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

RTP
RESEARCH
TO PRACTICE

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

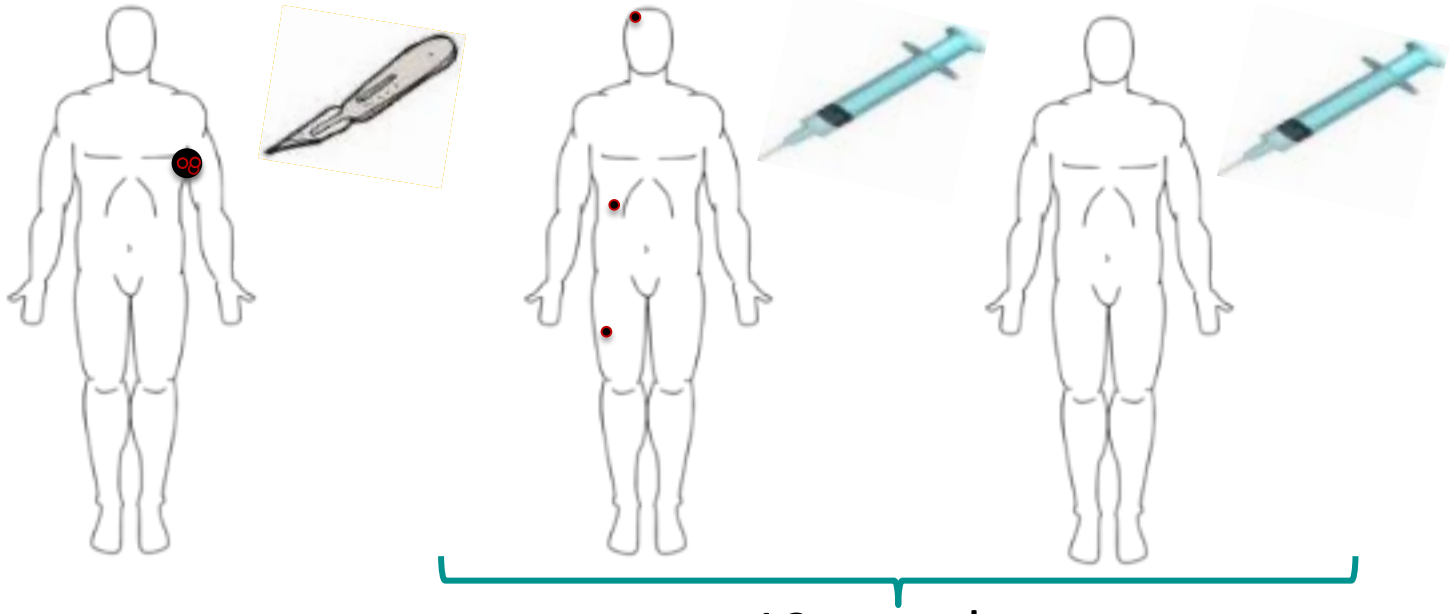
Prof Georgina Long, AO, BSc, PhD, MBBS
Co-Medical Director
Professor of Medical Oncology and Translational Research
Melanoma Institute Australia
Wollstonecraft, New South Wales, Australia

RTP
RESEARCH
TO PRACTICE

Neoadjuvant and Adjuvant Therapy Where are we now?

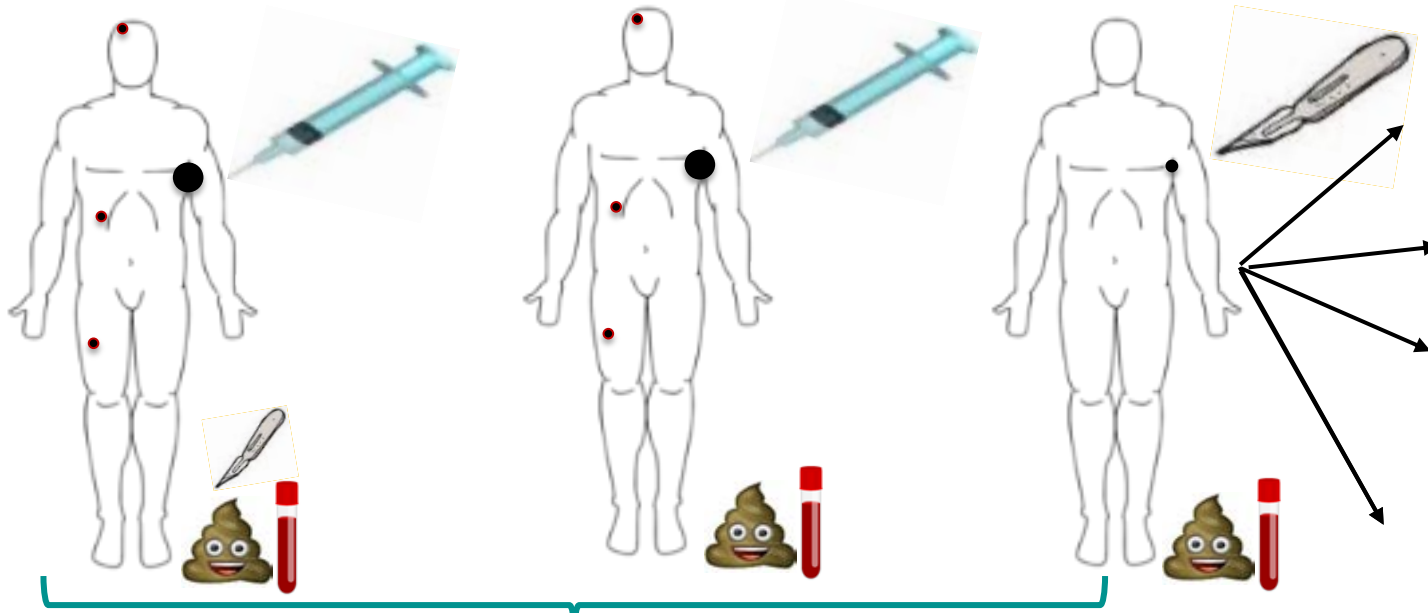
Georgina V Long
Melanoma Institute Australia, The University of Sydney
Royal North Shore and Mater Hospitals

Adjuvant



12 months

Neoadjuvant



6 weeks

Pathological Complete 0% TC

Pathological Near Complete ≤ 10% TC

Pathological Partial Respo >10%, ≤ 50% TC

No Pathological Response >50% TC

Presented by Georgina V Long @ProfGLongMIA

Outline

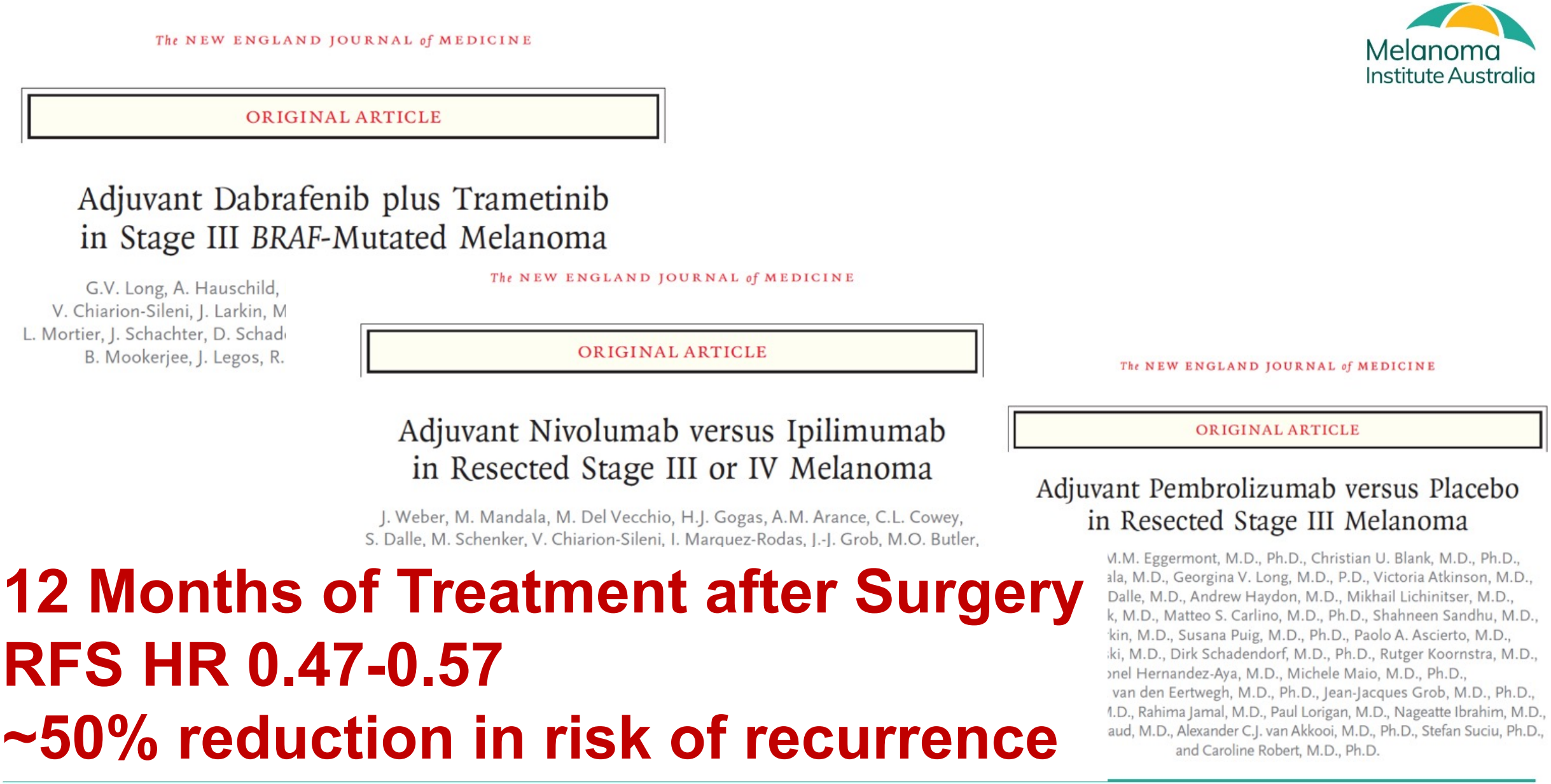
1. Adjuvant Therapy
    - Efficacy Update
    - BRAF targeted therapy vs Anti-PD1
2. Neoadjuvant Therapy
    - The Neoadjuvant Platform - Efficacy and Advantages
    - Next Steps

Outline

Melanoma Institute Australia

1. **Adjuvant Therapy**
    - **Efficacy Update**
    - **BRAF targeted therapy vs Anti-PD1**

2. Neoadjuvant Therapy
    - The Neoadjuvant Platform - Efficacy and Advantages
    - Next Steps



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

Melanoma Institute Australia

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Adjuvant Phase 3 Clinical Trials for Resected Melanoma

Primary Analyses of Efficacy Endpoints

Melanoma Institute Australia

AJCC Stage	Trial	Therapy	RFS HR (≥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)	-

Luke J Lancet 2022; Long Lancet Onc in press; Long NEJM 2017; Eggermont NEJM 2018; Eggermont Lancet Onc 2021; Weber NEJM 2017; Ascierto Lancet Onc 2020; Weber JCO 2022; Eggermont Lancet Onc 2015; Eggermont NEJM 2016; Zimmer Lancet

