

Abstract

Background

The phase III study CheckMate 238 demonstrated improved relapse-free survival (RFS) with NIVO 3 mg/kg vs IPI 10 mg/kg in patients (pts) with resected stage III/IV melanoma. Sustained efficacy benefit at 24 mo of follow-up with NIVO vs IPI was previously reported. Here we present a 36mo analysis of efficacy and biomarker data from this study.

Methods

Pts aged ≥ 15 y with completely resected stage IIIB/C or IV melanoma were randomized 1:1 to receive 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. RFS was the primary endpoint; exploratory endpoints included distant metastases-free survival (DMFS) in pts with stage III disease and potential biomarkers of efficacy.

Results

With 36 mo of follow-up, NIVO continued to demonstrate superior RFS vs IPI (HR, 0.68; $P < 0.0001$; 3-y RFS rates, 58% vs 45% and 188/453 vs 239/453 pts with events, respectively). Prespecified subgroup analyses demonstrated a consistent pattern similar to that of the 24-mo analysis, with HRs favoring NIVO (Table). DMFS analysis also continued to favor NIVO (Table). High levels of all biomarkers analyzed (interferon-gamma gene expression signature, tumor mutational burden, and CD8+ T-cell infiltration by immunohistochemistry) showed an association with improved RFS for both NIVO and IPI. Median RFS (mo; 24-mo follow-up) by high vs low values for each biomarker for NIVO was 30.8 vs 24.1, not reached (NR) vs 30.8, and 30.8 vs 24.9, respectively; and for IPI was NR vs 15.9, NR vs 18.3, and NR vs 13.8, respectively.

Conclusions

With 36 mo of follow-up, NIVO continued to demonstrate superior efficacy over IPI in pts with stage III/IV melanoma at high risk of recurrence across pt subgroups. Additional analyses using composite scoring of biomarker combinations will be presented.

Table:

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36-mo follow-up		
Pt group	NIVO vs IPI RFS HR (95% CI) ^a	NIVO vs IPI DMFS HR (95% CI) ^a
ITT population	0.68 (0.56–0.82)	0.78 (0.62–0.99)
Stage IIIB ^b	0.70 (0.48–1.00)	0.78 (0.52–1.17)
Stage IIIC ^b	0.68 (0.52–0.89)	0.81 (0.60–1.09)
Stage IV ^b	0.71 (0.46–1.08)	–
PD-L1 ≥ 5%	0.57 (0.39–0.83)	0.66 (0.41–1.06)
PD-L1 < 5%	0.73 (0.58–0.92)	0.83 (0.63–1.10) ^c
BRAF mutant	0.79 (0.59–1.06)	0.84 (0.58–1.20)
BRAF wild-type	0.60 (0.45–0.80)	0.75 (0.53–1.07)

^a

Stratified results for ITT population, unstratified results for subgroups.

^b

Per American Joint Committee on Cancer 7th edition.

^c

Includes pts with PD-L1 status categorized as indeterminate.

Clinical trial identification

NCT02388906.