Localized Melanoma and Other Types of Skin Cancer

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Adjuvant Therapy of Nivolumab Combined With Ipilimumab Versus Nivolumab Alone in Patients With Resected Stage IIIB-D or Stage IV Melanoma (CheckMate 915)

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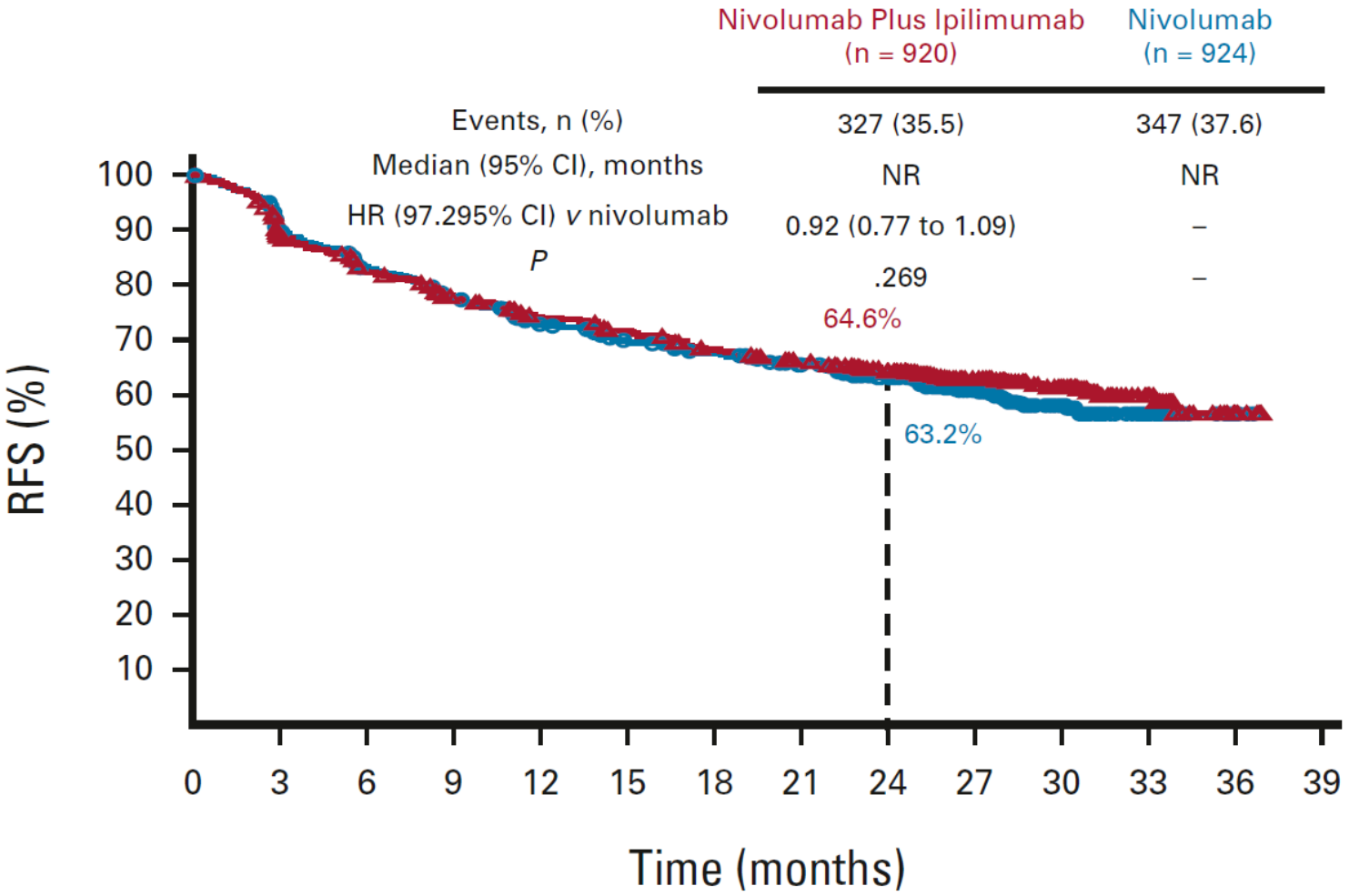
Weber JS et al. J Clin Oncol 2023;41(3):517-27.

No difference in recurrence-free survival (RFS) among ~1800 patients with resected stage IIIB-D or IV melanoma randomized to nivolumab + ipilimumab 1mg/kg q6W vs nivolumab alone



Weber JS et al. J Clin Oncol 2023;41(3):517-27.

Conclusions

- **Critical finding(s):** No difference in recurrence-free survival among ~1800 patients with resected stage IIIB-D or IV melanoma randomized to nivolumab + ipilimumab 1mg/kg q6W vs nivolumab alone, regardless of PD-L1 status.
- Treatment-related grade 3-4 adverse events were reported in 32.6% of patients in the combination group and 12.8% in the nivolumab group. Treatment-related deaths were reported in 0.4% of patients in the combination group and in no nivolumab-treated patients.

- **Clinical implication(s):** These results support administration of adjuvant anti-PD-1 monotherapy for patients with high-risk resected melanoma.

- **Research relevance:** Could other combinations (e.g., anti-PD-1 + anti-LAG-3) provide benefit over anti-PD-1 alone in this patient population?

Pembrolizumab Versus Placebo as Adjuvant Therapy in Stage IIB or IIC Melanoma: Final Distant Metastasis-Free Survival Analysis in the Phase 3 KEYNOTE-716 Study

Jason J. Luke[1]; Paolo A. Ascierto[2]; Muhammad A. Khattak[3]; Luis de la Cruz Merino[4]; Michele Del Vecchio[5]; Piotr Rutkowski[6]; Francesco Spagnolo[7]; Jacek Mackiewicz[8]; Vanna Chiarion-Sileni[9]; John M. Kirkwood[1]; Caroline Robert[10]; Jean-Jacques Grob[11]; Federica de Galitiis[12]; Dirk Schadendorf[13]; Matteo S. Carlino[14]; Xi Lawrence Wu[15]; Mizuho Fukunaga-Kalabis[15]; Clemens Krepler[15]; Alexander M. M. Eggermont[16]; Georgina V. Long[17]

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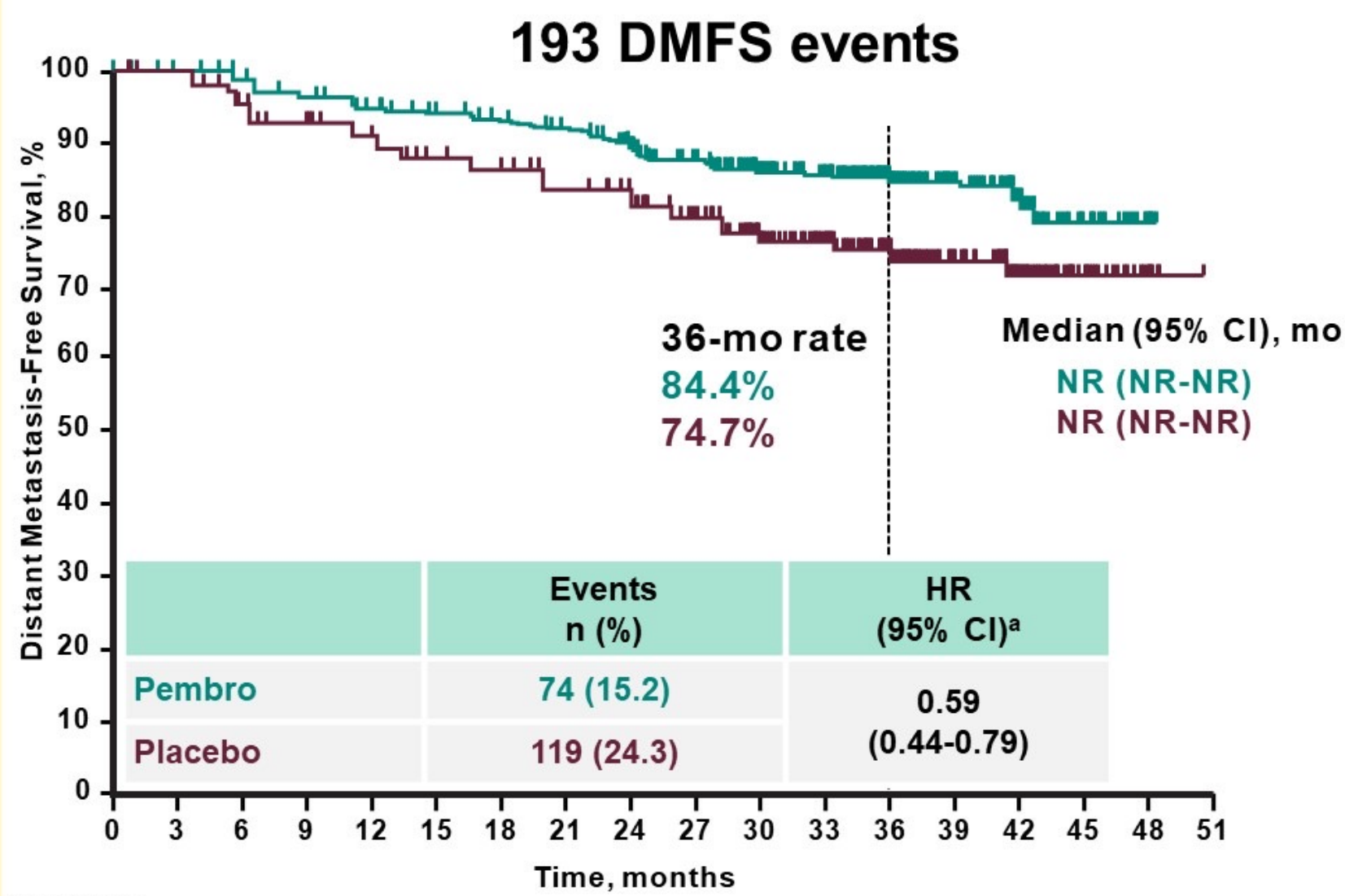
Luke JJ et al. ASCO 2023;Abstract LBA9505.

In patients with resected stage IIB/C melanoma, distant metastasis-free survival improved with adjuvant pembrolizumab vs. placebo.



Luke JJ et al. ASCO 2023;Abstract LBA9505.

