Melanoma: Have we Hit a Plateau or are we Making Progress?

Sanjiv S. Agarwala, MD

Co-Founder & CMO, Cancer Expert Now

Professor, Temple University School of Medicine

Overview

- Metastatic melanoma
- Adjuvant Therapy for surgically resected melanoma

Overview

- Metastatic melanoma
- Adjuvant Therapy for surgically resected melanoma

Metastatic Melanoma

- Immunotherapy
- Targeted therapy
- Choice of first line therapy between targeted and immunotherapy

Metastatic Melanoma

- Immunotherapy
- Targeted therapy
- Choice of first line therapy between targeted and immunotherapy

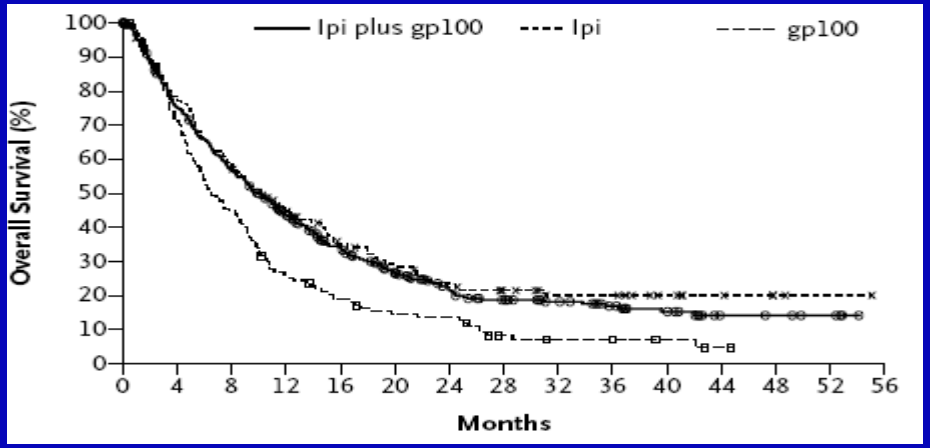
Immunotherapy

- Single agent
  - Anti-CTLA4 (ipilimumab)
  - Anti-PD1 (pembrolizumab or nivolumab)
- Combination
  - Anti-PD1/anti-CTLA4 (ipilimumab, nivolumab)
  - Anti-PD1/ anti-LAG3 (nivolumab, relatlimab)

Immunotherapy

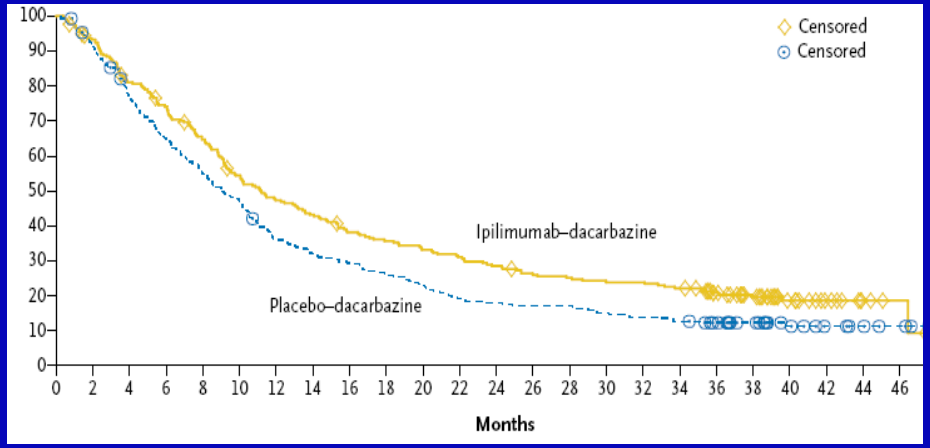
- Single agent
  - Anti-CTLA4 (ipilimumab)
  - Anti-PD1 (pembrolizumab or nivolumab)
- Combination
  - Anti-PD1/anti-CTLA4 (ipilimumab, nivolumab)
  - Anti-PD1/ anti-LAG3 (nivolumab, relatlimab)

Anti-CTLA4 Ipilimumab: First Positive Trial in Metastatic Melanoma



HR: 0.66 and 0.68
Pre-treated pts
Ipi 3 mg/kg +/- gp100

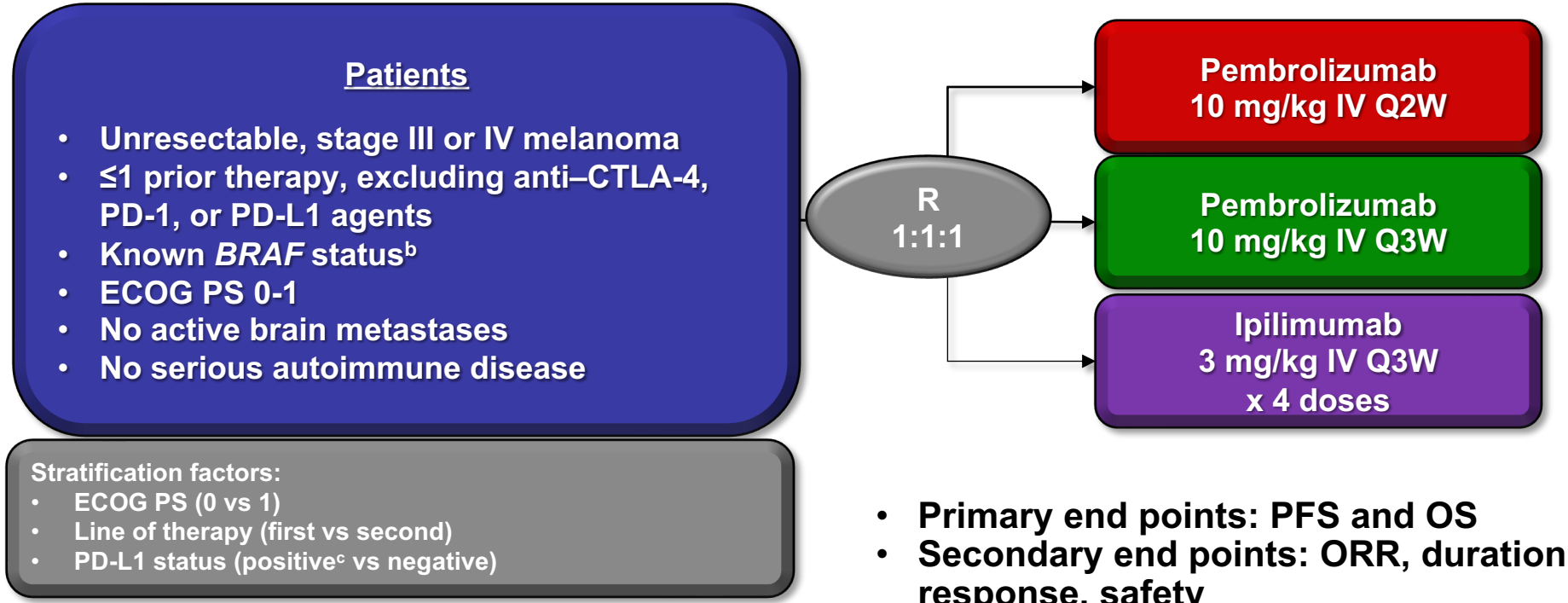
Hodi FS, et al. *N Engl J Med.* 2010;363:711-23.



HR: 0.72
First line
Ipi 10 mg/kg + DTIC

Robert C, et al. *N Engl J Med*. 2011;364:2517-26.

Keynote-006 Front-line Pembrolizumab vs Ipilimumab



- **Primary end points: PFS and OS**
- **Secondary end points: ORR, duration of response, safety**

[a]Patients enrolled from 83 sites in 16 countries.

[b]Prior anti-BRAF targeted therapy was not required for patients with normal LDH levels and no clinically significant tumor-related symptoms or evidence of rapidly progressing disease.

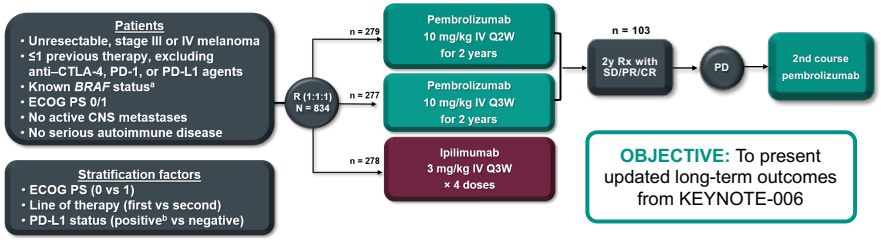
[c]Defined as membranous PD-L1 expression in ≥1% of tumor cells as assessed by IHC using the 22C3 antibody.

Long-Term Survival From Pembrolizumab Completion and Pembrolizumab Retreatment: Phase 3 KEYNOTE-006 in Advanced Melanoma

G. V. Long[1-4], J. Schachter[5], A. Arance[6], J.-J. Grob[7], L. Mortier[8], A. Daud[9], M. S. Carlino[1,2,10,11], A. Ribas[12], C. M. McNeil[2,13], M. Lotem[14], J. Larkin[15], P. Lorigan[16], B. Neyns[17], C. U. Blank[18], T. M. Petrella[19], O. Hamid[20], E. Jensen[21], C. Krepler[21], S. J. Diede[21], C. Robert[22]

ASCO 2020

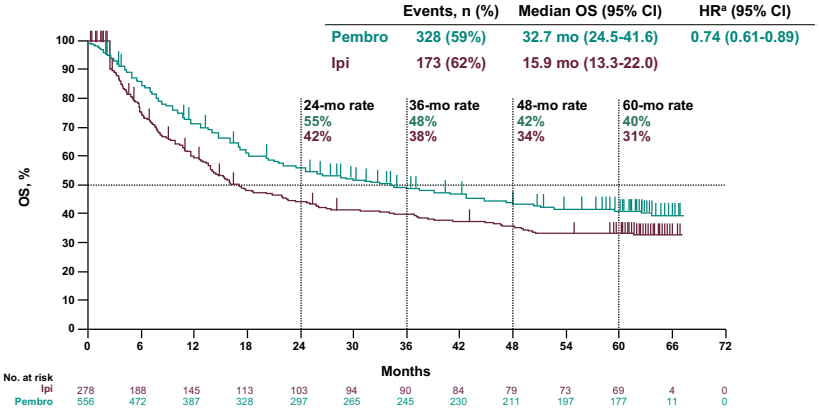
[1]Melanoma Institute Australia, Sydney, NSW, Australia; [2]University of Sydney, Sydney, NSW, Australia; [3]Royal North Shore Hospital, Sydney, NSW, Australia; [4]Mater Hospital, North Sydney, NSW, Australia; [5]Sheba Medical Center, Tel HaShomer Hospital, Tel Aviv, Israel, [6]Hospital Clinic de Barcelona, Barcelona, Spain; [7]Aix Marseille University, Hôpital de la Timone, Marseille, France; [8]Université Lille, Centre Hospitalier Regional Universitaire de Lille, Lille, France; [9]UCSF, San Francisco, CA, USA; [10]Blacktown Hospital, Blacktown, NSW, Australia; [11]Crown Princess Mary Cancer Centre, Westmead Hospital, Sydney, NSW, Australia; [12]David Geffen School of Medicine at UCLA, Los Angeles, CA, USA; [13]Chris O'Brien Lifehouse, Camperdown, NSW, Australia; [14]Sharett Institute of Oncology, Hadassah Hebrew Medical Center, Jerusalem, Israel; [15]Royal Marsden Hospital, London, England; [16]University of Manchester and the Christie NHS Foundation Trust, Manchester, England; [17]Universitair Ziekenhuis Brussel, Brussels, Belgium; [18]Netherlands Cancer Institute, Amsterdam, Netherlands; [19]Sunnybrook Health Sciences Centre, Toronto, ON, Canada; [20]The Angeles Clinic and Research Institute, Los Angeles, CA, USA; [21]Merck & Co., Inc., Kenilworth, NJ, USA; [22]Gustave Roussy and Paris-Sud University, Villejuif, France



- Two pembrolizumab arms pooled as similar efficacy[2]
- Patients completing ≥94 weeks of pembrolizumab with SD/PR/CR were considered to have completed 2 years of treatment
- Patients could receive a 2nd course of 1 year of pembrolizumab if progressed after SD/PR/CR
- Data cut-off: July 31, 2019; median follow-up: 66.8 months (range, 65.0-70.4); time from last patient enrolled to data cutoff, 65.0 months

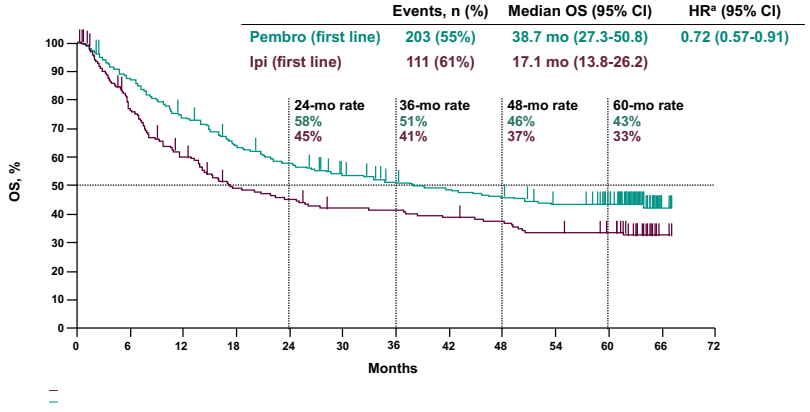
[a]Prior anti-BRAF therapy was not required for patients with normal LDH levels and no clinically significant tumor-related symptoms or evidence of rapidly progressing disease.
[b]Defined as ≥1% staining in tumor and adjacent immune cells as assessed by IHC using 22C3 antibody.

Overall Survival: Total Population



Data cut-off: July 31, 2019. [a]Based on Cox regression model with treatment as a covariate stratified by line of therapy (1st vs 2nd), PD-L1 status (positive vs negative) and ECOG (0 vs 1); in instances where there were no patients in one of the treatment groups involved in a comparison for a particular stratum, that stratum was excluded from the treatment comparison.

