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Five-year analysis on the long-term effects of dabrafenib plus trametinib (D + T) in patients with *BRAF V600*–mutant unresectable or metastatic melanoma.

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Background: First-line treatment with D+T demonstrated prolonged progression-free survival (PFS) and overall survival (OS) in patients with *BRAF* V600–mutant unresectable or metastatic melanoma. With 5 years of follow-up, we report survival and describe characteristics of patients in the phase 3 COMBI-d and COMBI-v trials with long-term benefit. **Methods:** Pooled 5-year landmark data for patients treated with D+T in the phase 3 COMBI-d (NCT01584648) and COMBI-v (NCT01597908) trials were analyzed. The trials enrolled patients with previously untreated *BRAF* V600E/K–mutant unresectable or metastatic melanoma. Patients received D 150 mg twice daily plus T 2 mg once daily vs either D + placebo (COMBI-d) or vemurafenib (COMBI-v). The primary endpoints were PFS in COMBI-d and OS in COMBI-v. **Results:** The pooled population included 563 patients who received D+T (COMBI-d, n = 211; COMBI-v, n = 352). Four- and 5-year PFS and OS rates were similar, suggesting a stabilization (4- and 5-year PFS, 21% [95% CI, 17%-24%] and 19% [95% CI, 15%-22%, respectively]; 4- and 5-year OS, 37% [95% CI, 33%-42%] and 34% [95% CI, 30%-38%], respectively). In patients with normal baseline lactate dehydrogenase (LDH) levels the 5-year PFS rate was 25% vs 8% in patients with elevated baseline LDH levels. Similarly, the 5-year OS rate was considerably higher in patients with normal baseline LDH levels vs those with elevated LDH levels at baseline (43% vs 16%). Among patients with normal baseline LDH levels and < 3 organ sites with metastases, the 5-year PFS and OS rates were 31% and 55%, respectively. In addition, exploratory analyses will be performed to characterize subgroup(s) of patients most likely to experience long-term benefit. Of 299 patients who received subsequent anticancer therapy following treatment with D+T, 151 (51%) received an anti–CTLA-4 therapy and 102 (34%) received an anti–PD-1 therapy. The safety profile of D+T was as previously reported, and no new safety signals were observed. No treatment-related deaths were reported. **Conclusions:** First-line treatment with D+T leads to durable long-term benefit in many patients with *BRAF* V600–mutant unresectable or metastatic melanoma. Clinical trial information: NCT01584648; NCT01597908.