

The Clinical Implications of Key Recent Data Sets in Oncology: A Daylong Multitumor Educational Symposium in Partnership with Florida Cancer Specialists

A CME/MOC- and NCPD-Accredited Event

**Saturday, October 22, 2022
7:30 AM – 5:30 PM ET**

Agenda

Module 1 — Lung Cancer: *Drs Langer and Lovly*

Module 2 — Chronic Lymphocytic Leukemia and Lymphomas:
Drs LaCasce and Smith

Module 3 — Prostate and Bladder Cancers: *Drs Morgans and Yu*

Module 4 — Renal Cell Carcinoma: *Prof Powles*

Module 5 — Multiple Myeloma: *Dr Usmani*

Module 6 — Hepatobiliary Cancers: *Dr Abou-Alfa*

Agenda

Module 7 — Breast Cancer: *Drs Goetz and Krop*

Module 8 — Endometrial Cancer: *Dr Westin*

Module 9 — Ovarian Cancer and PARP Inhibitors: *Dr O'Malley*

Module 10 — Gastrointestinal Cancers: *Drs Messersmith and Strickler*

Module 11 — Melanoma: *Prof Long*

Melanoma Faculty



Prof Georgina Long, AO, BSc, PhD, MBBS

Co-Medical Director

Professor of Medical Oncology and Translational Research

Melanoma Institute Australia

Wollstonecraft, New South Wales, Australia

Melanoma Agenda

MODULE 1: Neoadjuvant and Adjuvant Therapy for Melanoma

MODULE 2: Update on the Management of Metastatic Melanoma

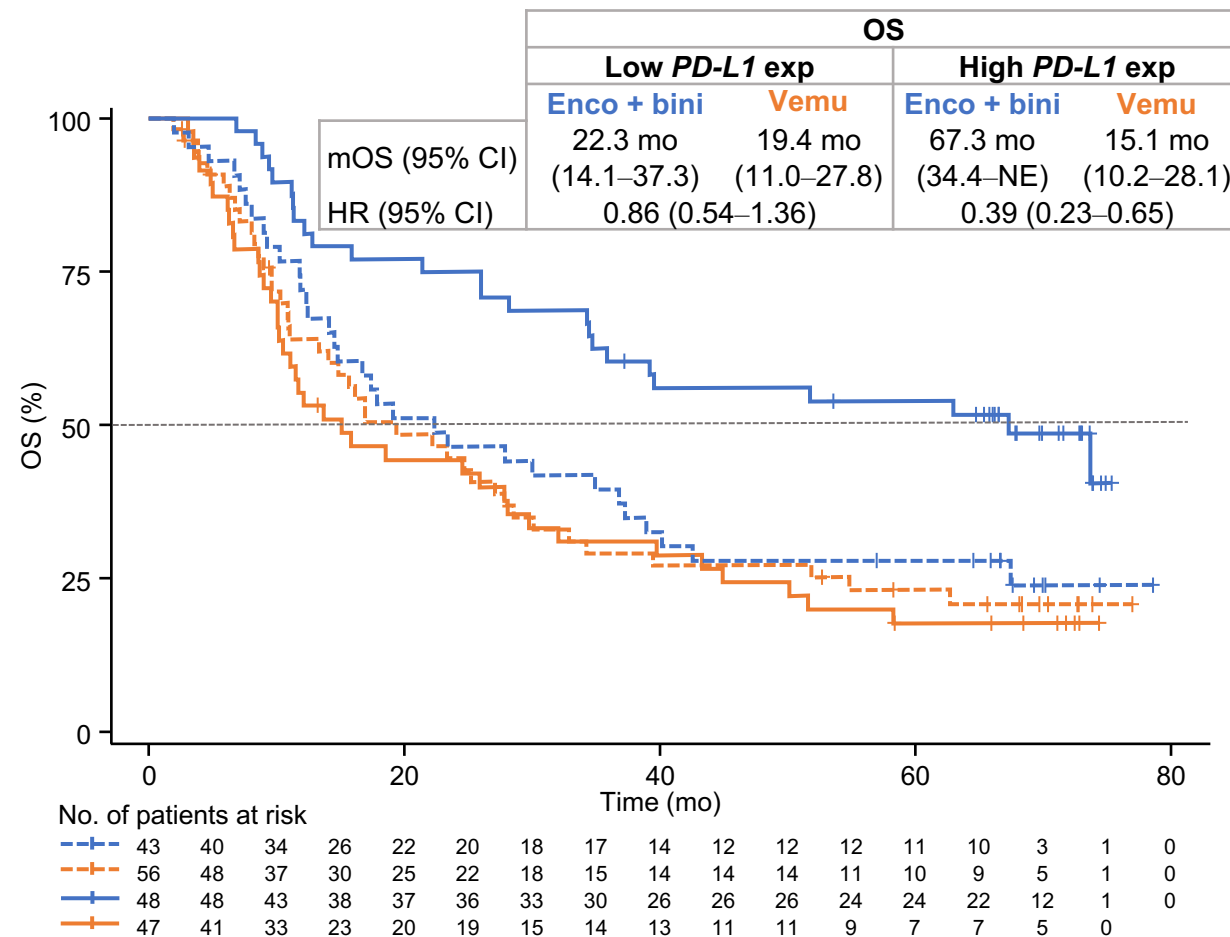
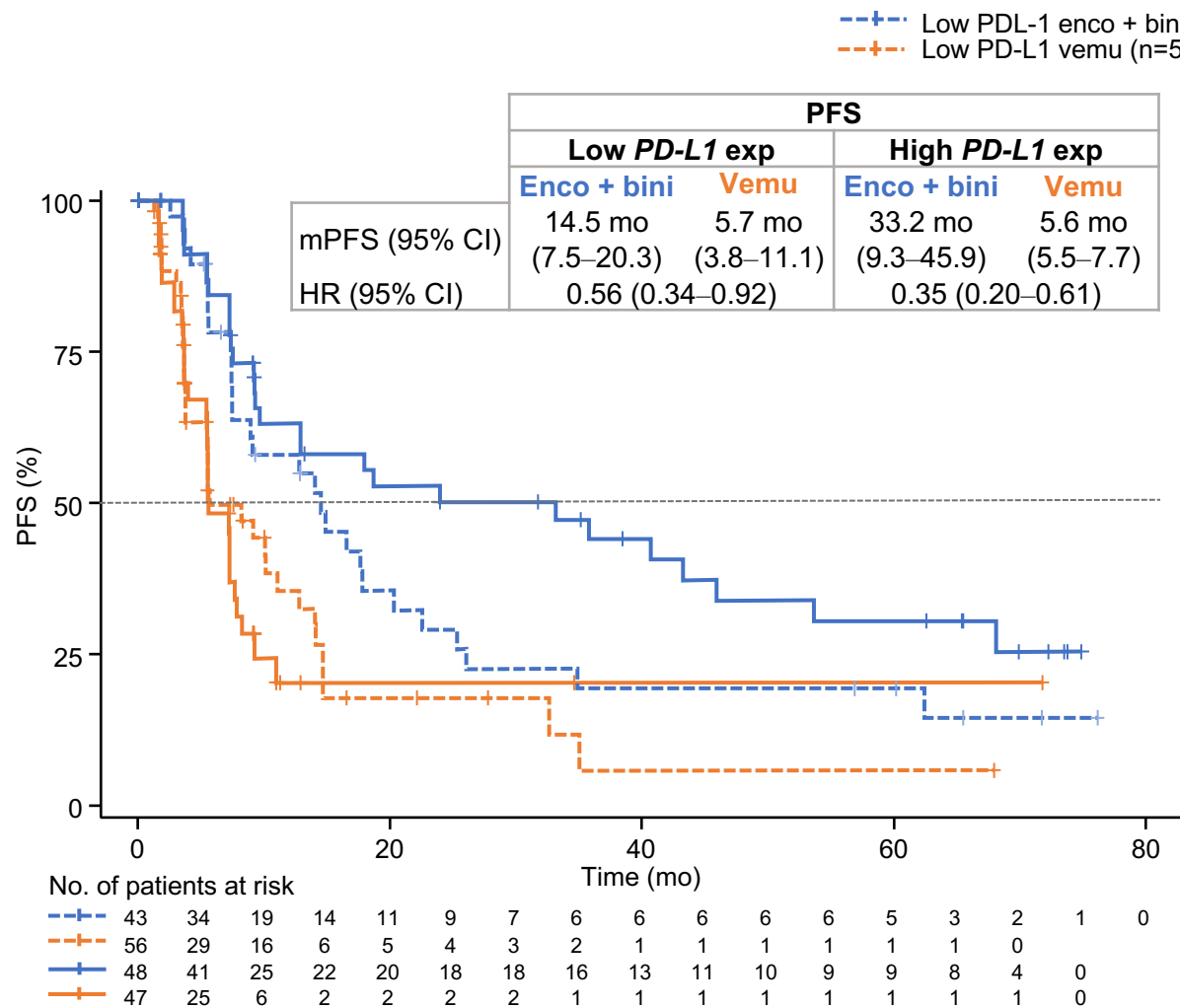
Tumor Biomarker Analysis From COLUMBUS Part 1: Encorafenib + Binimetinib for *BRAF* V600E/K-Mutant Advanced or Metastatic Melanoma

Reinhard Dummer,¹ Nuzhat Pathan,² Shibing Deng,³ Caroline Robert,⁴
Ana Arance,⁵ Jan Willem B. de Groot,⁶ Claus Garbe,⁷ Helen J. Gogas,⁸
Ralf Gutzmer,⁹ Ivana Krajsová,¹⁰ Gabriella Liskay,¹¹ Carmen Loquai,¹²
Mario Mandala,¹³ Dirk Schadendorf,¹⁴ Naoya Yamazaki,¹⁵ Alessandra di
Pietro,¹⁶ Tao Xie,³ Paolo A. Ascierto,¹⁷ Keith Flaherty¹⁸

¹University Hospital Zurich, Zurich, Switzerland; ²Pfizer, Inc, La Jolla, CA, USA; ³Pfizer, Inc, San Diego, CA, USA; ⁴Gustave Roussy and Paris-Saclay University, Villejuif, France; ⁵Hospital Clinic of Barcelona, Barcelona, Spain; ⁶Isala Oncology Center, Zwolle, Netherlands; ⁷University Hospital Tübingen, Tübingen, Germany; ⁸National and Kapodistrian University of Athens, Athens, Greece; ⁹Johannes Wesling Medical Center, Ruhr University Bochum Campus Minden, Minden, Germany; ¹⁰University Hospital Prague, Prague, Czech Republic; ¹¹National Institute of Oncology, Budapest, Hungary; ¹²University Medical Center of the Johannes Gutenberg University Mainz, Mainz, Germany; ¹³University of Perugia, Perugia, Italy; ¹⁴University Hospital Essen, West German Cancer Center and German Cancer Consortium, Partner Site Essen, Essen, Germany; ¹⁵National Cancer Center Hospital, Tokyo, Japan; ¹⁶Pfizer, Inc, Milan, Italy; ¹⁷Istituto Nazionale Tumori IRCCS Fondazione Pascale, Napoli, Italy; ¹⁸Massachusetts General Hospital, Boston, MA, USA



PFS and OS by *PD-L1* Gene Expression



There was a larger treatment effect of encorafenib + binimetinib vs vemurafenib on PFS and OS in the high *PD-L1* expression^a group compared with the low *PD-L1* expression group

COLUMBUS part 1 tumor biomarker analysis (data cutoff: Sep 15, 2020).

^aHigh *PD-L1* expression was defined as above median expression.

bini, binimetinib; enco, encorafenib; exp, expression; vemu, vemurafenib.

Melanoma Agenda

MODULE 1: Neoadjuvant and Adjuvant Therapy for Melanoma

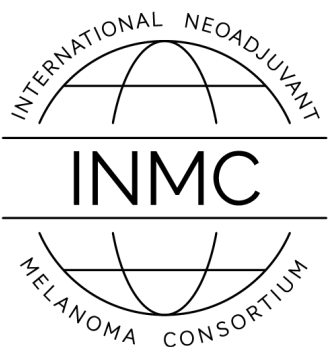
MODULE 2: Update on the Management of Metastatic Melanoma

Neoadjuvant and Adjuvant Therapy Where are we now?