Overall Survival: First Line Patients



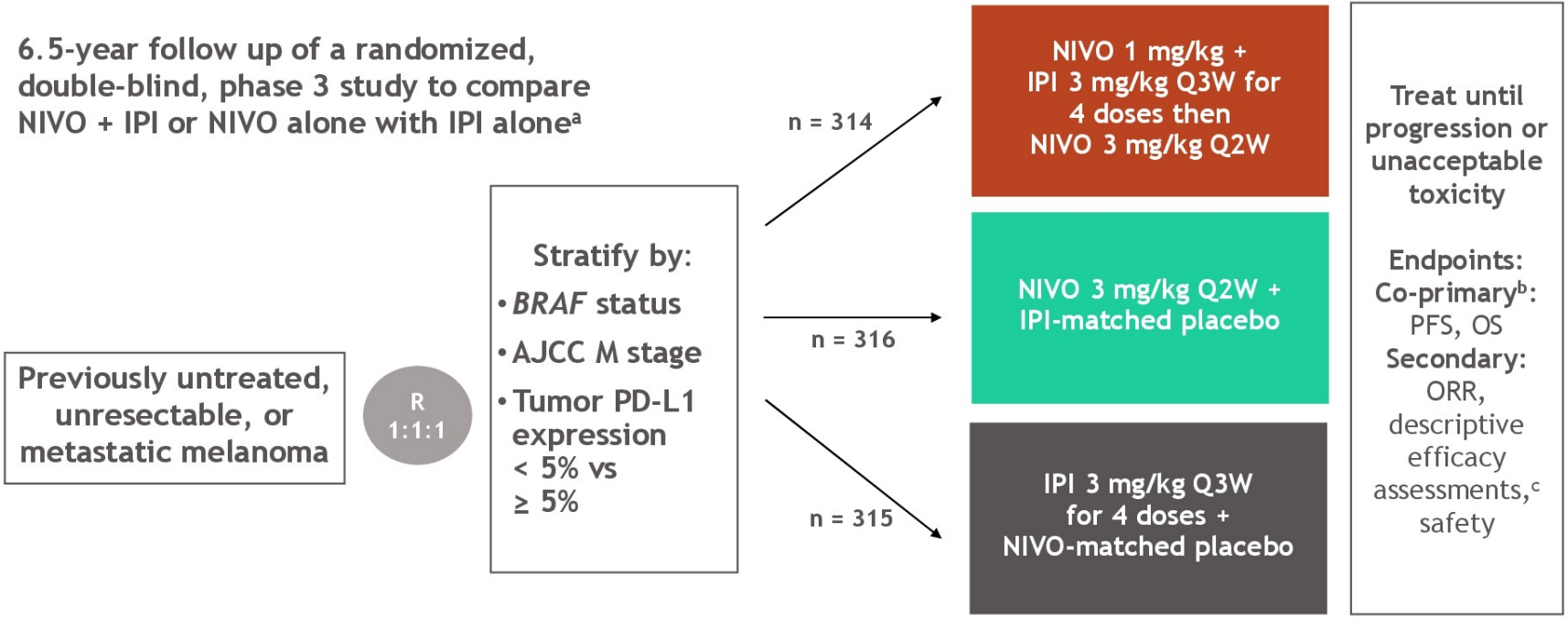
Data cut-off: July 31, 2019. [a]Based on Cox regression model with treatment as a covariate stratified by line of therapy (1st vs 2nd), PD-L1 status (positive vs negative) and ECOG (0 vs 1); in instances where there were no patients in one of the treatment groups involved in a comparison for a particular stratum, that stratum was excluded from the treatment comparison.

Immunotherapy

- Single agent
  - Anti-CTLA4 (ipilimumab)
  - Anti-PD1 (pembrolizumab or nivolumab)
- Combination
  - Anti-PD1/anti-CTLA4 (ipilimumab, nivolumab)
  - Anti-PD1/ anti-LAG3 (nivolumab, relatlimab)

CheckMate 067: study design

6.5-year follow up of a randomized, double-blind, phase 3 study to compare NIVO + IPI or NIVO alone with IPI alone[a]

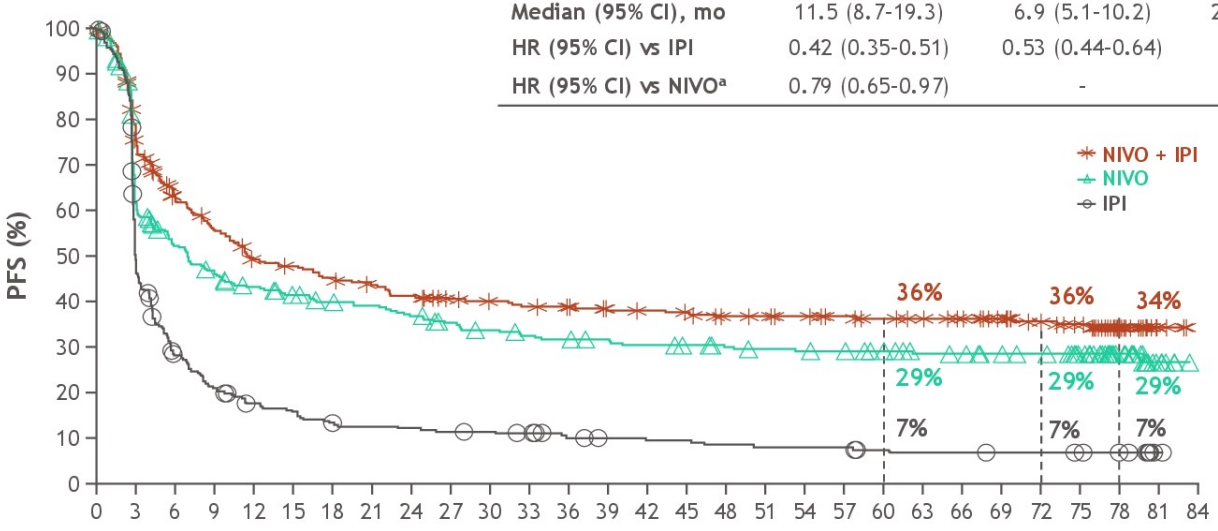


Database lock: October 19, 2020; minimum follow-up of 77 months for all patients

[a]The study was not powered for a comparison between NIVO+IPI and NIVO. [b]NIVO + IPI or NIVO vs IPI alone. [c]NIVO + IPI vs NIVO alone. AJCC, American Joint Committee on Cancer; M stage, metastasis stage; ORR, objective response rate; PD-L1, programmed death ligand 1; PFS, progression-free survival; Q2W, every 2 weeks; Q3W, every 3 weeks.

Progression-free survival

	NIVO + IPI (n = 314)	NIVO (n = 316)	IPI (n = 315)
Median (95% CI), mo	11.5 (8.7-19.3)	6.9 (5.1-10.2)	2.9 (2.8-3.2)
HR (95% CI) vs IPI	0.42 (0.35-0.51)	0.53 (0.44-0.64)	-
HR (95% CI) vs NIVO[a]	0.79 (0.65-0.97)	-	-



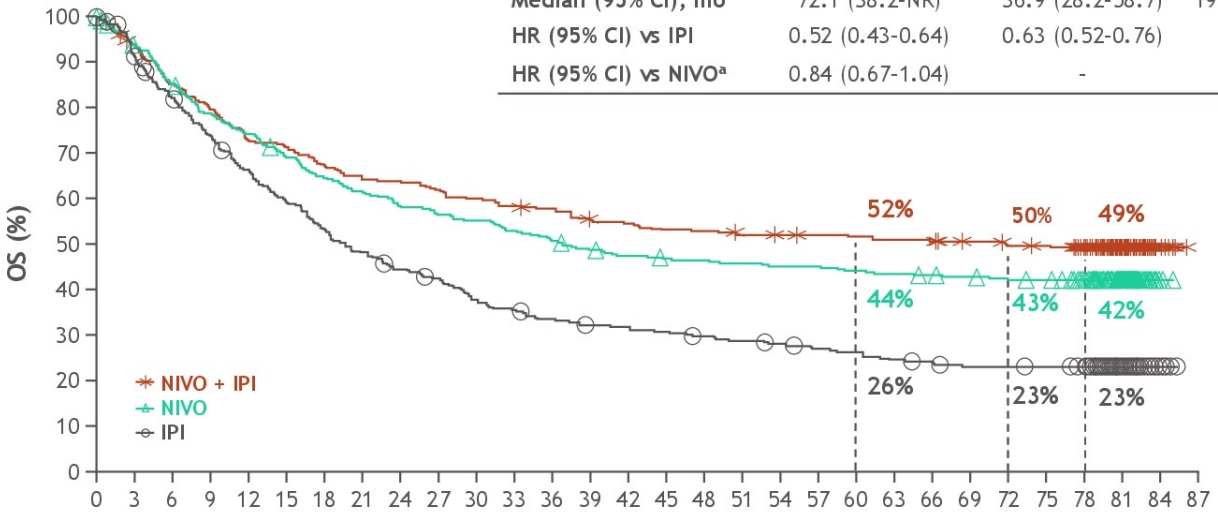
No. at risk

NIVO + IPI	314	218	174	155	136	131	124	117	110	104	101	98	96	92	90	88	83	82	80	77	74	72	69	64	58	52	29	3	0
NIVO	316	177	151	132	120	112	106	103	97	89	84	80	78	76	73	71	68	66	65	64	60	55	54	51	49	42	24	7	0
IPI	315	136	78	58	46	42	34	32	31	29	28	26	21	19	18	18	16	15	15	15	12	11	11	10	10	9	7	1	0

[a]Descriptive analysis.

Overall survival

	NIVO + IPI (n = 314)	NIVO (n = 316)	IPI (n = 315)
Median (95% CI), mo	72.1 (38.2-NR)	36.9 (28.2-58.7)	19.9 (16.8-24.6)
HR (95% CI) vs IPI	0.52 (0.43-0.64)	0.63 (0.52-0.76)	-
HR (95% CI) vs NIVO[a]	0.84 (0.67-1.04)	-	-



No. at risk

NIVO + IPI	314	292	265	248	227	222	210	201	199	193	187	181	179	172	169	164	163	159	158	157	156	154	153	150	147	145	138	66	10	0
NIVO	316	292	266	245	231	214	201	191	181	175	171	164	158	150	145	142	141	139	137	137	134	132	130	128	126	124	117	59	3	0
IPI	315	285	253	227	203	181	163	148	135	128	113	107	100	95	94	91	87	84	81	77	75	70	68	64	64	63	61	32	7	0

[a]Descriptive analysis.

Safety Summary

- With an additional 19 months of follow-up, safety was consistent with the initial report[1]

	NIVO+IPI (N=313)		NIVO (N=313)		IPI (N=311)	
Patients reporting event, %	Any Grade	Grade 3-4	Any Grade	Grade 3-4	Any Grade	Grade 3-4
Treatment-related adverse event (AE)	95.8	58.5	86.3	20.8	86.2	27.7
Treatment-related AE leading to discontinuation	39.6	31.0	11.5	7.7	16.1	14.1
Treatment-related death, n (%)	2 (0.6)[a]		1 (0.3)[b]		1 (0.3)[b]	

- Most select AEs were managed and resolved within 3-4 weeks (85–100% across organ categories)
- ORR was 70.7% for pts who discontinued NIVO+IPI due to AEs, with median OS not reached

[a]Cardiomyopathy (NIVO+IPI, n=1); Liver necrosis (NIVO+IPI, n=1). Both deaths occurred >100 days after the last treatment.
[b]Neutropenia (NIVO, n=1); colon perforation (IPI, n=1).[1]

1. Larkin J, et al. *NEJM* 2015;373:23–34.

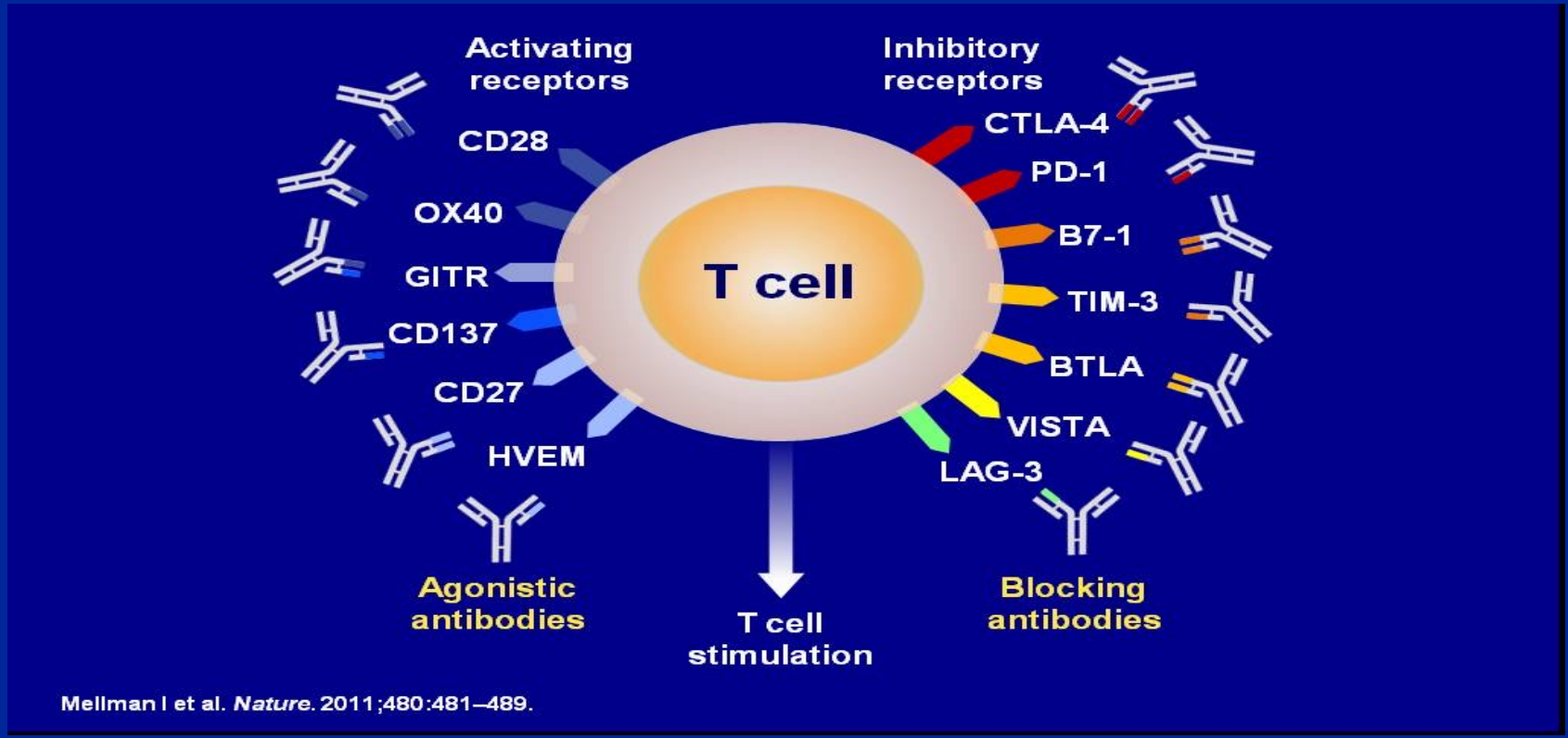
Combination anti-CTLA4 and anti-PD1 (ipilimumab + nivolumab) produced durable benefit in about 50% of patients but with significant toxicity

Is there another combination available?