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

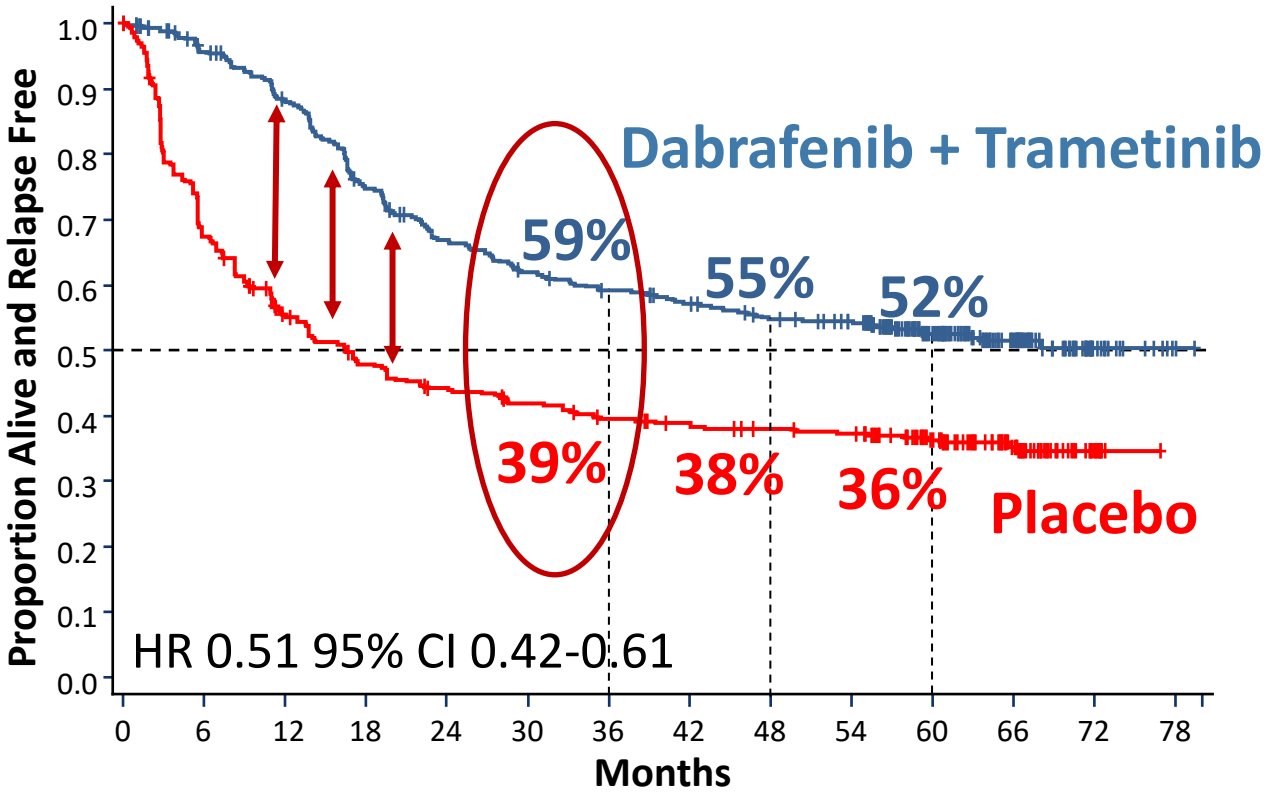
Presented by Georgina V Long @ProfGLongMIA

Relapse Free Survival in BRAF Mutant Melanoma

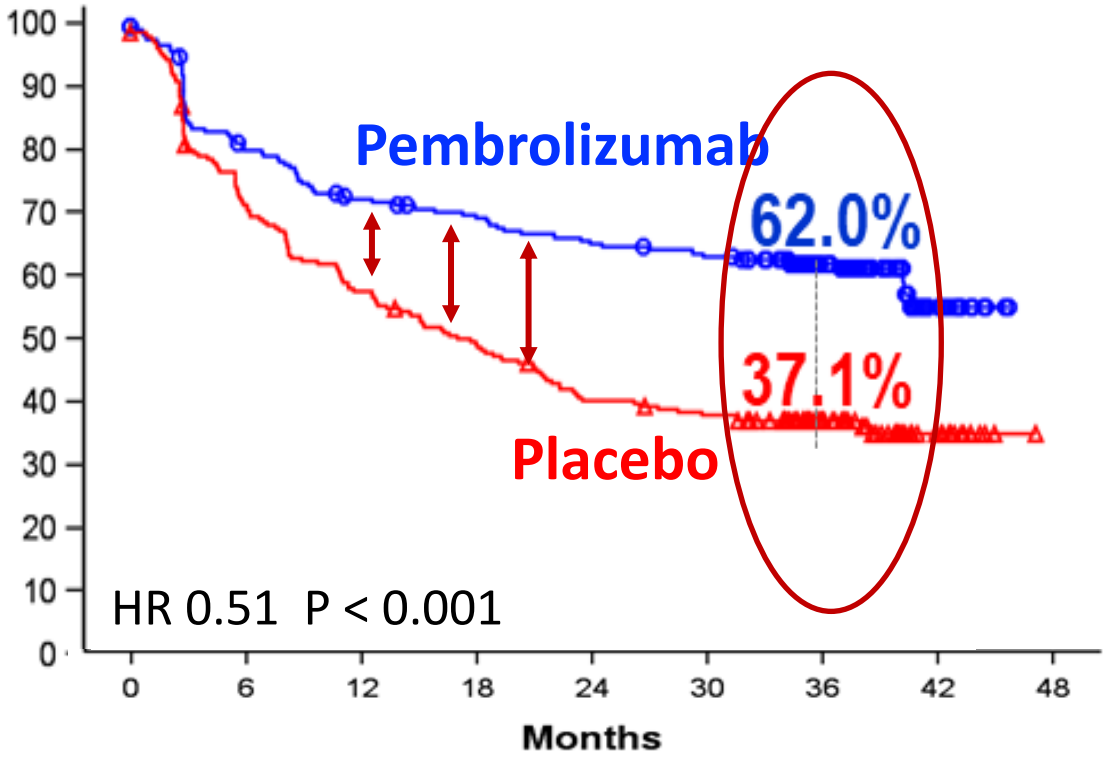
BRAF Targeted Therapy vs Anti-PD1

Melanoma Institute Australia

COMBI-AD



Keynote 054/EORTC 1325
V600 BRAF mutation positive only



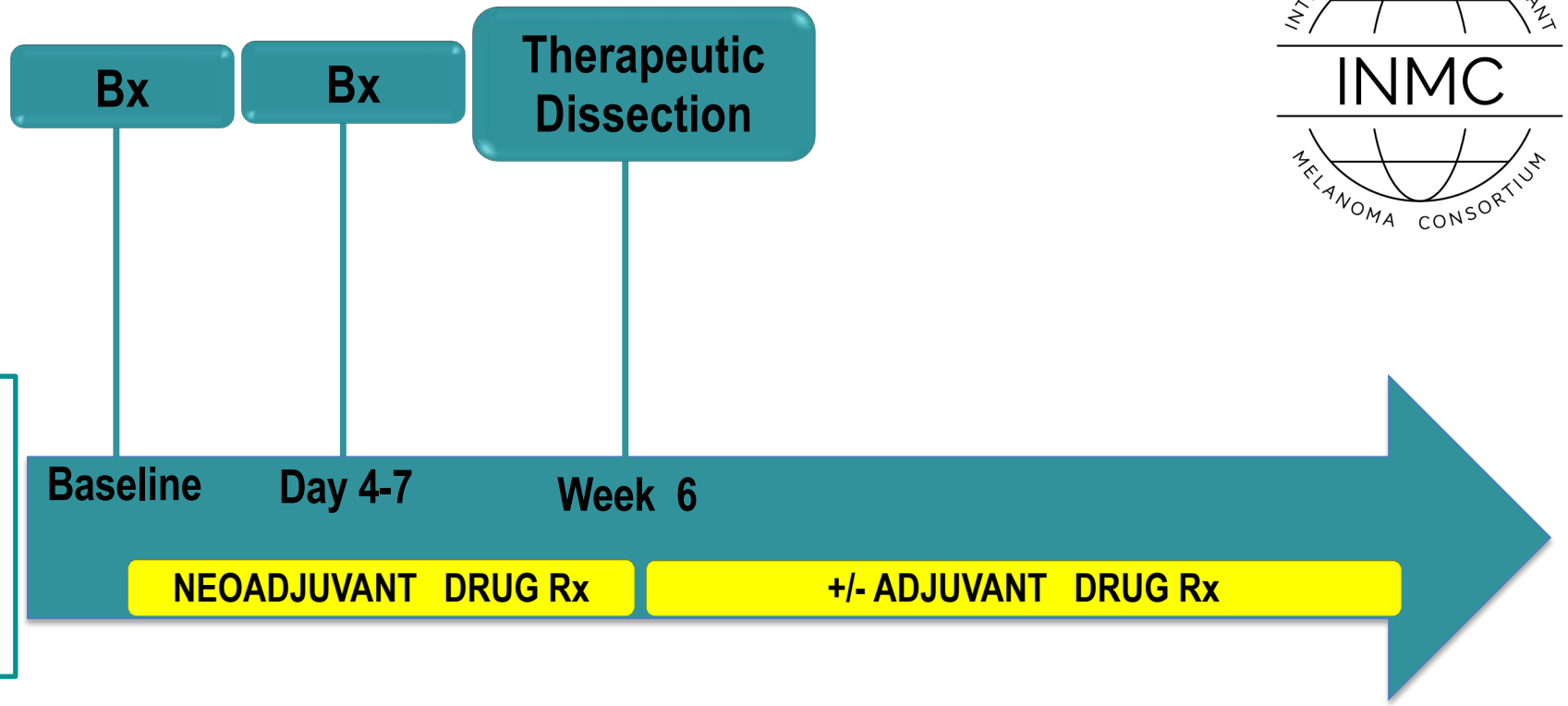
Dummer et al NEJM 2020; Eggermont et al JCO 2020

Outline

1. Adjuvant Therapy
    - Efficacy Update
    - BRAF targeted therapy vs Anti-PD1

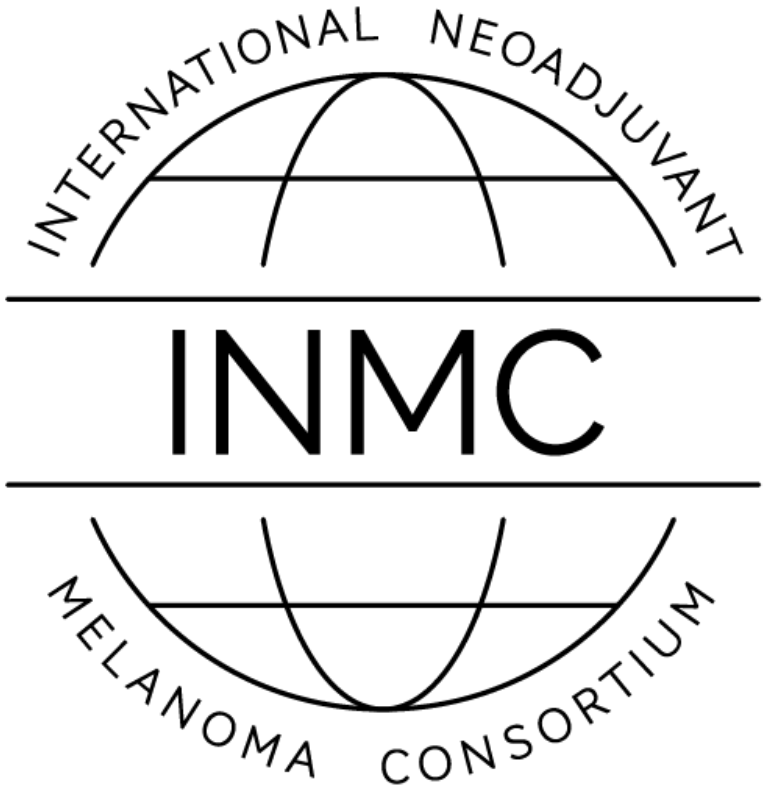
2. **Neoadjuvant Therapy**
    - **The Neoadjuvant Platform - Efficacy and Advantages**
    - **Next Steps**

Neoadjuvant Platform



Stage III Resectable
RECIST Measurable
Able to have two Biopsies

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

Melanoma Institute Australia

ESMO

Annals of Oncology 0: 1–8, 2018
doi: 10.1093/annonc/mdy226
Published online 25 June 2018

ORIGINAL ARTICLE

Annals Onc 2018

Pathological assessment of resection specimens after neoadjuvant therapy for metastatic melanoma