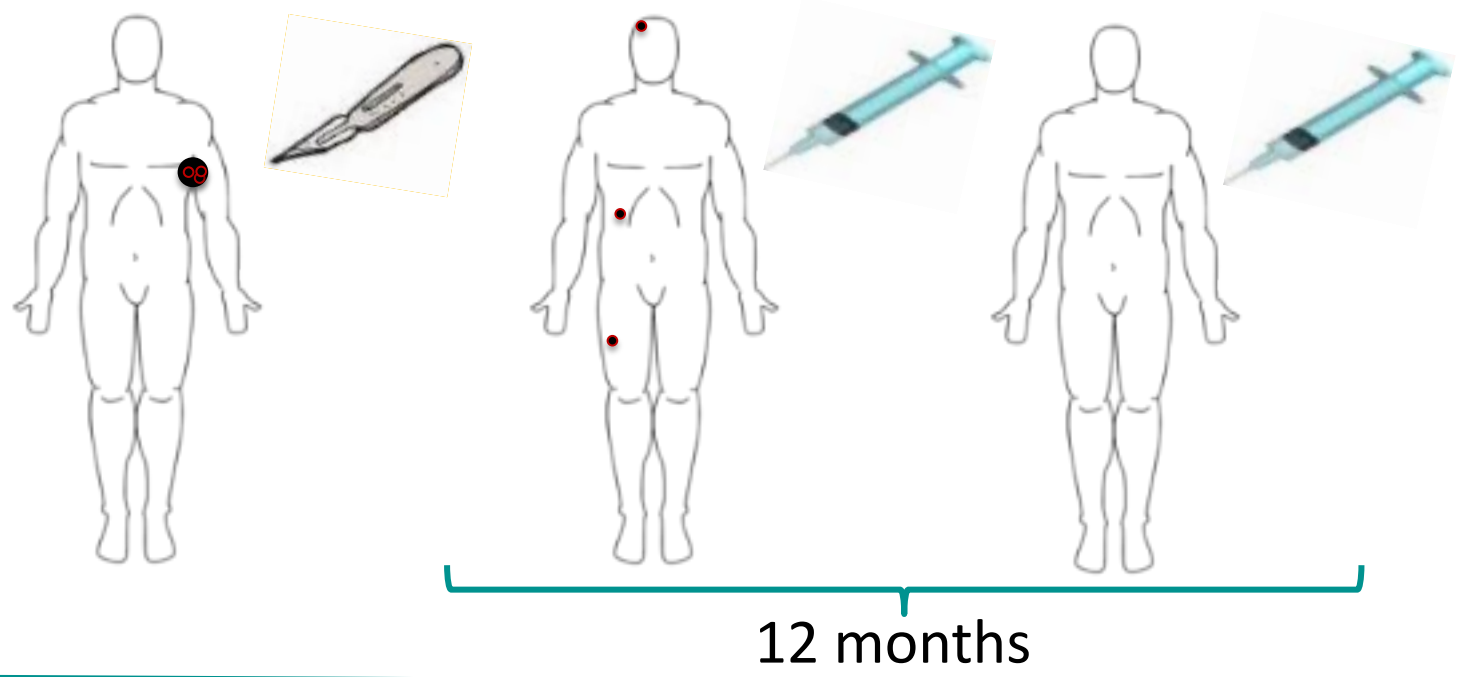
Georgina V Long

Melanoma Institute Australia, The University of Sydney

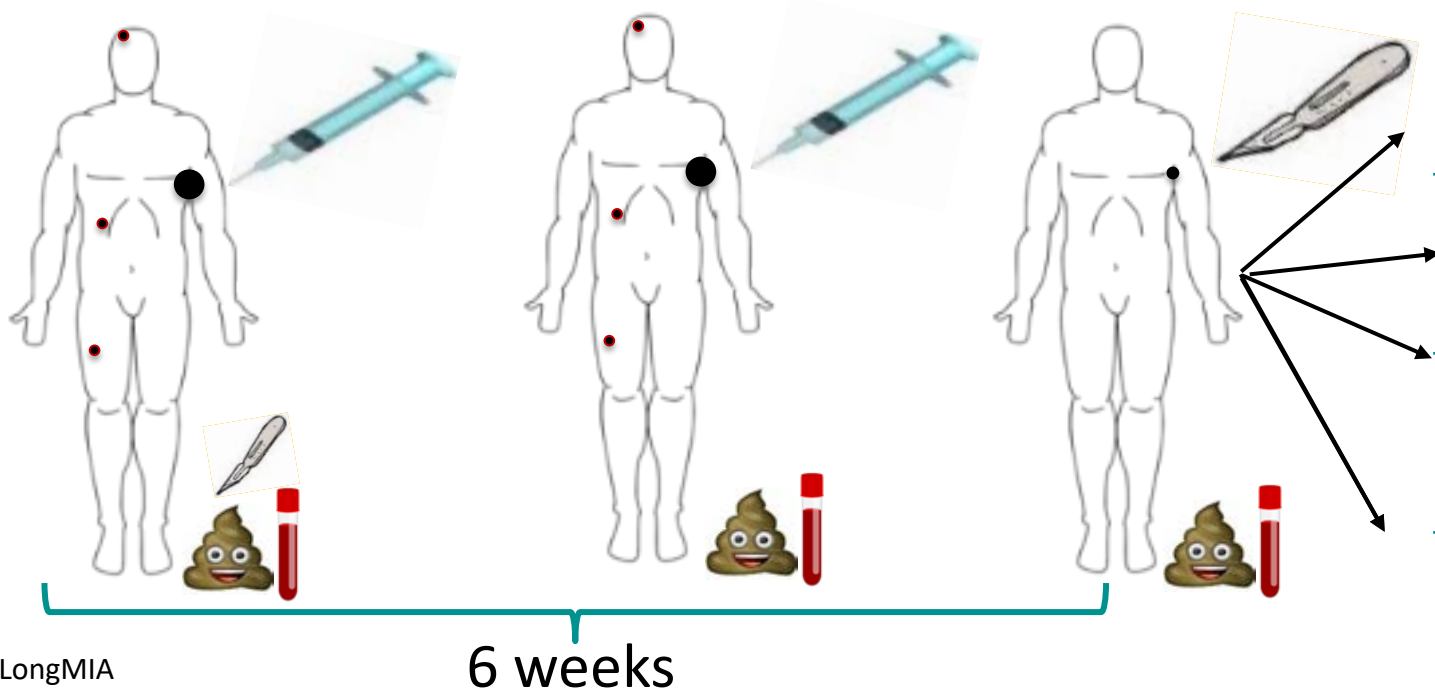
Royal North Shore and Mater Hospitals



Adjuvant



Neoadjuvant



- Pathological Complete **0% TC**
- Pathological Near Complete **≤ 10% TC**
- Pathological Partial Respo **>10%, ≤ 50% TC**
- No Pathological Response **>50% TC**

1. Adjuvant Therapy

- Efficacy Update
- BRAF targeted therapy vs Anti-PD1

2. Neoadjuvant Therapy

- The Neoadjuvant Platform - Efficacy and Advantages
- Next Steps

1. Adjuvant Therapy

- **Efficacy Update**
- **BRAF targeted therapy vs Anti-PD1**

2. Neoadjuvant Therapy

- The Neoadjuvant Platform - Efficacy and Advantages
- Next Steps

ORIGINAL ARTICLE

Adjuvant Dabrafenib plus Trametinib in Stage III BRAF-Mutated Melanoma

G.V. Long, A. Hauschild,
V. Chiarion-Sileni, J. Larkin, M.
L. Mortier, J. Schachter, D. Schadt,
B. Mookerjee, J. Legos, R.

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Adjuvant Nivolumab versus Ipilimumab in Resected Stage III or IV Melanoma

J. Weber, M. Mandala, M. Del Vecchio, H.J. Gogas, A.M. Arance, C.L. Cowey,
S. Dalle, M. Schenker, V. Chiarion-Sileni, I. Marquez-Rodas, J.-J. Grob, M.O. Butler,

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Adjuvant Pembrolizumab versus Placebo in Resected Stage III Melanoma

V.M. Eggermont, M.D., Ph.D., Christian U. Blank, M.D., Ph.D.,
ala, M.D., Georgina V. Long, M.D., P.D., Victoria Atkinson, M.D.,
Dalle, M.D., Andrew Haydon, M.D., Mikhail Lichinitser, M.D.,
k, M.D., Matteo S. Carlino, M.D., Ph.D., Shahneen Sandhu, M.D.,
kin, M.D., Susana Puig, M.D., Ph.D., Paolo A. Ascierto, M.D.,
iki, M.D., Dirk Schadendorf, M.D., Ph.D., Rutger Koornstra, M.D.,
onel Hernandez-Aya, M.D., Michele Maio, M.D., Ph.D.,
van den Eertwegh, M.D., Ph.D., Jean-Jacques Grob, M.D., Ph.D.,
1.D., Rahima Jamal, M.D., Paul Lorigan, M.D., Nageatte Ibrahim, M.D.,
aud, M.D., Alexander C.J. van Akkooi, M.D., Ph.D., Stefan Suciu, Ph.D.,
and Caroline Robert, M.D., Ph.D.

12 Months of Treatment after Surgery
RFS HR 0.47-0.57
~50% reduction in risk of recurrence

Adjuvant Phase 3 Clinical Trials for Resected Melanoma

Primary Analyses of Efficacy Endpoints

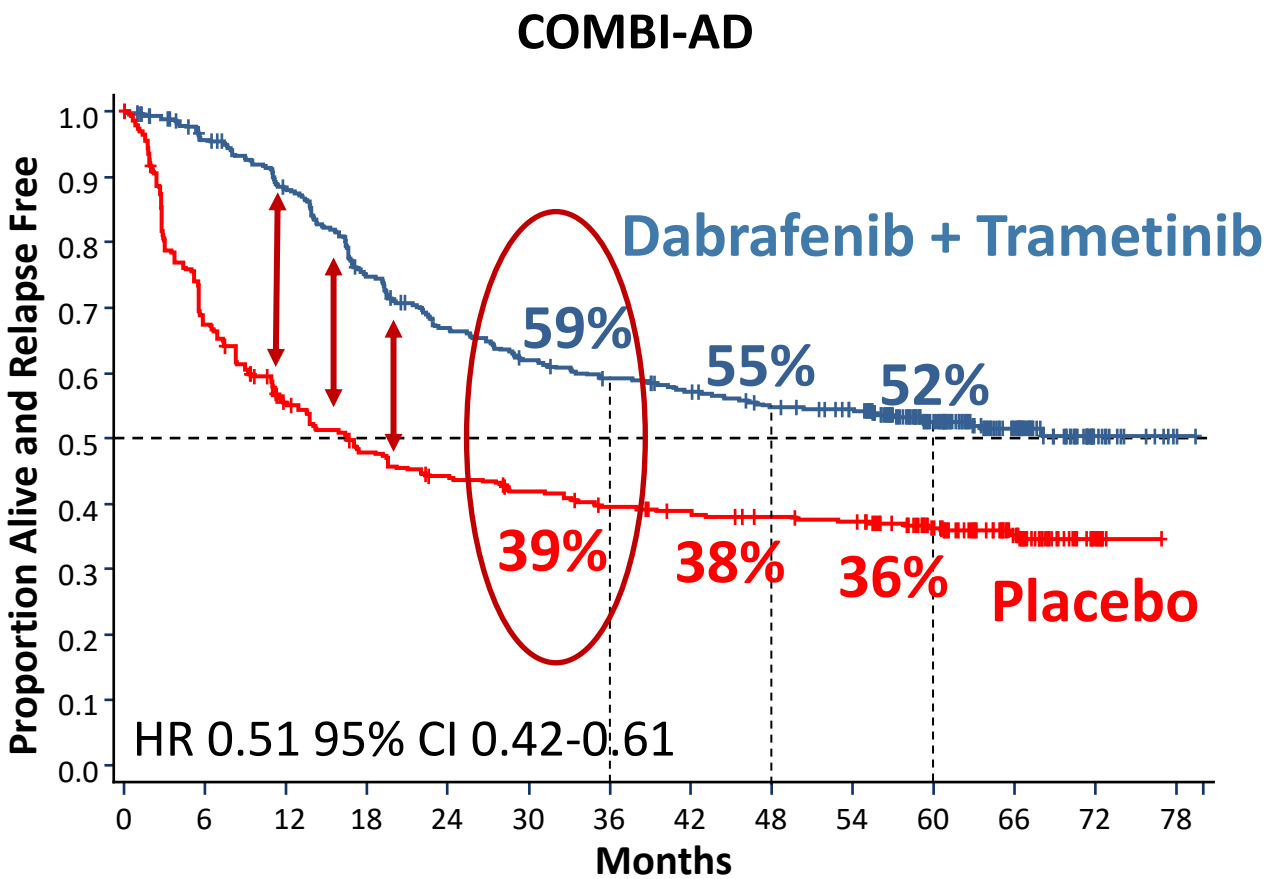


AJCC Stage	Trial	Therapy	RFS HR ($\geq 95\%$ CI)	DMFS HR	OS HR
Stage IIB,C	Keynote 716	Pembro vs Pbo	0.65 (0.46-0.92) P=0.00658	0.64 (0.47-0.88) P=0.0029	-
	Checkmate 76K	Nivo vs Pbo	0.42 (0.30-0.59) P<0.0001	0.47 (0.30-0.72)	-

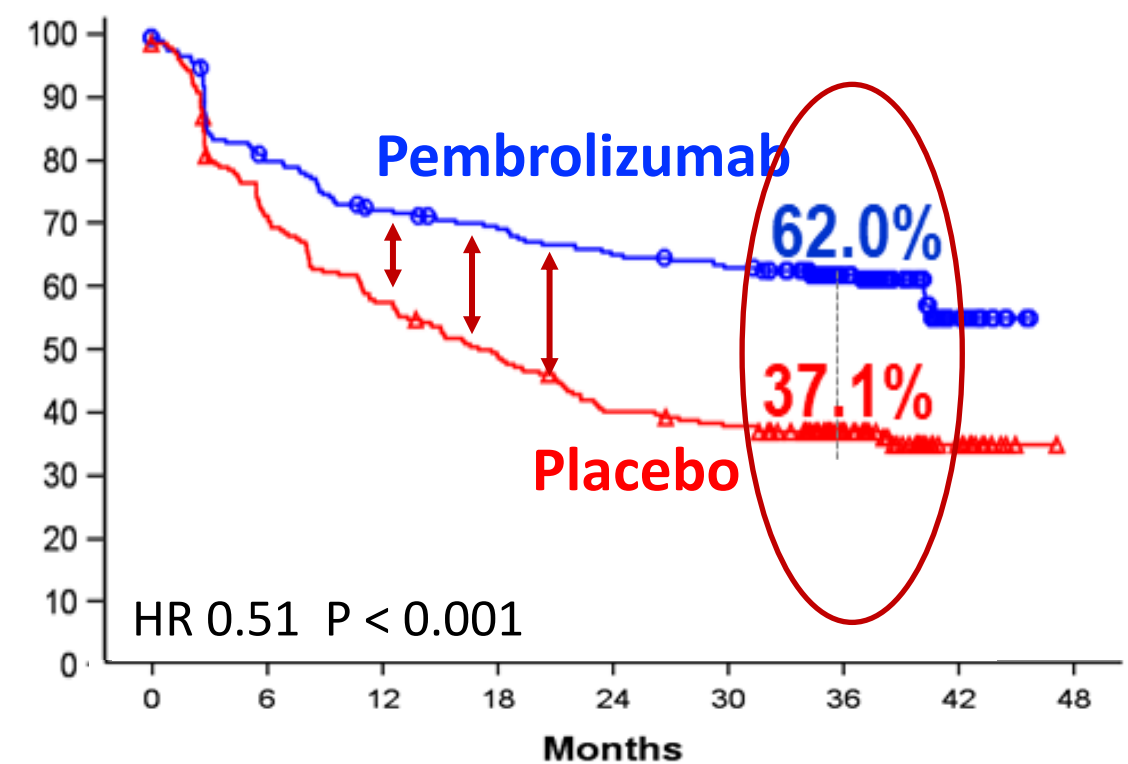
Adjuvant Anti-PD1 or BRAF+MEK inhibition for Adjuvant Therapy in V600 BRAF Mutant Melanoma?

