Immunotherapy of Melanoma

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Overview

- Metastatic Melanoma
- Adjuvant therapy for High-risk
- Practical Questions
- Future Directions

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- Metastatic Melanoma
- Adjuvant therapy for High-risk
- Practical Questions
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Today's Immunotherapy

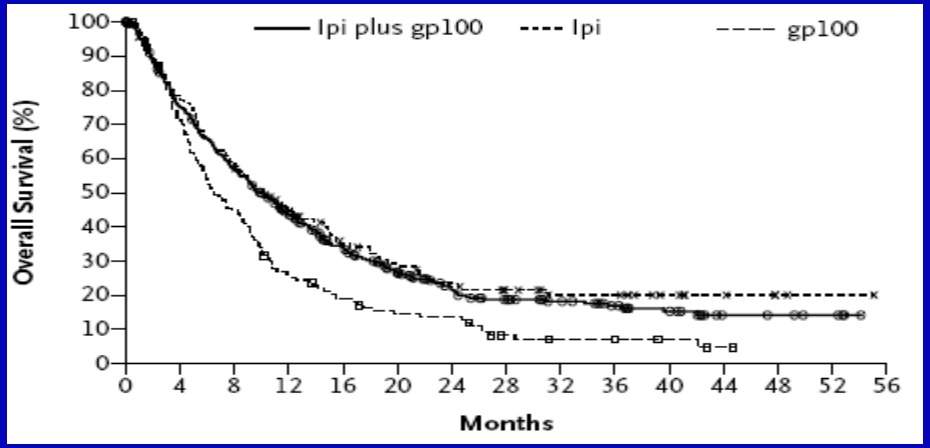
=

Checkpoint Inhibitors

Check-Point Inhibitors Approved for Melanoma

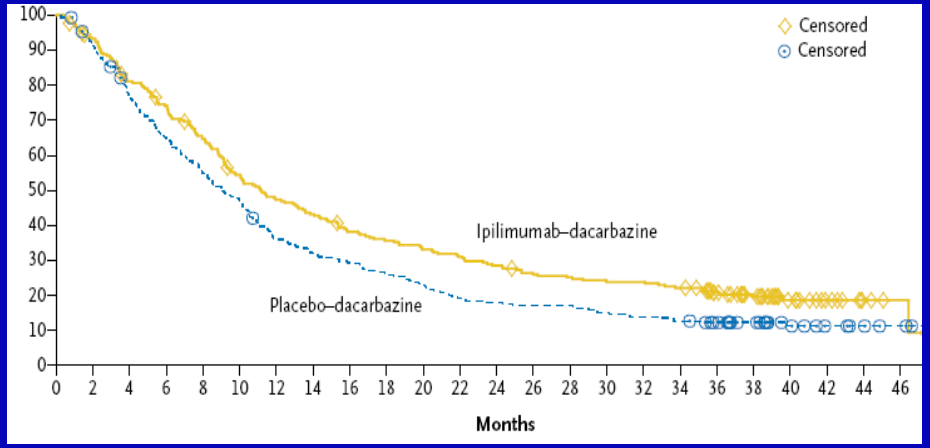
- Anti CTLA4 antibody: Ipilimumab
- Anti PD-1 inhibitors: pembrolizumab, nivolumab
- Combination anti CTLA-4 and anti-PD1 (ipilimumab and nivolumab)

Clinical Results with Ipilimumab (2nd and 1st line)
Ipilimumab vs vaccine and Ipi + DTIC vs DTIC



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

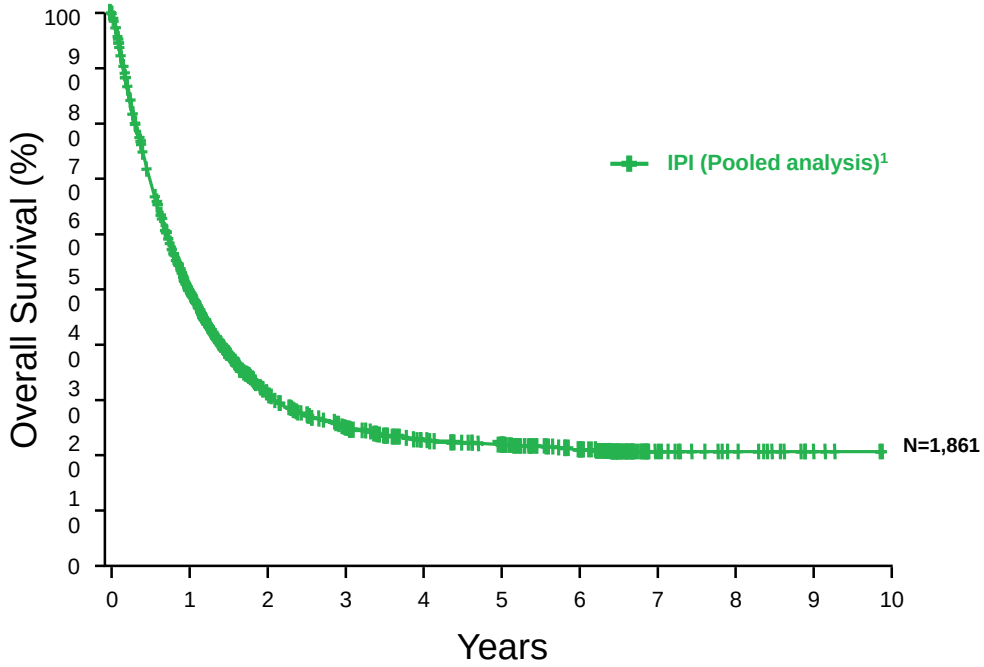
Hodi FS, et al. *N Engl J Med.* 2010;363:711-23.



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

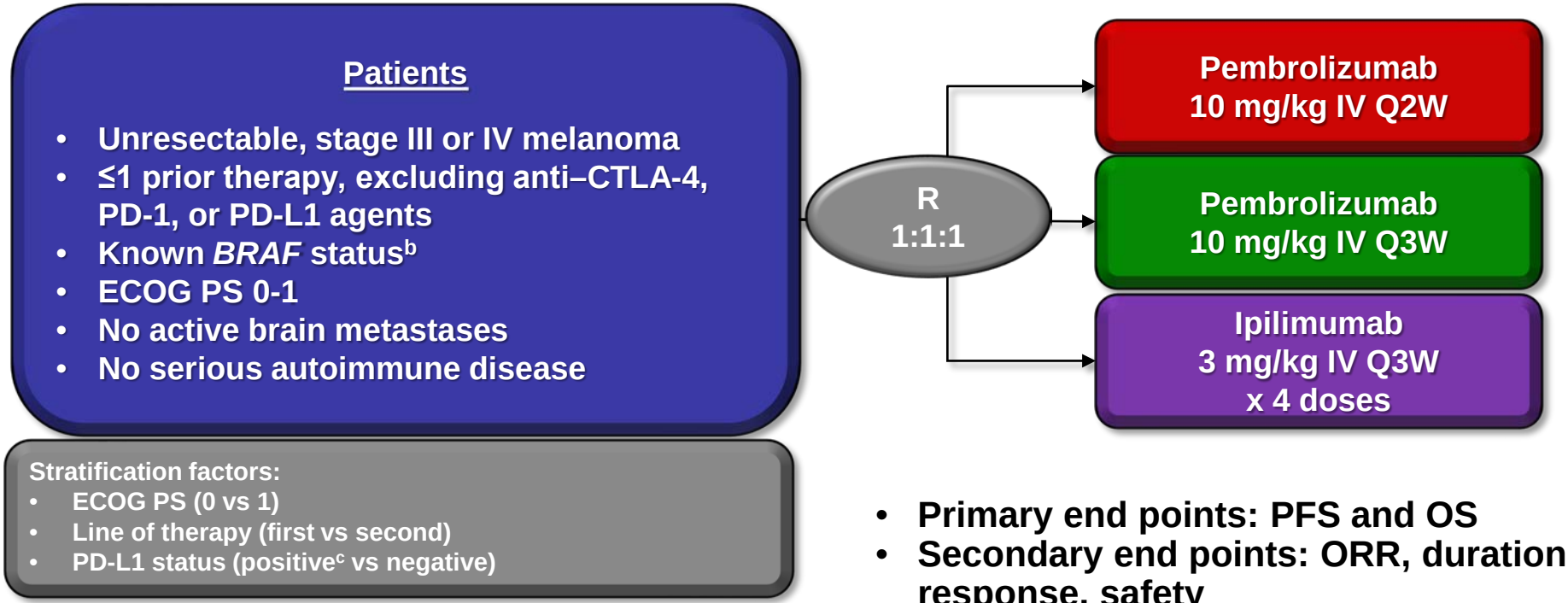
Robert C, et al. *N Engl J Med*. 2011;364:2517-26.

Immune Checkpoint Inhibitors Provide Durable Long-term Survival for Patients with Advanced Melanoma



1. Schadendorf et al. *J Clin Oncol* 2015;33:1889-1894; 2. Current analysis; 3. Poster presentation by Dr. Victoria Atkinson at SMR 2015 International Congress.

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.

Tumor Response (irRC, investigator)

	Pembrolizumab N = 556	Ipilimumab N = 278
ORR, % (95% CI)	42 (38-46)	16 (12-21)
Best overall response, % (95% CI)		
CR	13 (11-16)	3 (1-6)
PR	29 (25-33)	14 (10-18)
SD	21 (18-25)	25 (20 -31)
PD	29 (26-33)	39 (33-45)

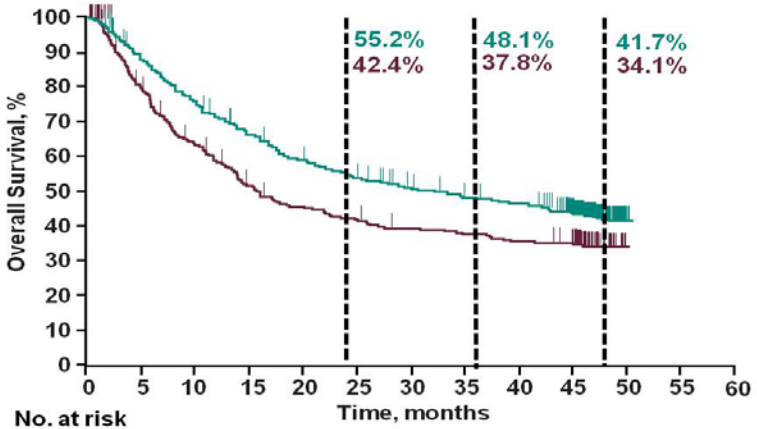
Analysis includes all randomized patients with measurable disease at baseline who received ≥1 pembrolizumab dose. Data cutoff date: Nov 3, 2016.

Overall Survival

Median Follow-Up 45.9 (0.3-50.0) Months

All Patients

	Events, n	HR[a] (95% CI)	Median,[b] mo (95% CI)
Pembro	309	0.73 (0.61-0.89)	32.7 (24.5-41.6)
Ipi	164	-	15.9 (13.3-22.0)

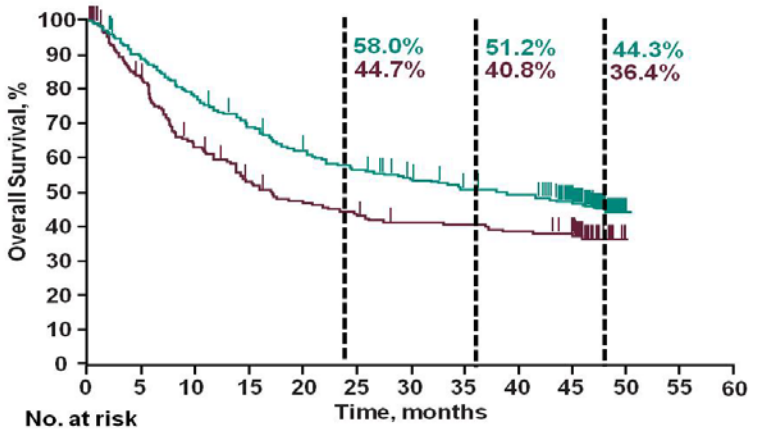


No. at risk

556	481	416	357	317	289	266	250	239	181	0	0	0
278	202	158	127	111	102	94	90	85	76	0	0	0

Treatment-Naive Patients

	Events, n	HR[a] (95% CI)	Median,[b] mo (95% CI)
Pembro	193	0.73 (0.57-0.93)	38.7 (27.3-NR)
Ipi	104	-	17.1 (13.8-26.2)

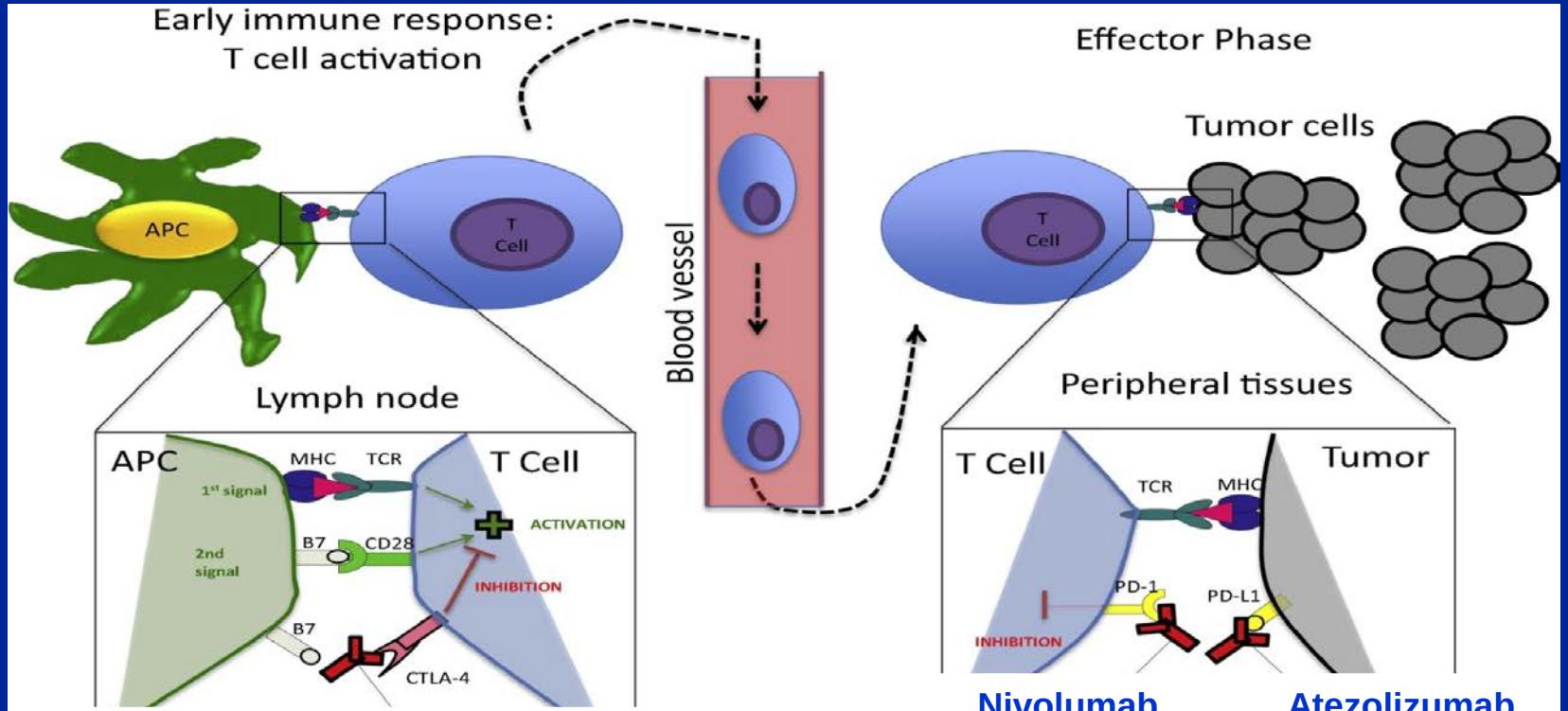


No. at risk

368	324	284	248	221	201	186	174	167	124	0	0	0
181	140	105	86	76	70	64	63	60	51	0	0	0

[a]Based on Cox regression model with treatment as covariate stratified by line of therapy (1st vs 2nd), PD-L1 status (positive vs negative), and ECOG (0 vs 1); if no patients are in one of the treatment groups involved in a comparison for a particular stratum, then that stratum was excluded from treatment comparison. [b]Derived by the product-limit (Kaplan-Meier) method for censored data. Data cutoff: Dec 4, 2017.