M. T. Tetzlaff[1,2*], J. L. Messina[3], J. E. Stein[4], X. Xu[5], R. N. Amaria[6], C. U. Blank[7], B. A. van de Wiel[7], P. M. Ferguson[8], R. V. Rawson[8], M. I. Ross[9], A. J. Spillane[10], J. E. Gershenwald[9,11], R. P. M. Saw[8], A. C. J. van Akkooi[7], W. J. van Houdt[7], T. C. Mitchell[12], A. M. Menzies[10], G. V. Long[13], 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, PhD[1], Tina J. Hieken, MD[2], Elizabeth M. Burton, MBA[3], Charlotte Ariyan, MD, PhD[4], Paolo A. Ascierto, MD, BC[5], Salvatore V. M. A. Asero, MD, PhD[6], Christian U. Blank, MD, PhD[1], Matthew S. Block, MD, PhD[2], Genevieve M. Boland, MD, PhD[7], Corrado Caraco, MD, PhD[5], Sydney Chng, MBBS, PhD, FRACS[8,9,10], B. Scott Davidson, MD[11], Joao Pedreira Duprat Neto, MD, PhD[12], Mark B. Faries, MD[13], Jeffrey E. Gershenwald, MD, FACS, FAAAS[3], Dirk J. Grunhagen, MD, PhD[14], David E. Gyorki, MBBS, MD, FRACS[15], Dale Han, MD[16], Andrew J. Hayes, MBBS, PhD[17], Winan J. van Houdt, MD, PhD[1], Giorgos C. Karakousis, MD, MS[18], Willem M. C. Klop, MD, PhD[1], Georgina V. Long, BSc, PhD, MBBS, FRACP, FAHMS[8,10,19,20], Michael C. Lowe, MD, MA, FACS, FSSO[21], Alexander M. Menzies, MBBS, PhD[8,10,19,20], Roger Olofsson Bagge, MD, PhD[22], Thomas E. Pennington, BSc, MBBS, MS, FRACS[8,10], Piotr Rutkowski, MD, PhD[23], 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, MD[24], Hussein Tawbi, MD, PhD[3], Alessandro A. E. Testori, MD[25], Mike T. Tetzlaff, MD, PhD[26], John F. Thompson, MD, FRACS, FACS[8,9,10,20], Jonathan S. Zager, MD, FACS[24], Charlotte L. Zuur, MD, PhD[1,27], Jennifer A. Wargo, MD[3], Andrew J. Spillane, MD[8,10,19,20], Merrick I. Ross, MD[3] on behalf of International Neoadjuvant Melanoma Consortium (INMC)

nature medicine

ARTICLES

https://doi.org/10.1038/s41591-020-01188-3

Check for updates

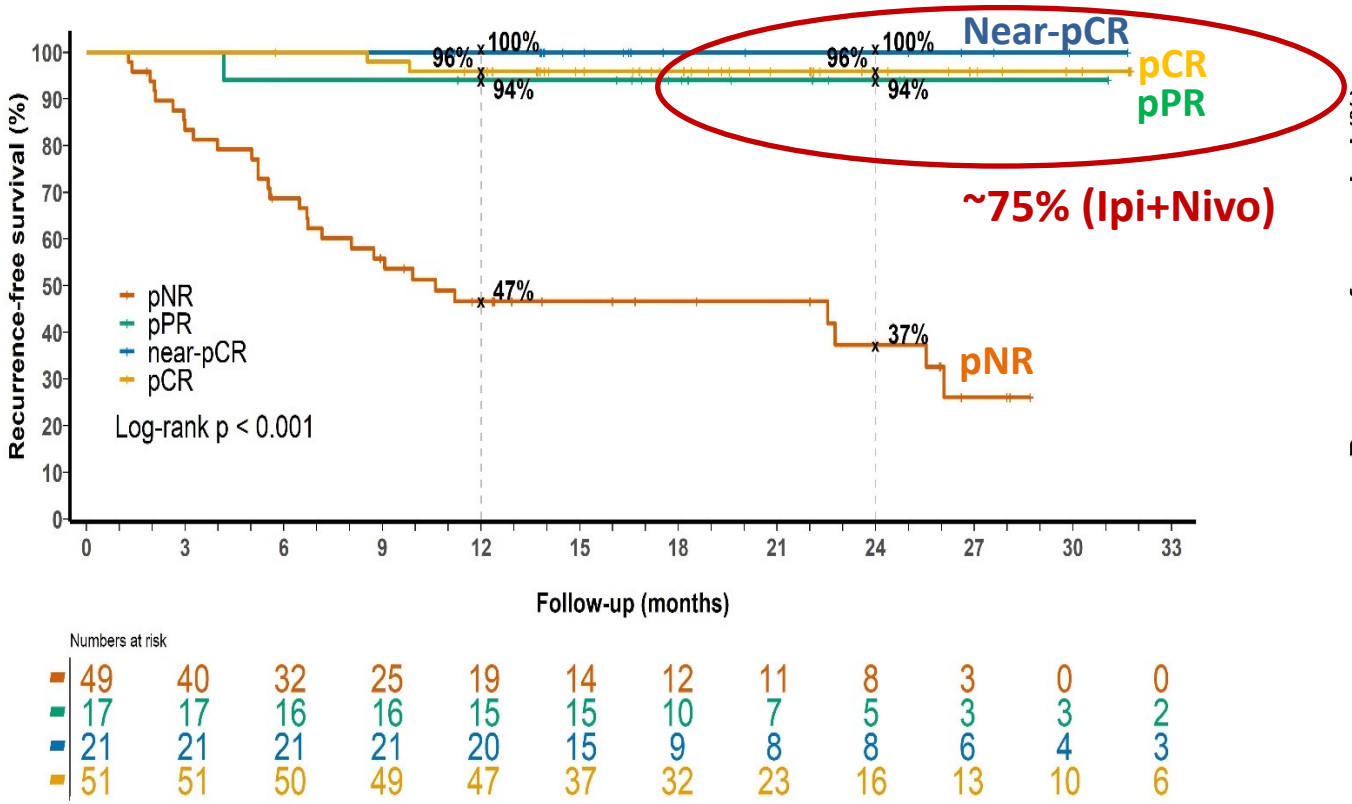
Nat Med 2021

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. Tarhini[8], Elizabeth M. Burton[4], Thomas E. Pennington[1,2,9], Robyn P. M. Saw[1,2,9], Xiaowei Xu[6], Giorgos C. Karakousis[6], Paolo A. Ascierto[10], Andrew J. Spillane[1,2,3], Alexander C. J. van Akkooi[5], 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] ✉

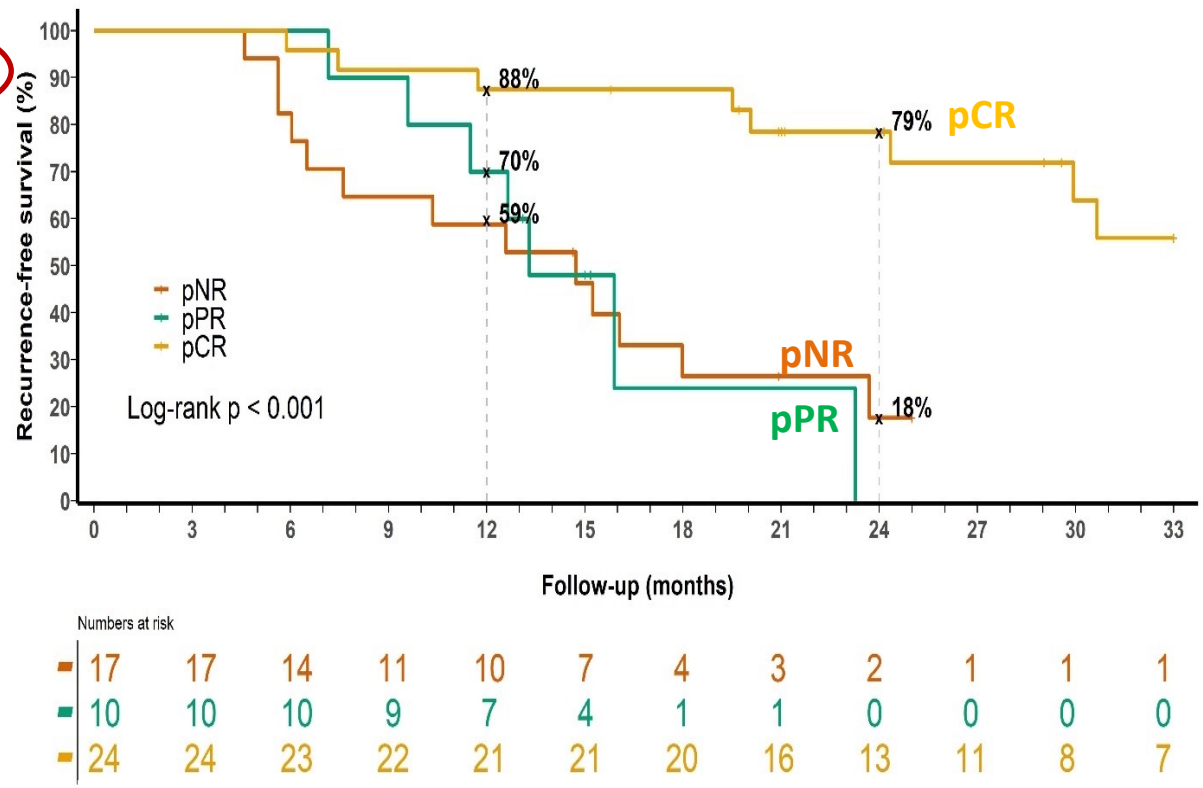
Pooled Analysis: Neoadjuvant Therapy in Stage III Melanoma
RFS by Pathological Response

Immunotherapy
Anti-PD1 pCR = 20%
Anti-PD1 + Anti-CTLA4 pCR = 43%



Med f/u 19.3 mo

Targeted Therapy
Dabrafenib + Trametinib pCR = 47%



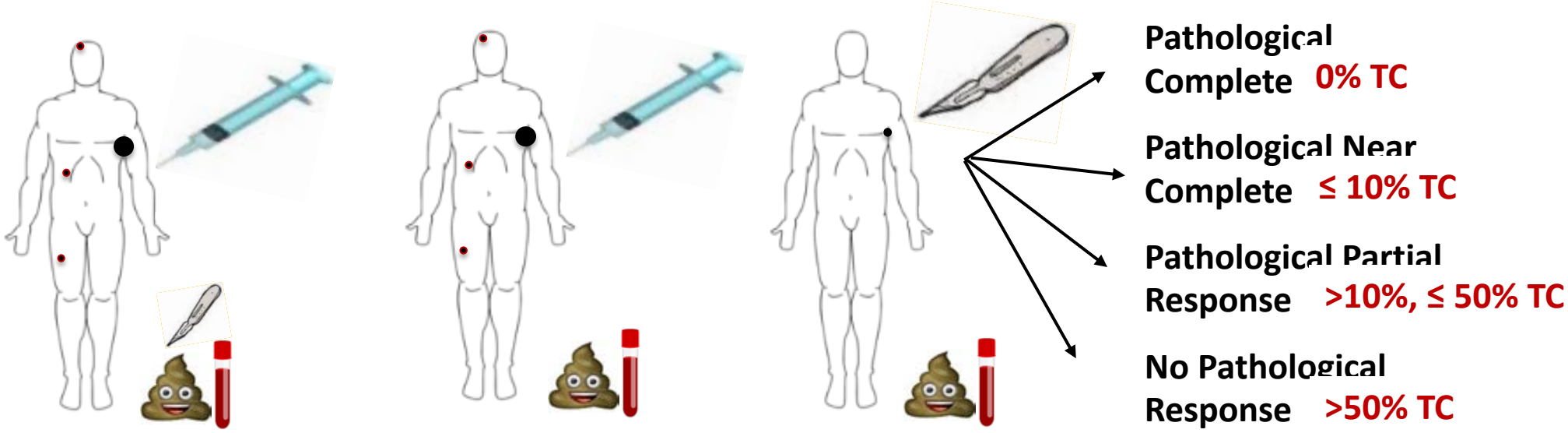
Med f/u 25.9 mo

Menzies A et al Nat Med 2021

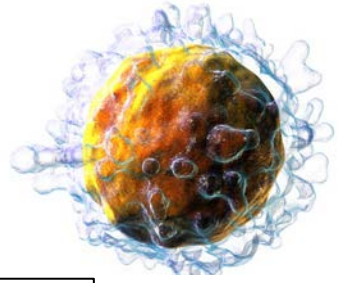
Presented by Georgina V Long @ProfGLongMIA