Relapse Free Survival in BRAF Mutant Melanoma

BRAF Targeted Therapy vs Anti-PD1



Keynote 054/EORTC 1325
V600 BRAF mutation positive only



Dummer et al NEJM 2020; Eggermont et al JCO 2020



Outline

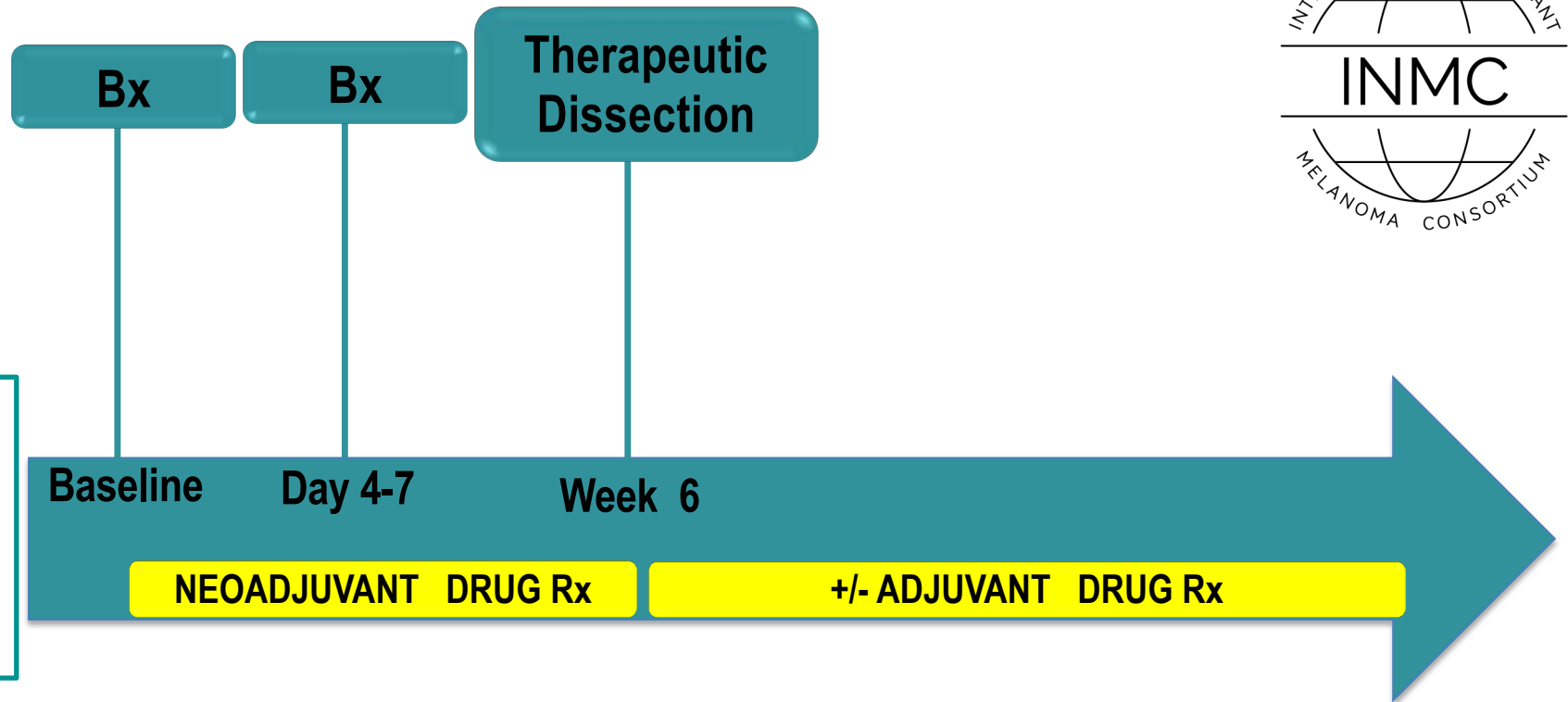
1. Adjuvant Therapy

- Efficacy Update
- BRAF targeted therapy vs Anti-PD1

2. Neoadjuvant Therapy

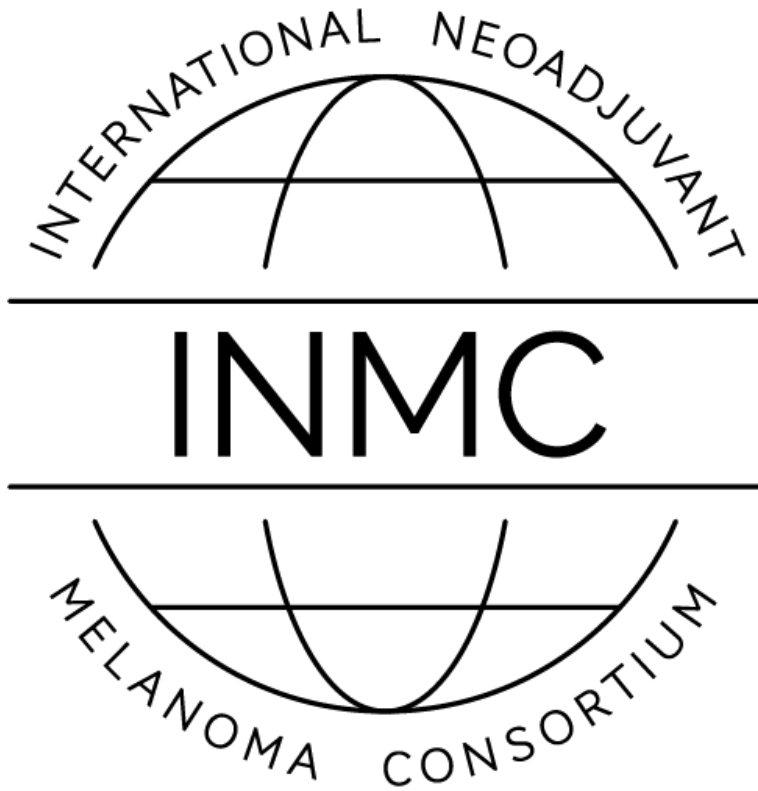
- **The Neoadjuvant Platform - Efficacy and Advantages**
- **Next Steps**

Neoadjuvant Platform



Primary Endpoint: Pathological Response

Secondary Endpoint: Relapse-Free Survival



<https://melanoma-inc.org/>

- 400 International members
- Pharma engagement
- Consultation FDA
- White papers/guidelines for:
 - Trial design
 - Pathological assessment
 - Surgical endpoints
 - Biospecimens
 - Translational Research
- Pooled data

Annals Onc 2018

Pathological assessment of resection specimens after neoadjuvant therapy for metastatic melanoma

M. T. Tetzlaff^{1,2*}, J. L. Messina³, J. E. Stein⁴, X. Xu⁵, R. N. Amaria⁶, C. U. Blank⁷, B. A. van de Wiel⁷, P. M. Ferguson⁸, R. V. Rawson⁸, M. I. Ross⁹, A. J. Spillane¹⁰, J. E. Gershenwald^{9,11}, R. P. M. Saw⁸, A. C. J. van Akkooi⁷, W. J. van Houdt⁷, T. C. Mitchell¹², A. M. Menzies¹⁰, G. V. Long¹³, J. A. Wargo^{9,14}, M. A. Davies^{2,6,15}, V. G. Prieto^{1,16}, J. M. Taube^{4†} & R. A. Scolyer^{8†}

Neoadjuvant systemic therapy in melanoma: recommendations of the International Neoadjuvant Melanoma Consortium

Lancet Onc 2019

Rodabe N Amaria*, Alexander M Menzies*, Elizabeth M Burton*, Richard A Scolyer*, Michael T Tetzlaff*, Robert Antdbacka, Charlotte Ariyan, Roland Bassett, Brett Carter, Adil Daud, Mark Faries, Leslie A Fecher, Keith Flaherty, Jeffrey E Gershenwald, Omid Hamid, Angela Hong, John Kirkwood, Serigne Lo, Kim Margolin, Jane Messina, Michael Postow, Helen Rizos, Merrick I Ross, Elisa A Rozeman, Robyn P M Saw, Vernon Sondak, Ryan J Sullivan, Janis M Taube, John F Thompson, Bart A van de Wiel, Alexander M Eggermont, Michael A Davies, The International Neoadjuvant Melanoma Consortium members†, Paolo A Ascierto†, Andrew J Spillane†, Alexander C J van Akkooi†, Jennifer A Wargo†, Christian U Blank†, Hussein A Tawbi†, Georgina V Long†

Ann Surg Oncol
https://doi.org/10.1245/s10434-021-11236-y

Annals of
SURGICAL ONCOLOGY
OFFICIAL JOURNAL OF THE SOCIETY OF SURGICAL ONCOLOGY



CONTINUING EDUCATION – MELANOMA

Annals Surg Onc 2022

Neoadjuvant Systemic Therapy (NAST) in Patients with Melanoma: Surgical Considerations by the International Neoadjuvant Melanoma Consortium (INMC)

Alexander C. J. van Akkooi, MD, PhD¹, Tina J. Hieken, MD², Elizabeth M. Burton, MBA³, Charlotte Ariyan, MD, PhD⁴, Paolo A. Ascierto, MD, BC⁵, Salvatore V. M. A. Asero, MD, PhD⁶, Christian U. Blank, MD, PhD¹, Matthew S. Block, MD, PhD², Genevieve M. Boland, MD, PhD⁷, Corrado Caraco, MD, PhD², Sydney Chng, MBBS, PhD, FRACS^{8,9,10}, B. Scott Davidson, MD¹¹, Joao Pedreira Duprat Neto, MD, PhD¹², Mark B. Faries, MD¹³, Jeffrey E. Gershenwald, MD, FACS, FFAAAS³, Dirk J. Grunhagen, MD, PhD¹⁴, David E. Gyorki, MBBS, MD, FRACS¹⁵, Dale Han, MD¹⁶, Andrew J. Hayes, MBBS, PhD¹⁷, Winan J. van Houdt, MD, PhD¹, Giorgos C. Karakousis, MD, MS¹⁸, Willem M. C. Klop, MD, PhD¹, Georgina V. Long, BSc, PhD, MBBS, FRACP, FAHMS^{8,10,19,20}, Michael C. Lowe, MD, MA, FACS, FSSO²¹, Alexander M. Menzies, MBBS, PhD^{8,10,19,20}, Roger Olofsson Bagge, MD, PhD²², Thomas E. Pennington, BSc, MBBS, MS, FRACS^{8,10}, Piotr Rutkowski, MD, PhD²³, Robyn P. M. Saw, MBBS, MS, FRACS^{8,9,10}, Richard A. Scolyer, MBBS, MD, FRCPA, FRCPATH, FAHMS^{8,9,10}, Kerwin F. Shannon, MBBS, FRACS^{8,10}, Vernon K. Sondak, MD²⁴, Hussein Tawbi, MD, PhD³, Alessandro A. E. Testori, MD²⁵, Mike T. Tetzlaff, MD, PhD²⁶, John F. Thompson, MD, FRACS, FACS^{8,9,10,20}, Jonathan S. Zager, MD, FACS²⁴, Charlotte L. Zuur, MD, PhD^{1,27}, Jennifer A. Wargo, MD³, Andrew J. Spillane, MD^{8,10,19,20}, Merrick I. Ross, MD³ on behalf of International Neoadjuvant Melanoma Consortium (INMC)

