Inhibiting BRAF V600E Kinase Signaling in Anaplastic Pleomorphic Xanthoastrocytomas

Usama Khalid Choudry¹, Areeba Nisar² and Mahwish Amin²

¹Department of Post Graduate Education, Aga Khan University Hospital, Karachi, Pakistan
²Jinnah Medical and Dental College, Karachi, Pakistan

Corresponding author: Choudry UK, Usama Khalid Choudry, Department of Post Graduate Education, Aga Khan University Hospital, Karachi, Pakistan, Tel: +923456165524; E-mail: uk_choudry@hotmail.com

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Editorial

Anaplastic pleomorphic xanthoastrocytoma (APXA) is an atypical astrocytic tumor. It is newly classified as Grade III (WHO) astrocytic neoplasm [1]. The treatment of APXA conventionally involves surgical resection followed by postsurgical radiotherapy [2]. It has a recurrence rate of 30% within five years and 40% within ten years, following primary resection [3]. The BRAF V600E mutation has been identified in 60% APXA patients particularly in younger patients. Researchers have explored this mutation as a ground for potential treatment option [4]. Selective inhibitors of the mutated BRAF V600E kinase (Vemurafenib) lead to reduced signaling through the aberrant mitogen-activated protein kinase (MAPK) pathway. However, resistance may develop due to BRAF V600E over amplification, bypassing mechanisms via up regulation and over expression of other components in the MAPK signaling cascade or activation of alternative pathways with potential to enhance cell growth, proliferation and cancer survival [5]. Vemurafenib is generally well tolerated with low frequency of adverse effects such as diarrhea, fatigue, nausea, alopecia and photosensitivity [6]. It has a reported response time of 10-14 days in APXA [7].

Vemurafenib is also used in combination with other cytotoxic chemotherapeutic agents as very effective regimens for metastatic melanoma [8]. Lee et al. [7] reported successful remission of APXA with Vemurafenib, at a dose of 720mg twice per day, which was confirmed with an MRI showing minimal residual enhancement after 12 weeks of therapy. Brown et al. also reported complete remission of APXA with BRAF inhibitors (Dabrafenib). Another retrospective case series of 4 patients with recurrent PXA showed median overall survival time of 8 months with single agent therapy of Vemurafenib [3]. Studies have reported that Treatment with Vemurafenib shows improved patient survival time in anaplastic PXA as compared to adjuvant therapy radiotherapy following resection [2,6]. Use of Vemurafenib may lead to enhanced clinical anti-tumor targeted therapy. The success rate of BRAF inhibitors for treatment of APXA need to be further explored through randomized control trials. Since the APXA tumors are evolving at a pace more rapid than the currently recommended regimens. It is imperative to find a more promising approach towards this tumor [9].

References