Best of Oncology
An ASCO Direct™ Conference

Best of ASCO: Melanoma Updates

PRESENTED BY

Douglas B. Johnson, MD, MSCI

Vanderbilt University Medical Center

Best of Oncology Conference

Adjuvant/ neoadjuvant therapy

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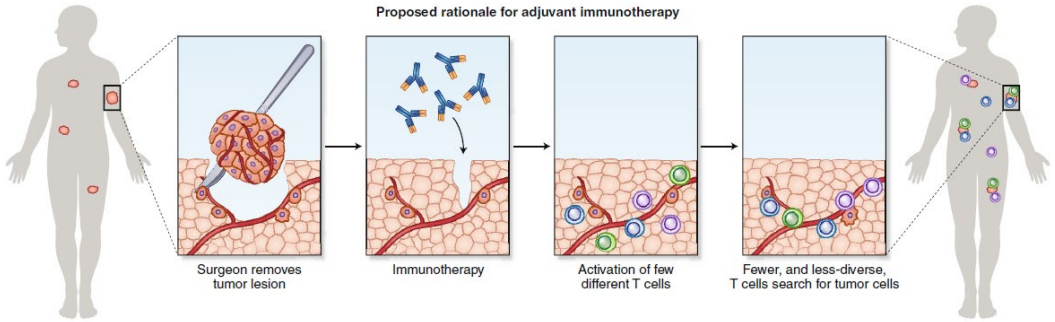
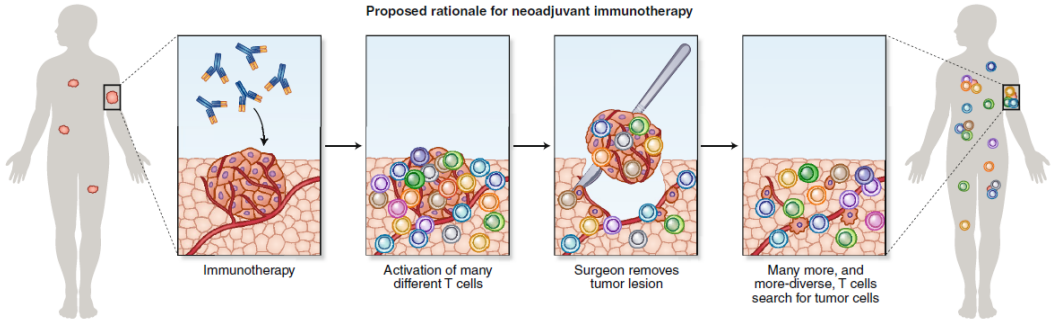
Biological & Early Clinical Rationale for Neoadjuvant Immunotherapy

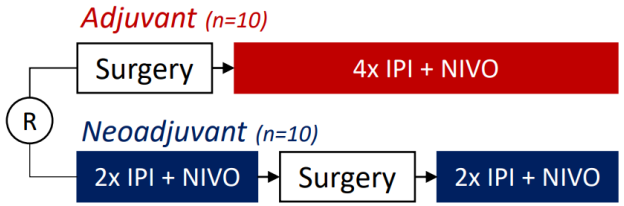
Adjuvant immunotherapy

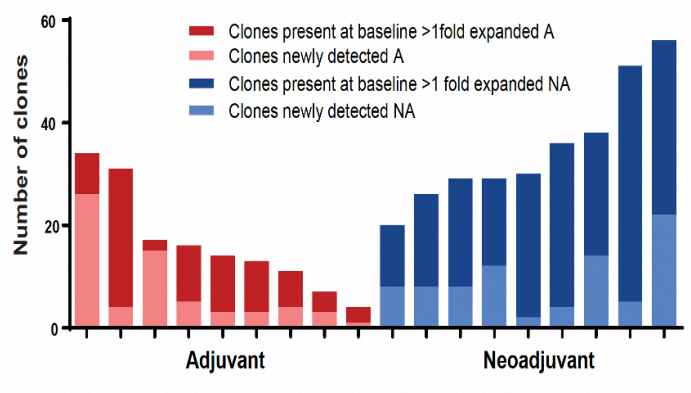


Neoadjuvant immunotherapy

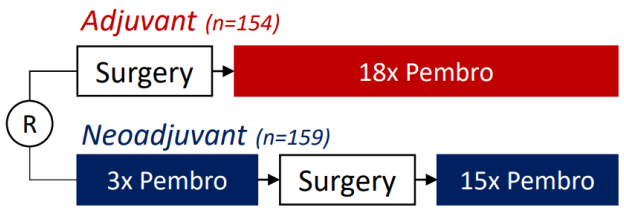


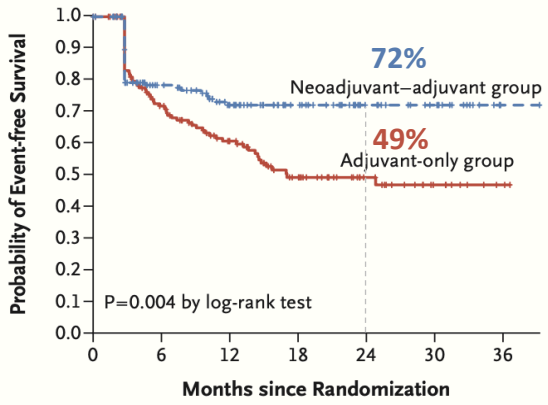
OpACIN (Phase1)
neoadjuvant ipilimumab + nivolumab





SWOG1801 (Phase 2)
neoadjuvant pembrolizumab





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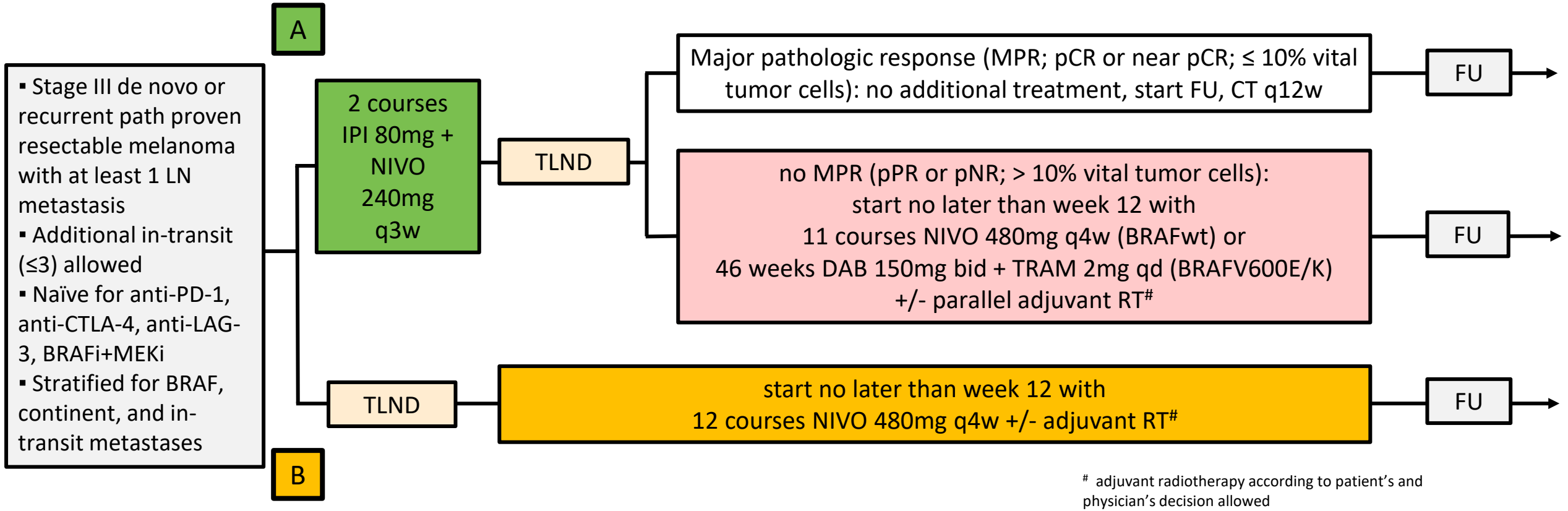
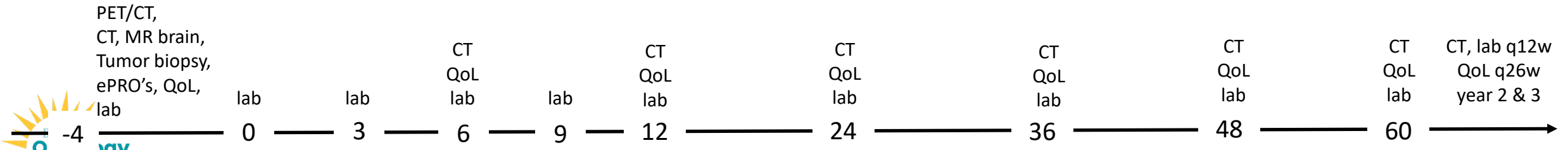
Versluis, Long and Blank, Nat Med 2020; Blank et al., Nat Med 2018; Patel et al., NEJM 2023