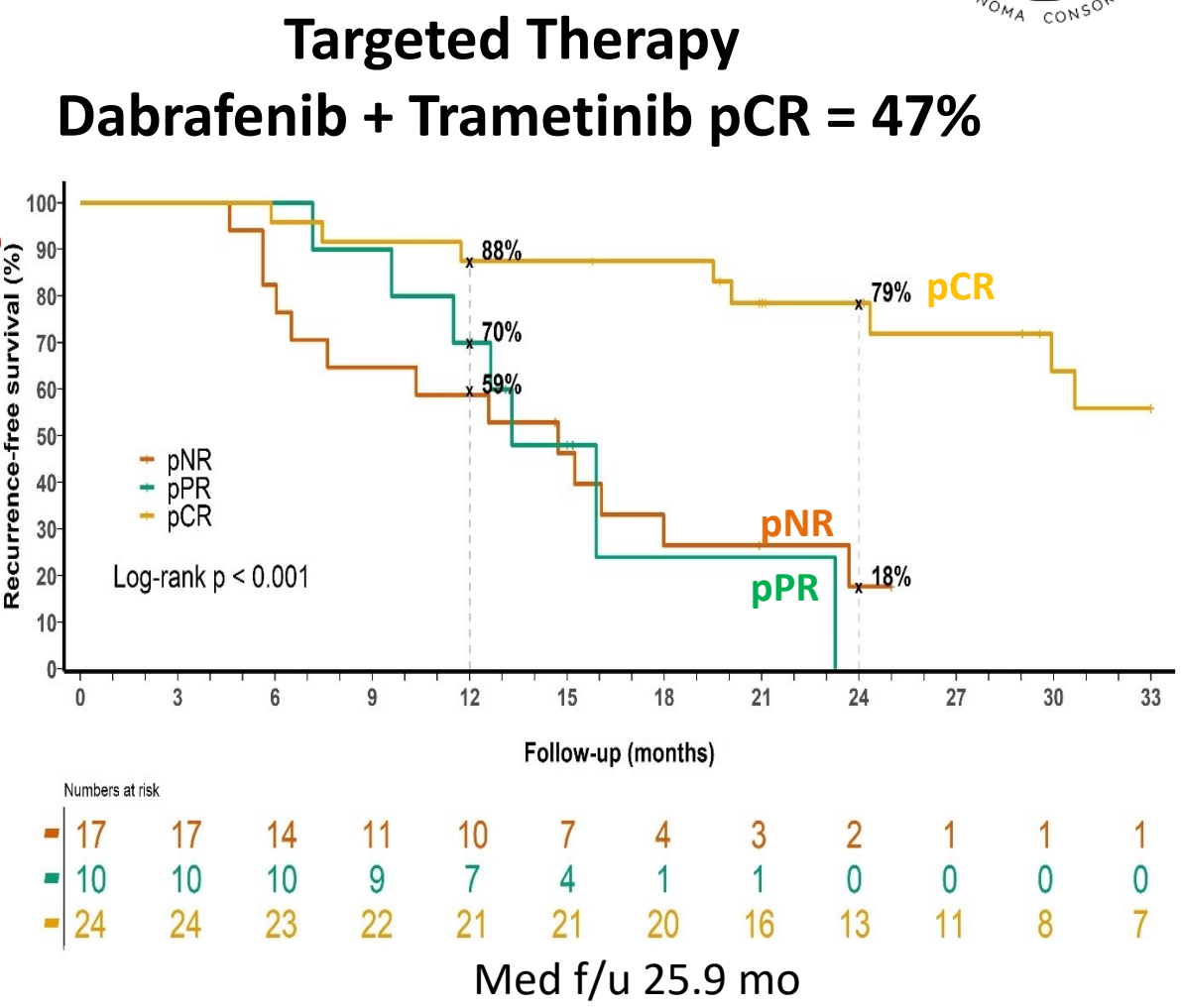
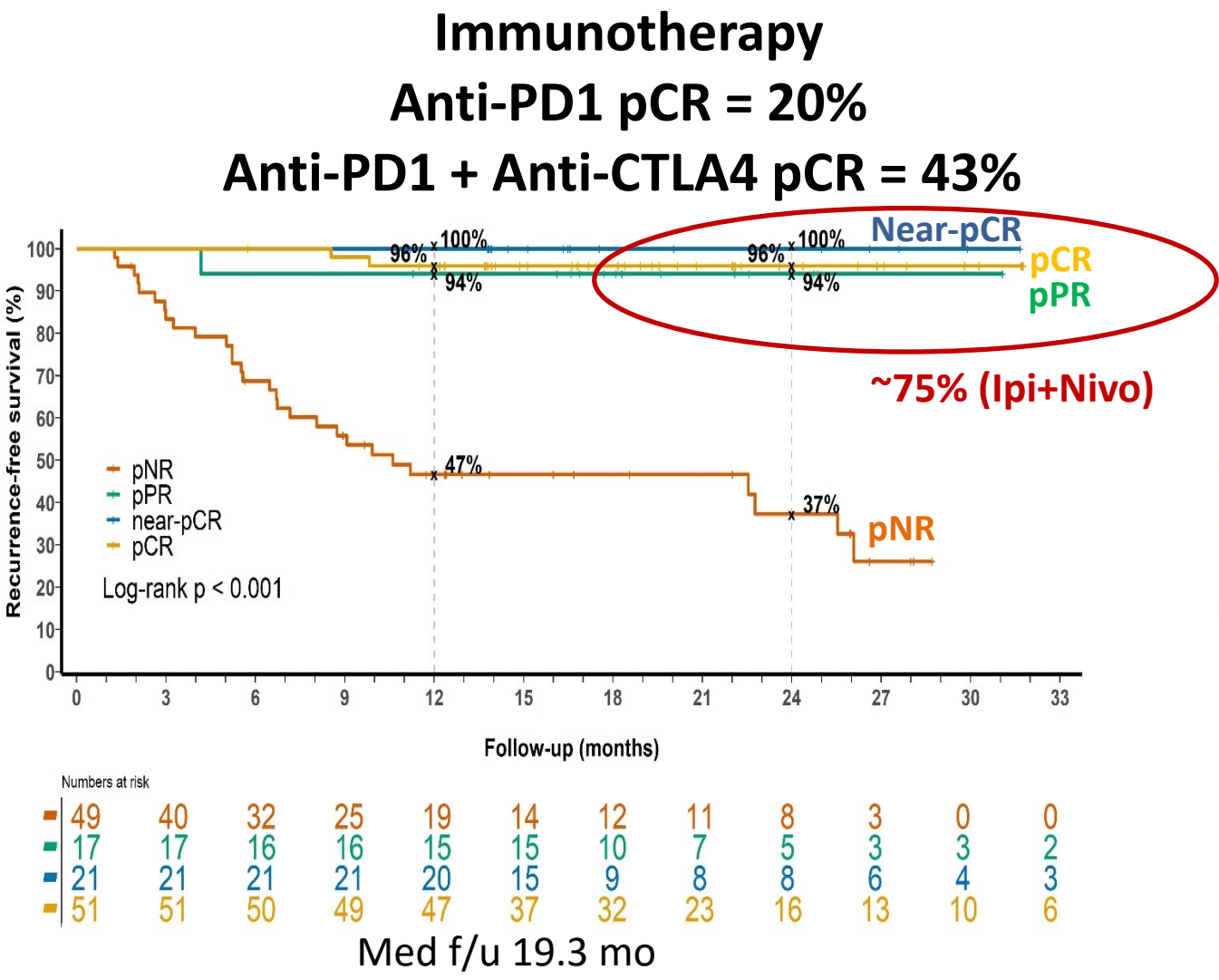


Pathological response and survival with neoadjuvant therapy in melanoma: a pooled analysis from the International Neoadjuvant Melanoma Consortium (INMC)

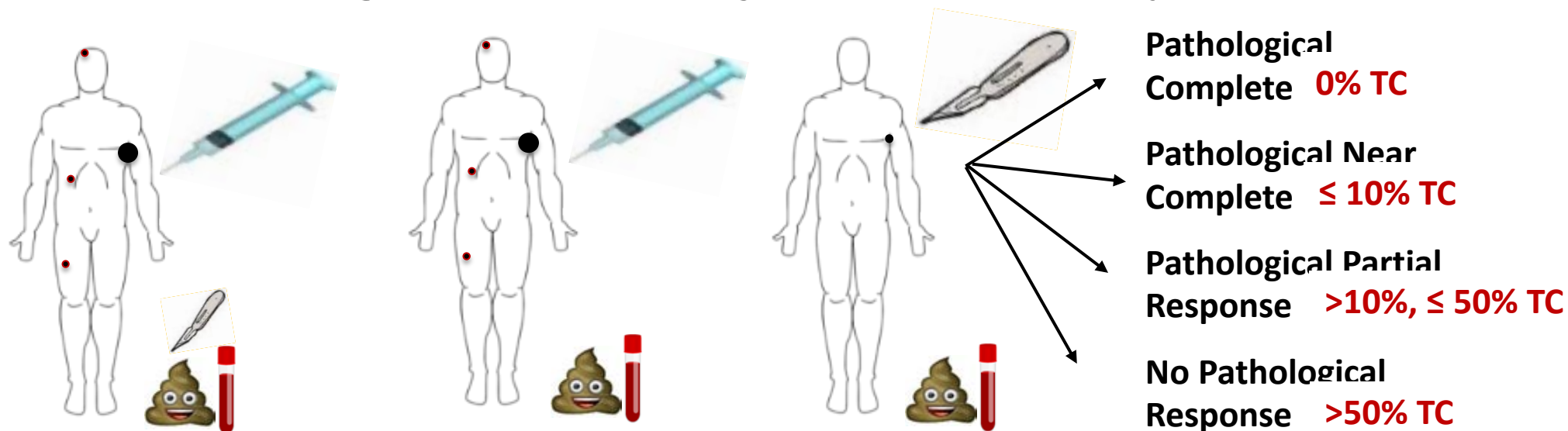
Alexander M. Menzies^{1,2,3,12}, Rodabe N. Amaria^{4,12}, Elisa A. Rozeman^{5,12}, Alexander C. Huang^{6,7,12}, Michael T. Tetzlaff^{4,12}, Bart A. van de Wiel^{5,12}, Serigne Lo^{1,2,12}, Ahmad A. Tarhini⁸, Elizabeth M. Burton⁴, Thomas E. Pennington^{1,2,9}, Robyn P. M. Saw^{1,2,9}, Xiaowei Xu⁶, Giorgos C. Karakousis⁶, Paolo A. Ascierto¹⁰, Andrew J. Spillane^{1,2,3}, Alexander C. J. van Akkooi⁵, Michael A. Davies^{4,13}, Tara C. Mitchell^{6,13}, Hussein A. Tawbi^{4,13}, Richard A. Scolyer^{1,2,11,13}, Jennifer A. Wargo^{4,13}, Christian U. Blank^{5,13} and Georgina V. Long^{1,2,3,13} ✉

Pooled Analysis: Neoadjuvant Therapy in Stage III Melanoma

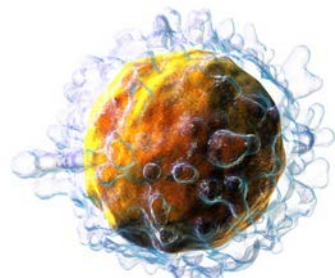
RFS by Pathological Response



The 5 Advantages of Neoadjuvant Therapy



1. ↑ Anti-cancer immunity compared with adjuvant



OpACIN Pilot
SWOG 18091

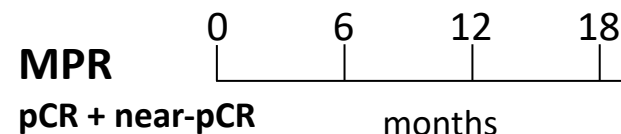
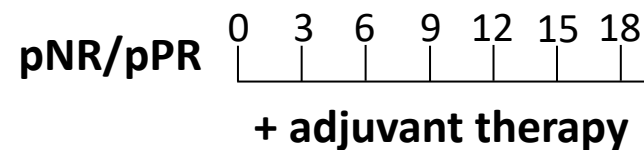
T Cell

2. Patient feedback. Refined prognosis



OpACIN-Neo

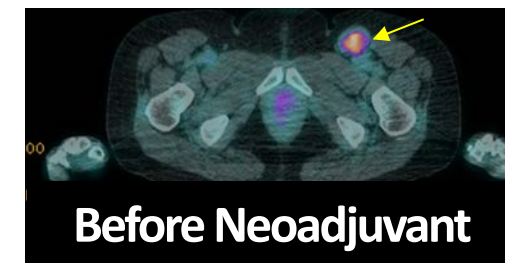
3. Tailor surveillance & adjuvant therapy



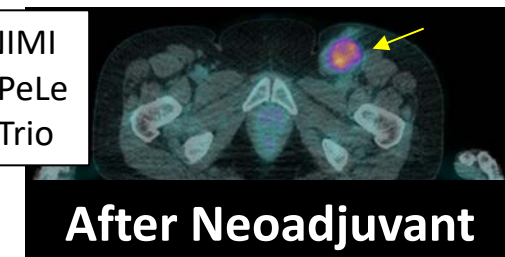
PRADO Trial

Less Surgery
No adjuvant therapy

4. Translational platform.
1) Biomarkers
2) Biology of Resistance



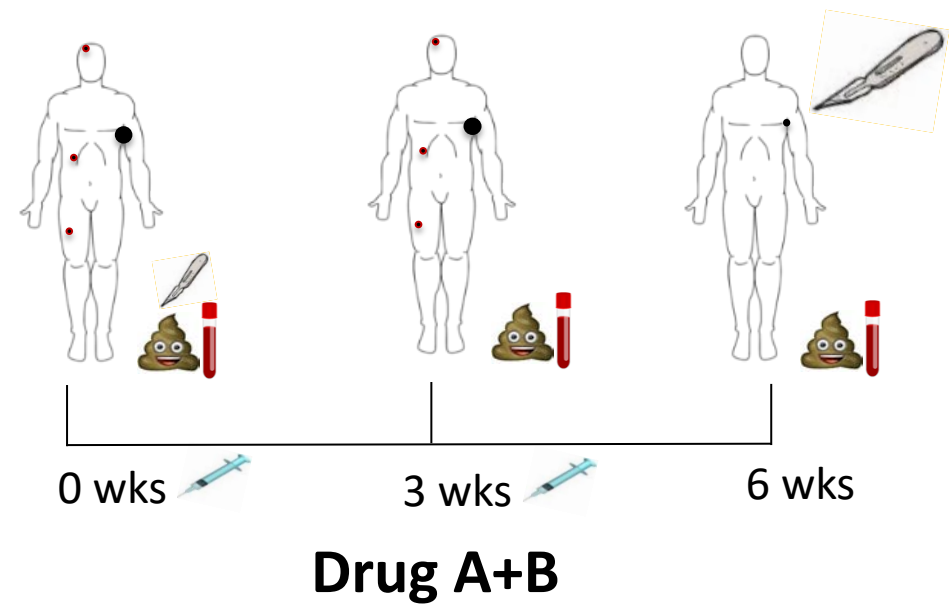
DONIMI
NeoPeLe
NeoTrio



5. Rapid Drug Development

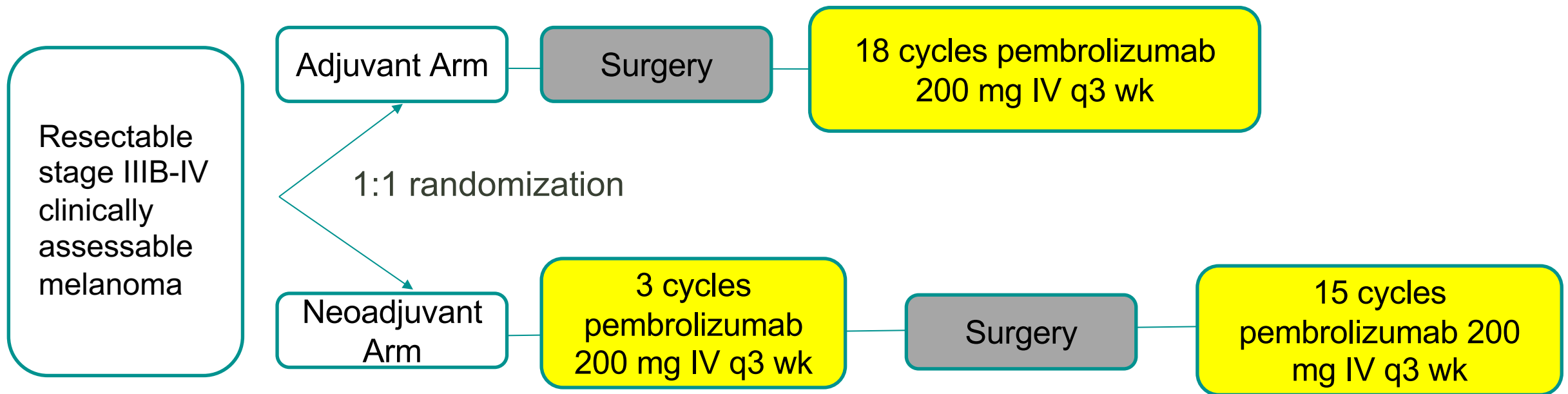
	pCR	Any path response
Nivo + Ipi	~45%	~75%
Dabraf + Tram	~50%	-
Pembro	30%	55%
Intralesional TVEC*	17%*	-
Nivo+anti-LAG3	~59%	~73%
Nivo+intralesion TLR9*	47%*	67%*
Pem+D+T	50%	80%
Nivo+HDACi	30%	55%
Nivo+Ipi+HDACi	~40%	~60%
Pem+Lenva	40%	75%

