Year in Review: Melanoma and Nonmelanoma Skin Cancers

A CME/MOC-Accredited Live Webinar

Wednesday, July 10, 2024
5:00 PM – 6:00 PM ET

Faculty

Evan J Lipson, MD

Moderator

Neil Love, MD

RTP Year in Review 2024

Faculty

Evan J Lipson, MD
Associate Professor, Medical Oncology
Bloomberg-Kimmel Institute
for Cancer Immunotherapy
Johns Hopkins School of Medicine
The Sidney Kimmel Comprehensive Cancer Center
Baltimore, Maryland

MODERATOR
Neil Love, MD
Research To Practice
Miami, Florida

Commercial Support

This activity is supported by an educational grant from Merck.

Dr Love — Disclosures

Dr Love is president and CEO of Research To Practice. Research To Practice receives funds in the form of educational grants to develop CME activities from the following companies: AbbVie Inc, Adaptive Biotechnologies Corporation, ADC Therapeutics, Agios Pharmaceuticals Inc, Alexion Pharmaceuticals, Amgen Inc, Array BioPharma Inc, a subsidiary of Pfizer Inc, Astellas, AstraZeneca Pharmaceuticals LP, Aveo Pharmaceuticals, Bayer HealthCare Pharmaceuticals, BeiGene Ltd, BeyondSpring Pharmaceuticals Inc, Blueprint Medicines, Boehringer Ingelheim Pharmaceuticals Inc, Bristol Myers Squibb, Celgene Corporation, Clovis Oncology, Coherus BioSciences, CTI BioPharma, a Sobi Company, Daiichi Sankyo Inc, Eisai Inc, Elevation Oncology Inc, EMD Serono Inc, Epizyme Inc, Exact Sciences Corporation, Exelixis Inc, Five Prime Therapeutics Inc, Foundation Medicine, G1 Therapeutics Inc, Genentech, a member of the Roche Group, Genmab US Inc, Gilead Sciences Inc, Grail Inc, GSK, Halozyme Inc, Helsinn Healthcare SA, ImmunoGen Inc, Incyte Corporation, Ipsen Biopharmaceuticals Inc, Janssen Biotech Inc, administered by Janssen Scientific Affairs LLC, Jazz Pharmaceuticals Inc, Karyopharm Therapeutics, Kite, A Gilead Company, Kronos Bio Inc, Legend Biotech, Lilly, Loxo Oncology Inc, a wholly owned subsidiary of Eli Lilly & Company, MEI Pharma Inc, Merck, Mersana Therapeutics Inc, Mirati Therapeutics Inc, Mural Oncology Inc, Natera Inc, Novartis, Novartis Pharmaceuticals Corporation on behalf of Advanced Accelerator Applications, Novocure Inc, Oncopeptides, Pfizer Inc, Pharmacyclics LLC, an AbbVie Company, Puma Biotechnology Inc, Regeneron Pharmaceuticals Inc, R-Pharm US, Sanofi, Seagen Inc, Servier Pharmaceuticals LLC, SpringWorks Therapeutics Inc, Stemline Therapeutics Inc, Sumitomo Dainippon Pharma Oncology Inc, Syndax Pharmaceuticals, Taiho Oncology Inc, Takeda Pharmaceuticals USA Inc, TerSera Therapeutics LLC, Tesaro, A GSK Company, TG Therapeutics Inc, Turning Point Therapeutics Inc, Verastem Inc, and Zymeworks Inc.

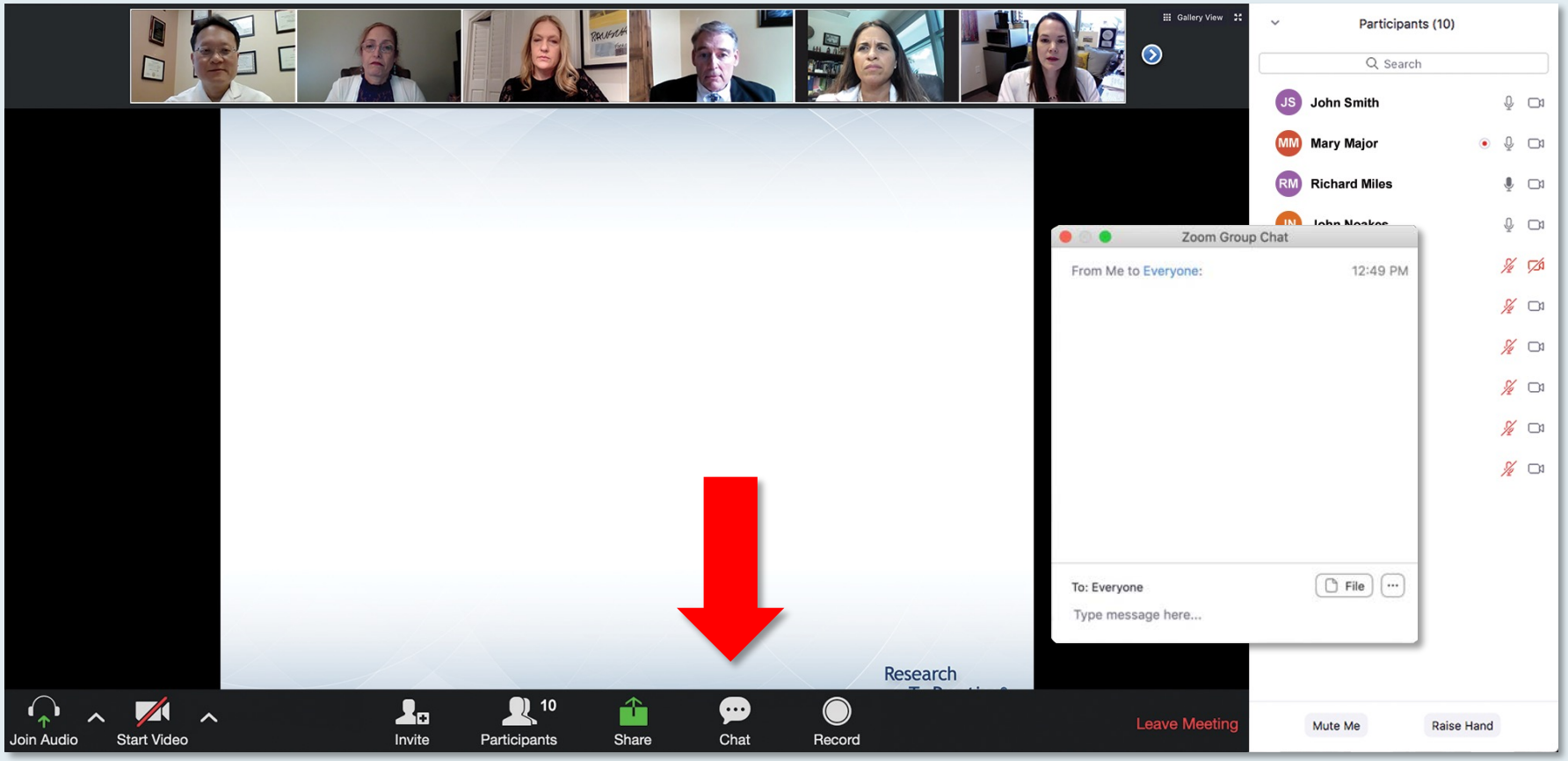
Research To Practice CME Planning Committee Members, Staff and Reviewers

Planners, scientific staff and independent reviewers for Research To Practice have no relevant conflicts of interest to disclose.

Dr Lipson — Disclosures

Consulting Agreements	Agenus Inc, Bristol Myers Squibb, CareDx, Eisai Inc, Genentech, a member of the Roche Group, HUYA Bioscience International, Immunocore, Instil Bio, Lyvgen Biopharma, Merck, Merck KGaA, Natera Inc, Nektar Therapeutics, Novartis, OncoSec Medical, Pfizer Inc, Rain Oncology, Regeneron Pharmaceuticals Inc, Replimune, Sanofi, Sun Pharmaceutical Industries Limited, Syneos Health
Contracted Research	Bristol Myers Squibb, Haystack Oncology, Merck, Regeneron Pharmaceuticals Inc, Sanofi
Stock Options/Stock — Public Company	Iovance Biotherapeutics (less than $10K)

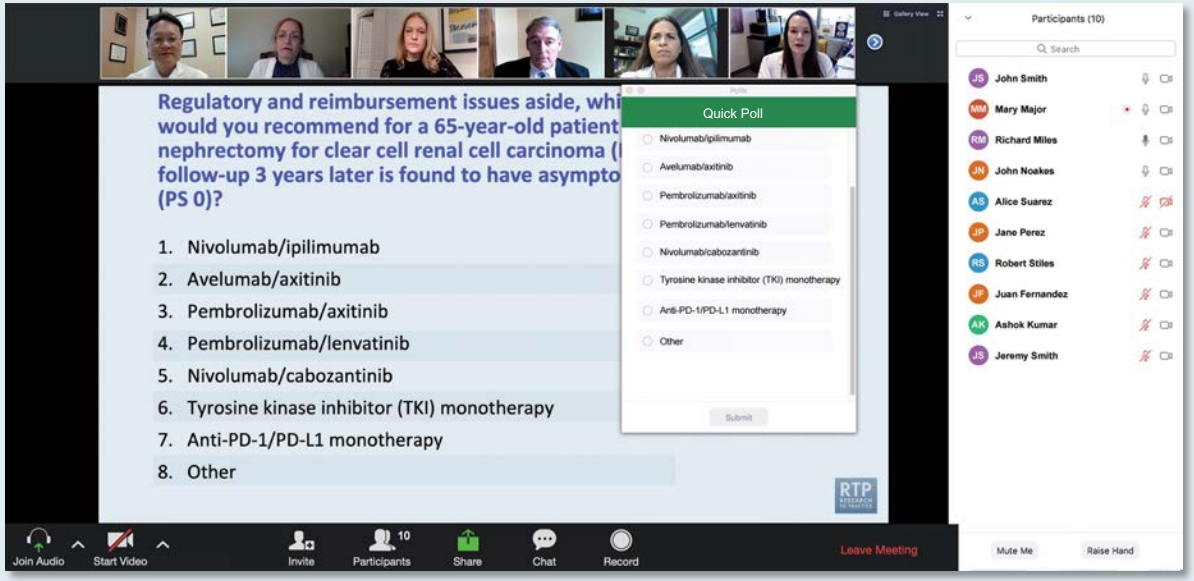
We Encourage Clinicians in Practice to Submit Questions



Feel free to submit questions now before the program begins and throughout the program.

RTP RESEARCH TO PRACTICE

Clinicians in the Audience, Please Complete the Pre- and Postmeeting Surveys



RTP RESEARCH TO PRACTICE

ONCOLOGY TODAY

WITH DR NEIL LOVE

Inside the Issue: Optimizing the Management of Nonmelanoma Skin Cancer

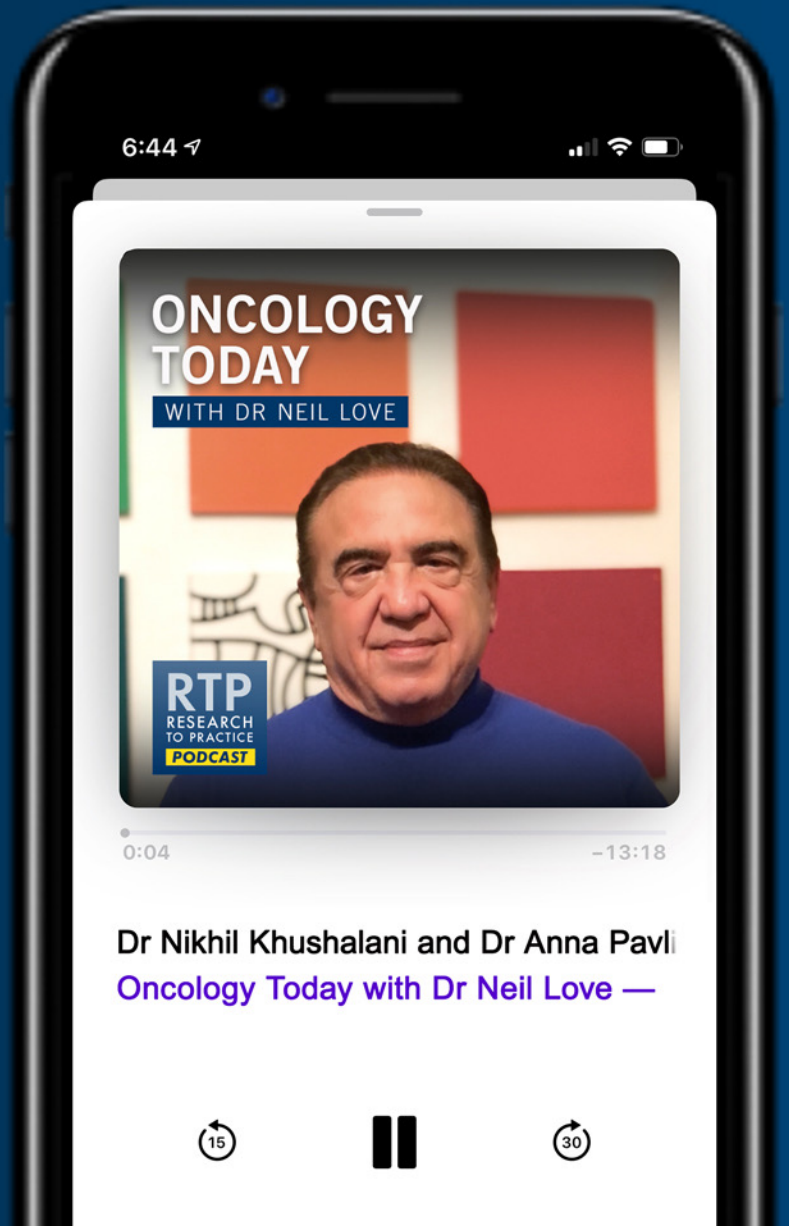
DR NIKHIL KHUSHALANI
MOFFITT CANCER CENTER

DR ANNA PAVLICK
WEILL CORNELL MEDICINE MEYER CANCER CENTER

Listen on Apple Podcasts

Spotify

Listen on Google Podcasts



Oncology Today with Dr Neil Love: Novel Agents and Strategies in Lung Cancer

A CME/MOC-Accredited Live Webinar

Thursday, July 11, 2024
5:00 PM – 6:00 PM ET

Faculty

Melissa Johnson, MD
Ticiana Leal, MD
Manish Patel, MD

Moderator

Neil Love, MD

RTP RESEARCH TO PRACTICE

Inside the Issue: Integrating Antibody-Drug Conjugates into the Management of HR-Positive and Triple-Negative Metastatic Breast Cancer

A CME/MOC-Accredited Live Webinar

Wednesday, July 17, 2024
5:00 PM – 6:00 PM ET

Faculty

Professor Peter Schmid, FRCP, MD, PhD
Sara M Tolaney, MD, MPH

Moderator

Neil Love, MD

RTP RESEARCH TO PRACTICE

Inside the Issue: Integrating ALK-Targeted Therapy into the Management of Localized Non-Small Cell Lung Cancer

A CME/MOC-Accredited Live Webinar

Thursday, July 18, 2024
5:00 PM – 6:00 PM ET

Faculty

Professor Solange Peters, MD, PhD
Professor Ben Solomon, MBBS, PhD

Moderator

Neil Love, MD

RTP
RESEARCH
TO PRACTICE

Inside the Issue: Integrating HER2-Targeted Strategies into the Management of Gastrointestinal Cancers

A CME/MOC-Accredited Live Webinar

Wednesday, August 21, 2024
5:00 PM – 6:00 PM ET

Faculty

Tanios Bekaii-Saab, MD
John Strickler, MD

Moderator

Neil Love, MD

RTP
RESEARCH
TO PRACTICE

Inside the Issue: Optimizing the Diagnosis and Treatment of Neuroendocrine Tumors

A CME/MOC-Accredited Live Webinar

Thursday, August 29, 2024
5:00 PM – 6:00 PM ET

Faculty

Pamela Kunz, MD
Simron Singh, MD, MPH

Moderator

Neil Love, MD

RTP
RESEARCH
TO PRACTICE

Agenda

INTRODUCTION: Johns Hopkins University

MODULE 1: Metastatic Melanoma

MODULE 2: Nonmetastatic Melanoma and Other Skin Cancers

Thank you for joining us!

CME and MOC credit information will be emailed to each participant within 5 business days.

RTP Year in Review 2024

Year in Review: Melanoma and Nonmelanoma Skin Cancers

A CME/MOC-Accredited Live Webinar

Wednesday, July 10, 2024
5:00 PM – 6:00 PM ET

Faculty

Evan J Lipson, MD

Moderator

Neil Love, MD

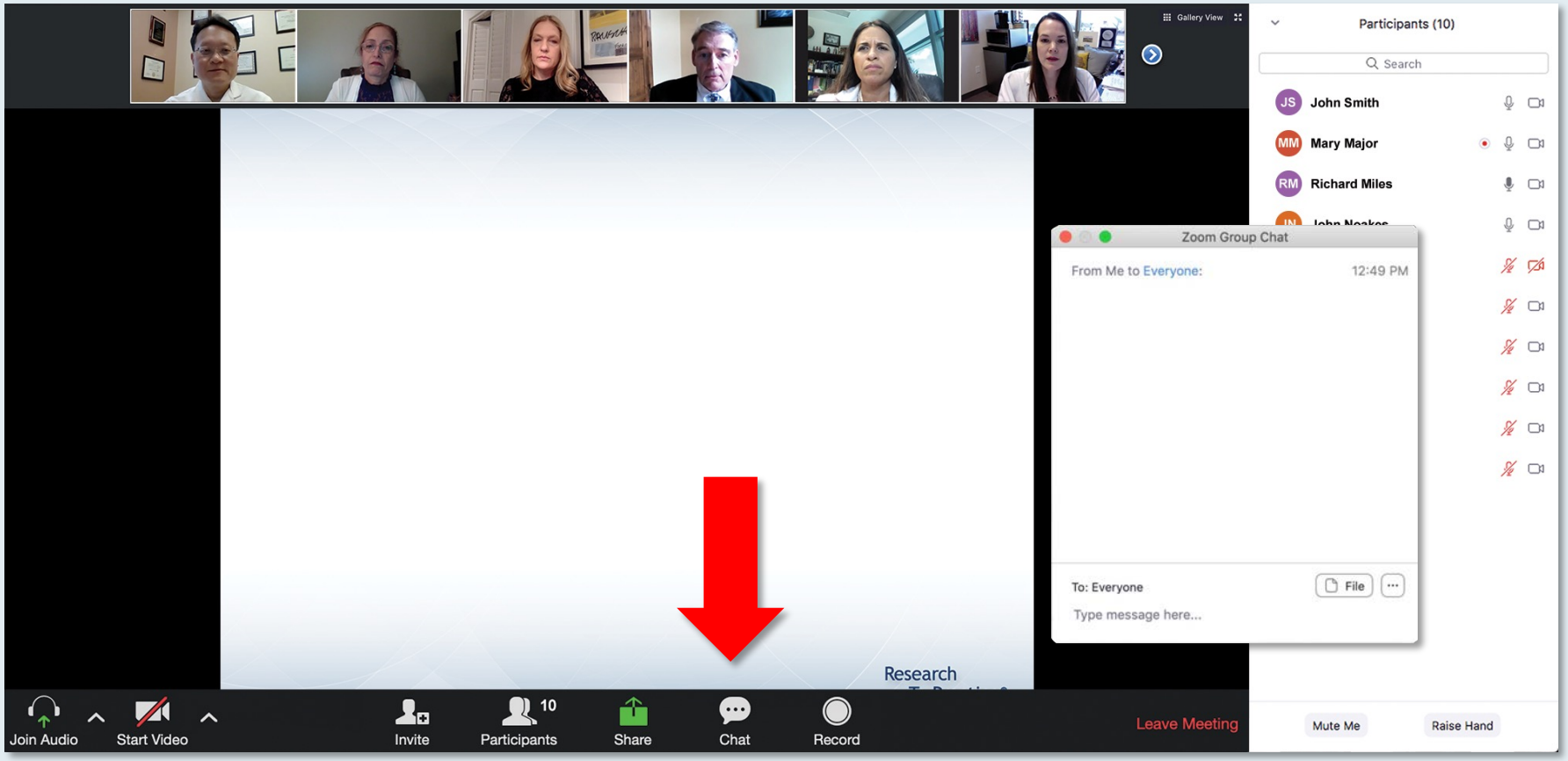
RTP Year in Review 2024

Faculty

Evan J Lipson, MD
Associate Professor, Medical Oncology
Bloomberg-Kimmel Institute
for Cancer Immunotherapy
Johns Hopkins School of Medicine
The Sidney Kimmel Comprehensive Cancer Center
Baltimore, Maryland

MODERATOR
Neil Love, MD
Research To Practice
Miami, Florida

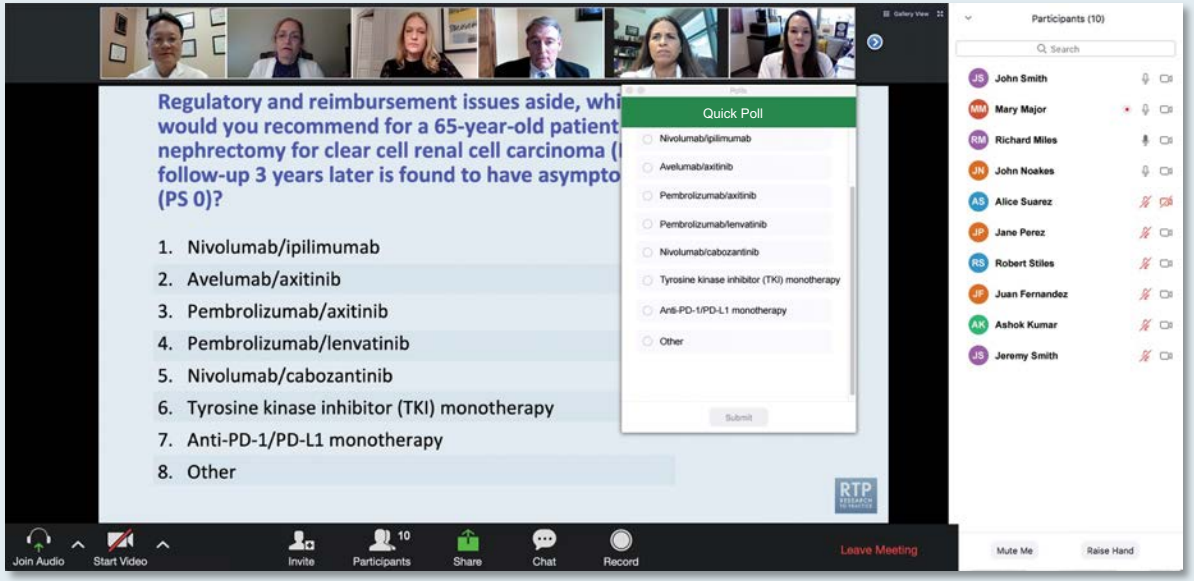
We Encourage Clinicians in Practice to Submit Questions



Feel free to submit questions now before the program begins and throughout the program.

RTP RESEARCH TO PRACTICE

Clinicians in the Audience, Please Complete the Pre- and Postmeeting Surveys



RTP RESEARCH TO PRACTICE

ONCOLOGY TODAY

WITH DR NEIL LOVE

Inside the Issue: Optimizing the Management of Nonmelanoma Skin Cancer

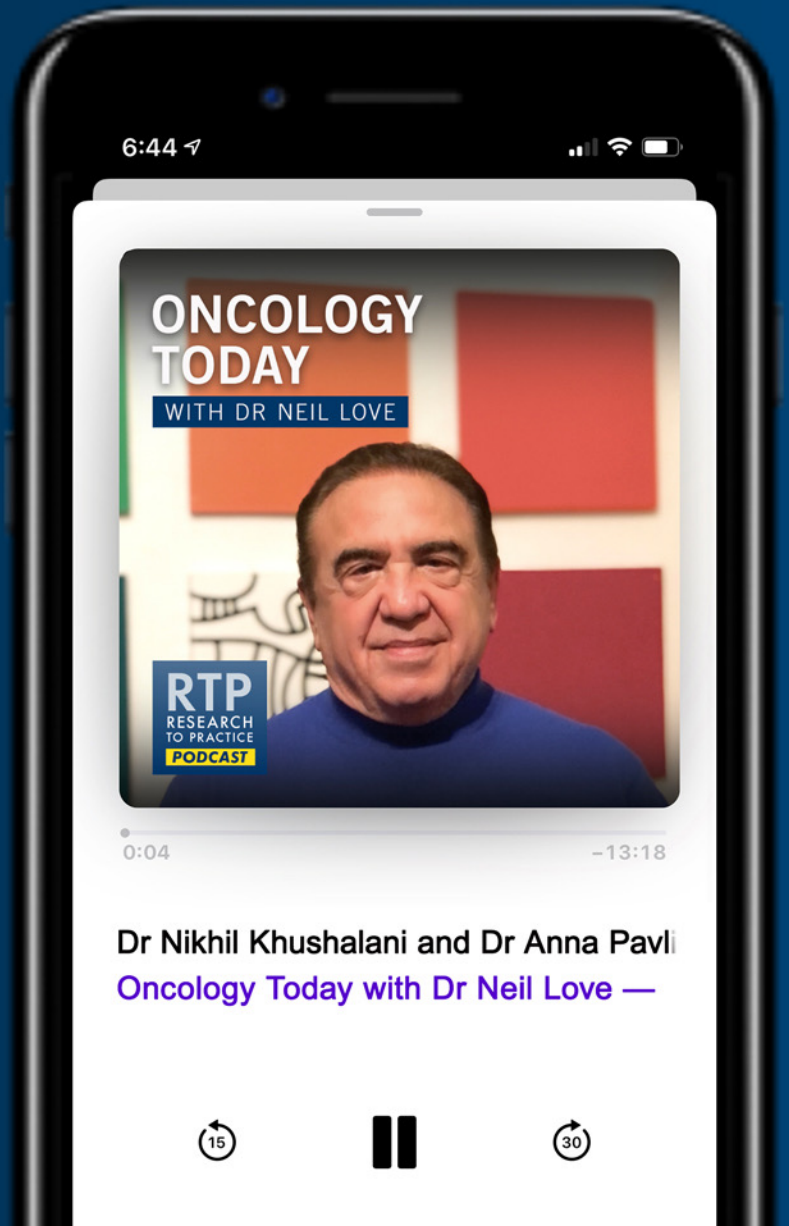
DR NIKHIL KHUSHALANI
MOFFITT CANCER CENTER

DR ANNA PAVLICK
WEILL CORNELL MEDICINE MEYER CANCER CENTER

Listen on Apple Podcasts

Spotify

Listen on Google Podcasts



Oncology Today with Dr Neil Love: Novel Agents and Strategies in Lung Cancer

A CME/MOC-Accredited Live Webinar

Thursday, July 11, 2024
5:00 PM – 6:00 PM ET

Faculty

Melissa Johnson, MD
Ticiana Leal, MD
Manish Patel, MD

Moderator

Neil Love, MD

RTP RESEARCH TO PRACTICE

Inside the Issue: Integrating Antibody-Drug Conjugates into the Management of HR-Positive and Triple-Negative Metastatic Breast Cancer

A CME/MOC-Accredited Live Webinar

Wednesday, July 17, 2024
5:00 PM – 6:00 PM ET

Faculty

Professor Peter Schmid, FRCP, MD, PhD
Sara M Tolaney, MD, MPH

Moderator

Neil Love, MD

RTP RESEARCH TO PRACTICE

Inside the Issue: Integrating ALK-Targeted Therapy into the Management of Localized Non-Small Cell Lung Cancer

A CME/MOC-Accredited Live Webinar

Thursday, July 18, 2024
5:00 PM – 6:00 PM ET

Faculty

Professor Solange Peters, MD, PhD
Professor Ben Solomon, MBBS, PhD

Moderator

Neil Love, MD

RTP
RESEARCH
TO PRACTICE

Inside the Issue: Integrating HER2-Targeted Strategies into the Management of Gastrointestinal Cancers

A CME/MOC-Accredited Live Webinar

Wednesday, August 21, 2024
5:00 PM – 6:00 PM ET

Faculty

Tanios Bekaii-Saab, MD
John Strickler, MD

Moderator

Neil Love, MD

RTP
RESEARCH
TO PRACTICE

Inside the Issue: Optimizing the Diagnosis and Treatment of Neuroendocrine Tumors

A CME/MOC-Accredited Live Webinar

Thursday, August 29, 2024
5:00 PM – 6:00 PM ET

Faculty

Pamela Kunz, MD
Simron Singh, MD, MPH

Moderator

Neil Love, MD

RTP
RESEARCH
TO PRACTICE

Year in Review: Melanoma and Nonmelanoma Skin Cancers

A CME/MOC-Accredited Live Webinar

Wednesday, July 10, 2024
5:00 PM – 6:00 PM ET

Faculty

Evan J Lipson, MD

Moderator

Neil Love, MD

RTP Year in Review 2024

Commercial Support

This activity is supported by an educational grant from Merck.

