In our recently published study (1), we describe genetic similarities between conjunctival and cutaneous melanoma and propose that the treatment rationale for patients with metastasized conjunctival melanoma should be adapted to that for metastasized cutaneous melanoma. Weber and colleagues (2) responded to this, reporting that a \textit{BRAF} V600E–mutant metastasized conjunctival melanoma patient treated with the BRAF inhibitor vemurafenib demonstrated only a mixed response, primarily with disease progression. Weber and colleagues interpret this finding as possible evidence that BRAF inhibitors may be less effective in metastasized conjunctival than cutaneous melanoma.

In contrast to their experience, we observed a partial response in a 43-year-old male patient with metastasized conjunctival melanoma treated with the BRAF inhibitor dabrafenib. The patient’s conjunctival melanoma, diagnosed in 2001, involved the caruncle of the right eye and had developed from a preexisting nevus. Initial treatment was surgical with adjuvant ruthenium therapy. Recurrences in 2003 and 2007 were treated surgically and by proton therapy. Metastatic disease with intramuscular and pulmonary metastasis was diagnosed in 2010. Disease progressed under dacarbazine (DTIC) chemotherapy. Having developed two small brain metastases (left frontal lobe <5 mm), the patient was admitted to the GlaxoSmithKline BR113929 study and received dabrafenib (3). The patient’s tumor showed a partial response [Response Evaluation Criteria in Solid Tumors (RECIST) 1.0] (Fig. 1), most pronounced 4.5 months after therapy initiation with target lesions demonstrating a 61.6% cumulative tumor reduction. Dabrafenib was discontinued after 6 months when progressive disease with appearance of additional pulmonary and lymph node metastases were observed.

Although also only a single patient, our report clearly shows that BRAF inhibitors can be of value in the treatment of patients with metastasized \textit{BRAF} V600–mutant conjunctival melanoma. Experience has taught us that not all patients with \textit{BRAF} V600–mutant metastasized cutaneous melanoma respond to BRAF inhibitors (4, 5). As such, individual patients with metastatic conjunctival melanoma not responding to therapy is not that surprising and cannot necessarily be assumed to be representative of the overall situation in conjunctival melanoma.

The genetic evidence we presented in our article strongly supports a link between conjunctival and cutaneous melanoma (1). In addition, our report on a patient with metastasized conjunctival melanoma who clearly profited from BRAF inhibitor therapy is further confirmation that patients with metastasized conjunctival melanoma can benefit from receiving treatment modalities available for metastasized cutaneous melanoma. Treating larger, representative numbers of patients (preferably in the context of prospective clinical trials) will be essential before allowing any objective assessment regarding which of the therapies available for metastasized cutaneous melanoma are also effective in metastasized conjunctival melanoma.

Figure 1. Response of pulmonary metastasis after 8 weeks of dabrafenib. Computer tomography image of the patient’s lung showing multiple metastases shortly before, and 8 weeks after receiving dabrafenib. The arrow points to a larger pulmonary metastasis whose diameter went from 25 to 15 mm in this time period.
Disclosure of Potential Conflicts of Interest

B. Schilling has honoraria from the Speakers Bureau of Roche. E. Livingstone has honoraria from the Speakers Bureau of Bristol-Myers Squibb, Roche, Amgen, Boehringer-Ingelheim, Merck, Sharp & Dohme, and Merck and has supplied expert testimony for Bristol-Myers Squibb. I. Zimmer has honoraria from the Speakers Bureau of Bristol-Myers Squibb and Roche, is a consultant/advisory board member of Bristol-Myers Squibb and Roche, and has supplied expert testimony for Bristol-Myers Squibb and Roche. D. Schadendorf has honoraria from the Speakers Bureau of Roche, Bristol-Myers Squibb, GlaxoSmithKline, Amgen, and Novartis and is a consultant/advisory board member of Roche, Bristol-Myers Squibb, GlaxoSmithKline, Amgen, and Novartis. No potential conflicts of interest were disclosed by the other authors.

Received August 30, 2013; accepted September 3, 2013; published OnlineFirst October 29, 2013.

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Conjunctival Melanomas Harbor *BRAF* and *NRAS* Mutations — Response

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