Immunotherapy

- Single agent
  - Anti-CTLA4 (ipilimumab)
  - Anti-PD1 (pembrolizumab or nivolumab)
- Combination
  - Anti-PD1/anti-CTLA4 (ipilimumab, nivolumab)
  - Anti-PD1/ anti-LAG3 (nivolumab, relatlimab)

T-Cell Immune Checkpoints



Study design

- RELATIVITY-047 is a global, randomized, double-blind, phase 2/3 study

Key eligibility criteria
- Previously untreated, unresectable, or metastatic melanoma
- ECOG PS 0–1

R 1:1
- NIVO 480 mg + RELA 160 mg FDC IV Q4W
- NIVO 480 mg IV Q4W

Primary endpoint
- PFS by BICR[a]

Secondary endpoints
- OS[b]
- ORR by BICR[c]

Stratified by: LAG-3,[d] PD-L1,[e] *BRAF*, and AJCC v8 M stage
Endpoints were tested in hierarchy: PFS → OS → ORR

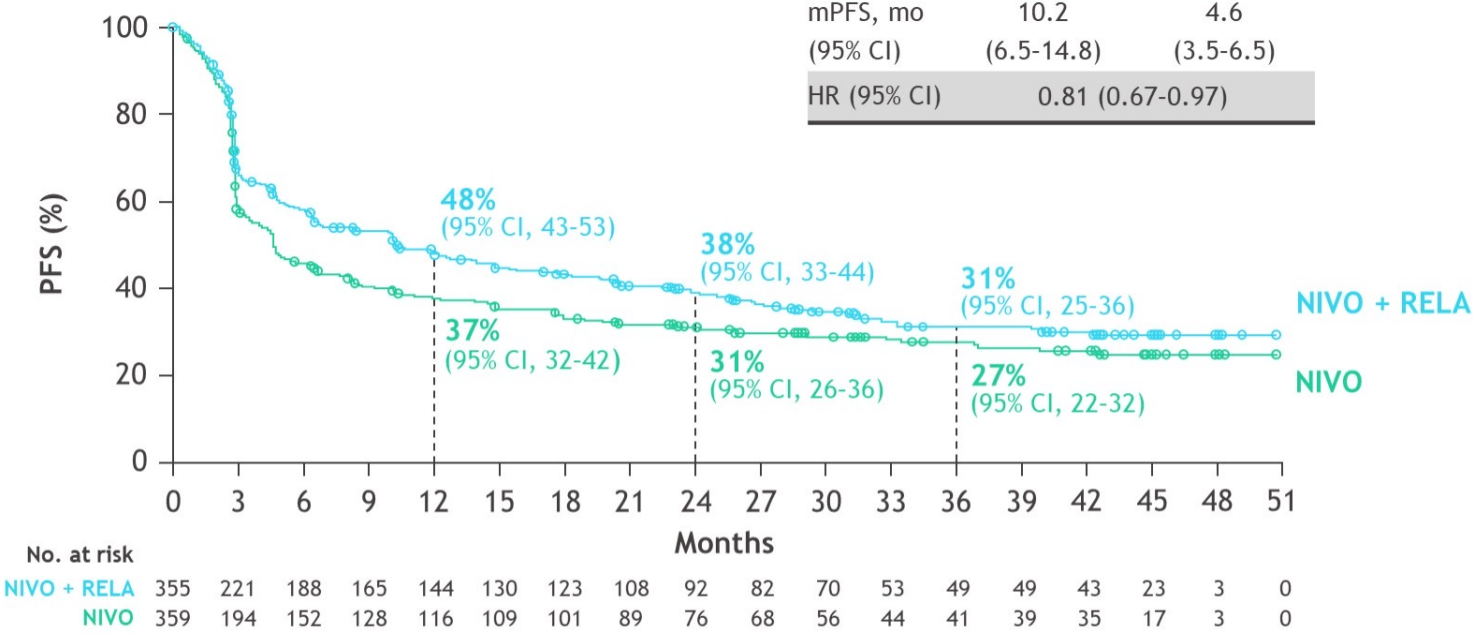
Database lock	March 9, 2021	October 28, 2021	October 27, 2022
Min. follow-up[f]	1.3 months	8.7 months	21.0 months
Median follow-up	13.2 months	19.3 months	25.3 months
Endpoint(s)	PFS per BICR	OS, ORR per BICR, and updated PFS per BICR	Updated PFS per BICR, OS, and ORR per BICR

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

PFS by BICR

Updated primary endpoint

	NIVO + RELA (n = 355)	NIVO (n = 359)
mPFS, mo	10.2	4.6
(95% CI)	(6.5-14.8)	(3.5-6.5)
HR (95% CI)	0.81 (0.67-0.97)	

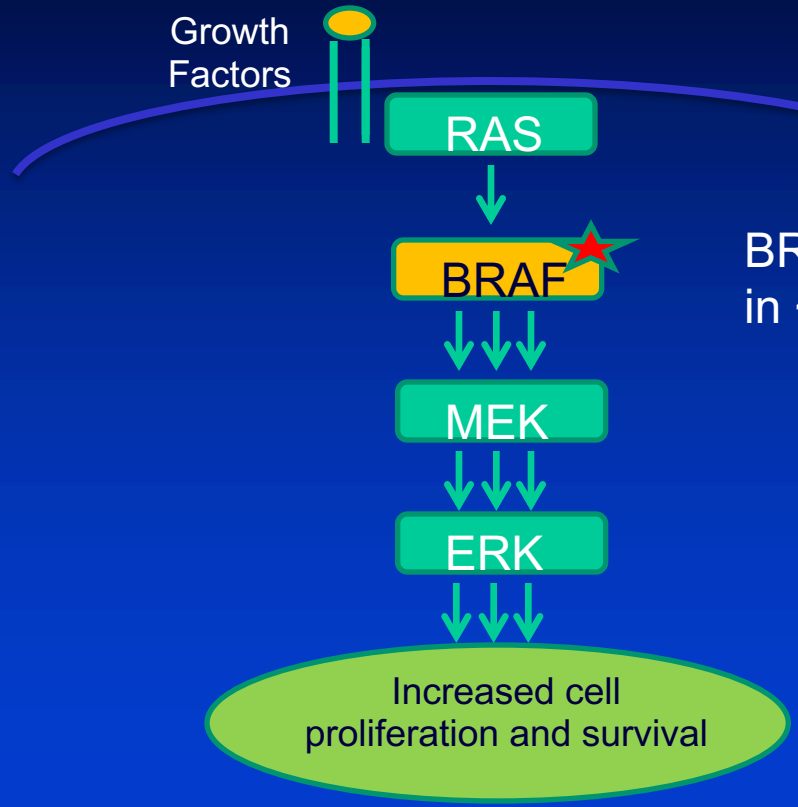


RELATIVITY-047 (NCT03470922). Median follow-up: 25.3 months.
Descriptive analysis. Statistical model for HR: stratified Cox proportional hazard model. Stratified by LAG-3, *BRAF* mutation status, and AJCC M stage. PD-L1 was removed from stratification because it led to subgroups with < 10 patients.

Metastatic Melanoma

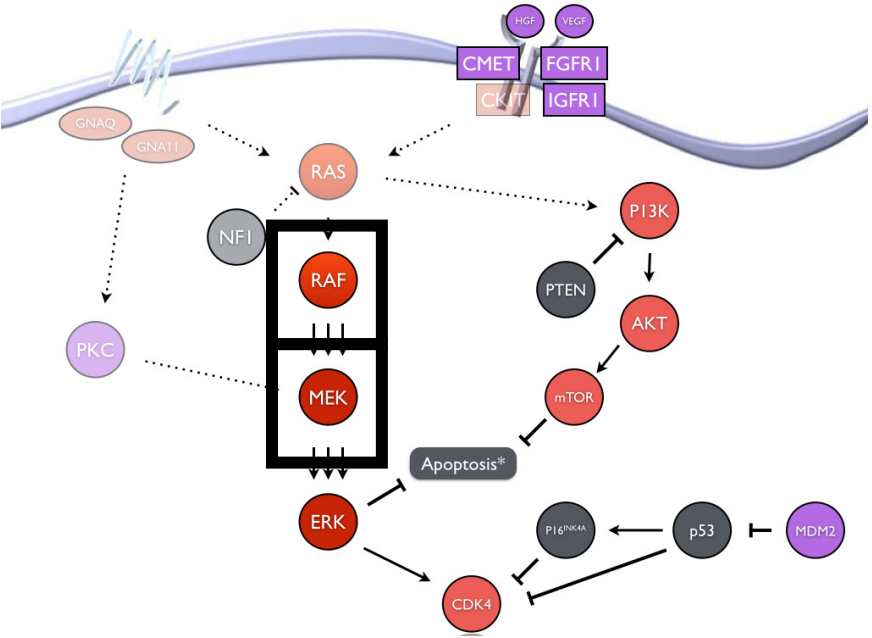
- Immunotherapy
- Targeted therapy
- Choice of first line therapy between targeted and immunotherapy

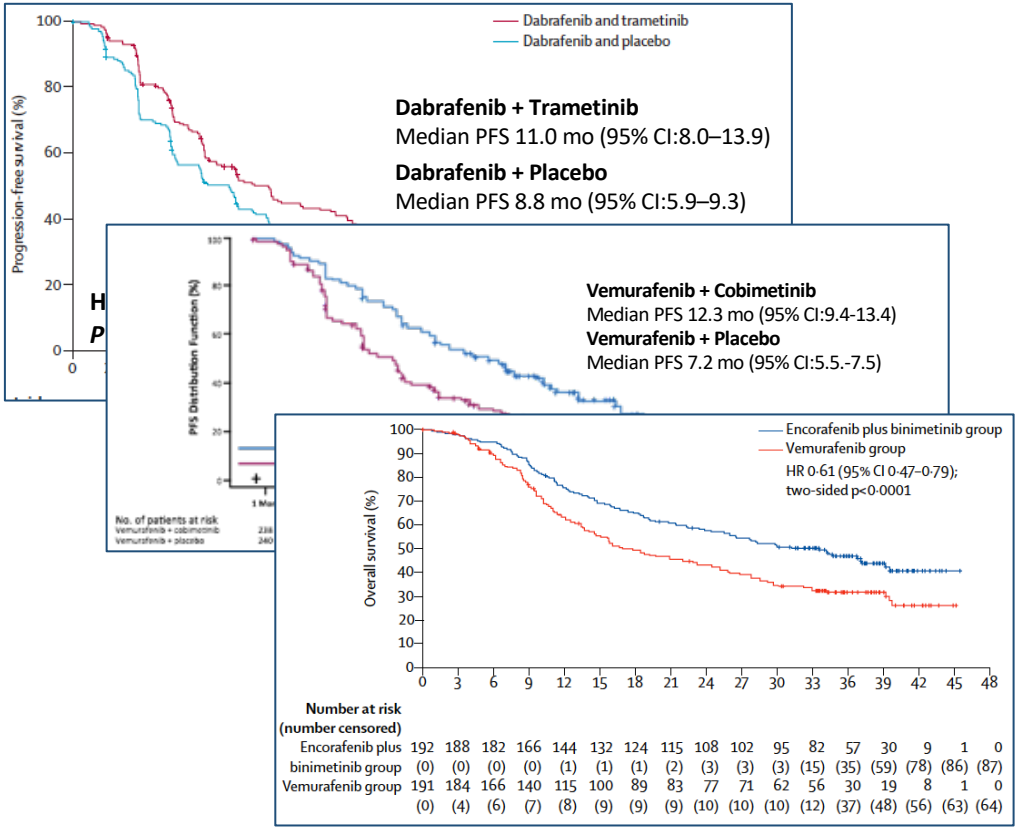
BRAF Mutation



BRAF mutation is present in ~50% of melanomas

Dual BRAF and MEK Inhibition Is Associated With High Response Rates and Improved PFS and OS



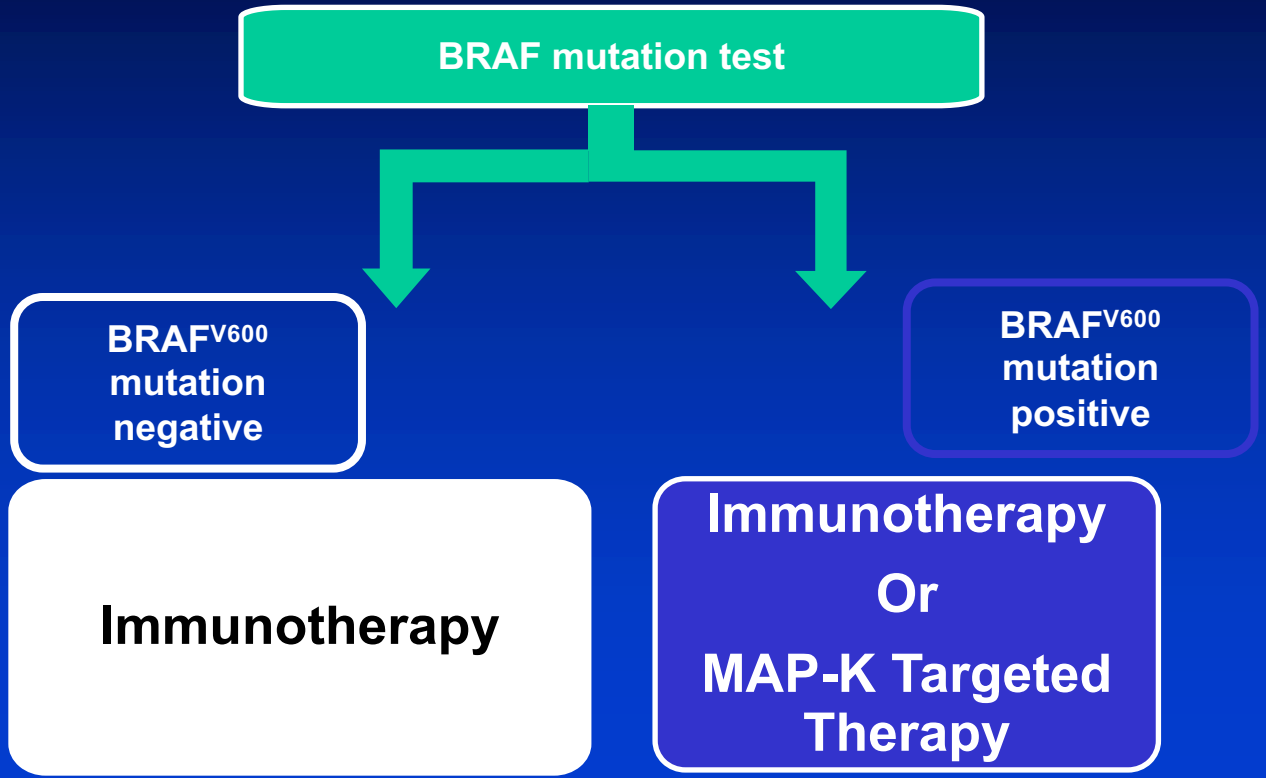


Long GV et al. *Lancet*. 2015.
Ascierto PA et al. *Lancet Oncol.* 2016.
Dummer R et al. *Lancet Oncol*. 2018.