Research To Practice CME Planning Committee Members, Staff and Reviewers

Planners, scientific staff and independent reviewers for Research To Practice have no relevant conflicts of interest to disclose.

Dr Lipson — Disclosures

Consulting Agreements	Agenus Inc, Bristol Myers Squibb, CareDx, Eisai Inc, Genentech, a member of the Roche Group, HUYA Bioscience International, Immunocore, Instil Bio, Lyvgen Biopharma, Merck, Merck KGaA, Natera Inc, Nektar Therapeutics, Novartis, OncoSec Medical, Pfizer Inc, Rain Oncology, Regeneron Pharmaceuticals Inc, Replimune, Sanofi, Sun Pharmaceutical Industries Limited, Syneos Health
Contracted Research	Bristol Myers Squibb, Haystack Oncology, Merck, Regeneron Pharmaceuticals Inc, Sanofi
Stock Options/Stock — Public Company	Iovance Biotherapeutics (less than $10K)

This educational activity contains discussion of non-FDA-approved uses of agents and regimens. Please refer to official prescribing information for each product for approved indications.

Key Data Sets

- Robert C et al. Seven-Year Follow-Up of the Phase III KEYNOTE-006 Study: **Pembrolizumab Versus Ipilimumab** in Advanced Melanoma. *J Clin Oncol* 2023;41(24):3998-4003.
- Thomas S et al. Efficacy and safety of **lifileucel**, an autologous tumor-infiltrating lymphocyte cell therapy, **and pembrolizumab** in patients with immune checkpoint inhibitor-naive unresectable or metastatic melanoma: Updated results from IOV-COM-202 cohort 1A. ASCO 2024;Abstract 9505.
- Hamid O et al. Significant durable response with **fianlimab (anti-LAG-3) and cemiplimab (anti-PD-1)** in advanced melanoma: Post adjuvant PD-1 analysis. ASCO 2023;Abstract 9501.
- Baramidze et al. A phase 3 trial of **fianlimab (anti–LAG-3) plus cemiplimab (anti-PD-1) versus pembrolizumab** in patients with previously untreated unresectable locally advanced or metastatic melanoma. ASCO 2023;Abstract TPS9602.
- Khushalani et al. A phase 3 trial of fixed dose combinations of **fianlimab (anti-LAG-3) + Cemiplimab (anti–PD-1) versus relatlimab + nivolumab** in patients with unresectable or metastatic melanoma. ASCO 2024;Abstract TPS9611.
- Luke JJ et al. **Pembrolizumab Versus Placebo as Adjuvant Therapy** in Resected Stage IIB or IIC Melanoma: Final Analysis of Distant Metastasis-Free Survival in the Phase III KEYNOTE-716 Study. *J Clin Oncol* 2024;42(14):1619-1624.

Key Data Sets (Continued)

- Patel SP et al. **Neoadjuvant-adjuvant or adjuvant-only pembrolizumab** in advanced melanoma. *N Engl J Med* 2023;388(9):813-23.
- Couselo E et al. **Pembrolizumab** (pembro) for locally advanced (LA) or recurrent/metastatic (R/M) cutaneous squamous cell carcinoma (cSCC): Long-term results of the phase 2 KEYNOTE-629 study. ASCO 2024;Abstract 9554.
- Maubec E et al. Final results of a Phase II study of **pembrolizumab as first-line treatment** in advanced cSCC. ESMO 2023;Abstract 1139P.
- Rapisuwon S et al. Phase II multi-center study of **adjuvant nivolumab in combination with ipilimumab** in patients with high-risk uveal melanoma (HCRN MEL17-309). ASCO 2024;Abstract 9509.
- Hassel JC et al. Three-year overall survival (OS) with **tebentafusp** in metastatic uveal melanoma. *N Engl J Med* 2023;389(24):2256-66.
- Piperno-Neumann et al. Three year survival with **tebentafusp** in previously untreated metastatic uveal melanoma in a phase 3 trial. ESMO 2023;Abstract LBA50.

Key Data Sets (Continued)

- Wermke M et al. Long-term efficacy and patterns of response of **lifileucel** tumor-infiltrating lymphocyte (TIL) cell therapy in patients with advanced melanoma: A 4-year analysis of the C-144-01 study. ESMO IO 2023;Abstract 1190.
- Blank CU et al. **Neoadjuvant nivolumab plus ipilimumab versus adjuvant nivolumab** in macroscopic, resectable stage III melanoma: The phase 3 NADINA trial. ASCO 2024;Abstract LBA2.
- Weber JS et al. Individualized neoantigen therapy **mRNA-4157 (V940) plus pembrolizumab** in resected melanoma: 3-year update from the mRNA-4157-P201 (KEYNOTE-942) trial. ASCO 2024;Abstract LBA9512.
- Tawbi HA et al. **Nivolumab (NIVO) plus relatlimab (RELA) vs NIVO** in previously untreated metastatic or unresectable melanoma (RELATIVITY-047): Overall survival (OS) and melanoma-specific survival (MSS) outcomes at 3 years. ASCO 2024;Abstract 9524.
- Ascierto PA et al. Efficacy and safety of **triplet nivolumab, relatlimab, and ipilimumab** (NIVO + RELA + IPI) in advanced melanoma: Results from RELATIVITY-048. ASCO 2024;Abstract 9504.
- Gross ND et al. **Neoadjuvant cemiplimab** and surgery for stage II-IV cutaneous squamous-cell carcinoma: follow-up and survival outcomes of a single-arm, multicentre, phase 2 study. *Lancet Oncol* 2023;24(11):1196-205.

Key Data Sets (Continued)

- Amaria RN et al. **OBX-115**, an interleukin 2 (IL2)-sparing engineered tumor-infiltrating lymphocyte (TIL) cell therapy, in patients (pts) with immune checkpoint inhibitor (ICI)-resistant unresectable or metastatic melanoma. ASCO 2024;Abstract 9515.
- Hauschild AH et al. Long-term follow up for **adjuvant dabrafenib plus trametinib** in stage III BRAF-mutated melanoma: Final results of the COMBI-AD study. ASCO 2024;Abstract 9500.
- Weber JS et al. Interleukin-6 receptor blockade with **tocilizumab to reduce immune-related toxicity with ipilimumab and nivolumab** in metastatic melanoma. ASCO 2024;Abstract 9538.
- Amaral T et al. Clinical validation of a prognostic **7-marker IHC assay (7-IHC)** in 382 patients (pts) with stage IB/IIA cutaneous melanoma (CM; MELARISK-001). ASCO 2024;Abstract 9572.
- Wong MK et al. Efficacy and safety of **RP1 combined with nivolumab** in patients with anti–PD-1–failed melanoma from the IGNYTE clinical trial. ASCO 2024;Abstract 9517.
- Ladwa R et al. A phase 2 study of de-escalation in resectable, locally advanced cutaneous squamous cell carcinoma (cSCC) with the use of **neoadjuvant pembrolizumab**: De-Squamate. ASCO 2024;Abstract 9514.

Agenda

INTRODUCTION: Johns Hopkins University

MODULE 1: Metastatic Melanoma

MODULE 2: Nonmetastatic Melanoma and Other Skin Cancers

Agenda

INTRODUCTION: Johns Hopkins University

MODULE 1: Metastatic Melanoma

MODULE 2: Nonmetastatic Melanoma and Other Skin Cancers

Bloomberg's $1 billion gift provides free tuition to Johns Hopkins medical students

BY SHERI WALSH *U.S. NEWS - UPI.COM*
UPDATED JULY 08, 2024 11:34 PM

Former mayor of New York City, Michael Bloomberg, donated $1 billion to Johns Hopkins University, which will provide free tuition to a majority of medical students and "reduce the financial barriers to these essential fields." File Pool Photo by Shannon Stapleton/UPI *upi*

Miami Herald
July 8, 2024

Agenda

INTRODUCTION: Johns Hopkins University

MODULE 1: Metastatic Melanoma

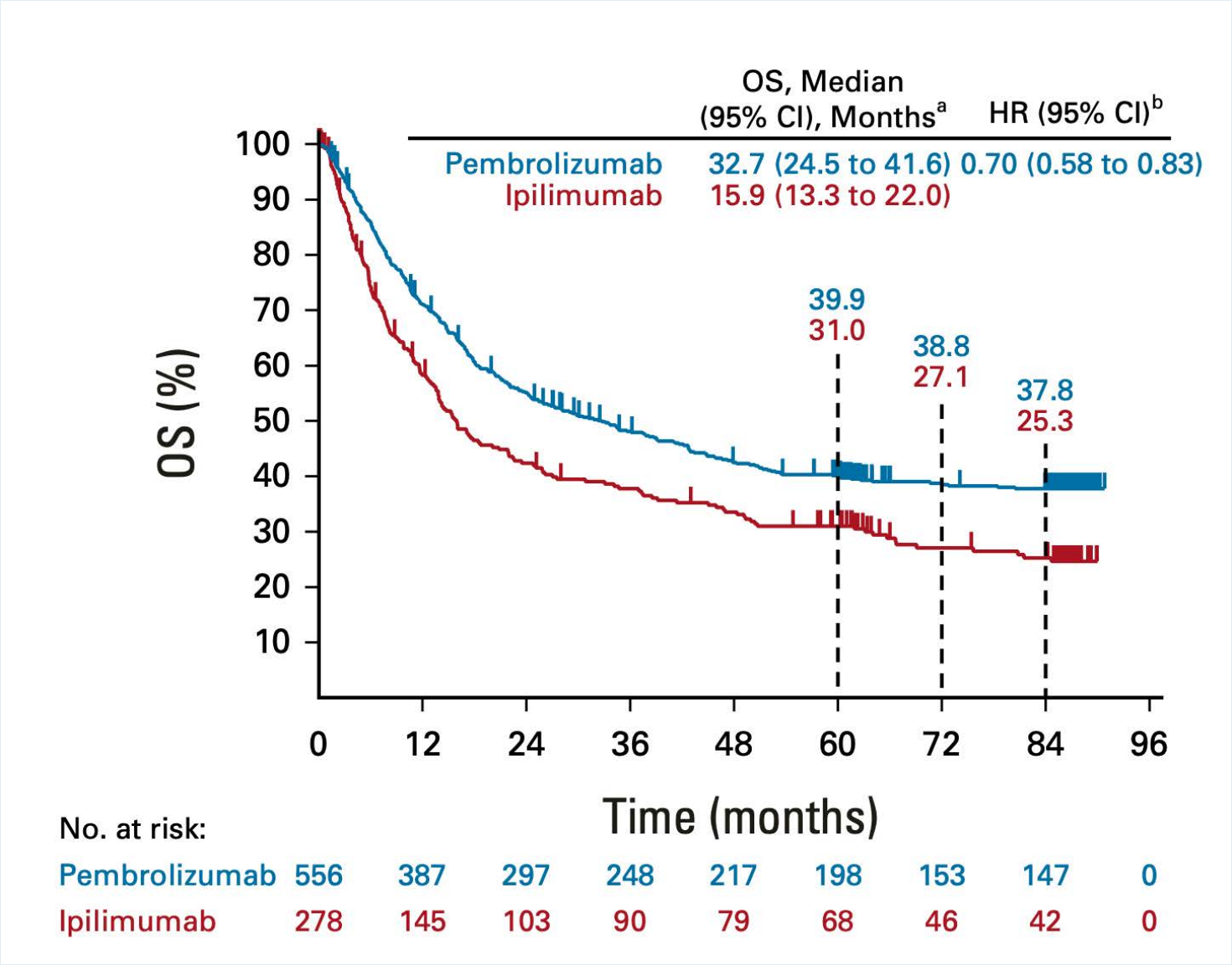
MODULE 2: Nonmetastatic Melanoma and Other Skin Cancers

Seven-Year Follow-Up of the Phase III KEYNOTE-006 Study: Pembrolizumab Versus Ipilimumab in Advanced Melanoma

Caroline Robert, MD, PhD[1]; Matteo S. Carlino, PhD, MBBS[2]; Catriona McNeil, MBBS, PhD[3]; Antoni Ribas, MD, PhD[4]; Jean-Jacques Grob, MD[5]; Jacob Schachter, MD[6]; Marta Nyakas, MD[7]; Damien Kee, DMedSc, MBBS[8]; Teresa M. Petrella, MD[9]; Arnold Blaustein, MD[10]; Michal Lotem, MD[11]; Ana Arance, MD, PhD[12]; Adil I. Daud, MD[13]; Omid Hamid, MD[14]; James Larkin, PhD[15]; James Anderson, PhD[16]; Clemens Krepler, MD[16]; Dmitri Grebennik, MD[16]; and Georgina V. Long, PhD, MBBS[17]

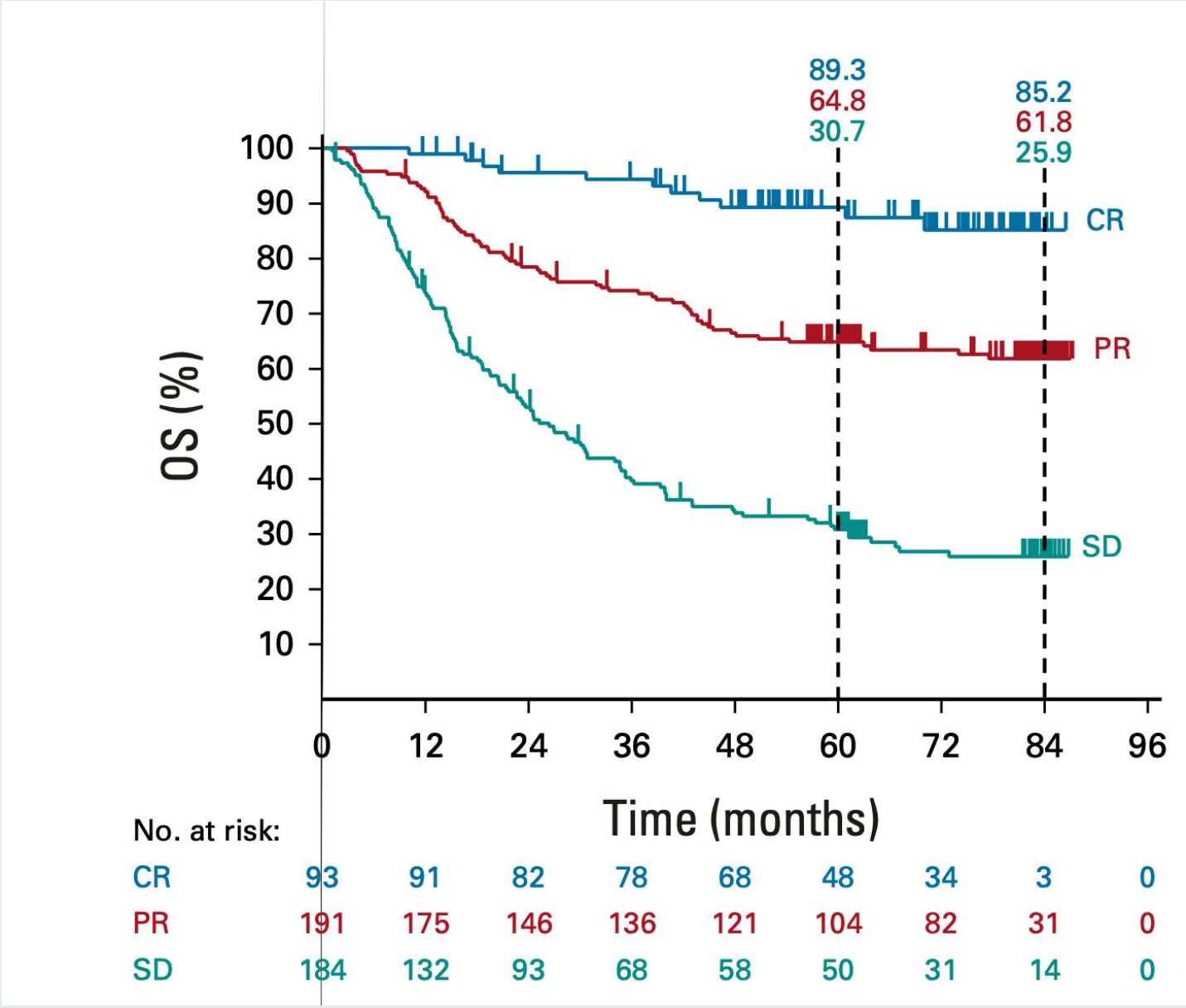
J Clin Oncol 2023;41(24):3998-4003.

KEYNOTE-006: Pembrolizumab versus Ipilimumab – Long-Term Overall Survival (OS)



Robert C et al. *J Clin Oncol* 2023;41(24):3998-4003.

KEYNOTE-006: Pembrolizumab versus Ipilimumab – OS by Response



CR = complete response; PR = partial response; SD = stable disease

Robert C et al. *J Clin Oncol* 2023;41(24):3998-4003.

2024 ASCO ANNUAL MEETING

Nivolumab plus relatlimab vs nivolumab in previously untreated metastatic or unresectable melanoma (RELATIVITY-047): Overall survival and melanoma-specific survival outcomes at 3 years

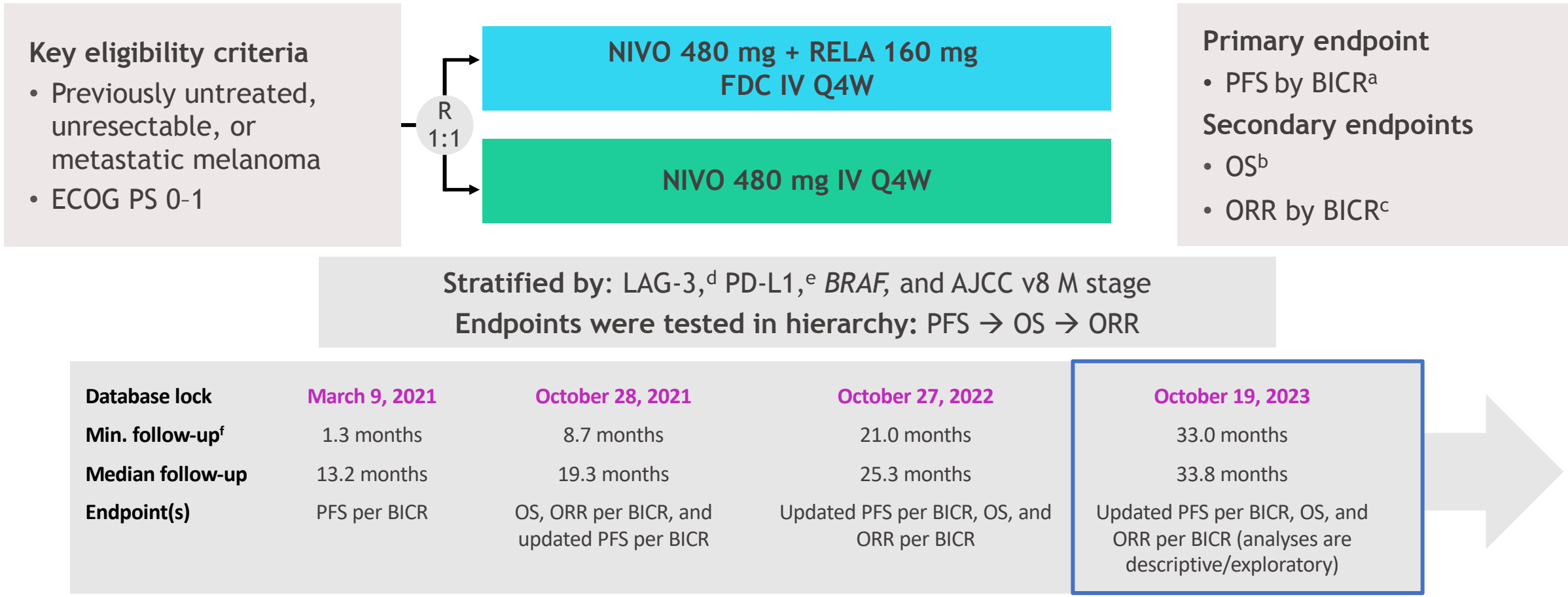
Hussein A. Tawbi,[1] F. Stephen Hodi,[2] Evan J. Lipson,[3] Dirk Schadendorf,[4] Paolo Antonio Ascierto,[5] Luis Matamala,[6] Erika Castillo Gutiérrez,[7] Piotr Rutkowski,[8] Helen Gogas,[9] Christopher D. Lao,[10] Juliana Janoski De Menezes,[11] Stéphane Dalle,[12] Ana Maria Arance,[13] Jean-Jacques Grob,[14] Barbara Ratto,[15] Saima Rodriguez,[15] Antonella Mazzei,[15] Sonia Dolfi,[15] Georgina V. Long[16]

[1]The University of Texas MD Anderson Cancer Center, Houston, TX; [2]Dana-Farber Cancer Institute, Boston, MA; [3]Bloomberg-Kimmel Institute for Cancer Immunotherapy, Johns Hopkins Medicine, The Sidney Kimmel Comprehensive Cancer Center, Baltimore, MD; [4]University of Essen and the German Cancer Consortium, Essen, Germany; [5]Istituto Nazionale dei Tumori IRCCS "Fondazione G. Pascale", Naples, Italy; [6]Instituto Oncológico Fundación Arturo López Pérez and Department of Oncology, Instituto Nacional del Cáncer, Santiago, Chile; [7]FAICIC Clinical Research, Veracruz, Mexico; [8]Maria Skłodowska-Curie National Research Institute of Oncology, Warsaw, Poland; [9]National and Kapodistrian University of Athens, Athens, Greece; [10]Michigan Medicine, Rogel Cancer Center, University of Michigan (current affiliation is Bristol Myers Squibb), Ann Arbor, MI; [11]Hospital Nossa Senhora da Conceição, Porto Alegre, Brazil; [12]Hospices Civils de Lyon, Cancer Research Center of Lyon, Pierre-Bénite, France; [13]Hospital Clinic Barcelona and IDIBAPS, Barcelona, Spain; [14]Aix-Marseille University, CHU Timone, Marseille, France; [15]Bristol Myers Squibb, Princeton, NJ; [16]Melanoma Institute Australia, The University of Sydney, Royal North Shore and Mater Hospitals, Sydney, NSW, Australia

Presentation number 9524

Courtesy of Evan J Lipson, MD

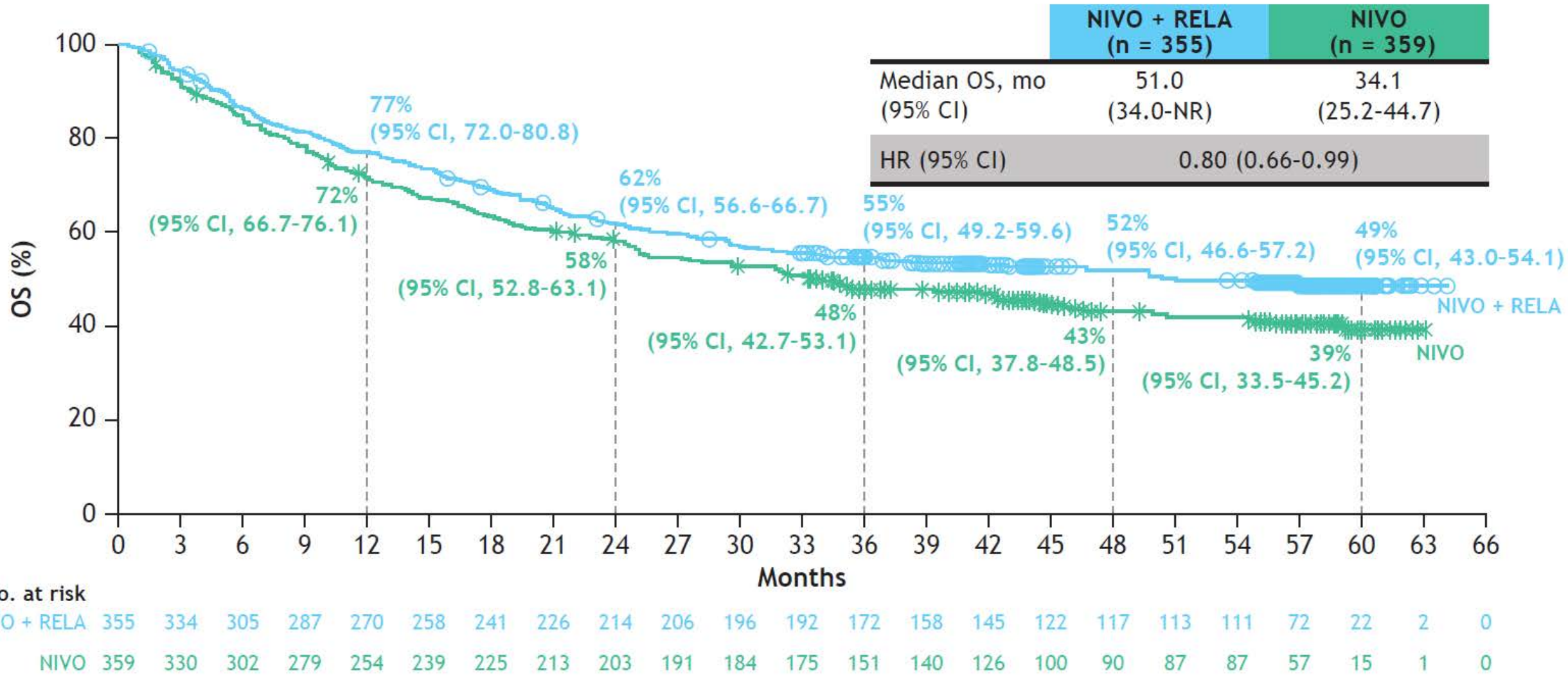
Figure 1. RELATIVITY-047 study design



Database lock	March 9, 2021	October 28, 2021	October 27, 2022	October 19, 2023
Min. follow-up[f]	1.3 months	8.7 months	21.0 months	33.0 months
Median follow-up	13.2 months	19.3 months	25.3 months	33.8 months
Endpoint(s)	PFS per BICR	OS, ORR per BICR, and updated PFS per BICR	Updated PFS per BICR, OS, and ORR per BICR	Updated PFS per BICR, OS, and ORR per BICR (analyses are descriptive/exploratory)

RELATIVITY-047 (NCT03470922).
[a]First tumor assessment (RECIST v1.1) was performed 12 weeks after randomization, every 8 weeks up to 52 weeks, and then every 12 weeks. [b]OS boundary for statistical significance was $P < 0.04302$ (2-sided) analyzed at 69% power; target HR, 0.75. [c]ORR could not be formally tested and was descriptively analyzed. [d]LAG-3 expression on immune cells (1%) was determined by an analytically validated IHC assay (Labcorp, Burlington, NC, USA). [e]PD-L1 expression on tumor cells (1%) was determined by a validated Agilent Dako PD-L1 IHC 28-8 pharmDx test (Agilent, Santa Clara, CA, USA). [f]Minimum potential follow-up was defined as the time from last patient randomized to last patient, last visit.