Blocking CTLA-4 and PD-1



Ipilimumab and Tremelimumab

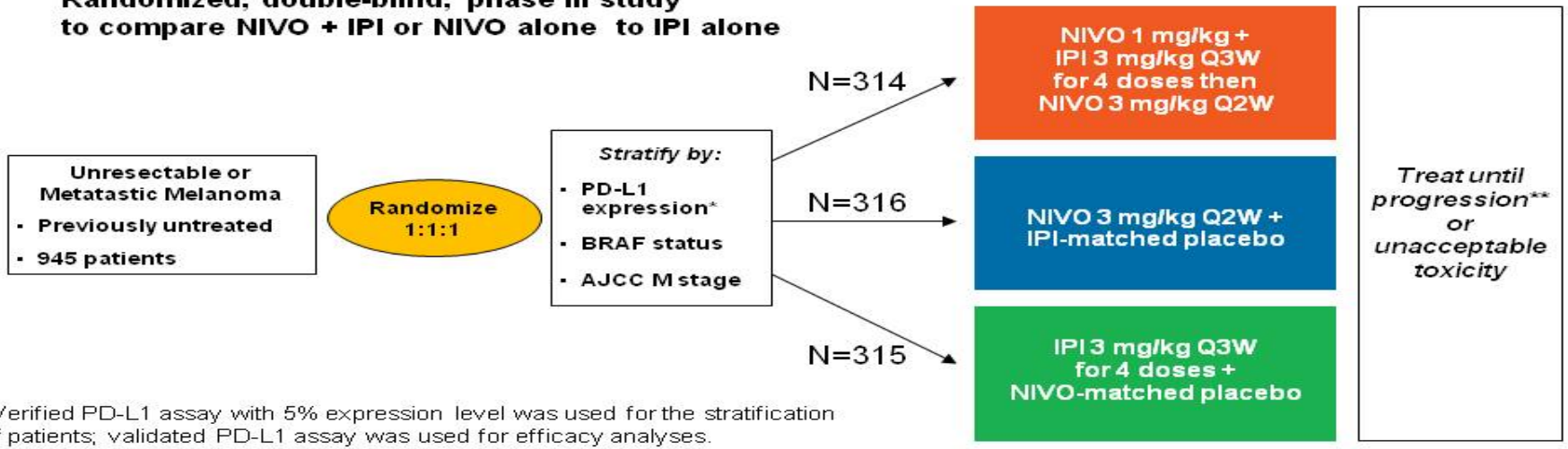
Nivolumab
Pembrolizumab
Pidilizumab

–

Atezolizumab
Durvalumab
Avelumab

CA209-067: Study Design

Randomized, double-blind, phase III study to compare NIVO + IPI or NIVO alone to IPI alone



*Verified PD-L1 assay with 5% expression level was used for the stratification of patients; validated PD-L1 assay was used for efficacy analyses.

**Patients could have been treated beyond progression under protocol-defined circumstances.

Presented By Jedd Wolchok at 2015 ASCO Annual Meeting

Updated Response To Treatment

	NIVO+IPI (N=314)	NIVO (N=316)	IPI (N=315)
ORR, % (95% CI)*	**58.9** (53.3–64.4)	**44.6** (39.1–50.3)	**19.0** (14.9–23.8)
Best overall response — %			
Complete response	17.2	14.9	4.4
Partial response	41.7	29.7	14.6
Stable disease	11.5	9.8	21.3
Progressive disease	23.6	38.6	51.1
Unknown	6.1	7.0	8.6
Median duration of response, months (95% CI)	**NR** (NR–NR)	**31.1** (31.1–NR)	**18.2** (8.3–NR)

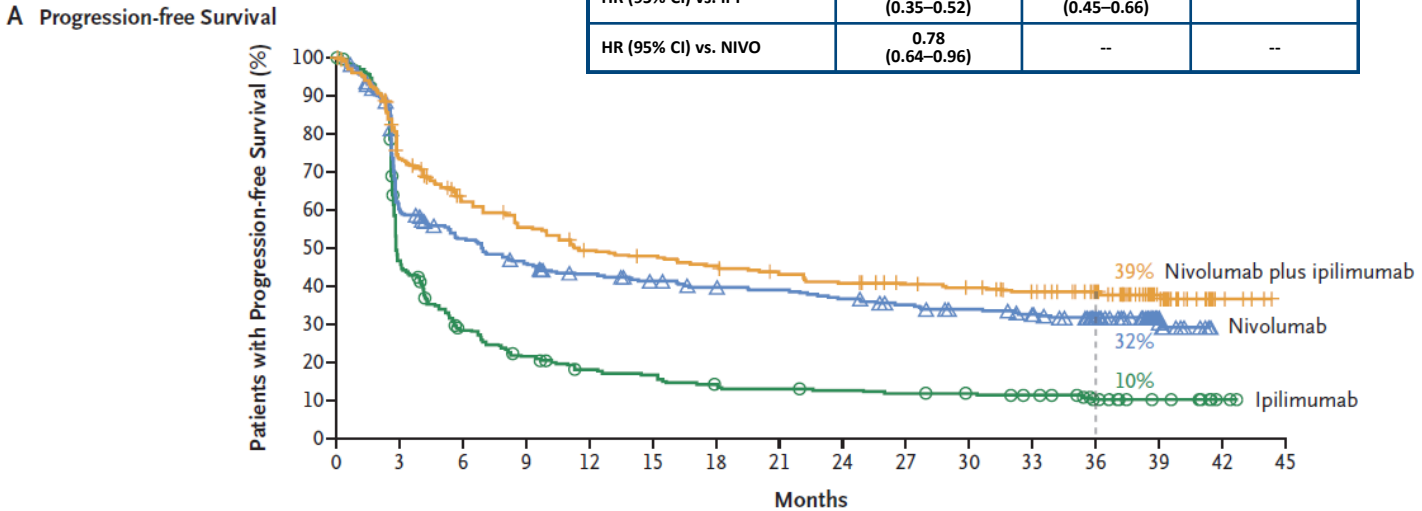
*By RECIST v1.1; NR = not reached.

- At the 18-month DBL, the CR rate for NIVO+IPI, NIVO and IPI was 12.1%, 9.8% and 2.2%, respectively

Database lock: Sept 13, 2016, minimum f/u of 28 months

CM-67 Progression-Free Survival

	NIVO+IPI (N=314)	NIVO (N=316)	IPI (N=315)
Median PFS, mo (95% CI)	11.5 (8.7–19.3)	6.9 (5;1–9.7)	2.9 (2.8–3.2)
HR (95% CI) vs. IPI	0.43 (0.35–0.52)	0.55 (0.45–0.66)	--
HR (95% CI) vs. NIVO	0.78 (0.64–0.96)	--	--



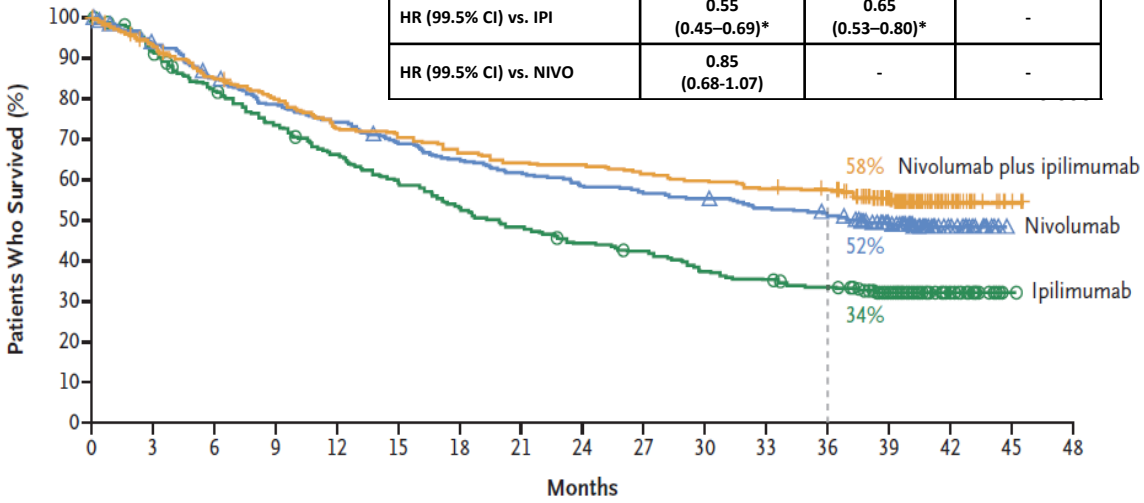
No. at Risk																
Nivolumab plus ipilimumab	314	218	175	155	136	131	124	117	110	104	100	92	75	29	5	0
Nivolumab	316	177	151	131	119	111	105	102	96	87	81	75	61	24	0	0
Ipilimumab	315	136	78	58	46	42	34	32	30	28	26	23	15	8	2	0

Database lock May 24, 2017

Wolchok, NEJM, 2017

CM-67 Overall Survival

	NIVO + IPI (N=314)	NIVO (N=316)	IPI (N=315)
Median OS, months (95% CI)	38.2-NR	37.6 (29.1-NR)	19.9 (16.9-24.6)
HR (99.5% CI) vs. IPI	0.55 (0.45–0.69)*	0.65 (0.53–0.80)*	-
HR (99.5% CI) vs. NIVO	0.85 (0.68-1.07)	-	-

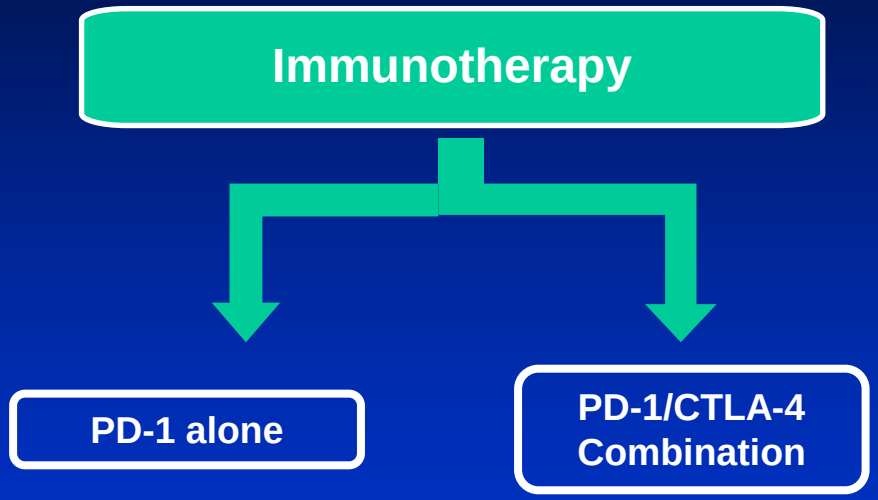


No. at Risk																	
Nivolumab plus ipilimumab	314	292	265	247	226	221	209	200	198	192	186	180	177	131	27	3	0
Nivolumab	316	292	265	244	230	213	201	191	181	175	171	163	156	120	28	0	0
Ipilimumab	315	285	253	227	203	181	163	148	135	128	117	107	100	68	20	2	0

Database lock May 24, 2017

Wolchok, NEJM, 2017

Decision Point….



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]	

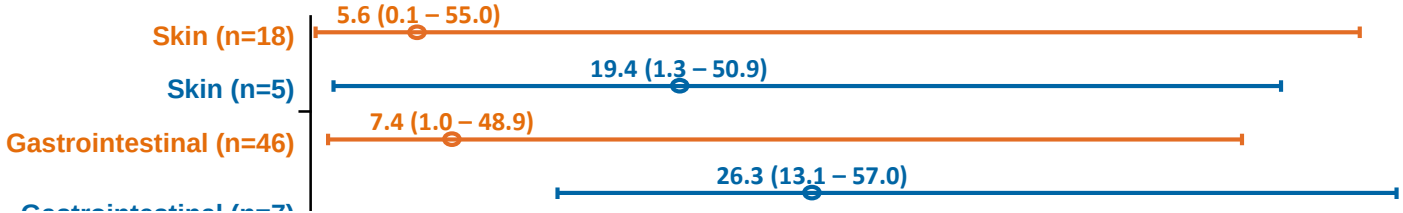
- Most select AEs were managed and resolved within 3-4 weeks (85–100% across organ categories)
- ORR was 70.7% for pts who discontinued NIVO+IPI due to AEs, with median OS not reached

[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.