The 5 Advantages of Neoadjuvant Therapy

Melanoma Institute Australia



1. ↑ Anti-cancer immunity compared with adjuvant



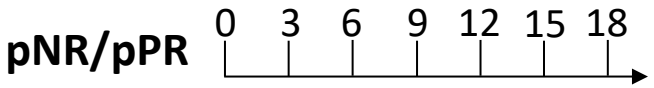
OpACIN Pilot
SWOG 18091

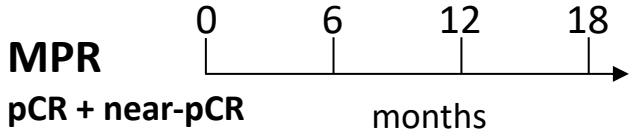
T Cell

2. Patient feedback. Refined prognosis

OpACIN-Neo

3. Tailor surveillance & adjuvant therapy



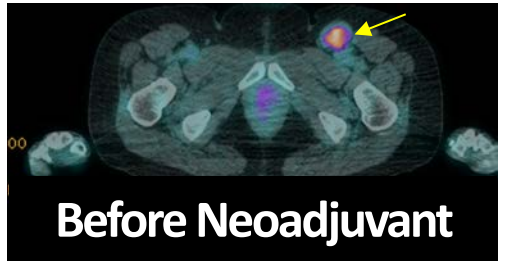


PRADO Trial

Less Surgery
No adjuvant therapy

4. Translational platform.

1) Biomarkers
2) Biology of Resistance



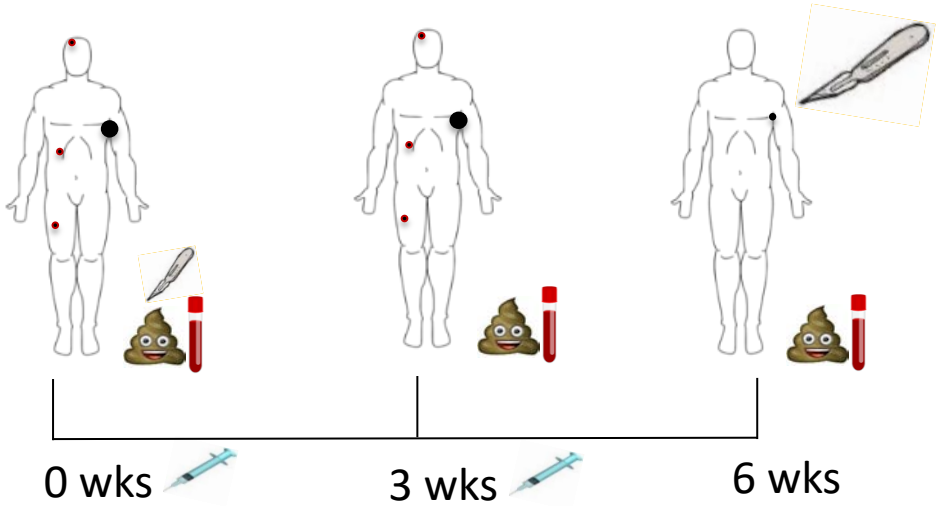
DONIMI
NeoPeLe
NeoTrio

Presented by Georgina V Long @ProfGLongMIA

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

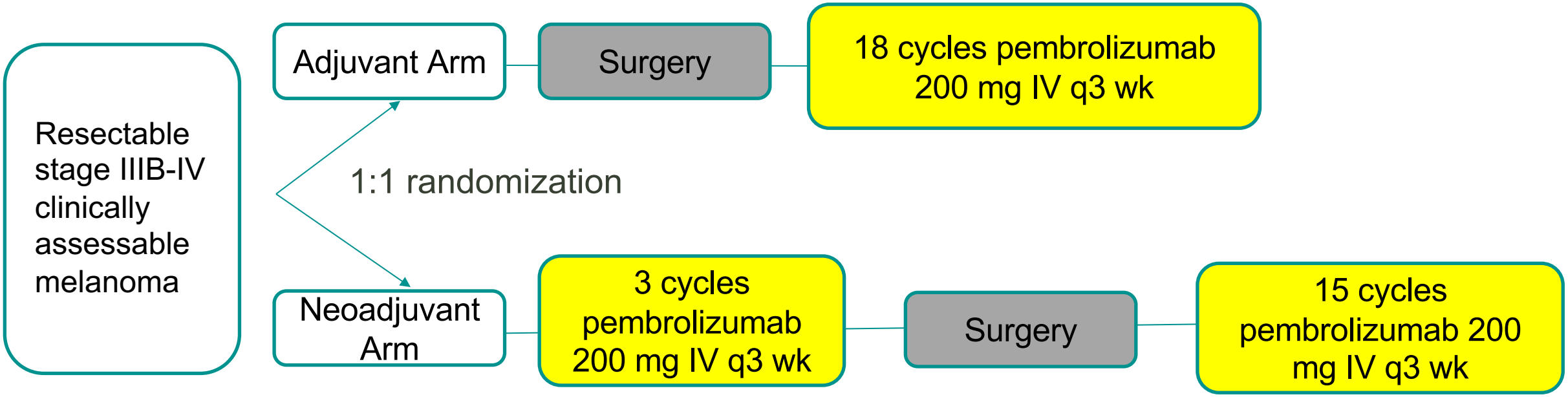


Drug A+B

Path response rate?

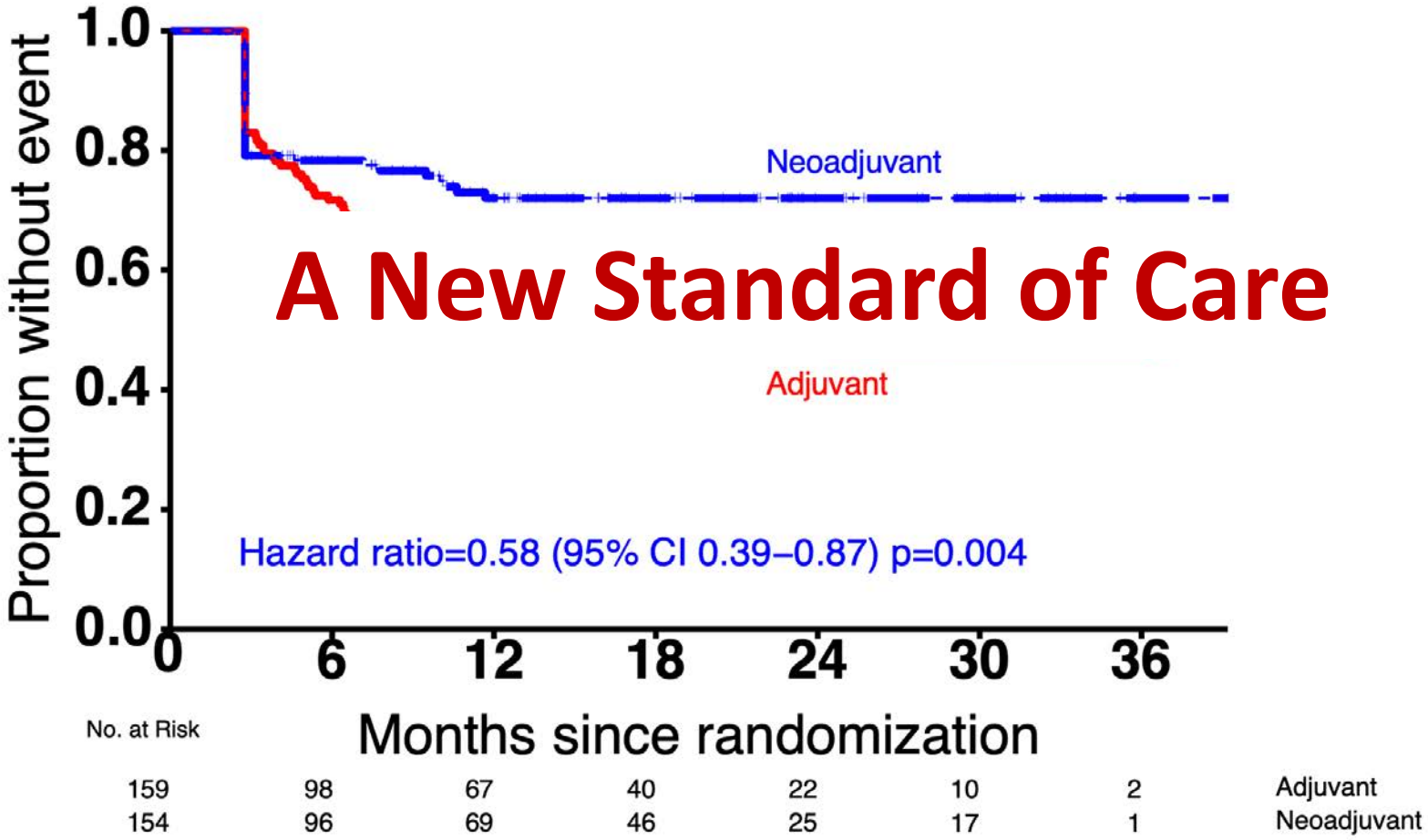
'Go' vs 'No Go' Decision

S1801 Study Design



Patel SP et al ESMO 2022

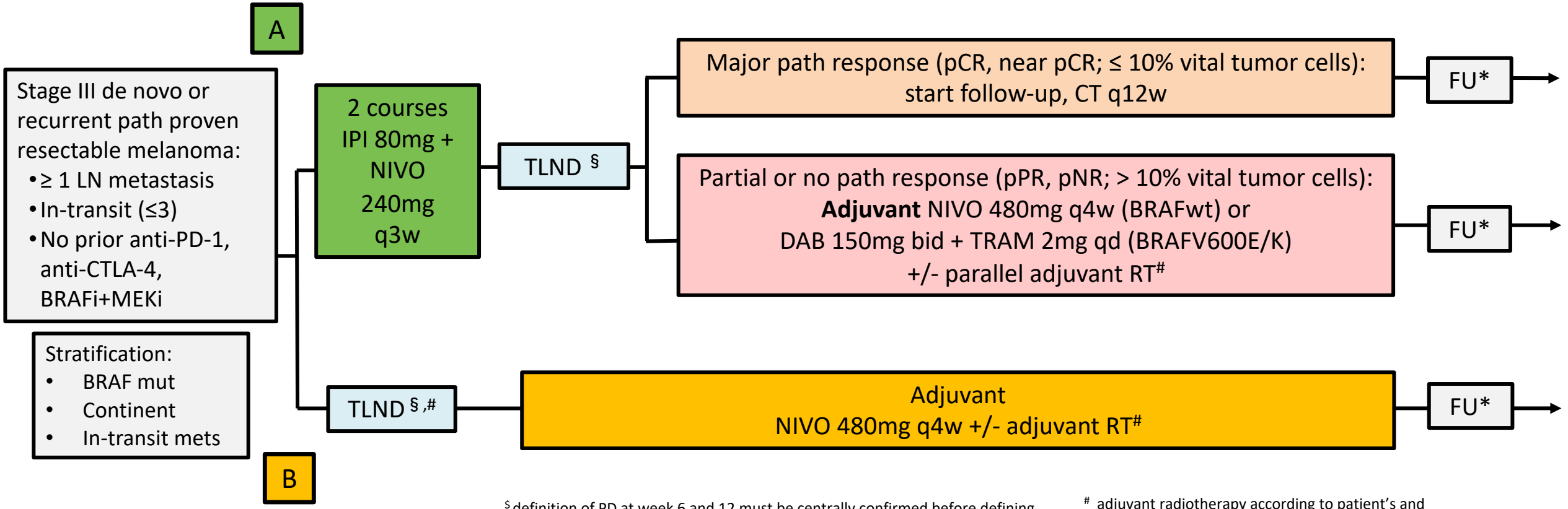
S1801 Primary Endpoint: Event-free Survival
(n=313)



A New Standard of Care

Patel SP et al ESMO 2022

Phase 3 trial comparing response driven **n**eo-**ad**juvant **i**pilimumab + **n**ivolumab vs **a**djuvant 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

	-4	0	3	6	9	12	24	36	48	60	
	PET/CT CT MR brain Tumor biopsy (3x14g) QoL lab	lab	lab	CT § QoL lab	lab	CT § QoL lab‡	CT QoL lab‡	CT QoL lab‡	CT QoL lab‡	CT QoL lab	CT, lab q12w QoL q26w year 2

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

Outline

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

Affiliated with THE UNIVERSITY OF SYDNEY

Acknowledgements

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

Adjuvant Dabrafenib + Trametinib (D + T) vs Placebo in Patients with Resected Stage III BRAF^{V600}-Mutant Melanoma: Updated 5-Year Distant-Metastases-Free Survival (DMFS) Analysis of COMBI-AD

Schadendorf D et al.

ASCO 2022;Abstract 9563.

COMBI-AD: Distant Metastasis-Free Survival (DMFS) in AJCC-8 Stage IIIA to IIID Subgroups

DMFS rates	Stage IIIA		Stage IIIB		Stage IIIC		Stage IIID	
	D + T (n = 50)	PBO (n = 39)	D + T (n = 145)	PBO (n = 154)	D + T (n = 217)	PBO (n = 214)	D + T (n = 22)	PBO (n = 17)
3 years	89%	85%	71%	55%	68%	54%	65%	26%
4 years	84%	85%	68%	54%	64%	53%	65%	26%
5 years	75%	85%	67%	53%	63%	51%	65%	26%
Hazard ratio	1.24		0.56		0.54		0.20	
p-value	0.695		0.004		0.0001		0.001	

AJCC-8 = American Joint Committee on Cancer melanoma staging system, eighth edition; D = dabrafenib; T = trametinib; PBO = placebo

Schadendorf D et al. ASCO 2022;Abstract 9563.