Courtesy of Evan J Lipson, MD



Descriptive analysis. Statistical model for HR: stratified Cox proportional hazards model. Stratified by LAG-3, *BRAF* mutation status, and AJCC M stage. PD-L1 was removed from stratification because it led to subgroups with < 10 patients. NR, not reached.

Courtesy of Evan J Lipson, MD

Conclusions

- **<u>Critical finding(s)</u>: At 3 years of follow-up, PFS benefit persists for patients with previously untreated metastatic or unresectable melanoma who were treated with NIVO + RELA vs NIVO.**
  - **Descriptive analyses suggest melanoma-specific survival benefit (MSS HR 0.75 (95% CI, 0.60–0.94))**
  - **No new or unexpected safety signals**

- **<u>Clinical implication(s)</u>: RELA+NIVO has replaced single agent anti-PD-1 as standard-of-care for treating many patients with advanced melanoma**

- **<u>Research relevance</u>: Biomarkers needed to better understand which patient needs which therapy.**

Courtesy of Evan J Lipson, MD

2024 ASCO® ANNUAL MEETING

Efficacy and safety of triplet nivolumab, relatlimab, and ipilimumab in advanced melanoma: results from RELATIVITY-048

Paolo Antonio Ascierto,[1] Reinhard Dummer,[2] Caroline Gaudy-Marqueste,[3] Samantha Bowyer,[4] Evan J. Lipson,[5] Eleonora Ghisoni,[6] Mark R. Middleton,[7] Barbara Ratto,[8a] William Joseph Jackson,[8] Alicia M. Y. Cheong,[9] Sourav Mukherjee,[8] Jenny Wu,[8] Georgina V. Long[10]

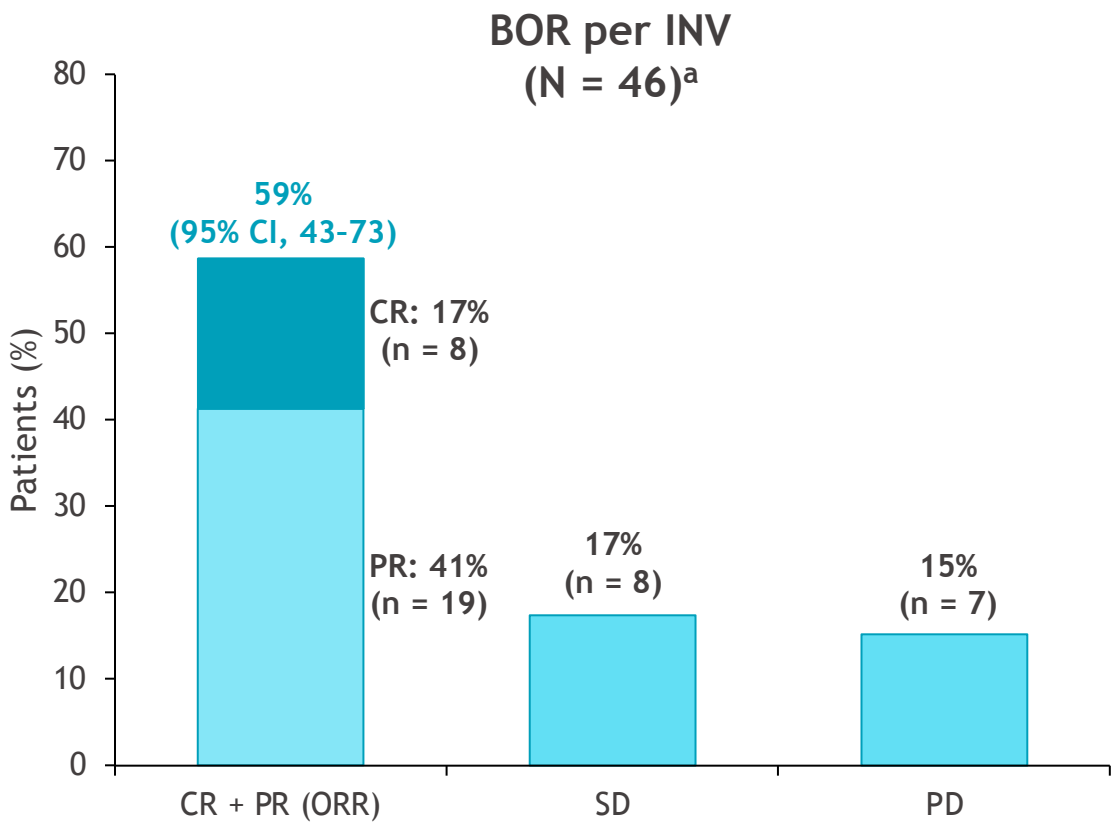
[1]Istituto Nazionale Tumori IRCCS "Fondazione G. Pascale," Naples, Italy; [2]University of Zurich, Zurich, Switzerland; [3]CEPCM, Aix-Marseille University, Assistance Publique-Hôpitaux de Marseille, Marseille, France; [4]Linear Clinical Research, Nedlands, WA, Australia; [5]The Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins Medicine, Baltimore, MD; [6]Lausanne University Hospital, and Ludwig Institute for Cancer Research, Lausanne, Switzerland; [7]University of Oxford, Headington, Oxford, United Kingdom; [8]Bristol Myers Squibb, Princeton, NJ; [9]Bristol Myers Squibb, Uxbridge, UK; [10]Melanoma Institute Australia, The University of Sydney, and Royal North Shore and Mater Hospitals, Sydney, NSW, Australia

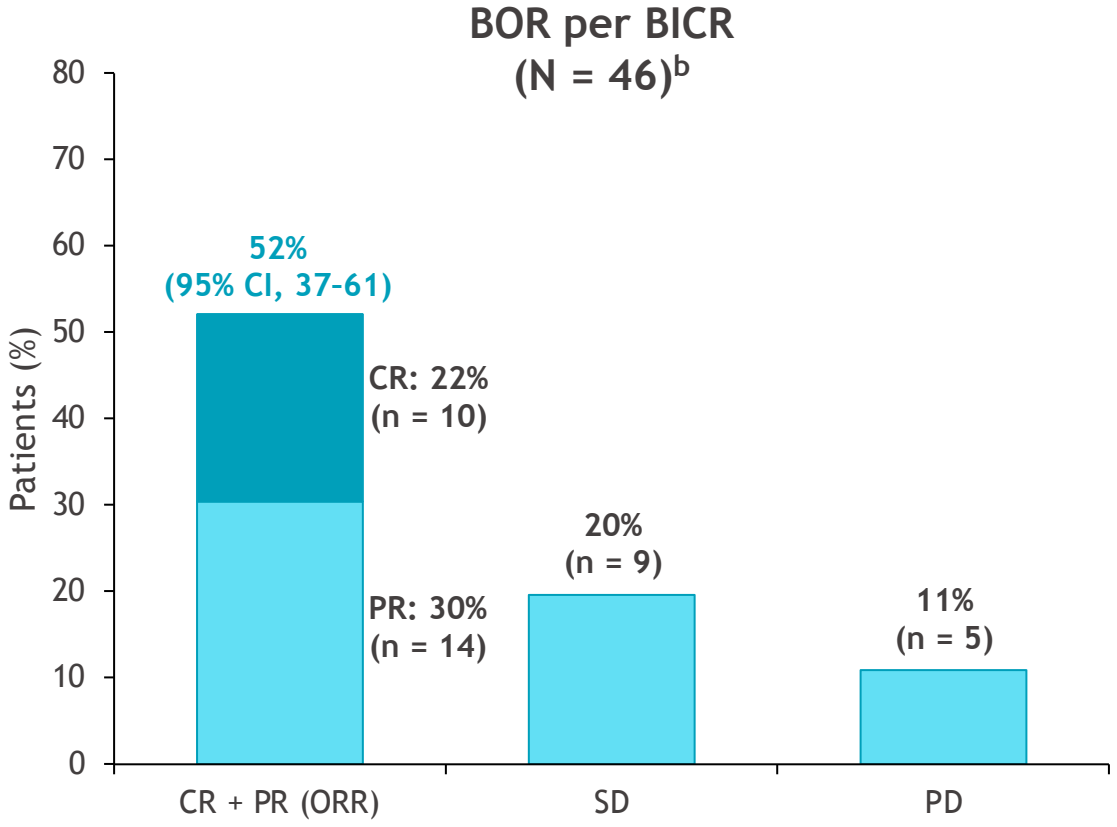
[a]Affiliation at the time the study was conducted.

Abstract number 9504

Courtesy of Evan J Lipson, MD

BOR per INV (primary endpoint) and BICR (exploratory endpoint)



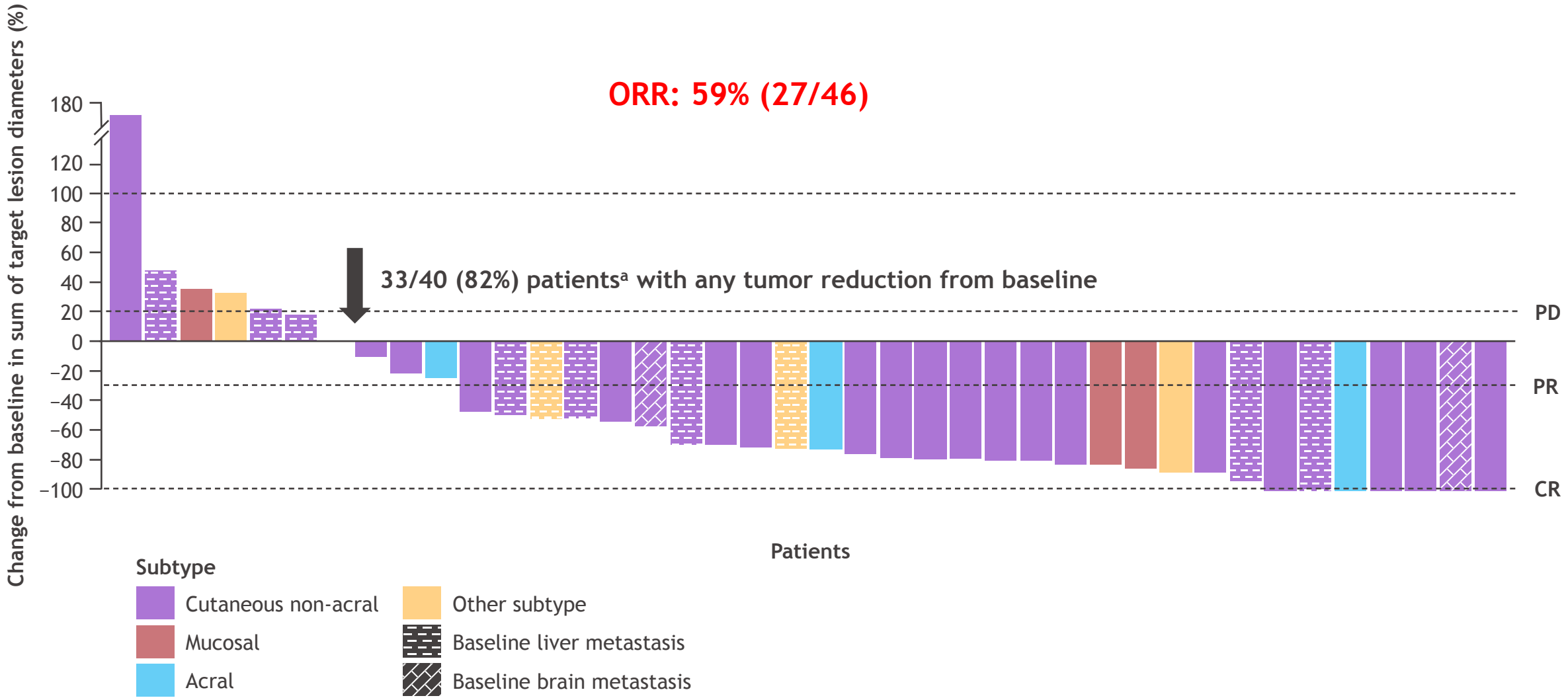


- Clinical benefit (CR + PR + SD) rate of 76% (95% CI, 61–87) per INV and 72% (95% CI, 56–84) per BICR
- Median duration of response per INV: NR (95% CI, NR–NR)

RELATIVITY-048 (NCT03459222). Median follow-up: 49.4 months. ORR determined using RECIST v1.1. [a]Undetermined in 4 patients (9%; due to death prior to the first post-baseline tumor assessment). [b]Undetermined in 8 patients (17%; 4 due to death prior to first post-baseline assessment, 2 due to no measurable disease at baseline per BICR, and 2 due to receiving palliative surgery before first post-baseline tumor assessment).

Courtesy of Evan J Lipson, MD

Best change from baseline in sum of target lesions per INV



RELATIVITY-048 (NCT03459222). Median follow-up: 49.4 months. [a]Included patients with both baseline and ≥ 1 post-baseline assessment of target lesions. Total of 6 patients not included (4 patients were nonevaluable due to death prior to first post-baseline tumor assessment and 2 patients receiving palliative subsequent surgery before the first post-baseline tumor assessment).

Courtesy of Evan J Lipson, MD

Safety summary

	NIVO + RELA + IPI (N = 46)	
	Any grade, n (%)	Grade 3-4, n (%)
Any AE	46 (100)	27 (59)
Any SAE	27 (59)	17 (37)
TRAE	44 (96)	18 (39)
TRAE leading to discontinuation	19 (41)	10 (22)
Most common TRAEs (≥ 20%)[a]		
Pruritus	16 (35)	0
Fatigue	14 (30)	0
Hypothyroidism	11 (24)	0
Asthenia	10 (22)	0
Colitis	10 (22)	2 (4)
Diarrhea	10 (22)	2 (4)
Lipase increased	10 (22)	6 (13)
Vitiligo	10 (22)	0
Deaths due to TRAEs	2 (4)	

- Treatment-related deaths occurring within 100 days of the last dose of study therapy were due to rectal hemorrhage and dyspnea (n = 1) and immune-mediated myositis (n = 1)

RELATIVITY-048 (NCT03459222). Median follow-up: 49.4 months. Includes AEs reported between first dose and 30 days after the last dose of study therapy.
[a]TRAEs occurring in < 20% of patients are not shown.

Courtesy of Evan J Lipson, MD

Conclusions

- **<u>Critical finding(s)</u>: NIVO + RELA + low-dose IPI demonstrated encouraging efficacy (ORR = 59%) in n= 46 patients with advanced treatment-naïve melanoma. Serious tox rate = 39%.**

- **<u>Clinical implication(s)</u>: Appropriate for patients in whom a single opportunity for therapy might exist?**

- **<u>Research relevance</u>: Larger studies are needed to confirm the efficacy and safety of PD-1+LAG-3+CTLA-4 blockade in this patient population.**

Courtesy of Evan J Lipson, MD

2024 ASCO ANNUAL MEETING

EFFICACY AND SAFETY OF RP1 COMBINED WITH NIVOLUMAB IN PATIENTS WITH ANTI–PD-1–FAILED MELANOMA FROM THE IGNYTE CLINICAL TRIAL

Michael K. Wong, Joseph J. Sacco, Caroline Robert, Judith Michels, Tawnya L. Bowles, Gino K. In, Katy K. Tsai, Céleste Lebbé, Caroline Gaudy-Marqueste, Eva Muñoz-Couselo, Mark R. Middleton, Adel Samson, Dirk Schadendorf, Georgia M. Beasley, Jiaxin Niu, Bartosz Chmielowski, Trisha M. Wise-Draper, Junhong Zhu, Marcus Viana, Mohammed M. Milhem

Dr. Michael K. Wong, MD, PhD, FRCPC

The University of Texas MD Anderson Cancer Center, Houston, TX, USA

Courtesy of Evan J Lipson, MD

Key takeaways

Clinical relevance

- Treatment of melanoma patients after progression on an anti-PD-1 containing regimen remains a considerable unmet need

IGNYTE data analysis by investigator review

- **Efficacy**
  - RP1 combined with nivolumab provides deep and durable responses in patients with advanced melanoma who had **confirmed disease progression, while on prior anti–PD-1** therapy for at least 8 weeks, including in combination with anti-CTLA-4
  - The **ORR** was **33%**, with a median **duration of response of >36 months** (N=156)
- **Safety**
  - The treatment showed a **favorable safety profile** with generally 'on target' and transient grade 1–2 side effects indicative of systemic immune activation

Courtesy of Evan J Lipson, MD

Efficacy

- The data presented today is the *investigator assessed data with all patients having at least 12 months follow up*
  - Centrally reviewed, primary endpoint data, will be presented separately once available

	All patients enrolled in IGNYTE						
BOR n (%)	All patients (n = 156)	Prior single-agent anti–PD-1 (n = 82)	Prior anti–PD-1/CTLA-4 Exposure (n = 74)[a]	Stage IIIb-IVM1a (n = 75)	Stage IVM1b-d (n = 81)	1° resistance to anti–PD-1 (n = 105)	2° resistance to anti–PD-1 (n = 51)[b]
CR	23 (14.7)	18 (22.0)	5 (6.8)	18 (24.0)	5 (6.2)	18 (17.1)	5 (9.8)
PR	28 (17.9)	13 (15.9)	15 (20.3)	13 (17.3)	15 (18.5)	18 (17.1)	10 (19.6)
SD	34 (21.8)	18 (22.0)	16 (21.6)	19 (25.3)	15 (18.5)	17 (16.2)	17 (33.3)
PD	63 (40.4)	31 (37.8)	32 (43.2)	24 (32.0)	39 (48.1)	47 (44.8)	16 (31.4)
ORR	**51 (32.7[c])**	**31 (37.8)**	**20 (27.0)**	**31 (41.3)**	**20 (24.7)**	**36 (34.3)**	**15 (29.4)**

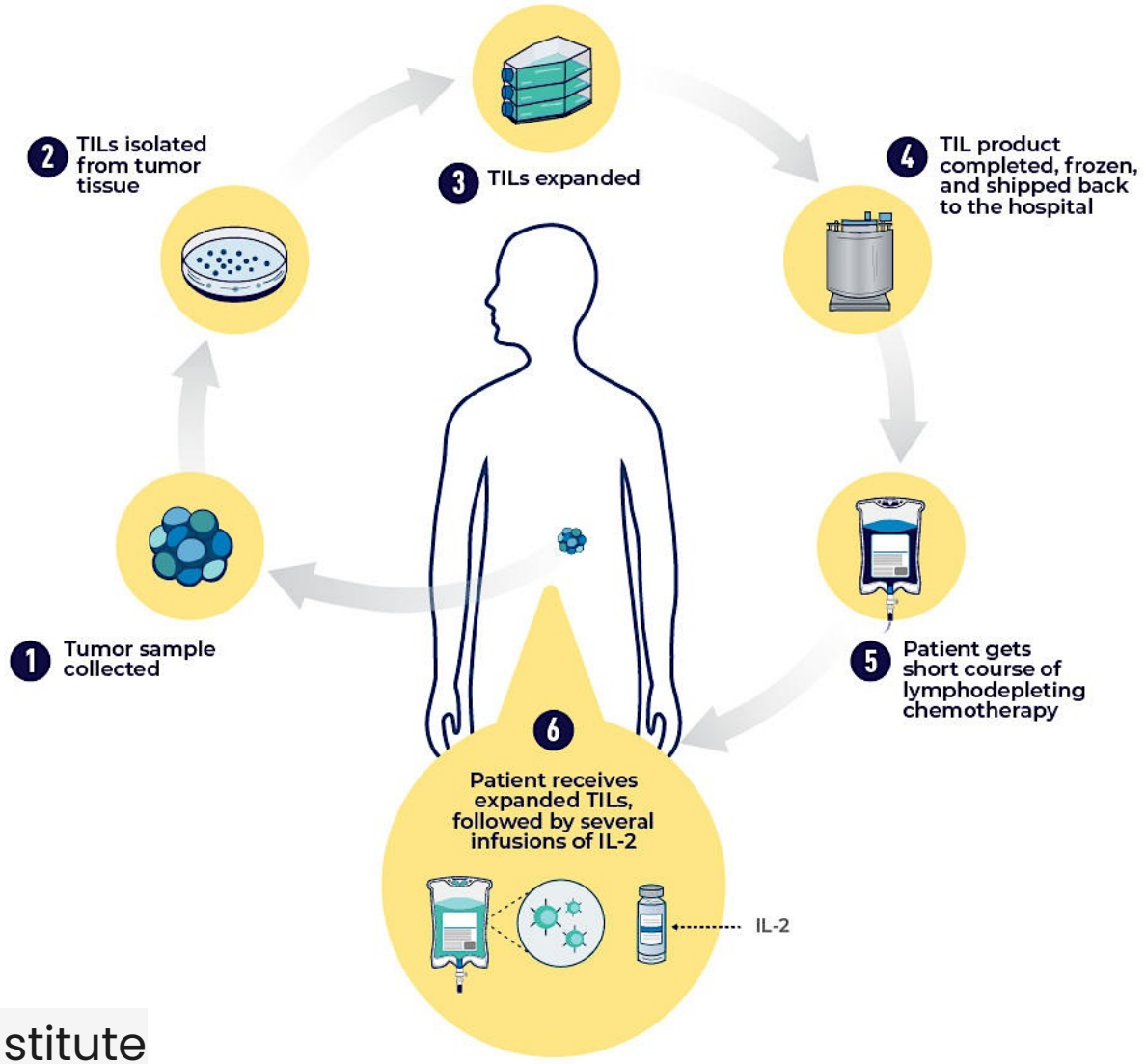
[a]Eight patients were treated with sequential anti-CTLA-4 and anti-PD-1 (ORR for prior combined anti-CTLA-4/anti-PD-1 was 25.8%). [b]Includes one patient with unknown resistance status.
[c]ORR for the 140 registration intended cohort was 32.1%

- Approximately 1 in 3 patients achieved an objective response (32.7%)
- Consistent ORR across subgroups, including:
  - 27% ORR in patients who had prior anti–PD-1 & anti–CTLA-4
  - 34% ORR in patients who are primary resistant to their prior anti-PD-1 therapy

Data cutoff: March 8th 2024. BOR, best overall response; CR, complete response; CTLA-4, cytotoxic T-lymphocyte antigen 4; PD-1, programmed cell death protein 1; PD, progressive disease; PR, partial response; ORR, objective response rate; SD, stable disease.