Conclusions

- **Critical finding(s):** Among ~1000 patients with resected stage IIB/C melanoma, at a median follow-up of 39.4 months, adjuvant pembrolizumab continued to demonstrate improved distant metastasis-free and recurrence-free survival compared with placebo.

- **Clinical implication(s):** These results support adjuvant pembrolizumab monotherapy for patients with resected stage IIB/C melanoma.

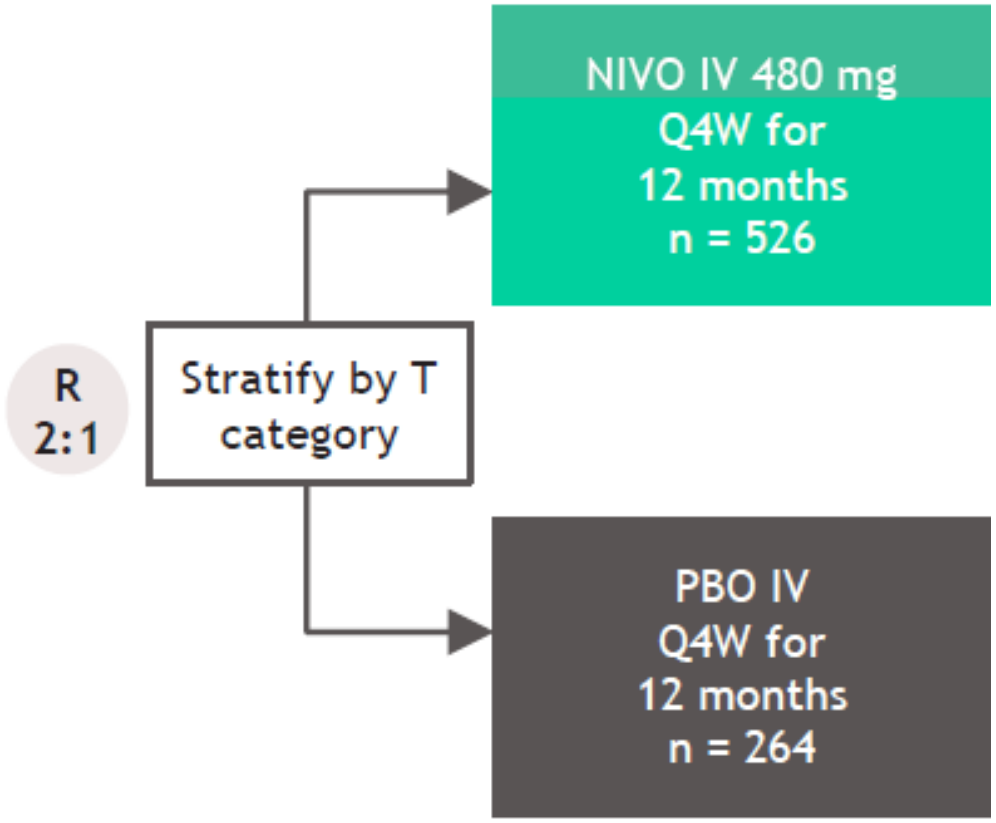
- **Research relevance:** Could other combinations (e.g., anti-PD-1 + anti-LAG-3) provide benefit over anti-PD-1 alone in this patient population?

Adjuvant therapy with nivolumab versus placebo in patients with resected stage IIB/C melanoma (CheckMate 76K)

Treatment naive patients ≥ 12 y with

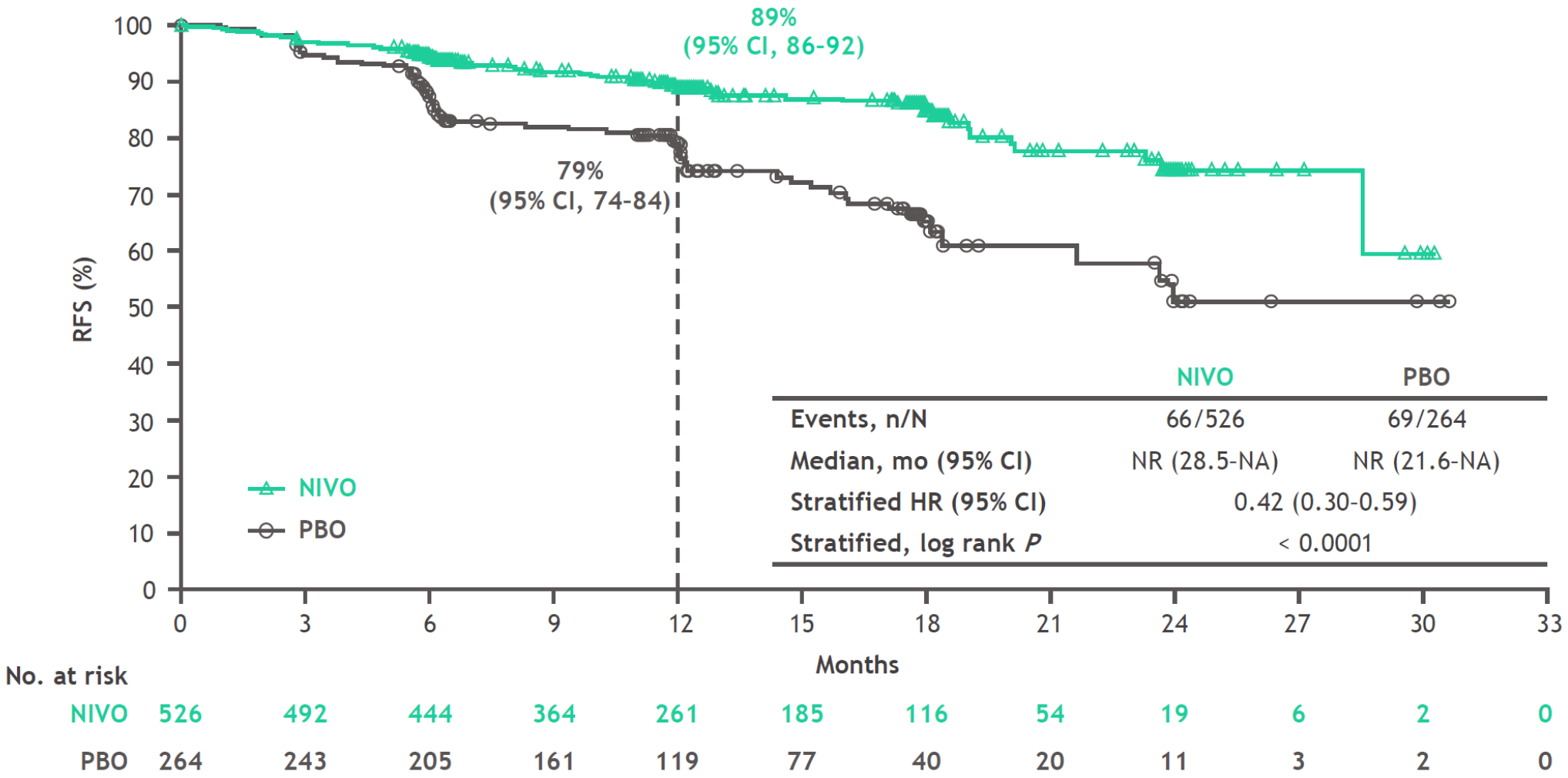
- Completely resected stage IIB/C melanoma with standard wide local excision
- Negative sentinel lymph node biopsy

N = 790



Long G et al. Society for Melanoma Research 2022.

In patients with resected stage IIB/C melanoma, recurrence-free survival (RFS) improved with adjuvant nivolumab (NIVO) vs. placebo (PBO)



	NIVO	PBO
Events, n/N	66/526	69/264
Median, mo (95% CI)	NR (28.5-NA)	NR (21.6-NA)
Stratified HR (95% CI)	0.42 (0.30-0.59)	
Stratified, log rank *P*	< 0.0001	

NA, not available; NR, not reached.

Long G et al. Society for Melanoma Research 2022.

Conclusions

- **Critical finding(s):** Among ~800 patients with resected stage IIB or IIC melanoma, nivolumab significantly reduced the risk of recurrence by 58% compared with placebo

- **Clinical implication(s):** These results demonstrate the benefit of adjuvant nivolumab for patients with resected stage IIB/C melanoma.

- **Research relevance:** Could other combinations (e.g., anti-PD-1 + anti-LAG-3) provide benefit over anti-PD-1 alone in this patient population?