*RFS for path responders low compared with checkpoint inhibitors alone

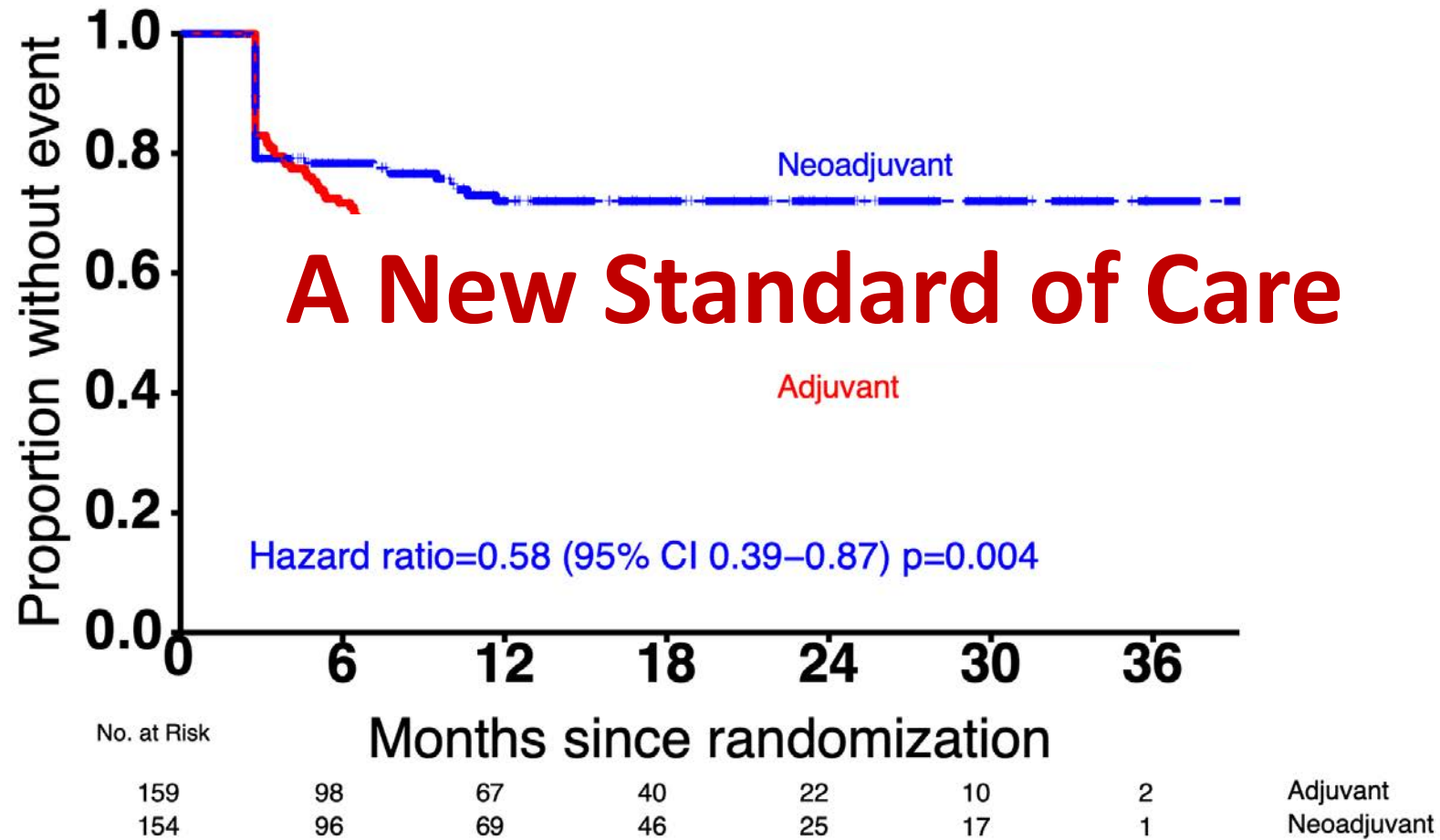


Path response rate?
‘Go’ vs ‘No Go’ Decision

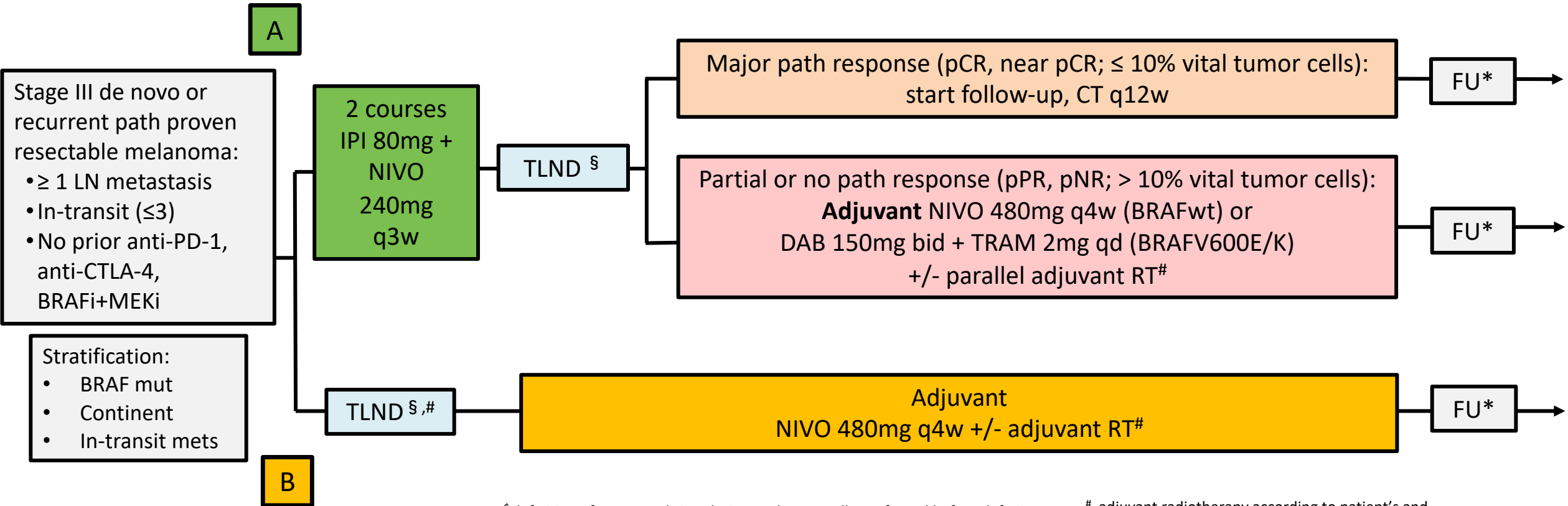
S1801 Study Design



S1801 Primary Endpoint: Event-free Survival (n=313)



Phase 3 trial comparing response driven **neo-adjuvant** ipilimumab + **nivolumab** vs **adjuvant** nivolumab (**NADINA**)

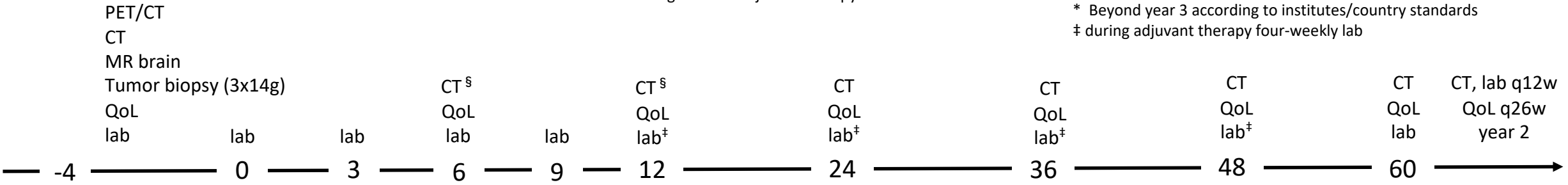


§ definition of PD at week 6 and 12 must be centrally confirmed before defining this as an event and omitting TLND or adjuvant therapy

$^{\#}$ adjuvant radiotherapy according to patient's and physician's decision allowed

* Beyond year 3 according to institutes/country standards

‡ during adjuvant therapy four-weekly lab



Additional Next Steps

- Neoadjuvant Pathological Assessment - International Implementation
- Commence Biomarker Selected Patient Trials
 - De-escalate therapy to anti-PD1 alone
 - Escalate therapy to those predicted to be non-responders
- Neoadjuvant therapy in stage 2 melanoma

1. Adjuvant Therapy

- Efficacy Update Sustained benefit in RFS and DMFS across all therapies
- BRAF targeted therapy vs Anti-PD1 Similar HR 0.51 → long term data needed

2. Neoadjuvant Therapy

- The Neoadjuvant Platform - Efficacy and Advantages
 - Next Steps Biomarker drive trials → enrich with predicted non-responders
Neoadjuvant therapy in Stage 2 melanoma
- No downsides!
 - 5 Major Advantages

Acknowledgements

- ♦ Patients and Families
- ♦ National and International Colleagues and Scientists working in Melanoma
- ♦ Melanoma Institute Australia and Trials Team





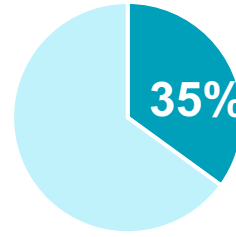
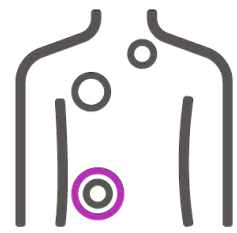
Adjuvant therapy with nivolumab versus placebo in patients with resected stage IIB/C melanoma (CheckMate 76K)

Georgina V. Long,¹ Michele Del Vecchio,² Jeffrey Weber,³ Christoph Hoeller,⁴ Jean-Jacques Grob,⁵ Peter Mohr,⁶ Stephan Grabbe,⁷ Caroline Dutriaux,⁸ Vanna Chiarion-Sileni,⁹ Jacek Mackiewicz,¹⁰ Piotr Rutkowski,¹¹ Petr Arenberger,¹² Gaëlle Quéreux,¹³ Tarek Meniawy,¹⁴ Paolo A. Ascierto,¹⁵ Piyush Durani,¹⁶ Maurice Lobo,¹⁶ Federico Campigotto,¹⁶ Brian R. Gastman,^{17*} John M. Kirkwood^{18*}

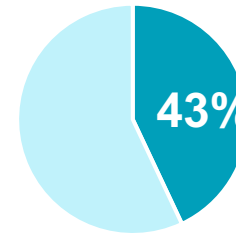
¹Melanoma Institute Australia, The University of Sydney, and Royal North Shore and Mater Hospitals, Sydney, New South Wales, Australia; ²IRCCS Istituto Nazionale dei Tumori, Milan, Italy; ³NYU Langone Medical Center, New York, NY, USA; ⁴Medizinische Universität Wien, Vienna, Austria; ⁵Hôpital de la Timone, Marseille, France; ⁶Elbe Klinikum Buxtehude, Buxtehude, Germany; ⁷University of Mainz Medical Center, Mainz, Germany; ⁸Hôpital Saint André, Bordeaux, France; ⁹Istituto Oncologico Veneto IOV-IRCCS, Padova, Italy; ¹⁰Institute of Oncology, Poznan University of Medical Sciences, Poznan, Poland; ¹¹Maria Skłodowska-Curie National Research Institute of Oncology, Warsaw, Poland; ¹²Charles University Third Faculty of Medicine and University Hospital of Královské Vinohrady, Prague, Czech Republic; ¹³Nantes University Hospital, Nantes, France; ¹⁴Sir Charles Gairdner Hospital, Perth, Australia; ¹⁵Istituto Nazionale Tumori IRCCS Fondazione Pascale, Naples, Italy; ¹⁶Bristol Myers Squibb, Princeton, NJ, USA; ¹⁷The Cleveland Clinic Foundation, Cleveland, OH, USA; ¹⁸UPMC Hillman Cancer Center, Pittsburgh, PA, USA

*Contributed equally

Introduction (1 of 2)