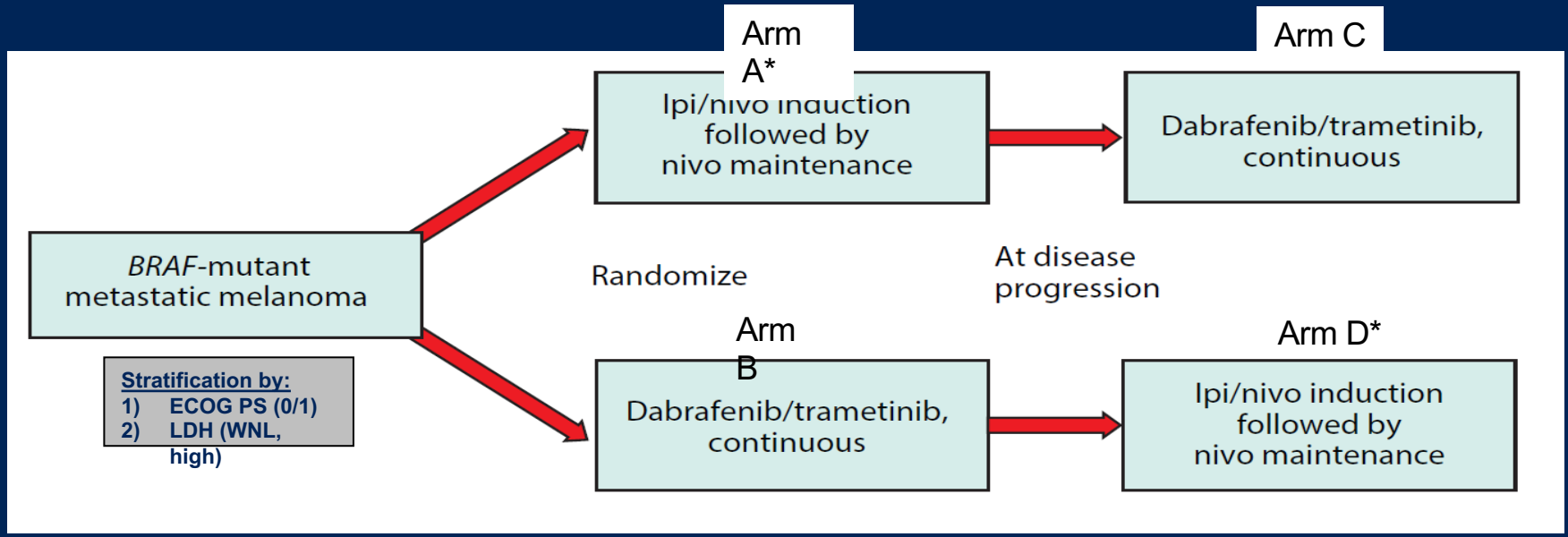
Metastatic Melanoma

- Immunotherapy
- Targeted therapy
- Choice of first line therapy between targeted and immunotherapy

Melanoma Therapy Decision Point

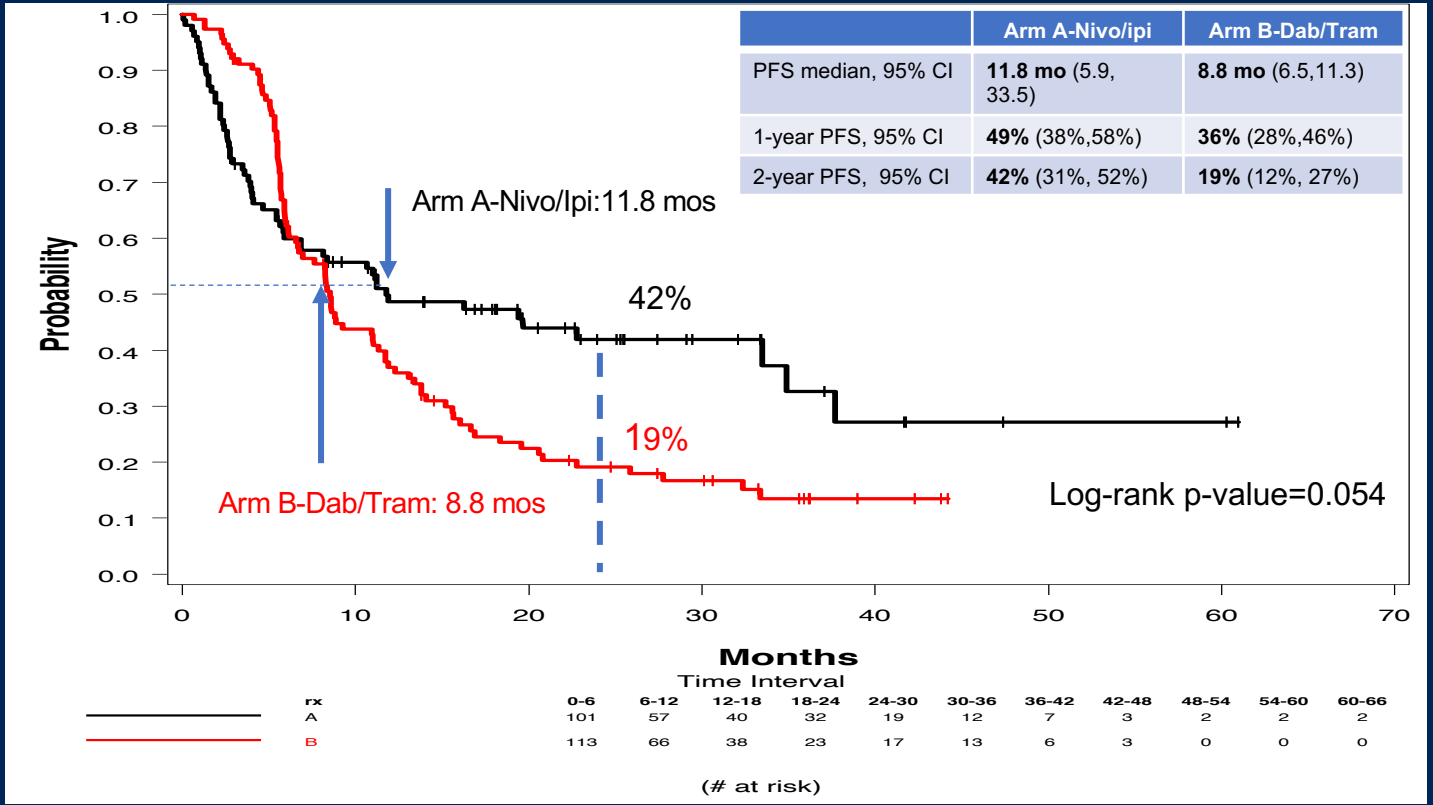


DREAMseq Trial Treatment Schema



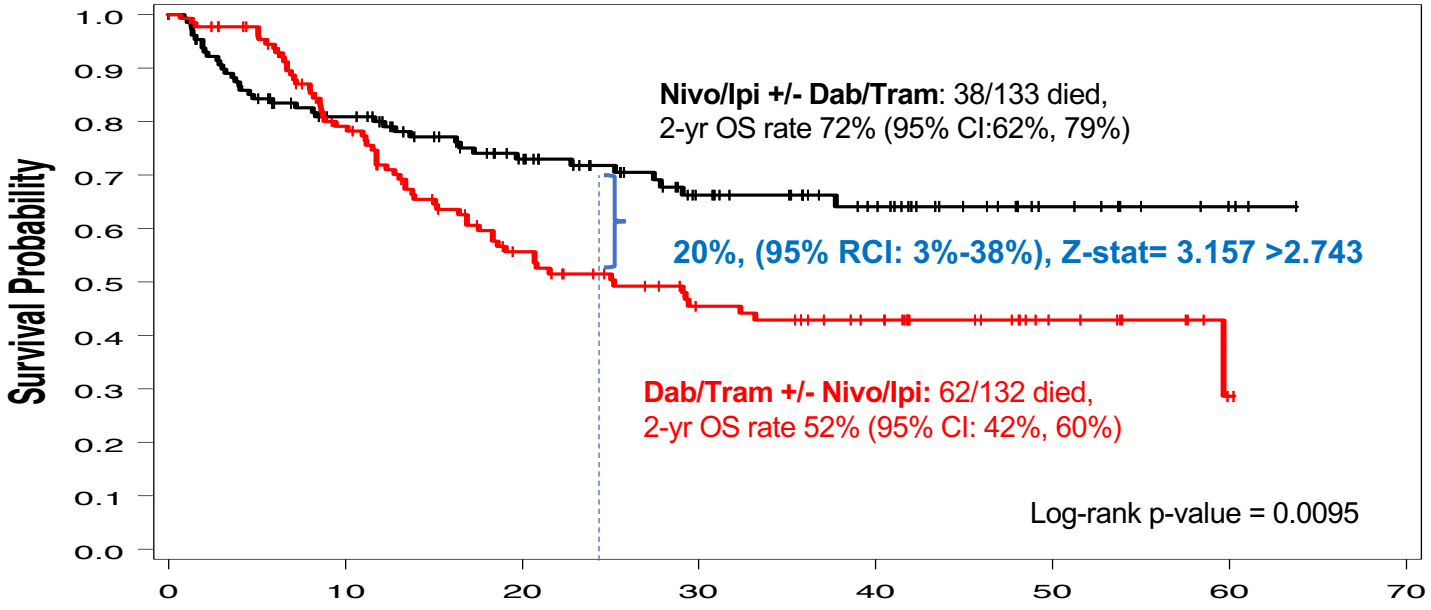
*Nivo/Ipi Induction = 12 wks; nivo maintenance = 72 wks

Progression Free Survival (PFS): Step1 (n=214)



	Arm A-Nivo/ipi	Arm B-Dab/Tram
PFS median, 95% CI	**11.8 mo** (5.9, 33.5)	**8.8 mo** (6.5,11.3)
1-year PFS, 95% CI	**49%** (38%,58%)	**36%** (28%,46%)
2-year PFS, 95% CI	**42%** (31%, 52%)	**19%** (12%, 27%)

Overall Survival (OS): Step 1 +/- Step 2



Time Interval

Treatment	0-6	6-12	12-18	18-24	24-30	30-36	36-42	42-48	48-54	54-60	60-66
IO+/-TT	133	99	87	71	55	42	33	23	15	6	3
TT+/-IO	132	115	78	60	47	35	30	18	15	6	1

(# at risk)

Overview

- Metastatic melanoma
- Adjuvant Therapy for surgically resected melanoma

Adjuvant Therapy

- Immunotherapy
- Targeted therapy

Adjuvant Therapy

- Immunotherapy
- Targeted therapy

CheckMate 238: Study Design

Patients with:

- **High-risk, completely resected stage IIIB/IIIC or stage IV[a] melanoma**
- **No prior systemic therapy**
- **ECOG PS 0/1**

1:1

n = 453 → **NIVO 3 mg/kg IV Q2W and IPI placebo IV Q3W for 4 doses, then Q12W from week 24**

n = 453 → **IPI 10 mg/kg IV Q3W for 4 doses, then Q12W from week 24 and NIVO placebo IV Q2W**

Follow-up

Maximum treatment duration of 1 year

Stratified by:

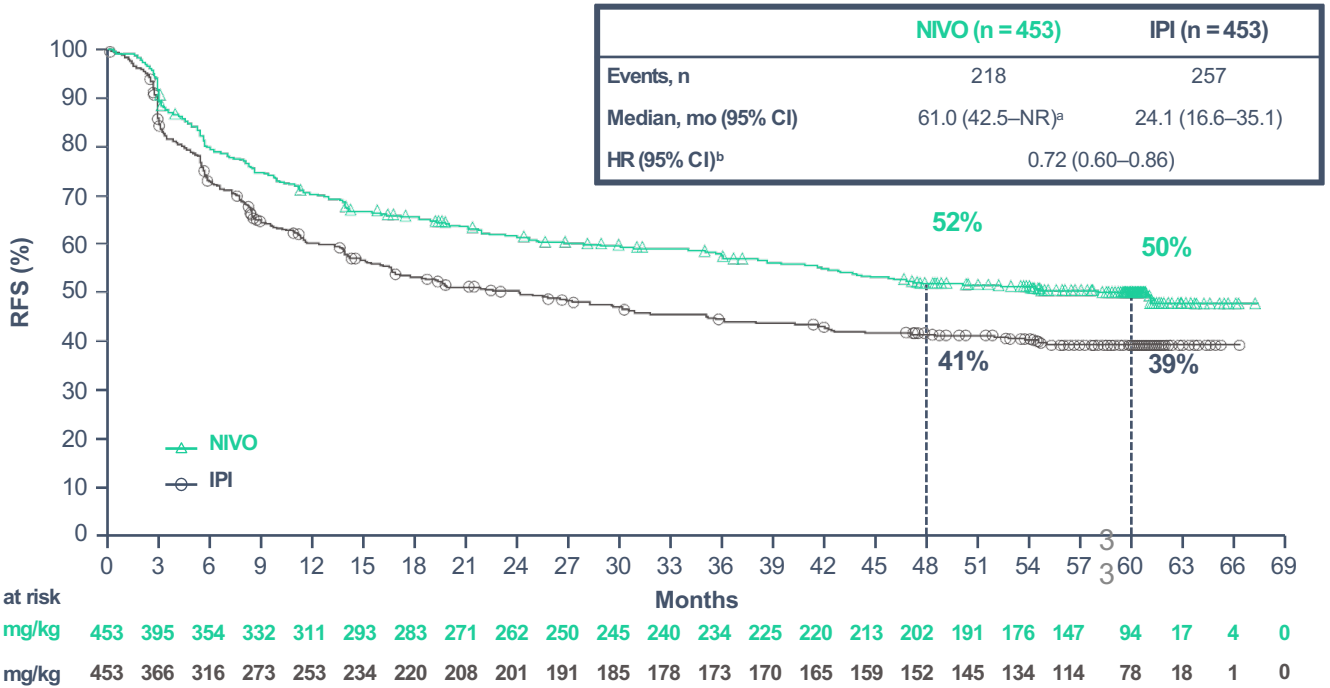
1) Disease stage: IIIB/IIIC vs IV M1a or M1b vs IV M1c
2) Tumor PD-L1 status at a 5% cutoff

Primary endpoint: RFS

Database lock: January 31, 2019; minimum follow-up of 36 months for all patients

NCT02388906.[a]Per American Joint Committee on Cancer (AJCC) Cancer Staging Manual, seventh edition.