Courtesy of Evan J Lipson, MD

Tumor Infiltrating Lymphocyte (TIL) therapy



Credit: National Cancer Institute

Courtesy of Evan J Lipson, MD

Lifileucel FDA accelerated approved Feb 2024 for:

- Adult patients with unresectable or metastatic melanoma
- Prior anti-PD-1 (and BRAF-directed therapy if BRAF V600 positive)

Courtesy of Evan J Lipson, MD

BASELINE PATIENT AND DISEASE CHARACTERISTICS

Most patients with advanced melanoma were heavily pretreated

Characteristic	Total (N=153)
Median age, years (range)	56 (20, 79)
PD-L1 Tumor Proportion Score,[a] n (%)	
≥1%	76 (49.7)
<1%	32 (20.9)
Liver and/or brain lesions by IRC, n (%)	72 (47.1)
Median target lesions SOD, mm (range)	101.1 (13.5, 552.9)
Baseline lesions in ≥3 anatomic sites, n (%)	109 (71.2)
>3 baseline target and nontarget lesions, n (%)	116 (75.8)
LDH, n (%)	
≤ULN	70 (45.8)
1–2 × ULN	54 (35.3)
>2 × ULN	29 (19.0)
Median number of prior therapies (range)	3 (1, 9)
Primary resistance to prior anti–PD-1/PD-L1 per SITC criteria,[b] n (%)	109 (71.2)

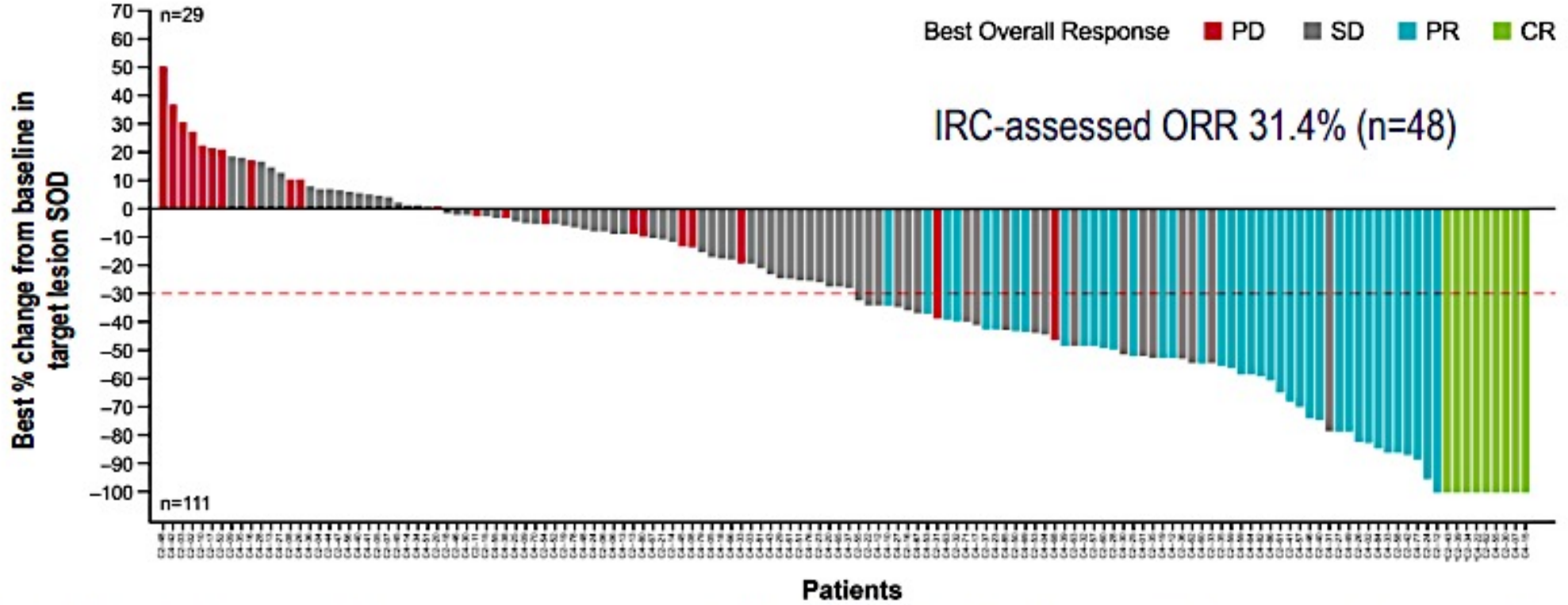
Data cut-off: June 30, 2023; median study follow-up of 48.1 months

[a]45 patients had missing PD-L1 status. [b]Includes primary resistance to prior anti–PD-1/PD-L1 in metastatic setting and primary resistance/early relapse to prior anti–PD-1/PD-L1 in adjuvant setting.
IRC, independent review committee; LDH, lactate dehydrogenase; PD-1, programmed cell death protein-1; PD-L1, programmed death-ligand 1; SITC, Society for Immunotherapy of Cancer; SOD, sum of diameters; ULN, upper limit of normal.

Courtesy of Evan J Lipson, MD

TUMOR BURDEN REDUCTION AND BEST RESPONSE TO LIFILEUCEL

Most patients had a reduction from baseline in tumor burden



13 patients in the Full Analysis Set are not included (best overall responses included not evaluable [n=6], non-CR/non-PD [n=1], and PD [n=6]) for reasons including no acceptable target lesions or no post-lifileucel target lesion SOD measurements.

[a]−100% change from baseline is presented for CR assessment that includes lymph node lesions.

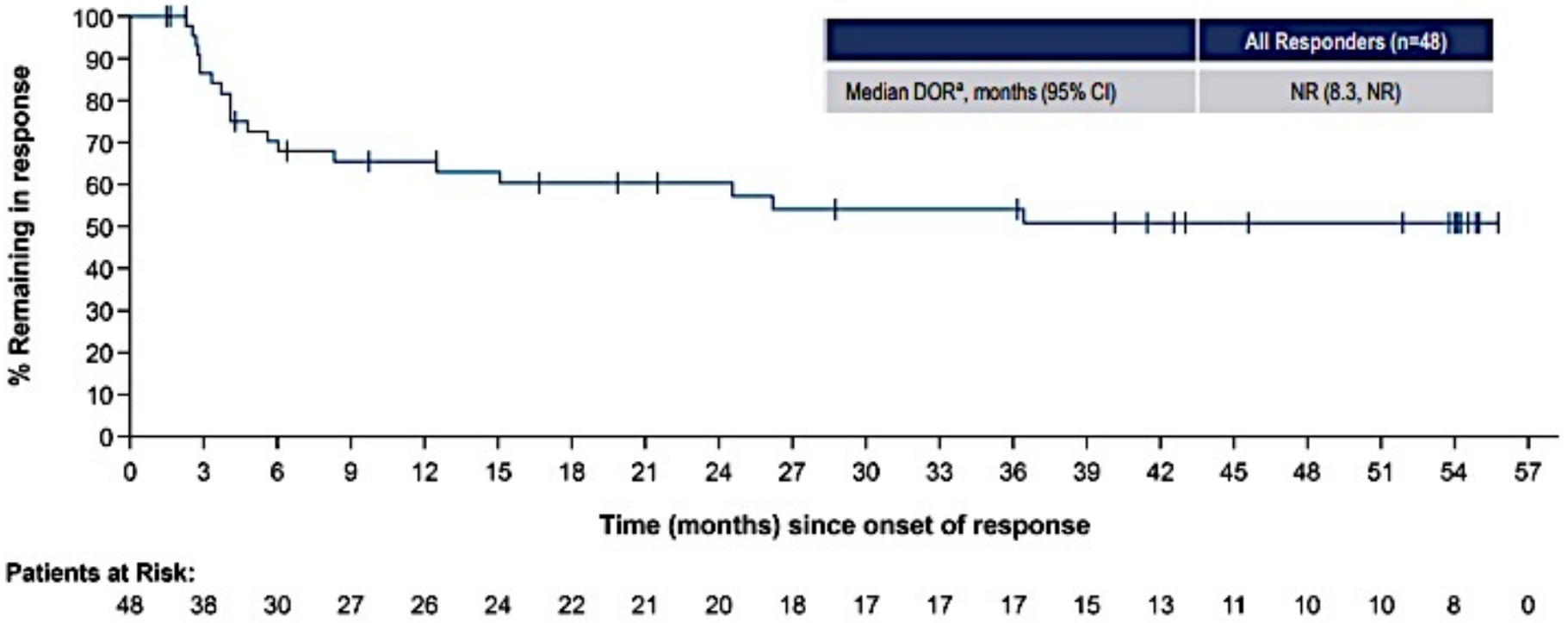
CR, complete response; IRC, independent review committee; ORR, objective response rate; PD, progressive disease; PR, partial response; SD, stable disease; SOD, sum of diameters.

Presenter: Martin Wermke

Courtesy of Evan J Lipson, MD

DURATION OF RESPONSE

Lifileucel demonstrated clinically meaningful antitumor activity with durable responses



DOR by Patterns of Response

	Early Responder[b] (n=39)	Late Responders[c] (n=9)	Responders With Deepened Response[d] (n=16)	Responders Without Deepened Response (n=32)	All Responders (n=48)
Median DOR, months (95% CI)	NR (6.1, NR)	19.8 (4.1, NR)	NR (8.3, NR)	26.2 (4.1, NR)	NR (8.3, NR)

[a]Based on Kaplan-Meier estimates. [b]Patients with CR or PR on Day 42 visit. [c]Patients with CR or PR after Day 42 visit. [d]Patients who had SD and improved to confirmed PR or had PR and improved to confirmed CR.
CI, confidence interval; CR, complete response; DOR, duration of response; NR, not reached; PR, partial response; SD, stable disease.

2023 ESMO IMMUNO-ONCOLOGY

Presenter: Martin Wermke

Courtesy of Evan J Lipson, MD

Safety

- Boxed Warning:
  - treatment-related mortality
  - prolonged severe cytopenia
  - severe infection
  - cardiopulmonary, renal impairment
- Most common AEs: chills, pyrexia, fatigue, tachycardia, diarrhea, febrile neutropenia, edema, rash hypotension, alopecia, infection, hypoxia, and dyspnea.

Courtesy of Evan J Lipson, MD

Conclusions

- **Critical finding(s): After decades of development, a TIL therapy is now FDA approved for patients with advanced melanoma.**

- **Clinical implication(s): Additional treatment option after ICI (+/- BRAF) for appropriate patients**

- **Research relevance: How best to maximize applicability / tolerability?**

Courtesy of Evan J Lipson, MD

2024 ASCO Annual Meeting
May 31–June 4, 2024 | Chicago, IL, USA

Efficacy and safety of lifileucel, an autologous tumor-infiltrating lymphocyte cell therapy, and pembrolizumab in patients with immune checkpoint inhibitor-naive unresectable or metastatic melanoma: updated results from IOV-COM-202 Cohort 1A

Sajeve Thomas,[1] Helen Gogas,[2] Young Ki Hong,[3] Gino K. In,[4] Bernard Doger de Speville Uribe,[5] Andrew J.S. Furness,[6] Almudena Garcia Castano,[7] Simon Häfliger,[8] Kai He,[9] Theresa Medina,[10] Donald Lawrence,[11] Sylvia Lee,[12] Juan Martin-Liberal,[13] Friedrich Graf Finckenstein,[14] Brian Gastman,[14] Jeffrey Chou,[14] Rana Fiaz,[14] Melissa Catlett,[14] Guang Chen,[14] Patrick Terheyden[15]

[1]Orlando Health Cancer Institute, Orlando, FL, USA; [2]Laiko General Hospital, School of Medicine, National and Kapodistrian University of Athens, Athens, Greece; [3]Cooper University Hospital, Camden, NJ, USA; [4]University of Southern California, Norris Comprehensive Cancer Center, Los Angeles, CA, USA; [5]START Madrid Fundación Jiménez Díaz, Madrid, Spain; [6]The Royal Marsden NHS Foundation Trust, London, UK; [7]Hospital Universitario Marqués de Valdecilla, Santander, Spain; [8]Inselspital, Bern University Hospital, Bern, Switzerland; [9]James Cancer Center, The Ohio State University, Columbus, OH, USA; [10]University of Colorado Cancer Center – Anschutz Medical Campus, Aurora, CO, USA; [11]Massachusetts General Hospital Cancer Center, Boston, MA, USA; [12]Fred Hutchinson Cancer Center, Seattle, WA, USA; [13]ICO L'Hospitalet – Hospital Duran i Reynals, Barcelona, Spain; [14]Iovance Biotherapeutics, Inc., San Carlos, CA, USA; [15]University of Lübeck, Lübeck, Germany

Courtesy of Evan J Lipson, MD

ABSTRACT 9515

OBX-115, an interleukin 2 (IL2)-sparing engineered tumor-infiltrating lymphocyte (TIL) cell therapy, in patients with immune checkpoint inhibitor (ICI)-resistant unresectable or metastatic melanoma

Rodabe N Amaria, MD[1]; Jennifer L McQuade, MD[1]; Michael A Davies, MD, PhD[1]; Isabella C Glitza Oliva, MD, PhD[1]; Steffy Jose, RN[1]; Erik Cressman, MD, PhD[2]; Ashlynd L Clausell, MPH[1]; Roland Bassett, MS[3]; Sapna Patel, MD[1]; Adi Diab, MD[1]; Hussein A. Tawbi, MD, PhD[1]; Michael K Wong MD, PhD[1]; Alexandra P Ikeguchi, MD[1]; Cara Haymaker, PhD[4]; Seoung-Ae Lee, PhD[4]; Madan Jagasia, MD, MS[5]; Giridharan Ramsingh, MD[5]; Prakash Prabhakar, PhD[5]; Raina Duan, PhD[5]; Parameswaran Hari, MD[5]

1. Department of Melanoma Medical Oncology, MD Anderson Cancer Center, Houston, TX, USA; 2. Department of Interventional Radiology, MD Anderson Cancer Center, Houston, TX, USA; 3. Department of Biostatistics, MD Anderson Cancer Center, Houston, TX, USA; 4. Department of Translational Molecular Pathology, MD Anderson Cancer Center, Houston, TX, USA; 5. Obsidian Therapeutics, Cambridge, MA, USA

OBX-115: Promising Efficacy Profile Without IL2 Administration

	Efficacy Cohort (n=9)
Objective response rate, n (%)	**4 (44.4)**
Complete response	**2 (22.2)**
Partial response	2 (22.2)
Stable disease ≥12 weeks	5 (55.6)
Progressive disease	0
Disease control rate,* n (%)	9 (100)
Progression-free survival at 24 weeks	75%

- Per-protocol efficacy analysis set (n=9)
  - 44.4% ORR, including 2 CRs
- Per-protocol high-risk cohort (n=1, *GNA11*-mutated rare uveal-equivalent subtype)
  - Best response of progressive disease

*Defined as stable disease (or better) for ≥12 weeks post-infusion.
CR, complete response; IL2, interleukin 2; ORR, objective response rate.

Conclusions

- OBX-115 is a highly differentiated TIL cell therapy product with optimized characteristics for response and persistence, which can be manufactured using tumor tissue obtained via core needle biopsy
  - ACZ-driven regulatable mbIL15 expression enables **elimination of IL2 from the regimen**
- In this Phase 1 first-in-human study exploring optimal dosing of OBX-115 + ACZ in this particularly **high unmet need population**, the OBX-115 regimen resulted in:
  - **Positively differentiated safety** from IL2-dependent non-engineered TIL cell therapy
  - **Promising efficacy profile without IL2 administration, including a 44% ORR across all dose-level cohorts (n=9)**
    - 50% ORR in patients receiving OBX-115 dose >30 × 10^9 cells
    - 100% disease control rate
    - Tumor burden reduction in all patients
    - 75% PFS at 24 weeks

Planned regimen optimization is **ongoing in a Phase 1/2 multicenter study**, currently enrolling patients with advanced melanoma and metastatic non-small cell lung cancer (NCT06060613 [Agni-01]; **Poster TPS9599**)

ACZ, acetazolamide; IL2, interleukin 2; PFS, progression-free survival; ORR, objective response rate; OS, overall survival; TIL, tumor-infiltrating lymphocyte; TKI, tyrosine kinase inhibitor.

Interleukin-6 Receptor Blockade With Tocilizumab Reduces Immune-Related Toxicity with Ipilimumab and Nivolumab in Metastatic Melanoma

Jeffrey S Weber[1], Amrutesh Puranik[1,4], Teruyuki Mizutani[1], Tomoaki Muramatsu[1], Judith Goldberg[1], Janice Mehnert[1], Xiaochun Li[1], Benjamin Levinson[1], Omid Hamid[2], Inderjit Mehmi[2], Mark Faries[2], F Stephan Hodi[3], Elizabeth Buchbinder[3], Patrick Ott[3], Sofia Bajwa[1], Perla Arriola[1], Naika Legros[4] and Ryan J Sullivan[4]

Laura and Isaac Perlmutter Cancer Center at NYU Langone Health[1], Bespoke MultiOmics Consultants[4], The Angeles Clinic and Research Institute[2], a Cedars Sinai Affiliate[2], Dana Farber Cancer Institute[3] and Massachusetts General Hospital Cancer Center[4]

2024 ASCO Poster #9538
Chicago, IL

INTRODUCTION

1. Interleukin-6, found at high levels in the serum of patients with metastatic melanoma and other cancers[1], may in part be responsible for immune-related adverse events, given that reversal of those toxicities is observed with IL-6 receptor blockade[2,3].

2. Murine data showed that IL-6 blockade reduced Th17, increased Th1 and TH17 ratio in immune checkpoint blockade (ICB)-treated tumors, with decreased toxicity and increased benefit[4].

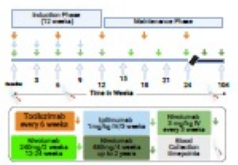
3. IL-6 may play a role as a chronic inflammatory mediator in raising levels of acute phase and complement-related proteins synthesized by the liver and circulating cells of the myeloid lineage[5] which have been shown to be immune suppressive and are associated with a short survival with checkpoint inhibition in melanoma and lung cancer[6-10].

4. A phase II trial of the established melanoma regimen[11] of ipilimumab at 1 mg/kg and nivolumab at 3 mg/kg for 4 induction doses followed by nivolumab maintenance at 480 mg every 4 weeks for up to 2 years to which tocilizumab, the IL-6 receptor blocking monoclonal antibody was added for the first 24 weeks was carried out to assess grade 3-4 immune related adverse events associated with ICB as well as response rate and progression-free survival (PFS).

5. Correlative marker studies were carried out to determine if baseline predictive or on-treatment pharmacodynamic markers were associated with toxicity and/or response.

TRIAL DESIGN

NCT03999749 is Phase II, open-label study assessing the safety and tolerability of tocilizumab (4 mg/kg every 6 weeks for 5 doses) in combination with ipilimumab and nivolumab induction therapy, followed by nivolumab maintenance therapy in patients with advanced melanoma.



DEMOGRAPHICS

Table 1. Demographic characteristics of Phase II PSMO/TOCI trial.

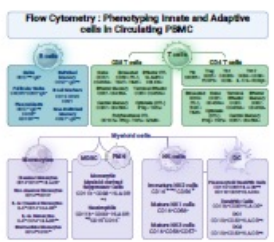
Category	Distribution
Age	Median 67 years
Sex	44 males, 26 females
Ethnicity	64 White, 3 Black, 1 Hispanic, 2 Unknown
Stage	IV-M1, III: 3
LDH > ULN at baseline	9/70 = 7%
Liver metastases at baseline	20/70 = 28%
M1c Subtype	23/67= 33%
Linear median baseline tumor measure	5.8 cm
Failed adjuvant immunotherapy	10
Performance status at baseline	0 = 23, 1 = 47
Number of patients by treatment center	NYU – 20, Angeles Clinic – 23, Dana Farber –12 , MGH - 10
Number of patients who stopped due to toxicity (%)	8 (11)
Best overall response rate, RECIST 1.1	57%
Number of patients with progression (%)	25 (35)
Number who have died (%)	24 (34)

BIOMARKER OBJECTIVES

#1: Identify Predictive Biomarkers for Treatment Efficacy
#2: Identify Biomarkers for Predicting and Monitoring Toxicity
#3 Correlate Biomarkers with Clinical Outcomes.

BIOMARKER METHODOLOGY

High-parametric flow cytometry was performed on cryopreserved patient PBMC from baseline, week 7 and 37 to estimate cell numbers of the following populations. Post-staining, the cells were acquired on a Sony ID7000 flow cytometer and analyzed using FlowJo. Quality control was conducted using PecoQC or FlowAI, and live cells were normalized across samples before concatenation. Dimensionality reduction (PHATE, UMAP) and Phenograph clustering were applied to approximately 1-2 million cells. Clusters were phenotyped using MEM and verified via cluster explorer.

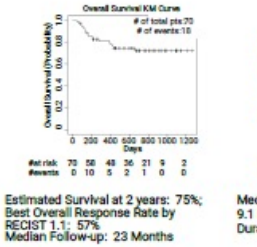


CLINICAL RESULTS

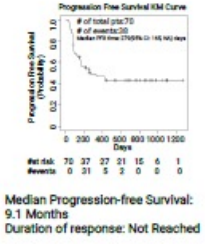
With 70 patients in two stages (Stage 1: 12+6 patients, Stage 2: 49 patients) we detect a reduction in the rate of the primary toxicity endpoint from 35% to 22% in grades 3-5 treatment related irAEs, with alpha of 0.05 and power of 80%.

Immune-related Adverse Events by week 24

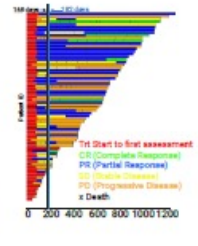
Category	Grades 1-2	Grades 3-4
Lipase/amylase elevation	11	3
ASTALT elevation	10	4
Pneumonitis	1	1
Colitis	4	3
Diarrhea	13	4
Adrenal Insufficiency	3	1
Skin Rash	21	1
Alkaline Phosphatase elevation	4	1
Hyperthyroidism	6	-
Hypothyroidism	8	-
Hypophysitis	1	-
Myositis	8	-
Nausea	5	-
Neuropathy	4	-
Thrombocytopenia	4	-
Arthralgia	13	-
Pruritis	23	-
Fatigue	14	-
Vitiligo	7	-
TOTAL number of patients	24/71 = 71%	10/71 = 22%



Estimated Survival at 2 years: 75%;
Best Overall Response Rate by RECIST 1.1: 57%
Median Follow-up: 23 Months

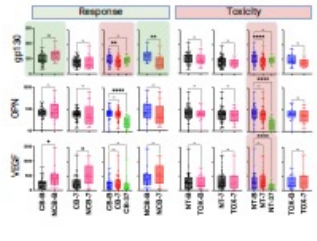


Median Progression-free Survival: 9.1 Months
Duration of response: Not Reached

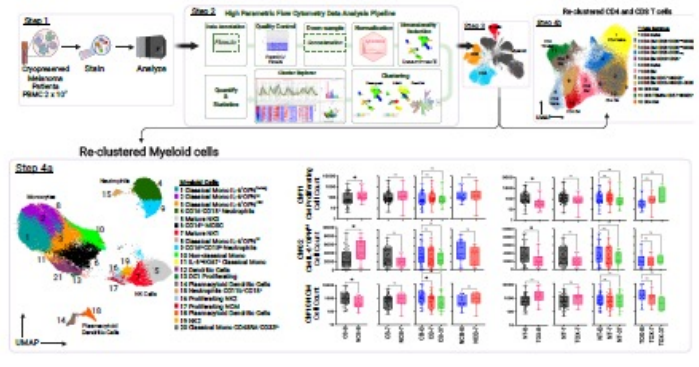


SERUM/PLASMA BIOMARKERS

We measured circulating IL-23, IL-6, IL-6R, gp130 (downstream of IL-6 signaling), IL-8, Osteopontin (SPP1), CXCL10, CXCL11, TNF-a, C5a, SAA, VEGF and other cytokines using ELISA and Luminex. gp130 (CD130) significantly reduced at week 7, in patients with clinical benefit (CB) and no clinical benefit (NCB).

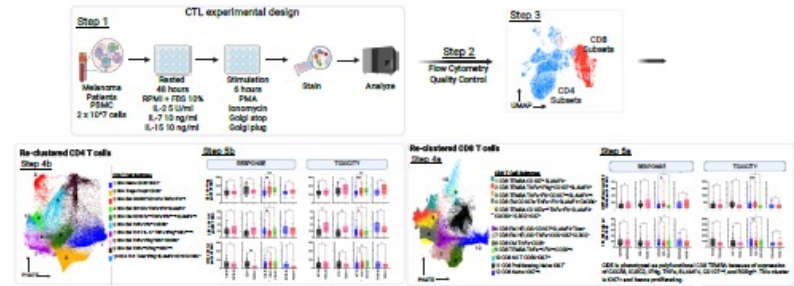


PERIPHERAL BLOOD MYELOID BIOMARKERS



PERIPHERAL BLOOD FUNCTIONAL T CELL BIOMARKERS

Cryopreserved peripheral blood mononuclear cells (PBMCs) are rested for 48 hours in media consisting of IL-2, IL-7 and IL-15, followed by stimulation with PMA/Ionomycin. Post-staining, the cells were acquired on a Sony ID7000 flow cytometer and analyzed using FlowJo. We identified 10 CD4 clusters and 12 CD8 clusters.



CONCLUSIONS

- Tocilizumab (TOCI) added to "flipped dose" IPI/NIVO reduced grade 3-4 immune-related adverse events by week 24 to 22% from expected 34% in Checkmate-511
- The best overall response rate with IPI/NIVO/TOCI was 57% compared to 47% for the same IPI/NIVO regimen in Checkmate-511
- Patients with partial responses had negative PET-CT scans.
- IL-6 expressing, osteopontin-positive classical monocytes at baseline were associated with progression and resistance to IPI/NIVO
- Biomarker data showed that circulating T_H17 cells and T_{reg} at baseline were significantly and reciprocally associated with grade 3-4 immune-related adverse events
- T_{reg} numbers at week 7 and 37 on treatment were associated with response to treatment
- Polyfunctional CD4 T_H1 cells are associated with response at week 7 and 37 in patients with no toxicity
- Polyfunctional CD8 T cells at baseline were significantly associated with response but not immune-related adverse events

REFERENCES

- Hoejberg L, Bastholt L, Schmidt H. Interleukin-6 and melanoma. Melanoma Res. 2012;22:327-333.
- Stroud CR, Hegde A, Cherry C et al Tocilizumab for the management of immune mediated adverse events secondary to PD-1 blockade. J Oncol Pharm Pract. 2019 Apr;25(3):551-557
- Brudno JN, Kochenderfer JN. Toxicities of chimeric antigen receptor T cells: recognition and management. *Blood*. 2016 Jun 30;127(26):3321-30.
- Scheller J, Chalaris A, Schmidt-Arras D, Rose-John S. The pro- and anti-inflammatory properties of the cytokine interleukin-6. Biochim Biophys Acta. 2011;1813(5):878–88.
- Weber JS, Sznol M, Sullivan RJ et al. A Serum Protein Signature Associated with Outcome after Anti-PD-1 Therapy in Metastatic Melanoma. *Cancer Immunol Res* 2018; 6: 79-86.
- Fang S, Wang Y, Sui D, et al. C-reactive protein as a marker of melanoma progression. *J Clin Oncol*. 2015 Apr 20;33(12):1389-96.
- Laino AS, Woods D, Vassallo M et al Serum Interleukin-6 and C-reactive protein are associated with survival in melanoma patients receiving immune checkpoint inhibition. J Immunother Cancer. 2020 Jun;8(1):e000842
- Shi Y, Liu X, Liu J et al Correlations between peripheral blood biomarkers and clinical outcomes in advanced non-small cell lung cancer patients who received immunotherapy-based treatments. *Transl Lung Cancer Res*. 2021 10(12):4477-4493
- Kauffmann-Guerrero D, Kahnert K, Kiefl R et al Systemic inflammation and pro-inflammatory cytokine profile predict response to checkpoint inhibitor treatment in NSCLC: a prospective study. *Sci Rep*. 2021;11(1):10919
- Weber J, Muramatsu T, Hamid O et al Phase II trial of ipilimumab, nivolumab and tocilizumab for unresectable metastatic melanoma ESMO 2021 abstr 10400
- Lebbe, C, Meyer, N, Mortier L et al Evaluation of Two Dosing Regimens for Nivolumab in Combination With Ipilimumab in Patients With Advanced Melanoma: Results From the Phase IIIb/IV CheckMate 511 Trial. *J Clin Oncol* 2019 Apr 10;37(11):867-875.