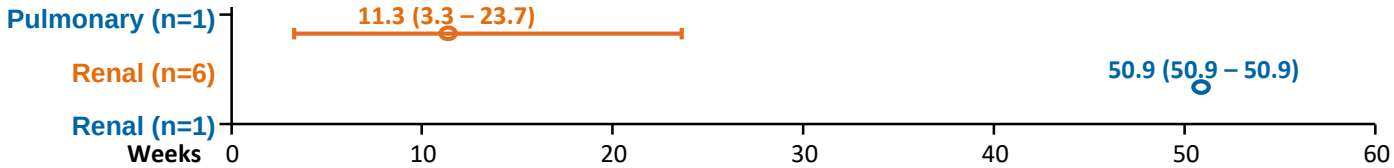
Checkmate 067: Safety

Onset Grade 3–4 Treatment-Related Select AEs



Toxicity Earlier

Longer Time to Resolution



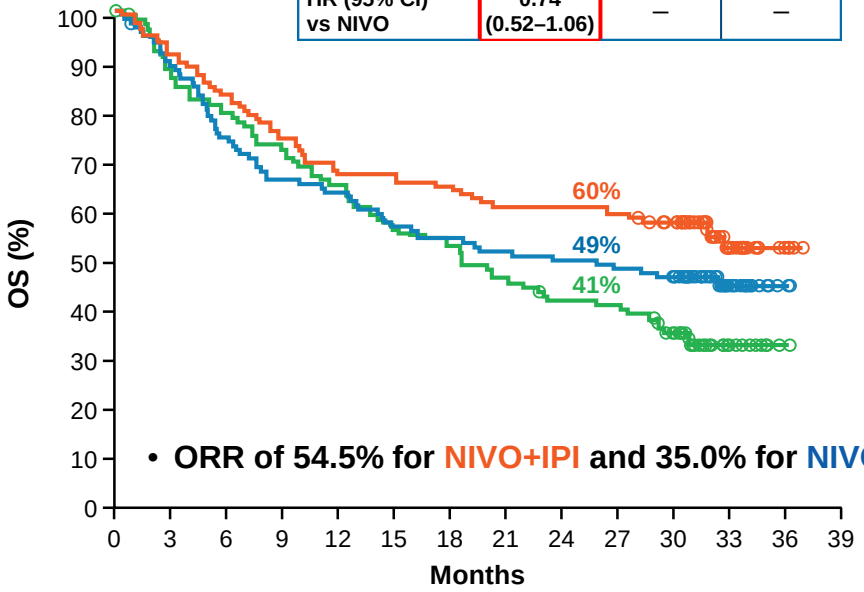
Circles represent medians; bars signify ranges

Larkin J et al ECC 2015

OS by Tumor PDL-1 Expression at a 1% Cutoff

PD-L1 Expression Level <1%

<1% PD-L1	NIVO+IPI	NIVO	IPI
Median OS, mo (95% CI)	NR (26.5–NR)	23.5 (13.0–NR)	18.6 (13.7–23.2)
HR (95% CI) vs NIVO	0.74 (0.52–1.06)	–	–



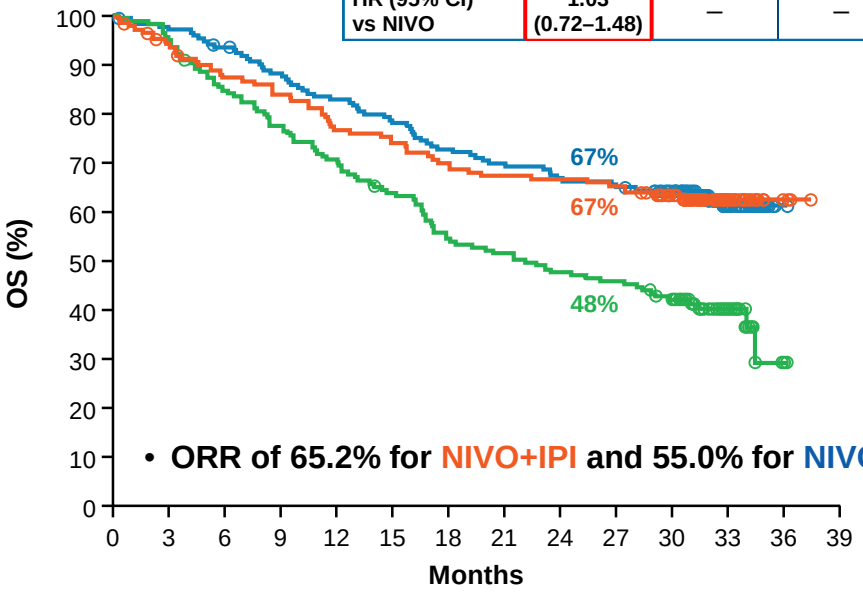
- ORR of 54.5% for NIVO+IPI and 35.0% for NIVO

Patients at risk:

NIVO+IPI	123	113	102	91	82	82	79	74	74	72	66	18	4	0
NIVO	117	103	86	76	73	65	62	59	57	55	50	16	2	0
IPI	113	96	87	79	71	61	57	50	44	43	32	10	1	0

PD-L1 Expression Level ≥1%

≥1% PD-L1	NIVO+IPI	NIVO	IPI
Median OS, mo (95% CI)	NR	NR	22.1 (17.1–29.7)
HR (95% CI) vs NIVO	1.03 (0.72–1.48)	–	–



- ORR of 65.2% for NIVO+IPI and 55.0% for NIVO

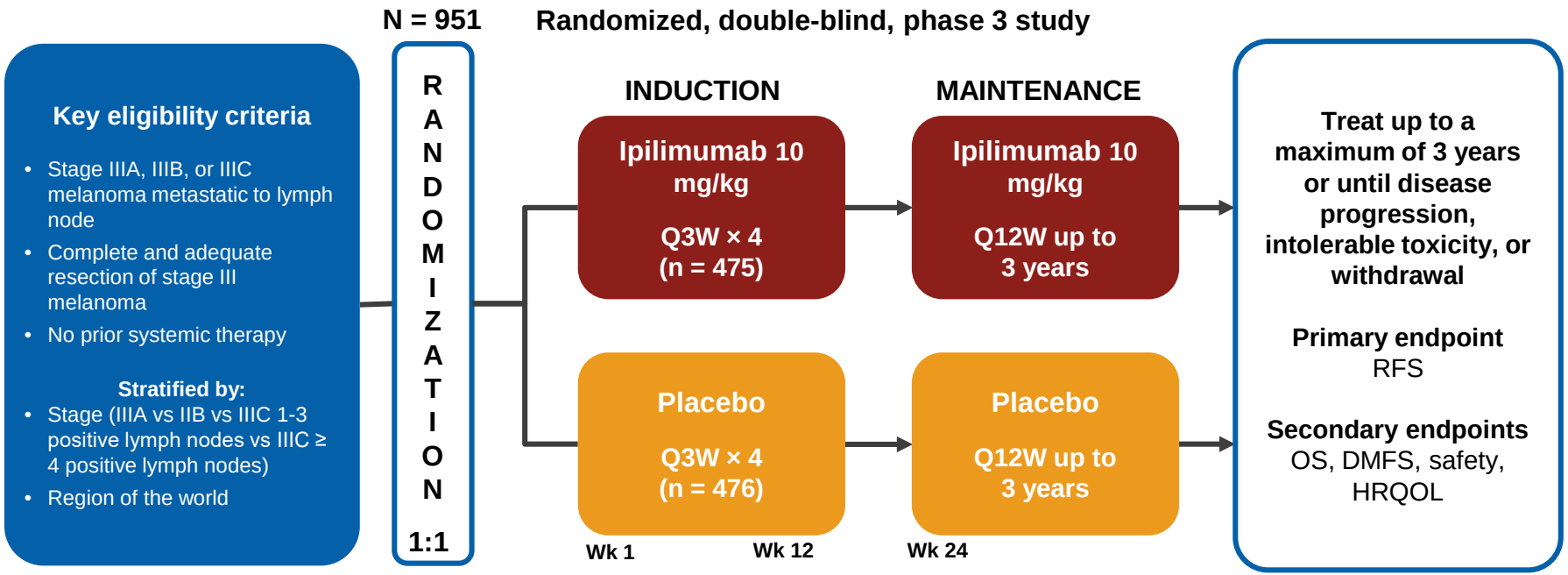
Patients at risk:

NIVO+IPI	155	144	132	127	116	112	105	102	101	99	85	27	3	0
NIVO	171	165	158	148	139	131	122	117	112	109	98	36	1	0
IPI	164	155	138	126	115	102	89	83	77	74	64	21	2	0

Overview

- Metastatic Melanoma
- Adjuvant therapy for High-risk
- Practical Questions
- Future Directions

EORTC 18071: phase 3 study design[1,2]

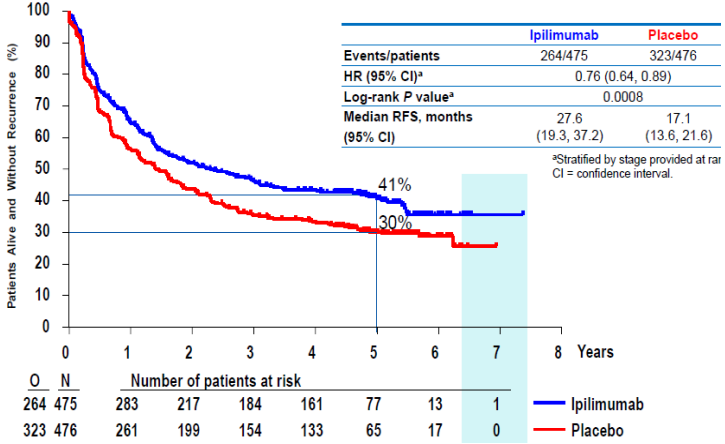


DMFS, distant metastasis-free survival; HRQOL, health-related quality of life; OS, overall survival; PFS, progression-free survival; Q3W, every 3 weeks; Q12W, every 12 weeks; RFS, relapse-free survival.

1. Eggermont AM, et al. *J Clin Oncol* 2014;32:5s(suppl; abstr LBA9008); 2. Eggermont A, et al. ESMO. 2016;[abstr LBA2_PR].

EORTC 18071
Ipilimumab vs Placebo

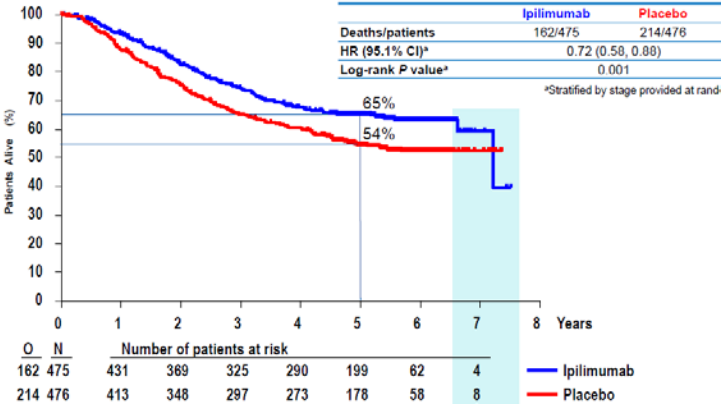
RFS (per IRC)



	Ipilimumab	Placebo
Events/patients	264/475	323/476
HR (95% CI)[a]	0.76 (0.64, 0.89)	
Log-rank *P* value[a]	0.0008	
Median RFS, months (95% CI)	27.6 (19.3, 37.2)	17.1 (13.6, 21.6)

[a]Stratified by stage provided at rar
CI = confidence interval.

OS



	Ipilimumab	Placebo
Deaths/patients	162/475	214/476
HR (95.1% CI)[a]	0.72 (0.58, 0.88)	
Log-rank *P* value[a]	0.001	

[a]Stratified by stage provided at rand

Safety Summary

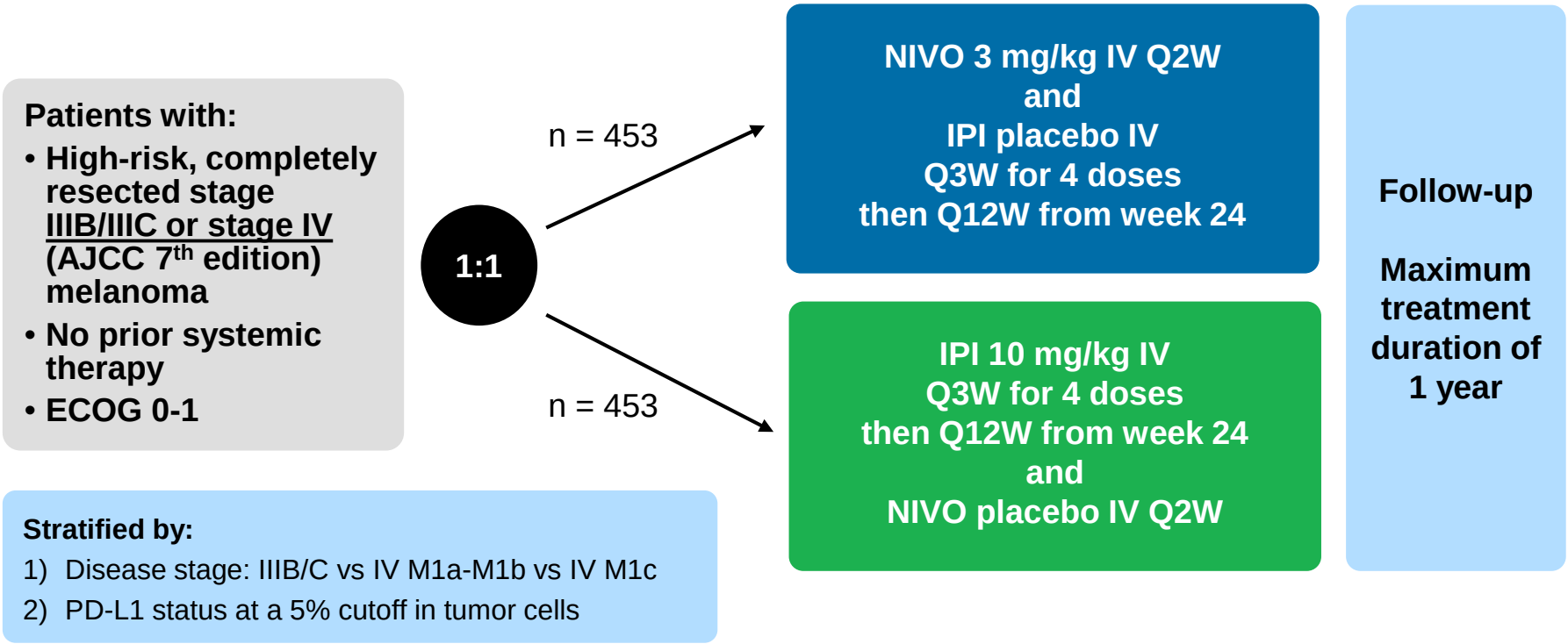
	Ipilimumab (n = 471)	
	Any Grade	Grade 3/4
Any AE, %	98.7	54.1
Treatment-related AE, %	94.1	45.4
Treatment-related AE leading to discontinuation, %	48.0	32.9
Any immune-related AE, %	90.4	41.6