Primary Endpoint: 60-Month RFS Update

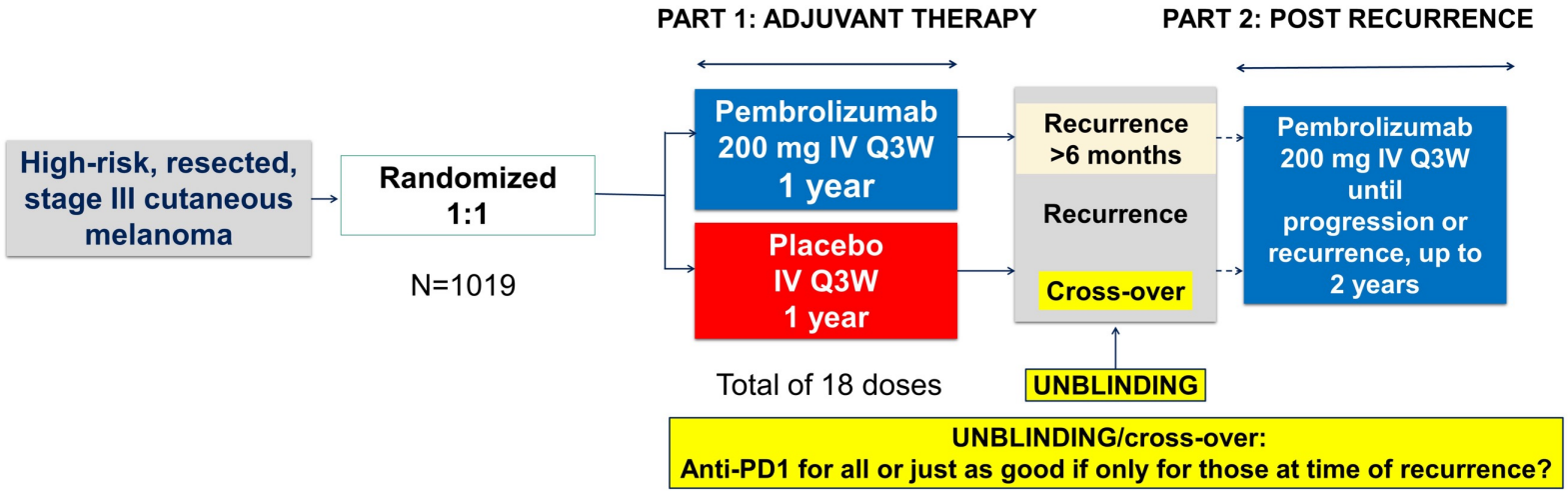


- New events since 4-year database lock: 6 (NIVO – 4 regional, 2 distant) and 4 (IPI – 1 each of local, distant, new primary, and death)

[a]Median not stable. [b]Stratified. Mo, month; NR, not reached.

Weber J et al. SMR 2021.

EORTC 1325/KEYNOTE-54 Study Design



Stratification factors:

✓**AJCC-7 Stage**: IIIA (>1 mm metastasis) vs. IIIB vs. IIIC 1-3 positive lymph nodes vs. IIIC ≥4 positive lymph nodes

✓**Region**: North America, European countries, Australia/New Zealand, other countries

Primary Endpoints:

- **RFS (per investigator) in overall ITT population,** and **in patients with PD-L1-positive tumors**

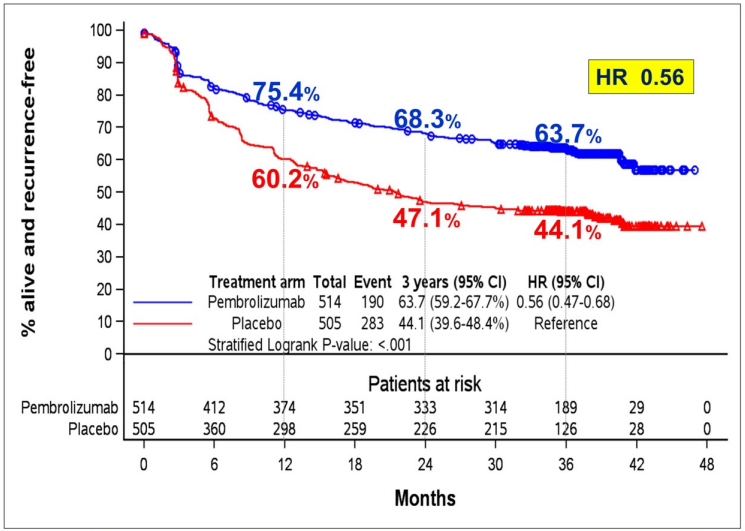
Secondary Endpoints:

- **DMFS and OS** in these 2 populations; **Safety, Health-related quality of life**

EORTC 1325/KEYNOTE-54: RFS ASCO (2020) and DMFS (ESMO 2020)

RFS updated analysis @ 3YR (ASCO 2020)[1]

- ***Cut-off date*** (30-Sep-2019); median follow-up: **3** years; **473 RFS events**

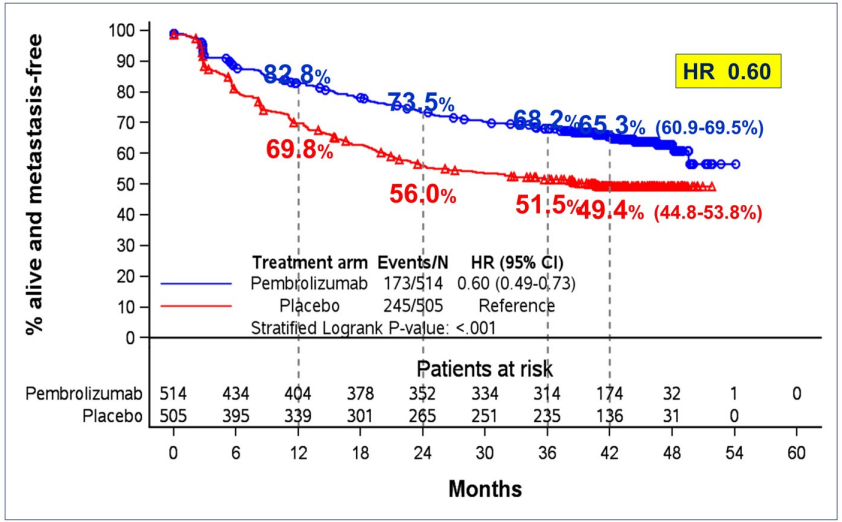


irAE: grade 1-5 (38%); grade 3-5 (7%)

[1]Eggermont AMM, et al. *J Clin Oncol* 2020;38:3925-36

DMFS final analysis @ 3.5 YR (ESMO 2020)[2]

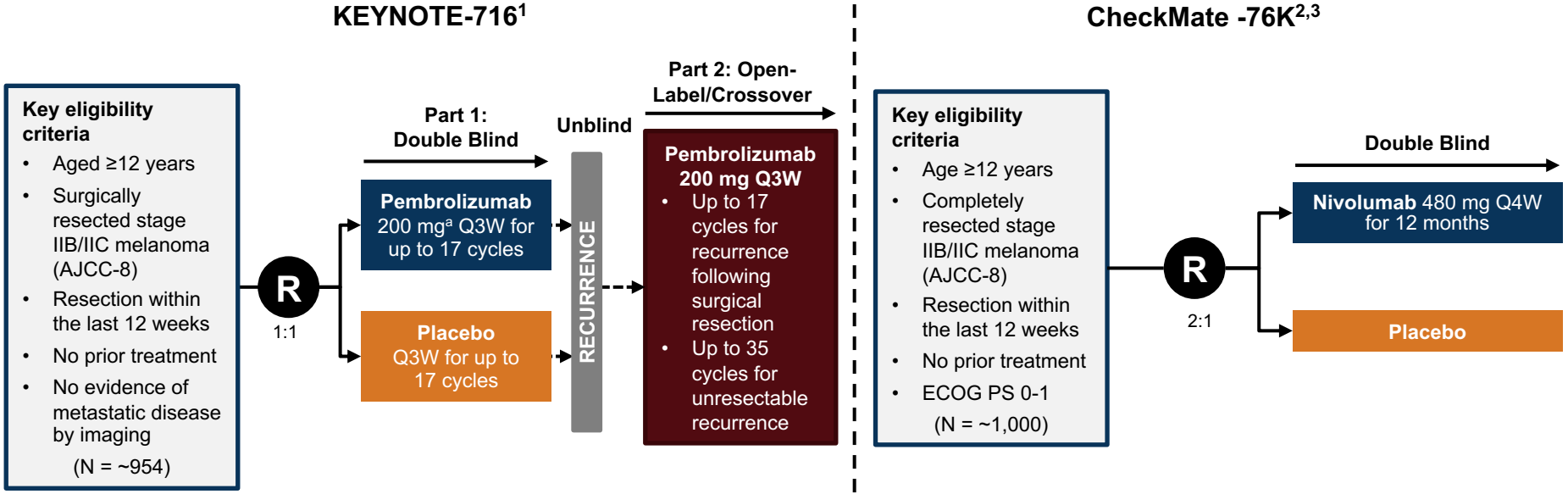
- ***Cut-off date*** (3-Apr-2020); median follow-up: **3.5** years; **418 DMFS events** (423 planned: ~87% power HR=0.725)



[2]Eggermont AMM, et al. *Lancet Oncol.* 2021;22:643-654

What about Stage II Melanoma?

Ongoing Trials of Adjuvant Anti–PD-1 Antibodies for Stage IIB/C Melanoma

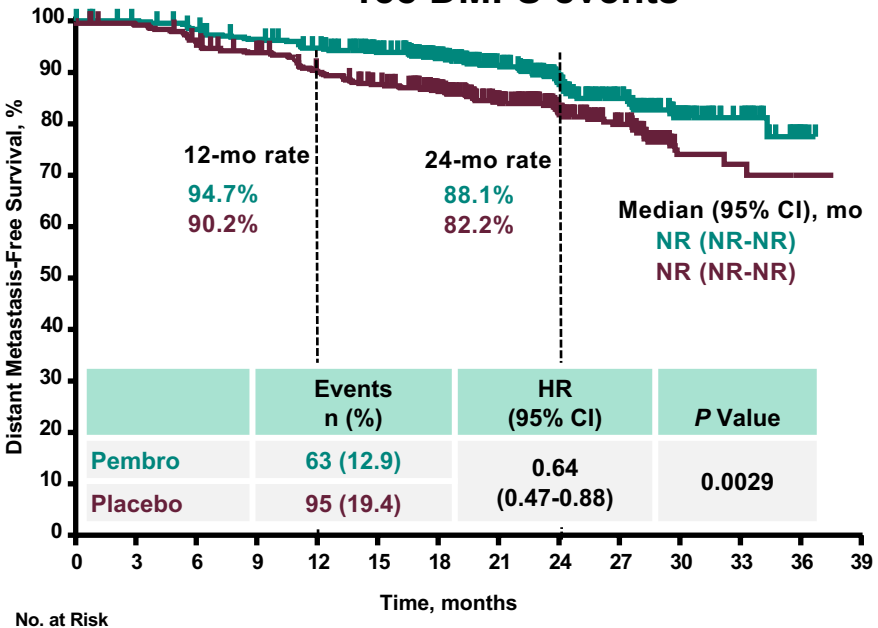


[a] Adult dosage; eligible patients aged 12 to <18 years receive 2 mg/kg Q3W.

1. Carlino MS et al. 2019 American Society of Clinical Oncology Annual Meeting (ASCO 2019). Abstract TPS9596. 2. https://clinicaltrials.gov/ct2/show/NCT04099
3. https://www.clinicaltrialsregister.eu/ctr-search/trial/2019-001230-34/AT.