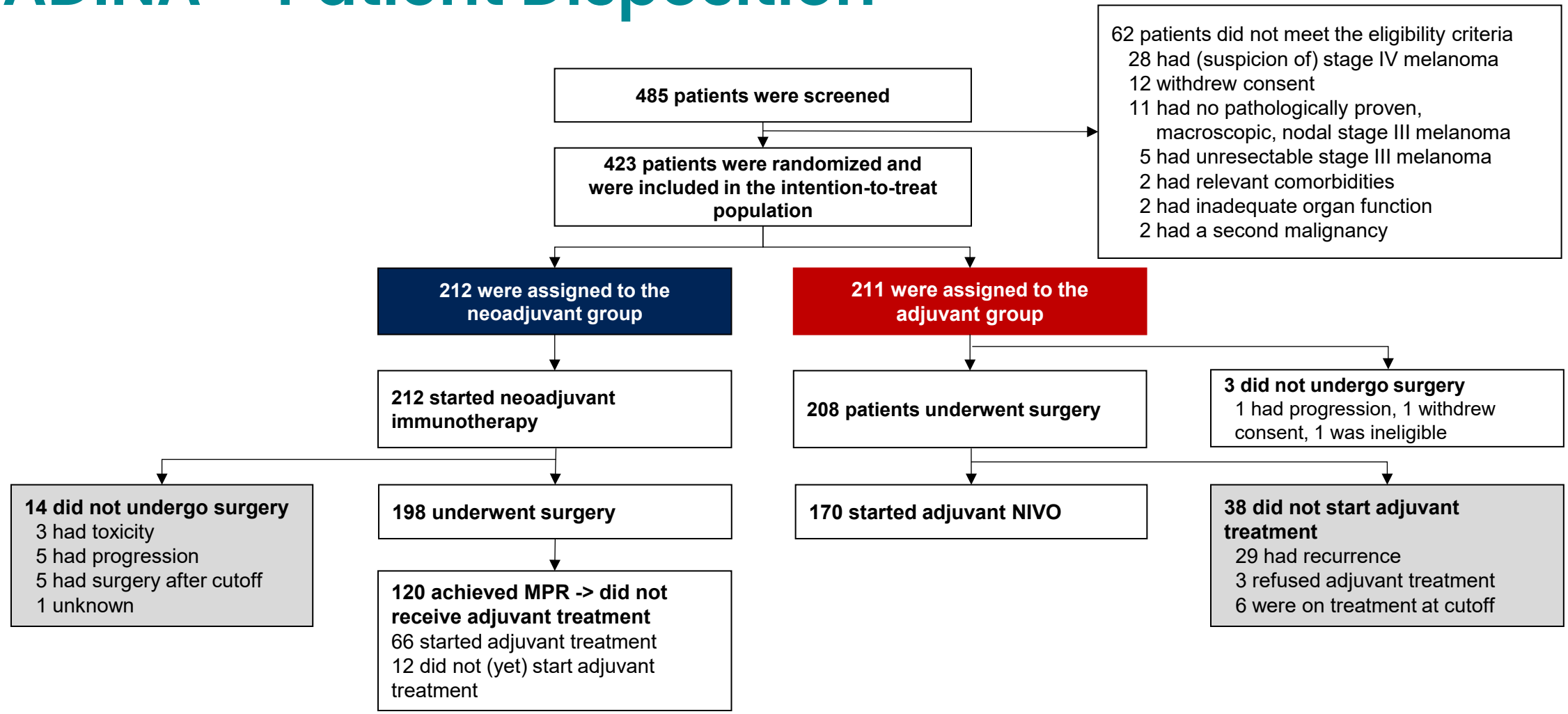
NADINA – Trial Design



adjuvant radiotherapy according to patient's and physician's decision allowed

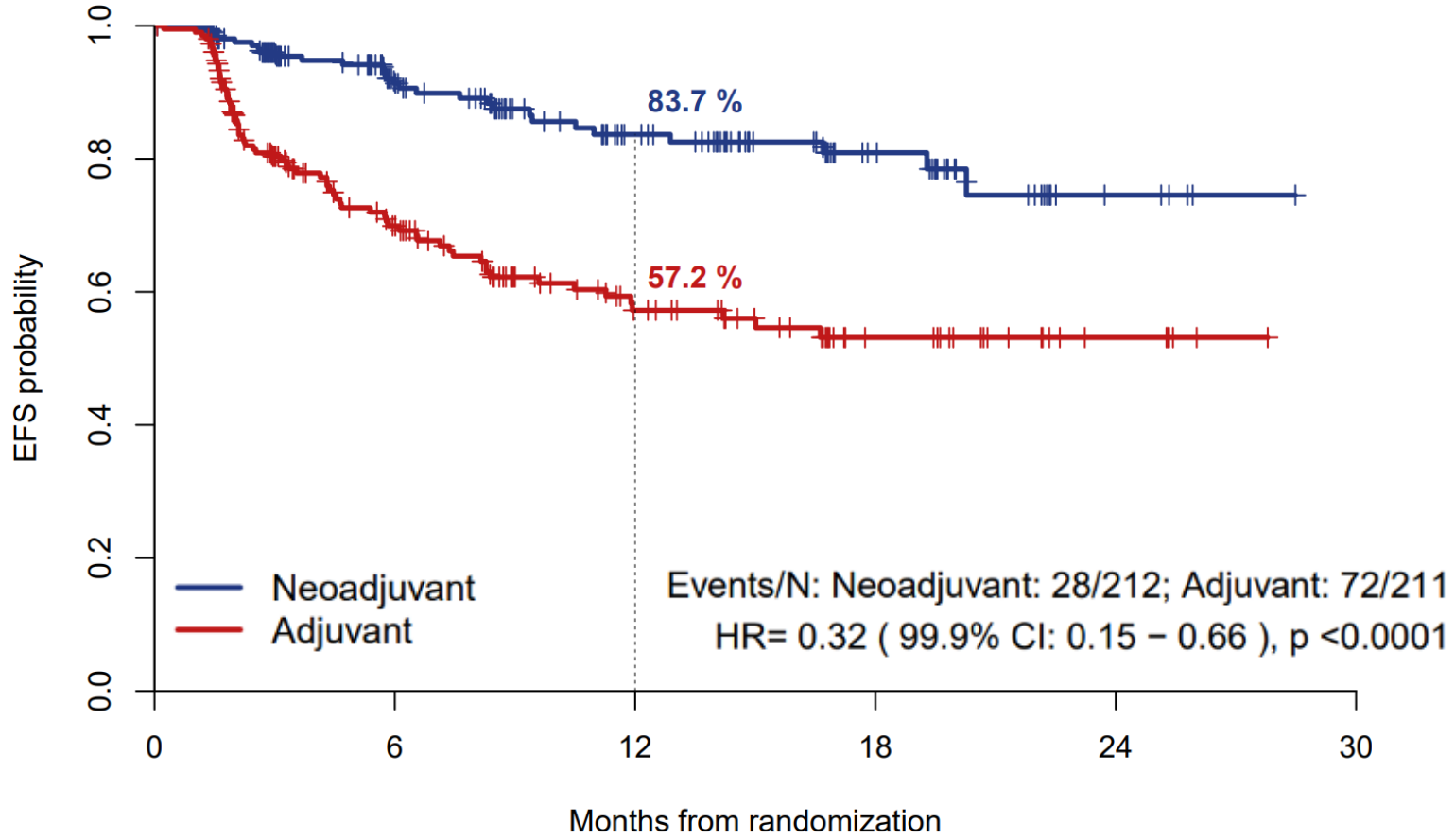


NADINA – Patient Disposition



At data cut-off (January 12, 2024) with a median follow-up of 9.9 months, 99 patients were still on treatment (31 neoadjuvant, 68 adjuvant arm)

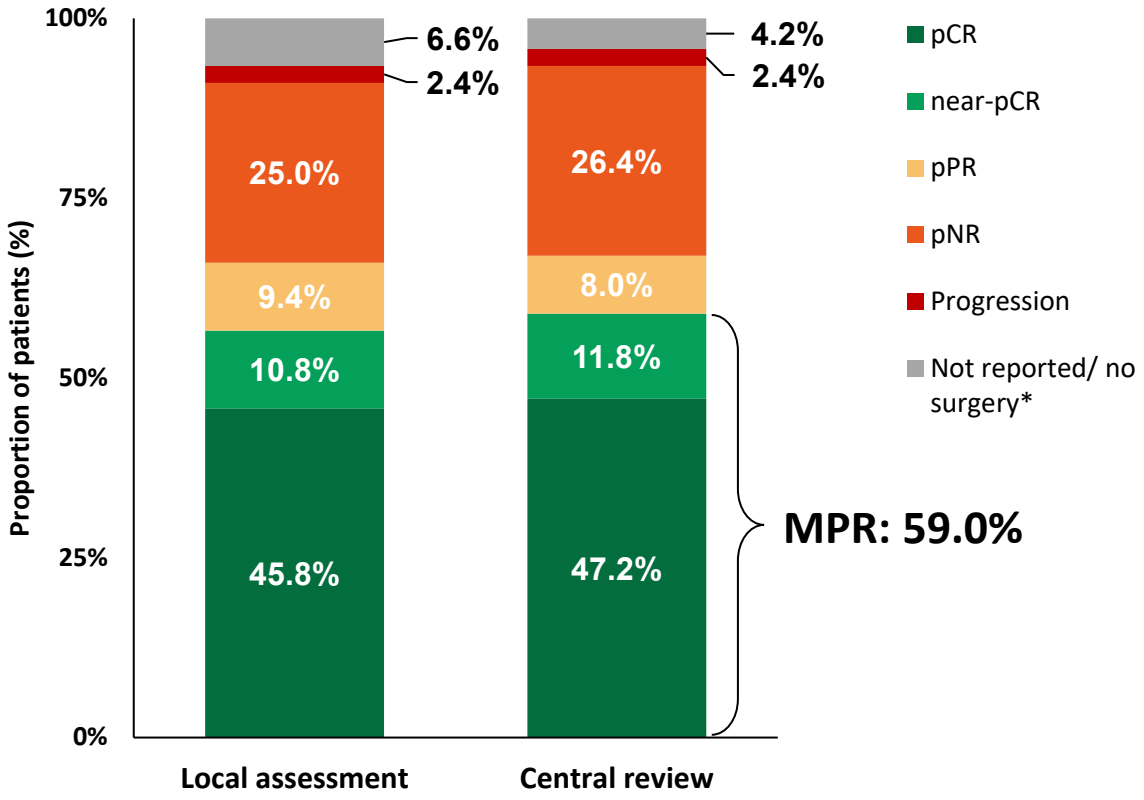
NADINA – Primary Endpoint: Event-Free Survival (EFS)



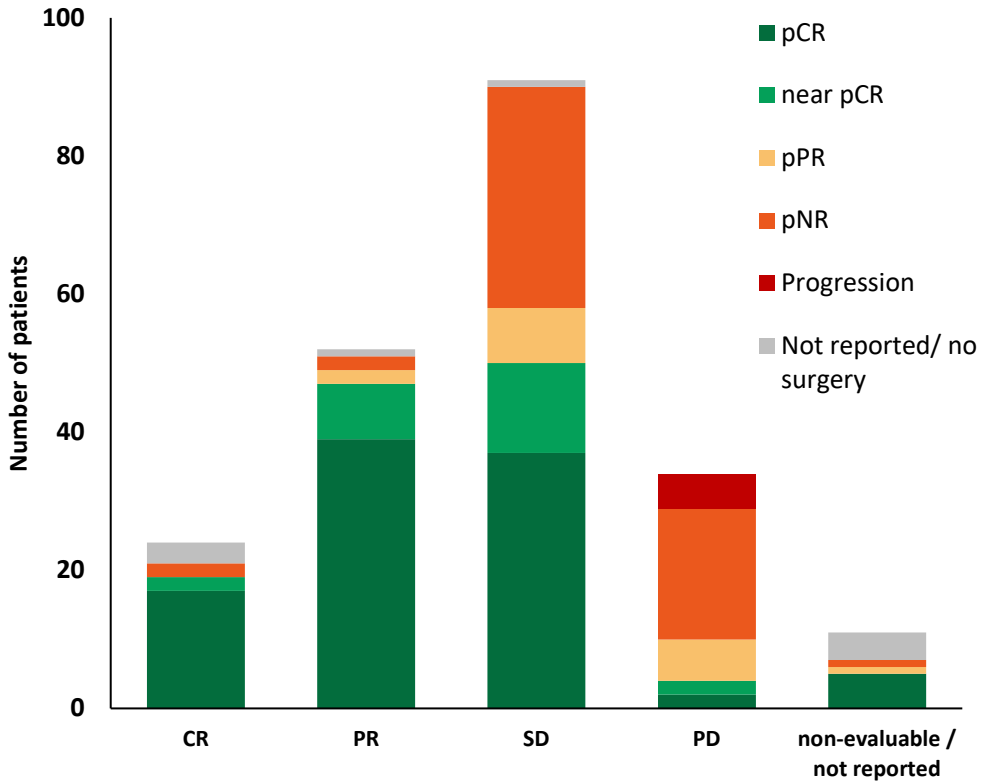
# at risk (censored)										
Neoadjuvant	212	(0)	126	(71)	77	(111)	34	(152)	5	(179)
Adjuvant	211	(0)	100	(57)	53	(89)	23	(116)	6	(133)

