10%	i31-SLNB predicted >10%
<u>T1-T4</u>			
n (positive/all)	3/114	13/185	28/131
% (95% CI)	2.6% (0-5.9)	7.0% (3.7-11.0)	21.4% (14.7-28.7)
<u>T1b-T2a</u>			
n (positive/all)	1/74	10/136	12/65
% (95% CI)	1.4% (0-4.4)	7.4% (3.3-12.1)	18.5% (9.1-28.4)

Comparing study and outcomes: T1b-T2a tumors

*** with all the caveats**



Study	Total T1b-T2a tumors with SLN assessed	% tumors that were T1b	% tumors with + SLNB	% tumors called low risk by test	% low risk tumors with + SLNB	NPV for low risk test result
DECIDE (i31-GEP)	275	57%	8.4%	27%	1.4%	98.6%, (95% CI $\approx$ 92.7%–99.8%)
MERLIN (CP-GEP)	1187	40.5%	12.5%	49%	6.5%	93.5% (95% CI, $\approx$ 91.2–95.2)

Melanoma: Cutaneous

Version 1.2026 — February 17, 2026

- ▶ Predictive GEP testing to differentiate melanomas at low versus high risk for nodal metastasis should not replace surgical oncology discussion of pathologic staging with SLNB in eligible patients. Findings of the prospective Merlin_001 trial suggest that CP-GEP testing may be used in select patients with T1b ± T2a melanoma to support shared decision-making, when a patient or provider would decide against SLNB if the true risk was <10%. A high-risk result in that scenario would portend a 3 times higher risk of SLN involvement based on trial results.⁵ Alternative GEP tests for SLNB risk prediction are not recommended outside of the context of a clinical study or trial based on current data. Additional prospective investigation and outcomes data (including impact of missing a positive SLNB) will further inform the utility of GEP tests, multivariable nomograms/risk calculators (eg, melanomarisks.org.au/snlland; mskcc.org/nomograms/melanoma/sentinel_lymph_node_metastasis), and other decision analytical models for SLNB risk prediction.⁶⁻⁸ Existing GEP tests for SLNB risk prediction should be prospectively compared with no-cost, contemporary models that incorporate readily available CP variables.⁹⁻¹⁹

Predictive GEP testing Should not replace surgical oncology discussion of pathologic staging with SLNB in eligible patients. Findings of the prospective Merlin_001 trial suggest that **CP-GEP testing may be used in select patients with T1b+/- T2a melanoma** to support shared decision making when a patient or provider would decide against SLNB if the true risk was <10%.

Take home points for the dermatologist



The University
of North Carolina
at Chapel Hill

- Screening: Not one size fits all → Risk based >> population based
- Multidisciplinary care is key: Find your team!

Thank you!

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