DMFS: ITT Population

Median follow-up: 27.4 months[1]
158 DMFS events

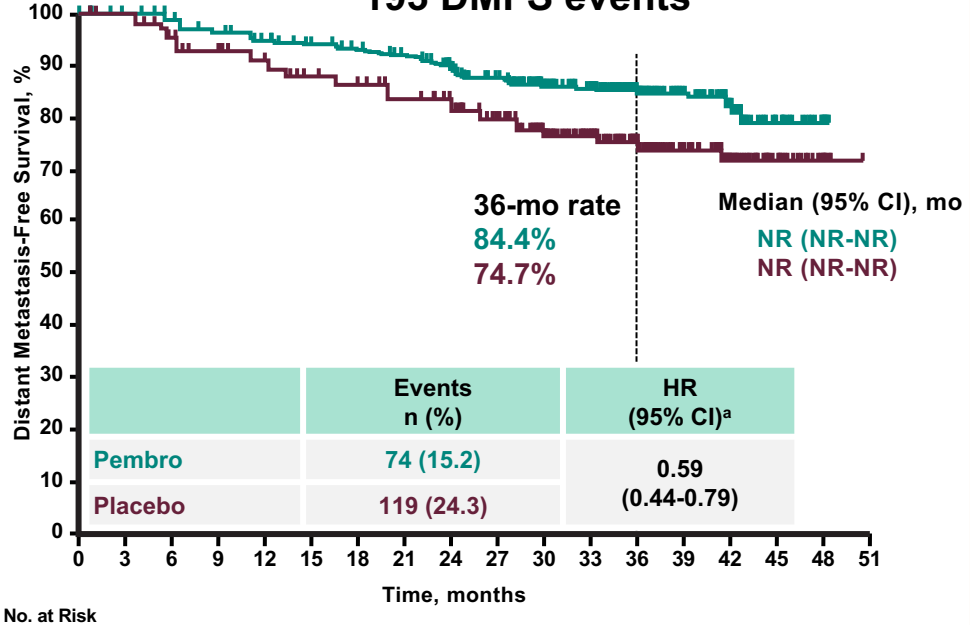


	Events n (%)	HR (95% CI)	*P* Value
Pembro	63 (12.9)	0.64 (0.47-0.88)	0.0029
Placebo	95 (19.4)		

No. at Risk

487	480	469	456	443	421	375	318	217	157	79	35	5	0
489	482	465	448	424	406	363	303	204	156	65	37	5	0

Median follow-up: 39.4 months
193 DMFS events



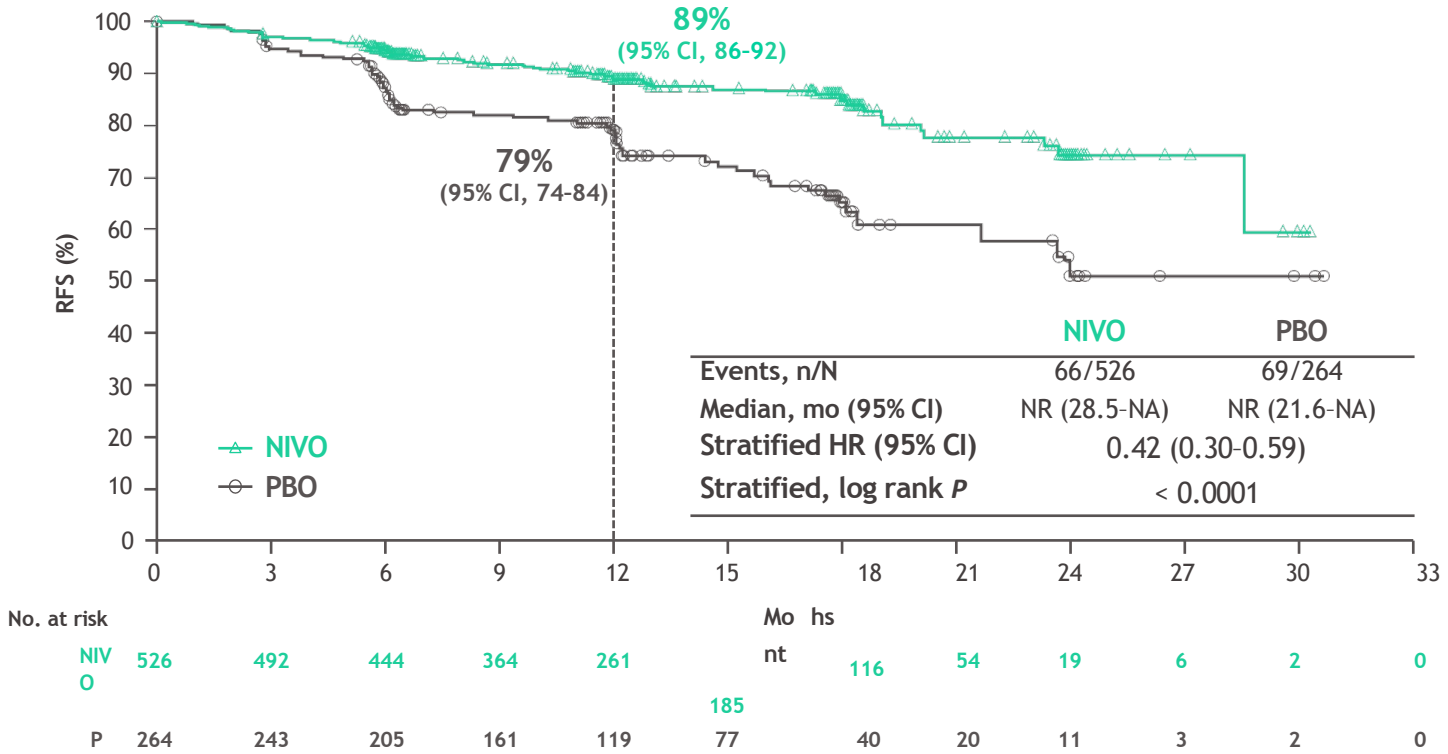
	Events n (%)	HR (95% CI)[a]
Pembro	74 (15.2)	0.59 (0.44-0.79)
Placebo	119 (24.3)	

No. at Risk

487	480	469	456	444	434	427	417	396	376	322	276	185	130	71	22	5	0
489	482	463	449	427	412	402	389	372	350	287	243	176	131	62	32	7	0

Long GV et al. *Lancet Oncol*. 2022;23(11):1378-1388.

Checkmate 76K: Primary endpoint RFS



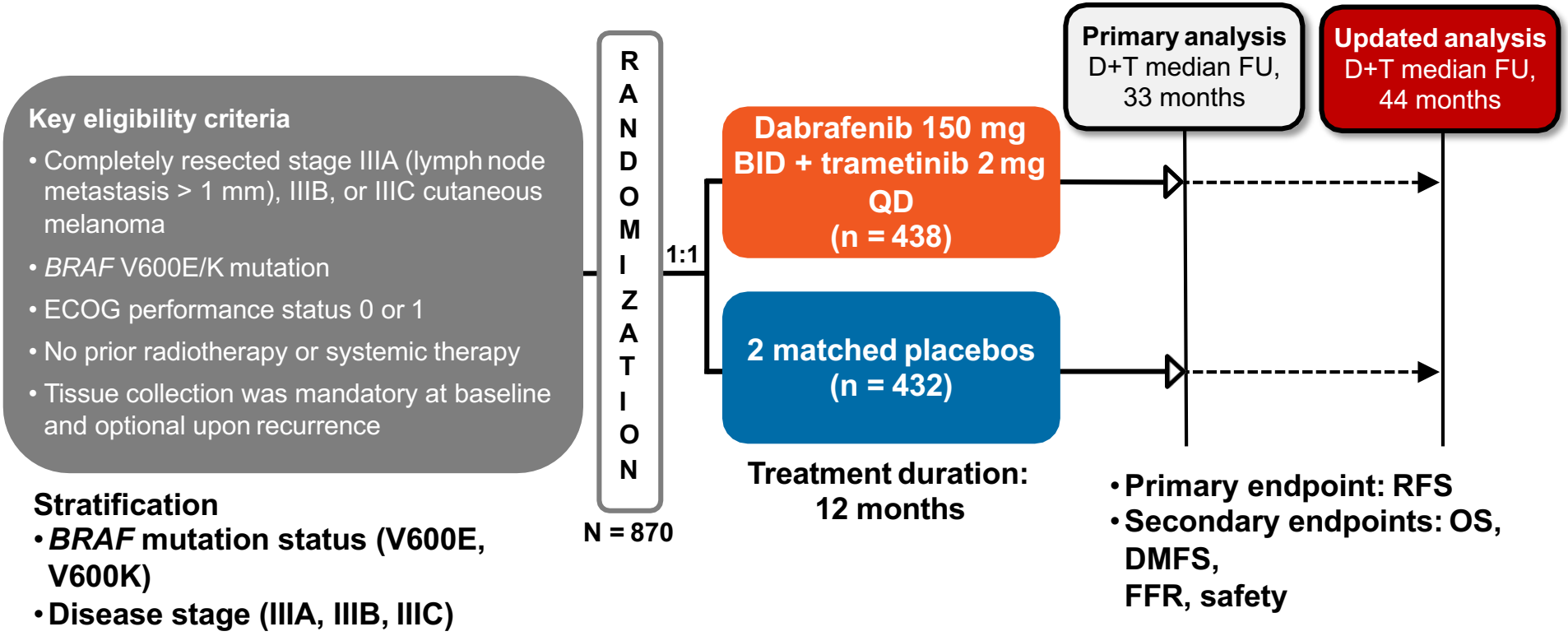
NA, not available; NR, not reached.

Presented by Georgina V Long

Adjuvant Therapy

- Immunotherapy
- Targeted therapy

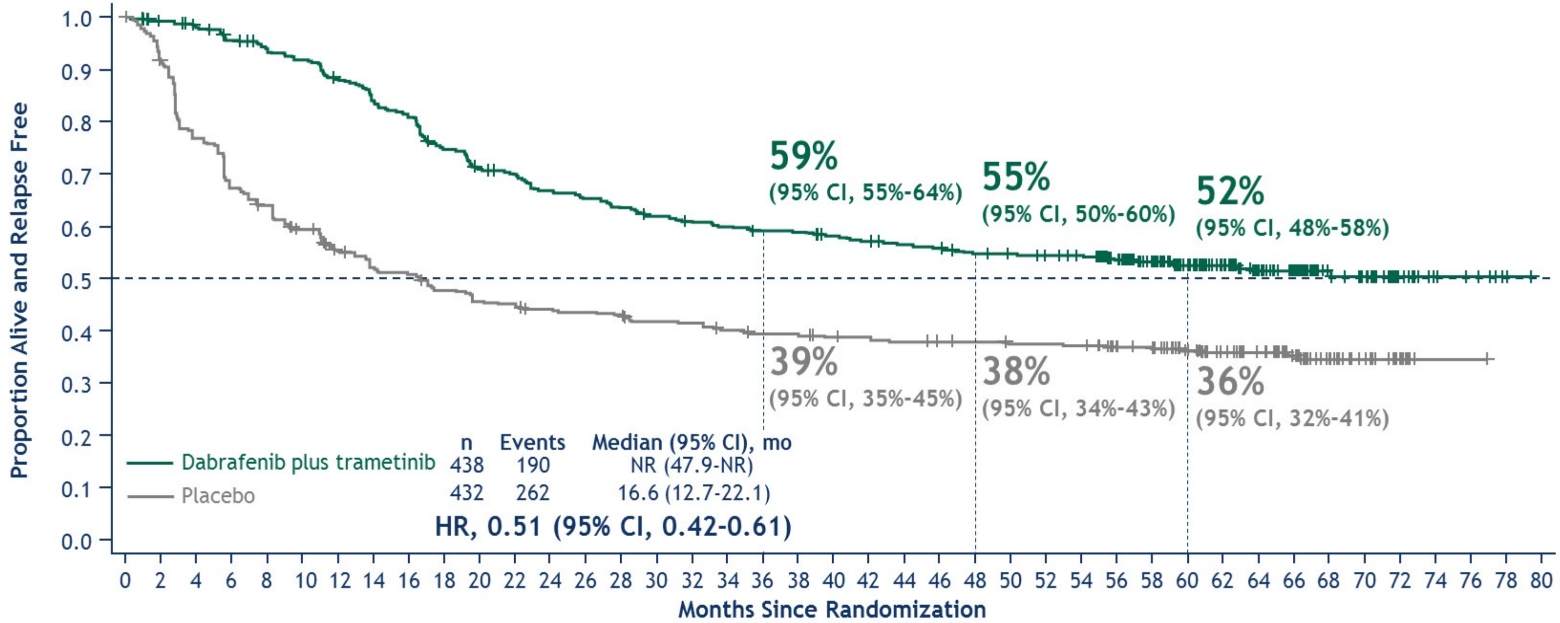
COMBI-AD: STUDY DESIGN—AND EXTENDED FOLLOW-UP ANALYSIS IN 2018



BID, twice daily; DMFS, distant metastasis–free survival; D+T, dabrafenib + trametinib; ECOG, Eastern Cooperative Oncology Group; FFR, freedom from relapse; FU, follow-up; QD, once daily.

Long GV, et al. *N Engl J Med*. 2017;377:1813-1823.

Relapse-Free Survival



No. at risk

Dabrafenib plus trametinib	438	413	405	391	381	372	354	335	324	298	281	275	262	256	249	242	236	233	229	228	221	217	213	210	204	202	199	195	176	156	133	109	92	80	45	38	17	8	6	2	0
Placebo	432	387	322	280	263	243	219	204	199	185	178	175	168	166	164	158	157	151	147	146	143	140	139	137	136	133	133	132	121	115	99	80	69	56	35	26	13	1	1	0	0

HR, hazard ratio; NR, not reached.

