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MASTERKEY-265: A phase III, randomized, placebo (Pbo)-controlled study of talimogene laherparepvec (T) plus pembrolizumab (P) for unresectable stage IIIB–IVM1c melanoma (MEL)

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Background

In the phase Ib part of MASTERKEY-265, T + P showed promising complete response rate (CRR) of 33% in 21 patients (pts) with advanced MEL. Here we report efficacy and safety from the phase III, randomized, double-blind MASTERKEY-265/KEYNOTE-034 study of T + P vs Pbo + P in pts with stage IIIB–IVM1c MEL (NCT02263508).

Methods

Unresectable stage IIIB-IVM1c, anti-PD-1 naïve, MEL pts with injectable lesions were randomized 1:1 to T + P or Pbo + P. T was given at ≤ 4 x 10^6 PFU followed by ≤ 4 x 10^8 PFU 3 weeks later and Q2W until dose 5, and Q3W thereafter. P was given IV 200 mg Q3W. Dual primary endpoints were progression-free survival (PFS) per mRECIST 1.1 by blinded independent central review and overall survival (OS). Secondary endpoints included objective response rate (ORR), complete response rate (CRR), durable response rate (DRR), duration of response (DOR), and safety. Results reported here are the primary PFS and interim OS analyses (data cutoff [DCO] PFS Mar 2, 2020; OS Sep 29, 2020).

Results

A total of 692 pts were randomized (346 to T + P, 346 to Pbo + P); as of the OS DCO, all pts were off study treatment (tx). Median follow-up was 31.0 mo (range: 0.3, 53.0). 6.9% had stage IVM1c disease, 32.7% had LDH > ULN, and 64.9% had PD-L1+ status. Median PFS was 14.3 mo (range: 10.3, 22.1) for the T + P arm and 8.5 mo (range: 5.7, 13.5) for the Pbo + P arm (HR 0.86, 95% CI 0.71, 1.04, P = 0.13). Median OS was not reached for the T + P arm and 49.2 mo (range: 40.6, NE) for the Pbo + P arm (HR 0.96, 95% CI 0.76, 1.24, P = 0.74). OS was not expected to achieve statistical significance at the primary OS analysis. ORR was 48.6% for the T + P arm (CRR 17.9%) and 41.3% for the Pbo + P arm (CRR 11.6%). DRR was 42.2% in the T + P arm and 34.1% for the Pbo + P arm. There was no difference in DOR between arms (P = 0.87, HR [95% CI] 1.04 [0.67, 1.60]). Gr 3+ TEAEs occurred in 161 (46.7%) pts receiving T + P and in 151 (44.0%) pts receiving Pbo + P. Gr 3+ tx-related AEs (TRAEs) occurred in 73 (21.2%) pts receiving T + P and in 55 (16%) pts receiving Pbo + P.

Conclusions

T + P did not significantly improve PFS or OS vs Pbo + P. There was a 5.8 mo numeric difference in PFS between arms. Safety results of T + P were acceptable and consistent with the known safety profiles of each agent.

Clinical trial identification

NCT02263508.

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Legal entity responsible for the study

Amgen Inc.

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Disclosure

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