The NEW ENGLAND JOURNAL of MEDICINE

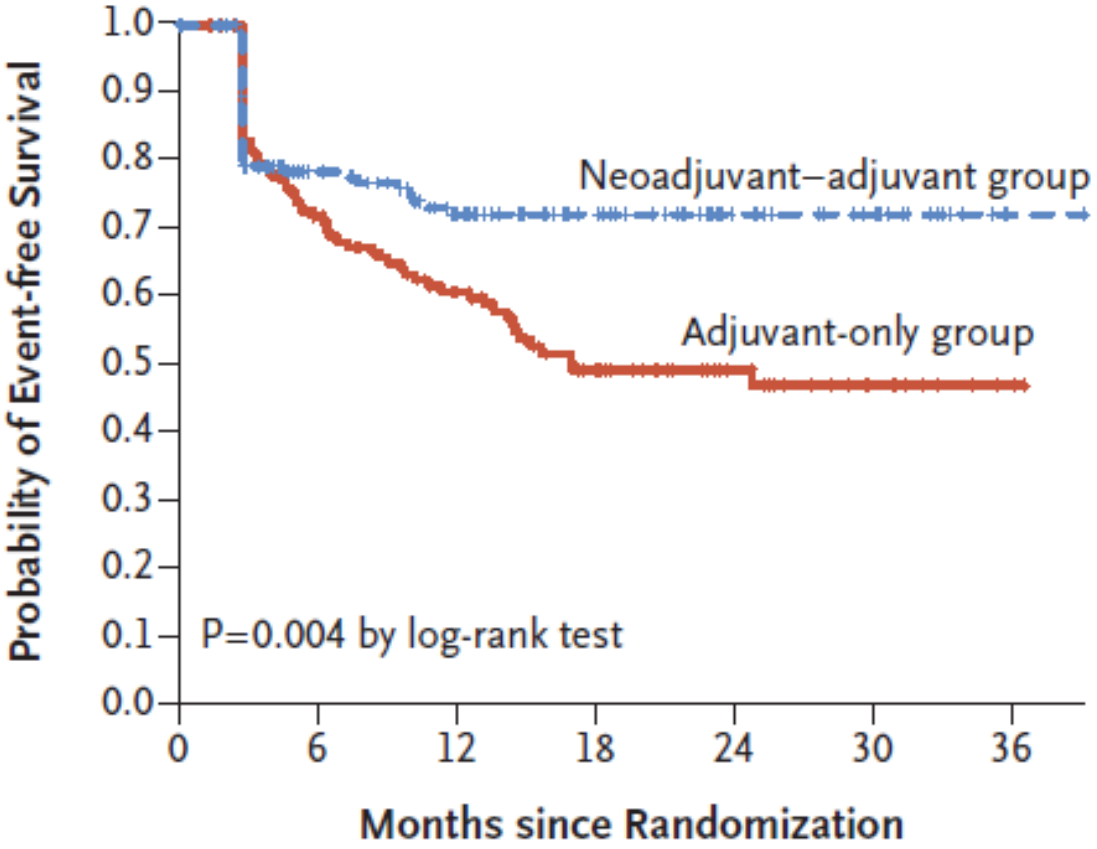
ORIGINAL ARTICLE

Neoadjuvant–Adjuvant or Adjuvant-Only Pembrolizumab in Advanced Melanoma

S.P. Patel, M. Othus, Y. Chen, G.P. Wright, Jr., K.J. Yost, J.R. Hyngstrom, S. Hu-Lieskovan, C.D. Lao, L.A. Fecher, T.-G. Truong, J.L. Eisenstein, S. Chandra, J.A. Sosman, K.L. Kendra, R.C. Wu, C.E. Devoe, G.B. Deutsch, A. Hegde, M. Khalil, A. Mangla, A.M. Reese, M.I. Ross, A.S. Poklepovic, G.Q. Phan, A.A. Onitilo, D.G. Yasar, B.C. Powers, G.C. Doolittle, G.K. In, N. Kokot, G.T. Gibney, M.B. Atkins, M. Shaheen, J.A. Warneke, A. Ikeguchi, J.E. Najera, B. Chmielowski, J.G. Crompton, J.D. Floyd, E. Hsueh, K.A. Margolin, W.A. Chow, K.F. Grossmann, E. Dietrich, V.G. Prieto, M.C. Lowe, E.I. Buchbinder, J.M. Kirkwood, L. Korde, J. Moon, E. Sharon, V.K. Sondak, and A. Ribas

Patel SP et al. N Engl J Med 2023;388(9):813-23.

In patients with resectable stage III/IV melanoma, event-free survival (EFS) improved with neoadjuvant + adjuvant pembrolizumab vs. adjuvant-only.



No. at Risk							
Neoadjuvant–adjuvant group	154	96	69	46	25	17	1
Adjuvant-only group	159	98	67	40	22	10	2

Patel SP et al. N Engl J Med 2023;388(9):813-23.

Conclusions

- **Critical finding(s):** Among ~150 patients with clinically detectable, measurable, surgically resectable, stage IIIB to IVC melanoma, event-free survival (EFS) improved with neoadjuvant + adjuvant pembrolizumab vs. adjuvant-only. Events were defined as:
  - disease progression or toxic effects that precluded surgery
  - inability to resect all gross disease
  - disease progression, surgical complications, or toxic effects of treatment that precluded the initiation of adjuvant therapy within 84 days after surgery
  - recurrence of melanoma after surgery
  - death from any cause

- **Clinical implication(s):** Neoadjuvant immunotherapy is becoming standard-of-care for patients with resectable, stage IIIB to IV melanoma.

- **Research relevance:** Which regimen is best, for how long, and is adjuvant therapy needed, especially in the setting of a pathologic complete response?

2023 ASCO ANNUAL MEETING

Distant Metastasis-Free Survival Results From the Randomized, Phase 2 mRNA-4157-P201/ KEYNOTE-942 Trial

Adnan Khattak,[1,2] Jeffrey S. Weber,[3] Tarek Meniawy,[4] Matthew H. Taylor,[5] George Ansstas,[6] Kevin B. Kim,[7] Meredith McKean,[8] Georgina V. Long,[9] Ryan J. Sullivan,[10] Mark B. Faries,[11] Thuy Tran,[12] C. Lance Cowey,[13] Theresa M. Medina,[14] Jennifer M. Segar,[15] Victoria Atkinson,[16] Geoffrey T. Gibney,[17] Jason J. Luke,[18] Elizabeth I. Buchbinder,[19] Robert S. Meehan,[20] Matteo S. Carlino,[9,21] Moderna Author's Group[20]

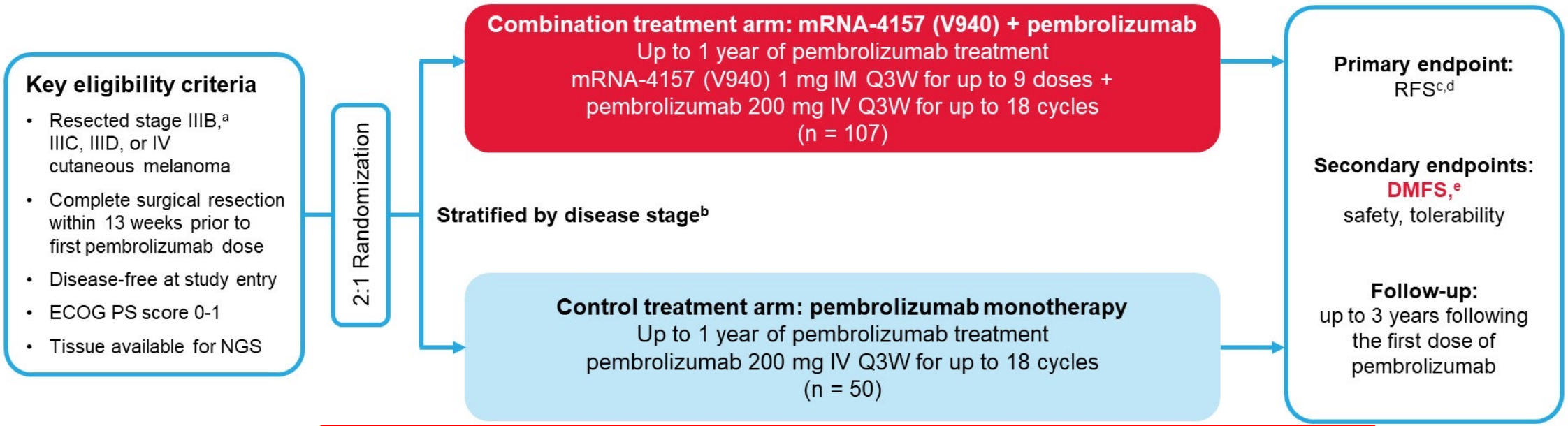
[1]Hollywood Private Hospital, Nedlands, Australia; [2]Edith Cowan University, Perth, Australia; [3]NYU Langone Medical Center, New York, NY; [4]Saint John of God Subiaco Hospital, Subiaco, Australia; [5]Earle A. Chiles Research Institute, Portland, OR, USA; [6]Washington University School of Medicine, St Louis, MO, USA; [7]California Pacific Medical Center Research Institute, Oakland, CA, USA; [8]Sarah Cannon Research Institute, Nashville, TN, USA; [9]Melanoma Institute Australia, Wollstonecraft, Australia; [10]Massachusetts General Hospital, Boston, MA, USA; [11]The Angeles Clinic and Research Institute, Los Angeles, CA, USA; [12]Yale-New Haven Hospital, New Haven, CT, USA; [13]Baylor Charles A. Sammons Cancer Center, Dallas, TX, USA; [14]University of Colorado, Aurora, CO, USA; [15]The University of Arizona Cancer Center, Tucson, AZ, USA; [16]Princess Alexandra Hospital, Woolloongabba, Australia; [17]Lombardi Cancer Center, Washington, DC, USA; [18]UPMC Hillman Cancer Center, Pittsburg, PA, USA; [19]Dana-Farber Cancer Institute, Boston, MA, USA; [20]Moderna Inc., Cambridge, MA, USA; [21]Westmead Hospital, Westmead, Australia.

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

Khattak MA et al. ASCO 2023;Abstract LBA9503.

