SUPPLEMENT

Treatment-free survival over extended follow-up of patients with advanced melanoma treated with immune checkpoint inhibitors in CheckMate 067

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Table S1 Number of endpoint events, Kaplan–Meier estimates of 60-month event-free proportions, and 60-month mean times by treatment assignment

		Treatment assignment		
		Nivolumab plus ipilimumab	**Nivolumab**	**Ipilimumab**
Number patients who initiated therapy		313	313	311
OS*	Number of events	151	175	228
	KM estimate event-free at 60 months, %	52	44	27
	60-month mean time, months†	38.6	36.1	28.4
Time to subsequent therapy initiation or death‡	Number of events	179	209	273
	KM estimate event-free at 60 months, %	43	33	11
	60-month mean time, months†	32.0	26.8	14.5
Time to protocol therapy cessation§	Number of events	301	289	311
	KM estimate event-free at 60 months, %	4	9	0
	60-month mean time, months†	12.3	16.9	2.6

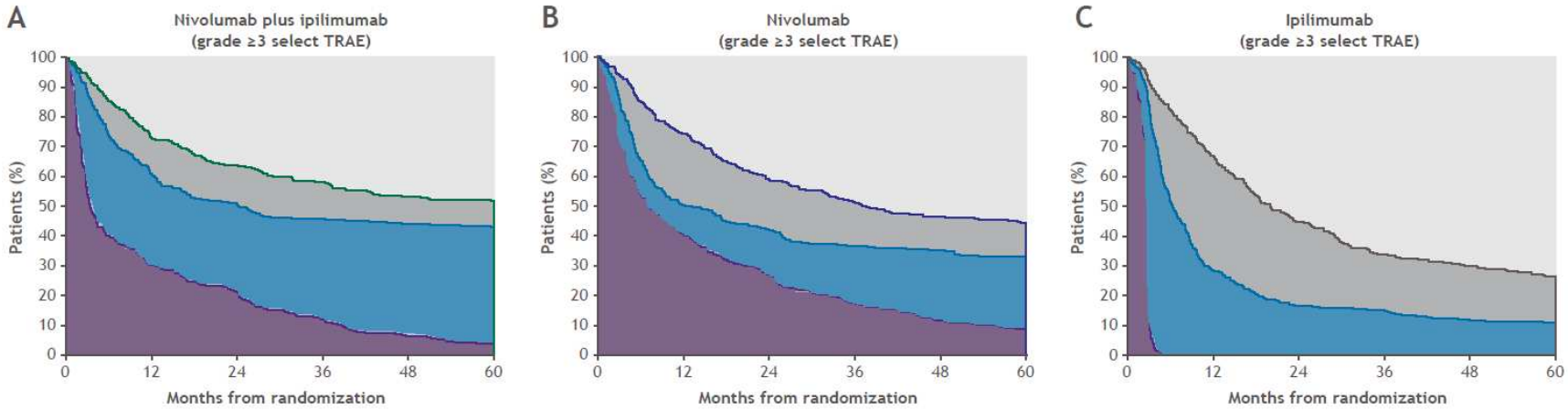
*Defined as the time from randomization until death from any cause or until censoring on the date last known alive.
†Interpreted as follows: on average, patients assigned to treatment *X* survived *Y* months of the 60-month period from randomization; on average, patients assigned to treatment *X* survived without initiating subsequent therapy *Y* months of the 60-month period from randomization; on average, patients assigned to treatment *X* were on protocol therapy *Y* months of the 60-month period from randomization.
‡Defined as the time from randomization until initiation of subsequent systemic anticancer therapy or death, whichever occurred first, or until censoring on the date last known alive and free of subsequent therapy.
§Defined as the time from randomization until cessation of protocol therapy or until censoring on the date last known alive on protocol therapy.
KM, Kaplan–Meier; OS, overall survival.

Table S2 Kaplan–Meier estimates of percentages of patients surviving free from subsequent therapy initiation, free from protocol therapy cessation, and treatment-free at 24, 36, 48, and 60 months*

Time since randomization, months	Event-free survival period	Treatment assignment		
		Nivolumab plus ipilimumab	Nivolumab	Ipilimumab
24	Free from subsequent therapy initiation, %	50	42	17
	Free from protocol therapy cessation, %	21	27	0
	Treatment-free, %	29	15	17
36	Free from subsequent therapy initiation, %	46	36	15
	Free from protocol therapy cessation, %	12	17	0
	Treatment-free, %	34	19	15
48	Free from subsequent therapy initiation, %	44	35	12
	Free from protocol therapy cessation, %	6	11	0
	Treatment-free, %	38	24	12
60	Free from subsequent therapy initiation, %	43	33	11
	Free from protocol therapy cessation, %	4	9	0
	Treatment-free, %	39	24	11