Deaths due to drug-related AEs

- 5 patients (1.1%) in the ipilimumab group
  - 3 patients with colitis (2 with gastrointestinal perforations)
  - 1 patient with myocarditis
  - 1 patient had multiorgan failure with Guillain-Barré

Eggermont et al. NEJM 2016

CheckMate 238: Study Design



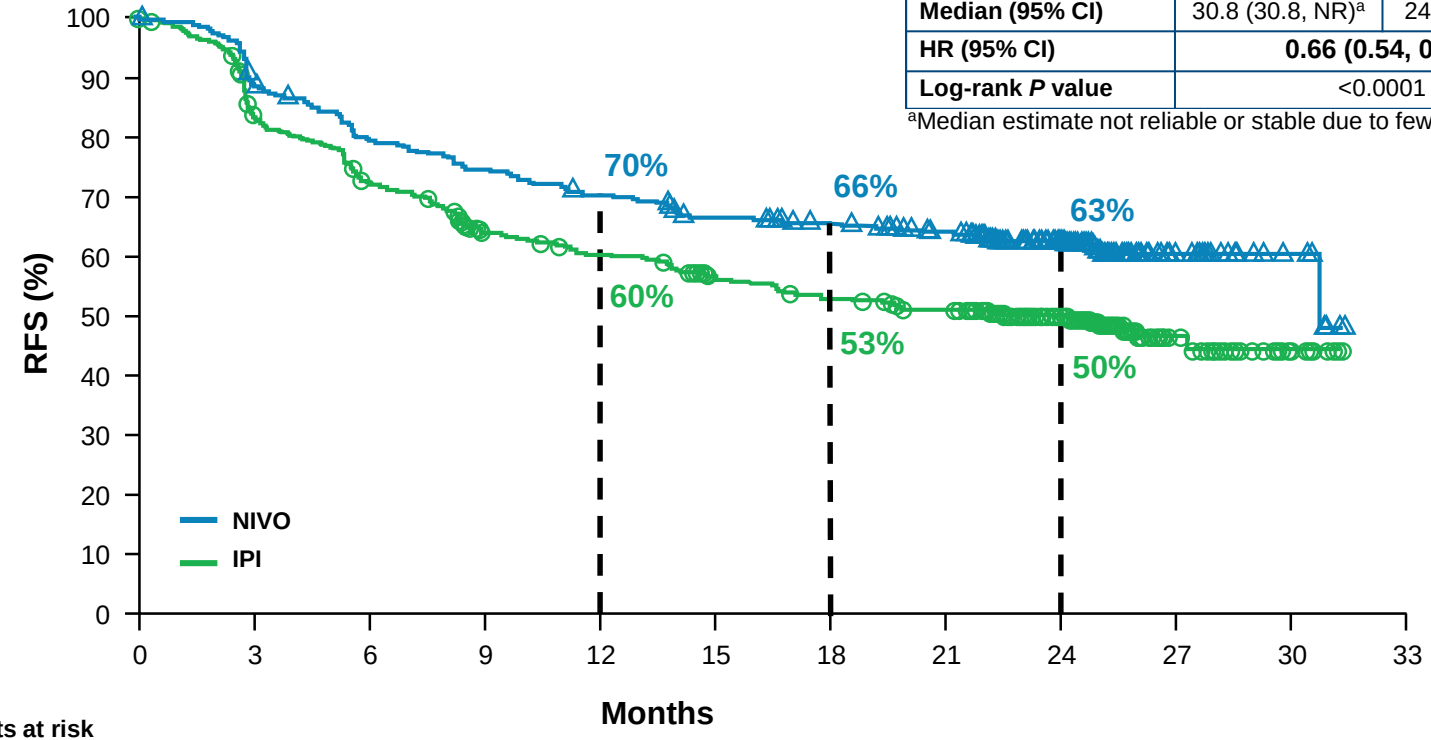
Enrollment period: March 30, 2015 to November 30, 2015

Jeffrey Weber, Oral Presentation ASCO 2018

Primary Endpoint: RFS in All Patients

	NIVO	IPI
Events/patients	171/453	221/453
Median (95% CI)	30.8 (30.8, NR)[a]	24.1 (16.6, NR)
HR (95% CI)	**0.66 (0.54, 0.81)**	
Log-rank *P* value	<0.0001	

[a]Median estimate not reliable or stable due to few patients at risk.



Number of patients at risk

NIVO	453	394	353	331	311	291	280	264	205	28	7	0
IPI	453	363	314	270	251	230	216	204	149	23	5	0

Jeffrey Weber, Oral Presentation ASCO 2018

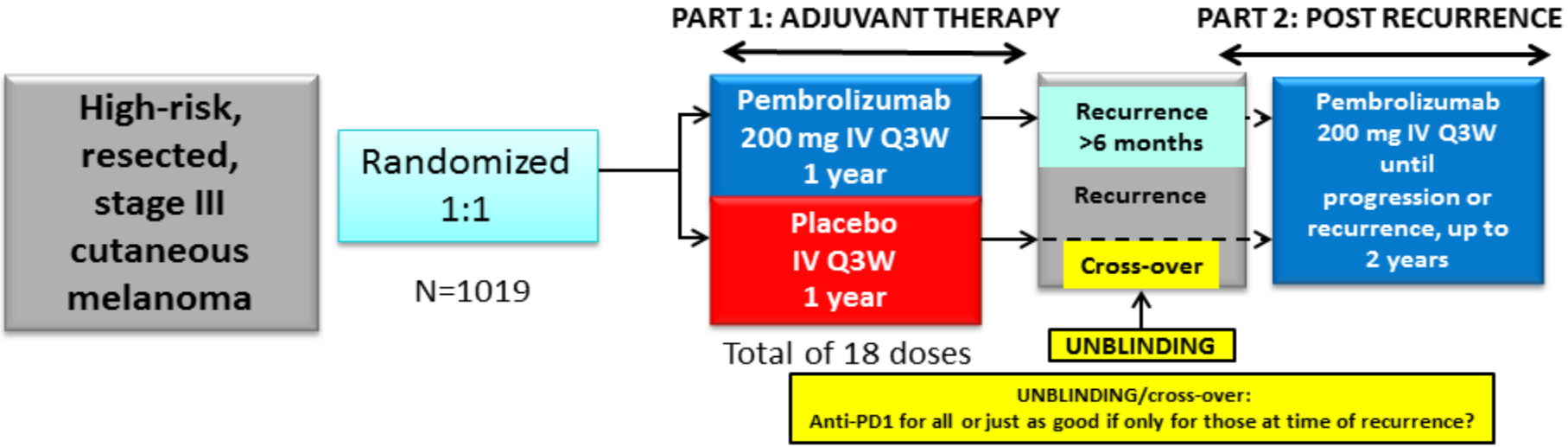
Safety Summary

AE, n (%)	NIVO (n = 452)		IPI (n = 453)	
	Any grade	Grade 3/4	Any grade	Grade 3/4
Any AE	438 (97)	115 (25)	446 (98)	250 (55)
Treatment-related AE	385 (85)	65 (14)	434 (96)	208 (46)
Any AE leading to discontinuation	44 (10)	21 (5)	193 (43)	140 (31)
Treatment-related AE leading to discontinuation	35 (8)	16 (4)	189 (42)	136 (30)

- There were no treatment-related deaths in the NIVO group
- There were 2 (0.4%) treatment-related deaths in the IPI group (marrow aplasia and colitis), both >100 days after the last dose

Weber, J et al ESMO 2017

EORTC 1325/KEYNOTE-54: Study Design



Stratification factors:

- ✓ **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:

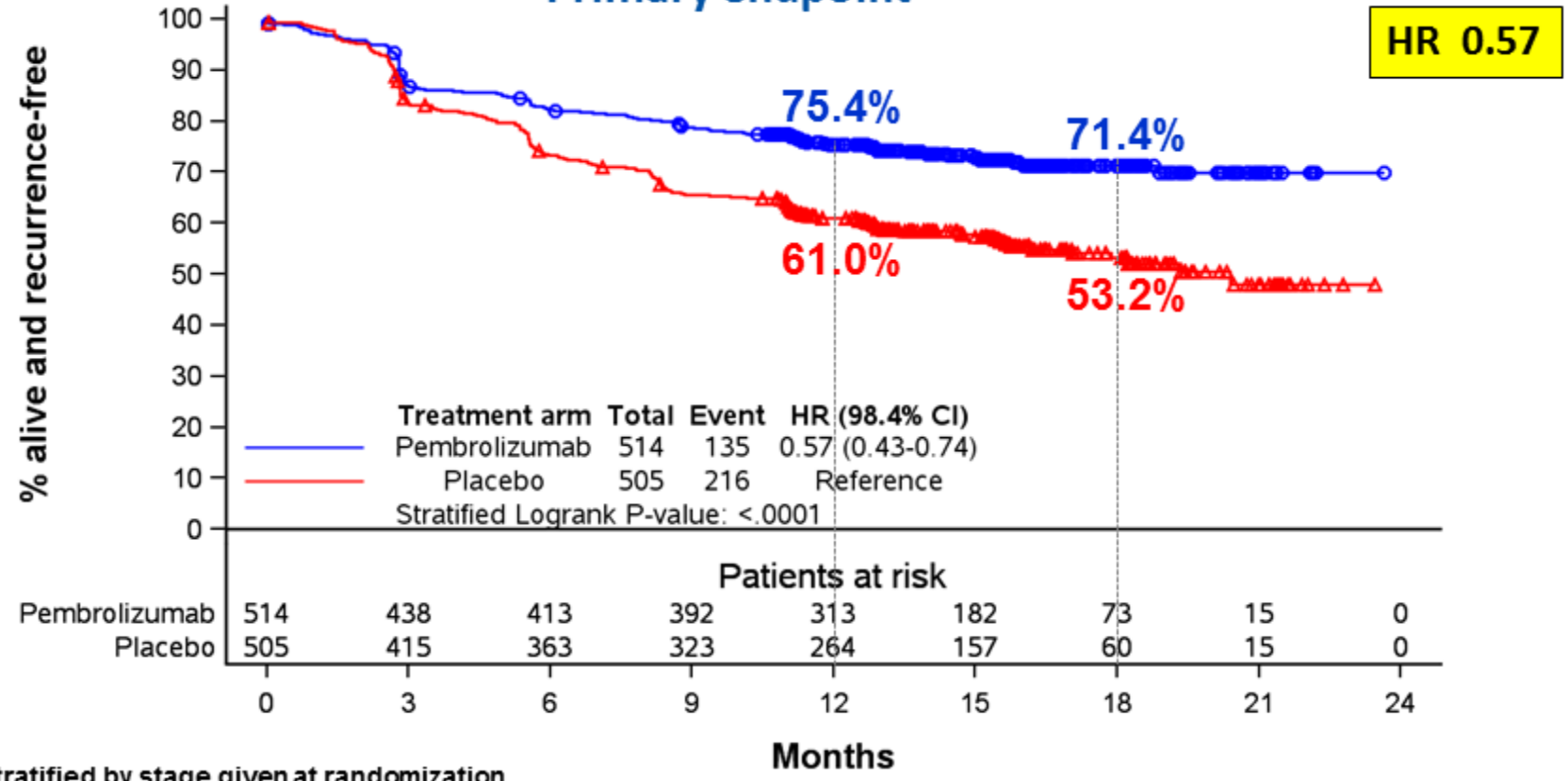
- **RFS (per investigator) in overall population,** and **RFS in patients with PD-L1-positive tumors**

Secondary Endpoints:

- **DMFS and OS** in all patients, and in patients with PD-L1-positive tumors; **Safety, Health-related quality of life**

Recurrence-Free Survival in the ITT Population

Primary endpoint



*Stratified by stage given at randomization

EORTC

The future of cancer therapy

Interferon

Overview

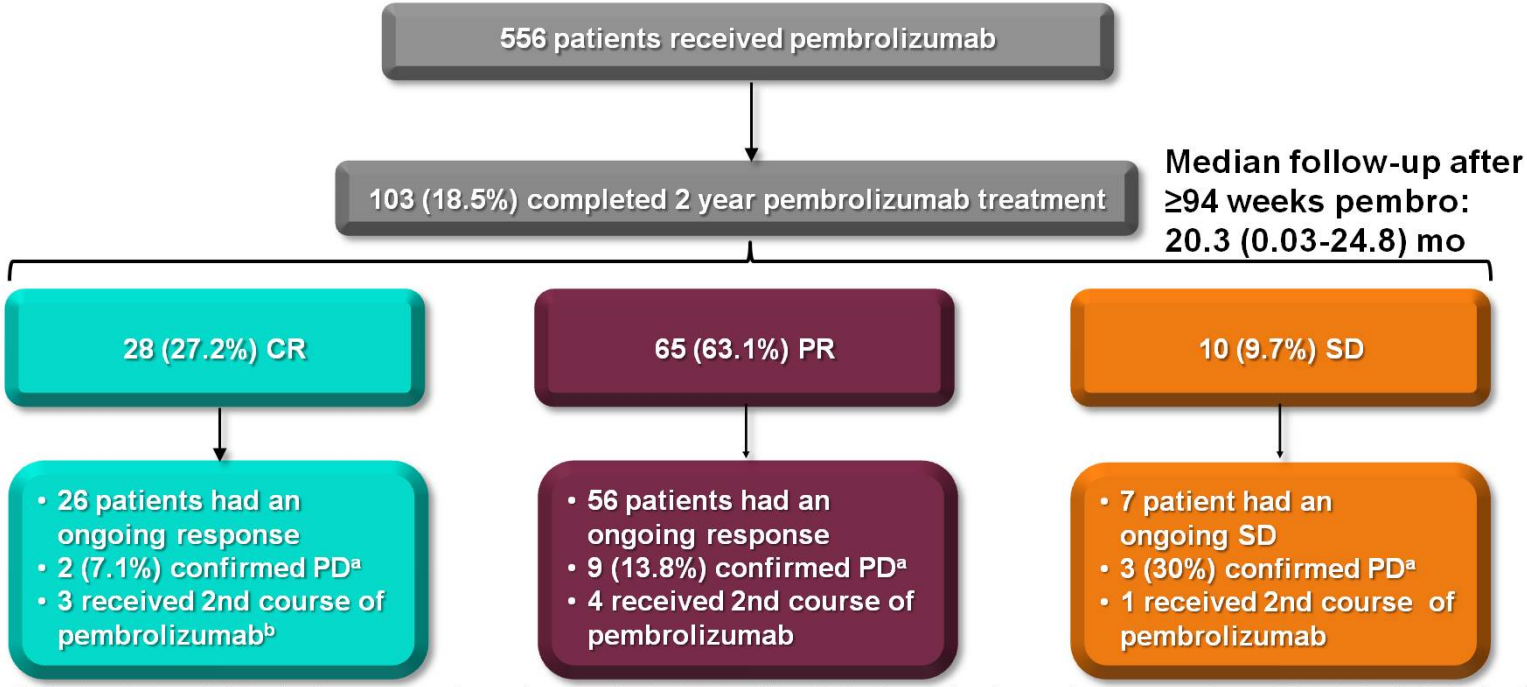
- Metastatic Melanoma
- Adjuvant therapy for High-risk
- Practical Questions
- Future Directions

Practical Questions

- What is the correct duration?
  - Are responses durable after stopping treatment?

