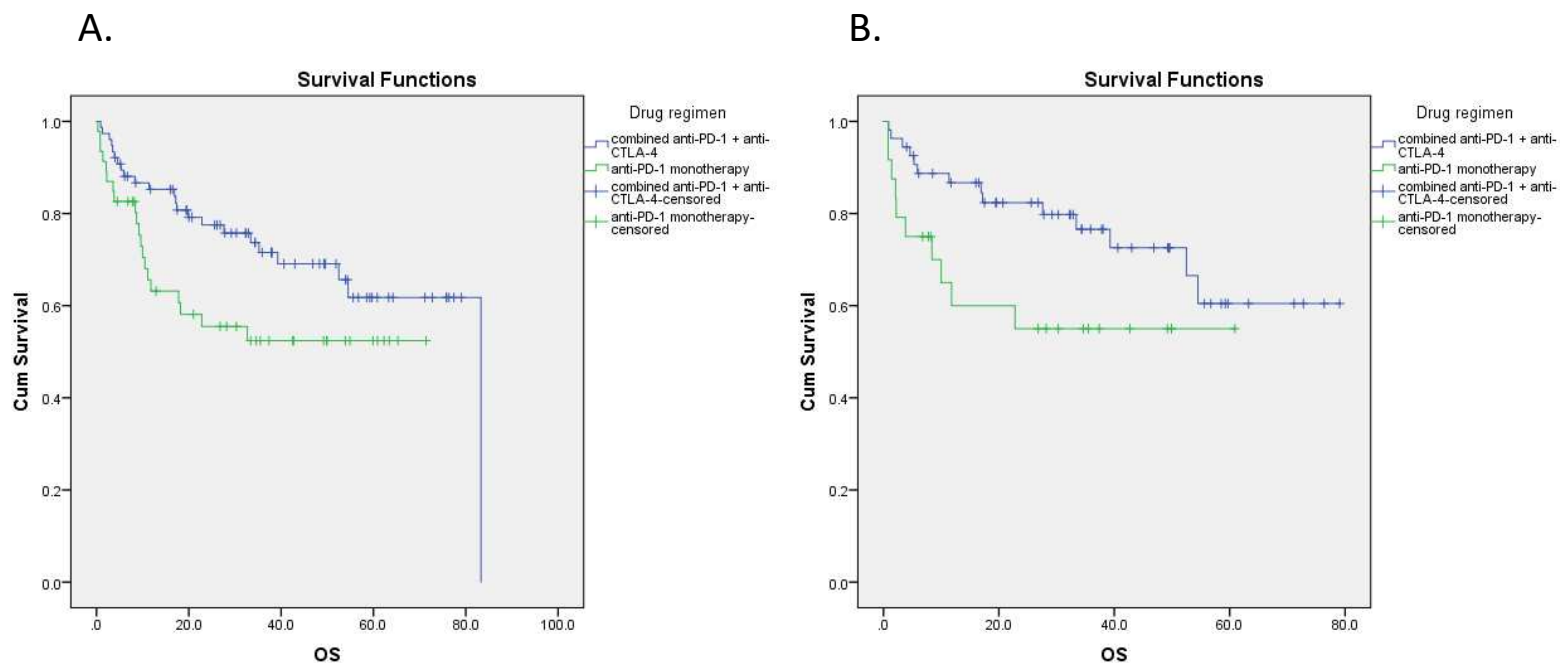


Supplemental Table 1. All Patient characteristics

Characteristics	Total (n=122)	Monotherapy (n=46)	Combo (n=76)	Statistics (mono vs combo)
Median age	64 years	69 years	59 years	P < 0.001 (t-test; ANOVA)
Male gender (%)	72 (59%)	32 (70%)	40 (53%)	P=0.065 (pearson chi-square)
ECOG 0-1(%)	115 (94%)	42 (91%)	73 (96%)	P=0.138 (pearson chi-square)
LDH elevated	50 (41%)	19 (41%)	31 (41%)	P=0.997 (pearson chi-square)
Primary tumor type				
Cutaneous	75 (62%)	27 (59%)	48 (63%)	P=0.086 (pearson chi-square)
Acral	7 (6%)	2 (4%)	5 (7%)	
Mucosal	13 (11%)	9 (20%)	4 (5%)	
Unknown	27 (22%)	8 (17%)	19 (25%)	
Disease stage at tx				
III	16 (13%)	10 (22%)	6 (8%)	P=0.028 (pearson chi-square)
IV	106 (87%)	36 (78%)	70 (92%)	
M stage at tx				
M1a	8 (7%)	3 (7%)	5 (7%)	P=0.893 (pearson chi-square)
M1b	23 (19%)	9 (20%)	14 (18%)	
M1c	37 (30%)	11 (24%)	26 (34%)	
M1d	38 (31%)	13 (28%)	25 (33%)	
BRAF mut (%)	50 (41%)*	13 (28%)**	37 (49%***)	P=0.037 (pearson chi-square)
Brain mets (%)	38 (31%)	13 (28%)	25 (33%)	P=0.592 (pearson chi-square)
Prior systemic tx				
Ipilimumab	44 (36%)	22 (48%)	22 (29%)	P=0.035 (pearson chi-square)
BRAFi/MEKi	20 (16%)	18 (39%)	2 (3%)	P<0.001 (pearson chi-square)
	15(12%)	6 (13%)	9 (12%)	P=0.845 (pearson chi-square)

