Vemurafenib

Anti-BRAF agents, including vemurafenib, have modified the prognosis for patients with melanoma. However, a difference can still be observed between extracerebral and cerebral responses.

While dabrafenib has demonstrated comparable efficacy to vemurafenib in BRAF V600E mutant melanoma patients, the BREAK-MB and dabrafenib/trametinib studies have taken BRAF inhibitor strategies further with evidence of disease activity in patients with metastatic melanoma brain metastases and potential abrogation of BRAF inhibitor resistance [1].

Case series

2015

Six patients treated with vemurafenib 960 mg twice daily had undergone a lumbar puncture because of suspicions of Leptomeningeal carcinomatosis, along with simultaneous blood sampling to measure vemurafenib level. The concentrations of vemurafenib in the CSF and the plasma were measured by high-performance liquid chromatography. The mean plasma and CSF concentrations of vemurafenib were 53.4±26.2 and 0.47±0.37 mg/l, respectively. The mean ratio of the CSF : plasma concentration was 0.98±0.84%. No relationship was found between plasma and CSF concentrations (P=0.8). In conclusion, the preliminary results highlight for the first time a low CSF vemurafenib penetration rate associated with a large interindividual variability in patients treated for metastatic BRAF-V600 mutated melanoma and brain metastases. Further investigations with larger cohorts are required to study the relationship between CSF vemurafenib concentrations and cerebral response [2].

2013

Retrospective analysis was performed on twelve patients who had the mutation and were treated with either stereotactic radiosurgery or whole brain radiation therapy prior to or along with vemurafenib at a dose of 960 mg orally twice a day. Clinical and radiological responses, development of new brain metastases, overall survival and toxicity were assessed. Improvement in neurological symptoms was seen in 7/11 (64 %) following therapy. Radiographic responses were noted in 36/48 (75 %) of index lesions with 23 (48 %) complete responses and 13 (27 %) partial responses. Six month local control, freedom from new brain metastases and overall survival were 75, 57 and 92 %. Four patients had intra-tumoral bleed prior to therapy and two patients developed steroid dependence. One patient experienced radiation necrosis. This retrospective study suggests that melanoma patients with brain metastases harboring BRAF mutation appear to be a distinct sub-group with a favorable response to vemurafenib and radiation therapy and acceptable morbidity [3].

Case reports

Finch et al., presented the case of a 16-year-old male with pleomorphic xanthoastrocytoma who responded to vemurafenib monotherapy initially and had an additional response to vemurafenib following progression after a brief time off the medication [4].

A patient had metastatic NSCLC with metastases to her brain. Due to the BRAF V600 mutation in her tumor and her poor functional status, Robinson et al. offered her off-label treatment with vemurafenib, a BRAF inhibitor approved for use in metastatic melanoma. The patient's visceral disease improved supporting vemurafenib's efficacy in the treatment of metastatic BRAF-mutated NSCLC. The regression of intracranial disease indicated vemurafenib was able to cross the blood brain barrier and was efficacious in treating brain metastases in this patient with lung cancer [5].

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