Stage IIB

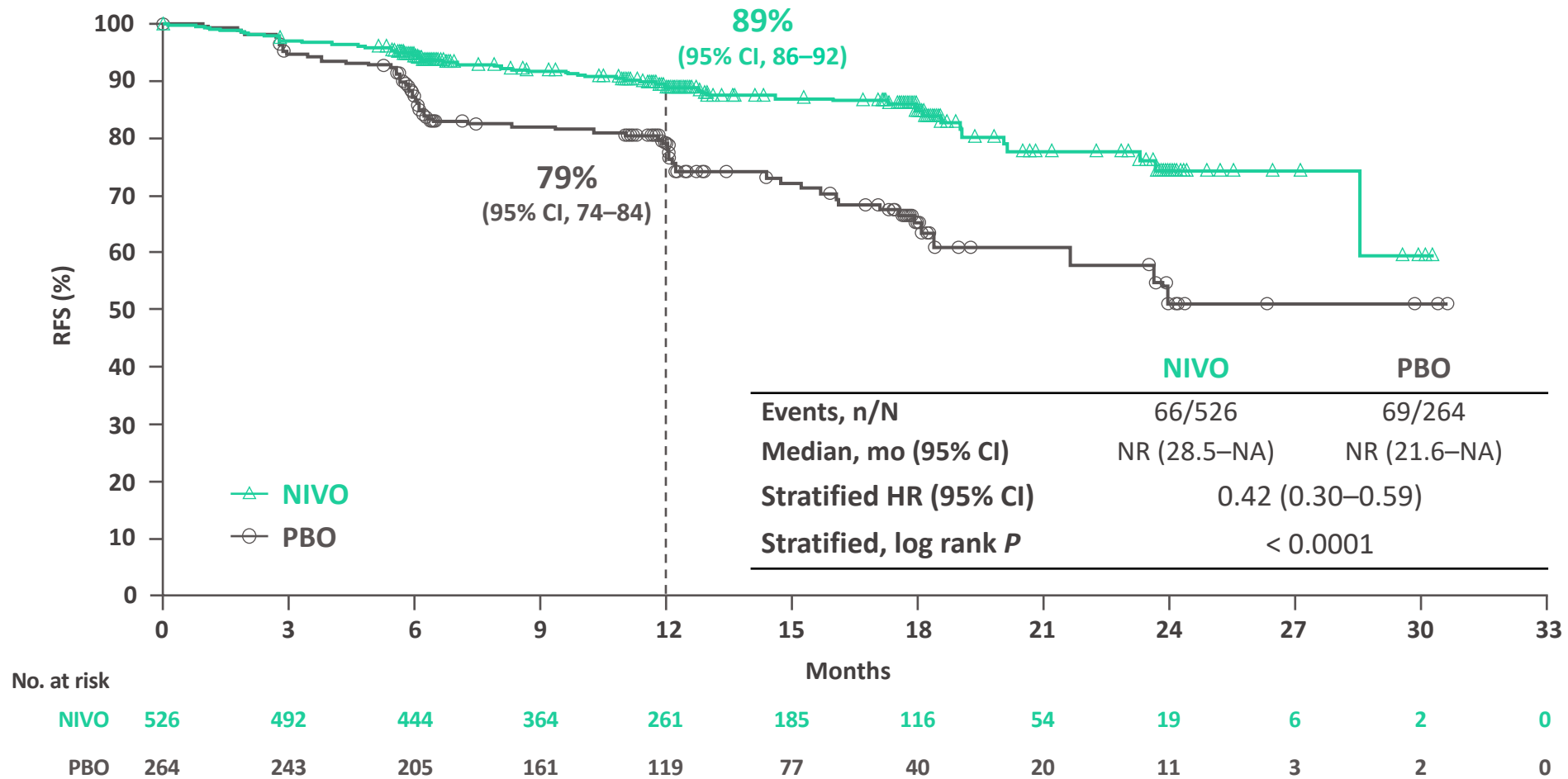


Stage IIC

**5-year risk of disease
recurrence^a (CMMR)¹**

^aConfirmatory cohort. CMMR, Central Malignant Melanoma Registry; MSS, melanoma-specific survival.
1. Garbe C, et al. *J Clin Oncol* 2022. doi: 10.1200/JCO.22.00202.

CheckMate 76K – Primary endpoint: RFS



NA, not available; NR, not reached.

Presented by Georgina V Long

Discussion Questions

- What is the optimal approach to adjuvant treatment for BRAF-mutant and BRAF wild-type melanoma?
- How do you prevent and ameliorate toxicity from treatment with BRAF/MEK inhibitors?

Melanoma Agenda

MODULE 1: Neoadjuvant and Adjuvant Therapy for Melanoma

MODULE 2: Update on the Management of Metastatic Melanoma

Discussion Questions

- What is the optimal first-line treatment for metastatic BRAF-mutant and BRAF wild-type disease?

2022 ASCO[®]
ANNUAL MEETING

Abstract 356154

DREAMseq (Doublet, Randomized Evaluation in Advanced Melanoma Sequencing) a Phase III Trial: ECOG-ACRIN EA6134

Michael B. Atkins¹, Sandra Lee², Bartosz Chmielowski³, Antoni Ribas³, Ahmad A. Tarhini⁴, Thach-Giao Truong⁵, Diwakar Davar⁶, Mark O'Rourke⁷, Brendan D. Curti⁸, Joanna M. Brell⁹, Kari L. Kendra¹⁰, Alexandra P. Ikeguchi¹¹, Jedd D. Wolchok¹², John M. Kirkwood⁶

¹Georgetown Lombardi Comprehensive Cancer Center, Washington DC; ²Dana-Farber Cancer Institute, Boston MA; ³Jonsson Comprehensive Cancer Center University of California Los Angeles, Los Angeles CA; ⁴H. Lee Moffitt Cancer Center and Research Institute, Tampa FL; ⁵Kaiser Permanente Northern California, Vallejo CA; ⁶Pittsburgh Cancer Institute, Pittsburgh PA; ⁷Greenville Health System Cancer Institute, Greenville SC; ⁸Providence Cancer Institute, Portland OR; ⁹MetroHealth Medical Center, Cleveland OH; ¹⁰Ohio State University Comprehensive Cancer Center, Columbus OH; ¹¹University of Oklahoma Medical Center, Oklahoma City OK; ¹²Memorial Sloan Kettering Cancer Center, New York NY

2022 ASCO[®]
ANNUAL MEETING

#ASC022

PRESENTED BY:

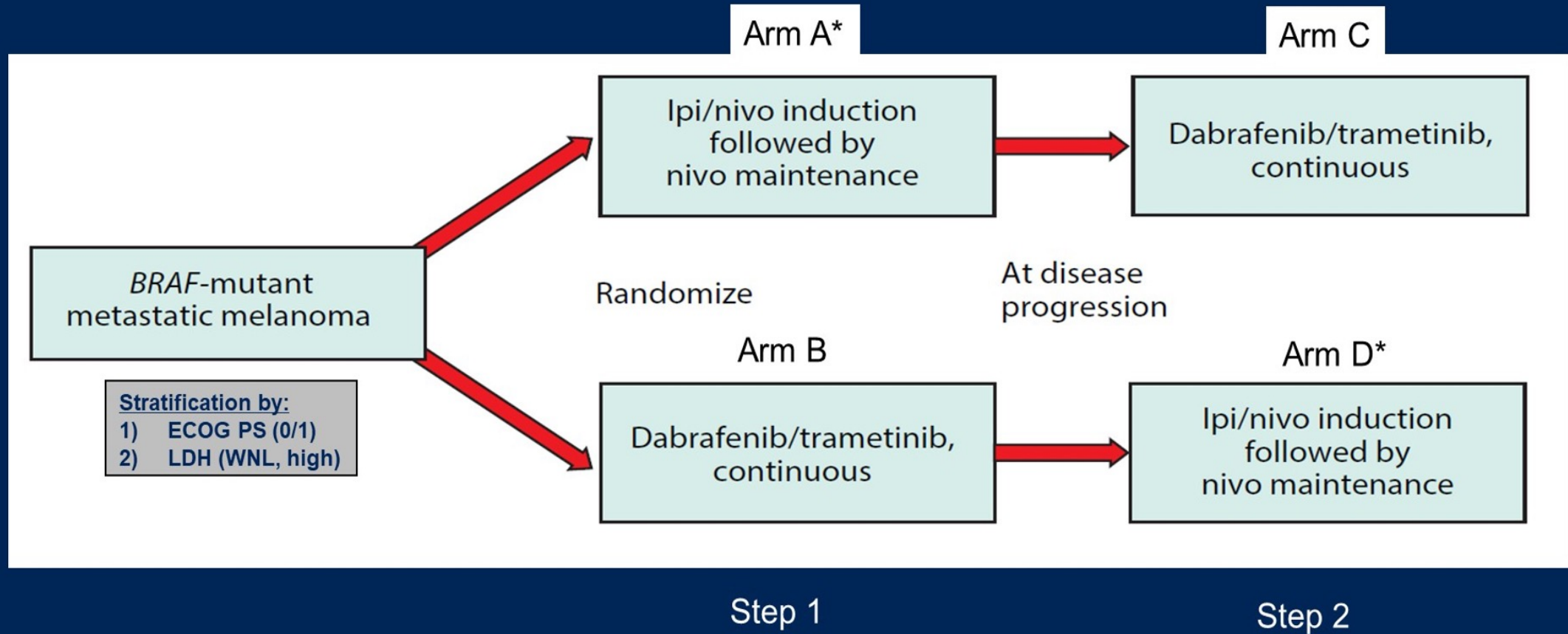
Michael B. Atkins, MD

Content of this presentation is the property of the author, licensed by ASCO. Permission required for reuse.

ASCO[®] AMERICAN SOCIETY OF
CLINICAL ONCOLOGY
KNOWLEDGE CONQUERS CANCER

RTP
RESEARCH
TO PRACTICE

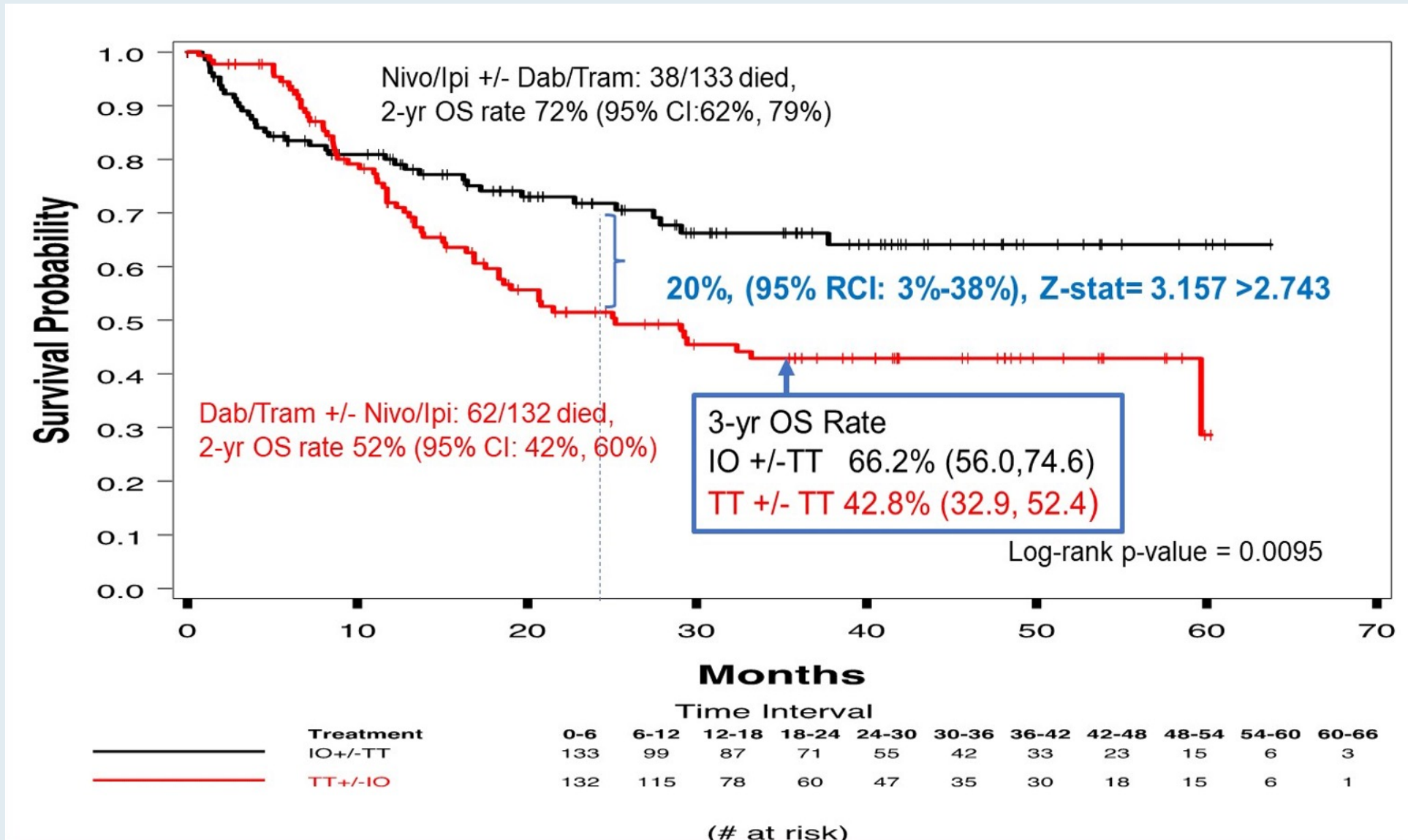
DREAMseq Study Schema



*Nivo/Ipi Induction = 12 wks; nivo maintenance = 72 wks

Ipi = ipilimumab; nivo = nivolumab

DREAMseq: Overall Survival (OS)