NADINA – Pathologic and Radiologic Response

Pathologic Response

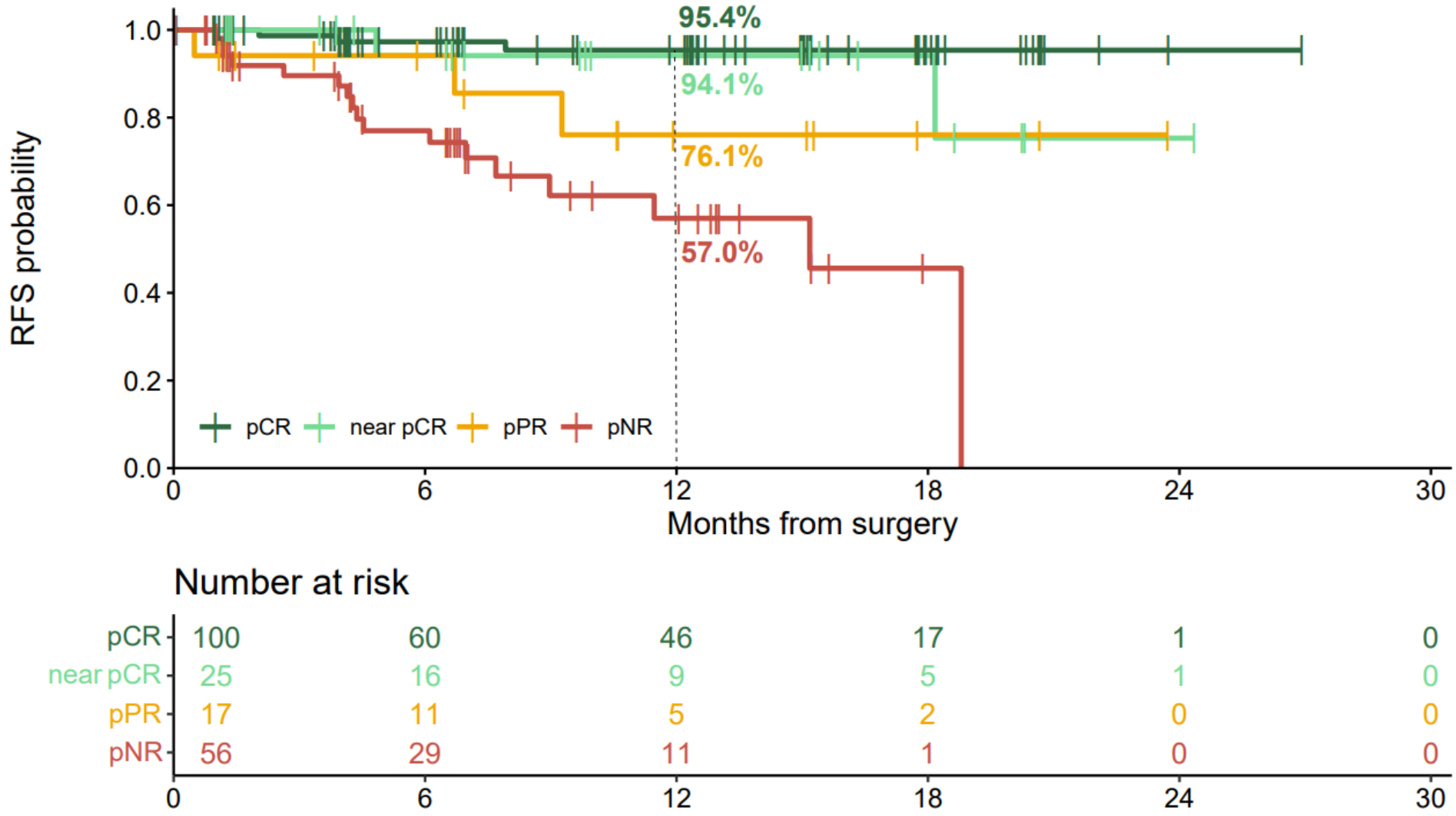


Radiologic- versus Pathologic Response



* Central review was completed for all patients who underwent surgery. At data cutoff, patients had not (yet) undergone surgery (4.2%); 5 patients had surgery after data cutoff.

NADINA – RFS According to Pathologic Response



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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]

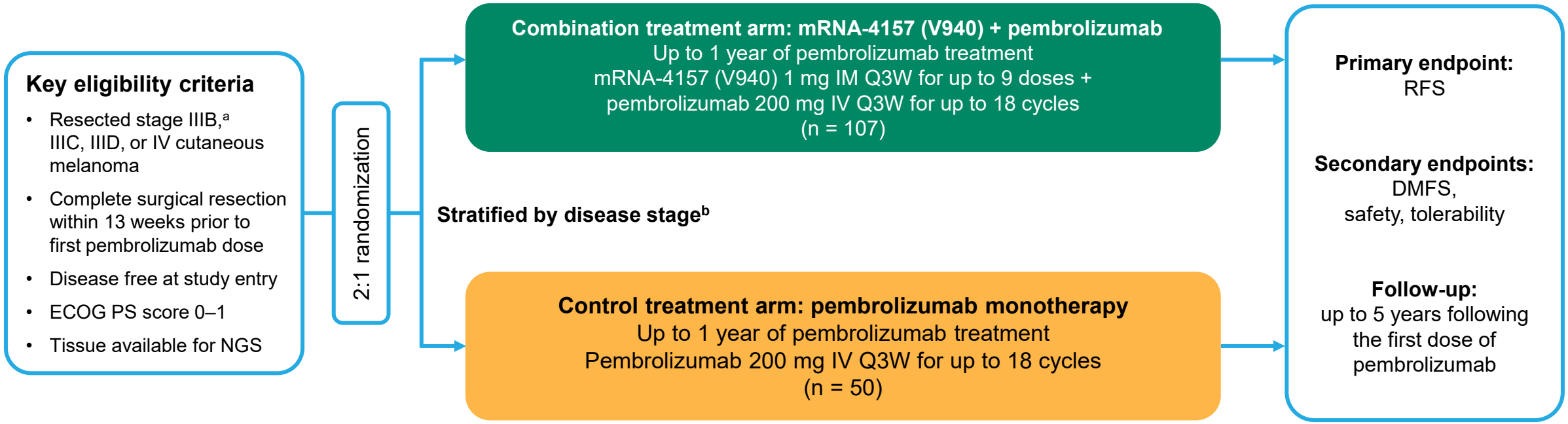
[a]Manju Morrissey,[20] Igor Feldman,[20] Vasudha Sehgal,[20] Huzhang Mao,[20] Jia Guo,[20] Min Liu,[20] Anjali Rao,[20] Wei Zheng,[20] Praveen Aanur,[20] Lakshmi Srinivasan,[20] Mo Huang,[21] Tal Zaks,[20] Michelle Brown,[20] Tracey Posadas[20]

[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.

mRNA-4157-P201/KEYNOTE-942 (NCT03897881) study design

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

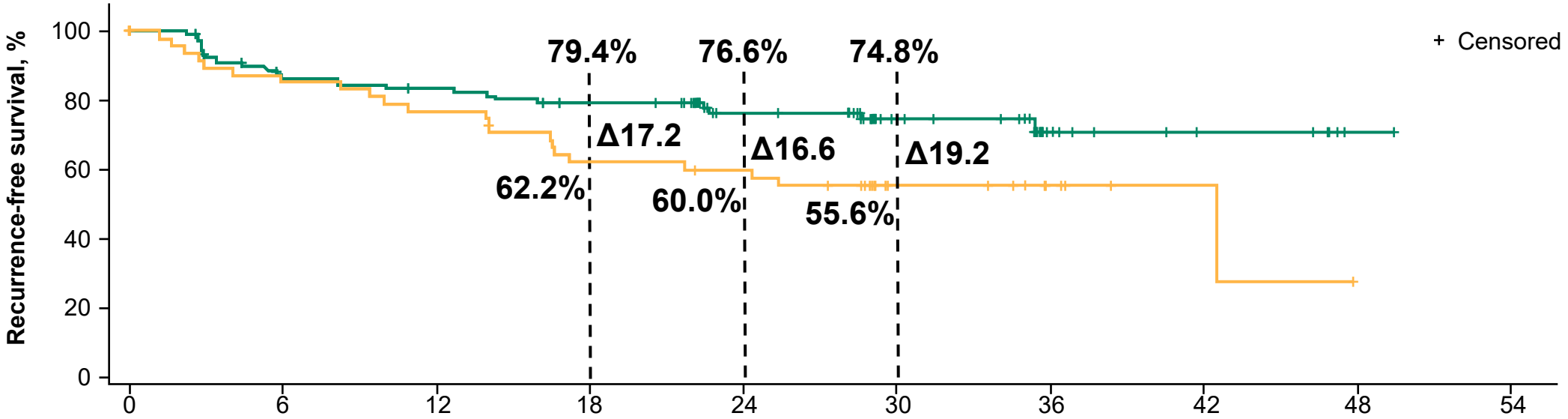


Designed with 80% power to detect a hazard ratio of 0.5 with 40 RFS events (with a 1-sided alpha of 0.1 per protocol)
Primary analysis **triggered after a minimum of 1-year planned follow-up[c]** (November 14, 2022 data cut) and at least 40 RFS events have been observed. DMFS analysis was prespecified for testing following positive RFS in the ITT population

Supportive analysis was **triggered after a minimum of 2 years of planned follow-up[c]** (November 3, 2023 data cut)
Median planned follow-up[c]: ~3yrs

[a]Patients with stage IIIB disease were eligible only if relapse occurred within 3 months of prior surgery of curative intent; [b]According to the 8th edition of the American Joint Committee on Cancer Staging Manual [c]Defined as the time from the first dose date (or date of randomization if not treated) to date of clinical cut-off.
ECOG PS, Eastern Cooperative Oncology Group performance status; IM, intramuscular; ITT, intent-to-treat; IV, intravenous; NGS, next-generation sequencing; Q3W, every 3 weeks.

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.