ACKNOWLEDGEMENTS

The staff of the Laura and Isaac Perlmutter Clinical Trials Office; Nurse Practitioners Nila Delarosa and Kathleen Madden; Iman Osman, MD; Anthony Salvatore MD, Corey Ritchings MD and Leon Sekkal MD, BMS; Barbara Blechele MD, Genentech; Eddy Yang for his technical assistance; This work was supported by a grant from the National Cancer Institute R01 CA244936

Agenda

INTRODUCTION: Johns Hopkins University

MODULE 1: Metastatic Melanoma

MODULE 2: Nonmetastatic Melanoma and Other Skin Cancers

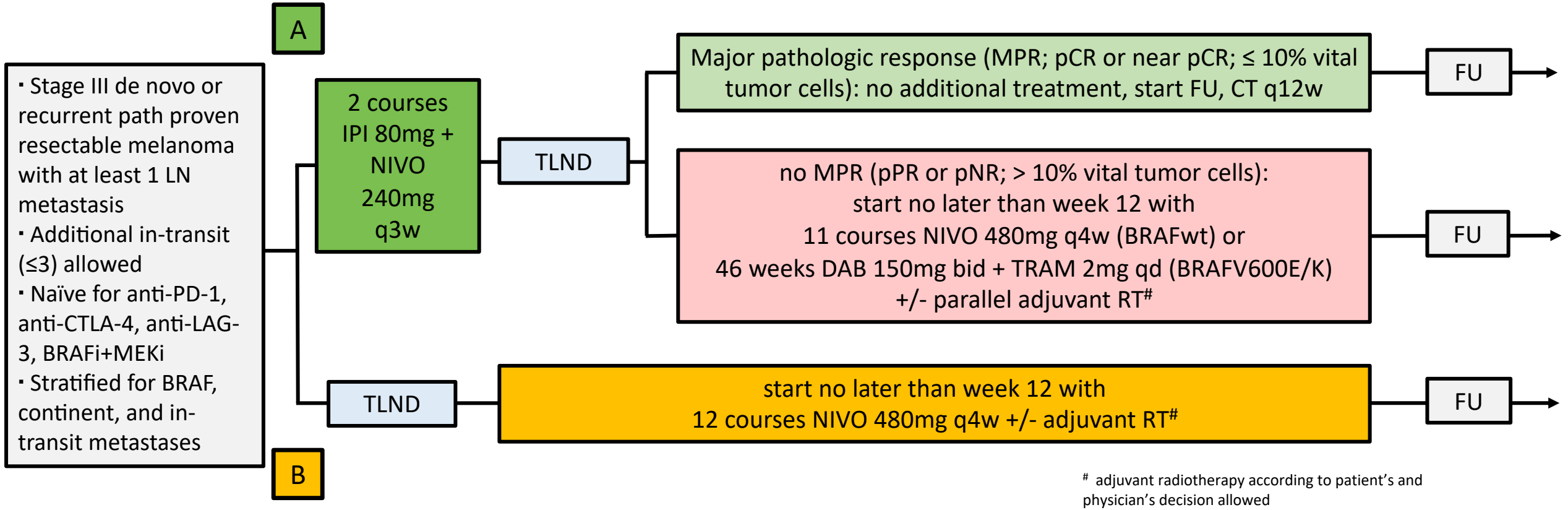
2024 ASCO ANNUAL MEETING

Neoadjuvant Nivolumab Plus Ipilimumab Versus Adjuvant Nivolumab in Macroscopic, Resectable Stage III Melanoma: The Phase 3 NADINA Trial

Christian U. Blank, M.W. Lucas, R.A. Scolyer, B.A. van de Wiel, A.M. Menzies, M. Lopez-Yurda, A.C.J. van Akkooi, W.J. van Houdt, R.P.M. Saw, A. Torres-Acosta, S.N. Lo, G.A.P. Hospers, M.S. Carlino, J.W.B. de Groot, E. Kapiteijn, K.P.M. Suijkerbuijk, P. Rutkowski, S. Sandhu, A.A.M. van der Veldt, G.V. Long

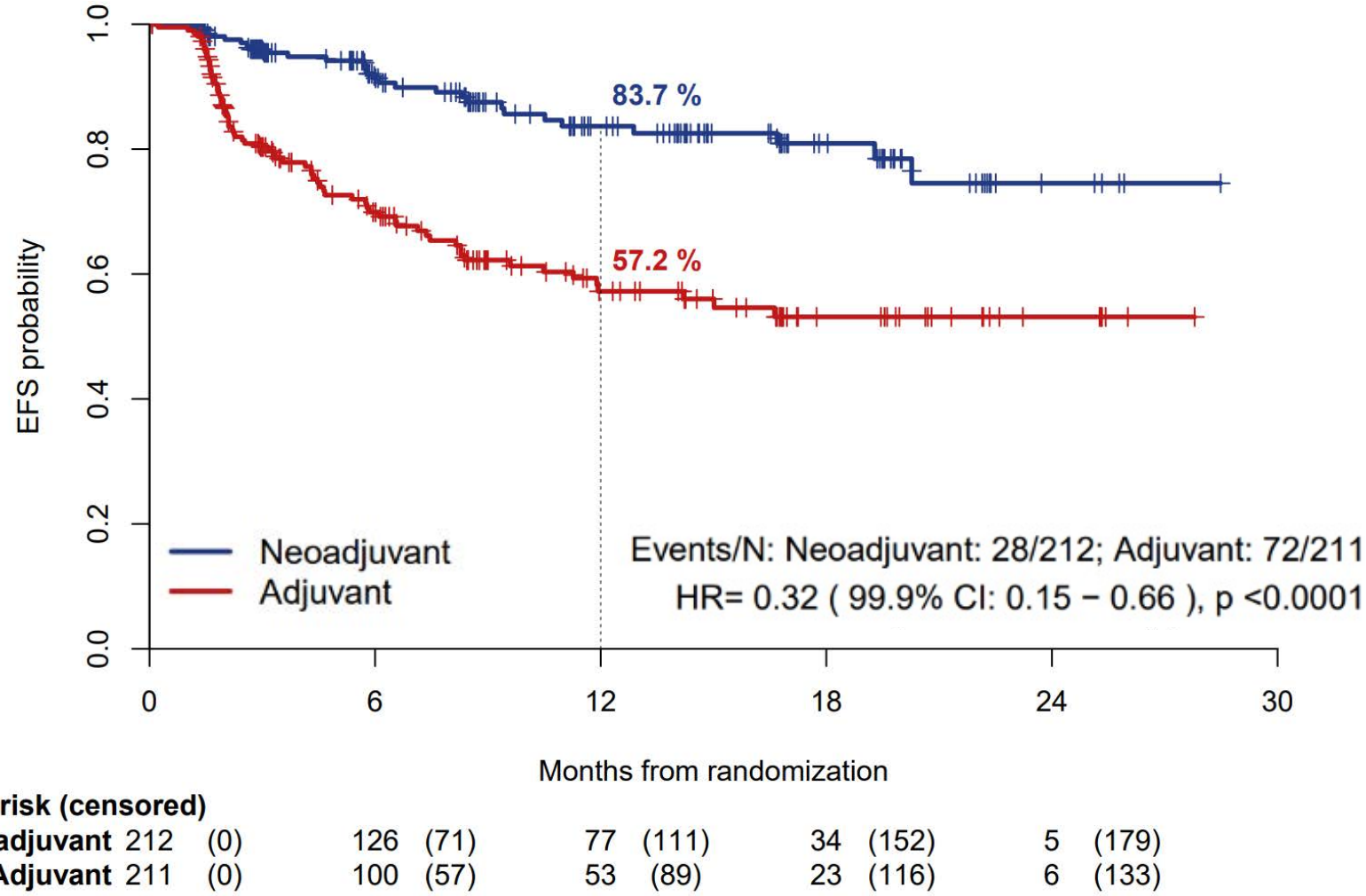
lay abstract

NADINA - Trial Design



Courtesy of Evan J Lipson, MD

NADINA – Primary Endpoint: Event-Free Survival (EFS)



# at risk (censored)										
Neoadjuvant	212	(0)	126	(71)	77	(111)	34	(152)	5	(179)
Adjuvant	211	(0)	100	(57)	53	(89)	23	(116)	6	(133)

Conclusions

- **Critical finding(s): NADINA shows a significant event-free survival (EFS) benefit for neoadjuvant ipilimumab + nivolumab compared to adjuvant nivolumab in patients with macroscopic stage III melanoma**
- **Of the 59% of patients who experienced a major pathologic response, some were able to avoid adjuvant therapy altogether, limiting their total treatment time to 6 weeks.**
- **Clinical implication(s): new standard of care for the treatment of patients with resectable macroscopic stage III melanoma.**
- **Research relevance: What is the optimal approach for patients who do not experience an MPR following neoadjuvant therapy? What is the optimal neoadjuvant regimen?**

Courtesy of Evan J Lipson, MD

ORIGINAL ARTICLE

Neoadjuvant–Adjuvant or Adjuvant-Only Pembrolizumab in Advanced Melanoma

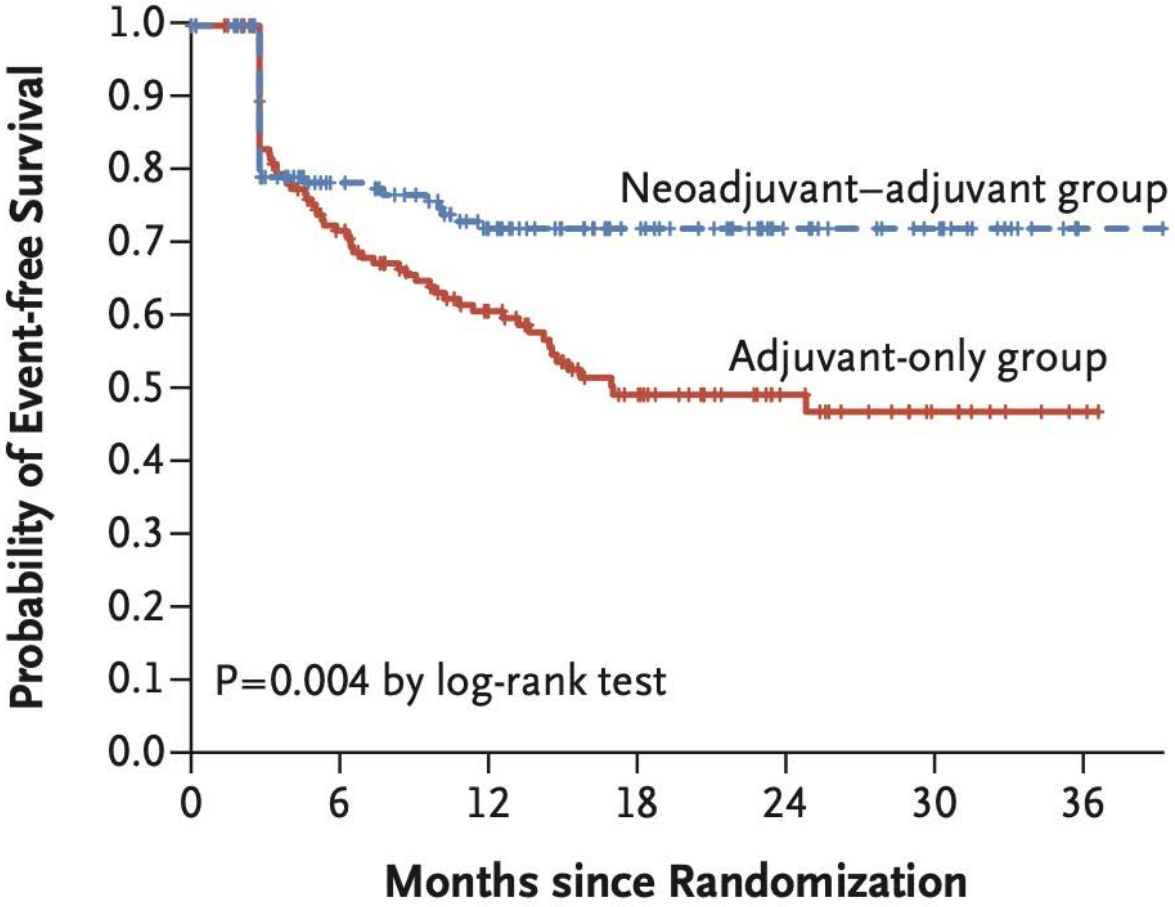
S.P. Patel, M. Othus, Y. Chen, G.P. Wright, Jr., K.J. Yost, J.R. Hyngstrom, S. Hu-Lieskovan, C.D. Lao, L.A. Fecher, T.-G. Truong, J.L. Eisenstein, S. Chandra, J.A. Sosman, K.L. Kendra, R.C. Wu, C.E. Devoe, G.B. Deutsch, A. Hegde, M. Khalil, A. Mangla, A.M. Reese, M.I. Ross, A.S. Poklepovic, G.Q. Phan, 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

N Engl J Med 2023;388(9):813-23.

Neoadjuvant and Adjuvant or Adjuvant-Only Pembrolizumab: EFS

EFS at 2 years was 72% (95% CI, 64 to 80) in the neoadjuvant–adjuvant group.

EFS at 2 years was 49% (95% CI, 41 to 59) in the adjuvant-only group.



No. at Risk

Neoadjuvant–adjuvant group	154	96	69	46	25	17	1
Adjuvant-only group	159	98	67	40	22	10	2

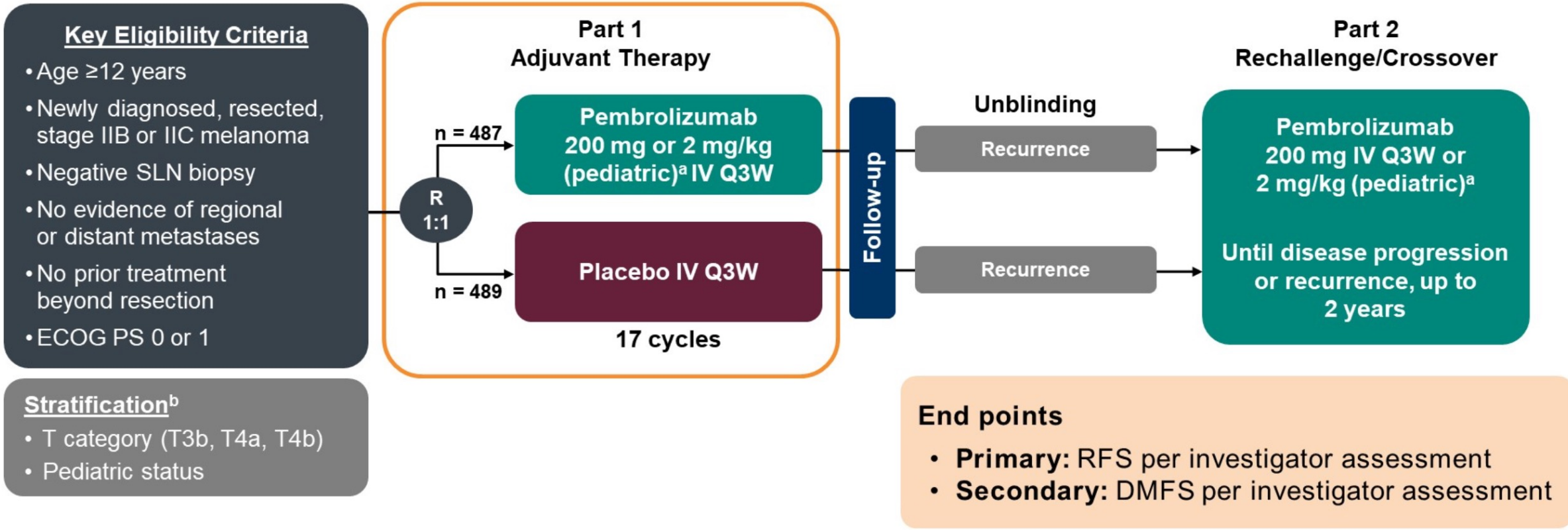
Patel SP et al. *N Engl J Med* 2023;388(9):813-23.

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

Jason J. Luke, MD, FACP[1]; Paolo A. Ascierto, MD, PhD[2]; Muhammad A. Khattak, MD, PhD[3]; Luis de la Cruz Merino, MD, PhD[4,5]; Michele Del Vecchio, MD, PhD[6]; Piotr Rutkowski, MD, PhD[7]; Francesco Spagnolo, MD[8]; Jacek Mackiewicz, MD, PhD[9]; Vanna Chiarion-Sileni, MD[10]; John M. Kirkwood, MD[1]; Caroline Robert, MD, PhD[11,12]; Jean-Jacques Grob, MD, PhD[13]; Federica de Galitiis, MD[14]; Dirk Schadendorf, MD, PhD[15,16]; Matteo S. Carlino, BMedSc, MBBS, FRACP[17,18]; Xi Lawrence Wu, DrPH[19]; Mizuho Fukunaga-Kalabis, MD[19]; Clemens Krepler, MD[19]; Alexander M.M. Eggermont, MD, PhD[20,21]; and Georgina V. Long, PhD, MBBS (Hons), BSc (Hons1, UM), AO, FRACP[17,22]

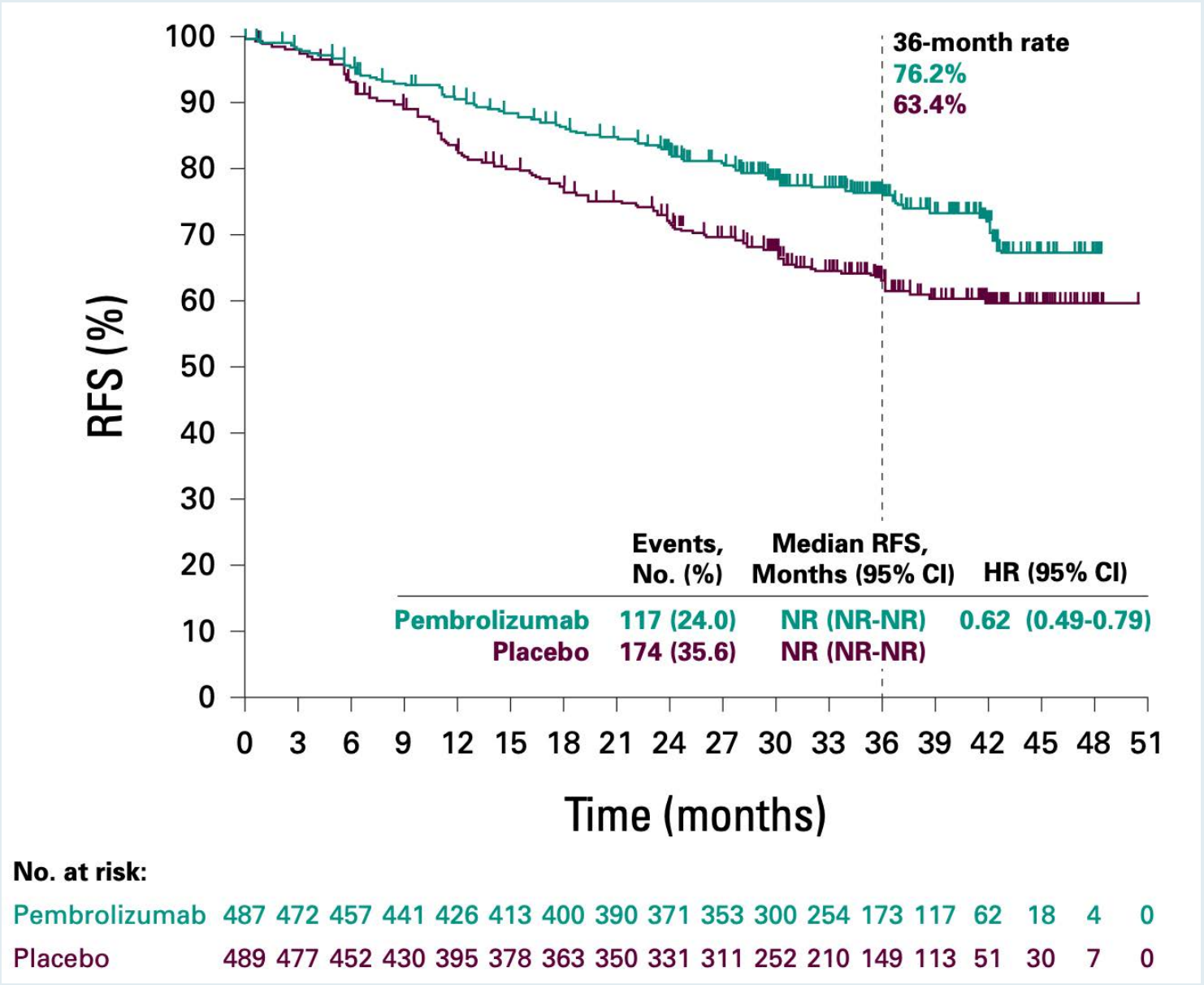
J Clin Oncol 2024;42(14):1619-24.

KEYNOTE-716 Study Design



Luke JJ et al. ASCO 2023;Abstract LBA9505.

KEYNOTE-716: Recurrence-Free Survival (RFS) in the ITT Population



Luke JJ et al. *J Clin Oncol* 2024;42(14):1619-24.

2024 ASCO® ANNUAL MEETING

Individualized neoantigen therapy mRNA-4157 (V940) plus pembrolizumab in resected melanoma: 3-year update from the mRNA-4157-P201 (KEYNOTE-942) trial

Jeffrey S. Weber,[1] Muhammad Adnan Khattak,[2] Matteo S. Carlino,[3] Tarek Meniawy,[4] Matthew H. Taylor,[5] George Ansstas,[6] Kevin B. Kim,[7] Meredith McKean,[8] Ryan J. Sullivan,[9] Mark B. Faries,[10] Thuy Tran,[11] C. Lance Cowey,[12] Theresa M. Medina,[13] Jennifer M. Segar,[14] Victoria Atkinson,[15] Geoffrey T. Gibney,[16] Jason J. Luke,[17] Elizabeth I. Buchbinder,[18] Georgina V. Long,[19] INT Research and Development Author Group,[20,21,a] Robert S. Meehan[20]

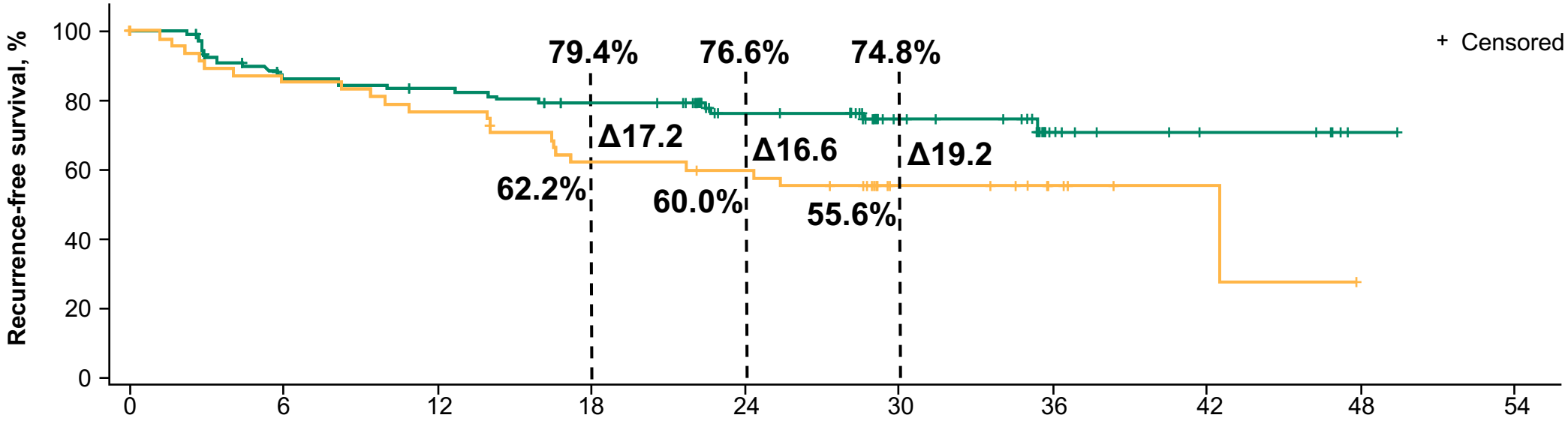
[a]Manju Morrissey,[20] Igor Feldman,[20] Vasudha Sehgal,[20] Huzhang Mao,[20] Jia Guo,[20] Min Liu,[20] Anjali Rao,[20] Wei Zheng,[20] Praveen Aanur,[20] Lakshmi Srinivasan,[20] Mo Huang,[21] Tal Zaks,[20] Michelle Brown,[20] Tracey Posadas[20]

[1]Laura and Isaac Perlmutter Cancer Center at NYU Langone Health, New York, NY, USA; [2]Hollywood Private Hospital and Edith Cowan University, Perth, Australia; [3]Melanoma Institute Australia and Westmead Hospital, Sydney, Australia; [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, San Francisco, CA, USA; [8]Sarah Cannon Research Institute, Nashville, TN, USA; [9]Massachusetts General Hospital, Boston, MA, USA; [10]The Angeles Clinic and Research Institute, Los Angeles, CA, USA; [11]Yale-New Haven Hospital, New Haven, CT, USA; [12]Baylor Charles A. Sammons Cancer Center, Dallas, TX, USA; [13]University of Colorado, Aurora, CO, USA; [14]University of Arizona Cancer Center, Tucson, AZ, USA; [15]Princess Alexandra Hospital, Woolloongabba, Australia; [16]Lombardi Comprehensive Cancer Center, Washington, DC, USA; [17]UPMC Hillman Cancer Center, Pittsburgh, PA, USA; [18]Dana-Farber Cancer Institute, Boston, MA, USA; [19]Melanoma Institute Australia, Sydney, Australia; [20]Moderna, Inc., Cambridge, MA, USA; [21]Merck & Co., Inc., Rahway, NJ, USA.