FDA-Approved Adjuvant Immunotherapy Options for Melanoma

Monotherapy	FDA approval	Pivotal study	BRAF status	HR (RFS)			Treatment discontinuation
				ITT	BRAF wt	BRAF mutant	
Pembrolizumab	2/14/19	KEYNOTE-054	All comers	0.59	0.61	0.59	14%
Nivolumab	12/20/17	CheckMate 238	All comers	0.71	0.69	0.79	10%
Ipilimumab	10/28/15	EORTC-18071	All comers	0.75	NR	NR	53%

RFS = relapse-free survival; wt = wild type; NR = not reported

Eggermont AMM et al. *N Engl J Med* 2018; *Eur J Cancer* 2019; *N Engl J Med* 2021. Ascierto PA et al. *Lancet Oncol* 2020. Bai X et al. *Br J Dermatol* 2021.

2022 ASCO® ANNUAL MEETING

Abstract LBA9500

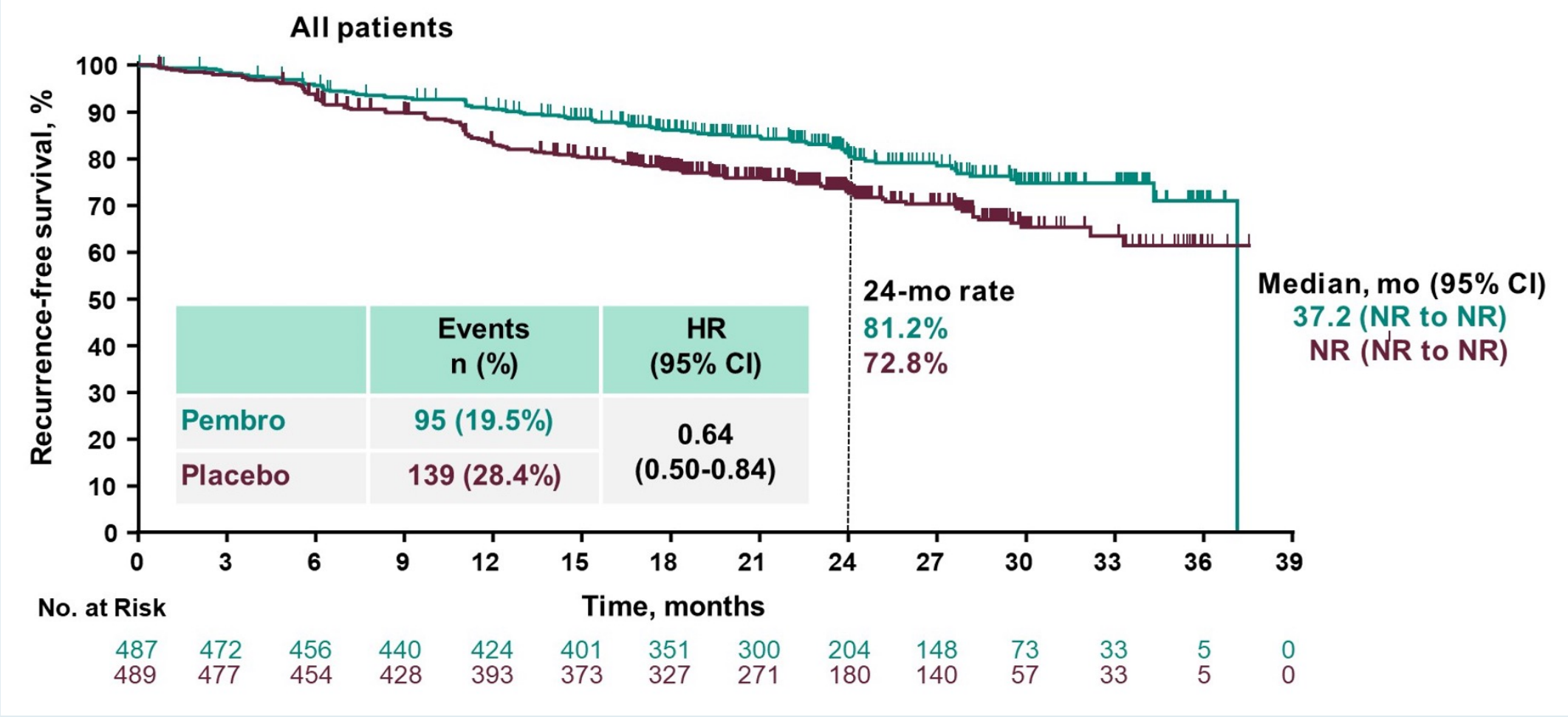
Distant Metastasis-free Survival With Pembrolizumab Versus Placebo as Adjuvant Therapy in Stage IIB or IIC Melanoma: The Phase 3 KEYNOTE-716 Study

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

[1]Melanoma Institute Australia, The University of Sydney, Sydney, Australia; [2]Royal North Shore & Mater Hospitals, Sydney, Australia; [3]UPMC Hillman Cancer Center, Pittsburgh, PA, USA; [4]Fiona Stanley Hospital, Perth, Australia; [5]Edith Cowan University, Perth, Australia; [6]Hospital Universitario Virgen Macarena, Seville, Spain; [7]Fondazione IRCCS Istituto Nazionale dei Tumori, Milano, Italy; [8]Maria Sklodowska-Curie National Research Institute of Oncology, Warsaw, Poland; [9]IRCCS San Martino Polyclinic Hospital, Genoa, Italy; [10]Poznan University of Medical Sciences, Poznan, Poland; [11]Greater Poland Cancer Center, Poznan, Poland; [12]Istituto Oncologico Veneto, IOV-IRCCS, Padova, Italy; [13]Institut Gustave Roussy, Villejuif, France and Paris-Saclay University, Villejuif, France; [14]AP-HM Hospital, Aix-Marseille University, Marseille, France; [15]Dermopathic Institute of the Immaculate IDI-IRCCS, Rome, Italy; [16]University Hospital Essen & German Cancer Consortium Partner Site, Essen, Germany; [17]Westmead and Blacktown Hospitals, Sydney, Australia; [18]Merck & Co., Inc., Rahway, NJ, USA; [19]UMCUtrecht & Princess Máxima Center, Utrecht, NL; CCC Munich, Munich, Germany; [20]Istituto Nazionale Tumori IRCCS Fondazione Pascale, Naples, Italy

RTP RESEARCH TO PRACTICE

KEYNOTE-716: Relapse-Free Survival with Longer Follow-Up at Third Interim Analysis



Long GV et al. ASCO 2022;Abstract LBA9500.

RTP RESEARCH TO PRACTICE

2022 ASCO® ANNUAL MEETING

Abstract 356154

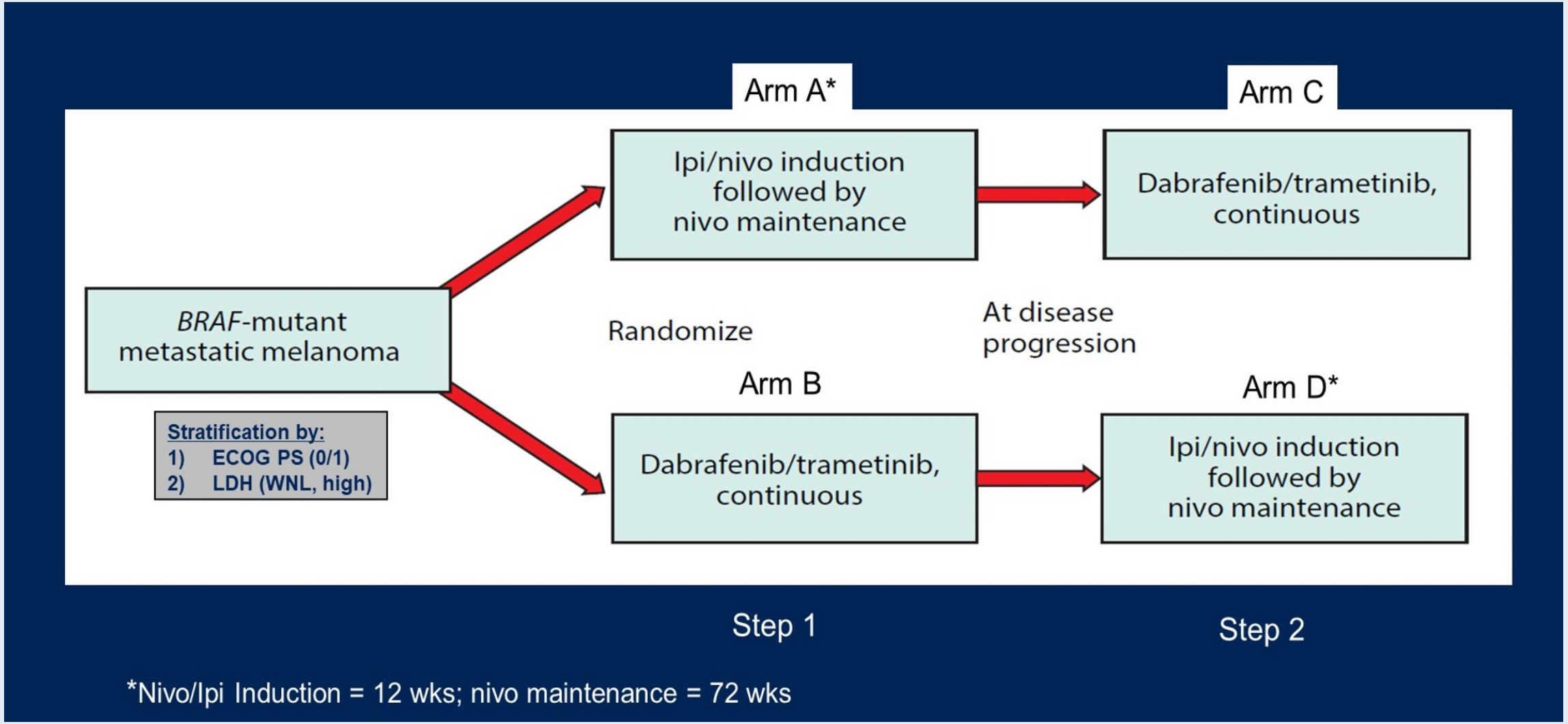
DREAMseq (Doublet, Randomized Evaluation in Advanced Melanoma Sequencing) a Phase III Trial: ECOG-ACRIN EA6134

Michael B. Atkins[1], Sandra Lee[2], Bartosz Chmielowski[3], Antoni Ribas[3], Ahmad A. Tarhini[4], Thach-Giao Truong[5], Diwakar Davar[6], Mark O'Rourke[7], Brendan D. Curti[8], Joanna M. Brell[9], Kari L. Kendra[10], Alexandra P. Ikeguchi[11], Jedd D. Wolchok[12], John M. Kirkwood[6]