Metastatic: front-line

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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

RELATIVITY-048: study design

Phase 1/2, nonrandomized trial: advanced melanoma expansion cohort (Part 2B)

Key eligibility criteria
- Previously untreated advanced unresectable, or metastatic melanoma
- Prior neoadjuvant/adjuvant I-O therapies permitted ≥ 6 months prior
- ECOG PS 0–1
- Patients with controlled brain metastases[a] were allowed

N = 46

NIVO 480 mg Q4W + RELA 160 mg Q4W + IPI 1 mg/kg Q8W

Database lock: November 1, 2023[b]
Median follow-up: 49.4 months (range, 0.4–55.0)[c]

Primary endpoints
- Key safety (AE, SAE, AEs leading to discontinuation)
- ORR,[d] DCR,[d] median DOR[d] per INV

Secondary endpoints
- PFS[d] per INV (rates at 6 and 12 months)

Key exploratory endpoints
- OS (rates at 1 and 2 years)

Overall study — phase 1/2, nonrandomized trial evaluating I-O triplets for patients with select solid tumors
Part 1: dose finding for I-O triplets in select solid tumors (except primary CNS); **Part 2: specific tumor-type expansion cohorts**
- Part 1A/2A: NIVO + RELA + IDOi
- Part 1B/**2B: NIVO + RELA + IPI**

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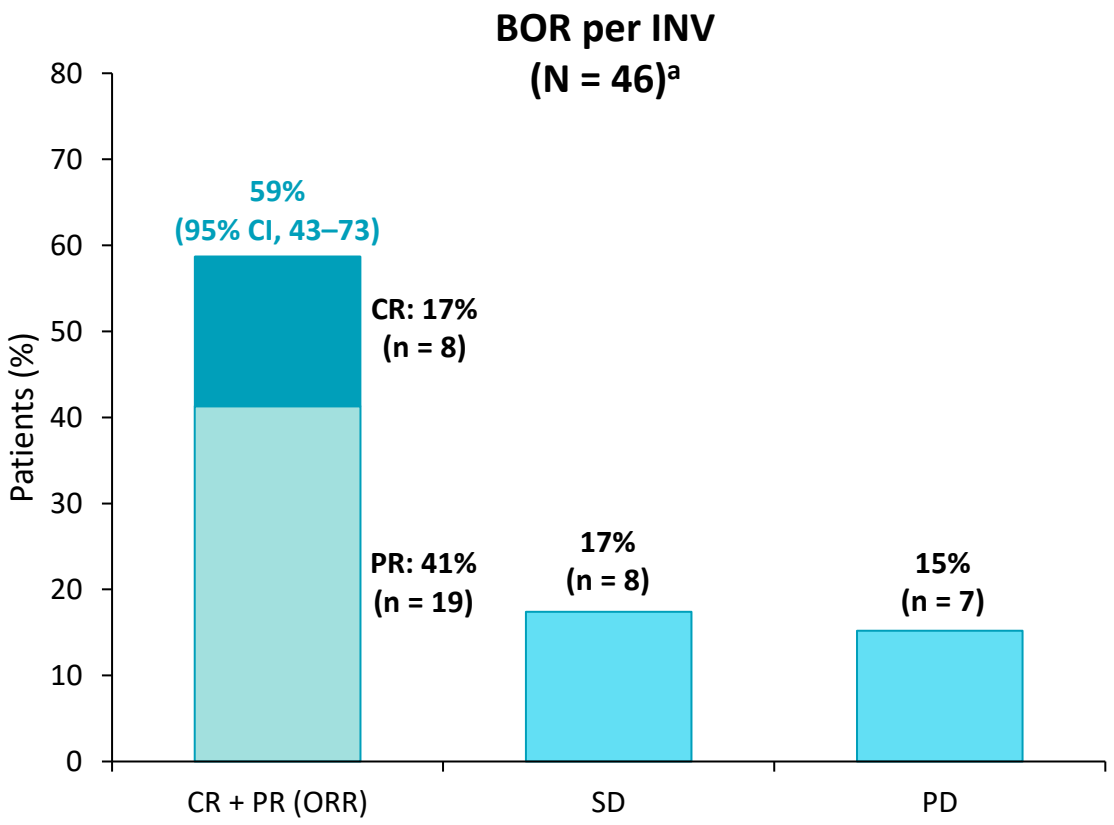
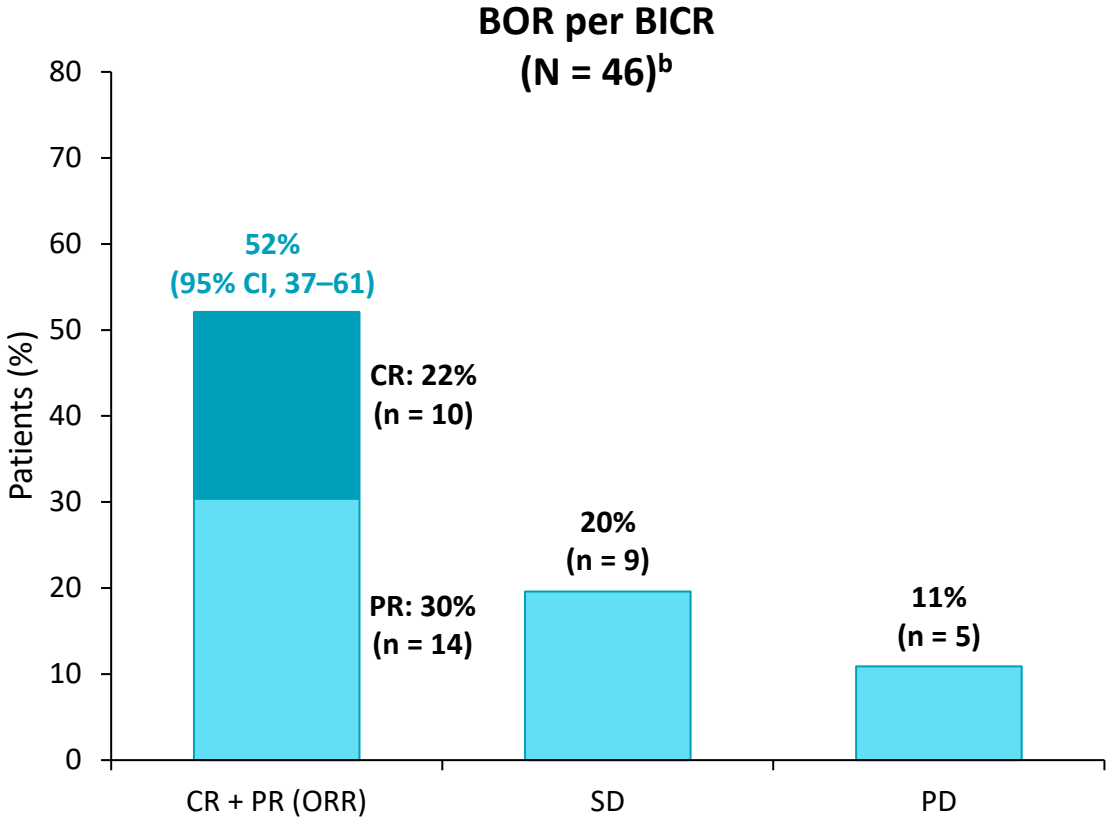
RELATIVITY-048 (NCT03459222). [a]Controlled brain metastases defined as no radiographic progression ≥ 4 weeks after radiation and/or surgery and no steroid use > 2 weeks prior to informed consent. [b]Clinical cutoff date: September 27, 2023; last patient, first visit August 8, 2019. [c]Minimum potential follow-up: 49.7 months. [d]Per RECIST v1.1.

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).

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).

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.

Summary

In RELATIVITY-048, the triplet of NIVO 480 mg + RELA 160 mg + IPI 1 mg/kg demonstrated encouraging efficacy in patients with untreated advanced melanoma at a median follow-up of 49.4 months

- Confirmed ORR per INV: 59% (95% CI, 43–73)
- 48-month PFS rate: 52% (95% CI, 35–66)
- 48-month OS rate: 72% (95% CI, 56–82)

Preliminary efficacy data from 46 patients with advanced melanom… with the triplet combination compare favorably with historical published da… + IPI[1] and NIVO + RELA[2]; cross-trial comparisons should be interpr… caution

There were no new safety signals with NIVO + REL… pared with other I-O combinations

- Grade 3–4 TRAEs: 39%
- Any-grade TRAEs leading to discont…

Larger studies are needed to confirm… efficacy and safety of the PD-1, LAG-3, and CTLA-4 inhibitor triplet combination in this patient group

Jury is still out – need more data

RELATIVITY-048 (NCT03459222). 1. Hodi SF, et al. Presented at the American Society of Medical Oncology (ASCO) Annual Meeting; June 3–7, 2022; Chicago, IL, USA & Online. Abstract 9522. 2. Tawbi HA, et al. Presented at the American Society of Medical Oncology (ASCO) Annual Meeting; June 2–7, 2023; Chicago, IL, USA & Online. Abstract 9502.

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

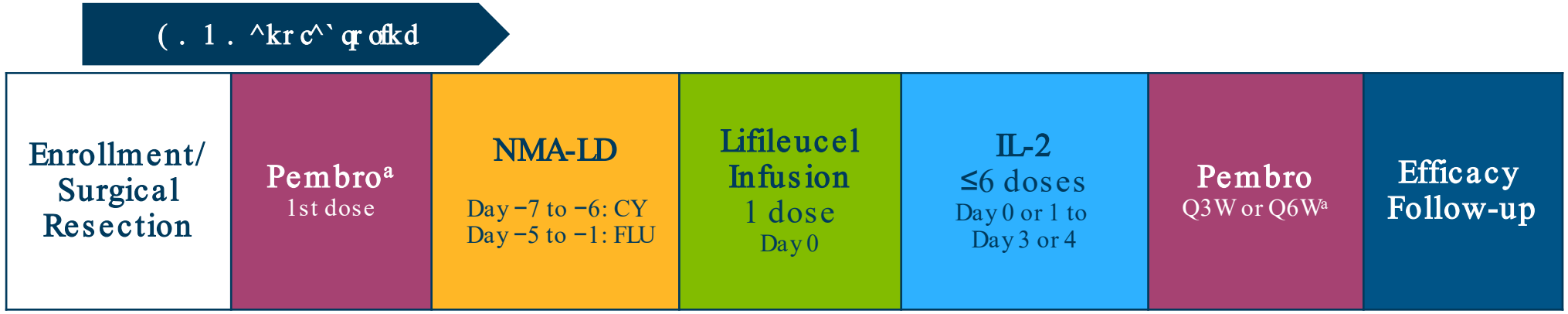
Sajeve Thomas,[1] Helen Gogas,[2] Young Ki Hong,[3] Gino K. In,[4] Bernard Doger de Speville Uribe,[5] Andrew J.S. Furness,[6] Almudena Garcia Castano,[7] Simon Häfliger,[8] Kai He,[9] Theresa Medina,[10] Donald Lawrence,[11] Sylvia Lee,[12] Juan Martin-Liberal,[13] Friedrich Graf Finckenstein,[14] Brian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

IOV-COM-202: Phase 2, Multicohort, Multicenter Study of Lifileucel + Pembrolizumab in Patients With Solid Tumors

- Cohort 1A of IOV-COM-202 (NCT03645928) assesses the efficacy and safety of lifileucel + pembrolizumab in patients with ICI-naive unresectable or metastatic melanoma
  - Patients may have received BRAF/MEK inhibitor treatment if they are *BRAF* mutation positive
  - Eligible patients must have ≥1 resectable lesion (≥1.5-cm diameter) and ≥1 measurable lesion for response assessment per RECIST v1.1
- Trial designed as a proof-of-concept study to support a registrational study in the frontline treatment setting

Treatment Schema



[a]First administration of single-dose pembrolizumab IV 200 mg or 400 mg, followed by pembrolizumab IV 200 mg Q3W or 400 mg Q6W for 24 months or until disease progression or unacceptable toxicity.
CY, cyclophosphamide; EOA, end of assessment; FLU, fludarabine; GMP, Good Manufacturing Practice; ICI, immune checkpoint inhibitor; IL-2, interleukin-2; NMA-LD, nonmyeloablative lymphodepletion; pembro, pembrolizumab; Q3W, every 3 weeks; Q6W, every 6 weeks; RECIST, Response Evaluation Criteria in Solid Tumors.