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

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

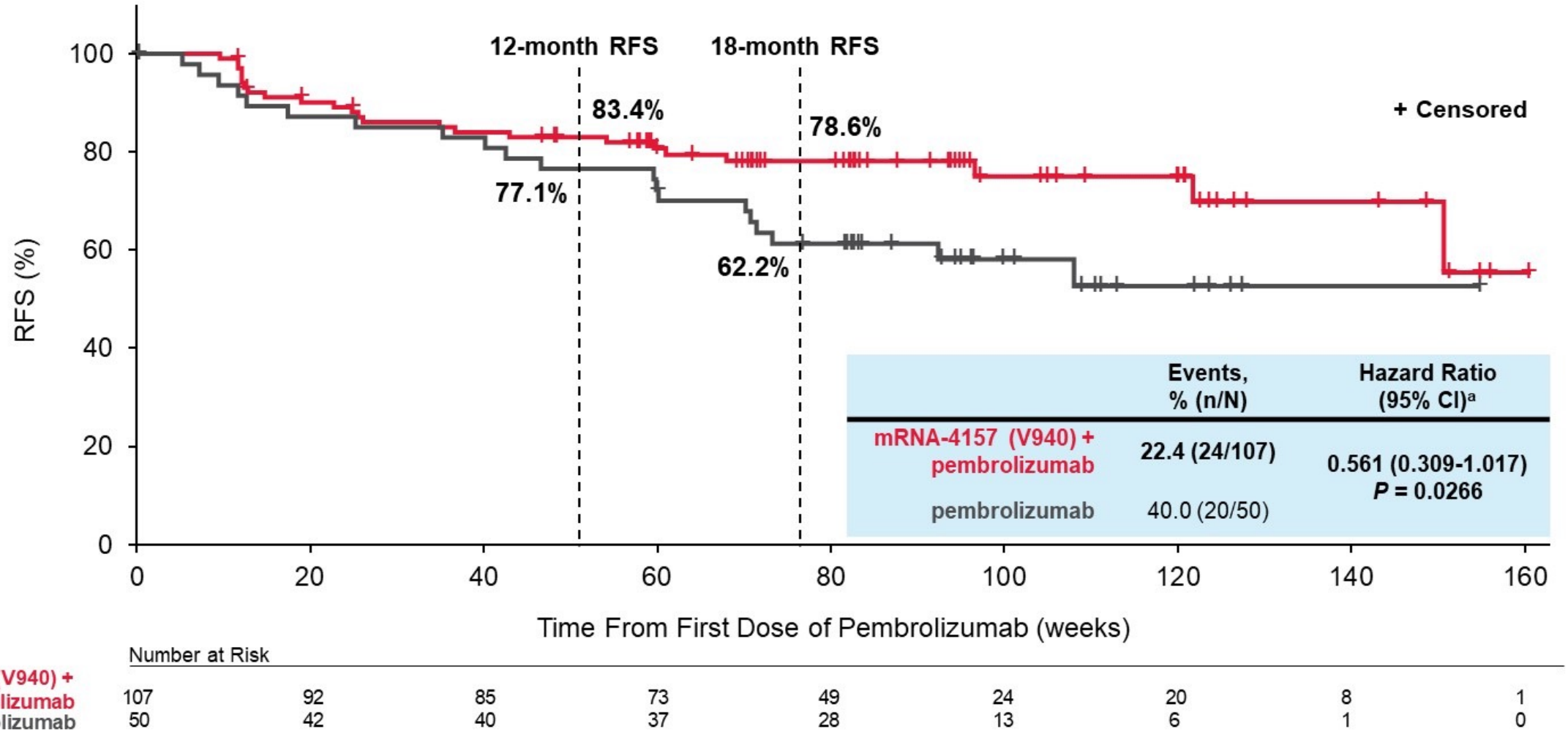


Designed with 80% power to detect an HR of 0.5 with ≥40 RFS events (with a 1-sided alpha of 0.1)
DMFS analysis was prespecified for testing following positive RFS in the ITT population[f]
Median follow-up[g]: 23 months for mRNA-4157 (V940) + pembrolizumab
24 months for pembrolizumab monotherapy

[a]Patients with stage IIIB disease were eligible only if relapse occurred within 3 months of prior surgery of curative intent. [b]According to the 8th edition of the American Joint Committee on Cancer Staging Manual. [c]The primary endpoint was investigator-assessed RFS (defined as the time from first dose of pembrolizumab until the date of first recurrence [local, regional, or distant metastasis], a new primary melanoma, or death from any cause) in the intention-to-treat population. [d]The primary analysis for RFS was specified to occur after all patients completed ≥12 months on study and ≥40 RFS events were observed. Descriptive analysis was specified to occur when ≥51 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.

Khattak MA et al. ASCO 2023;Abstract LBA9503.

Recurrence-free survival among patients with resected stage IIIB-IV melanoma who received adjuvant pembrolizumab alone or mRNA-4157 (V940) + pembrolizumab.



Khattak MA et al. ASCO 2023;Abstract LBA9503.

Conclusions

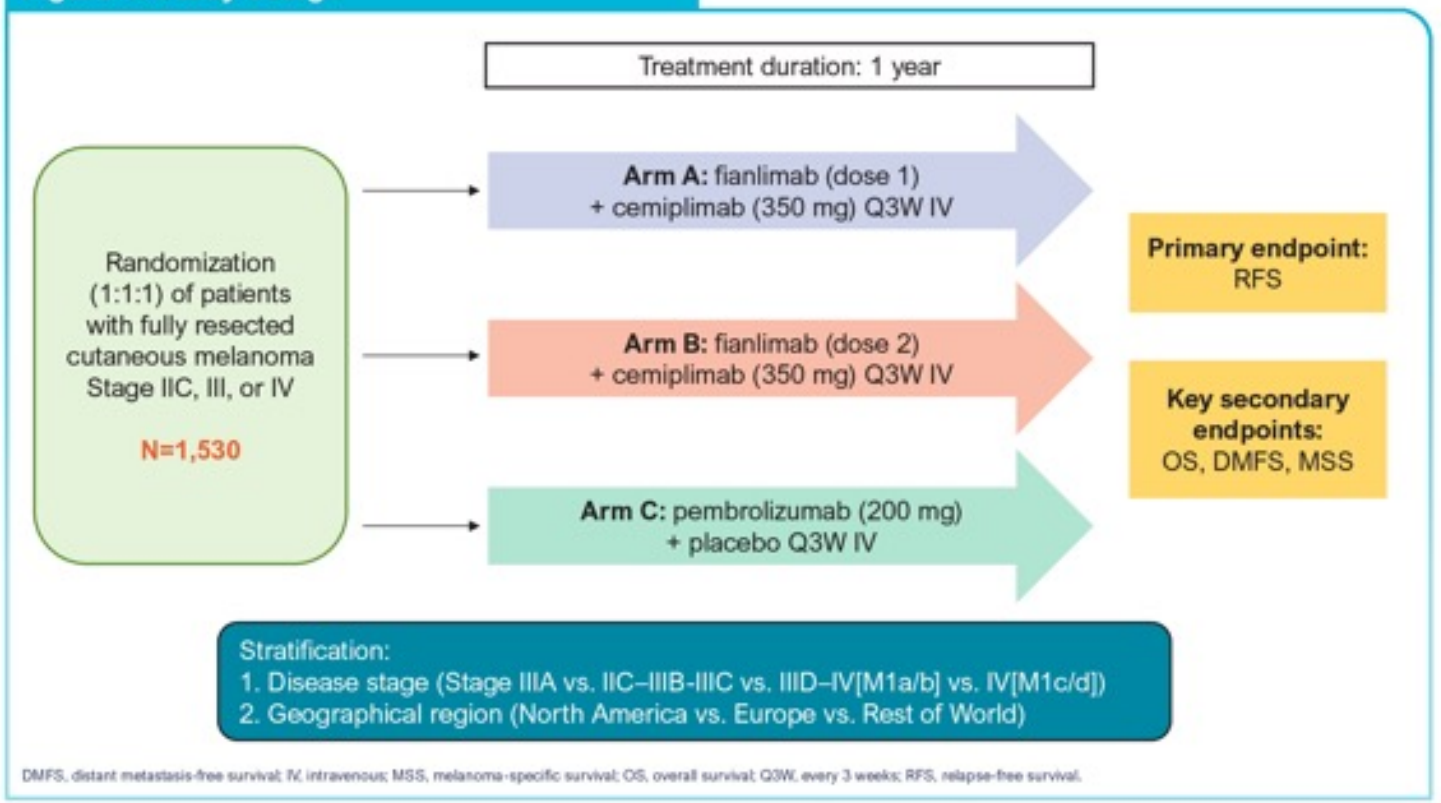
- **Critical finding(s):** Compared to pembrolizumab alone, mRNA-4157 (V940) + pembrolizumab led to a 44% reduction in the risk of recurrence or death and a 65% reduction in the risk of distant metastasis or death among patients with resected stage IIIB-IV melanoma.
- **Clinical implication(s):** Further testing needed. Sample size was relatively small and statistical outcomes are borderline, requiring additional investigation.
- **Research relevance:** Phase 3 trial opening soon.

Abstract TPS9598: A Phase 3 trial comparing fianlimab (anti-LAG-3) plus cemiplimab (anti-PD-1) to pembrolizumab in patients with completely resected high-risk melanoma

Timothy J Panella,[1] Sajeve S Thomas,[2] Meredith McKean,[3] Kim Margolin,[4] Ryan Weight,[5] Jayakumar Mani,[6] Shraddha Patel,[6] Priya Desai,[6] Rossella Marullo,[6] Mark Salvati,[6] Israel Lowy,[6] Matthew G Fury,[6] Giuseppe Gullo[6]

[1]University of Tennessee Medical Center, Knoxville, TN, USA; [2]Orlando Health Cancer Institute, Lake Mary, FL, USA; [3]Sarah Cannon Research Institute/Tennessee Oncology PLLC, Nashville, TN, USA; [4]Saint John's Cancer Institute, Santa Monica, CA, USA; [5]The Melanoma And Skin Cancer Institute, Denver, CO, USA; [6]Regeneron Pharmaceuticals, Inc., Tarrytown, NY, USA

Figure 1. Study design



DMFS, distant metastasis-free survival; IV, intravenous; MSS, melanoma-specific survival; OS, overall survival; Q3W, every 3 weeks; RFS, relapse-free survival.

Panella TJ et al. ASCO 2023;Abstract TPS9598.

Conclusions

- **Critical finding(s):** This is a phase 3 trial comparing recurrence-free survival among patients with resected stage IIC, III or IV melanoma who receive pembrolizumab or cemiplimab+fianlimab (anti-PD-1 + anti-LAG-3).

- **Clinical implication(s):** If successful, this trial could introduce a combination adjuvant immunotherapy option for patients with resected high-risk melanoma.