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

PRESENTED BY:
Michael B. Atkins, MD

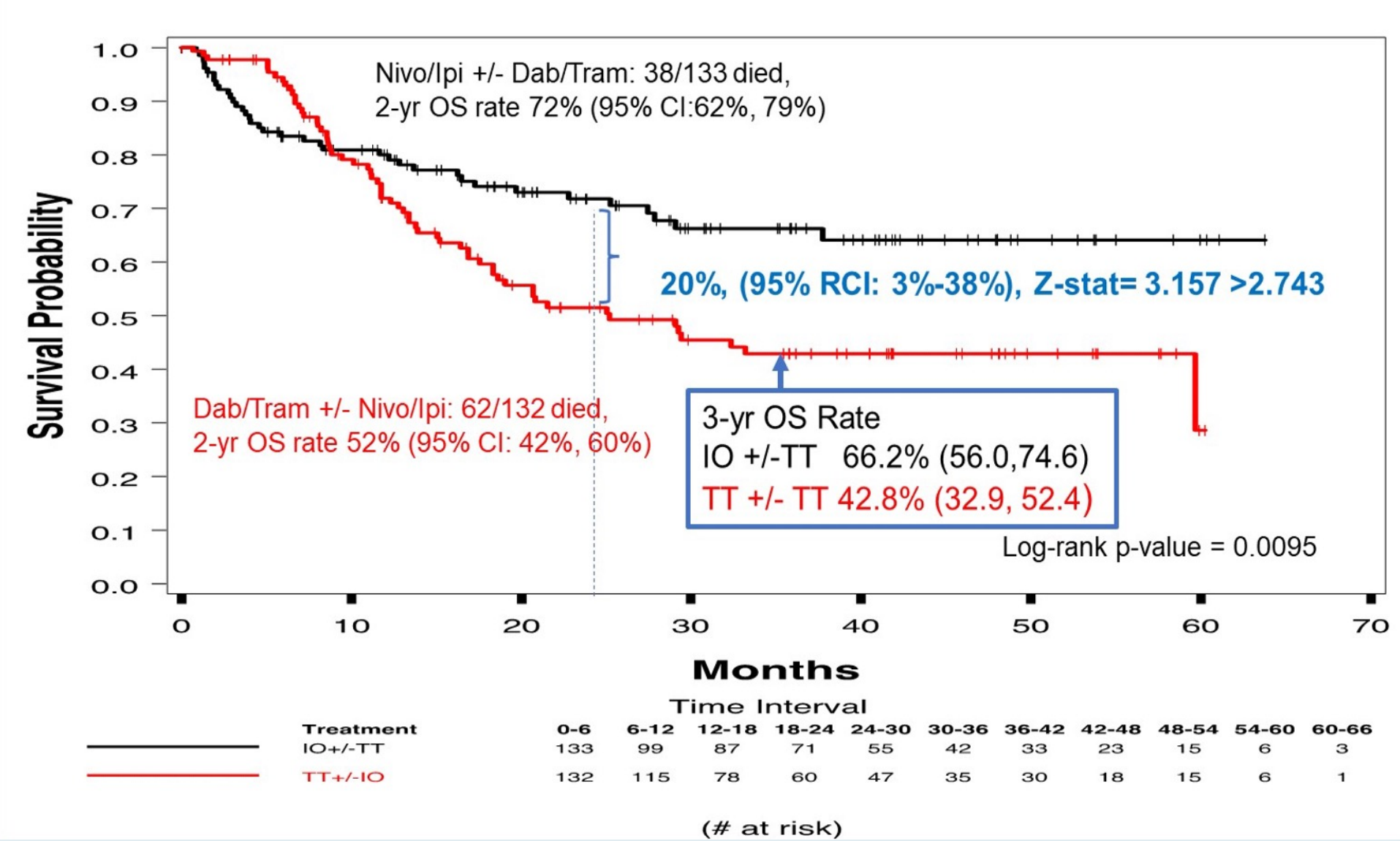
DREAMseq Study Schema



Ipi = ipilimumab; nivo = nivolumab

Atkins MB. ASCO 2022;Abstract 356154.

DREAMseq: Overall Survival (OS)



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

Atkins MB. ASCO 2022;Abstract 356154.

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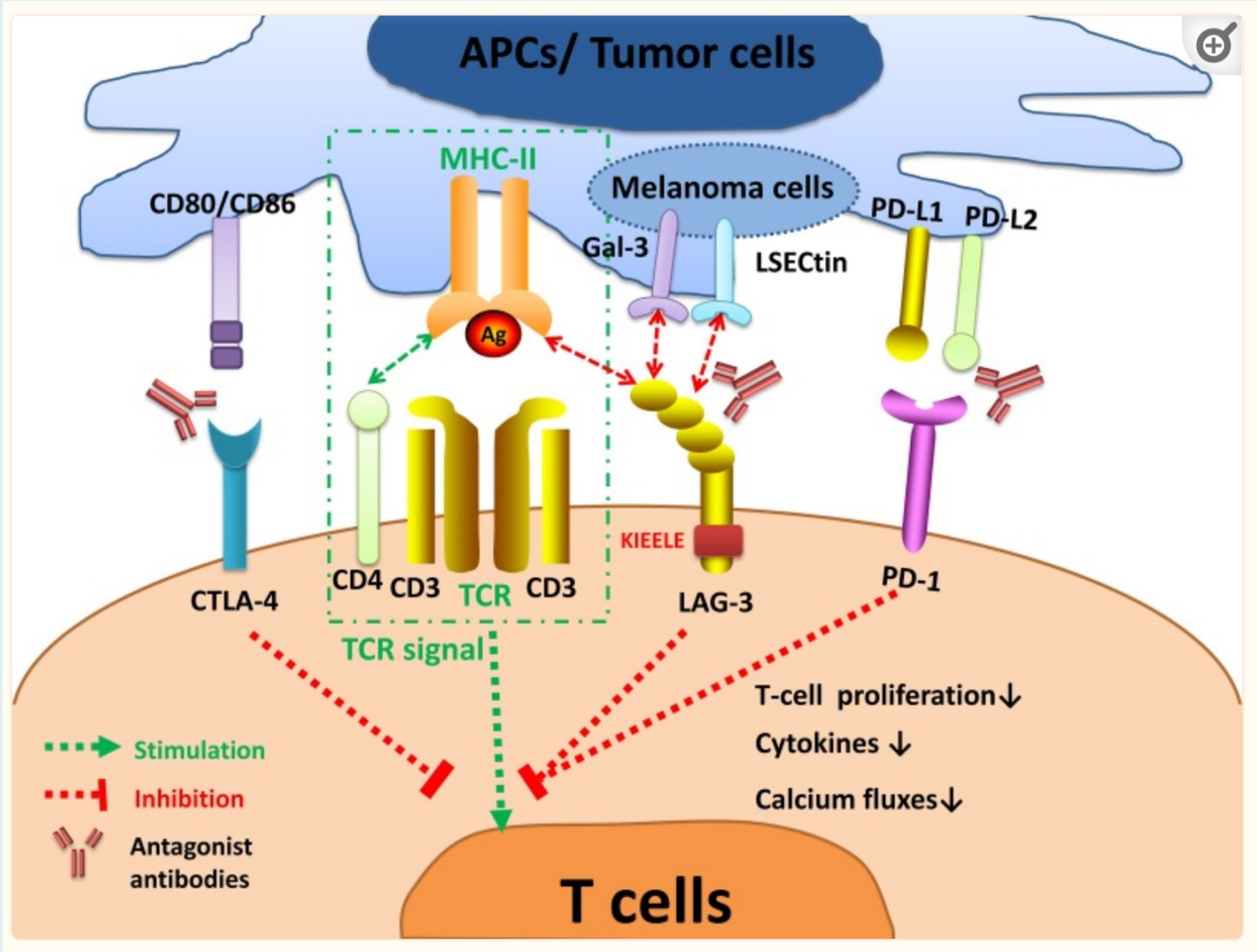
DREAMseq: Conclusions

- 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

Atkins MB. ASCO 2022;Abstract 356154.

LAG-3 Signaling and Interplay with Other Immune Checkpoints



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

Long L et al. *Genes Cancer* 2018;9(5-6):176-89.

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."

https://www.fda.gov/drugs/resources-information-approved-drugs/fda-approves-opdualag-unresectable-or-metastatic-melanoma

RTP RESEARCH TO PRACTICE

2022 ASCO® ANNUAL MEETING

ADVANCING EQUITABLE CANCER CARE THROUGH INNOVATION

Abstract 9505

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

Hussein A. Tawbi[1], F. Stephen Hodi[2], Evan J. Lipson[3], Dirk Schadendorf[4], Paolo A. Ascierto[5], Luis Matamala[6], Pamela Salman[6*], Erika Castillo Gutiérrez[7], Piotr Rutkowski[8], Helen J. Gogas[9], Christopher D. Lao[10], Juliana Janoski De Menezes[11], Stéphane Dalle[12], Ana Arance[13], Jean-Jacques Grob[14], Sarah Keidel[15], Karin Jonczak[15], Anne Marie Sobiesk[15], Sonia Dolfi[15], Georgina V. Long[16]

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

**Affiliation during the time of the trial*

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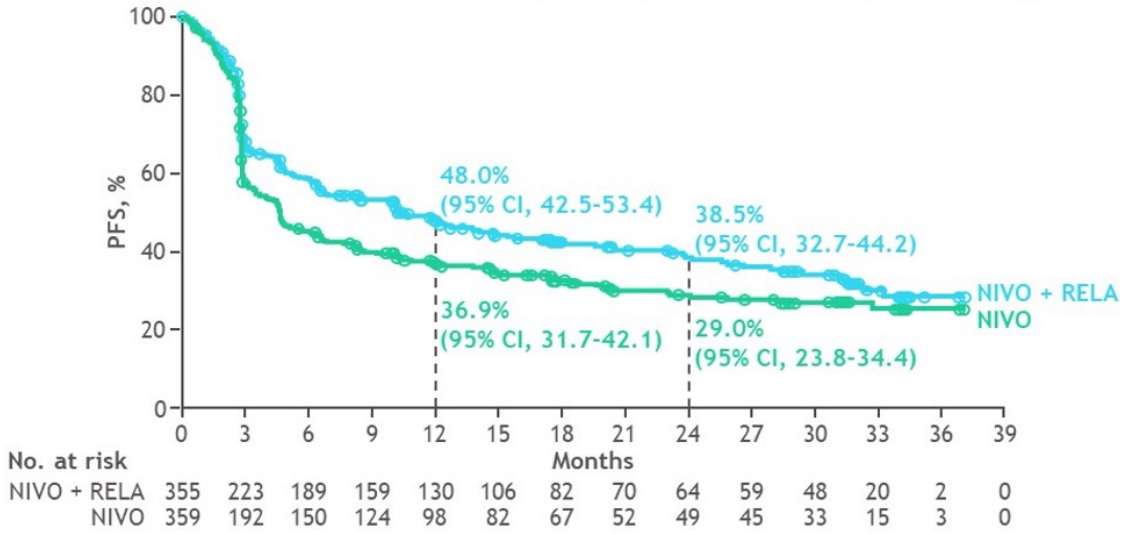
Tawbi HA et al. ASCO 2022;Abstract 9505.

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

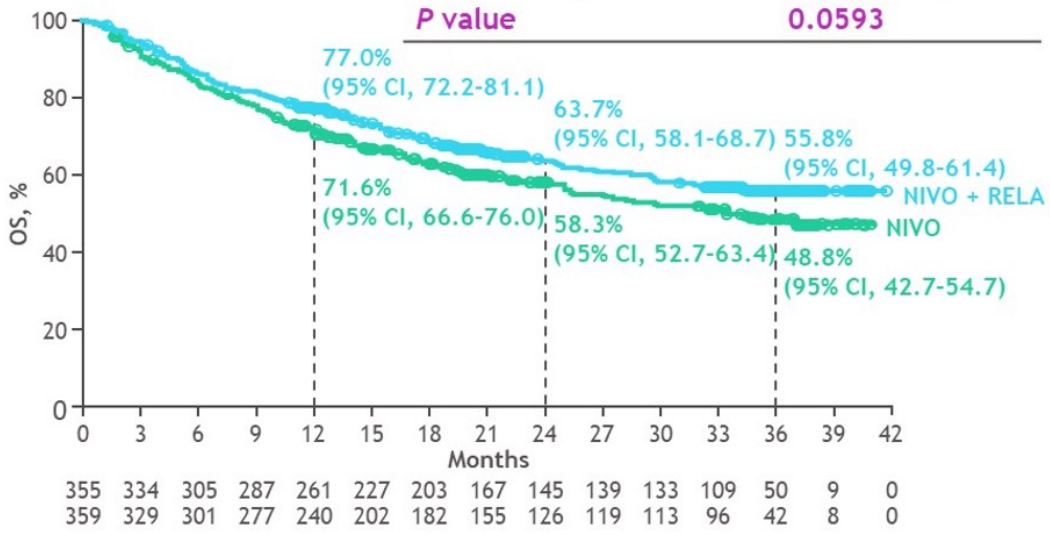
Updated PFS by BICR

	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)	



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	



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

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

Tawbi HA et al. ASCO 2022;Abstract 9505.

RTP RESEARCH TO PRACTICE

PARIS 2022 ESMO congress

Abstract 790MO

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 Gullo[16]

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

*Formerly with Regeneron Pharmaceuticals, Inc.