Safety

Nonhematologic TEAEs in ≥30% of Patients[a]

	N=23	
Preferred Terms, n (%)	Any grade	Grade 3/4
Chills	19 (82.6)	3 (13.0)
Pyrexia	18 (78.3)	4 (17.4)
Nausea	18 (78.3)	0
Vomiting	15 (65.2)	0
Fatigue	14 (60.9)	1 (4.3)
Febrile neutropenia	11 (47.8)	10 (43.5)
Headache	11 (47.8)	0
Diarrhea	10 (43.5)	1 (4.3)
Cough	10 (43.5)	0
Dyspnea	9 (39.1)	1 (4.3)
Alopecia	9 (39.1)	0
Decreased appetite	9 (39.1)	0
Hypertension	8 (34.8)	5 (21.7)
Rash maculopapular	8 (34.8)	3 (13.0)
Peripheral edema	8 (34.8)	1 (4.3)
Hypokalemia	8 (34.8)	0
Abdominal pain	7 (30.4)	0

Grade 3/4 Hematologic Lab Abnormalities[b]

	N=23
Preferred Terms, n (%)	Grade 3/4
Neutropenia	23 (100)
Lymphopenia	23 (100)
Leukopenia	22 (95.7)
Thrombocytopenia	22 (95.7)
Anemia	10 (43.5)

- By Day 30, Grade 3/4 hematologic lab abnormalities resolved to Grade ≤2:
  - Neutropenia: 91.3%
  - Lymphopenia: 78.3%
  - Leukopenia: 95.5%
  - Thrombocytopenia: 95.5%
  - Anemia: 90.0%
- No unexpected AEs
- AEs consistent with the lifileucel regimen occurred and resolved early
- AEs occurring later than 30 days after lifileucel infusion were generally consistent with pembrolizumab monotherapy
- **Safety was consistent with the underlying disease and known safety profiles of pembrolizumab, NMA-LD, lifileucel, and IL-2**

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-(o^ab/ßEebj ^ql il df i^_l o^ql ovql uf fqvar ofkd qeb mboflla ool j qeb pq^oql c/. "≥%ql /◊a^vp^oqboqeb 5*- fkcr pfl k Tfql ^kv obpl ir qfl k a^qb´°
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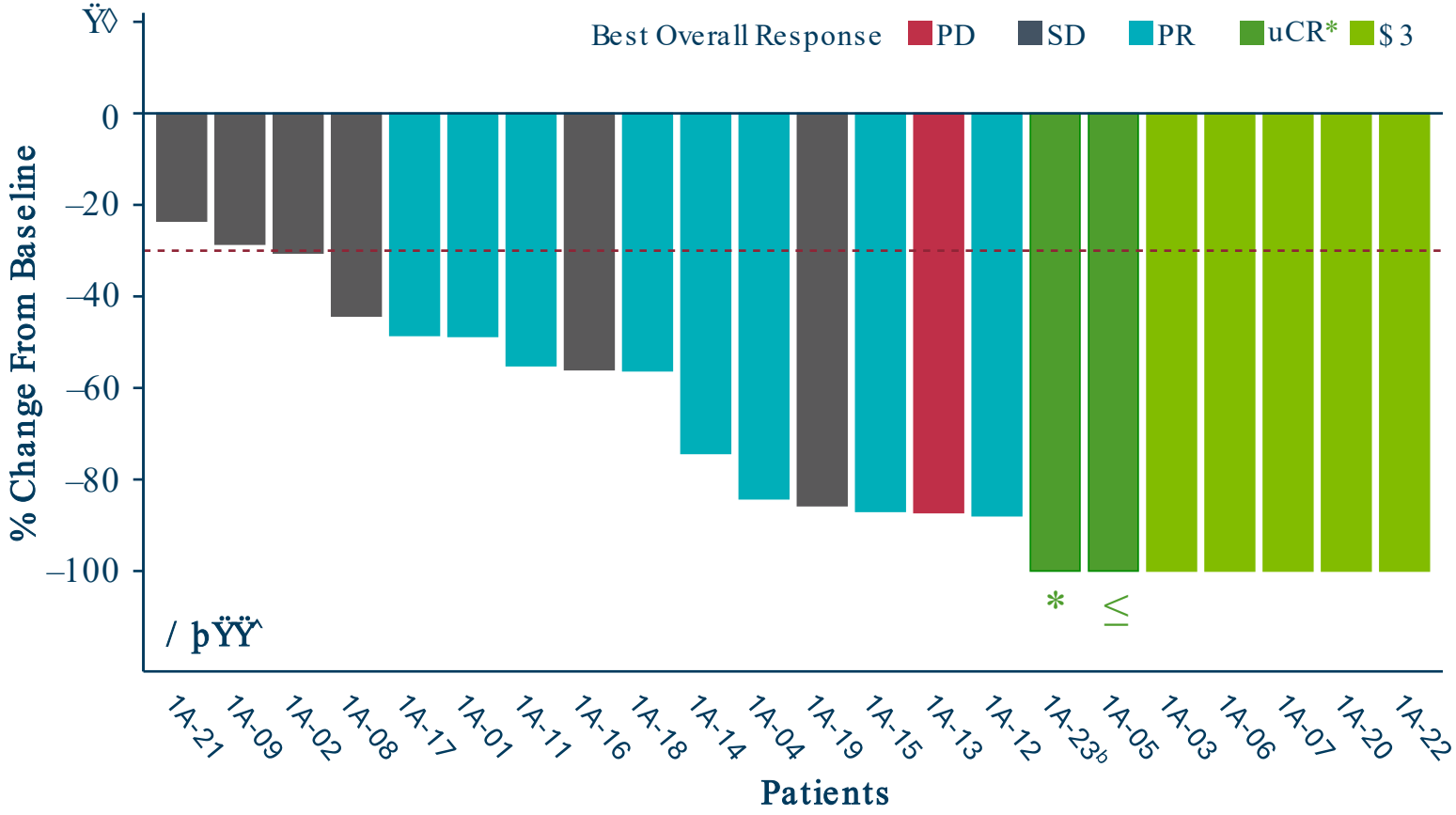
ORR was 65.2%; CR rate was 30.4%

Best Percentage Change From Baseline in Target Lesion SOD



Investigator-Assessed Response (RECIST v1.1)

	N=23
ORR, n (%) (95% CI)	15 (65.2) (42.7, 83.6)
CR	7 (30.4)
PR	8 (34.8)
SD	6 (26.1)
PD	1 (4.3)
NE	1 (4.3)

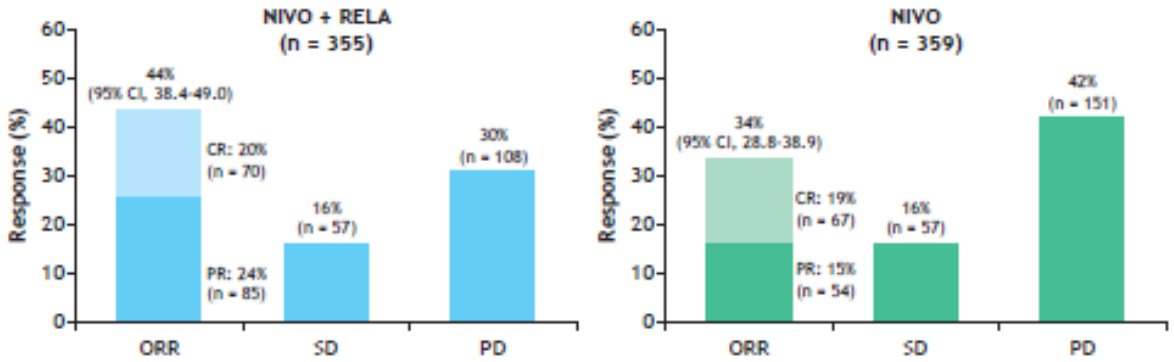
All response-evaluable patients demonstrated regression of target lesions

***The two uCRs have been confirmed post-data cut**

[a]One patient without a postdose tumor response assessment was not included. [b]Target lesion lymph node at baseline decreased by 50% is no longer pathological, and thus is shown here as -100% representing uCR. CI, confidence interval; CR, complete response; NE, not evaluated; ORR, objective response rate; PD, progressive disease; PR, partial response; RECIST, Response Evaluation Criteria in Solid Tumors; SD, stable disease; SOD, sum of diameters; uCR, unconfirmed complete response.

