

Does BRAF V600E Mutation Enable Vemurafenib to be a Universal Candidate for Treating a Plethora of Cancers?

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Commentary

Thanks to molecular pathology, BRAF V600E mutation was detected in several head and neck neoplasms such as ameloblastoma [1], isthmus malignant thyroid nodules [2], primary and metastatic papillary thyroid carcinoma [3-5].

Neurologically, BRAF V600E mutation was detected in cerebellar anaplastic pilocytic astrocytoma [6], ganglioglioma [7], desmoplastic infantile astrocytoma [8], indeterminate cell tumor and interdigitating dendritic cell sarcoma [9]. Hematologically, BRAF V600E mutation was also detected in multiple myeloma [10] and several leukemias (hairy cell, chronic lymphocytic, prolymphocytic and acute lymphoblastic leukaemia) [11-13].

In GIT, BRAF V600E mutation induces gastrointestinal crypt senescence and promotes tumor progression as in gastroenteropancreatic neuroendocrine tumors, colorectal cancer [14-19].

Other miscellaneous targets include melanoma (and conjunctival melanoma) [20,21], Japanese lung adenocarcinoma [22], non-small cell lung cancer [23], metanephric adenoma (and the associated active hyperplastic perilobar nephrogenic rests) [24,25], papillary craniopharyngioma [26], syringocystadenoma papilliferum [27], Erdheim-Chester disease [28,29], pleomorphic xanthoastrocytoma [30] and in in serous ovarian tumors [31].

Taken together, this shared mutation may explain the metastatic map of some cancers and may help pathologists understand confusing syndromes. This was the case when a genodermatosis syndrome associated with BRAF V600E mosaicism has been recently introduced. Similar to Schimmelpenning-Feuerstein-Mims syndrome, this neoplastic syndrome is expected to be driven by mosaicism of HRAS and/or KRAS activating mutations [32].

The immunohistochemical marker VE1 was successfully introduced to appreciate these mutations in the histological specimens of such tumor cells [33-35].

This promoted BRAF V600E oncogene to be a potential target for therapy with variable degrees of success. However, it takes two arms to embrace success. Encoding the "other" arm warrants more therapeutic success as in the case of targeting MAP2K1 and BRAF mutations in hairy cell leukemia [36], BRAF V600E-BRAFV600K in melanoma [37], as well as BRAF V600E-TERT promoter mutations in papillary thyroid cancers [38].

Accordingly, this overview may highlight the significance and efficacy of vemurafenib in treating BRAF-V600E-mutated cancers [37].

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