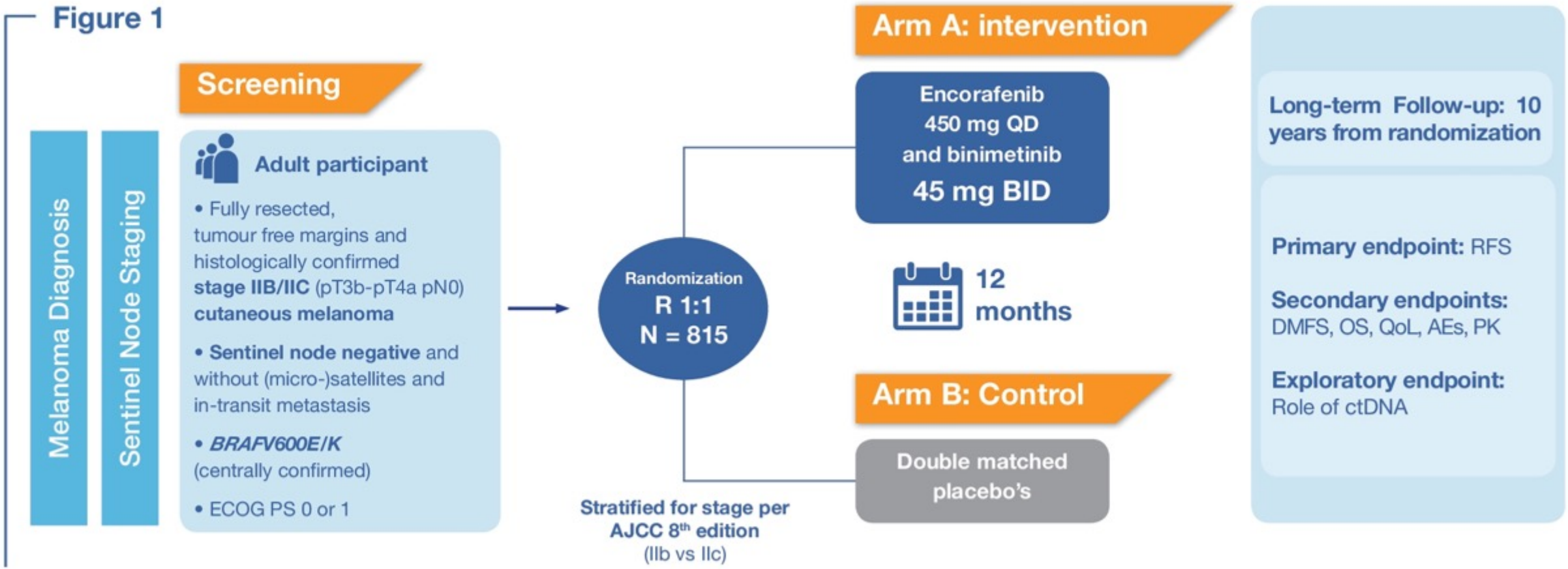
- **Research relevance:** Phase 3 trial in progress.

Phase III Study of Adjuvant Encorafenib Plus Binimetinib Versus Placebo In Fully Resected Stage IIB/C *BRAFV600*-Mutated Melanoma : COLUMBUS-AD Study Design

Alexander C. J. van Akkooi[1], Axel Hauschild[2], Georgina V. Long[3], Mario Mandala[4] Michal Kicinski[5], Anne-Sophie Govaerts[5], Isabelle Klauck[6], Monia Ouali[6], Paul C. Lorigan[7], Alexander M. M. Eggermont[8]

[1]Melanoma Institute Australia, the University of Sydney, and Mater and Royal Hospitals, Sydney, NSW, Australia; [2]Department of Dermatology, University Hospital (UKSH), Kiel, Germany; [3]Melanoma Institute Australia, the University of Sydney, and Mater and Royal North Shore Hospitals, Sydney, NSW, Australia; [4]University of Perugia, Ospedale Santa Maria della Misericordia, Perugia, Italy; [5]EORTC Headquarters, Brussels, Belgium; [6]Pierre Fabre, France; [7]Christie NHS Foundation Trust, Manchester, United Kingdom; [8]University Medical Center Utrecht, Utrecht, the Netherlands.

Figure 1



Van Akkooi ACJ et al. ASCO 2023;Abstract TPS9601.

Conclusions

- **Critical finding(s):** This phase 3 study will evaluate whether encorafenib (BRAF inhibitor) plus binimetinib (MEK inhibitor) can decrease the risk of recurrence and improve distant metastasis-free survival and overall survival versus placebo in patients with resected stage IIB/C BRAF V600E/K-mutant melanoma.

- **Clinical implication(s):** If successful, this trial could introduce a combination adjuvant targeted therapy option for patients with resected stage IIB/C BRAF V600E/K-mutant melanoma.

- **Research relevance:** Phase 3 trial in progress.

nature medicine

Article

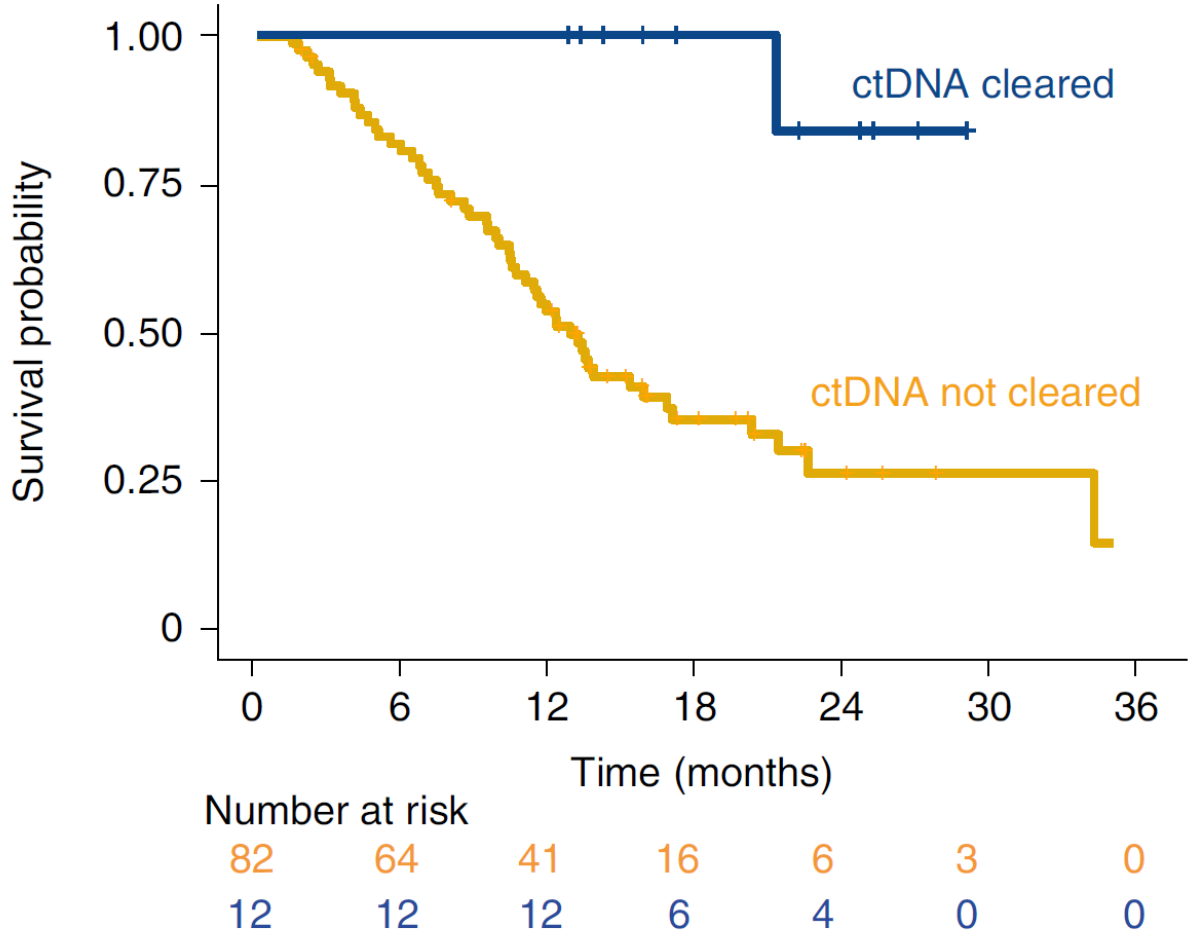
https://doi.org/10.1038/s41591-022-02015-7

Clinical and molecular response to tebentafusp in previously treated patients with metastatic uveal melanoma: a phase 2 trial

Carvajal RD et al. Nat Med 2022;28(11):2364-73.

Tebentafusp may improve OS compared to historical controls. Early on-treatment reduction in circulating tumor DNA was associated with overall survival, even in patients with radiographic progression.

	Historical controls	Tebentafusp
1-year OS rate (%)	37	62
Median OS (mos)	7.8	16.8



Carvajal RD et al. Nat Med 2022;28(11):2364-73.

Conclusions

- **Critical finding(s):** 127 patients with previously treated metastatic uveal melanoma received tebentafusp (T cell receptor bispecific (gp100×CD3))
  - Despite an overall response rate of only 5%, 1-year overall survival rate was 62% and median overall survival was 16.8 months, suggesting benefit beyond traditional imaging-based response criteria.
  - In an exploratory analysis, early on-treatment reduction in circulating tumor DNA was strongly associated with overall survival, even in patients with radiographic progression.

- **Clinical implication(s):** In patients with metastatic uveal melanoma who had previously received immunotherapy, chemotherapy, targeted therapy, radiotherapy, liver-directed therapy, and/or surgery, tebentafusp demonstrated promising clinical activity. ctDNA appears to be an early indicator of clinical benefit.

- **Research relevance:** The findings above need validation in a randomized trial.

Society for Immunotherapy of Cancer (SITC) clinical practice guideline on immunotherapy for the treatment of nonmelanoma skin cancer

Ann W Silk ,[1] Christopher A Barker,[2] Shailender Bhatia ,[3] Kathryn B Bollin,[4] Sunandana Chandra,[5] Zeynep Eroglu ,[6] Brian R Gastman,[7] Kari L Kendra,[8] Harriet Kluger,[9] Evan J Lipson ,[10] Kathleen Madden,[11] David M Miller ,[12] Paul Nghiem ,[13] Anna C Pavlick,[14] Igor Puzanov ,[15] Guilherme Rabinowits,[16] Emily S Ruiz,[17] Vernon K Sondak,[6] Edward A Tavss,[18] Michael T Tetzlaff,[19] Isaac Brownell [20]

Silk AW et al. J Immunother Cancer 2022;10(7):e004434.

Conclusions

- **Critical finding(s):** With the goal of improving patient care by providing expert guidance to the oncology community, the Society for Immunotherapy of Cancer (SITC) convened a multidisciplinary panel of experts to develop a clinical practice guideline for treating patients with basal, cutaneous squamous and Merkel cell carcinomas.

- The expert panel drew on the published literature as well as their own clinical experience to develop recommendations for healthcare professionals on important aspects of immunotherapeutic treatment for these patients, including staging, biomarker testing, patient selection, therapy selection, post-treatment response evaluation and surveillance, and patient quality of life considerations.

- **Clinical implication(s):** The evidence- and consensus-based recommendations in this clinical practice guideline are intended to provide guidance to cancer care professionals treating patients with non-melanoma skin cancers.

- **Research relevance:** Some of the evidence- and consensus-based recommendations included in the clinical practice guideline are undergoing formal testing in clinical trials.