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

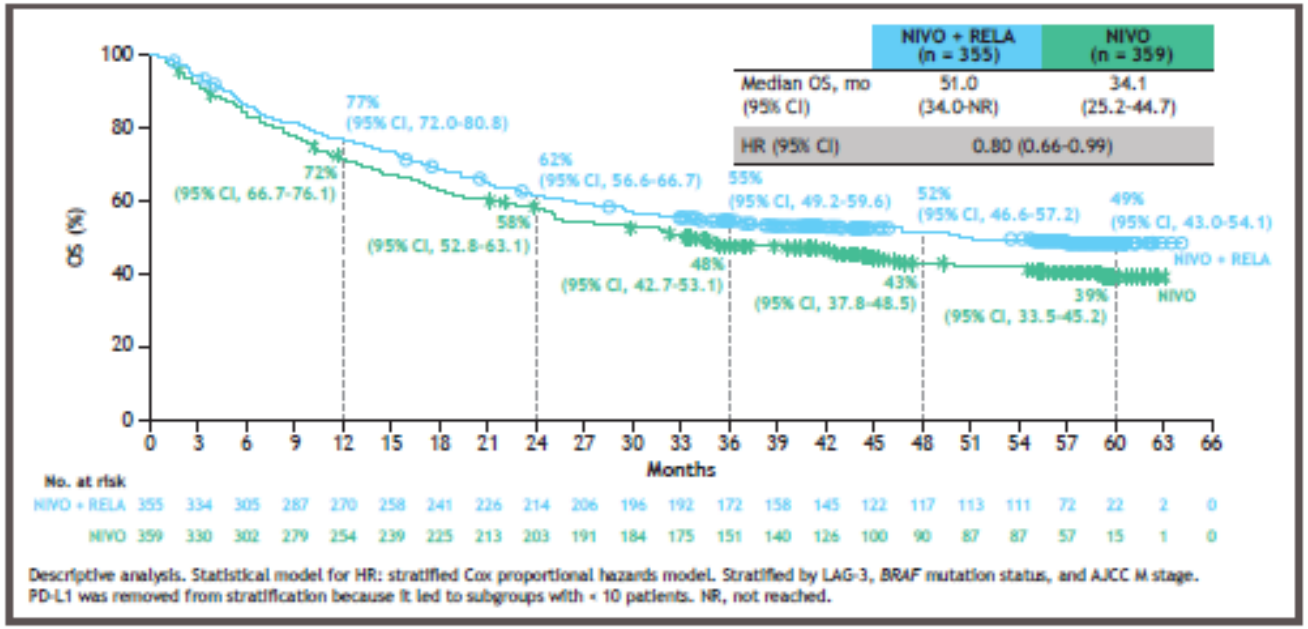
Hussein A. Tawbi,[1] F. Stephen Hodi,[2] Evan J. Lipson,[3] Dirk Schadendorf,[4] Paolo Antonio Ascierto,[5] Luis Matamala,[6] Erika Castillo Gutiérrez,[7] Piotr Rutkowski,[8] Helen Gogas,[9] Christopher D. Lao,[10] Juliana Janoski De Menezes,[11] Stéphane Dalle,[12] Ana Maria Arance,[13] Jean-Jacques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



- ORR difference: 9.8% (95% CI, 2.8-16.8)
- Median DOR was NR (95% CI, 46.9-NR) with NIVO + RELA and NR (95% CI, 39.8-NR) with NIVO

Descriptive analysis. 27 patients (8%) in the NIVO + RELA arm and 26 patients (7%) in the NIVO arm were classified as unable to determine. Tumor response was assessed at 12 weeks, followed by Q8W up to 52 weeks, and then Q12W until disease progression or treatment discontinuation.
BOR, best overall response; DOR, duration of response; PD, progressive disease; SD, stable disease.

Figure 3. OS



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.

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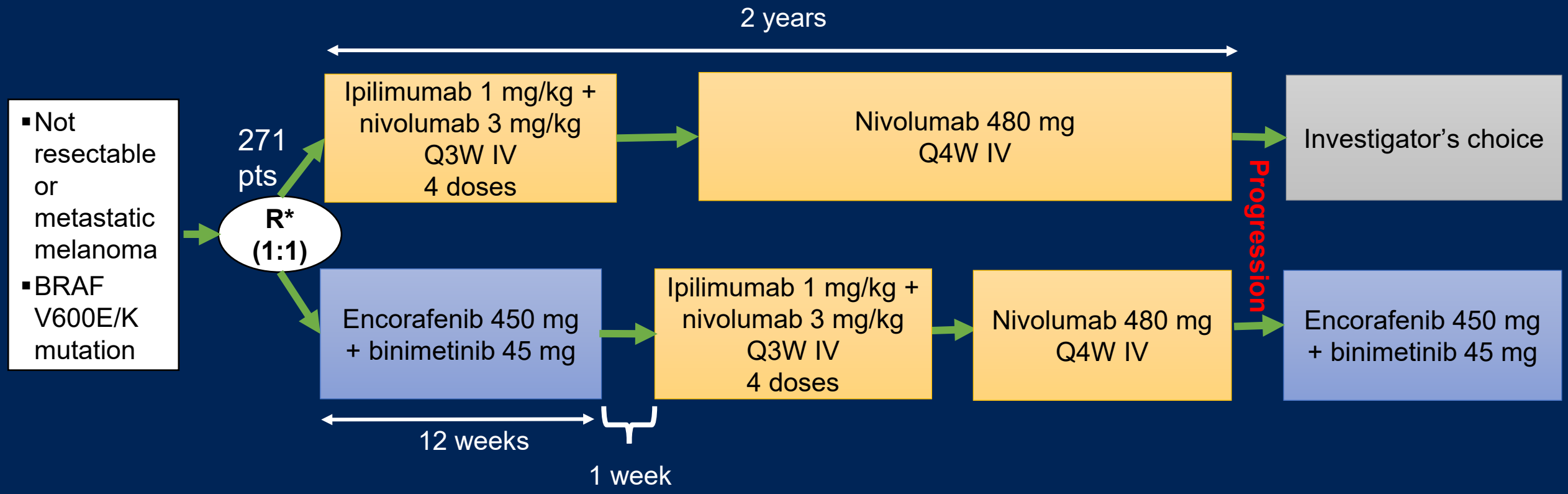
Combination of encorafenib and binimetinib followed by ipilimumab and nivolumab versus ipilimumab and nivolumab in patients with advanced BRAF-V600E/K melanoma: the primary analysis of an EORTC randomized phase II study (EBIN)

Caroline Robert, Caroline Dutriaux, Felix Oppong, Michal Kicinski, Émilie Routier, Eve-Marie Neidhardt, Xavier Durando, Barouyr Baroudjian, Philippe Saiag, Caroline Gaudy-Marqueste, Paolo A. Ascierto, Ana Arance, Michelangelo Russillo, Jean-Luc Perrot, Anne-sophie Govaerts, Emanuel Bührer, Bastian Schilling, Mario Mandalà, Paul Lorigan, Alexander C.J. van Akkooi

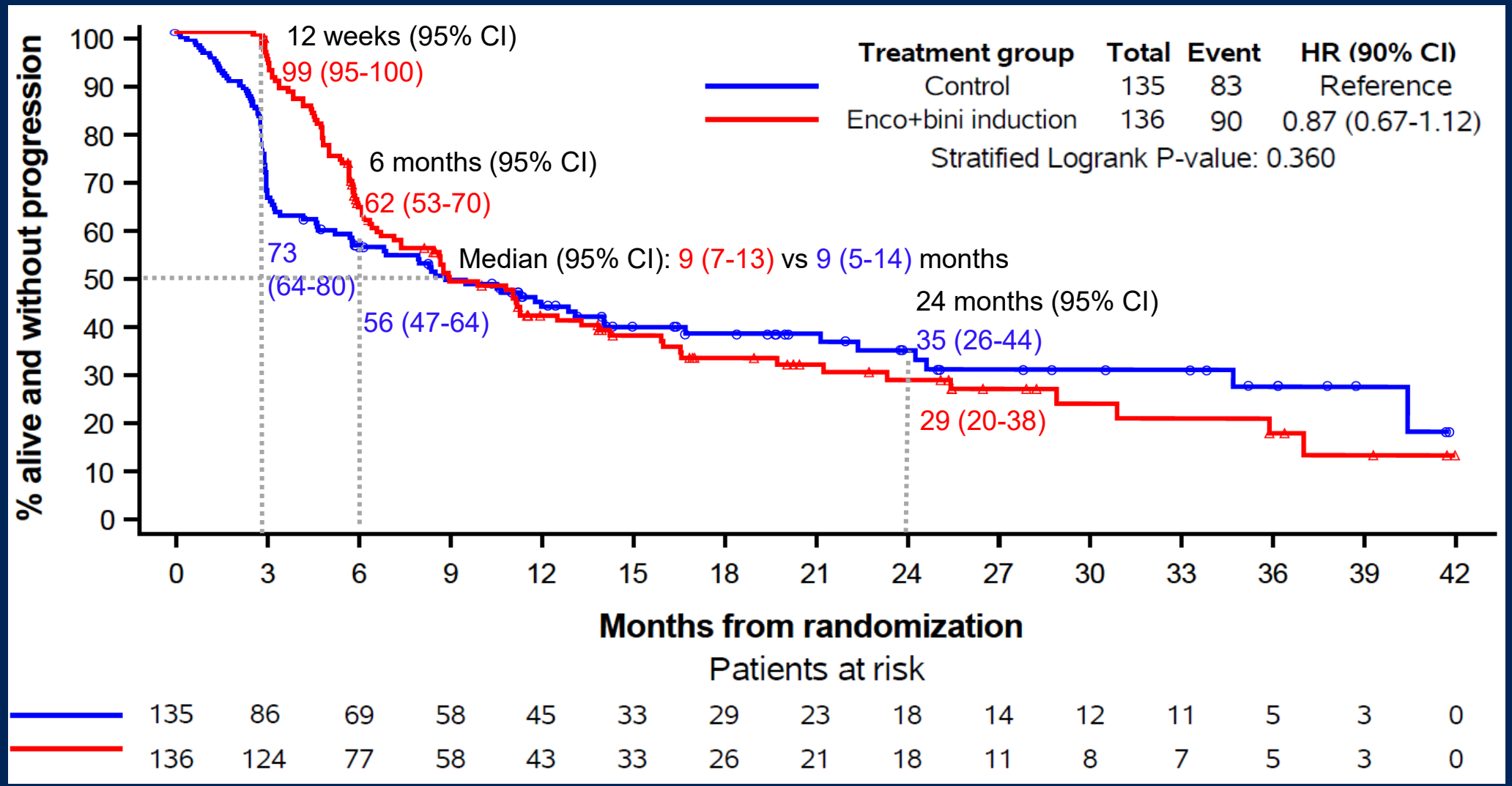
Funding: Bristol-Myers Squibb and Pierre Fabre

Study design



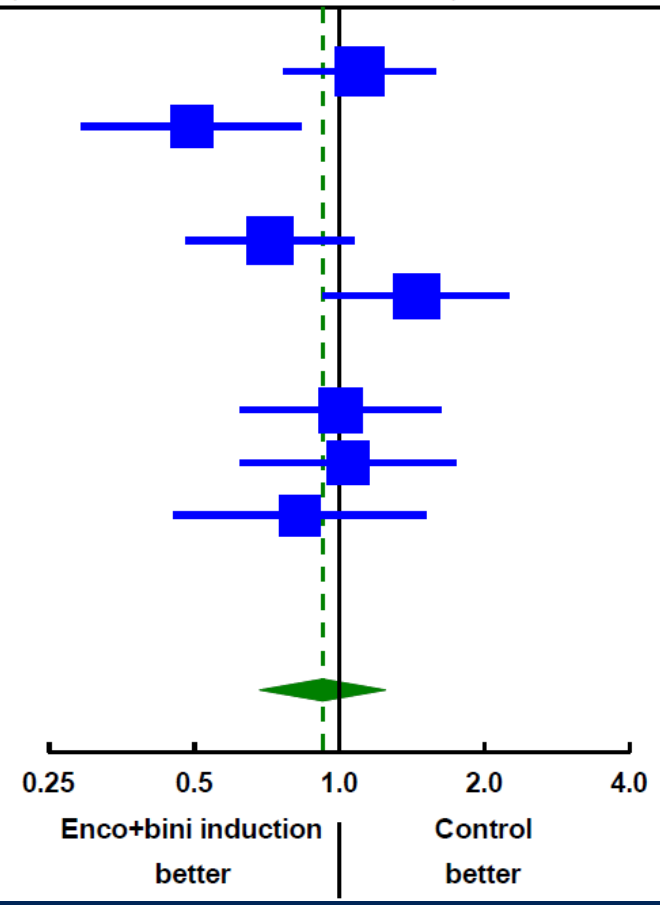
***Stratified by stage/LDH (unresectable stage III/M1a with LDH≤ULN vs M1b/M1c with LDH≤ULN vs ULN<LDH≤2ULN vs LDH>2ULN) and center**