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Fianlimab and Cemiplimab for Advanced Melanoma

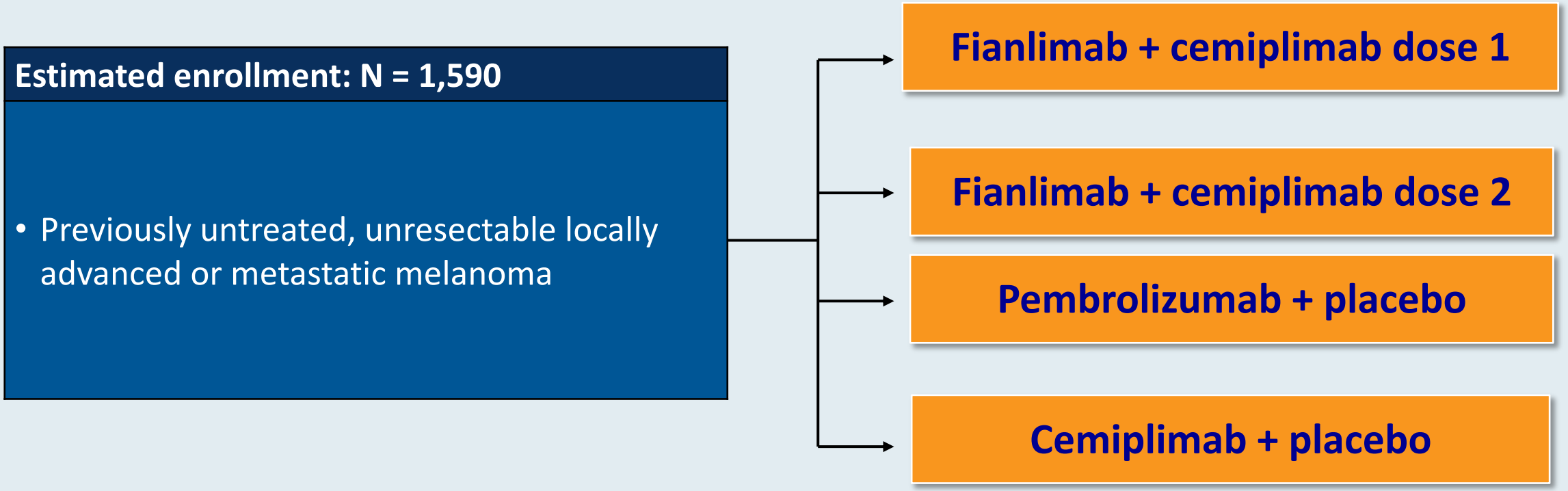
% (n), unless otherwise stated	Anti-PD-(L)1-naive		
	Cohort 6 (N=40)	Cohort 15 (N=40)	Cohorts 6 + 15 (N=80)
ORR, % (95% CI)	**62.5 (45.8, 77.3)**	**65 (48.3, 79.4)**	**63.8 (52.2, 74.2)**
Complete response	15.0 (6)	2.5 (1)	8.8 (7)
Partial response	47.5 (19)	62.5 (25)	55.0 (44)
Stable disease	17.5 (7)	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

Hamid O et al. ESMO 2022;Abstract 790MO.

R3767-ONC-2011 Phase III Trial Design

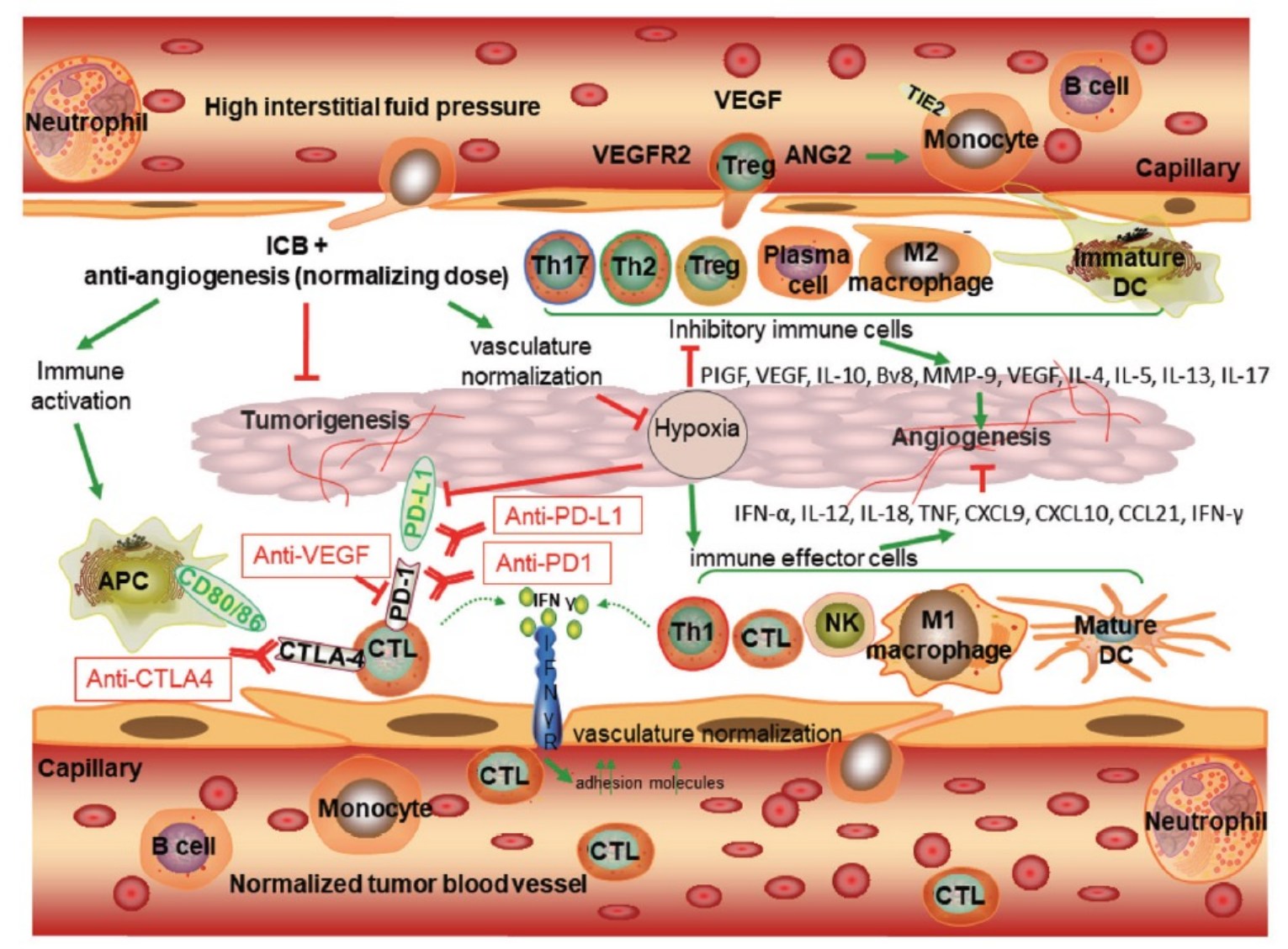


Primary endpoints: Progression-free survival (BICR)

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

www.clinicaltrials.gov. NCT05352672. Accessed September 2022.

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



Zhu L et al. *Oncogenesis* 2021;10:47.

RTP RESEARCH TO PRACTICE

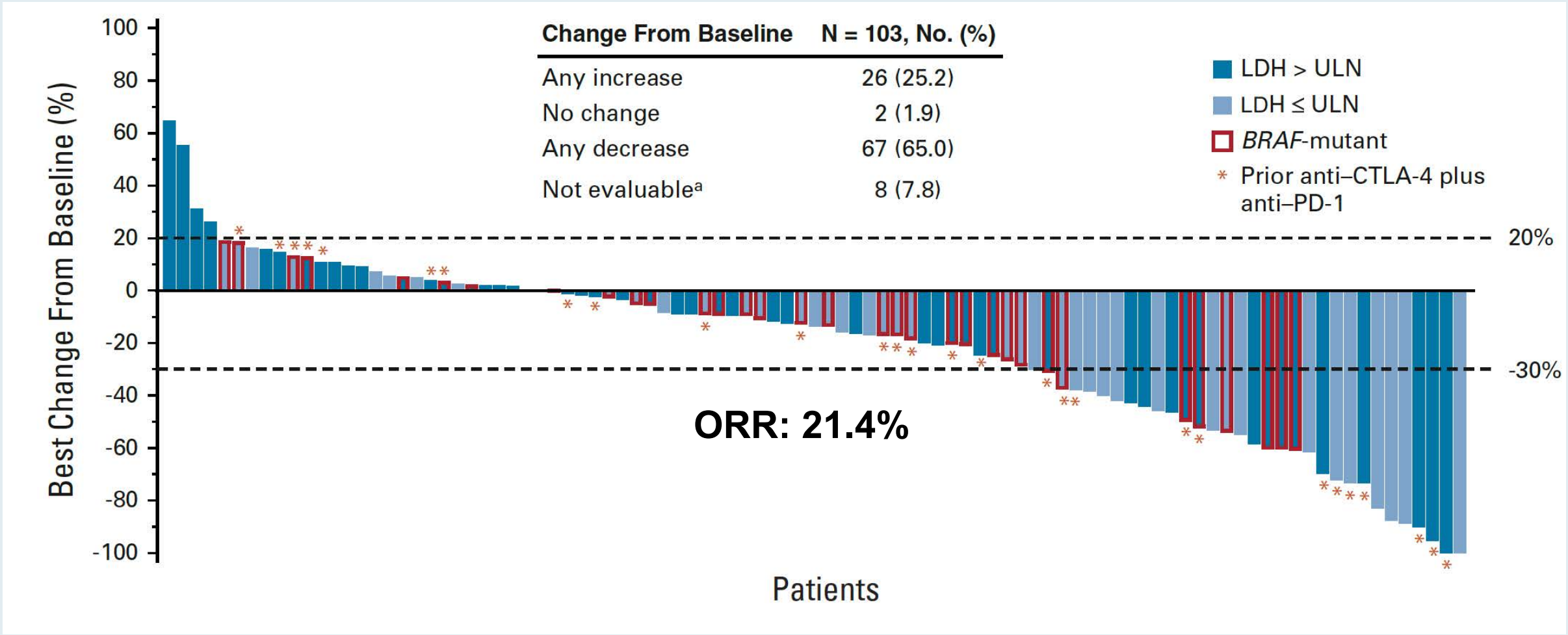
original reports

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, PhD[1]; Luis de la Cruz-Merino, MD, PhD[2]; Teresa M. Petrella, MD[3]; Rahima Jamal, MD[4]; Lars Ny, MD, PhD[5]; Ana Carneiro, MD, PhD[6]; Alfonso Berrocal, MD[7]; Ivan Márquez-Rodas, MD, PhD[8]; Anna Spreafico, MD, PhD[9]; Victoria Atkinson, MD[10]; Fernanda Costa Svedman, MD, PhD[11]; Andrew Mant, MBBS[12]; Muhammad A. Khattak, MBBS, FRACP[13]; Catalin Mihalcioiu, MD[14]; Sekwon Jang, MD[15]; C. Lance Cowey, MD[16]; Alan D. Smith, MD[17]; Natalyn Hawk, MD, PhD[18]; Ke Chen, MS[19]; Scott J. Diede, MD, PhD[19]; Clemens Krepler, MD[19]; and Georgina V. Long, MBBS, PhD[20,21,22,23]

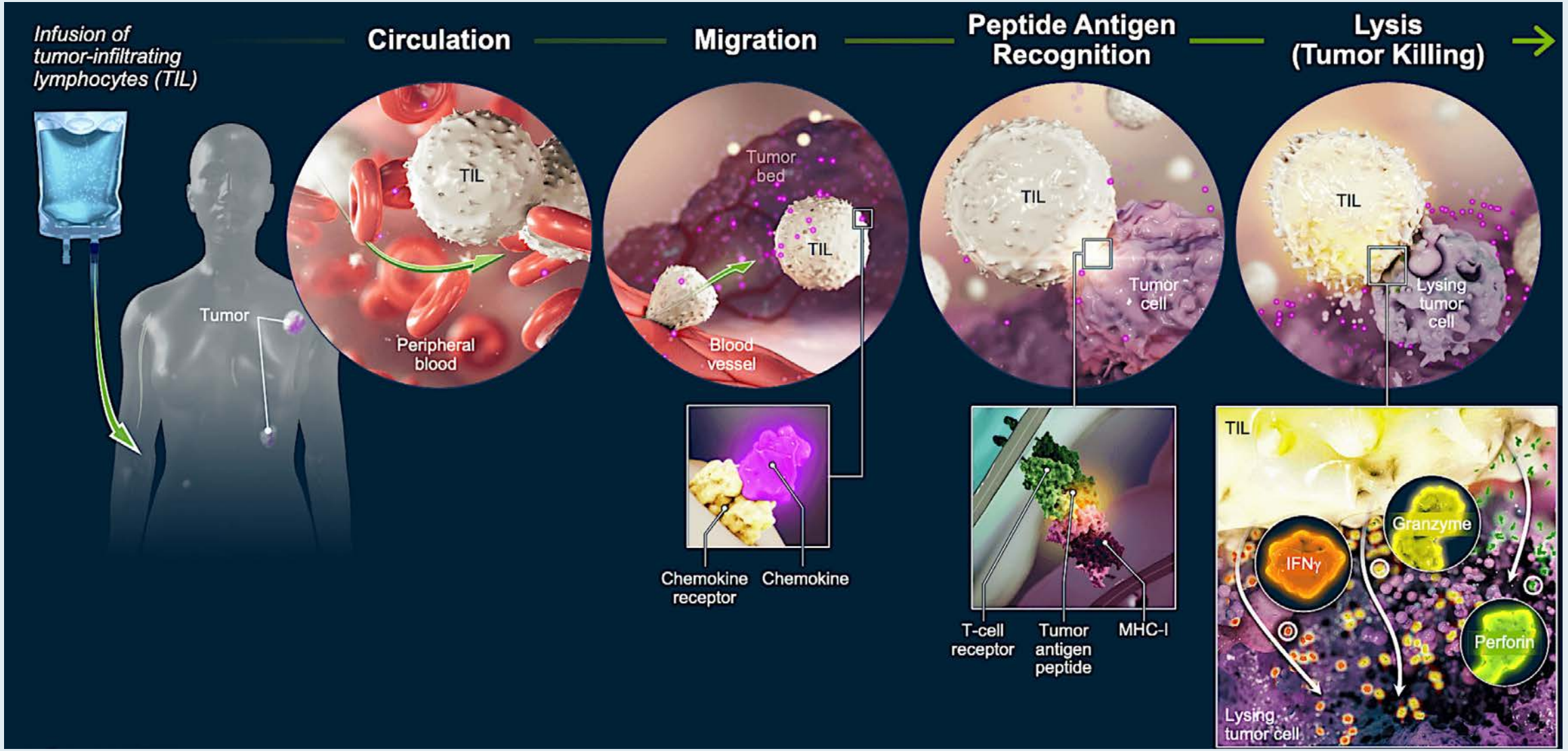
J Clin Oncol 2022 June 2;[Online ahead of print].

