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Adjuvant nivolumab (NIVO) vs ipilimumab (IPI) in resected stage III/IV melanoma: 4-y recurrence-free and overall survival (OS) results from CheckMate 238

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Background

NIVO has shown improved recurrence-free survival (RFS) vs IPI in patients (pts) with resected stage III/IV melanoma in the phase III CheckMate 238 study. Updated 48-mo RFS and distant metastases-free survival (DMFS) and primary OS are presented.

Methods

Pts aged ≥ 15 y with completely resected stage IIIB/C or IV melanoma were stratified by stage and tumor programmed death ligand 1 (PD-L1) status and randomized 1:1 to NIVO (3 mg/kg Q2W; n = 453) or IPI (10 mg/kg Q3W for 4 doses, Q12W thereafter; n = 453) for ≤ 1 y or until disease recurrence/unacceptable toxicity. The primary endpoint was RFS. Secondary endpoints included OS and safety; DMFS in stage III disease was exploratory.

Results

At 48 mo of follow-up, NIVO continued to demonstrate superior RFS vs IPI (HR 0.71; 95% CI 0.60–0.86; *P* = 0.0003; Table). DMFS in pts with stage III disease favored NIVO (HR 0.79; 95% CI 0.63–0.99). At 48 mo, the number of OS events (n = 211) was lower than anticipated (n = 302) and OS rates were comparable: 78% (95% CI 73.7–81.5) with NIVO and 77% (95% CI 72.2–80.3) with IPI (HR 0.87, 95.03% CI 0.66–1.14, *P* = 0.3148). Subsequent systemic next-line therapy was received by 150 (33%) NIVO-treated pts and 189 (42%) IPI-treated pts; more IPI-treated pts (34% vs 23%) received subsequent systemic immunotherapy (IO). Any-grade late-emergent treatment-related adverse events (TRAEs; reported > 100 d after last dose) were observed in 18 (4%) NIVO-treated pts and 25 (6%) IPI-treated pts, with grade 3/4 in 3 (1%) and 7 (2%), respectively.

Conclusions

NIVO continued to demonstrate improved RFS and DMFS vs IPI at 48 mo in pts with stage III/IV melanoma at high risk of recurrence. OS events (n = 211) were lower than anticipated (n = 302). OS rates were similar to NIVO and IPI, although use of subsequent IO therapy was higher in the IPI arm. Late-emergent TRAEs were consistent with the established safety profile of NIVO and IPI, with more events reported with IPI.Table: 10760

	RFS	DMFS	OS
ITT population[a]	0.71 (0.60–0.86)	0.79 (0.63–0.99)	0.87 (0.66–1.14)[b]
Stage[c]			
IIIB	0.70 (0.50–0.98)	0.78 (0.54–1.14)	0.88 (0.53–1.47)
IIIC	0.74 (0.57–0.96)	0.82 (0.62–1.09)	0.96 (0.67–1.39)
IV	0.74 (0.49–1.11)	-	0.72 (0.38–1.38)

	RFS	DMFS	OS
PD-L1			
≥ 1%	0.68 (0.54–0.86)	0.77 (0.58–1.04)	0.73 (0.51–1.04)
< 1%/ind	0.76 (0.57–1.02)	0.80 (0.56–1.14)	1.09 (0.72–1.67)
≥ 5%	0.67 (0.47–0.96)	0.79 (0.51–1.22)	0.74 (0.43–1.27)
< 5%/ind	0.74 (0.59–0.91)	0.80 (0.61–1.04)	0.92 (0.68–1.26)
BRAF			
Mutant	0.79 (0.60–1.05)	0.82 (0.57–1.16)	1.13 (0.73–1.74)
Wild-type	0.69 (0.53–0.91)	0.79 (0.57–1.09)	0.76 (0.51–1.12)

Data are HR (95% CI) for NIVO vs IPI; [a]Stratified; [b]95.03% CI; [c]AJCC 7th ed.; Ind, indeterminate.

Clinical trial identification

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