PFS in the ITT population (primary analysis)

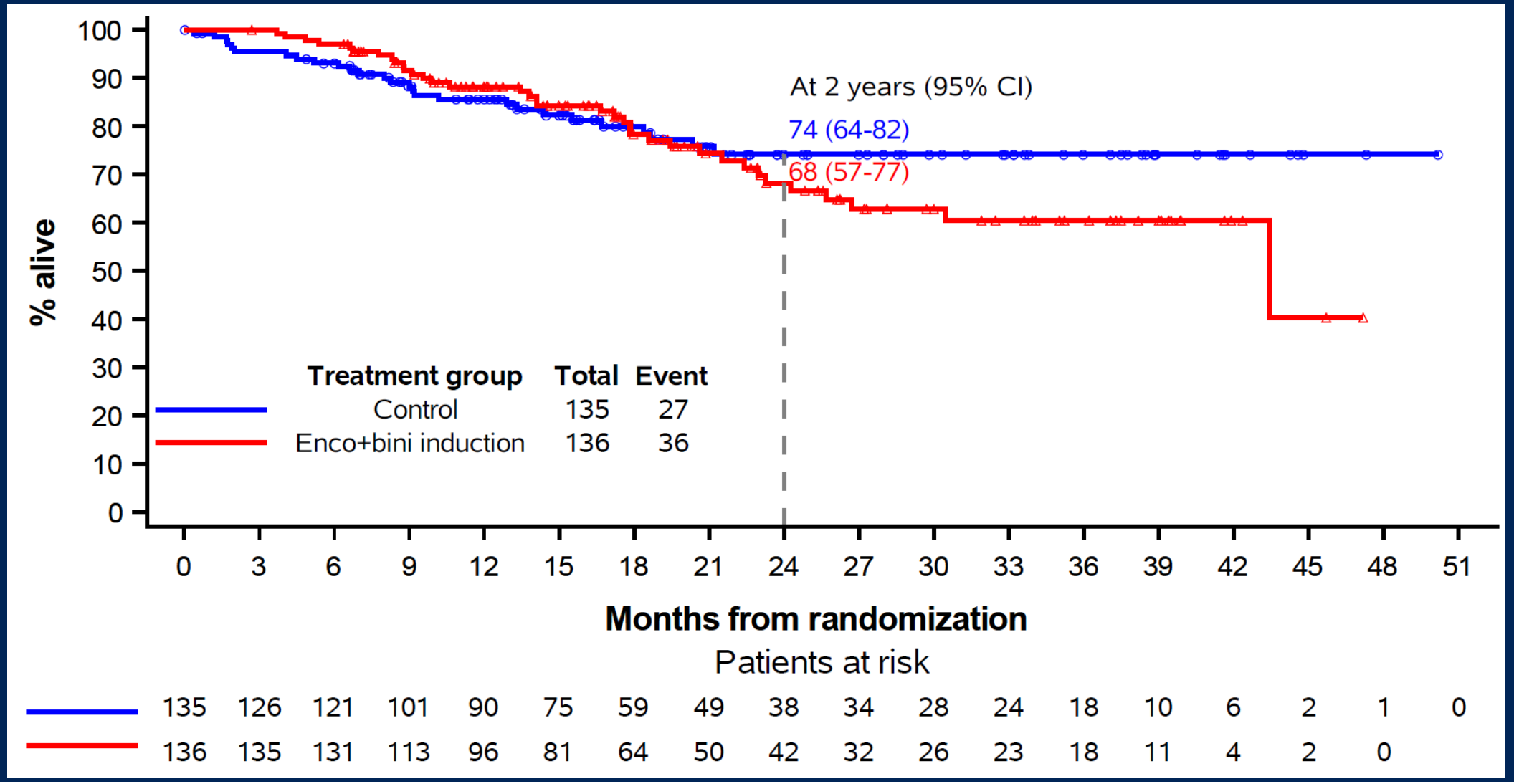


PFS in subgroups given by other indicators of tumour burden (post-hoc)

	Events / Patients Enco+bini induction	Events / Patients Control	HR (95% CI)		Interaction test
Liver metastasis					
No	61 / 95	56 / 103	1.10	(0.76 ; 1.58)	p=0.013 (df=1)
Yes	29 / 41	27 / 32	0.49	(0.29 ; 0.84)	
Number of involved sites					
<3	49 / 87	46 / 73	0.72	(0.48 ; 1.08)	p=0.022 (df=1)
≥3	41 / 49	37 / 62	1.45	(0.92 ; 2.26)	
Sum ot target lesions					
<5cm	43 / 66	27 / 50	1.01	(0.62 ; 1.63)	p=0.831 (df=2)
5-<10cm	29 / 45	30 / 46	1.04	(0.62 ; 1.74)	
≥10cm	18 / 25	26 / 39	0.83	(0.45 ; 1.51)	
Total	**90 / 136 (66.2 %)**	**83 / 135 (61.5 %)**	**0.92**	**(0.68 ; 1.25)**	



Exploratory analysis of overall survival



Refractory setting

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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

OBX-115 autologous engineered TIL cell therapy does not require co-administration of IL2 due to inducible and regulatable expression of mbIL15 using a carbonic anhydrase-2 drug-responsive domain (DRD), making its expression inducible with the FDA-approved small-molecule drug ACZ

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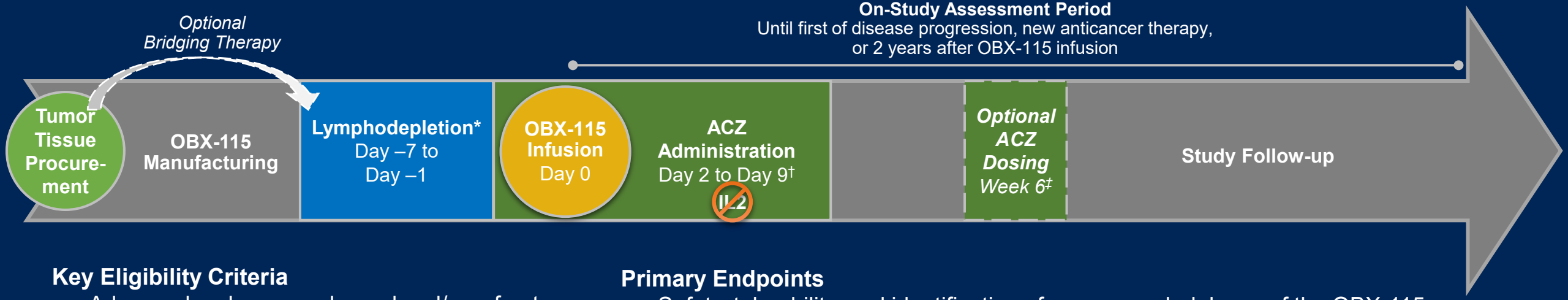
First-in-human Study Design (NCT05470283)



Key Eligibility Criteria

- Advanced melanoma relapsed and/or refractory to ICI therapy
- ≥1 lesion suitable for tumor tissue procurement (TTP) for manufacturing and ≥1 remaining lesion amenable to RECIST v1.1 response assessment
- Protocol-defined high-risk patients (e.g. mucosal and uveal or genomically equivalent mutations) may be enrolled after initial safety established

Primary Endpoints

- Safety, tolerability, and identification of recommended doses of the OBX-115 regimen: all treated patients
  - Incidence and severity of adverse events (AEs), serious AEs (SAEs), and dose-limiting toxicities (DLTs)

Key Secondary Endpoints

- Investigator-assessed ORR, DOR, and PFS: by dose level for full efficacy set
  - Protocol-defined high-risk patients assessed separately

Data cutoff: April 4, 2024 (10 patients who had started study treatment by December 31, 2023 are included).
*Standard- or low-dose lymphodepletion options. †Or until absolute lymphocyte count ≥5000 cells/μL, whichever is earlier. ‡Patients may receive additional ACZ dosing at Week 6.
ACZ, acetazolamide; AE, adverse event; DLT, dose-limiting toxicity; DOR, duration of response; ICI, immune checkpoint inhibitor; ORR, objective response rate; PFS, progression-free survival; RECIST, Response Evaluation Criteria in Solid Tumors; SAE, serious adverse event; TTP, tumor tissue procurement.

PRESENTED BY: Rodabe N Amaria, The University of Texas MD Anderson Cancer Center, Houston, TX

OBX-115 Has a Positively Differentiated Safety Profile

No treatment- or disease-related mortality at median study follow-up of ~30 weeks
No ICU care needed in any patient

At a median study follow-up of 29.5 weeks (range, 13.0–69.3):

- ✓ No DLTs reported at any dose level
- ✓ No confirmed CRS, ICANS, or capillary leak syndrome
- ✓ No AEs related to outpatient ACZ redosing at Week 6 (n=7)
- ✓ No patient discontinued study due to AEs
- ✓ No Grade 4+ nonhematologic TEAEs (Grade 3 events, n=3 in 2 patients)*

	All Patients (N=10)		
Nonhematologic TEAE,* n (%)	All Grades	Grade 3	Grade 4+
Increased alanine aminotransferase	4 (40.0)	1 (10.0)	0
Abdominal pain†	1 (10.0)	1 (10.0)	0
Syncope	1 (10.0)	1 (10.0)	0

