Editorial

iMedPub Journals
http://www.imedpub.com/

Journal of Surgery and Emergency Medicine

2017
Vol.1 No.1:e104

Inhibiting BRAF V600E Kinase Signaling in Anaplastic Pleomorphic Xanthoastrocytomas

Usama Khalid Choudry[1], Areeba Nisar[2] and Mahwish Amin[2]

[1]Department of Post Graduate Education, Aga Khan University Hospital, Karachi, Pakistan

[2]Jinnah 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

Received date: January 02, 2017; **Accepted date:** January 04, 2017; **Published date:** January 06, 2017

Citation: Choudry UK, Nisar A, Amin M (2017) Inhibiting BRAF V600E Kinase Signaling in Anaplastic Pleomorphic Xanthoastrocytomas. J Surgery Emerg Med 1:1.

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 post-surgical 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 photosentivity [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

1. Kleihues P, Louis DN, Scheithauer BW, Rorke LB, Reifenberger G, et al. (2002) The WHO classification of tumors of the nervous system. Journal of Neuropathology and Experimental Neurology 61: 215-225.
2. Choudry UK, Khan SA, Qureshi A, Bari E (2016) Primary anaplastic pleomorphic xanthoastrocytoma in adults. International Journal of Surgery Case Reports 27: 183-188.
3. Kepes JJ, Rubinstein LJ, Eng LF (1979) Pleomorphic xanthoastrocytoma: A distinctive meningocerebral glioma of young subjects with relatively favorable prognosis a study of 12 cases. Cancer 44: 1839-1852.
4. Dias-Santagata D, Lam Q, Vernovsky K, Vena N, Lennerz JK, et al. (2011) BRAF V600E mutations are common in pleomorphic xanthoastrocytoma: diagnostic and therapeutic implications. PloS one 6: e17948.
5. Sosman JA, Kim KB, Schuchter L, Gonzalez R, Pavlick AC, et al. (2012) Survival in BRAF V600-mutant advanced melanoma treated with vemurafenib. New England Journal of Medicine 366: 707-714.
6. Chamberlain MC (2013) Salvage therapy with BRAF inhibitors for recurrent pleomorphic xanthoastrocytoma: a retrospective case series. Journal of neuro-oncology 114: 237-240.
7. Lee EQ, Ruland S, LeBoeuf NR, Wen PY, Santagata S (2016) Successful treatment of a progressive BRAF V600E-mutated anaplastic pleomorphic xanthoastrocytoma with vemurafenib monotherapy. Journal of Clinical Oncology 34: e87-e89.
8. Heakal Y, Kester M, Savage S (2011) Vemurafenib (PLX4032): an orally available inhibitor of mutated BRAF for the treatment of metastatic melanoma. Annals of Pharmacotherapy 45: 1399-1405.
9. Brown NF, Carter T, Mulholland P (2016) Dabrafenib in BRAFV600-mutated anaplastic pleomorphic xanthoastrocytoma. CNS oncology.