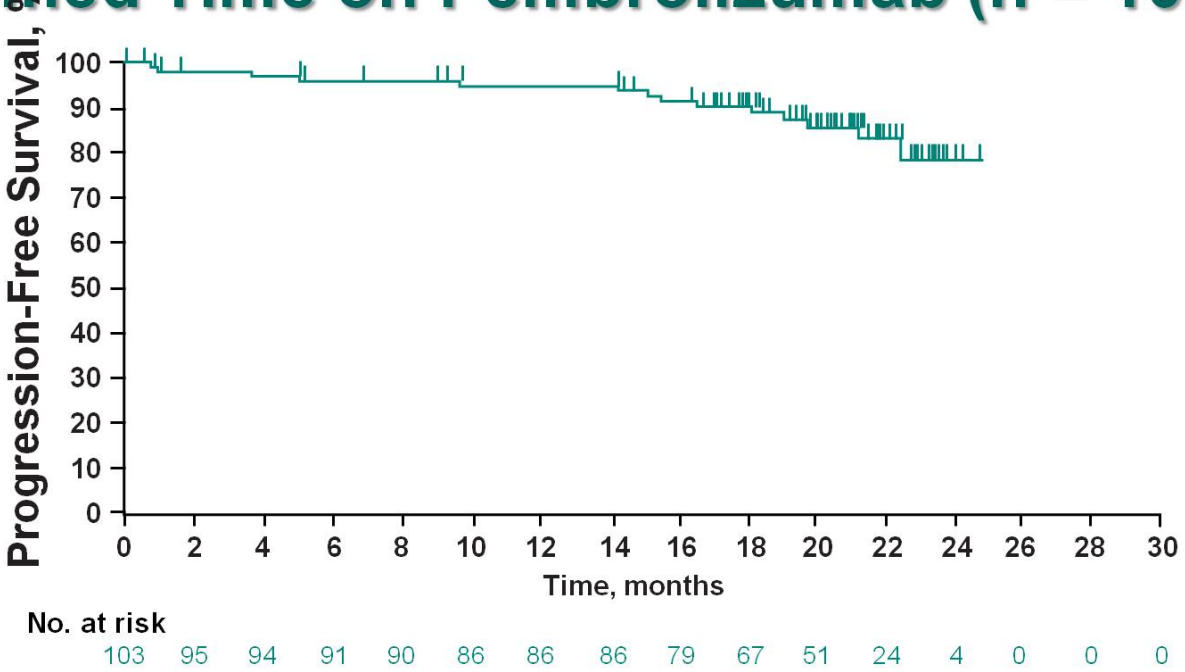
- What is the correct first choice for BRAF+ patients?

Disposition of Patients Completing ≥94 Weeks of Pembrolizumab Treatment



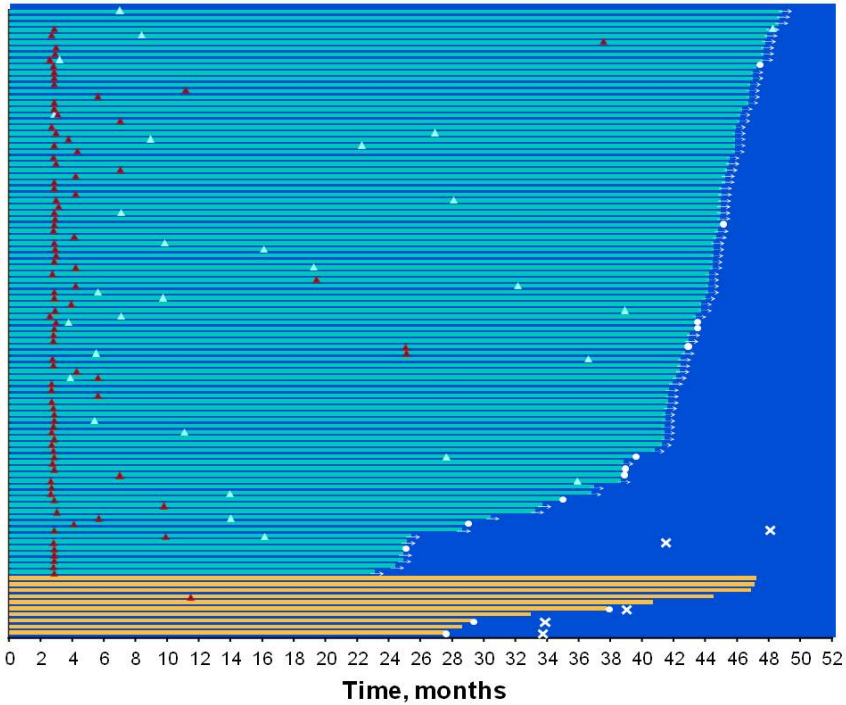
[a]Confirmed PD by investigator per irRC (confirmatory scan or no subsequent scan or not evaluable). An additional 5 pts with unconfirmed progressive disease were observed. [b]Includes 1 patient who discontinued early with CR and then progressed. Data cutoff: Dec 4, 2017.

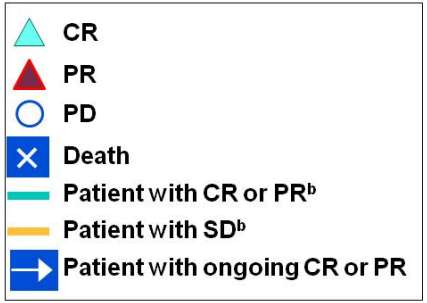
PFS[a] in Patients Who Completed Protocol-Specified Time on Pembrolizumab (n = 103)



[a]Per immune-related response criteria by investigator review; time is measured from last dose of pembrolizumab. Data cutoff: Dec 4, 2017.

Duration of Response in Patients With ≥94 Weeks of Pembrolizumab[a] (n = 103)





- 89[c] (86%) patients who completed 2 years on pembrolizumab were progression-free at 20 months after end of therapy

[a]With SD, CR, or PR. [b]Length of each bar represents time to the last scan. [c]An additional 5 patients have unconfirmed progression. Data cutoff: Dec 4, 2017.

Practical Questions

- What is the correct duration?
  - Are responses durable after stopping treatment?

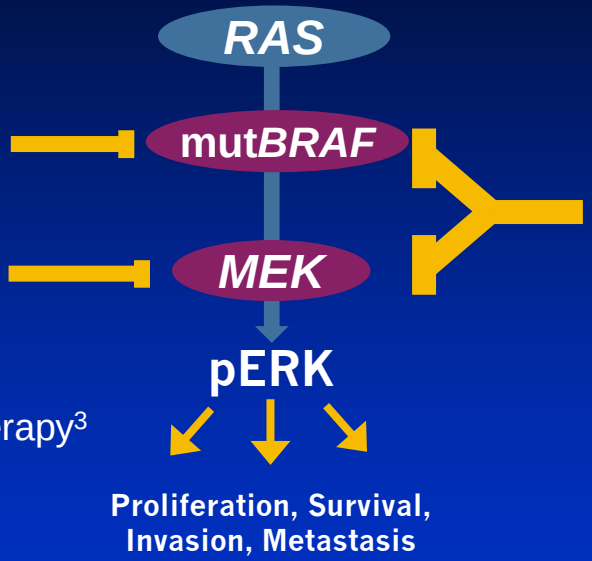
- What is the correct first choice for BRAF+ patients?

MAPK Pathway Targeted Therapy

BRAFi (dabrafenib)
PFS HR, 0.37 vs DTIC[1]
Hyperproliferative skin AEs

BRAFi (vemurafenib)
PFS HR, 0.38 vs DTIC[2]
Hyperproliferative skin AEs

MEKi (trametinib)
PFS HR, 0.45 vs chemotherapy[3]



BRAFi + MEKi ph III studies

Dabrafenib + trametinib (D + T)
PFS HR, 0.67 vs dabrafenib[4]
OS HR, 0.71 vs dabrafenib[4]

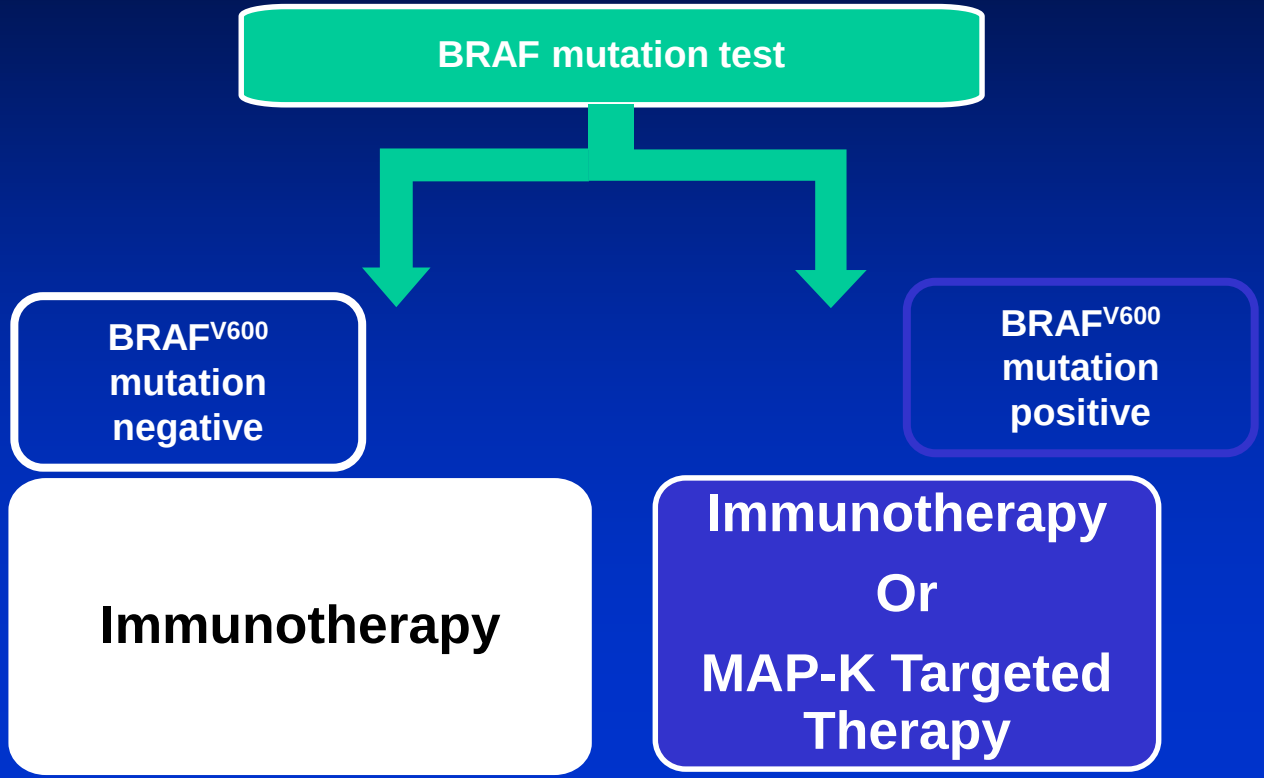
PFS HR, 0.56 vs vemurafenib[5]
OS HR, 0.69 vs vemurafenib[5]

Vemurafenib + cobimetinib
PFS HR, 0.58 vs vemurafenib[6]
OS HR, 0.70 vs vemurafenib[6]

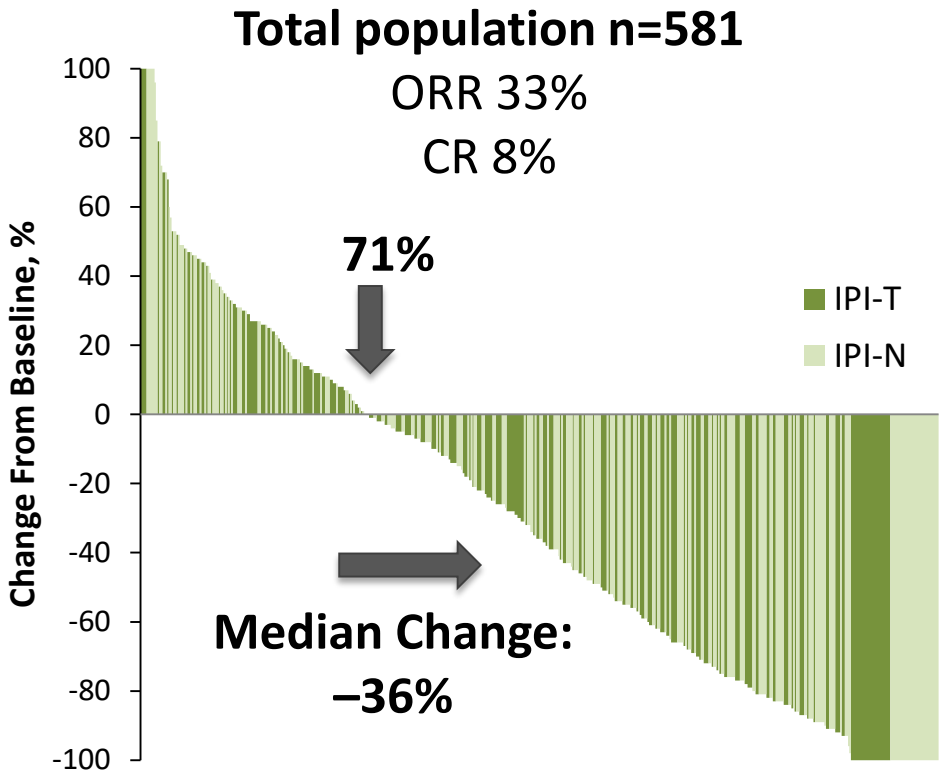
Decreased hyperproliferative skin AEs[4,5,6]