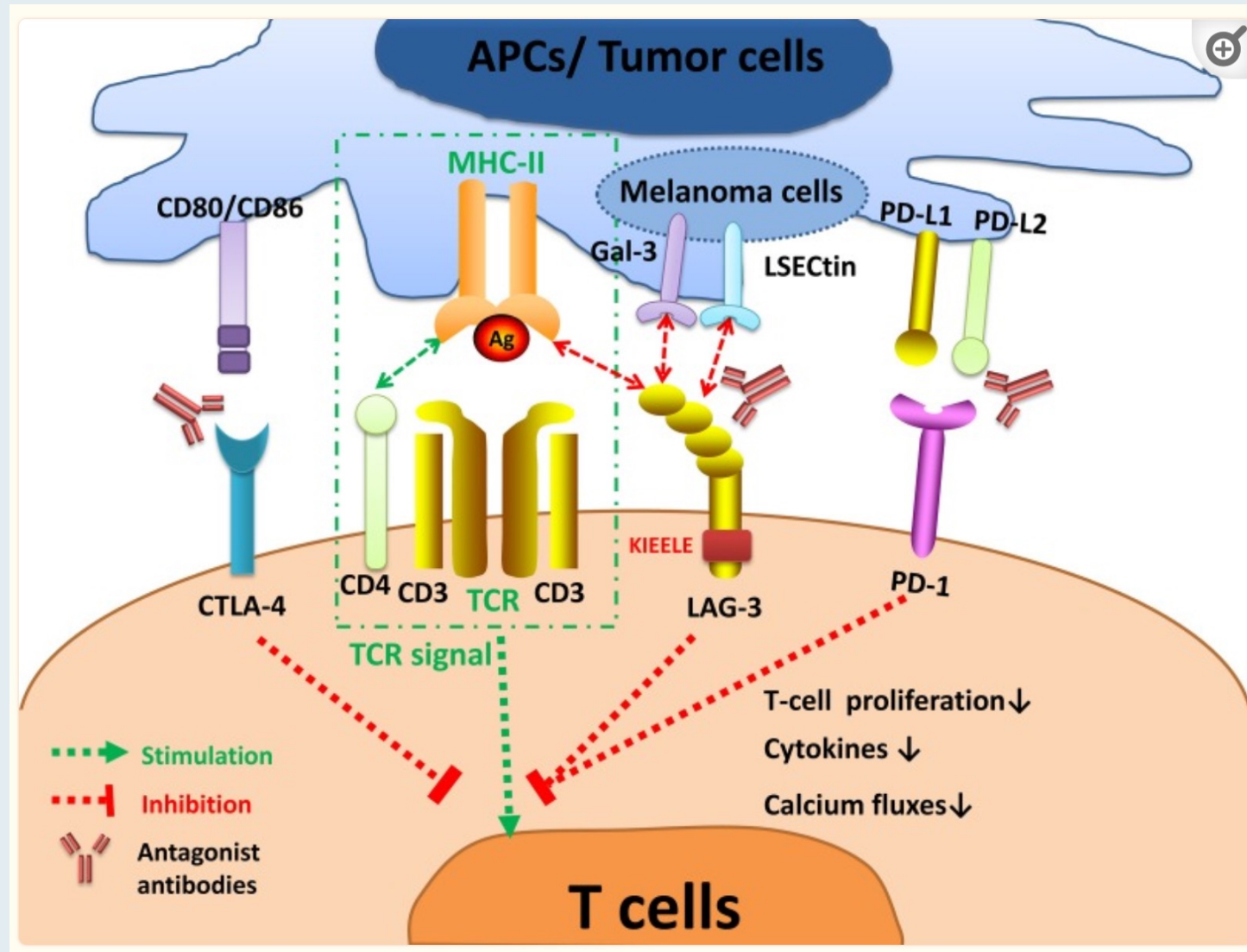
IO = immuno-oncology (immunotherapy); TT = targeted therapy

DREAMseq: Conclusions

- Nivo/ipi followed by dab/tram is associated with greater OS at 2 and 3 yrs than the converse sequence
 - Nivo/ipi results in more durable and ongoing responses in the frontline and is less effective in the second line
 - OS benefit for nivo/ipi initial sequence was seen in all subgroups
 - 2nd line dab/tram is a critical contributor to overall efficacy
- Crossover was frequently not feasible - in many cases due to CNS progression making pts ineligible
 - Pts dying early had worse prognosis and rarely crossed over
- QOL was initially worse with IO, but converged by 24 weeks

Nivo/ipi followed by BRAF/MEKi (if necessary) should be the preferred treatment sequence for the majority of pts with BRAF mutant melanoma

LAG-3 Signaling and Interplay with Other Immune Checkpoints



APC = antigen-presenting cell; TCR = T-cell receptor

FDA Approves Nivolumab/Relatlimab-rmbw for Unresectable or Metastatic Melanoma

Press Release: March 18, 2022

“The Food and Drug Administration approved nivolumab and relatlimab-rmbw for adult and pediatric patients 12 years of age or older with unresectable or metastatic melanoma. [This therapy] is a fixed-dose combination of the LAG-3-blocking antibody relatlimab and the programmed death receptor-1 blocking antibody nivolumab.

Efficacy was evaluated in RELATIVITY-047 (NCT03470922), a randomized (1:1), double-blinded trial in 714 patients with previously untreated metastatic or unresectable Stage III or IV melanoma. The trial excluded patients with active autoimmune disease, medical conditions requiring systemic treatment with moderate or high dose corticosteroids or immunosuppressive medications, uveal melanoma, and active or untreated brain or leptomeningeal metastases. Patients were randomized to receive nivolumab 480 mg and relatlimab 160 mg by intravenous infusion every 4 weeks or nivolumab 480 mg by intravenous infusion every 4 weeks until disease progression or unacceptable toxicity.”

Nivolumab (NIVO) + relatlimab (RELA) vs NIVO in previously untreated metastatic or unresectable melanoma: OS and ORR by key subgroups from **RELATIVITY-047**

Hussein A. Tawbi¹, F. Stephen Hodi², Evan J. Lipson³, Dirk Schadendorf⁴, Paolo A. Ascierto⁵, Luis Matamala⁶, Pamela Salman^{6*}, Erika Castillo Gutiérrez⁷, Piotr Rutkowski⁸, Helen J. Gogas⁹, Christopher D. Lao¹⁰, Juliana Janoski De Menezes¹¹, Stéphane Dalle¹², Ana Arance¹³, Jean-Jacques Grob¹⁴, Sarah Keidel¹⁵, Karin Jonczak¹⁵, Anne Marie Sobiesk¹⁵, Sonia Dolfi¹⁵, Georgina V. Long¹⁶

¹Department of Melanoma Medical Oncology, Division of Cancer Medicine, The University of Texas MD Anderson Cancer Center, Houston, TX, USA; ²Dana-Farber Cancer Institute, Boston, MA, USA;

³Sidney Kimmel Comprehensive Cancer Center, Bloomberg-Kimmel Institute for Cancer Immunotherapy, Johns Hopkins University School of Medicine, Baltimore, MD, USA; ⁴Department of Dermatology, University Hospital Essen, Essen, Germany & German Cancer Consortium, Partner Site, Essen, Germany; ⁵Istituto Nazionale Tumori IRCCS Fondazione "G. Pascale," Naples, Italy;

⁶Department of Oncology, Instituto Oncológico Fundación Arturo López Pérez, Santiago, Chile; ⁷FAICIC Clinical Research, Veracruz, Mexico; ⁸Maria Skłodowska-Curie National Research Institute of Oncology, Warsaw, Poland; ⁹Department of Medicine, National and Kapodistrian University of Athens, Athens, Greece; ¹⁰Michigan Medicine, Rogel Cancer Center, University of Michigan, Ann Arbor, MI, USA; ¹¹Hospital Nossa Senhora da Conceição, Porto Alegre, Brazil; ¹²Unit of Dermatology, Hospices Civils de Lyon, Cancer Research Center of Lyon, Pierre-Bénite, France;

¹³Department of Medical Oncology, Hospital Clinic Barcelona and IDIBAPS, Barcelona, Spain; ¹⁴Aix-Marseille University, CHU Timone, Marseille, France; ¹⁵Bristol Myers Squibb, Princeton, NJ, USA;

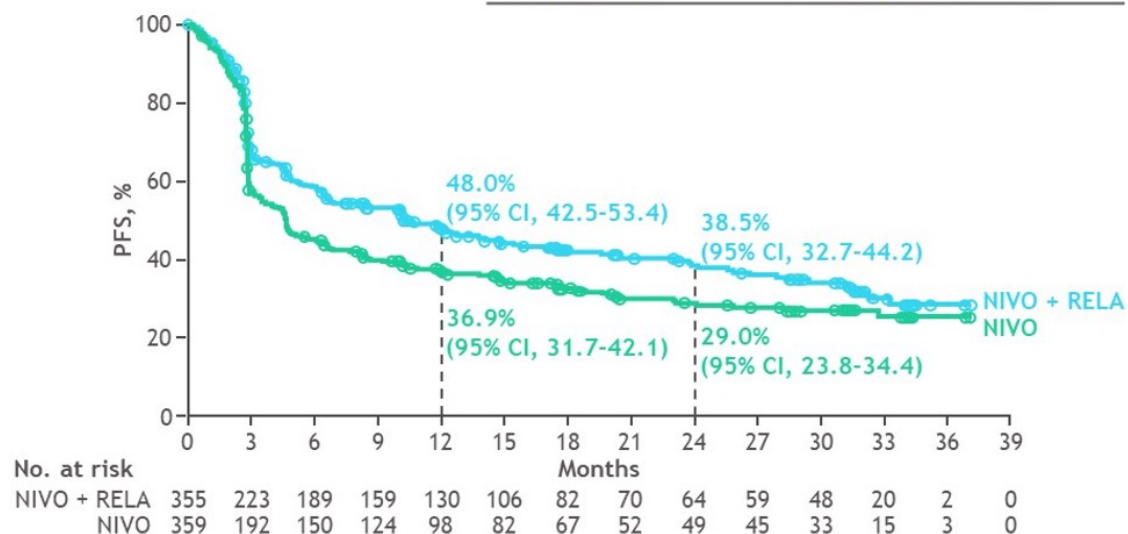
¹⁶Melanoma Institute Australia, The University of Sydney, Royal North Shore and Mater Hospitals, Sydney, Australia

*Affiliation during the time of the trial

RELATIVITY-047: PFS, OS and ORR for All Randomized Patients

Updated PFS by BICR

	NIVO + RELA (n = 355)	NIVO (n = 359)
mPFS, mo (95% CI)	10.22 (6.51-14.75)	4.63 (3.48-6.44)
HR (95% CI)	0.78 (0.64-0.94)	



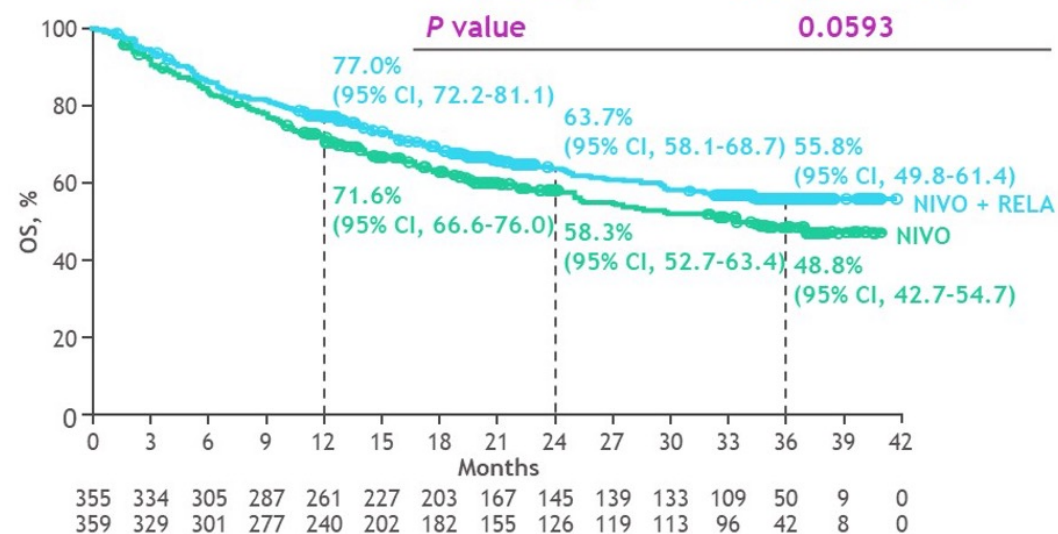
Confirmed ORR by BICR

	NIVO + RELA (n = 355)	NIVO (n = 359)
ORR % (95% CI)	43.1 (37.9-48.4)	32.6 (27.8-37.7)

DBL date: October 28, 2021. Median follow-up: 19.3 mo

OS

	NIVO + RELA (n = 355)	NIVO (n = 359)
mOS, mo (95% CI)	NR (34.20-NR)	34.10 (25.23-NR)
HR (95% CI)	0.80 (0.64-1.01)	
P value	0.0593	



PFS = progression-free survival; OS = overall survival; ORR = objective response rate; BICR = blinded independent central review; DBL = database lock

Phase 1 study of fianlimab, a human lymphocyte activation gene-3 (LAG-3) monoclonal antibody, in combination with cemiplimab in advanced melanoma

Omid Hamid,¹ Karl Lewis,² Amy Weise,³ Meredith McKean,⁴ Kyriakos P Papadopoulos,⁵ John Crown,⁶ Tae Min Kim,⁷ Nehal J Lakhani,⁸ John Kaczmar,⁹ Ragini Kudchadkar,¹⁰ Alexander Spira,¹¹ Guilherme Rabinowits,¹² Kevin Kim,¹³ Richard Carvajal,¹⁴ Stephen Williamson,¹⁵ Ella Ioffe,¹⁶ Shuquan Chen,¹⁶ Jayakumar Mani,¹⁶ Vladimir Jankovic,¹⁶ Laura Brennan,¹⁶ Glenn Kroog,¹⁶ Tasha Sims,^{16*} Israel Lowy,¹⁶ Giuseppe Gullo¹⁶

¹The Angeles Clinical and Research Institute, a Cedars-Sinai Affiliate, Los Angeles, CA, USA; ²University of Colorado Hospital, CO, USA; ³Henry Ford Hospital, Detroit, MI, USA; ⁴Sarah Cannon Research Institute/Tennessee Oncology PLLC, Nashville, TN, USA; ⁵START San Antonio, San Antonio, TX, USA; ⁶St Vincent's University Hospital, Dublin, Ireland; ⁷Seoul National University Hospital, Seoul, South Korea; ⁸START Midwest, Grand Rapids, MI, USA; ⁹MUSC Hollings Cancer Center, North Charleston, SC, USA; ¹⁰Emory University School of Medicine, Atlanta GA, USA; ¹¹Virginia Cancer Specialists, Fairfax, VA, USA; ¹²Miami Cancer Institute, Miami, FL, USA; ¹³Sutter Health Research Enterprise, San Francisco, CA, USA; ¹⁴Columbia University Medical Center, New York, NY, USA; ¹⁵University of Kansas Medical Center, Fairway, KS, USA; ¹⁶Regeneron Pharmaceuticals, Inc., Tarrytown, NY, USA

*Formerly with Regeneron Pharmaceuticals, Inc.