*N=13 or 11% unknown BRAF status / **N=8 or 17% unknown BRAF status / ***N=5 or 7% unknown BRAF status

Supplemental Figure 1. Overall survival. Panel A, all patients with advanced melanoma treated with anti-PD-1 therapy. The anti-PD-1 monotherapy cohort had 20/46 events and median OS was not reached. The anti-PD-1 combination therapy cohort had 23/76 events and median OS was 83.3 mos. Log-rank $P=0.052$. Panel B, all treatment naive patients with advanced melanoma treated with anti-PD-1 therapy. The anti-PD-1 monotherapy cohort had 10/24 events and median OS not reached. The anti-PD-1 combination therapy cohort had 14/54 events and median OS was not reached. Log-rank $P=0.053$.



Supplemental Table 2. EFS outcomes and estimated survival.

	Choice (N=24)	Toxicity (N=28)
1yr EFS	100%	87%
2yr EFS	95%	83%
3yr EFS	95%	71%
4yr EFS	81%	71%
EFS Events	2 (8%)	6 (21%)
Subsequent systemic therapy	1 (7%)	4 (14%)
Deceased	1 (7%)	2 (7%)
Median follow up	30.9 months	39.3 months

Supplemental Table 3. Baseline characteristics and treatment outcomes for patients with an event. BOR, best overall response. M, male; F, female. Nivo/Ipi, nivolumab plus ipilimumab. mos, months. Vem/cobi, vemurafenib plus cobimetinib. Bev, bevacizumab; given for radiation necrosis. Dab/Tram, dabrafenib plus trametinib. Pembro, pembrolizumab. NED, no evidence of active disease.

Patient	Age	Gender	BRAF V600 Mutant	Treatment Received	BOR	Reason off treatment	Treatment Duration	EFS	Subsequent management	Outcome
1	61 yr	M	No	Nivo/Ipi	CR	CR on CT	16 mos	20 mos	Surgery (LN metastasis)	Alive
2	70 yr	M	No	Nivo/Ipi	PR	PET/CT neg	12 mos	38 mos	Nivo/Ipi	Deceased
3	54 yr	F	Yes	Nivo/Ipi	SD	Immune colitis	8 mos	1 mos	Ipi Dab/Tram	Alive
4	53 yr	M	No	Nivo/Ipi	PR	Immune colitis	2 mos	30 mos	Surgery Bev	Lost to follow up with progressive CNS disease
5	36 yr	F	Yes	Nivo/Ipi	PR	Immune colitis	1 mos	17 mos	Pembro Dab/Tram	Alive
6	64 yr	F	Yes	Nivo/Ipi	PR	Immune myositis	4 mos	7 mos	Dab/Tram Pembro	Deceased
7	48 yr	F	No	Nivo/Ipi	PR	Immune colitis	2 mos	10 mos	Pembro Surgery	Deceased
8	66 yr	M	No	Pembro	PR	Immune hepatitis	12 mos	25 mos	Surgery (brain metastasis)	Alive

Supplemental Table 4. EFS Associations with Baseline Variables by Cox Regression (Univariate).

	Events	HR	95% CI	P value
Primary type				
Mucosal vs Cutaneous	2/4 mucosal 5/31 cutaneous	1.964	0.863-4.473	0.108
Mucosal vs Unknown Primary	2/4 mucosal 1/16 unknown primary	15.625	1.391-175.502	0.026
LDH level (elevated vs normal)	3/15 elevated 4/36 normal	2.385	0.530-10.744	0.258
Brain metastasis (present vs absent)	1/17 present 7/35 absent	0.309	0.038-2.521	0.273
Stage M1c-M1d vs IIIb-M1b	6/34 M1c-M1d 2/18 IIIb-M1b	1.896	0.381-9.423	0.434
Prior systemic tx (yes vs no)	3/15 yes 5/37 no	1.394	0.331-5.864	0.651
Prior Ipilimumab (yes vs no)	1/9 yes 7/43 no	0.647	0.079-5.285	0.685
Prior BRAF targeted treatment (yes vs no) <i>only BRAF V600 mut</i>	1/5 yes 3/11 no	0.938	0.097-9.110	0.956
Drug regimen (mono vs combo)	1/17 mono 7/35 combo	0.274	0.034-2.229	0.226
Gender (female vs male)	4/18 female 4/34 male	2.126	0.531-8.506	0.287
Reason for DC (toxicity vs choice)	6/28 toxicity 2/24 choice	2.991	0.601-14.885	0.181
ECOG PS (1 vs 0)	3/19 ECOG PS 1 4/32 ECOG PS 0	1.317	0.292-5.941	0.720
BRAF mutation (mutant vs wild-type)	4/16 BRAF mutant 4/28 BRAF wild-type	2.226	0.553-8.956	0.260