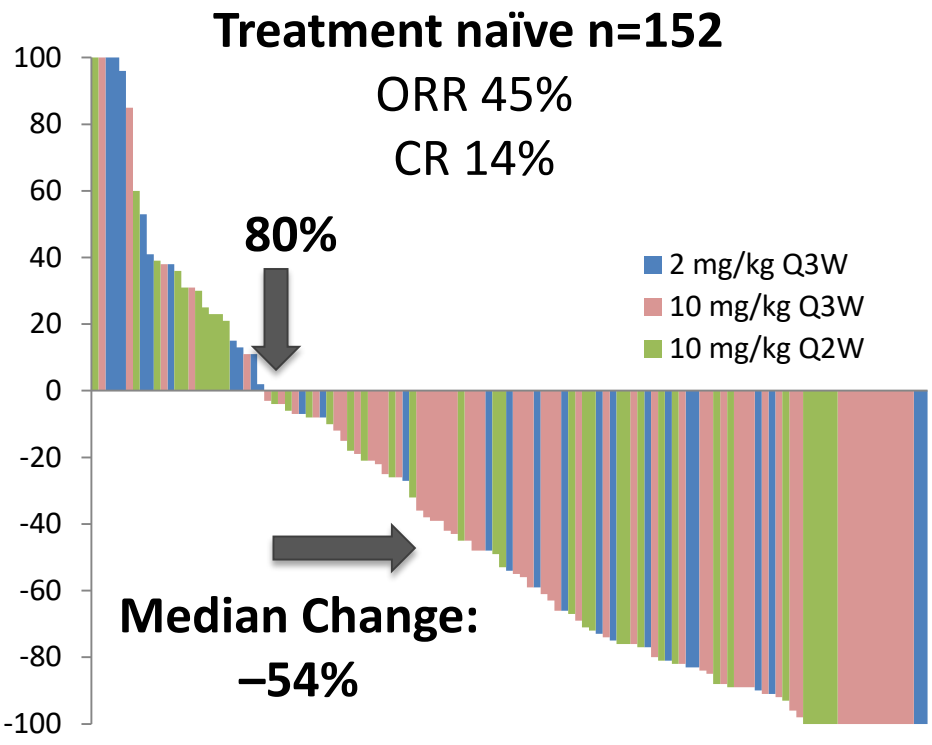
1. Hauschild A, et al. *Lancet.* 2012;380(9839):358-365.
2. McArthur GA, et al. *Lancet Oncol.* 2014;15(3):323-332.
3. Flaherty KT, et al. *N Engl J Med.* 2012;367(2):107-114.
4. Long GV, et al. *Lancet.* 2015;386(9992):444-451.
5. Robert C, et al. *N Engl J Med.* 2015;372(1):30-39.
6. Atkinson V, et al. Presented at:Society for Melanoma Research 2015 Congress.

Decision Point….



KEYNOTE-001: Phase I
RECIST Response (v1.1)





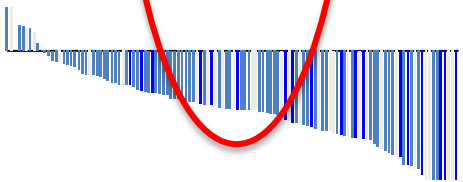
Analysis cut-off date: October 18, 2014; Median follow up 21 mo

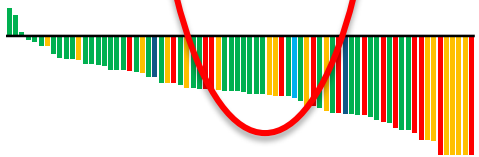
Daud A et al ASCO 2015

BRAF Inhibitors

Second line

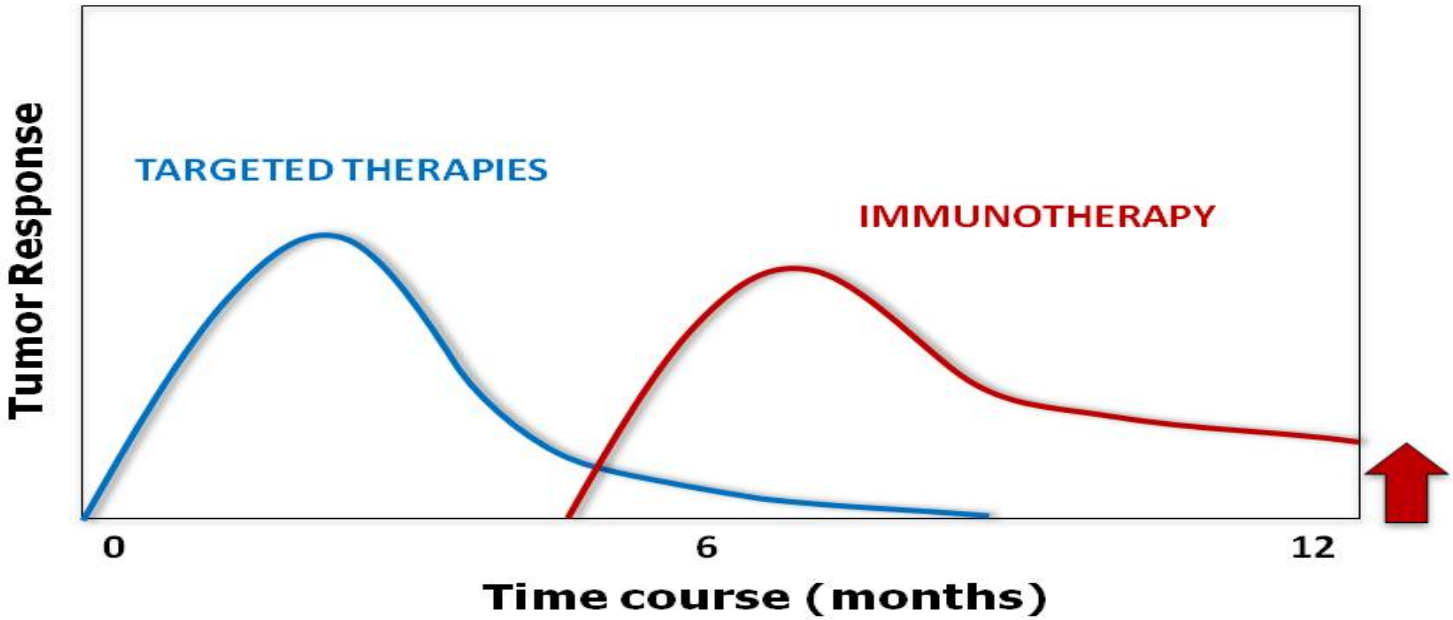
	Vemurafenib[1]			Dabrafenib[2]		
Phase	1	2	3	1	2	3
RR	56%	57%	57%	56%	59%	59%
PFS		6.7	6.9	5.5	6.3	6.9
OS	13.8	15.9	13.6		13.1	18.2





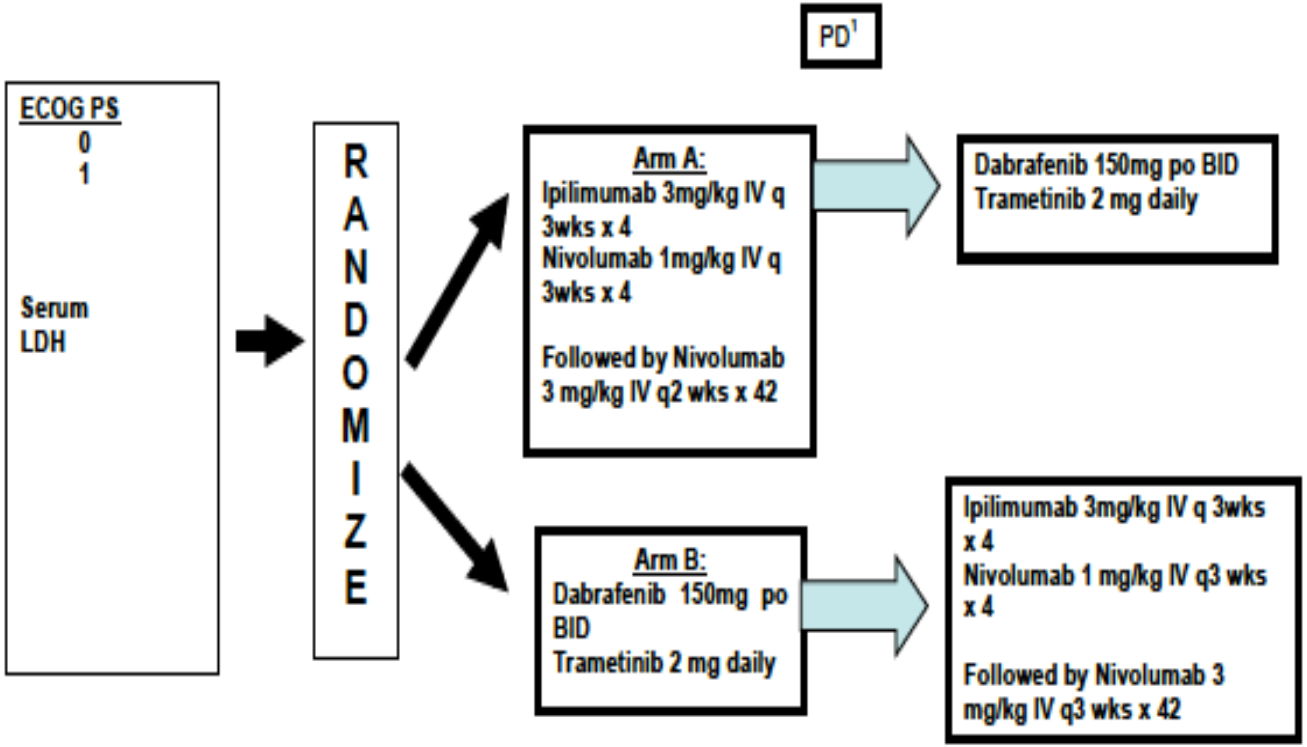
1. Chapman PB, *et al. N Engl J Med* 2011;364:2507–2516 (updated Chapman *et al.* ASCO 2012); Sosman JA, *et al. N Engl J Med* 2012;366:707–714;
2. Hauschild A, *et al. Lancet* 2012;380:358–365 (updated Hauschild *et al.* ASCO 2013); Ascierto PA, *et al. J Clin Oncol* 2013; 31:3205–3211.

Antitumoral response: Targeted therapies vs. Immunotherapies (CTLA-4 antibodies)



Presented By Axel Hauschild at 2014 ASCO Annual Meeting

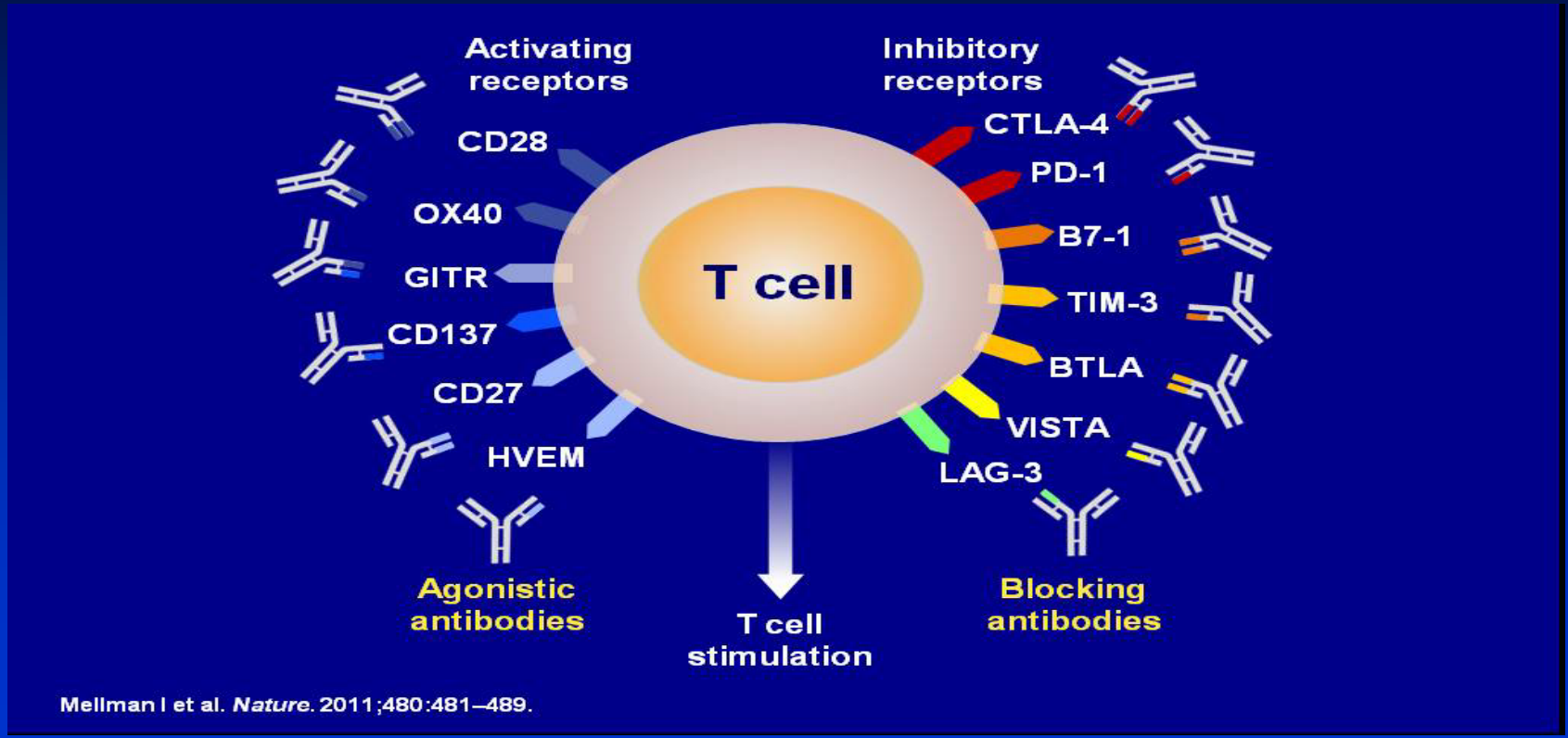
EA6134


PD[1]
ECOG PS
0
1
Serum
LDH
RANDOMIZE
Arm A:
Ipilimumab 3mg/kg IV q 3wks x 4
Nivolumab 1mg/kg IV q 3wks x 4
Followed by Nivolumab 3 mg/kg IV q2 wks x 42
Dabrafenib 150mg po BID
Trametinib 2 mg daily
Arm B:
Dabrafenib 150mg po BID
Trametinib 2 mg daily
Ipilimumab 3mg/kg IV q 3wks x 4
Nivolumab 1 mg/kg IV q3 wks x 4
Followed by Nivolumab 3 mg/kg IV q3 wks x 42