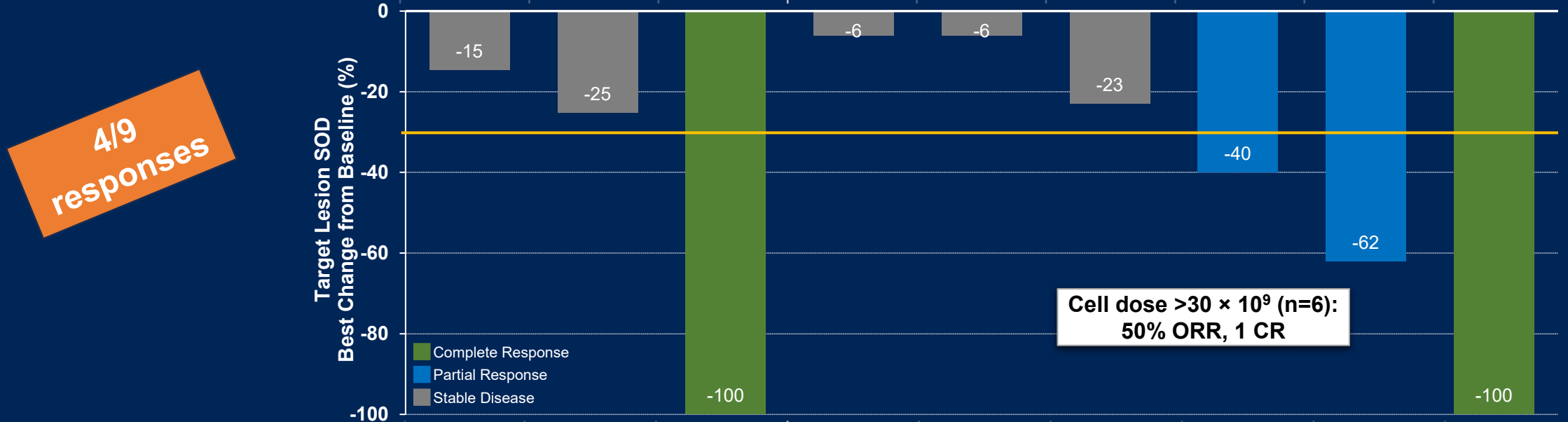
- Hematologic AEs were consistent with known lymphodepletion safety profile
- Eight patients experienced rash / pruritus (all Grade 1–2)
- Uveitis / iritis (all Grade 1–2) in 4 patients, 1 of whom reported optic neuritis (Grade 3) that has resolved

*Grade ≥3 events reported within 30 days after OBX-115 infusion. †Included increased alanine aminotransferase and required prolonged hospitalization (only patient with TEAE resulting in prolonged hospitalization).
ACZ, acetazolamide; AE, adverse event; DLT, dose-limiting toxicity; CRS, cytokine release syndrome; ICANS, immune effector cell-associated neurotoxicity syndrome; ICU, intensive care unit; TEAE, treatment-emergent adverse event.

PRESENTED BY: **Rodabe N Amaria**, The University of Texas MD Anderson Cancer Center, Houston, TX

All Patients Experienced Tumor Burden Reduction

	Infused OBX-115 Dose ≤30 × 10^9 Cells			Infused OBX-115 Dose >30 × 10^9 Cells					
BRAF Mutation / TKI Exposure		+ / -		+ / +	+ / +				
Prior Lines of Systemic Therapy	1	2	2	4	6	6	3	3	3
Prior Brain Metastasis Therapy				+					+
Patient	4	2	3	9*	6	7	5	10*	1



Isolated Brain Progression†			+	+					
Progression Requiring Subsequent Systemic Therapy		+			+	+	+		
Time to Progression‡	36 wks+	24 wks	36 wks	13 wks	25 wks	12 wks	25 wks	12 wks+	60 wks+

*Patient received cryopreserved OBX-115. †Patients with isolated brain progression did not receive systemic treatment post-progression. ‡"+" indicates no progression at latest follow-up.
CR, complete response; ORR, objective response rate; SOD, sum of diameters; TKI, tyrosine kinase inhibitor; wks, weeks.

PRESENTED BY: **Rodabe N Amaria**, The University of Texas MD Anderson Cancer Center, Houston, TX

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

IGNYTE Study design (Anti-PD-1 failed melanoma cohort)

Anti–PD-1–failed cutaneous melanoma cohort (140 pts; 16 pts treated in prior cohorts: Total 156)

Screening — *28 days* → **First dose** RP1 1×10^{6} pfu/mL — *2 weeks* → **RP1+nivolumab**[a] 1×10^{7} pfu/mL, 240 mg — *2 weeks* → **Nivolumab** 240 mg — *2 weeks* → **Nivolumab** 480 mg (Q4W)

Cycle 1 | **Cycles 2–8** | **Cycle 9** | **Cycles 10–30**[b]

3-year follow-up from last patient enrolled

100-day safety follow-up

***Tumor response assessment**: Radiographic imaging (CT) at baseline and every 8 weeks from first dose and every 12 weeks after confirmation of response*

Primary objectives

- To assess the safety and efficacy (by independent central review [mRECIST]) of RP1 in combination with nivolumab

Secondary objective

- **ORR by investigator review (mRECIST)**
- To assess the efficacy of RP1 in combination with nivolumab as determined by DOR, CR rate, DCR, PFS, by central & investigator review, 1-year and 2-year OS

Key eligibility

Advanced melanoma having ***confirmed progression while on prior anti-PD-1 therapy***[c]; at least 1 measurable and injectable lesion (≥1 cm LD), including deep/visceral; adequate organ function; no prior treatment with oncolytic therapy; ECOG performance status 0–1

Criteria for prior anti–PD-1–failure

≥8 weeks of prior anti–PD-1, confirmed progression while on anti–PD-1; anti–PD-1 must be the last therapy before the clinical trial. Patients on prior adjuvant therapy must have progressed while on prior adjuvant treatment (progression can be confirmed by biopsy)

Primary analysis to be conducted when all patients have ≥ 12 months follow up

[a]Dosing with nivolumab begins at dose 2 of RP1 (C2D15). [b]Option to reinitiate RP1 for 8 cycles if criteria are met.
c. Non-neurological solid tumors CR, complete response; CT, computed tomography; DCR, disease control rate; DOR, duration of response; ECOG, Eastern Cooperative Oncology Group; LD, longest diameter; ORR, objective response rate; OS, overall survival; PD-1, programmed cell death protein 1; PFS, progression-free survival; pfu, plaque-forming unit; Q4W, every 4 weeks; RECIST, Response Evaluation Criteria in Solid Tumors.

PRESENTED BY: Dr. Michael K. Wong, MD, PhD, FRCPC

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)	1º resistance to anti–PD-1 (n = 105)	2º 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)**

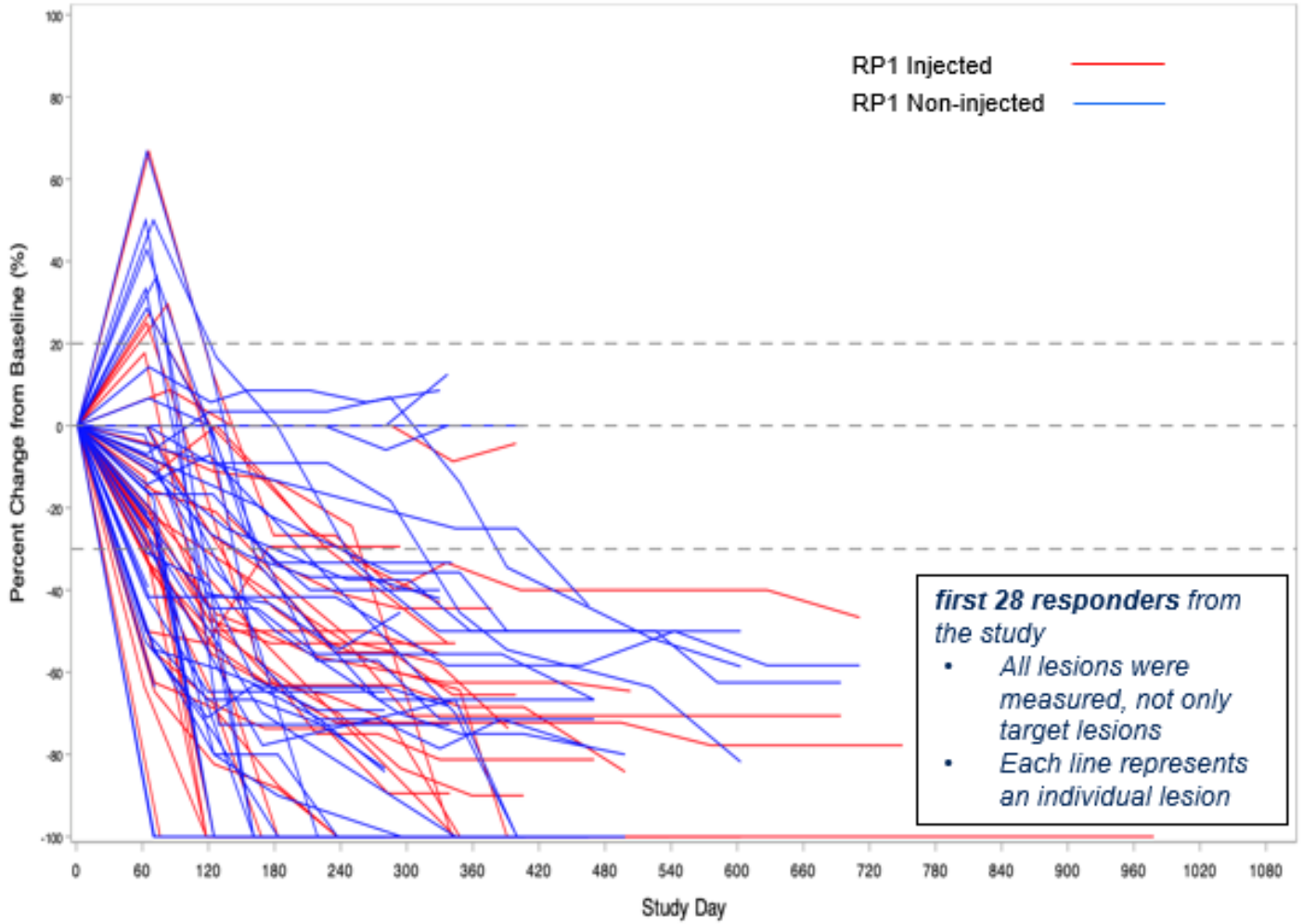
[a]Eight patients were treated with sequential anti-CTLA-4 and anti-PD-1 (ORR for prior combined anti-CTLA-4/anti-PD-1 was 25.8%). [b]Includes one patient with unknown resistance status.
[c]ORR for the 140 registration intended cohort was 32.1%

- 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.

Responses are Systemic

Change in Size of Individual Injected and Non-injected Lesions



- 70.4% of responding patients had non-injected lesions
  - Responders include patients with minority of lesions injected
- Injected and non-injected lesions responded with similar duration and kinetics
- Depth of response independent of whether injected

Responses in non-injected lesions demonstrate systemic benefit

Includes both target and non-target lesions for RECIST assessment, measured from CT/MRI scans for radiologically assessable lesions (responders from the first 75 patients enrolled into the registration intended cohort). 58/75 patients had at ≥ 1 non-injected lesion, of whom 15 achieved a response based on those lesions only (excludes possible response in injected lesions); ORR of 25.9% on the basis of non-injected lesions only. First presented at ASCO 2023.

Thanks!

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