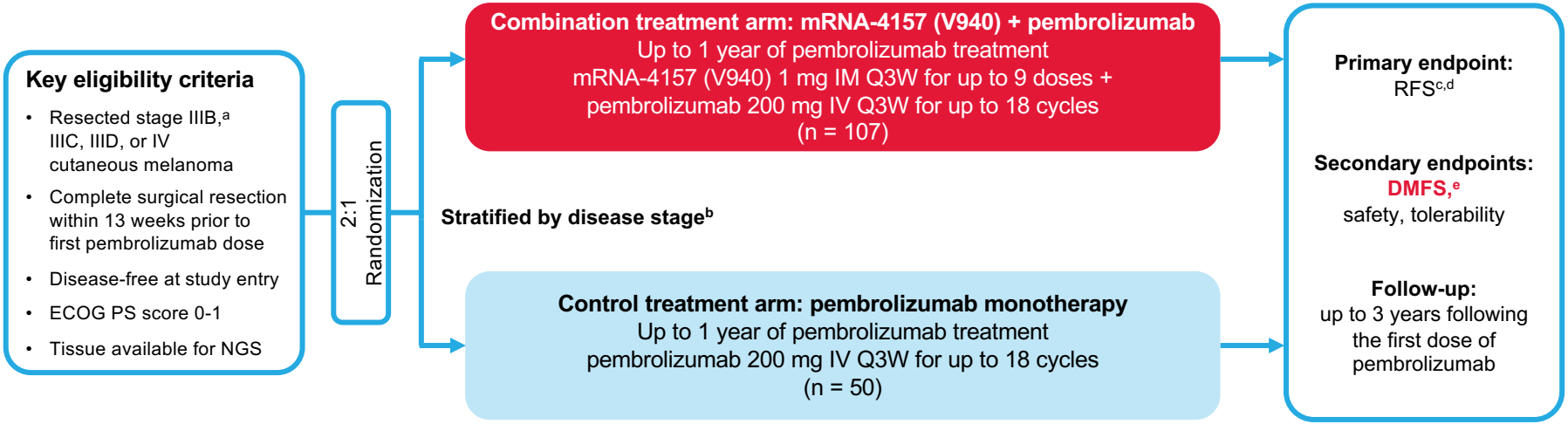
ASCO 2020

Where is Progress Being Made?

- RNA vaccine for adjuvant therapy
- Neoadjuvant therapy
- Overcoming immunotherapy resistance

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

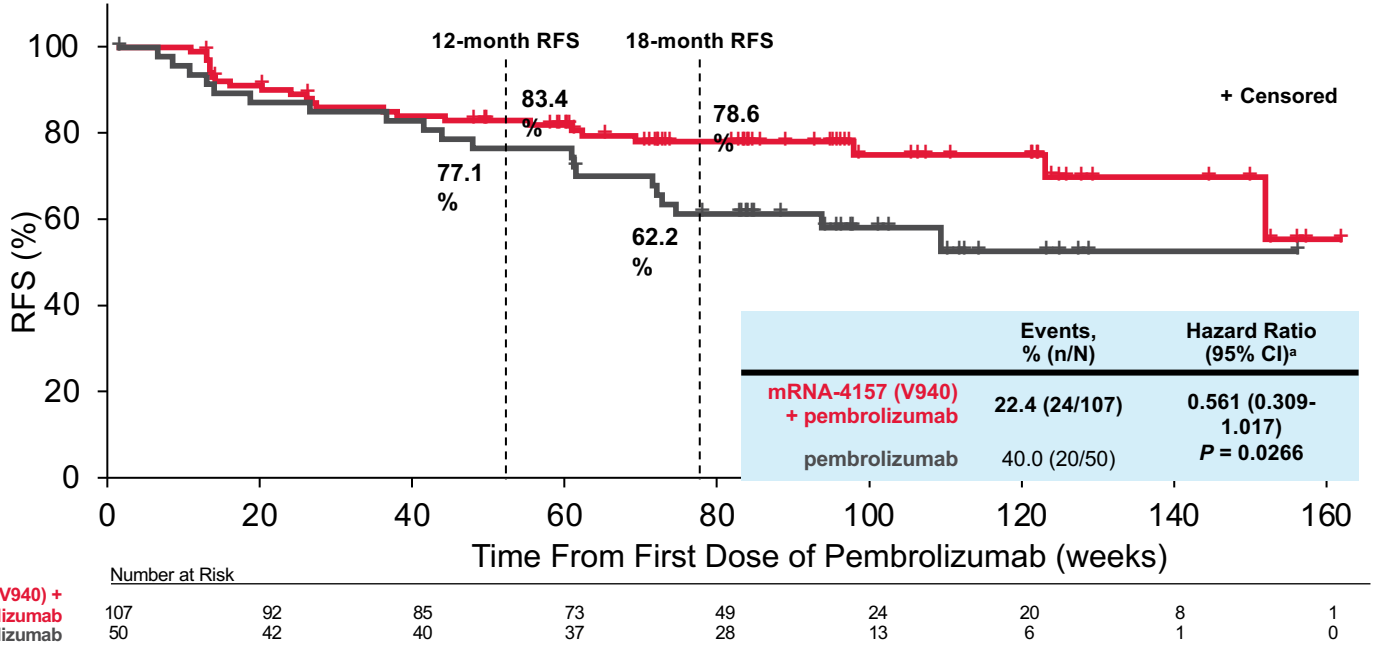
Randomized, phase 2, open-label study in adjuvant resected melanoma patients at high risk of recurrence



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

[a]Patients with stage IIIB disease were eligible only if relapse occurred within 3 months of prior surgery of curative intent. [b]According to the 8th edition of the American Joint Committee on Cancer Staging Manual. [c]The primary endpoint was investigator-assessed RFS (defined as the time from first dose of pembrolizumab until the date of first recurrence [local, regional, or distant metastasis], a new primary melanoma, or death from any cause) in the intention-to-treat population. [d]The primary analysis for RFS was specified to occur after all patients completed ≥12 months on study and ≥40 RFS events were observed. Descriptive analysis was specified to occur when ≥51 RFS events were observed. [e]Investigator-assessed DMFS was defined as the time from first dose of pembrolizumab until the date of first distant recurrence or death from any cause. [f]The stratified log-rank test was used for comparison. [g]Time of database cutoff was November 14, 2022.

Primary Efficacy Endpoint: RFS[1]

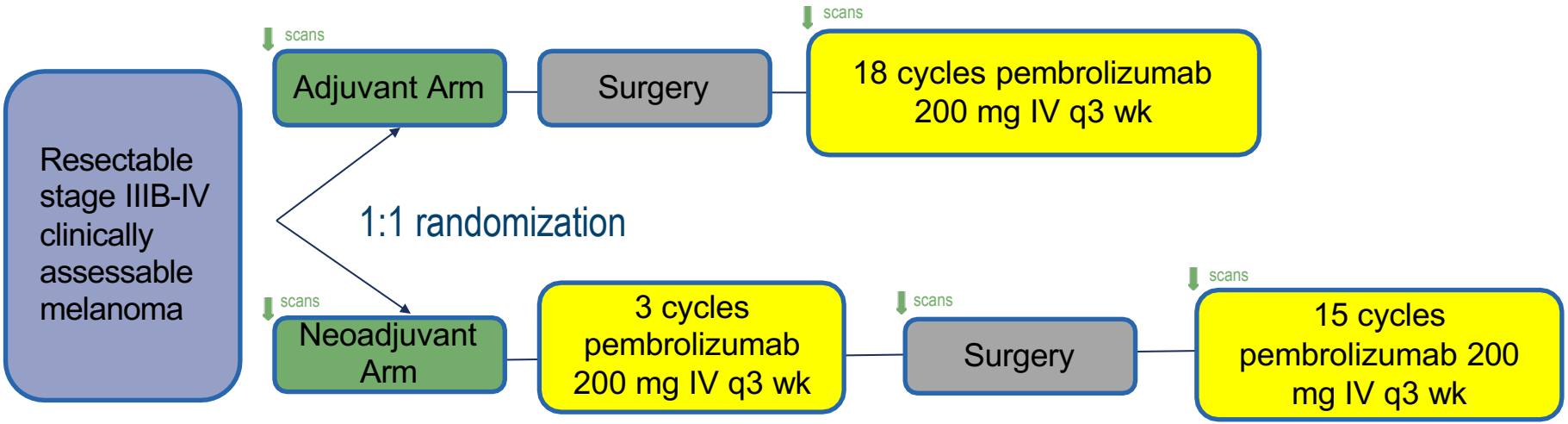


[a]The hazard ratio and 95% CI for mRNA-4157 (V940) plus pembrolizumab versus pembrolizumab is estimated using a Cox proportional hazards model with treatment group as a covariate, stratified by disease stage (stages IIIB or IIIC or IIID vs stage IV) used for randomization. The *P* value is based on a 1-sided log-rank test stratified by disease stage (stages IIIB or IIIC or IIID vs stage IV) used for randomization.

1. Khattak A, et al. Presented at the American Association for Cancer Research® (AACR) Annual Meeting; April 14-19, 2023; Orlando, FL, USA. Oral presentation CT001.

S1801 Study Schema

Primary endpoint: Event-free survival

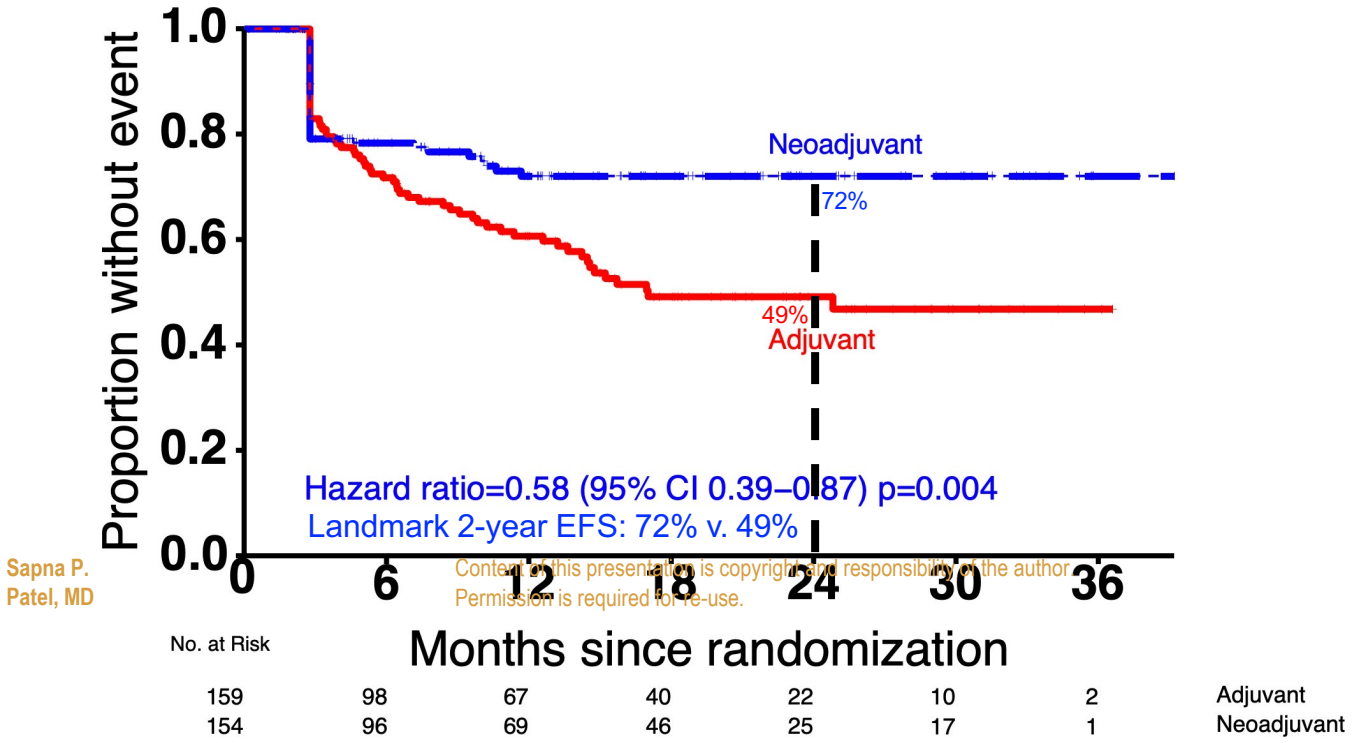


radiographic assessment (scans)

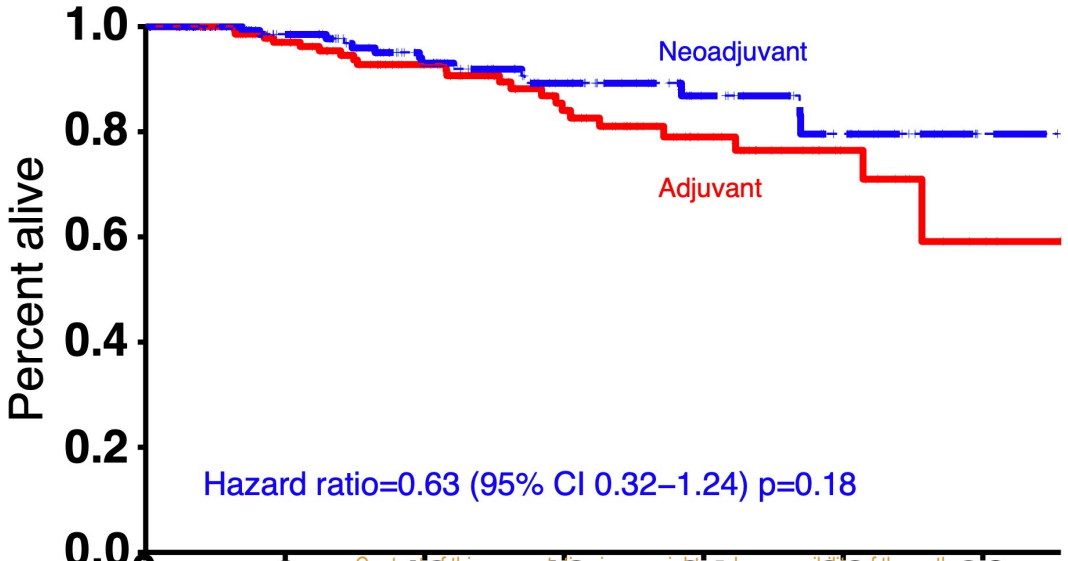
Additional criteria: strata included AJCC 8th ed. stage and LDH, adjuvant radiation allowed, concomitant radiation & pembrolizumab was not allowed, brain metastasis excluded, uveal melanoma excluded

Surgery type and extent was required to be pre-specified and carried out regardless of radiologic response to therapy

