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Long-term outcomes in patients with BRAF V600-mutant metastatic melanoma receiving dabrafenib monotherapy: Analysis from phase 2 and 3 clinical trials

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Abstract

Background: Previous analyses of BREAK-2 and BREAK-3 showed that durable outcomes lasting ≥3 years are achievable with dabrafenib in some patients with BRAF V600-mutant metastatic melanoma (MM); however, additional follow-up is needed to fully characterise the long-term impact of dabrafenib in these patients.

Methods: BREAK-2 was a single-arm phase 2 study evaluating dabrafenib in treatment-naive or previously treated BRAF V600E/K-mutant MM. BREAK-3, a randomised (3:1) phase 3 study, assessed dabrafenib versus dacarbazine in previously untreated unresectable or metastatic BRAF V600E-mutant melanoma. Five-year analyses were performed.

Results: All BREAK-2 patients (N = 92 [V600E, n = 76; V600K, n = 16]) discontinued treatment by the data cutoff. Median follow-up was 13.0 months. In BRAF V600E patients, 5-year progression-free survival (PFS) and overall survival (OS) were 11% and 20%, respectively. Subsequent immunotherapy was received by 22% of patients. In BREAK-3, median follow-up was 17.0 and 12.0 months in the dabrafenib (n = 187) and dacarbazine (n = 63) arms, respectively. Thirty-seven patients (59%) receiving dacarbazine crossed over to dabrafenib following disease progression as per protocol. Five-year PFS was 12% in the dabrafenib arm; all dacarbazine-arm patients progressed or were censored by 5 years. Dabrafenib improved PFS versus dacarbazine, regardless of baseline lactate dehydrogenase levels. Five-year OS rates were 24% and 22% in the dabrafenib and dacarbazine arms, respectively. Subsequent therapy in each arm included anti-CTLA-4 (dabrafenib [24%] and dacarbazine [24%]) and/or anti-PD-1 (8% and 2%) treatment. No new safety signals were observed.

Conclusions and relevance: These data, representing extended follow-up for dabrafenib monotherapy, demonstrate that durable benefit lasting ≥5 years is achievable in a subset of patients.

Trial registration: ClinicalTrials.gov (BREAK-2, NCT01153763; BREAK-3, NCT01227889).

Keywords: BRAF; Dabrafenib; Long-term outcomes; Melanoma; Metastatic.

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