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



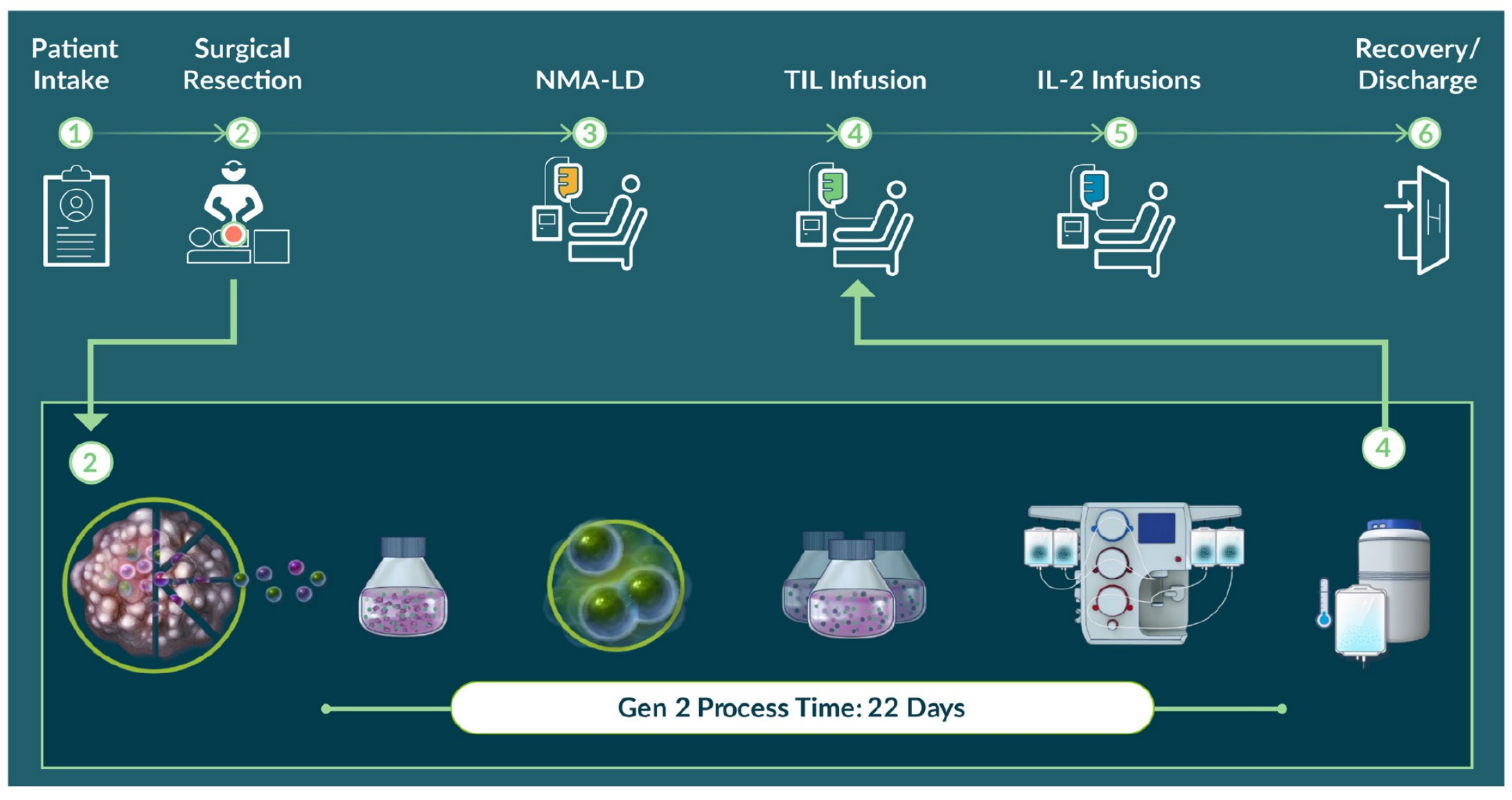
Arance A et al. *J Clin Oncol* 2022 June 2;[Online ahead of print].

Tumor-Infiltrating Lymphocytes (TIL) Mechanism of Action



Fardis M et al. *Cell Gene Ther Insights* 2020;6(6):855-63.

Proprietary TIL Therapy Process



NMA-LD = a nonmyeloablative lymphodepleting regimen

Fardis M et al. *Cell Gene Ther Insights* 2020;6(6):855-63.

RTP RESEARCH TO PRACTICE

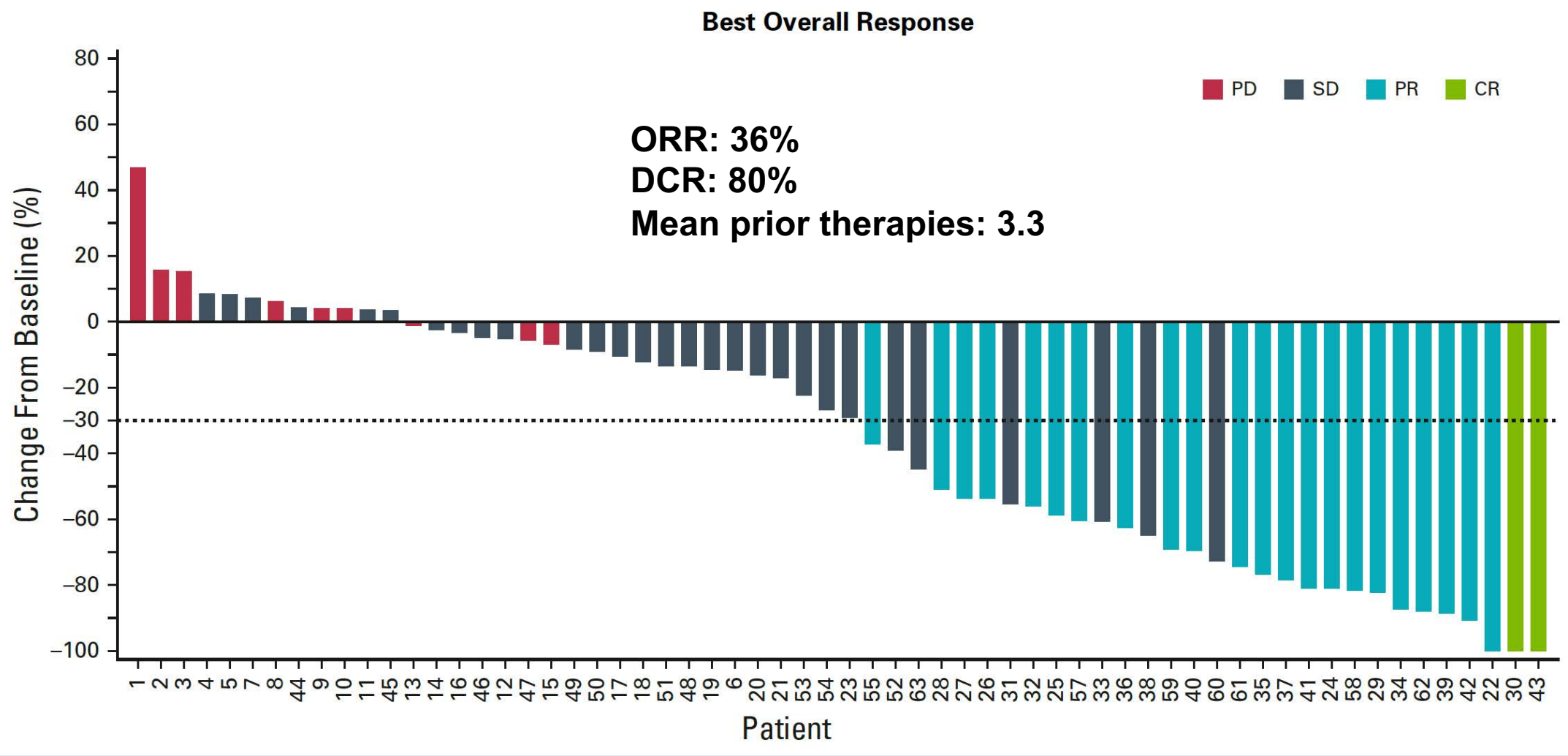
rapid communications

Lifileucel, a Tumor-Infiltrating Lymphocyte Therapy, in Metastatic Melanoma

Amod A. Sarnaik, MD[1]; Omid Hamid, MD[2]; Nikhil I. Khushalani, MD[1]; Karl D. Lewis, MD[3]; Theresa Medina, MD[3]; Harriet M. Kluger, MD[4]; Sajeve S. Thomas, MD[5]; Evidio Domingo-Musibay, MD[6]; Anna C. Pavlick, DO, MBA[7]; Eric D. Whitman, MD[8]; Salvador Martin-Algarra, MD, PhD[9]; Pippa Corrie, PhD, FRCP[10]; Brendan D. Curti, MD[11]; Judit Oláh, MD, DSc[12]; Jose Lutzky, MD[13]; Jeffrey S. Weber, MD, PhD[7]; James M. G. Larkin, MD, PhD[14]; Wen Shi, MD, PhD[15]; Toshimi Takamura, BA, BS[15]; Madan Jagasia, MD[15]; Harry Qin, PhD[15]; Xiao Wu, PhD[15]; Cecile Chartier, PhD[15]; Friedrich Graf Finckenstein, MD[15]; Maria Fardis, PhD, MBA[15]; John M. Kirkwood, MD[16]; and Jason A. Chesney, MD, PhD[17]

J Clin Oncol 2021;39:2656-66.

Lifileucel: Investigator-Assessed ORR in Metastatic Melanoma



ORR = objective response rate

Sarnaik AA et al. *J Clin Oncol* 2021;39:2656-66.

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Regenerative Medicine Advanced Therapy Designation

"As described in Section 3033 of the 21st Century Cures Act, a drug is eligible for regenerative medicine advanced therapy (RMAT) designation if:

a. The drug is a regenerative medicine therapy, which is defined as a cell therapy, therapeutic tissue engineering product, human cell and tissue product, or any combination product using such therapies or products, except for those regulated solely under Section 361 of the Public Health Service Act and part 1271 of Title 21, Code of Federal Regulations;

b. The drug is intended to treat, modify, reverse, or cure a serious or life-threatening disease or condition; and

c. Preliminary clinical evidence indicates that the drug has the potential to address unmet medical needs for such disease or condition

Based on FDA's interpretation of Section 506(g) of the Federal Food, Drug, and Cosmetic Act (as added by Section 3033 of the 21st Century Cures Act), certain human gene therapies and xenogeneic cell products may also meet the definition of a regenerative medicine therapy."

https://www.fda.gov/vaccines-blood-biologics/cellular-gene-therapy-products/regenerative-medicine-advanced-therapy-designation

Thank you for joining us!

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

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