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

Courtesy of Evan J Lipson, MD

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.

Conclusions

- **Critical finding(s): 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**

- **Clinical implication(s): If platform is feasible and RFS benefit is sustained in Phase III study, with no new safety signals, this approach could replace single agent anti-PD-1 as standard-of-care.**

- **Research relevance: The treatment landscape for patients with resectable Stage IIIB-IV melanoma is changing. How does this approach compare to neoadjuvant therapy?**

Courtesy of Evan J Lipson, MD

CONQUER CANCER® THE ASCO FOUNDATION

MERIT AWARD

9572: Clinical validation of a prognostic 7-marker IHC assay (7-IHC) in 382 patients with stage IB/IIA cutaneous melanoma
The MELARISK-001 study

Authors: Teresa Amaral, MD, PhD[1]*, Stephan Forchhammer, MD[1]*, Eftychia Chatziioannou, MD, Iva Johansson, MD, PhD, Eduardo Nagore, MD, PhD, Esperanza Manrique-Silva, MD, Víctor Través-Zapata, MD, Barbara van Leeuwen, MD, PhD, Marnix R. Jansen, MD, Jose Bañuls, MD, PhD, Noelia Jara-Rico, MD, María Niveiro de Jaime, MD, PhD, Ann-Sophie Bohne, MD, Jüri Teras, MD, Merrick I. Ross, MD, Alexander van Akkooi, MD, PhD, Jeffrey S. Weber, MD, PhD, Dirk Schadendorf, MD, Roger Olofsson Bagge, MD, PhD**, and Axel Hauschild, MD**

1. Background

- Approx. 40% of the globally reported 59,000 melanoma deaths (2022) occur within stage **IB-IIA** (1,2). These patients (pts) lack access to adjuvant therapy.
- Adjuvant clinical trials in this "early"-stage setting may be merited. However, this subgroup cannot be identified using AJCC staging alone.
- A seven-biomarker assay based on immunohistochemistry (**7-IHC**), that includes five risk markers (**Bax, Bcl-X, CD20, COX-2, PTEN**) and two protective markers (**MTAP, ß-Catenin**), has demonstrated ability to stratify CM pts into a high-risk (HR) group or a low-risk (LR) group for recurrence and melanoma-specific survival (MSS) (3).
- **7-IHC** was analytically (4) and prospectively clinically validated (5) to identify stage **IB/IIA** pts at high risk of relapse and death and may be useful in selecting pts for trials investigating adjuvant therapy.
- The multicenter, multinational MELARISK-001 study sought to further clinically validate **7-IHC**.

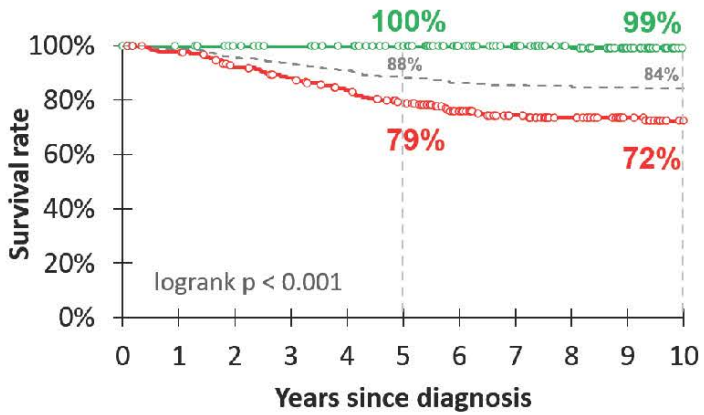
2. Methods

- MELARISK-001 enrolled consecutive pts diagnosed with stage IB/IIA CM from 2000-2016, with available formalin-fixed paraffin-embedded (FFPE) primary CM and outcome data from 6 centers and 4 countries - Germany, Spain, The Netherlands, Sweden.
- Specimens were analyzed by **7-IHC** and classified as high-risk (HR) or low-risk (LR).
- Primary endpoint was recurrence-free survival (RFS) and secondary endpoint was MSS.

3. Results

- 382 pts included, 247 (65%) stage IB, 135 (35%) stage IIA, all sentinel node-negative.
- Median Breslow thickness was 1.6 mm, median age 60y.
- Median follow-up was 90 months (RFS), 98 months (MSS).
- **7-IHC** classified **212 pts (55%) as HR** and **170 (45%) as LR.**
- **7-IHC HR pts** had significantly worse survival outcome (log-rank p<0.001) than did **7-IHC LR pts.**

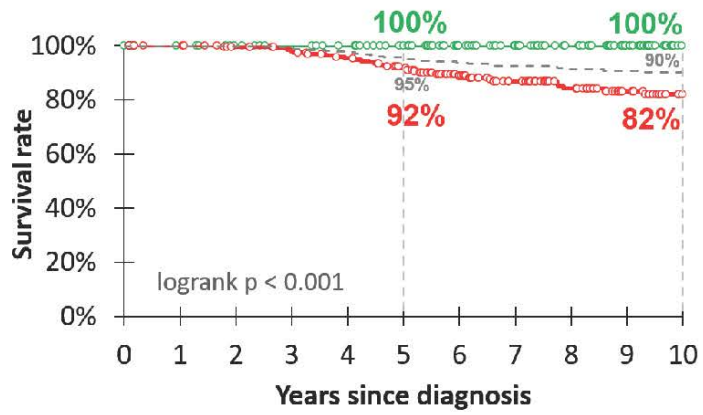
3.1 Relapse-free survival



No. at risk

Low-risk	170	164	159	155	151	141	125	112	99	80	53
High-risk	212	205	187	175	160	144	116	97	81	65	50

3.2 Melanoma-specific survival



No. at risk

Low-risk	170	164	159	155	151	141	125	112	100	81	54
High-risk	212	210	202	195	185	171	141	118	96	77	59

3.3 Multivariate Cox regression

In multivariate analysis, **7-IHC** risk class was the strongest independent prognosticator of survival.

Prognostic factor	Range	RFS		MSS	
		Hazard ratio (CI)	*p*	Hazard ratio (CI)	*p*
7-IHC[U]	Low: 170, High: 212	22.33 (7.0 - 70.9)	**<0.001**	n/a[(1)]	
Breslow mm[U]	Continuous	1.5 (1.1 - 1.9)	**0.003**	1.7 (1.2 – 2.4)	**0.002**
Ulceration	No: 344; Yes: 38	1.1 (0.6 - 2.0)	0.849	1.6 (0.7 - 3.4)	0.271
Age (years)[U]	Dichotomized at median 60 years	1.6 (1.0 - 2.5)	**0.034**	1.8 (1.0 - 3.3)	**0.05**
Sex	F: 166; M: 216	1.1 (0.7 - 2.3)	0.703	1.7 (1.0 - 3.1)	0.066

U = statistically significant in univariate Cox-Regression, p<0.05
(1) Not calculable due to 7-IHC risk class' 100% sensitivity for MSS events

Conclusions

- **7-IHC HR** status identified **98% of relapses** and **100% of melanoma- related deaths** in stage IB/IIA.
- Pts with stage IB/IIA melanoma and **7-IHC HR** have a relapse rate comparable to pts for whom adjuvant therapy is approved.
- **MELARISK-001 further validated 7-IHC in pts with stage IB/IIA melanoma, suggesting its utility to aid in pts selection for adjuvant studies.**

[1]Center for Dermatooncology, University of Tübingen, Germany *,** contributed equally

References: 1. Whiteman et al *J Invest Dermatol 2015*; 2. Bray et al *CA Cancer J Clin 2024;* 3. Meyer et al *PloS ONE 2012*; 4. Ziemer et al *Diagnostics 2023*; 5. Meyer et al *Eur J Cancer 2023*

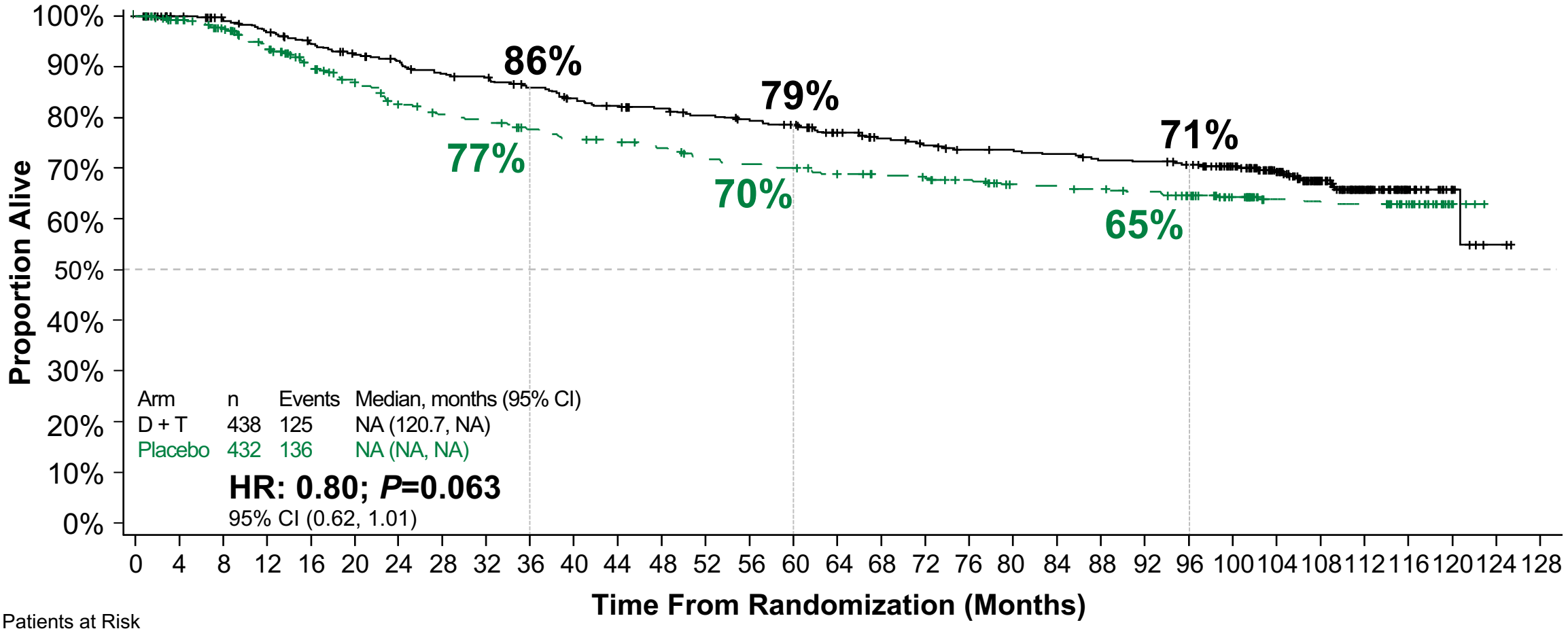
Courtesy of Evan J Lipson, MD

2024 ASCO® ANNUAL MEETING

Long-Term Follow-Up for Adjuvant Dabrafenib Plus Trametinib in Stage III BRAF-Mutated Melanoma: Final Results of the COMBI-AD Study

Axel Hauschild, Reinhard Dummer, Mario Santinami, Victoria Atkinson, Mario Mandala, Barbara Merelli, Vanna Chiarion-Sileni, Andrew Mark Haydon, Jacob Schachter, Dirk Schadendorf, Thierry Lesimple, Elizabeth Ruth Plummer, James Larkin, Monique Tan, Sachin Bajirao Adnaik, Paul Burgess, Tarveen Jandoo, Georgina V. Long

Overall Survival (ITT)



Patients at Risk

D + T	438	416	407	395	381	370	362	351	347	336	325	318	312	305	299	294	279	268	261	255	254	251	246	245	240	222	173	124	75	27	8	2	0
Placebo	432	415	400	377	346	328	308	297	292	282	274	270	264	255	251	248	241	236	233	228	218	216	213	208	201	185	157	115	67	26	4	0	0

End of study 31 July 2023. Median follow-up: D+T 100.0 (0−125) months; Placebo 82.5 (1−122) months.

Conclusions

- **Longest follow-up (up to 10 years)** in adjuvant treatment of stage III melanoma
- **Durable improvements in RFS and DMFS** with dabrafenib plus trametinib over placebo
- **Overall survival and melanoma-specific survival** were numerically improved (not statistically significant) with D+T vs placebo, despite post-relapse systemic therapy
  - **20% risk reduction for death** with dabrafenib plus trametinib over placebo (***P*=0.063)**
  - **22% reduction for risk of death due to melanoma** with dabrafenib plus trametinib over placebo
- ***BRAF* V600E** showed a **benefit for OS** with dabrafenib plus trametinib over placebo
  - ***BRAF* V600K** population did not appear to have an OS benefit from adjuvant dabrafenib plus trametinib although caution warranted given this small subgroup
- **No new safety concerns**
  - No irreversible toxicities during the long-term follow-up
  - Skin and other cancers incidence was similar in each arm

Conclusions

- **Critical finding(s): Longest follow-up (≤10 years) in adjuvant treatment of patients with stage III melanoma demonstrated durable improvements in RFS and DMFS with dabrafenib plus trametinib vs placebo.**

No statistically significant improvement in overall survival with D+T vs placebo

  - **20% risk reduction for death with dabrafenib plus trametinib over placebo (P=0.063)**
  - **22% reduction for risk of death due to melanoma with dabrafenib plus trametinib over placebo**

- **Clinical implication(s): data continue to support adjuvant administration of D+T in patients with resected stage III BRAF-mutant melanoma**

- **Research relevance: The treatment landscape for patients with resectable Stage III melanoma is changing. How does this approach compare to neoadjuvant therapy?**

Courtesy of Evan J Lipson, MD

Neoadjuvant cemiplimab and surgery for stage II–IV cutaneous squamous-cell carcinoma: follow-up and survival outcomes of a single-arm, multicentre, phase 2 study

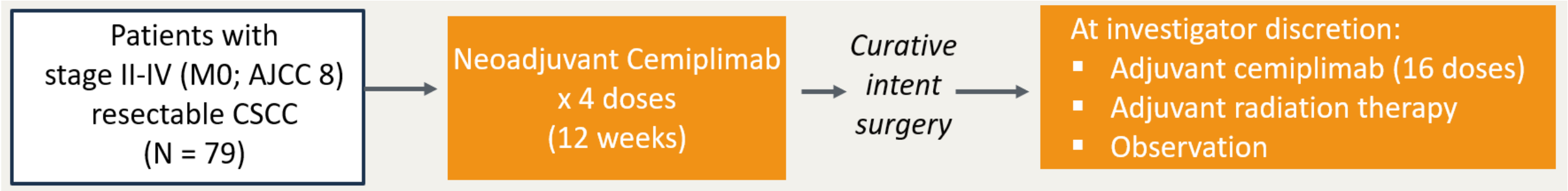
Neil D Gross, David M Miller, Nikhil I Khushalani, Vasu Divi, Emily S Ruiz, Evan J Lipson, Friedegund Meier, Yungpo Bernard Su, Paul L Swiecicki, Jennifer Atlas, Jessica L Geiger, Axel Hauschild, Jennifer H Choe, Brett G M Hughes, Dirk Schadendorf, Vishal A Patel, Jade Homsi, Janis M Taube, Annette M Lim, Renata Ferrarotto, Suk-Young Yoo, Melissa Mathias, Hyunsil Han, Frank Seebach, Israel Lowy, Matthew G Fury, Danny Rischin

Lancet Oncology 2023

Courtesy of Evan J Lipson, MD

Neoadjuvant Cemiplimab in CSCC: Study Design

- Multicenter phase II study



- **Primary endpoint:** pCR rate (0% residual viable tumor) by central review
- **Key secondary endpoints:** Major Pathologic Response (MPR) rate (>0% and ≤10% residual viable tumor) by central review, EFS, DFS, OS

Gross et al. Lancet Oncol. 2023

Courtesy of Evan J Lipson, MD

NEOADJUVANT CEMIPLIMAB IN CSCC

Patient Characteristics

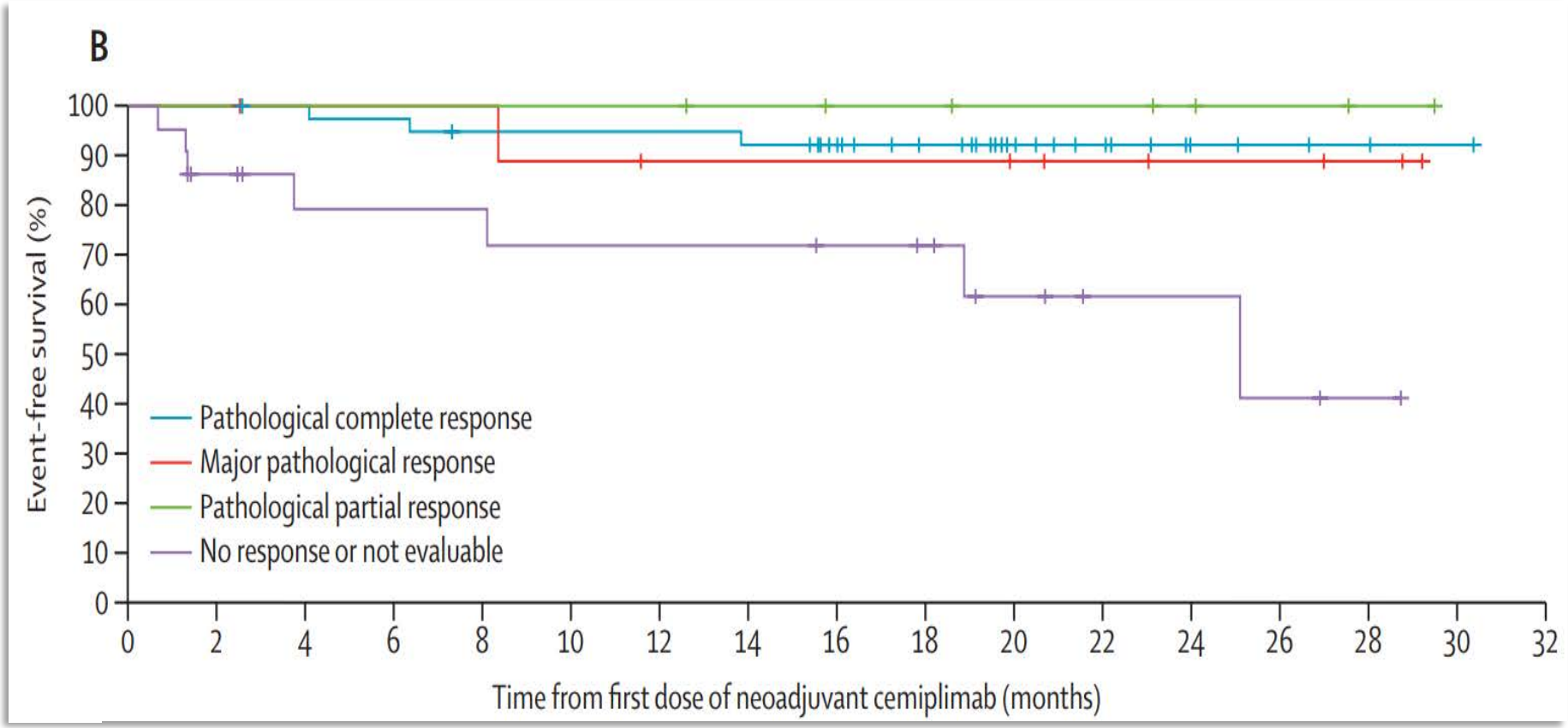
Characteristic	Neoadjuvant cemiplimab (N=79)
Age, median (range), years	73.0 (24–93)
Male, no. (%)	67 (84.8)
Race, no. (%)	
White	69 (87.3)
Other	2 (2.5)
Not reported	8 (10.1)
Primary site of CSCC, no. (%)	
Head and neck	72 (91.1)
Trunk/extremities	7 (8.9)
CSCC stage group, no. (%)	
Stage II	5 (6.3)
Stage III	38 (48.1)
Stage IV (M0)	36 (45.6)
ECOG performance status, no. (%)	
0	60 (75.9)
1	19 (24.1)

Gross et al. Lancet Oncol. 2023

Courtesy of Evan J Lipson, MD

NEOADJUVANT CEMIPLIMAB IN CSCC

EFS Results by Depth of Response



No recurrence occurred in the 40 pCR patients

Only 3 EFS events occurred in pCR patients - deaths unrelated to study drug

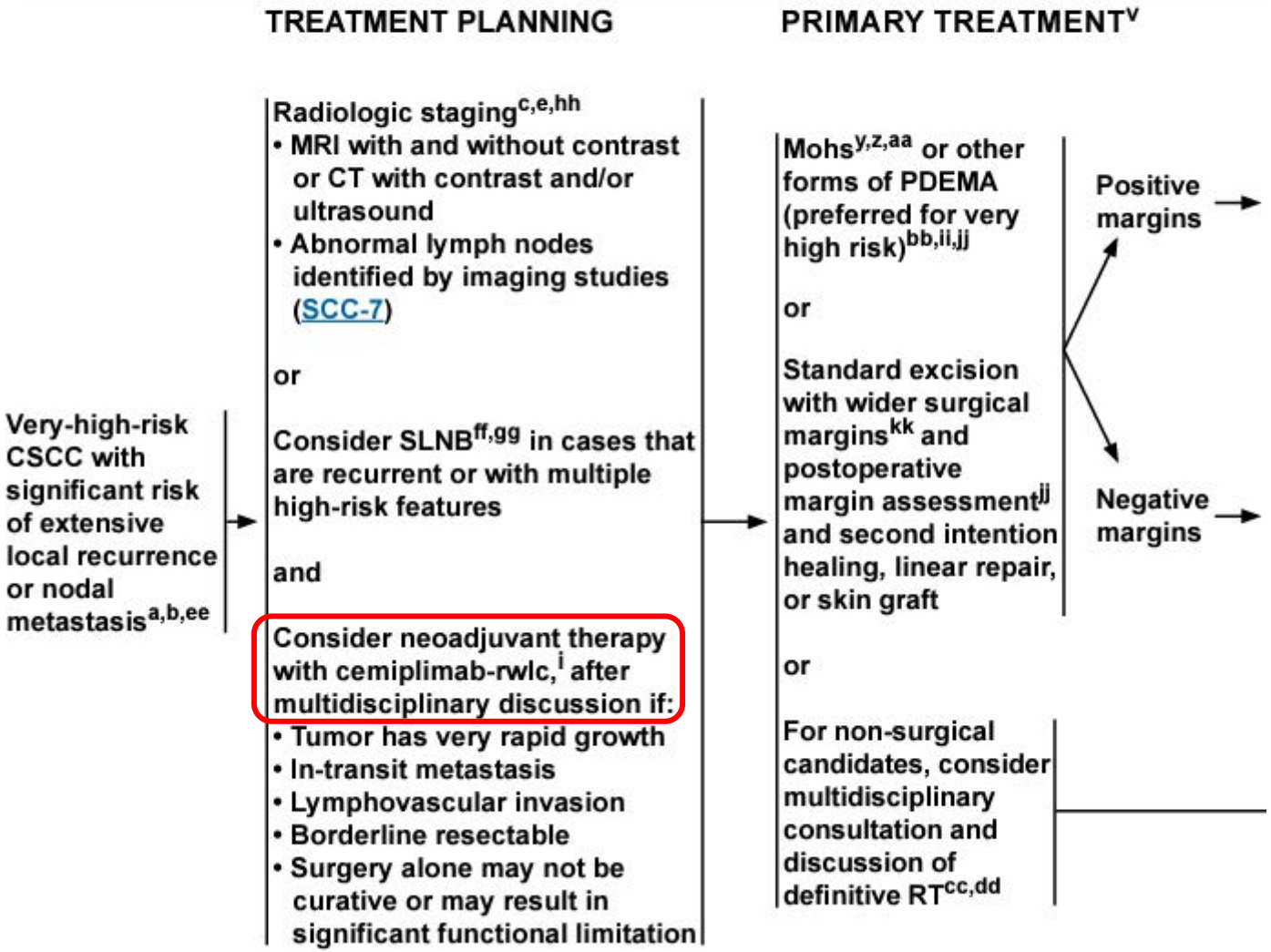
EFS: time from first dose of neoadjuvant cemiplimab to progressive disease that precluded surgery, inability to undergo R0, R1 resection, disease recurrence by imaging criteria, or death due to any cause.

Gross et al. Lancet Oncol. 2023

Courtesy of Evan J Lipson, MD

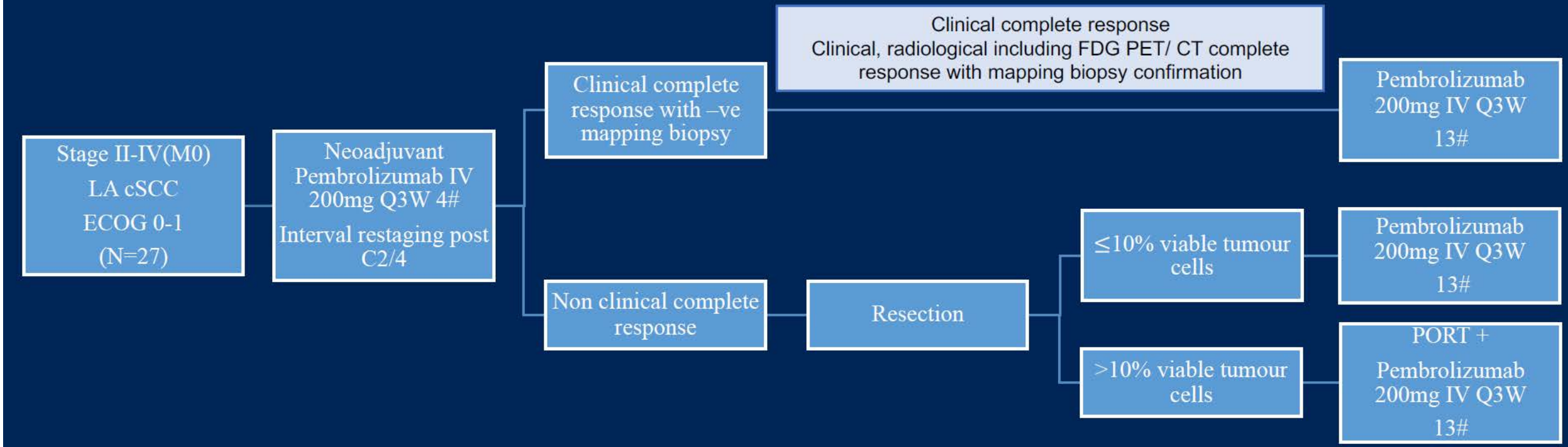
National Comprehensive Cancer Network®

NCCN Guidelines Version 1.2024
Squamous Cell Skin Cancer



Courtesy of Evan J Lipson, MD

DESQUAMATE Study Design



Primary Endpoint
Histopathological response as determined by a combination of pCR: (no viable tumour cells) + mPR: (≤10% viable tumour cells) + Clinical CR following up to 4 cycles of neoadjuvant therapy

Courtesy of Evan J Lipson, MD

Pembrolizumab for Locally Advanced or Recurrent/Metastatic Cutaneous Squamous Cell Carcinoma: Long-Term Results of the Phase 2 KEYNOTE-629 Study

E. Munoz-Couselo[1]; B. G. M. Hughes[2]; L. Mortier[3]; J. J. Grob[4]; R. Gutzmer[5]; O. Roshdy[6]; R. González Mendoza[7]; J. Schachter[8]; A. Arance[9]; F. Grange[10]; N. Meyer[11]; A. Joshi[12]; S. Billan[13]; S. E. Ojavee[14]; J. Yuan[14]; B. Gumuscu[14]; Å. Bratland[15]

ASCO 2024;Abstract 9554.

