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MELANOMA

Blocking BRAF to the BRIM

In the past few years, the treatment of melanoma has been revolutionised by the approval of the CTLA-4 antibody, ipilimumab, and protein kinase inhibitors—such as vemurafenib, dabrafenib, and trametinib. These agents have significantly extended the overall survival of patients with mutations in *BRAF*. In fact, 40–60% of patients with melanoma harbour mutations in codon 600 of BRAF, the most prevalent of which are BRAF V600E (found in 80% of patients) and BRAF V600K (found in 5–30% of patients).

The BRIM-3 phase III trial was launched in 2010 to compare the efficacy of vemurafenib with the chemotherapeutic agent dacarbazine in 675 patients with *BRAF*-mutated metastatic melanoma, showing a clear benefit for vemurafenib, which led to approval of the drug by the US FDA in this setting. Now, McArthur *et al.* have published the results from the extended follow-up of patients, with a median follow-up of 12.5 months for patients assigned to receive vemurafenib and 9.5 months for those assigned to receive dacarbazine. The study also analysed whether there was any difference regarding the efficacy and safety of vemurafenib versus dacarbazine between patients with BRAF V600E or BRAF V600K mutations.

Treatment with vemurafenib prolonged median overall survival (13.6 months) compared with dacarbazine (9.7 months). Median progression-free survival was also significantly longer in the vemurafenib group than in the dacarbazine group (6.9 months versus 1.6 months).

Interestingly, a significant survival benefit was observed in patients with the BRAF V600E mutation in the vemurafenib group (13.3 months versus 10.0 months in the dacarbazine group). This difference was also seen in patients with the rarer BRAF V600K mutation (14.5 months in the vemurafenib group versus 7.6 months in the dacarbazine group). However, these patients had a higher incidence of keratocanthomas than the patients with BRAF V600E mutation, although the incidence of squamous-cell carcinoma was similar in both populations. These results confirm that vemurafenib is an appropriate treatment option for patients with both types of mutation in *BRAF*.

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Original article McArthur, G. A. *et al*. Safety and efficacy of vemurafenib in BRAFV600E and BRAFV600K mutation-positive melanoma (BRIM-3): extended follow-up of a phase 3, randomised, open-label study. *Lancet Oncol.* doi:10.1016/S1470-2045(14)70012-9