2023 ASCO® ANNUAL MEETING

Non-comparative, open-label, international, multicenter phase 1/2 study of nivolumab (NIVO) ± ipilimumab (IPI) in patients (pts) with recurrent/metastatic Merkel cell carcinoma (MCC) (CheckMate 358)

Shailender Bhatia,[1] Suzanne L. Topalian,[2] William Sharfman,[2] Tim Meyer,[3] Christopher D. Lao,[4] Lorena Fariñas-Madrid,[5] Lot A Devriese,[6] Raid Aljumaily,[7] Robert L. Ferris,[8] Yoshitaka Honma,[9] Tariq Aziz Khan,[10] Anjaiah Srirangam,[10] Charlie Garnett-Benson,[10] Michelle Lee,[10,11] Paul Nghiem[12]

[1]Division of Medical Oncology, University of Washington and Fred Hutchinson Cancer Center, Seattle, WA, USA; [2]Johns Hopkins Bloomberg-Kimmel Institute for Cancer Immunotherapy and Sidney Kimmel Comprehensive Cancer Center, Baltimore, MD, USA; [3]Department of Oncology, University College London Cancer Institute, London, UK; [4]Michigan Medicine, Rogel Cancer Center, Ann Arbor, MI, USA; [5]Vall d'Hebron University Hospital, Vall d'Hebron Institute of Oncology, Barcelona, Spain; [6]Department of Medical Oncology, Cancer Center, University Medical Center Utrecht, Utrecht, the Netherlands; [7]Stephenson Cancer Center at the University of Oklahoma Health Sciences Center, Oklahoma City, OK, USA; [8]Department of Otolaryngology, University of Pittsburgh, Pittsburgh, PA, USA; [9]Department of Head and Neck, Esophageal Medical Oncology, National Cancer Center Hospital, Tokyo, Japan; [10]Bristol Myers Squibb, Princeton, NJ, USA; [11]Syneos Health, Morrisville, NC, USA; [12]University of Washington Medical Center, Seattle, WA, USA

Presentation number 9506

Efficacy: all treated patients

- In this non-randomized trial, ORR appeared to be similar in the two cohorts
- NIVO + IPI combination appeared to be associated with shorter DOR, PFS, and OS

	NIVO (n = 25)	NIVO + IPI (n = 43)
ORR,[a] % (95% CI)	60.0 (38.7-78.9)	58.1 (42.1-73.0)
n	15	25
CR, n (%)	8 (32.0)	8 (18.6)
PR, n (%)	7 (28.0)	17 (39.5)
SD, n (%)	5 (20.0)	4 (9.3)
PD, n (%)	3 (12.0)	10 (23.3)
NE, n (%)	2 (8.0)	4 (9.3)
Median PFS, months (95% CI)	21.3 (9.2-62.5)	8.4 (3.7-24.3)
Median OS, months (95% CI)	80.7 (23.3-NA)	29.8 (8.5-48.3)

	NIVO (n = 25)	NIVO + IPI (n = 43)
Median DOR, months (95% CI)	60.6 (16.7-NA)	25.9 (10.4-NA)
Patients with DOR of at least:		
12 months, n (%)	12 (80.0)	17 (68.0)
18 months, n (%)	8 (53.3)	15 (60.0)
24 months, n (%)	6 (40.0)	13 (52.0)

Database lock: November 28, 2022. [a]ORR and PFS were investigator-assessed.
CR, complete response; DOR, duration of response; IPI, ipilimumab; NA, not applicable; NE, not evaluable; NIVO, nivolumab; ORR, objective response rate; OS, overall survival; PD, progressive disease; PFS, progression-free survival; PR, partial response; SD, stable disease.

Bhatia S et al. ASCO 2023;Abstract 9506.

Conclusions

- **Critical finding(s):** This multicenter, international phase 1 /2 study investigated NIVO ± IPI 1 mg/kg Q6W in patients with advanced MCC, some treatment-naïve, some previously treated.
  - Both NIVO and NIVO + low-dose IPI were associated with frequent and durable responses.
  - While the non-randomized trial design limits comparisons between cohorts, results do not suggest additional efficacy (ORR, PFS, OS) in the combination arm.

- **Clinical implication(s):** Although this study does not support administration of IPI+NIVO to patients with advanced Merkel cell carcinoma, reports from other groups suggest some benefit associated with this combination. For now, anti-PD-(L)1 monotherapy remains the standard of care for this patient population, though the addition of ipilimumab might be considered in patients with refractory MCC.

- **Research relevance:** Further research is needed to assess a potential role for combination immune checkpoint inhibitor therapy in this patient population.

2023 ASCO ANNUAL MEETING

Towards organ preservation and cure via two infusions of immunotherapy only, in patients normally undergoing extensive and mutilating curative surgery for cutaneous squamous cell carcinoma (CSCC)

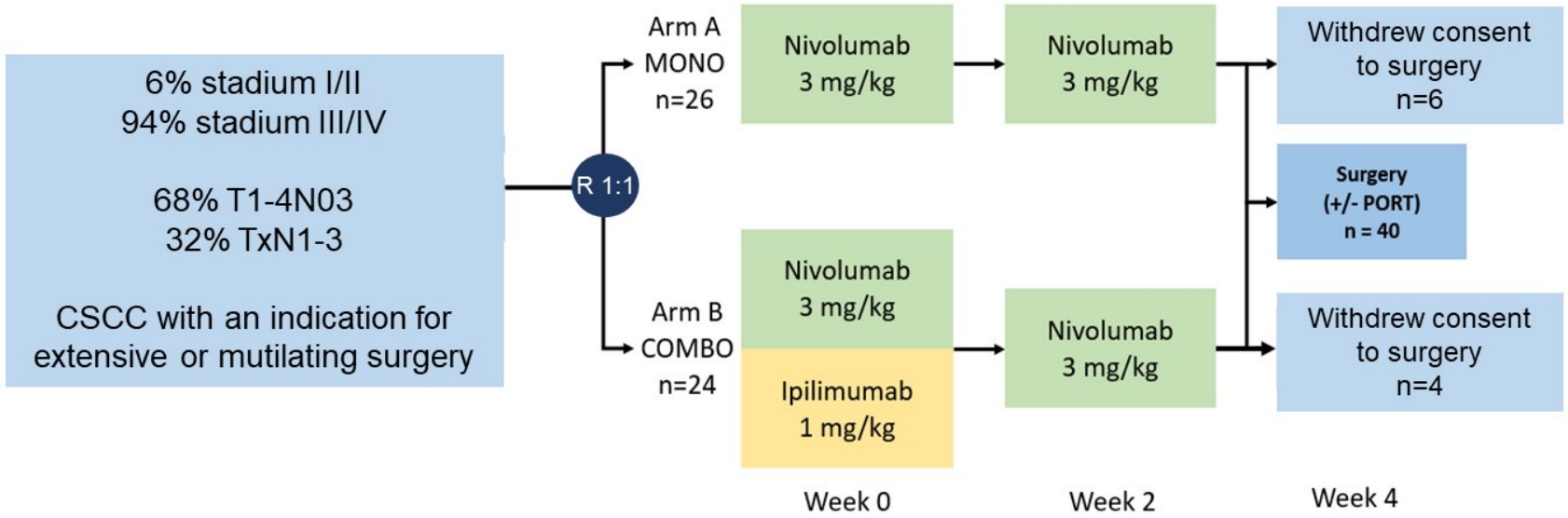
The MATISSE trial, NCT04620200

Charlotte (Lotje) Zuur, MD PhD, Head and Neck Surgeon, c.zuur@nki.nl

The Netherlands Cancer Institute, Amsterdam, The Netherlands.

Zuur CL et al. ASCO 2023;Abstract 9507.

MATISSE: Included patients

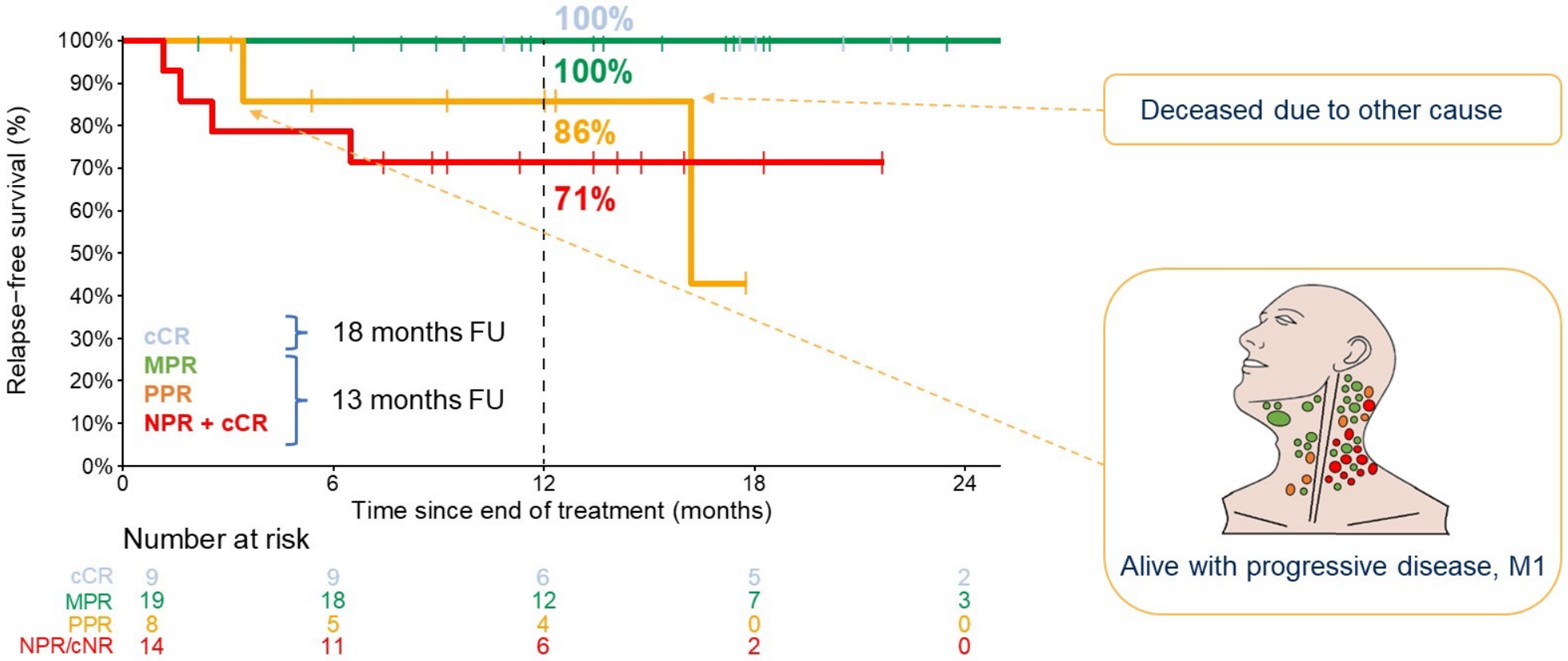


10 patients withdrew consent to surgery w/wo adjuvant RT and were 'not evaluable' according to the primary endpoint of the trial >> accrual of 10 extra patients

9/10 patients refused surgery w/wo RT as they themselves noticed remission of their cancer upon 2 infusions of immunotherapy only.