KEYNOTE-629: Pembrolizumab for Locally Advanced (LA) or Recurrent or Metastatic (R/M) Cutaneous Squamous Cell Carcinoma (cSCC)

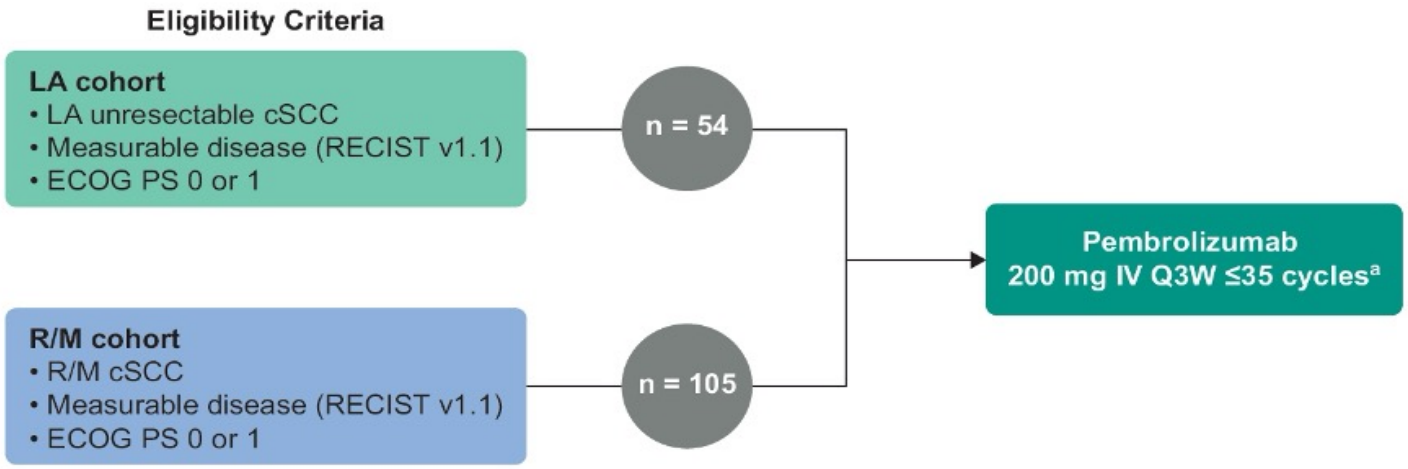


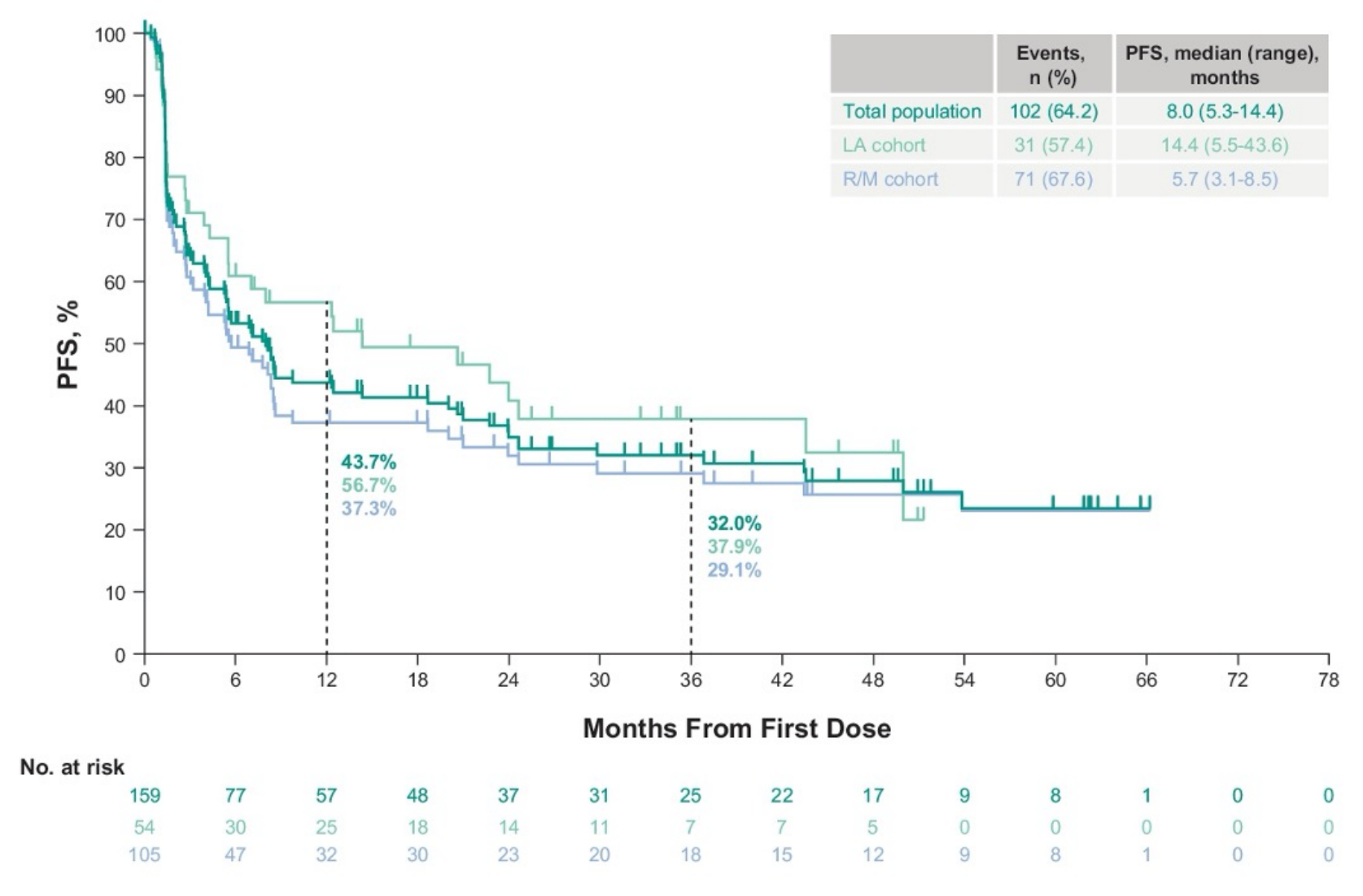
Table 2. ORR per RECIST v1.1 by BICR in the LA cohort, R/M cohort, and total population

	LA cohort n = 54	R/M cohort n = 105	Total population N = 159
ORR, % (95% CI)	51.9 (37.8-65.7)	35.2 (26.2-45.2)	40.9 (33.2-48.9)
DCR, % (95% CI)	64.8 (50.6-77.3)	52.4 (42.4-62.2)	56.6 (48.5-64.4)
Best overall response, n (%)			
CR	12 (22.2)	13 (12.4)	25 (15.7)
PR	16 (29.6)	24 (22.9)	40 (25.2)
SD	12 (22.2)	30 (28.6)	42 (26.4)
SD ≥12 weeks	7 (13.0)	18 (17.1)	25 (15.7)
PD	9 (16.7)	28 (26.7)	37 (23.3)
NE/NA[a]	5 (9.3)	10 (9.5)	15 (9.4)

Couselo E et al. ASCO 2024;Abstract 9554.

ORR = objective response rate

KEYNOTE-629: Progression-Free Survival (PFS) Outcomes by BICR



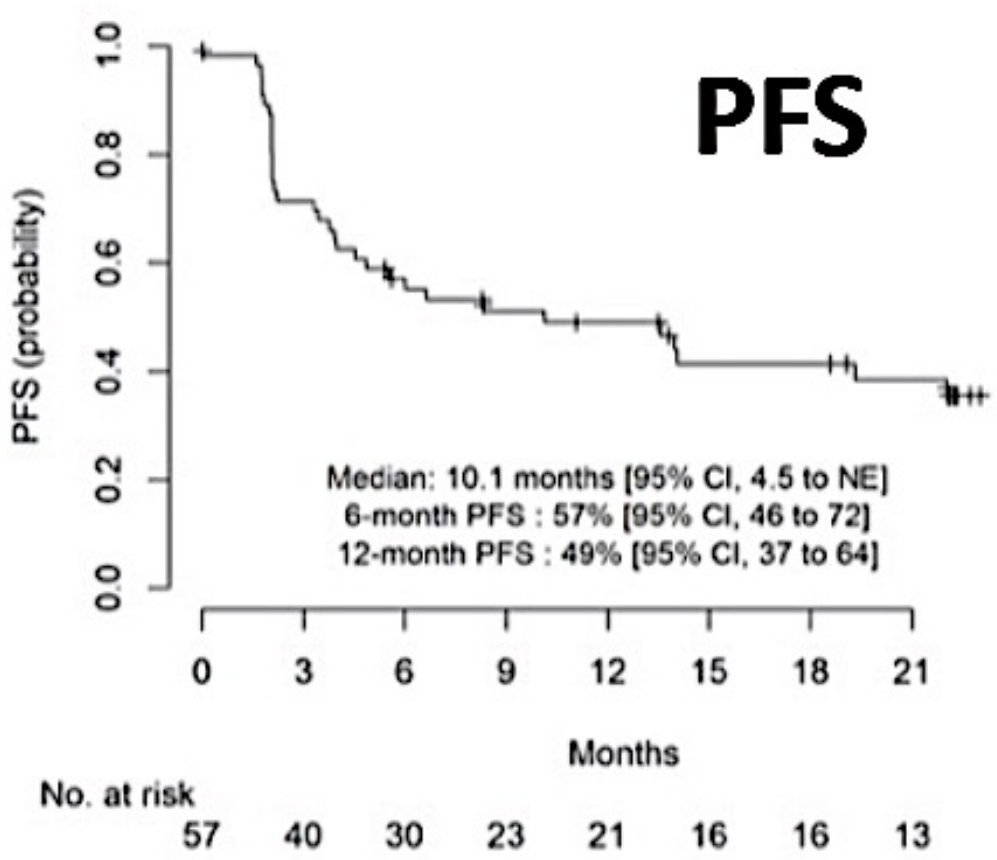
Couselo E et al. ASCO 2024;Abstract 9554.

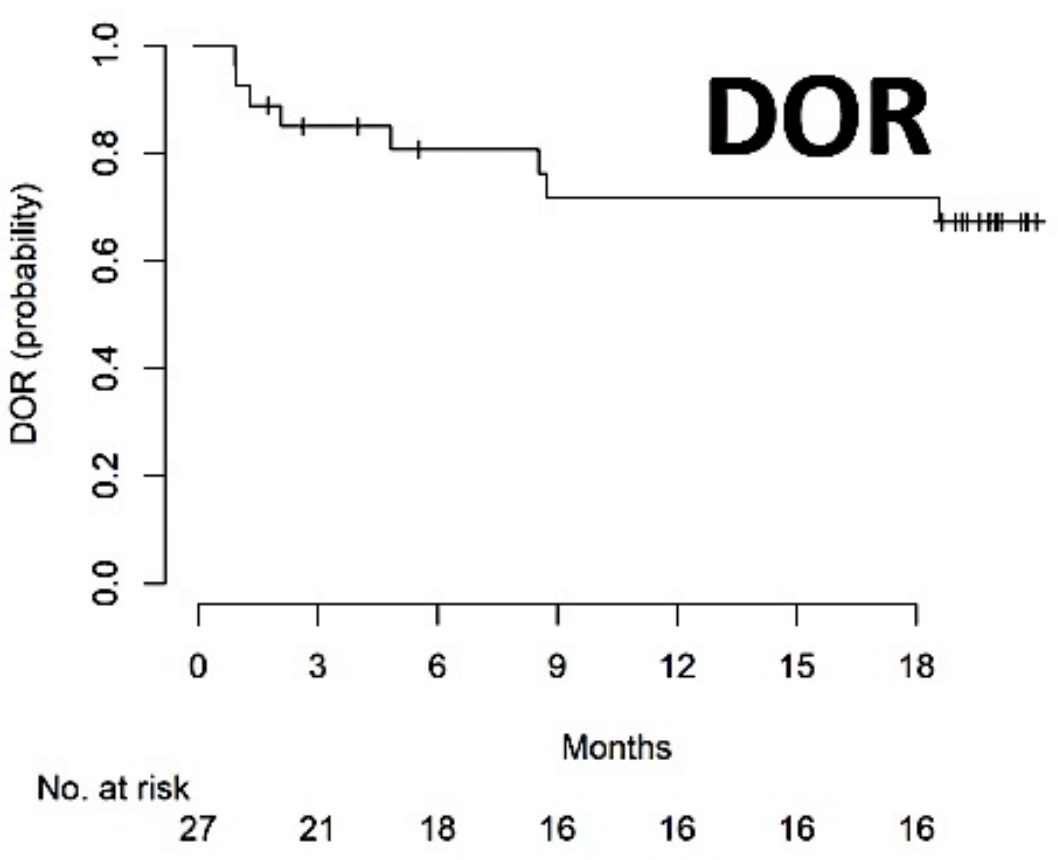
Final results of a phase 2 study of pembrolizumab as first-line treatment in advanced cutaneous squamous cell carcinomas (CSCCs)

Eve Maubec[1,2], Marouane Boubaya[1], Lydia Deschamps[3], Marie Beylot-Barry[4], Peter Petrow[5], Isabelle Scheer-Senyarich[1], Nicole Basset-Seguin[6], Caroline Gaudy[7], Gaëlle Quereux[8], Coralie Bloch-Queyrat[1], Marie-Thérèse Leccia[9], Andrea Stefan[10], Philippe Saiag[11], Florent Grange[12], Nicolas Meyer[13], Sophie Dalac[14], Céline Alloux[15], Isabelle Lopez[5], Annick Tibi[15], and Vincent Lévy[1,2]

ESMO 2023;Abstract 1139P.

First-Line Pembrolizumab for Advanced Cutaneous Squamous Cell Carcinoma





Maubec E et al. ESMO 2023;Abstract 1139P.

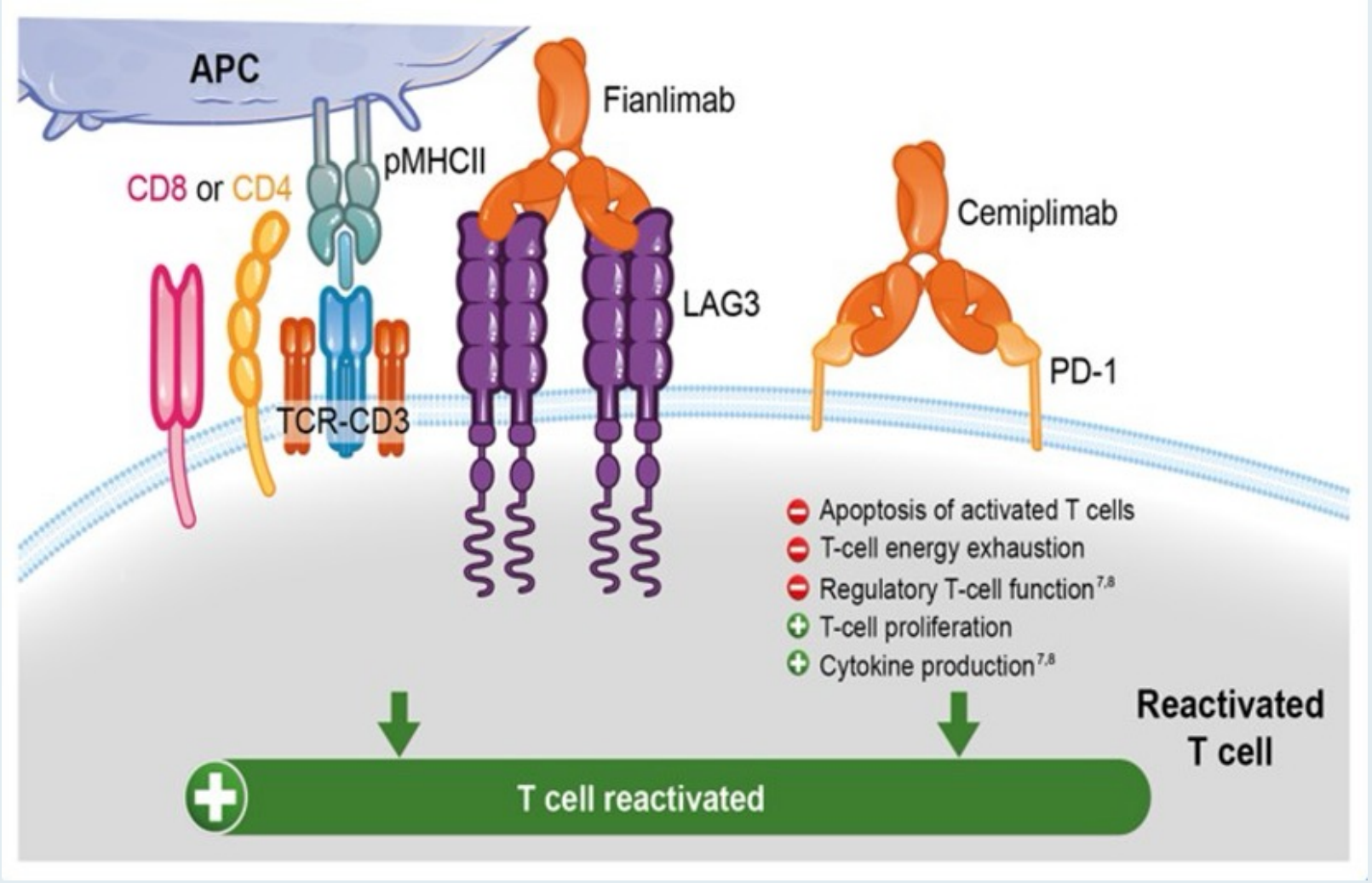
APPENDIX

Significant durable response with fianlimab (anti-LAG-3) and cemiplimab (anti-PD-1) in advanced melanoma: post adjuvant PD-1 analysis

Omid Hamid,[1] Karl D Lewis,[2] Amy Weise,[3] Meredith McKean,[4] Kyriakos P Papadopoulos,[5] John Crown,[6] Sajeve S Thomas,[7] Eugenia Girda,[8] John Kaczmar,[9] Kevin B Kim,[10] Nehal J Lakhani,[11] Melinda Yushak,[12] Tae Min Kim,[13] Guilherme Rabinowits,[14] Alexander Spira,[15] Jayakumar Mani,[16] Fang Fang,[16] Shuquan Chen,[16] JuAn Wang,[16] Laura Brennan,[16] Vladimir Jankovic,[16] Anne Paccaly,[16] Sheila Masinde,[16] Mark Salvati,[16] Matthew G Fury,[16] Israel Lowy,[16] Giuseppe Gullo[16]

ASCO 2023;Abstract 9501.

Fianlimab (Anti-LAG-3) and Cemiplimab for Advanced Melanoma



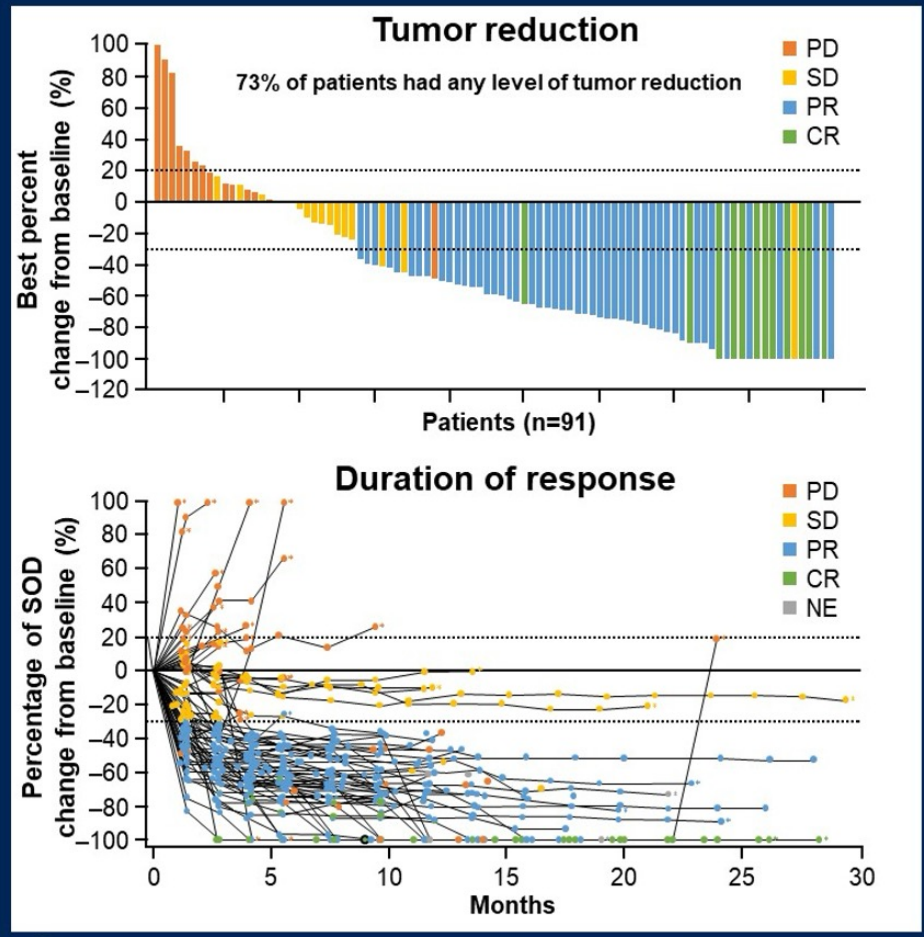
Hamid O et al. ASCO 2023;Abstract 9501.

Fianlimab and Cemiplimab for Advanced Melanoma: Response

Tumor response: combined cohorts

Median follow-up combined (IQR): 12.6 months (8.6–19)

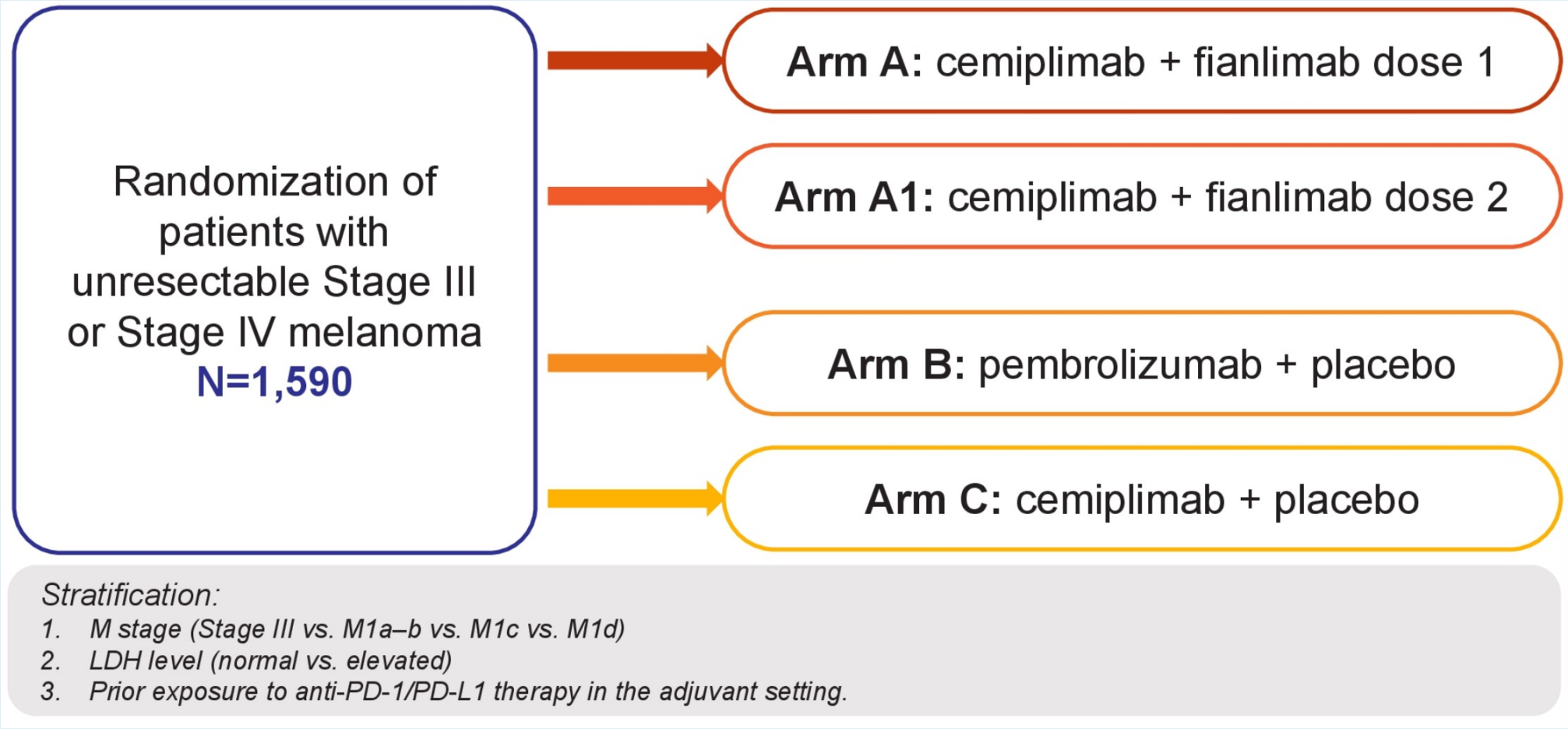
	Cohorts MM1# + MM2# + MM3# Advanced melanoma (N=98)
Treatment exposure, median (IQR), weeks	**33 (15–54)**
ORR, (n)	**61% (60)**
95% CI for ORR	(51, 71)
DoR, median (95% CI), months	**NR (23–NE)**
DCR, (n)	**78% (76)**
95% CI for DCR	(68–85)
Best overall response, (n)	
CR	12% (12)
PR	49% (48)
SD	16% (16)
PD	17% (17)
NE	5% (5)



MM1#, Cohort 6; MM2#, Cohort 15; MM3#, Cohort 16. *Completion or discontinuation of the treatment. All subsequent analyses combining cohorts MM1+MM2+MM3 were post hoc.
CI, confidence interval; CR, complete response; DCR, disease control rate; DoR, duration of response; IQR, interquartile range; MM, metastatic melanoma; n, number; NE, not estimated; NR, not reached; ORR, objective response rate; PD, progressive disease; PR, partial response; SD, stable disease; SOD, sum of diameters.