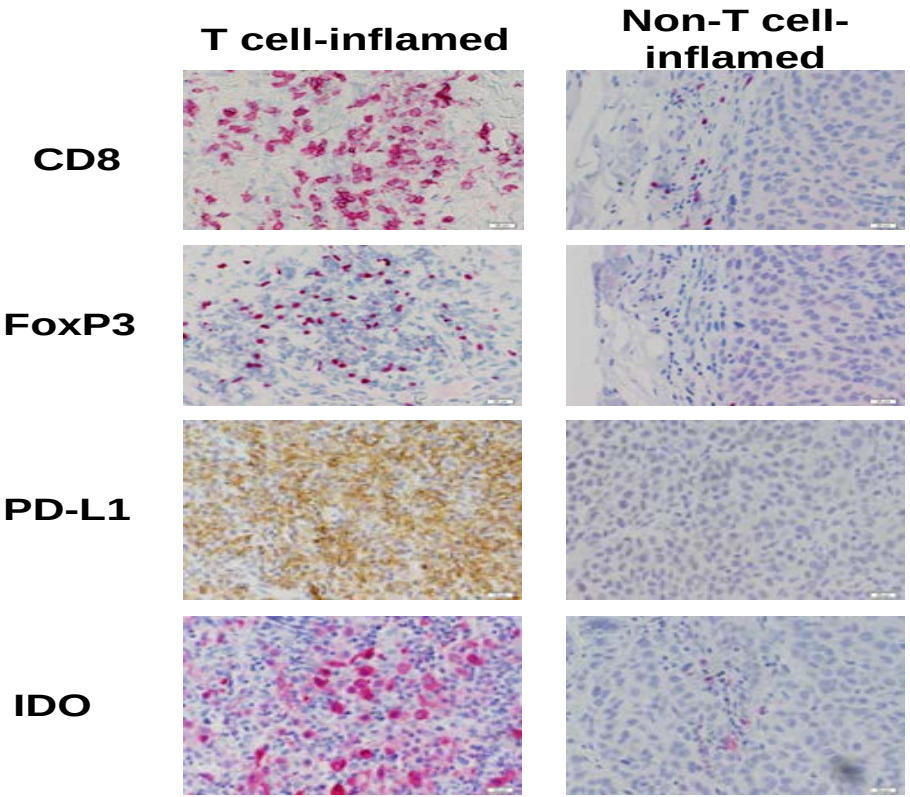
Overview

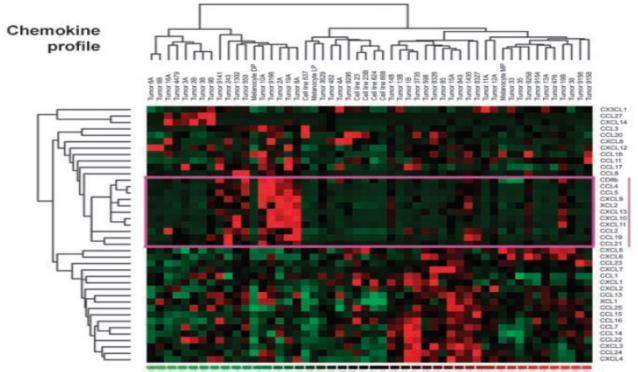
- Metastatic Melanoma
- Adjuvant therapy for High-risk
- Practical Questions
- Future Directions

T-Cell Immune Checkpoints

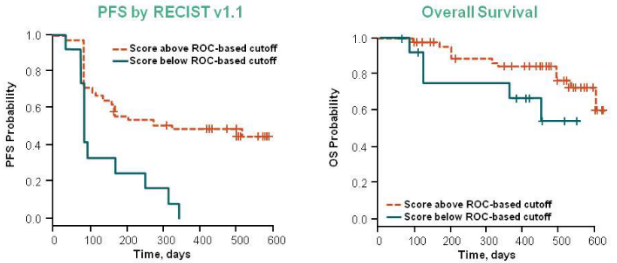


The T Cell-Inflamed Tumor Microenvironment is Characterized by Expression of Immune-Inhibitory Pathways and Predicts Outcomes to Immunotherapy





PFS and OS in Patients With Melanoma and IFNγ Signature Score Above and Below the Cutoff



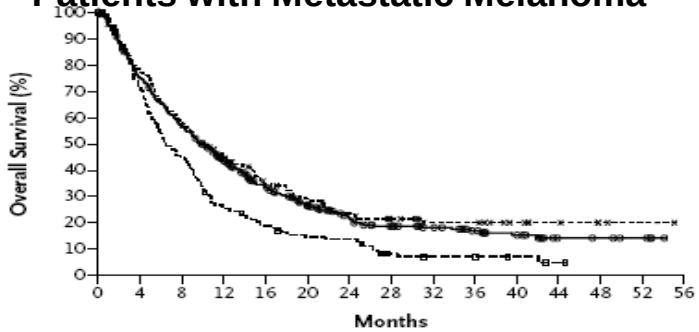
Spranger *et al.*, Science Trans. Med. 2013

Harlin *et al*. Clin Can Res 2009

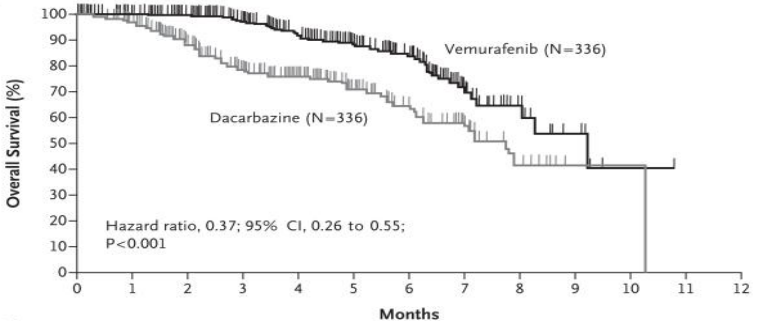
Ribas *et al*. J Clin Oncol 33, 2015 (suppl; abstr 3001)

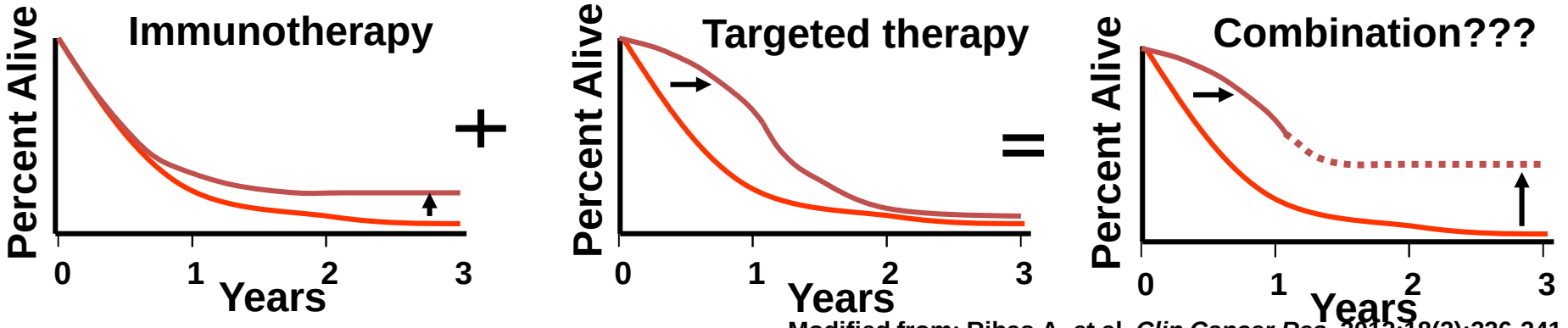
Combining Immunotherapy and Targeted Therapy for Melanoma?

Improved Survival With Ipilimumab in Patients with Metastatic Melanoma[1]



Improved Survival With Vemurafenib in Melanoma With BRAF V600E Mutation[2]





Modified from: Ribas A, et al. *Clin Cancer Res*. 2012;18(2):336-341.

1. Hodi FS, et al. *N Engl J Med*. 2010;363(8):711-723. 2. Chapman PB, et al. *N Engl J Med*. 2011;364(26):2507-2516.

Targeted-Immuno Triplets: BRAF + MEK + PD1/L1

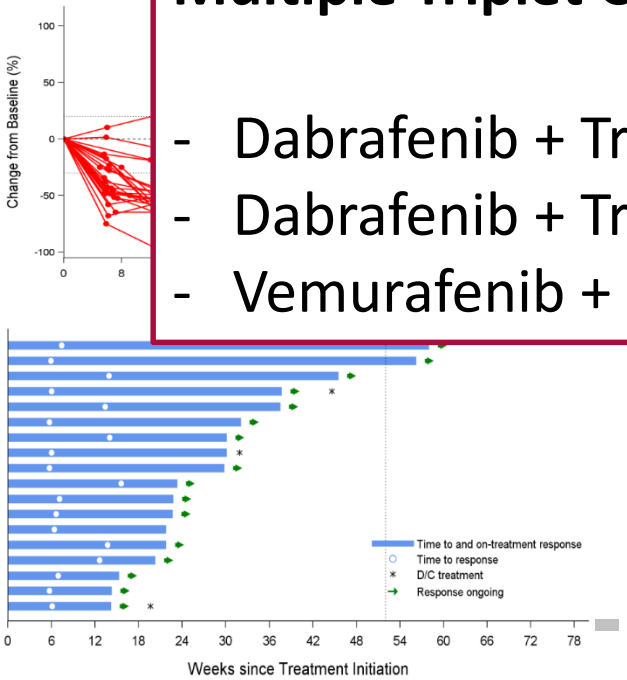
Dabrafenib+Trametinib +Durvalumab

Dabrafenib+Trametinib +Pembrolizumab

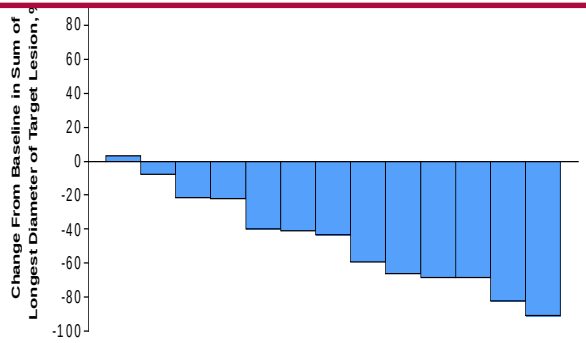
Vemurafenib+Cobimetinib +Atezolizumab

Multiple Triplet Combinations Launching Into Phase III:

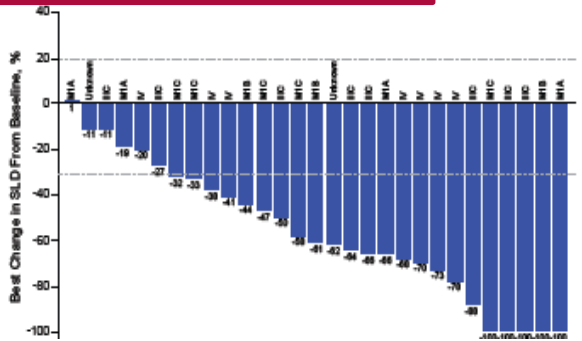
- Dabrafenib + Trametinib + Pembrolizumab
- Dabrafenib + Trametinib + PDR-001
- Vemurafenib + Cobimetinib + Atezolizumab



Ribas *et al*. ASCO 2015



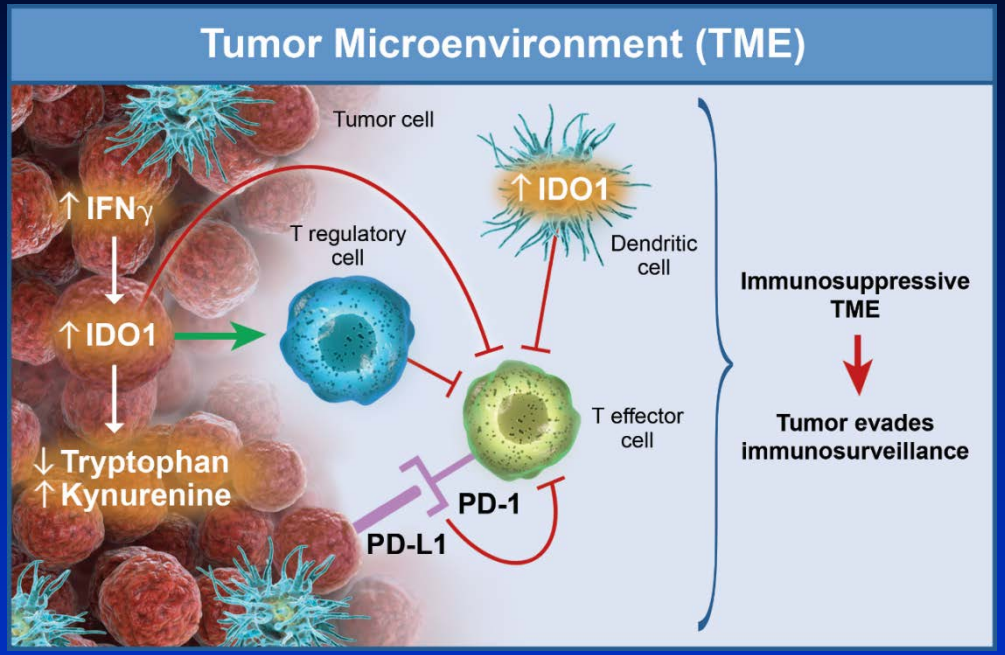
Ribas *et al*. ASCO 2016



Hwu *et al*. ECCO 2016

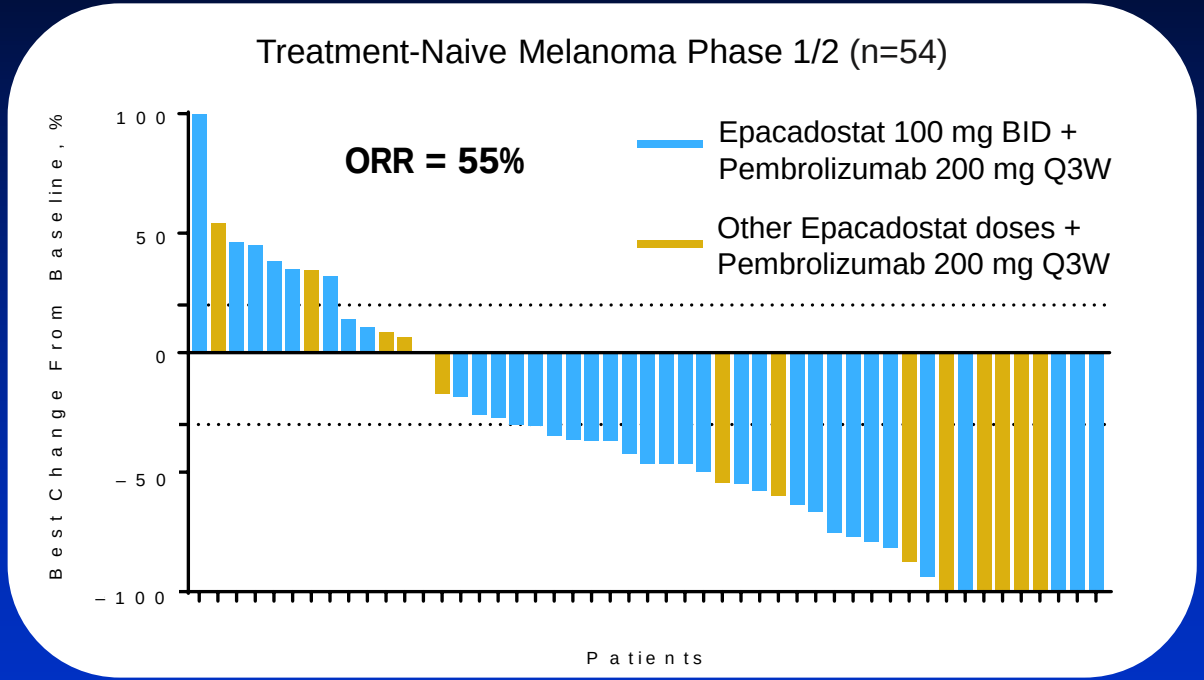
IDO Inhibitors: Background

- Upregulation of IDO1 is a potential mechanism to evade immunosurveillance
  - ↓ Tryptophan ↑ Kynurenine
  - ↓ T_{eff} and NK cells
  - ↑ T_{reg} cells, MDSCs, TAMs
- Epacadostat: IDO1 enzyme inhibitor
- Pembrolizumab: anti-PD-1 humanized antibody



IDO1, indoleamine 2,3 dioxygenase 1; IFNγ, interferon gamma; MDSC, myeloid-derived suppressor cell; NK, natural killer; PD-1, programmed death 1; PD-L1, programmed death ligand-1; TAM, tumor-associated macrophage; T_{eff}, effector T cell; T_{reg}, regulatory T cell.