Zuur CL et al. ASCO 2023;Abstract 9507.

MATISSE, RFS:



Excellent clinical outcome in patients with an **MPR** or **CCR**,
at an overall median Follow-Up of 14 months.

PRESENTED BY: Charlotte (Lotje) Zuur, MD PhD, Head and Neck Surgeon, The Netherlands Cancer Institute, Amsterdam, The Netherlands.

Zuur CL et al. ASCO 2023;Abstract 9507.

Conclusions

- **Critical finding(s):** Among 40 patients with locally-advanced cutaneous squamous cell carcinoma who received NIVO or IPI+NIVO, major pathologic response rates were 40% and 53%, respectively.

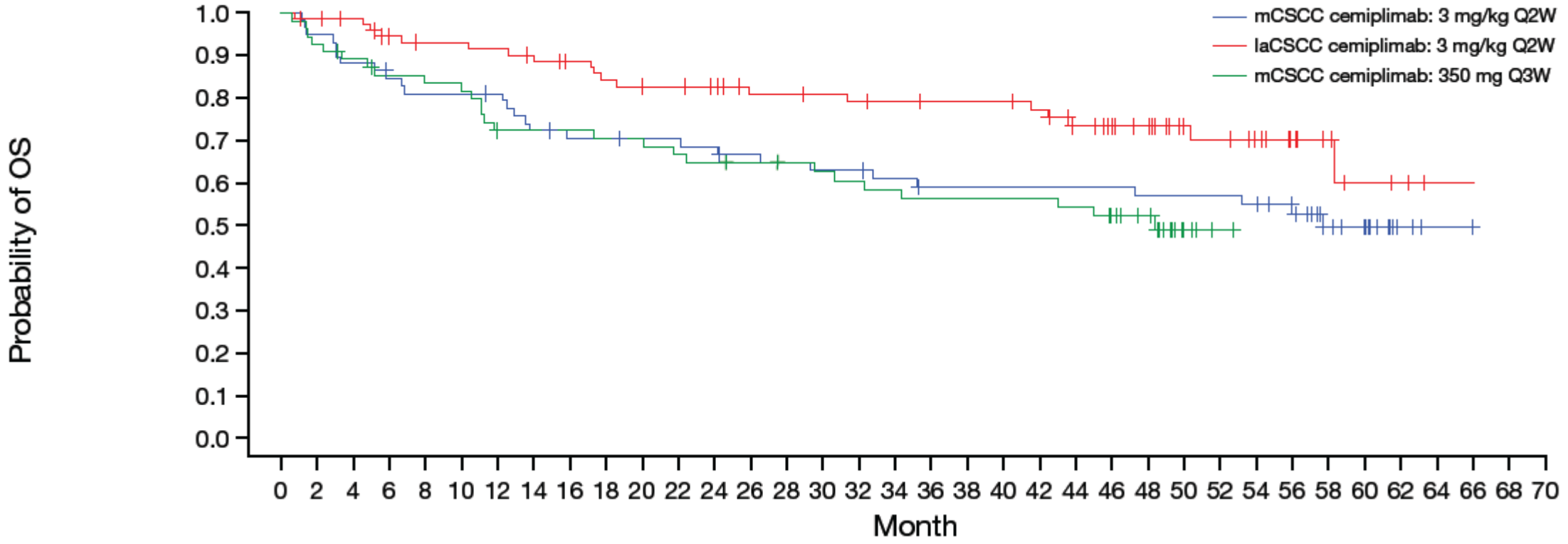
- 9 pts declined surgery because of self-reported substantial clinical remission upon neoadjuvant immunotherapy. These clinical responses were confirmed via FDG-PET evaluation in week 4. All 9 pts were “cancer free” at median follow-up of 12 months (range 4 to 27) with superior quality-of-life compared to MATISSE pts undergoing standard of care surgery.

- **Clinical implication(s):** Neoadjuvant immunotherapy is becoming standard-of-care for patients with locally-advanced resectable CSCC. In the setting of substantial tumor regression, it remains unclear whether surgical resection is necessary.

- **Research relevance:** Which regimen is best, for how long, and are surgery and/or adjuvant therapy needed, particularly in the setting of substantial tumor regression or a pathologic complete response?

Phase 2 study of cemiplimab in patients with advanced cutaneous squamous cell carcinoma (CSCC): Final analysis from EMPOWER-CSCC-1 Groups 1, 2 and 3

Michael R Migden,[1] Chrysalyne D Schmults,[2] Nikhil I Khushalani,[3] Alexander Guminski,[4] Anne Lynn S Chang,[5] Karl D Lewis,[6] George Ansstas,[7] Samantha Bowyer,[8] Brett G Hughes,[9] Dirk Schadendorf,[10] Badri Modi,[11] Lara A Dunn,[12] Lukas Flatz,[13] Axel Hauschild,[14] Suk-Young Yoo,[15] Jocelyn Booth,[15] Frank Seebach,[15] Israel Lowy,[15] Matthew G Fury,[15] Danny Rischin[16]



Migden MR et al. ESMO 2022;Abstract 814P.

Conclusions

- **Critical finding(s):** 193 patients with advanced cutaneous squamous cell carcinoma received cemiplimab. Median duration of follow up was 15.7 months.
  - Median PFS = 22.1 months
  - Median duration of response = 41.3 months
  - Median OS not reached; Kaplan–Meier estimated probability of OS at 48 months was 61.8%

- **Clinical implication(s):** This study confirms the efficacy, durability, and safety profile of cemiplimab in patients with advanced CSCC.

- **Research relevance:** Could other combinations (e.g., anti-PD-1 + anti-LAG-3) provide benefit over anti-PD-1 alone in this patient population?

The NEW ENGLAND JOURNAL of MEDICINE

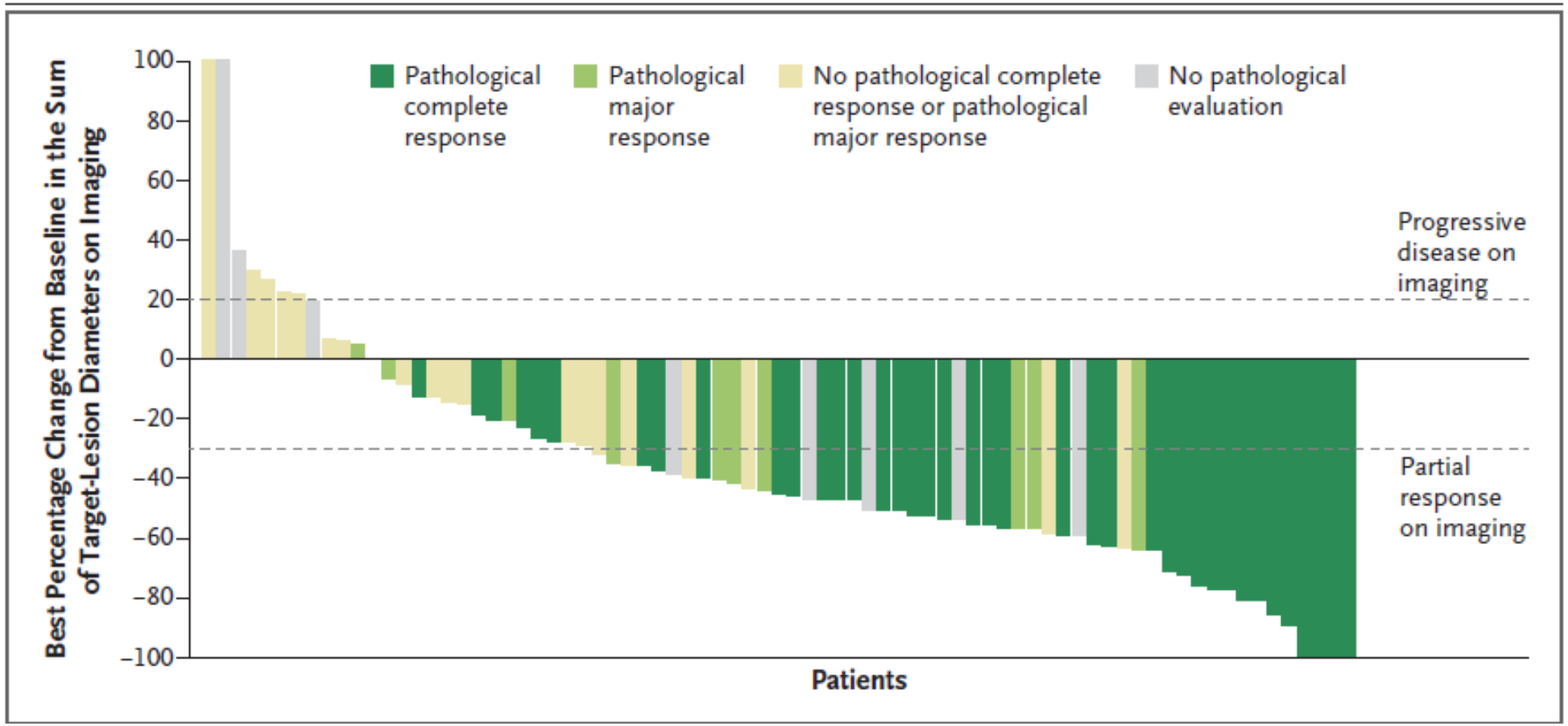
ORIGINAL ARTICLE

Neoadjuvant Cemiplimab for Stage II to IV Cutaneous Squamous-Cell Carcinoma

N.D. Gross, D.M. Miller, N.I. Khushalani, V. Divi, E.S. Ruiz, E.J. Lipson, F. Meier, Y.B. Su, P.L. Swiecicki, J. Atlas, J.L. Geiger, A. Hauschild, J.H. Choe, B.G.M. Hughes, D. Schadendorf, V.A. Patel, J. Homsi, J.M. Taube, A.M. Lim, R. Ferrarotto, H.L. Kaufman, F. Seebach, I. Lowy, S.-Y. Yoo, M. Mathias, K. Fenech, H. Han, M.G. Fury, and D. Rischin

Gross ND et al. N Engl J Med 2022;387(17):1557-68.