S1801 primary endpoint: Event-free survival



Overall survival



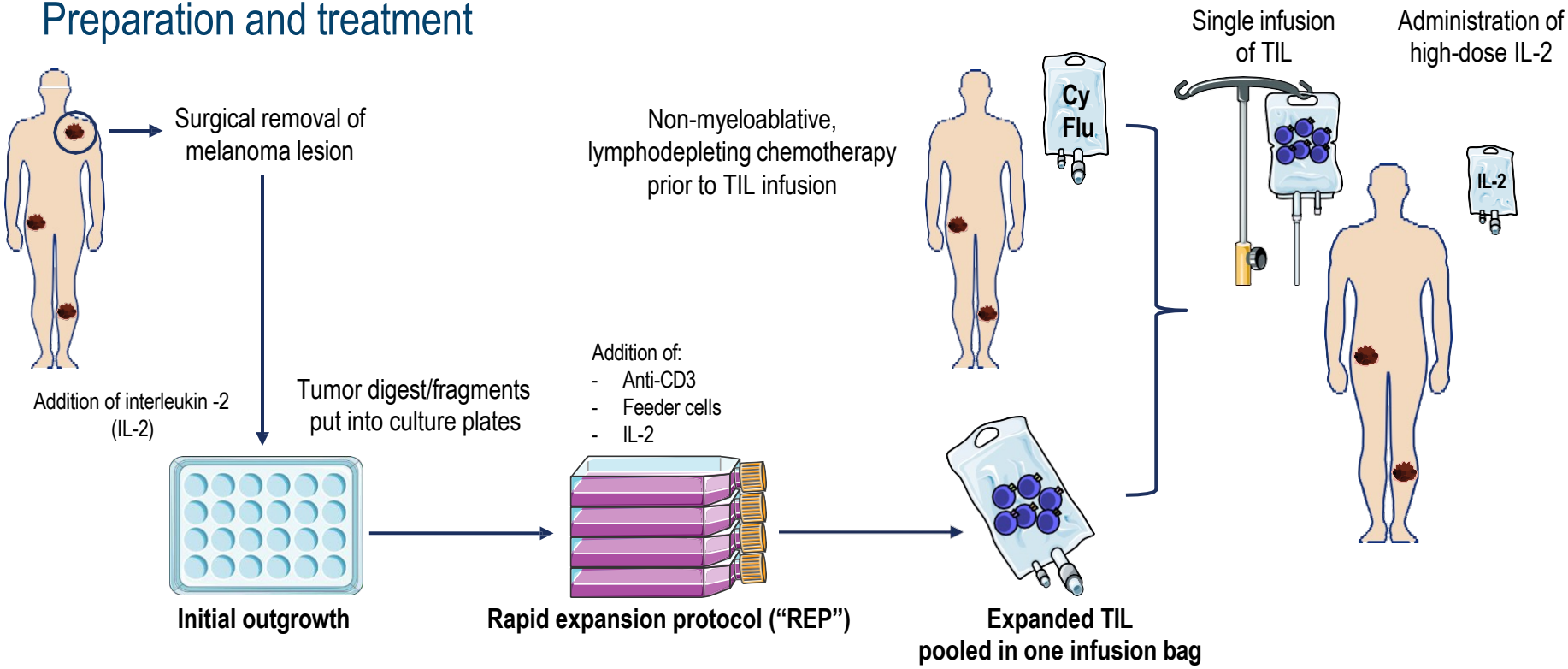
No. at Risk

159	124	93	60	33	15	3	Adjuvant
154	124	90	59	30	19	1	Neoadjuvant

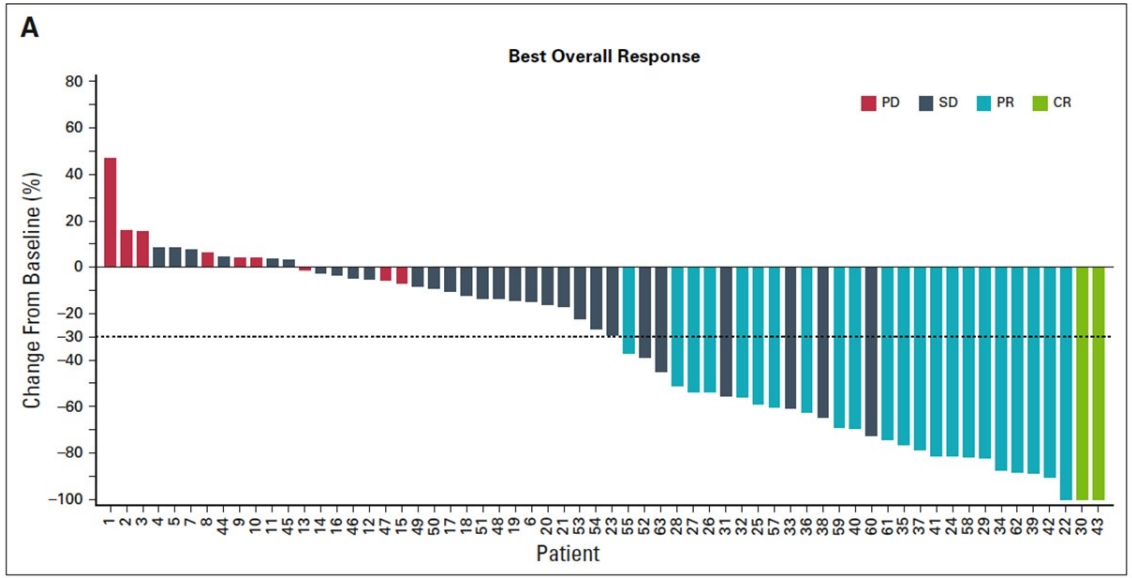
Sapna P. Patel, MD

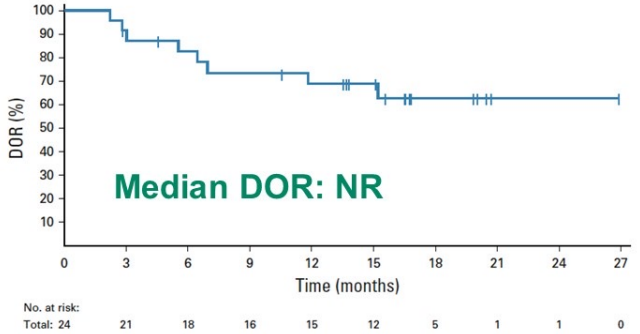
Tumor-infiltrating lymphocytes (TIL)

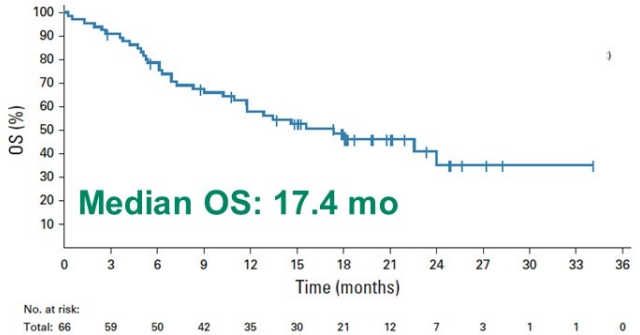
Preparation and treatment



Lifileucel for PD-1 Refractory Melanoma







ORR: 36%
(95% CI, 25 to 49)

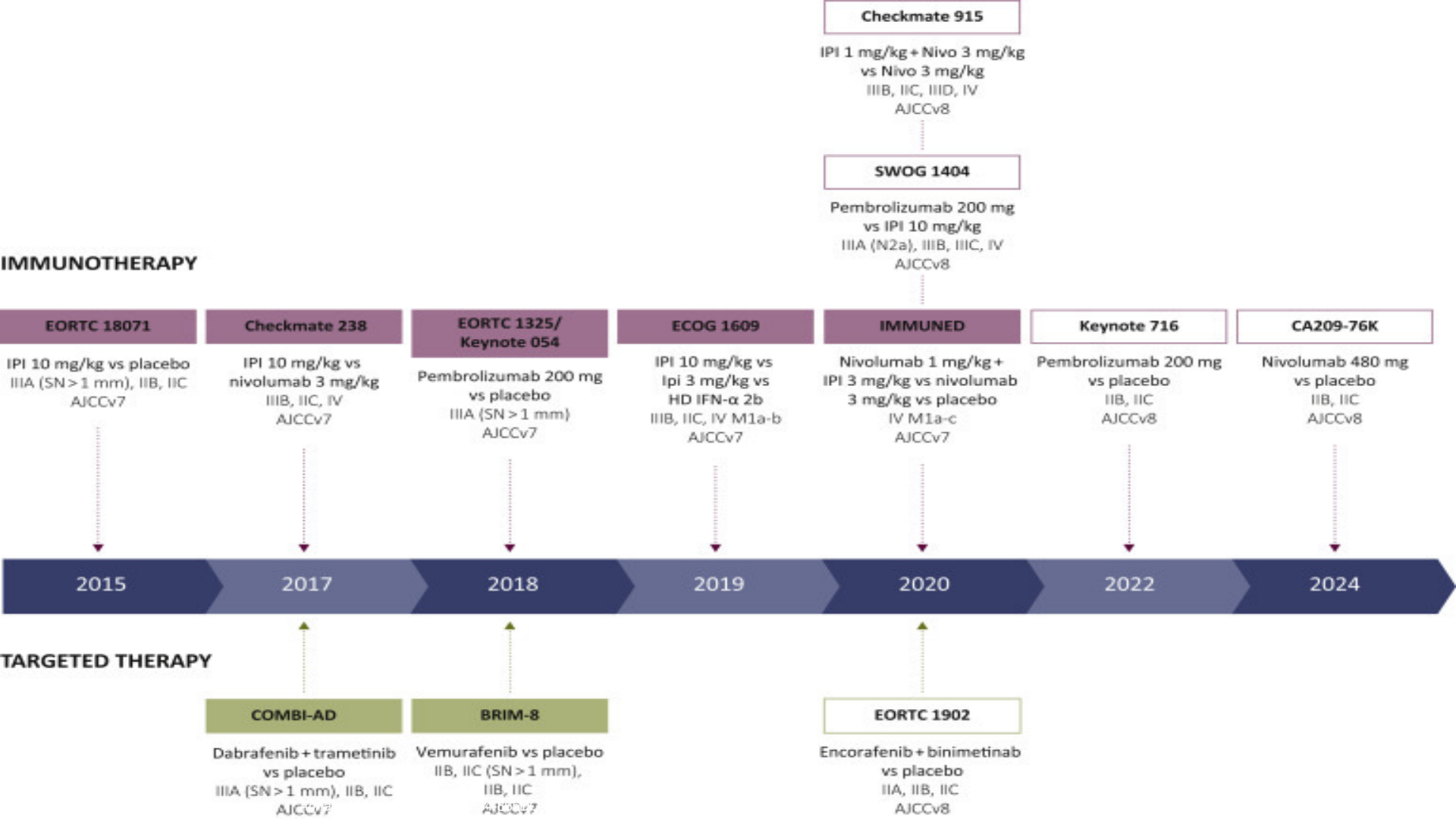
(Sarnaik et al. *J Clin Oncol* 2021)

Metastatic Melanoma: Summary & Conclusions

- For first-line therapy of metastatic melanoma, combination immunotherapy has emerged as the preferred first-line option regardless of BRAF mutation status
  - Ipi/Nivo in most patients
  - Rela/Nivo in selected patients

Adjuvant Therapy
Summary & Conclusions

- Most patients with stage III disease are offered adjuvant therapy
  - Anti-PD1 an option for all appropriate patients
  - Targeted therapy (BRAF+MEK) for BRAF-MT patients
- Choice between targeted therapy or immunotherapy for BRAF-MT stage III patients remains a clinical decision
- Adjuvant anti-PD1 therapy is effective in terms of RFS for Stage IIB and IIC melanoma


Checkmate 915
IPI 1 mg/kg + Nivo 3 mg/kg vs Nivo 3 mg/kg
IIIB, IIC, IIID, IV
AJCCv8
SWOG 1404
Pembrolizumab 200 mg vs IPI 10 mg/kg
IIIA (N2a), IIIB, IIIC, IV
AJCCv8
IMMUNOTHERAPY
EORTC 18071
IPI 10 mg/kg vs placebo
IIIA (SN > 1 mm), IIB, IIC
AJCCv7
Checkmate 238
IPI 10 mg/kg vs nivolumab 3 mg/kg
IIIB, IIC, IV
AJCCv7
EORTC 1325/ Keynote 054
Pembrolizumab 200 mg vs placebo
IIIA (SN > 1 mm)
AJCCv7
ECOG 1609
IPI 10 mg/kg vs Ipi 3 mg/kg vs HD IFN-α 2b
IIIB, IIC, IV M1a-b
AJCCv7
IMMUNED
Nivolumab 1 mg/kg + IPI 3 mg/kg vs nivolumab 3 mg/kg vs placebo
IV M1a-c
AJCCv7
Keynote 716
Pembrolizumab 200 mg vs placebo
IIB, IIC
AJCCv8
CA209-76K
Nivolumab 480 mg vs placebo
IIB, IIC
AJCCv8
2015
2017
2018
2019
2020
2022
2024
TARGETED THERAPY
COMBI-AD
Dabrafenib + trametinib vs placebo
IIIA (SN > 1 mm), IIB, IIC
AJCCv7
BRIM-8
Vemurafenib vs placebo
IIB, IIC (SN > 1 mm), IIB, IIC
AJCCv7
EORTC 1902
Encorafenib + binimetinab vs placebo
IIA, IIB, IIC
AJCCv8

Systemic Therapy for Melanoma: ASCO Guideline Update

Rahul Seth, DO[1]; Sanjiv S. Agarwala, MD[2]; Hans Messersmith, MPH[3]; Krishna C. Alluri, MD[4]; Paolo A. Ascierto, MD[5]; Michael B. Atkins, MD[6]; Kathryn Bollin, MD[7]; Matias Chacon, MD[8]; Nancy Davis, MD[9]; Mark B. Faries, MD[10]; Pauline Funchain, MD[11]; Jason S. Gold, MD[12]; Samantha Guild, JD[13]; David E. Gyorki, MBBS[14]; Varinder Kaur, MD[15]; Nikhil I. Khushalani, MD[16]; John M. Kirkwood, MD[17]; Jennifer Leigh McQuade, MD[18]; Michael O. Meyers, MD[19]; Anthony Provenzano, MD[20]; Caroline Robert, MD, PhD[21]; Mario Santinami, MD[22]; Amikar Sehdev, MPH, MD[23]; Vernon K. Sondak, MD[16]; Gilliosa Spurrier, MSc[24]; Umang Swami, MS, MD[25]; Thach-Giao Truong, MD[26]; Katy K. Tsai, MD[27]; Alexander van Akkooi, MD, PhD[28]; and Jeffrey Weber, MD, PhD[29]

DOI https://doi.org/10.1200/JCO.23.01136

ASCO Committee Chairs: Rahul Seth, DO and Sanjiv Agarwala, MD