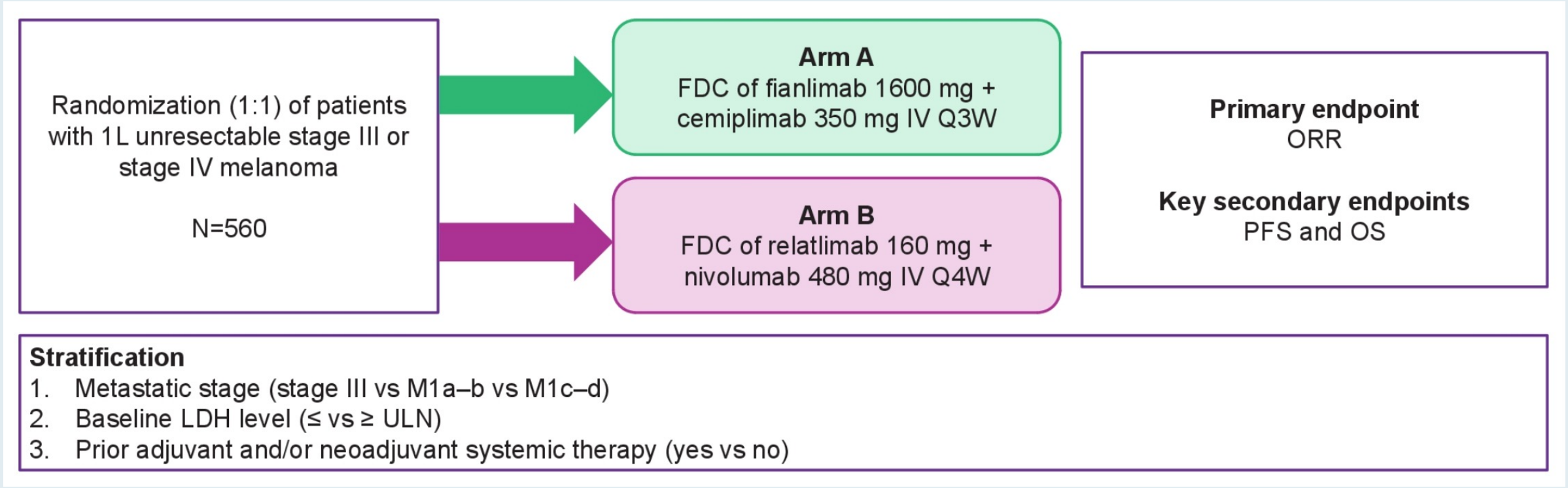
Hamid O et al. ASCO 2023;Abstract 9501.

Ongoing Phase III Trial of Fianlimab/Cemiplimab versus Pembrolizumab for Unresectable or Metastatic Melanoma



Baramidze A et al. ASCO 2023;Abstract TPS9602.

Ongoing Phase III Trial of Fianlimab/Cemiplimab versus Relatlimab/Nivolumab for Unresectable or Metastatic Melanoma



Khushalani NI et al. ASCO 2024;Abstract TPS9611.

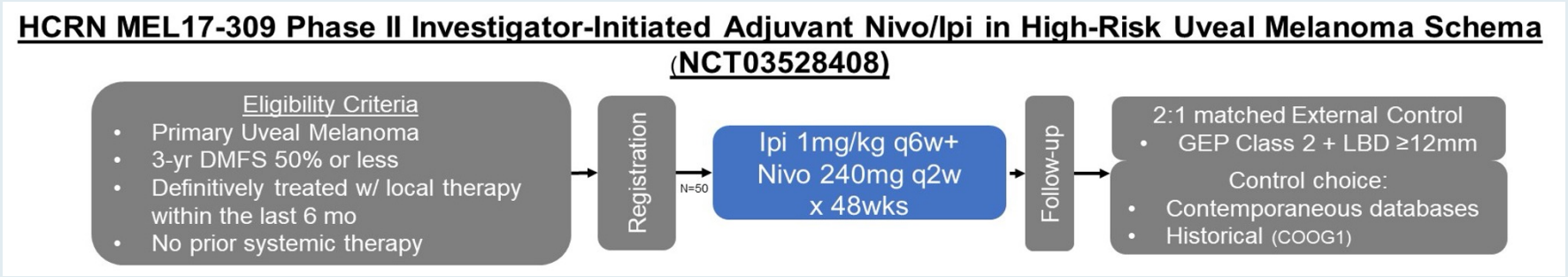
2024 ASCO ANNUAL MEETING

Phase II single-arm multi-center study of adjuvant nivolumab in combination with ipilimumab in patients with high-risk uveal melanoma (UM) (HCRN MEL17-309)

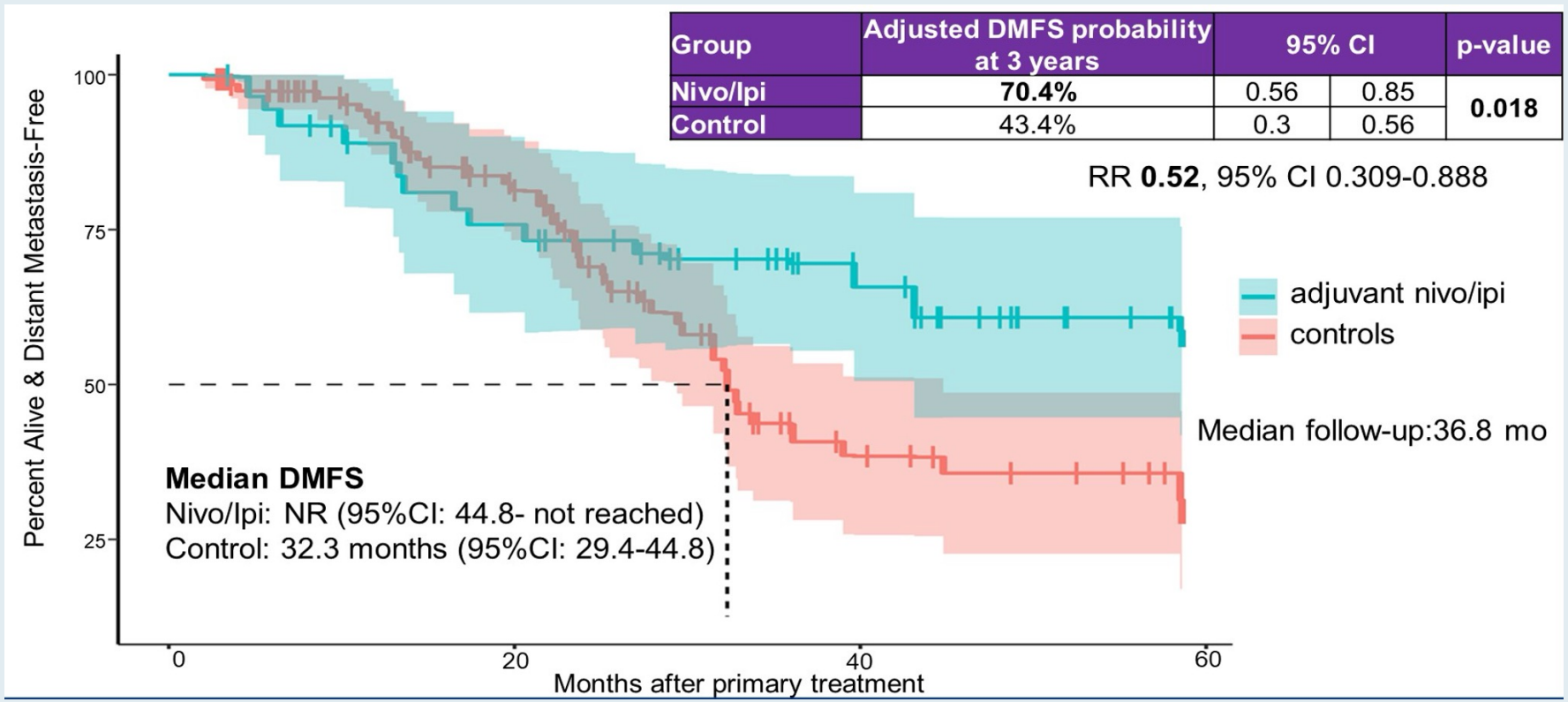
Suthee Rapisuwon, Richard D. Carvajal, George Ansstas, Katy K. Tsai, Leonel F. Hernandez-Aya, Shaheer Khan, Sunandana Chandra, J. William Harbour, Jeffrey A. Sosman, Adil Daud, Christina Decatur, Deniz Ozisik, Ming T. Tan, Michael B. Atkins, Sapna P. Patel*

Abstract 9509

Phase II Study of Adjuvant Nivolumab/Ipilimumab for High-Risk Uveal Melanoma



Group	Adjusted DMFS probability at 3 years	95% CI		p-value
Nivo/Ipi	**70.4%**	0.56	0.85	**0.018**
Control	43.4%	0.3	0.56	



Rapisuwon S et al. ASCO 2024;Abstract 9509.

ORIGINAL ARTICLE

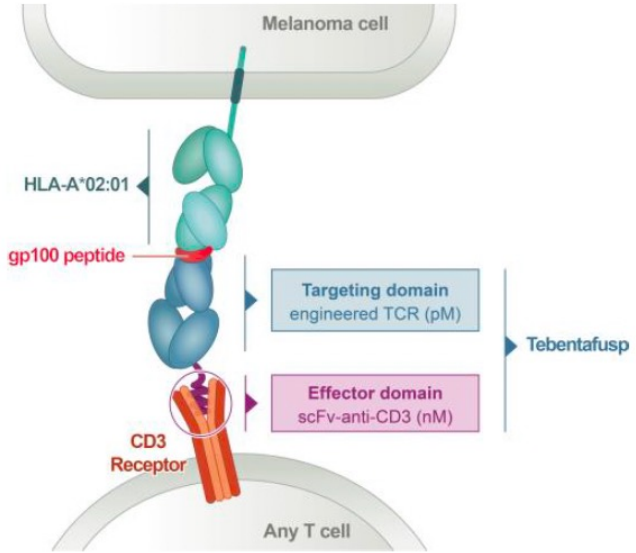
Three-Year Overall Survival with Tebentafusp in Metastatic Uveal Melanoma

Jessica C. Hassel, M.D., Sophie Piperno-Neumann, M.D., Piotr Rutkowski, M.D., Ph.D., Jean-Francois Baurain, M.D., Ph.D., Max Schlaak, M.D., Marcus O. Butler, M.D., Ryan J. Sullivan, M.D., Reinhard Dummer, M.D., John M. Kirkwood, M.D., Marlana Orloff, M.D., Joseph J. Sacco, M.D., Ph.D., Sebastian Ochsenreither, M.D., Anthony M. Joshua, M.B., B.S., Ph.D., Lauris Gastaud, M.D., Brendan Curti, M.D., Josep M. Piulats, M.D., Ph.D., April K.S. Salama, M.D., Alexander N. Shoushtari, M.D., Lev Demidov, M.D., Mohammed Milhem, M.D., Bartosz Chmielowski, M.D., Ph.D., Kevin B. Kim, M.D., Richard D. Carvajal, M.D., Omid Hamid, M.D., Laura Collins, M.S., Koustubh Ranade, Ph.D., Chris Holland, M.S., Constance Pfeiffer, Pharm.D., and Paul Nathan, M.D., Ph.D.

N Engl J Med 2023;389(24):2256-66.

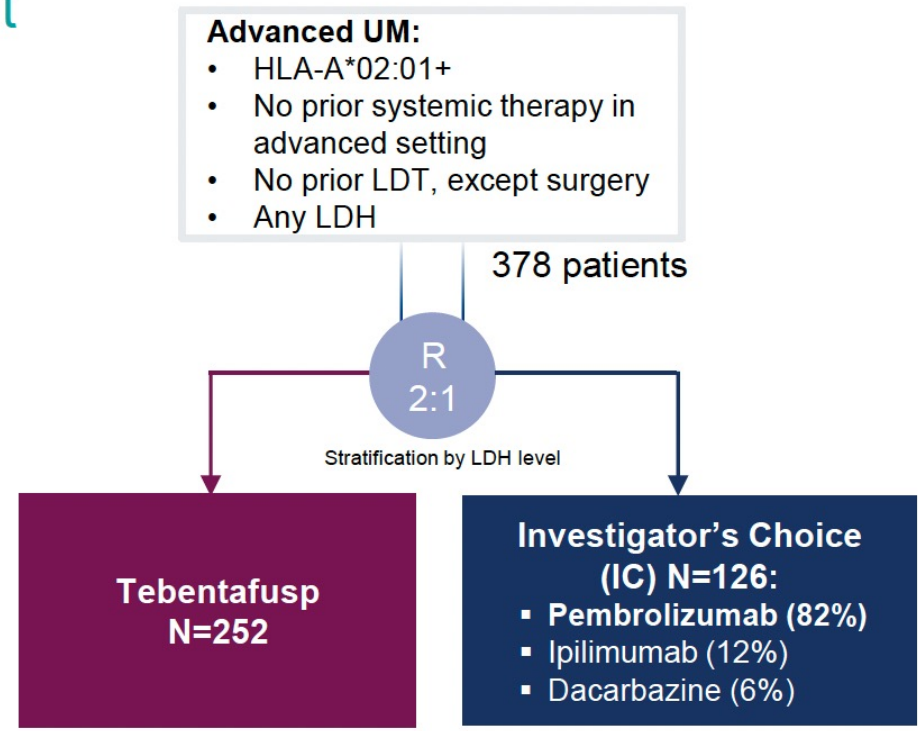
Tebentafusp for Metastatic Uveal Melanoma (UM)

First TCR therapeutic to demonstrate survival benefit



TCR bispecific targeting gp100-HLA*02:01 complexes

- Bispecific, soluble TCR therapeutic
- Affinity-enhanced TCR fused to anti-CD3
- Designed to redirect T cells to gp100+ melanocytic cells



Primary endpoint: OS

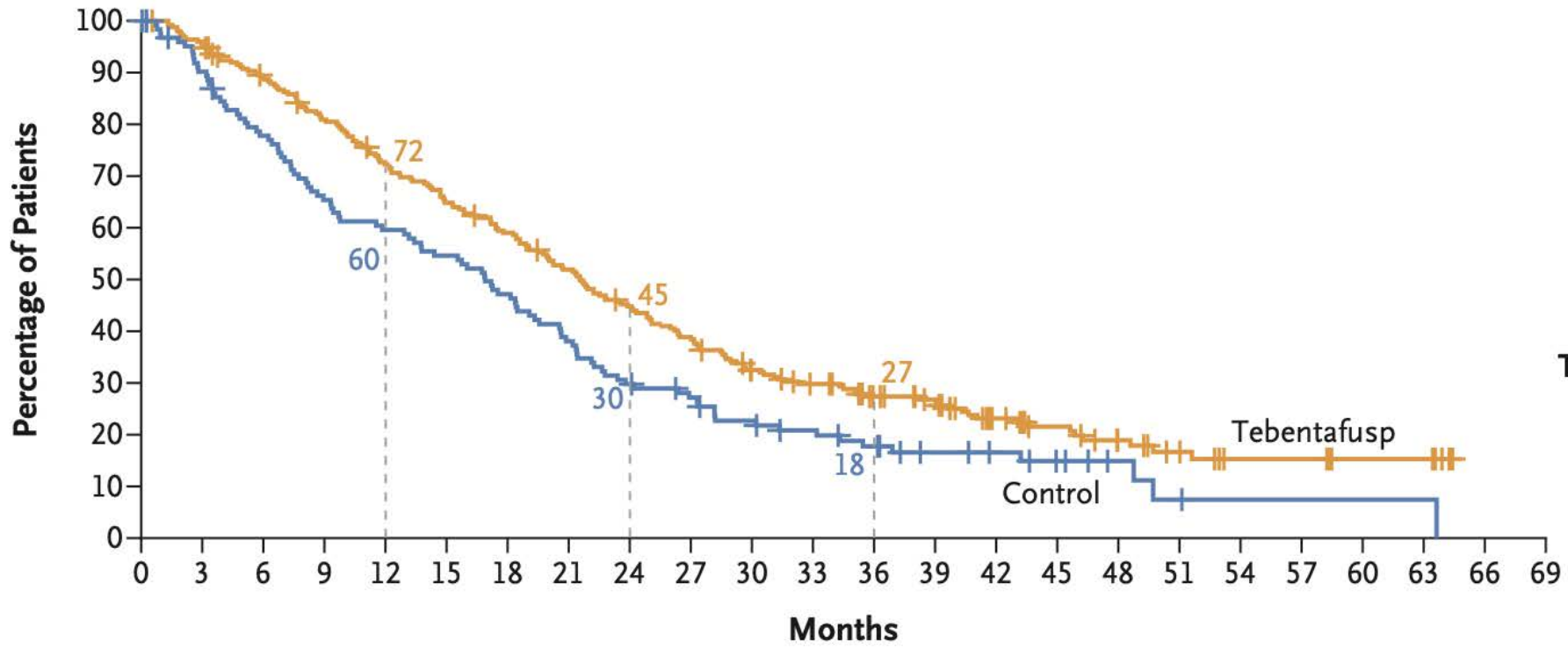
Secondary endpoints: ORR, PFS, DCR, DoR, Safety

- Baseline characteristics were well balanced[1]
- Minimum follow-up for OS: 36 months

LDT = liver-directed therapy; TCR = T-cell receptor

Piperno-Neumann et al. ESMO 2023;Abstract LBA50.

Tebentafusp for Metastatic Uveal Melanoma – Long-Term OS



Median Overall Survival (95% CI)

	mo
Tebentafusp	21.6 (19.0–24.3)
Control	16.9 (12.9–19.5)

Stratified hazard ratio for death, 0.68 (95% CI, 0.54–0.87)

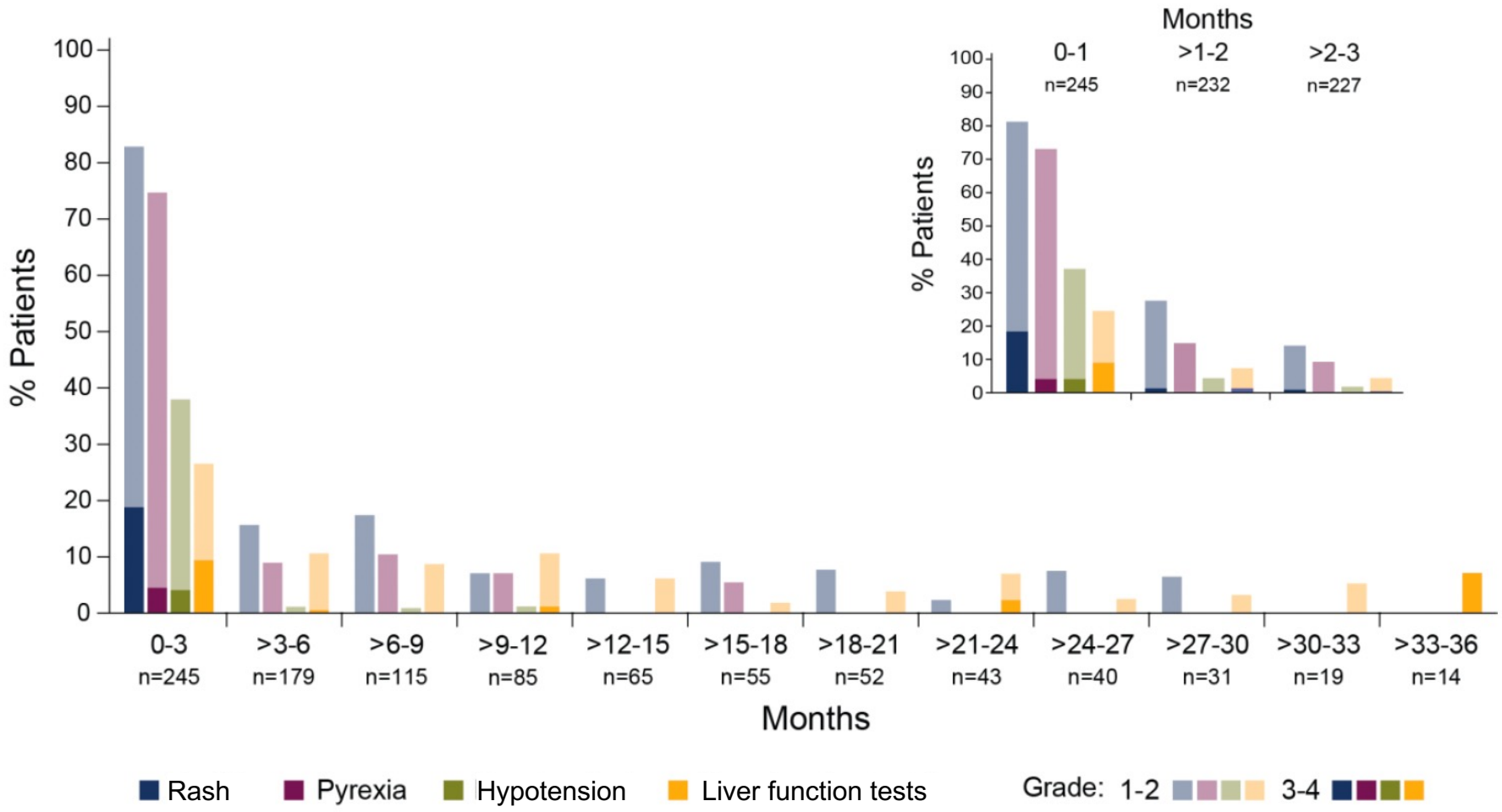
No. at Risk

Tebentafusp	252	239	218	197	175	157	142	124	106	92	73	64	53	47	32	25	18	13	8	8	5	5	0
Control	126	110	94	79	72	66	57	46	36	31	25	21	17	12	10	7	4	2	1	1	1	1	0

Hassel JC et al. *N Engl J Med* 2023;389(24):2256-66.

Tebentafusp for Metastatic Uveal Melanoma – Safety

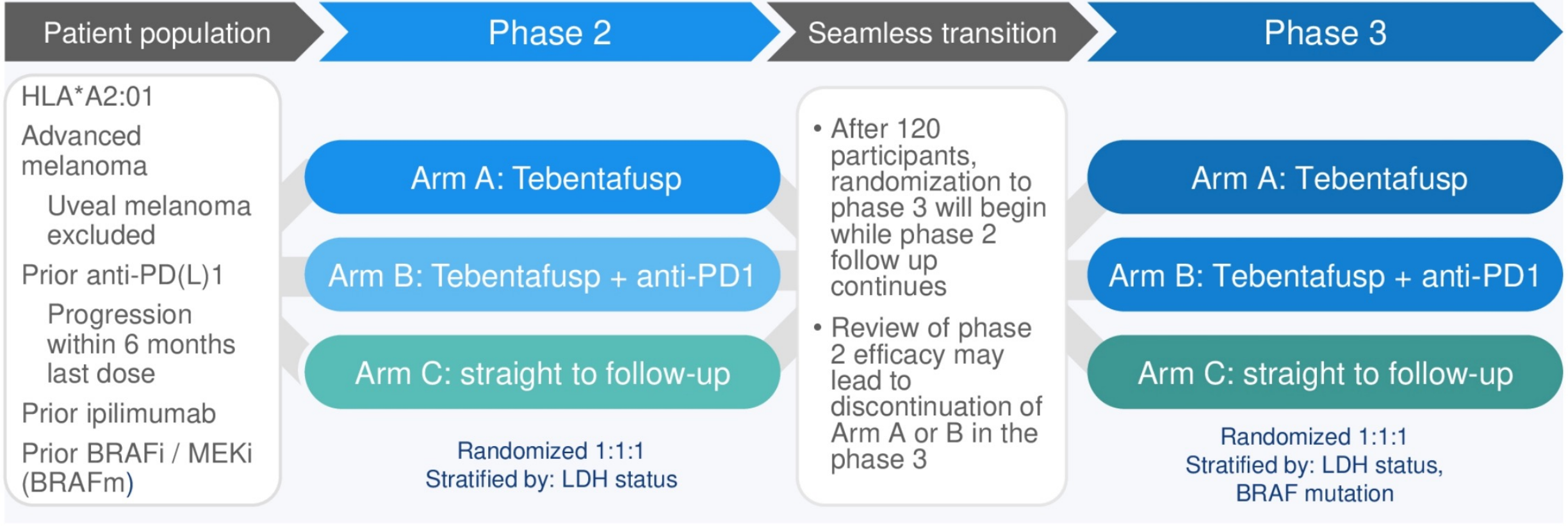
AEs manageable, very low rate of discontinuation (2%) & no treatment-related deaths



Piperno-Neumann et al. ESMO 2023;Abstract LBA50.

Ongoing Phase II/III Trial of Tebentafusp with or without Pembrolizumab

Figure 3: TEBE-AM is a multicenter, open-label, seamless phase 2/3 trial



Daver D et al. ASCO 2023;Abstract TPS9594.

Oncology Today with Dr Neil Love: Novel Agents and Strategies in Lung Cancer

A CME/MOC-Accredited Live Webinar

Thursday, July 11, 2024
5:00 PM – 6:00 PM ET

Faculty

Melissa Johnson, MD
Ticiana Leal, MD
Manish Patel, MD

Moderator

Neil Love, MD

RTP RESEARCH TO PRACTICE

Thank you for joining us!

CME and MOC credit information will be emailed to each participant within 5 business days.

RTP Year in Review 2024