Among 79 patients with advanced CSCC who received neoadjuvant cemiplimab, complete or major pathological response was observed in 64%. Objective response on imaging was observed in 68%.



Gross ND et al. N Engl J Med 2022;387(17):1557-68.

Conclusions

- **Critical finding(s):** Among 79 patients with resectable stage II, III, or IV (M0) CSCC who received neoadjuvant cemiplimab x 12 weeks, complete or major pathological response was observed in 64%. Objective response on imaging was observed in 68%.
- **Clinical implication(s):** Neoadjuvant immunotherapy is becoming standard-of-care for patients with locally-advanced resectable CSCC.
- **Research relevance:** Which regimen is best, for how long, and are surgery and/or adjuvant therapy needed, particularly in the setting of substantial tumor regression or a pathologic complete response? Larger trials addressing these questions are in process.

HSR23-097: Health-Related Quality of Life in Patients With Metastatic Basal Cell Carcinoma Treated With Cemiplimab: Analysis of a Phase 2 Open-Label Clinical Trial

Authors: Karl D. Lewis MD, Timothy J. Inocencio PharmD, PhD, Ruben G.W. Quek PhD, Patrick R. LaFontaine PharmD, PhD, Zeynep Eroglu MD, Anne Lynn S. Chang MD, Cristina Ivanescu PhD, LNMB, Alexander J. Stratigos PhD, Ketty Peris MD, Aleksandar Sekulic MD, PhD, Matthew G. Fury MD, PhD, and Chieh-I Chen MPH

Lewis KD et al. EADO 2023;Abstract HSR23-097.

- Phase 2 Trial of Cemiplimab in patients with metastatic basal cell carcinoma who progressed on or were intolerant to hedgehog inhibitor (HHI) treatment

- Objective response rate = 24.1%

- This analysis evaluated health-related quality of life data using validated questionnaires (European Organisation for Research and Treatment of Cancer Quality of Life-Core 30 and Skindex-16).

- Baseline scores showed moderate to high levels of functioning and low symptom burden. Responder analysis showed clinically meaningful improvement or maintenance of functioning and symptoms in 76–88% of patients at week 3 that were generally maintained at ~6 months.

Lewis KD et al. EADO 2023;Abstract HSR23-097.

Conclusions

- **Critical finding(s):** Most patients with metastatic BCC treated with cemiplimab reported maintenance in global health status/quality of life and functioning while maintaining low symptom burden.

- **Clinical implication(s):** Cemiplimab remains a standard-of-care therapy for patients with metastatic basal cell carcinoma who previously received a hedgehog inhibitor (HHI) or for whom a HHI is not appropriate.

- **Research relevance:** Response rates of BCC to anti-PD-1 after HHI seem low compared to tumors with similar tumor mutation burdens (CSCC, Merkel cell). An ongoing front-line anti-PD-1 study reports response rates of ~50% in patients with treatment-naïve BCC.

Cemiplimab for Kidney Organ Transplant Recipients with Advanced Cutaneous Squamous Cell Carcinoma (**CONTRAC-1**)

Glenn J. Hanna, M.D., Harita Dharaneeswaran, Anita Giobbe-Hurder, John J. Harran, Zixi Liao, Lori Pai, M.D., Vatche Tchekmedyian, M.D., Emily S. Ruiz, M.D., Abigail Waldman, M.D., Chrysalyne D. Schmults, M.D., Patrick Lizotte, Ph.D., Cloud Paweletz, Ph.D., Leonardo V. Riella, M.D., Ph.D., Naoka Murakami, M.D., Ph.D., Ann W. Silk, M.D.

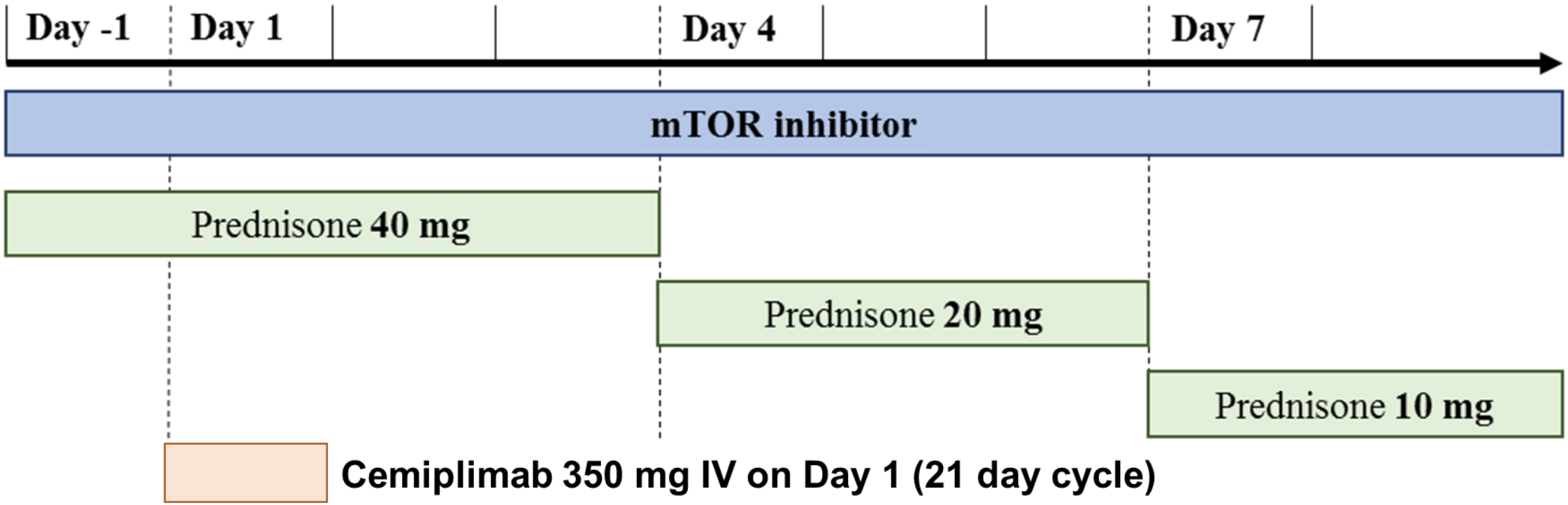


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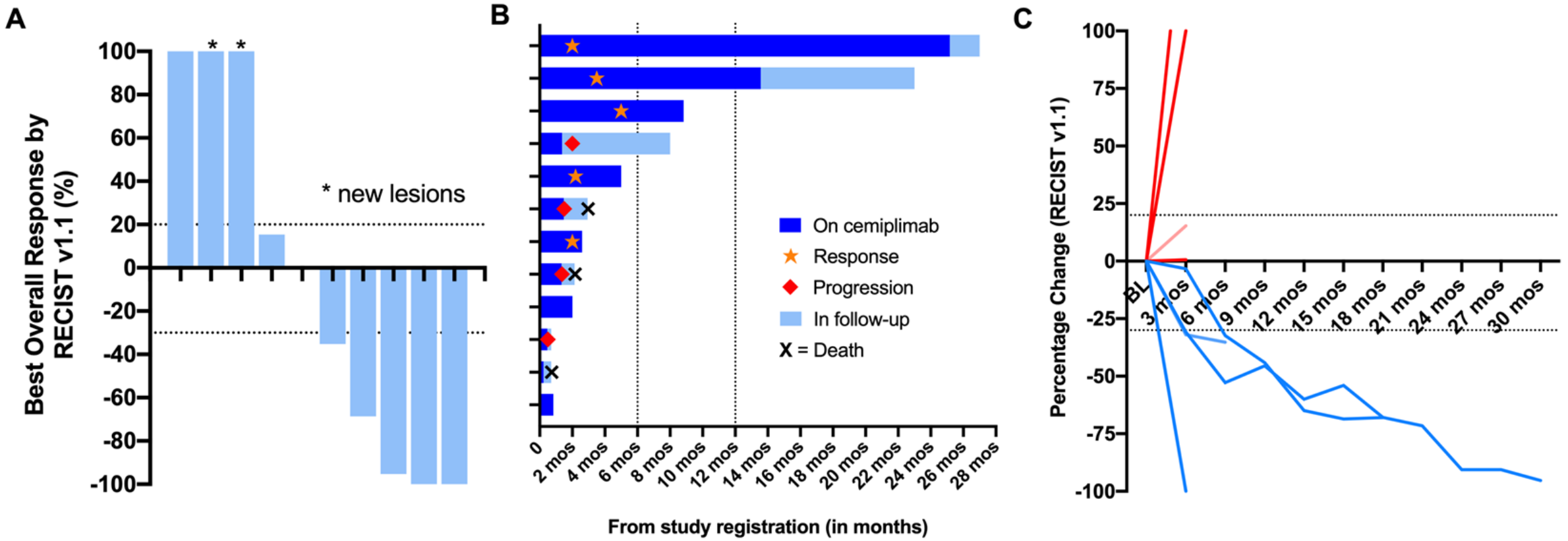
Figure 1. Efficacy Measurements



Conclusions

- **Critical finding(s):** Among 12 patients, no kidney rejection observed. ORR= 50% (5/10 patients); some responses were durable (>2 years in 2/10 patients)
- **Clinical implication(s):** To date, mTor inhibition + pulsed prednisone is the regimen associated with the lowest risk of organ rejection that does not preclude responses to Cemiplimab in kidney transplant recipients with cutaneous squamous cell carcinoma.
- **Research relevance:** Larger trials are planned to further test combinatorial regimens that can activate anti-tumor immunity and maintain allograft tolerance.