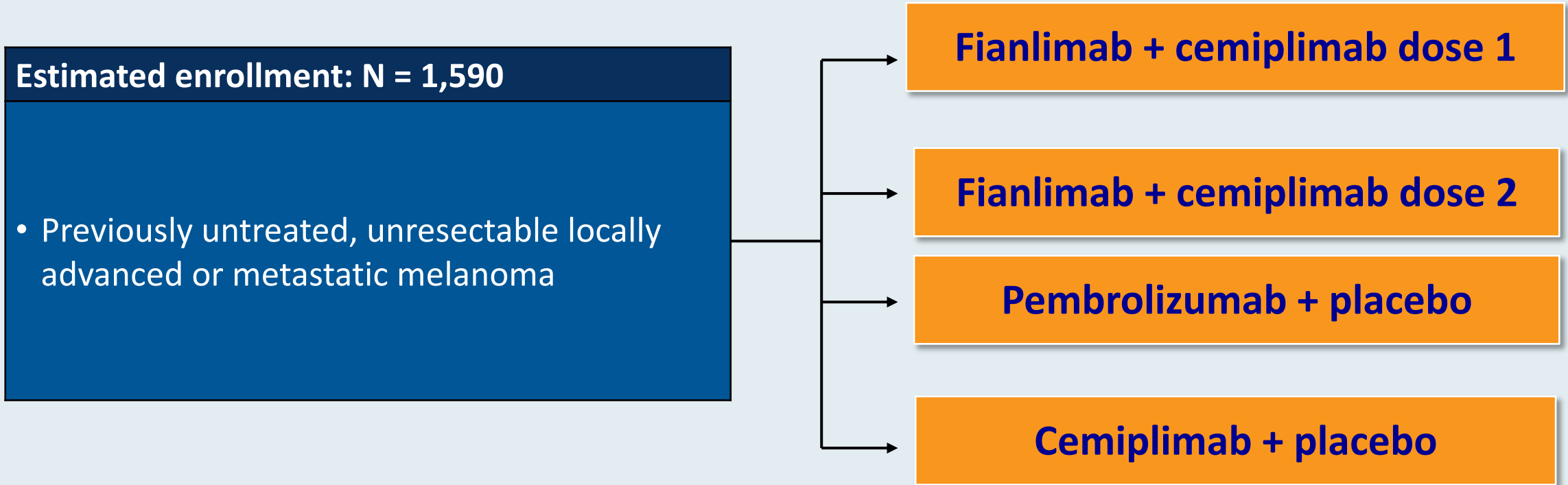
Fianlimab and Cemiplimab for Advanced Melanoma

% (n), unless otherwise stated	Anti-PD-(L)1-naive		Cohorts 6 + 15 (N=80)
	Cohort 6 (N=40)	Cohort 15 (N=40)	
ORR, % (95% CI)	62.5 (45.8, 77.3)	65 (48.3, 79.4)	63.8 (52.2, 74.2)
Complete response	15.0 (6)	2.5 (1)	8.8 (7)
Partial response	47.5 (19)	62.5 (25)	55.0 (44)
Stable disease	17.5 (7)	15.0 (6)	16.3 (13)
Progressive disease	15.0 (6)	15.0 (6)	15.0 (12)
NE	5.0 (2)	5.0 (2)	5.0 (4)
DCR	80.0 (32)	80.0 (32)	80.0 (64)
KM-estimated PFS, median (95% CI), months	24 (4.2, NE)	NR (7.5, NE)	24 (9.9, NE)
DOR, median (95% CI), months	NR (11.9, NE)	NR (6.3, NE)	NR (22.6, NE)
ORR: baseline LDH, n/N1 (%)			
LDH > ULN	10/17 (58.8)	6/11 (54.5)	16/28 (57.1)
LDH normal	15/23 (65.2)	18/24 (75.0)	33/47 (70.2)
ORR: liver metastasis, n/N2 (%)			
Yes	6/14 (42.9)	3/5 (60.0)	9/19 (47.4)
No	19/26 (73.1)	23/35 (65.7)	42/61 (68.9)

Anti-PD-(L)1-experienced (cohort 7)	
% (n), unless otherwise stated	Total (N=15)
ORR, % (95% CI)	13.3 (1.7–40.5)
Complete response	0
Partial response	13.3 (2)
Stable disease	26.7 (4)
Progressive disease	53.3 (8)
NE	6.7 (1)
DCR	40.0 (6)
KM-estimated PFS, median (95% CI), months	1.5 (1.3–7.7)
DOR, median (95% CI), months	NR (3.4–NE)
ORR by LAG-3 expression, %	
<1%	NA
≥1%	18.2
ORR by PD-L1 expression, %	
<1%	18.2
≥1%	0

ORR = objective response rate; NE = not estimated; DCR = disease control rate; KM = Kaplan-Meier; DOR = duration of response

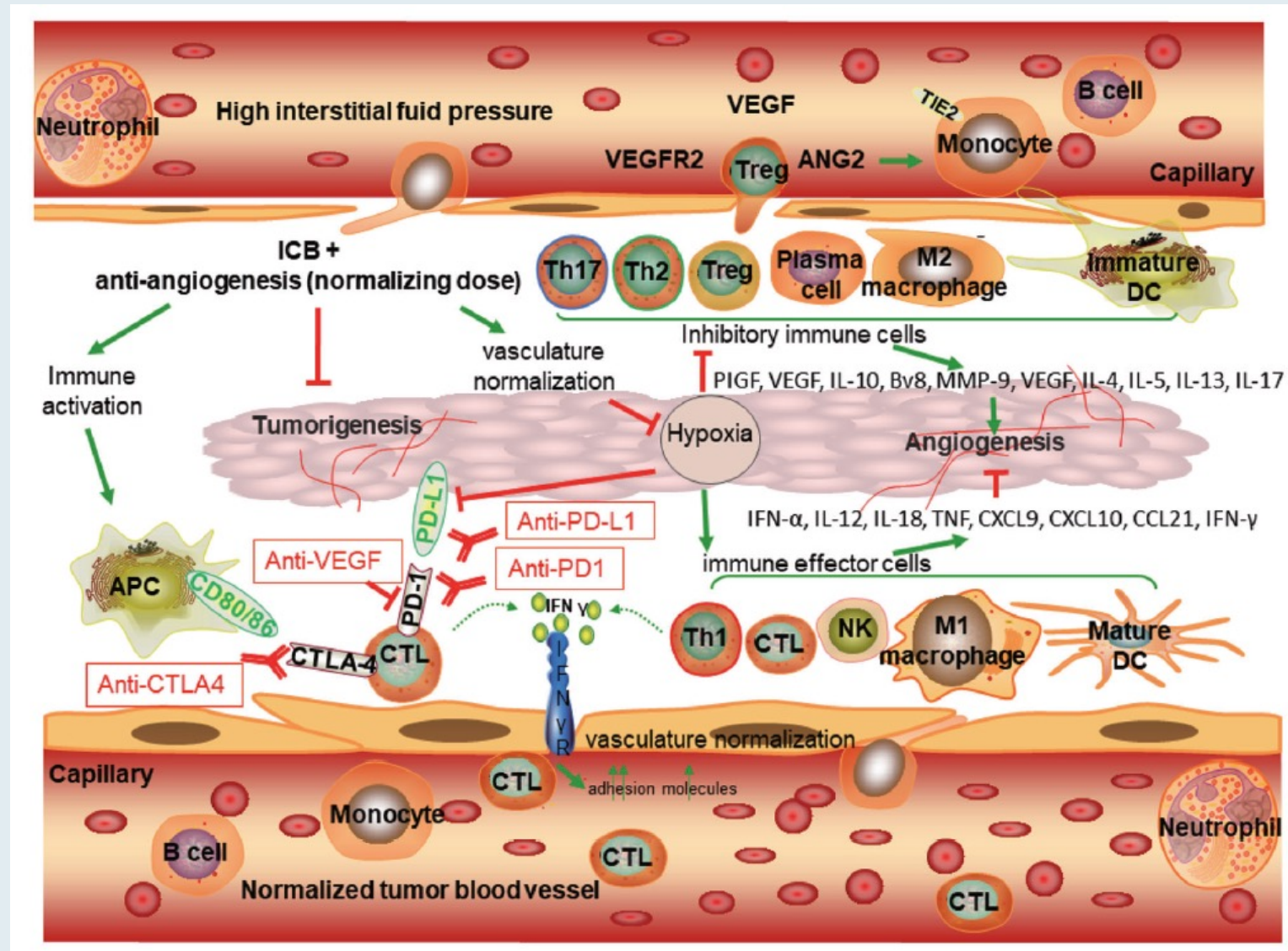
R3767-ONC-2011 Phase III Trial Design



Primary endpoints: Progression-free survival (BICR)

Secondary endpoints: Overall survival, objective response rate, disease-control rate, duration of response, incidence of adverse events

Mechanistic Rationale for Immune Checkpoint Blockade (ICB) in Combination with Anti-Angiogenic Agents

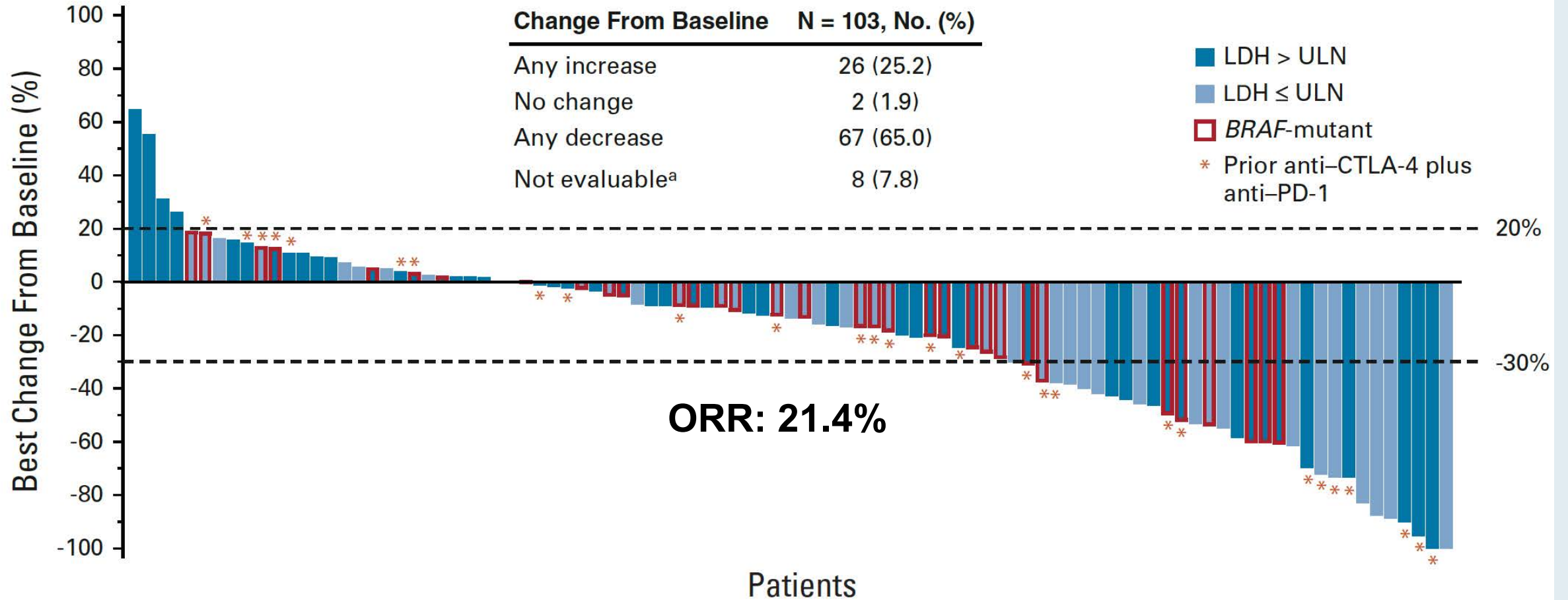


Phase II LEAP-004 Study of Lenvatinib Plus Pembrolizumab for Melanoma With Confirmed Progression on a Programmed Cell Death Protein-1 or Programmed Death Ligand 1 Inhibitor Given as Monotherapy or in Combination

Ana Arance, MD, PhD¹; Luis de la Cruz-Merino, MD, PhD²; Teresa M. Petrella, MD³; Rahima Jamal, MD⁴; Lars Ny, MD, PhD⁵; Ana Carneiro, MD, PhD⁶; Alfonso Berrocal, MD⁷; Ivan Márquez-Rodas, MD, PhD⁸; Anna Spreafico, MD, PhD⁹; Victoria Atkinson, MD¹⁰; Fernanda Costa Svedman, MD, PhD¹¹; Andrew Mant, MBBS¹²; Muhammad A. Khattak, MBBS, FRACP¹³; Catalin Mihalciou, MD¹⁴; Sekwon Jang, MD¹⁵; C. Lance Cowey, MD¹⁶; Alan D. Smith, MD¹⁷; Natalyn Hawk, MD, PhD¹⁸; Ke Chen, MS¹⁹; Scott J. Diede, MD, PhD¹⁹; Clemens Krepler, MD¹⁹; and Georgina V. Long, MBBS, PhD^{20,21,22,23}

J Clin Oncol 2022 June 2;[Online ahead of print].

LEAP-004 Primary Endpoint: Objective Response Rate (ORR) by Independent Review Committee



Thank you for joining us!

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