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Pembrolizumab versus placebo after complete resection of high-risk stage II melanoma: Efficacy and safety results from the KEYNOTE-716 double-blind phase III trial

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Background

Current standard of care for patients (pts) after resection of high-risk stage II melanoma is observation. In the phase 3 double-blind KEYNOTE-716 trial we evaluated pembrolizumab (pembro) versus placebo in pts with resected AJCC-8 stage IIB or IIC melanoma. We present results of the first recurrence-free survival (RFS) interim analysis.

Methods

Eligible pts aged ≥12 years with complete resection of cutaneous stage IIB or IIC melanoma with negative sentinel lymph node biopsy were randomized 1:1 to pembro 200 mg (2 mg/kg for pediatric pts) or placebo Q3W for 17 cycles (up to 1 year). Randomization was stratified by T category 3b, 4a, 4b (adults) with a separate stratum for pediatric pts. Treatment continued until disease recurrence or unacceptable toxicity. The primary endpoint was RFS per investigator assessment. Safety was also evaluated. The data cutoff date for the interim analysis was December 4, 2020.

Results

Overall, 976 pts (64% stage IIB; 34.8% stage IIC) were randomized (487 pembro; 489 placebo). At median follow-up of 14.4 months, pembro significantly prolonged RFS vs placebo (HR 0.65, 95% CI 0.46-0.92; P=0.00658; median not reached for both). 54 (11.1%) vs 82 (16.8%) pts had a recurrence with almost halving of distant recurrence events in the pembro (23) vs placebo (38) group. The 12-month RFS rate was 90.5% vs 83.1%. Grade ≥3 any-cause AEs occurred in 125 (25.9%) vs 83 (17.1%) pts in the pembro vs placebo group. Grade ≥3 drug-related AEs occurred in 78 (16.1%) vs 21 (4.3%) pts; 74 (15.3%) vs 12 (2.5%) discontinued due to a drug-related AE. No deaths due to any-cause AE or drug-related AEs occurred with pembro; four deaths due to any-cause AEs occurred with placebo. Immune-mediated AEs occurred in 36.2% vs 8.4%, most commonly hypothyroidism (15.7% vs 3.5%) and hyperthyroidism (10.4% vs 0.6%). Most were grade 1-2 in severity.

Conclusions

Adjuvant pembrolizumab for resected stage IIB and IIC melanoma decreased the risk of disease recurrence or death by 35% compared with placebo and was associated with significantly prolonged RFS and a favorable benefit-risk profile.

Clinical trial identification

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