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Final, 9-year results from the CheckMate 238 phase III trial of adjuvant nivolumab vs ipilimumab in resected stage IIIB–C or IV melanoma

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Background

Nivolumab (NIVO) improved recurrence-free survival (RFS) vs ipilimumab (IPI) in pts with high-risk, resected stage IIIB–C or IV melanoma in CheckMate 238, which led to the first approval of a PD-1 inhibitor as adjuvant melanoma treatment. Final, 9-y results and new analyses are presented.

Methods

Pts aged > 15 y (stratified by disease stage and PD-L1 status) were randomized 1:1 to NIVO 3 mg/kg Q2W (n = 453) or IPI 10 mg/kg Q3W for 4 doses then Q12W (n = 453) for up to 1 y or until disease recurrence/unacceptable toxicity. Endpoints included RFS, overall survival (OS), distant metastasis-free survival (DMFS) in stage III pts, and safety. Other post hoc analyses included progression-free survival through next-line therapy (PFS2), melanoma-related mortality analyzed via melanoma-specific survival (MSS) and competing risks methodology, and the impact the timing of dose administration has on outcomes.

Results

At 9-y minimum follow-up, RFS with NIVO remained significantly improved vs IPI (HR 0.76 [95% CI 0.63–0.90]), DMFS and PFS2 continued to favor NIVO; OS and MSS outcomes remained high (Table). Since the 7-y analysis, there were 8 new recurrence events for NIVO (2 regional, 2 local, 2 new primary, 2 death) and 2 for IPI (1 new primary, 1 death). For NIVO vs IPI respectively, there were a total of 7 and 10 new deaths (4 and 7 due to melanoma). Subsequent systemic therapy was less frequent with NIVO than with IPI (45% vs 51%), including subsequent immunotherapy in 26% vs 37% of pts. There were no new voluntarily reported late-emergent treatment-related adverse events since the 4-y database lock, and overall rates remain low.

	NIVO (n = 453)	IPI (n = 453)
	9-y rates, % (95% CI)	HR ^a (95% CI)
RFS	44 (39–49)	37 (32–42)
	0.76 (0.63–0.90)	
OS	69 (64–74)	65 (60–70)
	0.88 (0.69–1.11)	
MSS	74 (69–78)	70 (65–74)
	0.87 (0.67–1.12)	
DMFS ^b	54 (48–59)	48 (42–53)

	NIVO (n = 453)	IPI (n = 453)
	9-y rates, % (95% CI)	HR ^a (95% CI)
0.81 (0.65–1.00)		
PFS2	55 (49–59)	47 (42–52)
0.77 (0.63–0.93)		

^aNIVO vs IPI (stratified Cox proportional hazards model)^bIn stage III patients (NIVO = 370; IPI = 366)

Conclusions

In this final analysis for CheckMate 238, NIVO continued to show superior long-term RFS vs IPI in pts with stage IIIB–C or IV resected melanoma. These data, which are the longest follow-up of a checkpoint inhibitor in any adjuvant solid tumor setting, show that DMFS and PFS2 favored NIVO. Moreover, OS and MSS rates are high, at least 70% in the NIVO arm.

Clinical trial identification

NCT02388906.

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Legal entity responsible for the study

Bristol Myers Squibb.

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Disclosure

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