Phase I/II Combination Epacadostat + Pembrolizumab



ECHO-202 / KEYNOTE-037

- Phase 1: Epacadostat 50, 100, or 300 mg PO BID + Pembrolizumab 200 mg IV Q3W
- MTD of epacadostat not reached
- Phase 2: Epacadostat 100 mg PO BID
- Phase 1/2 efficacy in treatment-naive melanoma:
  - ORR = 55%
  - Median PFS = 22.8 mo (12.4 mo all melanoma)

BID, twice daily; MTD, maximally tolerated dose; PD-L1, programmed death ligand-1; Q3W, every 3 weeks.
Hamid O, et al. *Ann Oncol*. 2017;28(suppl 5):1214O.

Phase III Randomized Placebo Controlled Trial

Key Eligibility Criteria

- Unresectable stage III or IV melanoma, advanced/metastatic disease
  - Patients with *BRAF* mutation could have received prior BRAF/MEK therapy
  - Prior anti-CTLA-4 or interferon in adjuvant setting permitted
- ECOG performance status 0–1
- No active CNS metastases

Stratification

- PD-L1 status (positive[a] vs negative)
- *BRAF* mutation status
  - Wild type
  - Mutant with prior *BRAF*-directed therapy
  - Mutant without prior *BRAF*-directed therapy

N=706
R 1:1

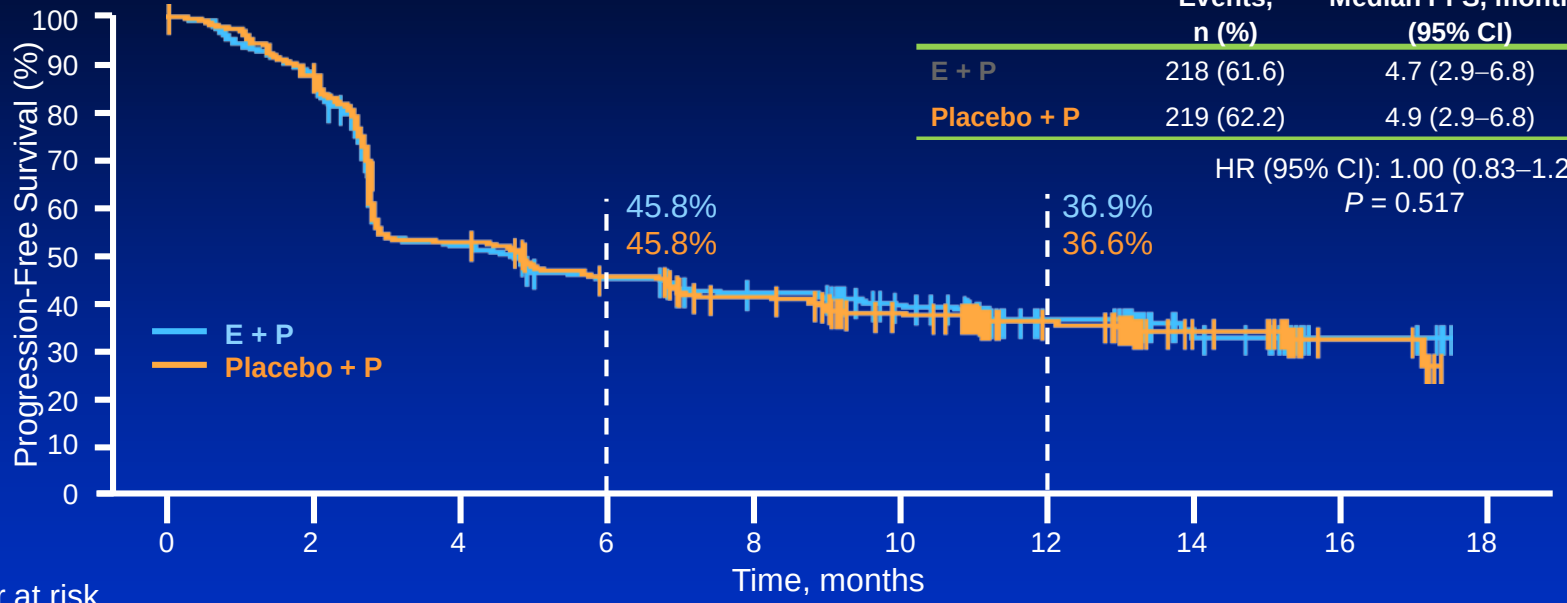
Epacadostat 100 mg PO BID
+
Pembrolizumab 200 mg IV Q3W
n=354

Placebo
+
Pembrolizumab 200 mg IV Q3W
n=352

- **Primary endpoints:** PFS (RECIST v1.1) and OS
- **Secondary endpoints:** ORR (RECIST v1.1), DOR, safety

BID, twice daily; DOR, duration of response; ECOG, Eastern Cooperative Oncology Group; ORR, objective response rate; OS, overall survival; PD-L1, programmed death-ligand 1; PFS, progression-free survival; Q3W, every 3 weeks; RECIST, Response Evaluation Criteria In Solid Tumors.
[a]≥1% staining in tumor and adjacent immune cells as assessed by IHC (22C3 antibody).

Progression-Free Survival



	Events, n (%)	Median PFS, months (95% CI)
E + P	218 (61.6)	4.7 (2.9–6.8)
Placebo + P	219 (62.2)	4.9 (2.9–6.8)

HR (95% CI): 1.00 (0.83–1.21)
P = 0.517

Number at risk

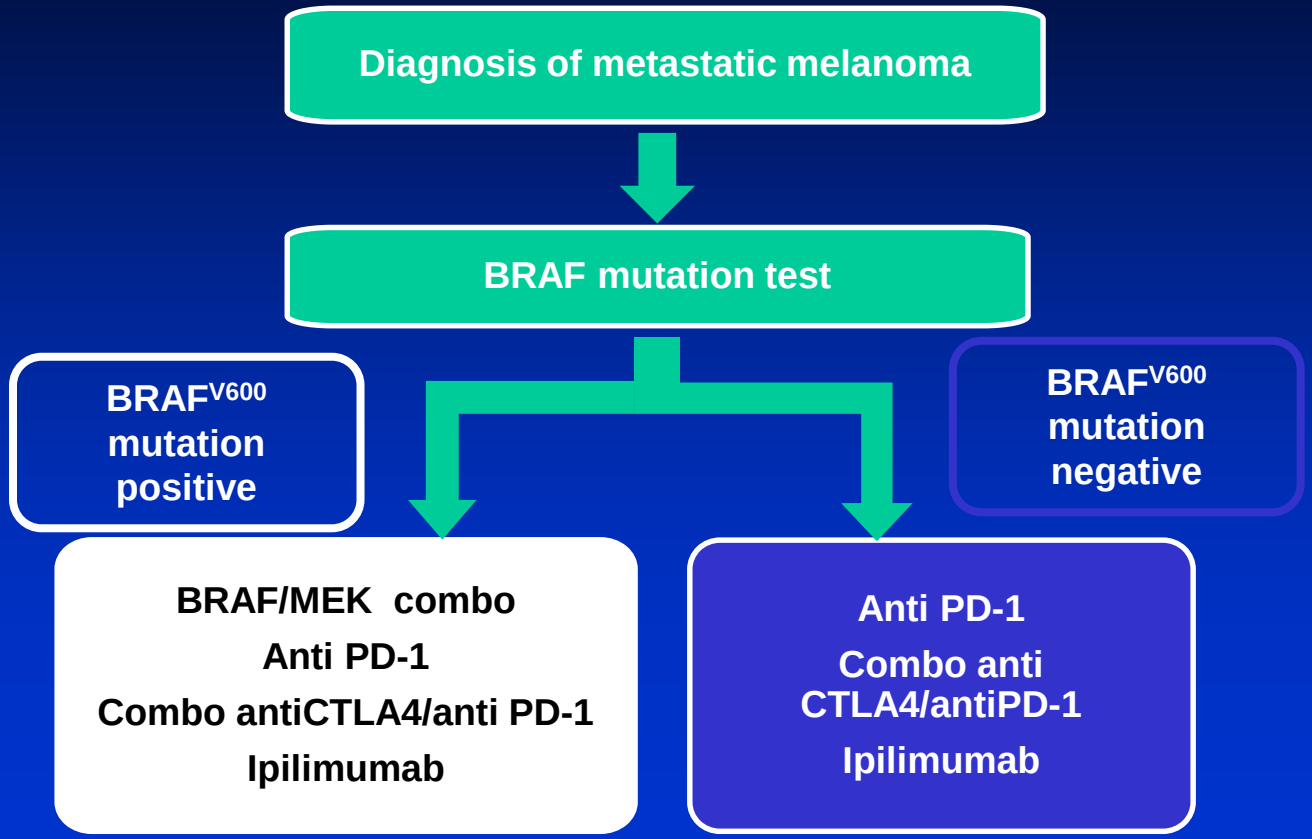
E + P	354	309	181	155	137	114	57	25	5	0
Placebo + P	352	304	181	151	132	109	65	28	7	0

BICR, blinded independent central review; CI, confidence interval; E, epacadostat; HR, hazard ratio; P, pembrolizumab; PFS, progression-free survival; RECIST, Response Evaluation Criteria In Solid Tumors.
PFS defined as time from randomization to disease progression or death, whichever occurred first.

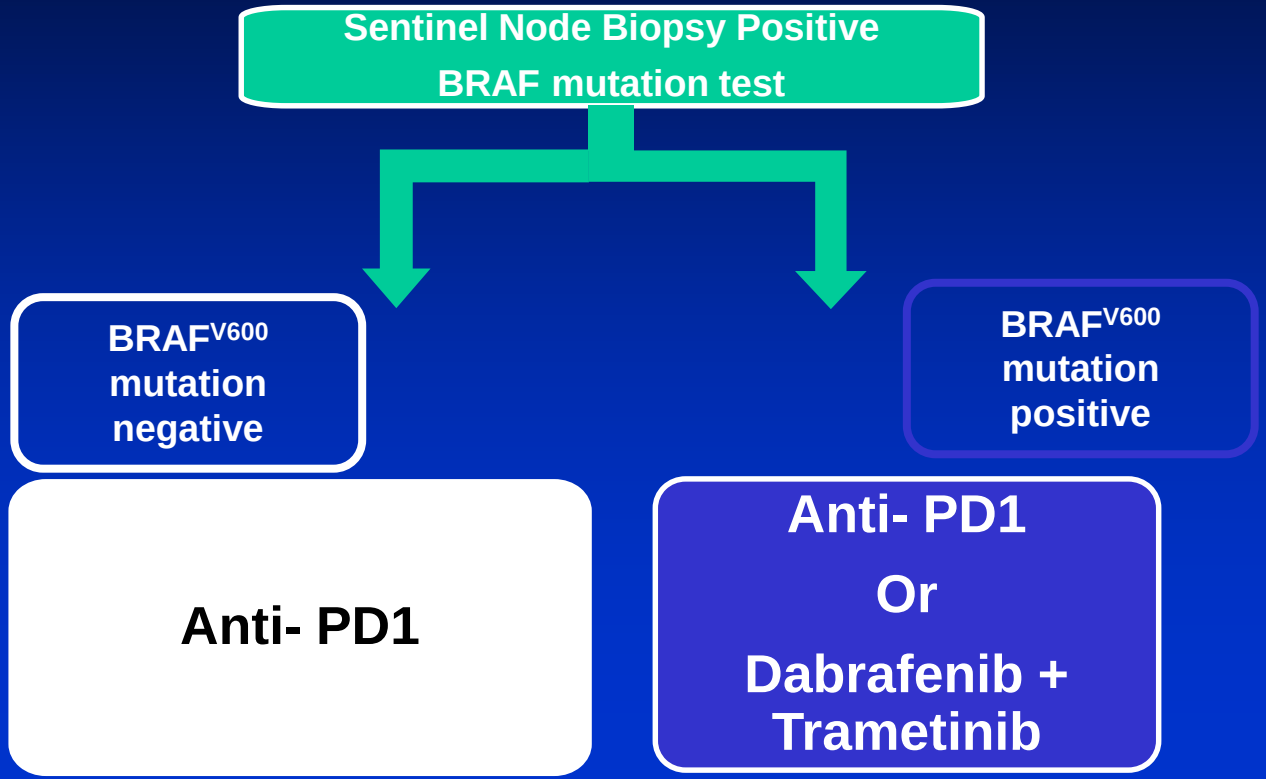
Summary & Conclusions

- Immunotherapy with checkpoint inhibitors is standard of care for most patients
  - Single agent PD1
  - Combination PD-1/CTLA-4
- For BRAF+ patients the choice is based on clinical judgment
- It has recently been approved for adjuvant therapy
- Future therapies will address better combinations and overcoming resistance

How I Treat Metastatic Melanoma



How I treat High Risk Melanoma Adjuvant Therapy



Clinical Trials!