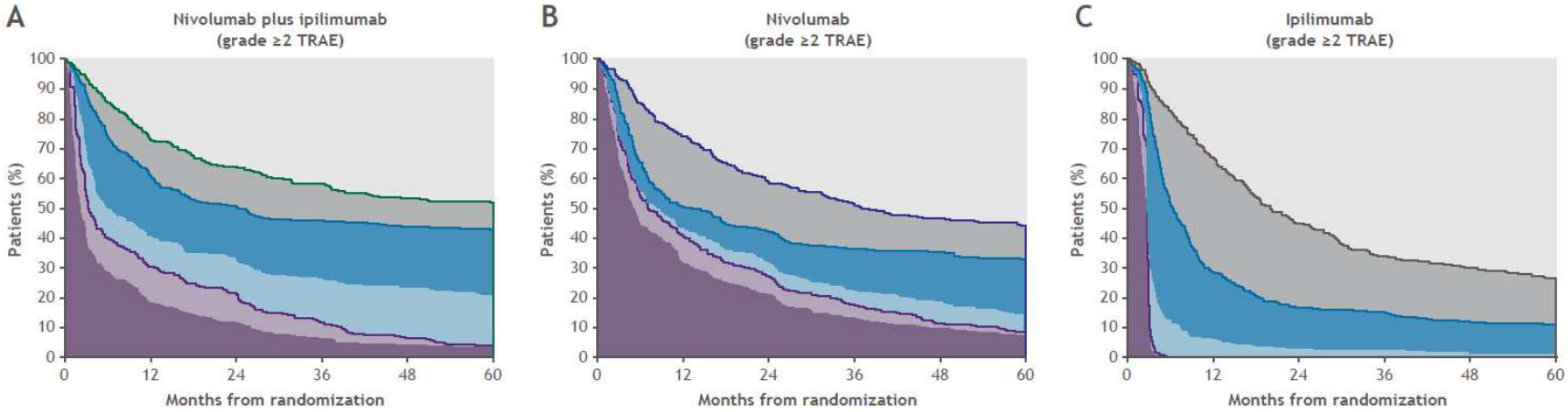
*Estimated by the differences in Kaplan–Meier estimates of the two defining endpoints.

Figure S1 Kaplan–Meier estimates of endpoints, TFS, and survival states characterizing how overall time was spent over the 60-month follow-up period from randomization. Toxicity was defined as grade ≥3 select TRAEs (i.e., those of potential immunologic etiology). OS, overall survival; TFS, treatment-free survival; TRAE, treatment-related adverse event.



Survival state	Nivolumab plus ipilimumab		Nivolumab		Nivolumab plus ipilimumab vs nivolumab	Ipilimumab		Nivolumab plus ipilimumab vs ipilimumab
	60-month mean time, months	60-month period, %	60-month mean time, months	60-month period, %	Difference (95% CI), months	60-month mean time, months	60-month period, %	Difference (95% CI), months
OS	38.6	64	36.1	60	2.5 (−1.1 to 6.2)	28.4	47	10.2 (6.6 to 13.9)
Survival after subsequent therapy initiation	6.6	11	9.3	15	−2.7 (−4.9 to −0.4)	13.9	23	−7.3 (−9.8 to −4.8)
TFS	19.7	33	9.9	17	9.8 (6.7 to 12.8)	11.9	20	7.8 (4.6 to 11.0)
Without grade ≥3 select TRAE	19.0	32	9.5	16	9.5 (6.5 to 12.5)	11.8	20	7.3 (4.1 to 10.4)
With grade ≥3 select TRAE	0.7	1	0.4	1	0.2 (−0.4 to 0.9)	0.1	<1	0.5 (0 to 1.0)
Time on protocol therapy	12.3	21	16.9	28	−4.6 (−7.3 to −1.8)	2.6	4	9.8 (7.9 to 11.6)
With grade ≥3 select TRAE	0.3	<1	0.4	1	−0.2 (−0.9 to 0.5)	0.0	<1	0.2 (0 to 0.4)
Without grade ≥3 select TRAE	12.1	20	16.5	27	−4.4 (−7.1 to −1.7)	2.5	4	9.5 (7.7 to 11.4)

Figure S2 Kaplan–Meier estimates of endpoints, TFS, and survival states characterizing how overall survival time was spent over the 60-month follow-up period from randomization. Toxicity was defined as grade ≥2 TRAEs. OS, overall survival; TFS, treatment-free survival; TRAE, treatment-related adverse event.



Survival state	Nivolumab plus ipilimumab		Nivolumab		Nivolumab plus ipilimumab vs nivolumab	Ipilimumab		Nivolumab plus ipilimumab vs ipilimumab
	60-month mean time, months	60-month period, %	60-month mean time, months	60-month period, %	Difference (95% CI), months	60-month mean time, months	60-month period, %	Difference (95% CI), months
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Survival after subsequent therapy initiation	6.6	11	9.3	15	−2.7 (−4.9 to −0.4)	13.9	23	−7.3 (−9.8 to −4.8)
TFS	19.7	33	9.9	17	9.8 (6.7 to 12.8)	11.9	20	7.8 (4.6 to 11.0)
Without grade ≥2 TRAE	11.3	19	6.9	12	4.3 (1.7 to 7.0)	9.4	16	1.9 (−0.9 to 4.8)
With grade ≥2 TRAE	8.4	14	3.0	5	5.4 (3.3 to 7.6)	2.5	4	5.9 (3.7 to 8.0)
Time on protocol therapy	12.3	21	16.9	28	−4.6 (−7.3 to −1.8)	2.6	4	9.8 (7.9 to 11.6)
With grade ≥2 TRAE	5.0	8	4.5	8	0.5 (−1.3 to 2.2)	0.4	1	4.5 (3.3 to 5.8)
Without grade ≥2 TRAE	7.3	12	12.4	21	−5.0 (−7.1 to −2.9)	2.1	4	5.2 (3.9 to 6.6)