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Editorial

KV7 Potassium Channel Modulator BHV-7000: A Novel Therapy in the Treatment of Epilepsy and Other Neurological Disorders

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Epilepsy is a neurological disorder that arises due to abnormal electrical activity in the brain leading to unprovoked seizures. The cause for this abnormal electrical activity includes trauma, malformations, infection, drug toxicity etc. There are two major forms of epilepsy - generalised and focal epilepsy. Focal seizures constitute 60% of prevalence worldwide, making it the most common type of epilepsy.

Treatment of focal epilepsy depends on the cause and the specific area of the brain involved. There are multiple anti-epileptic drugs, surgical options, neurostimulation therapy, lifestyle modifications. But focal epilepsies are challenging to treat due to their unpredictability of relapse.

The new drug has been discovered BHV-7000 by the company Biohaven. It is a potent and selective activator of KV 7.2/7.3 potassium channels. These potassium channels are voltage dependent regulating the vascular smooth muscle contractility eventually modulating neuronal activity. They are also regulated by neurotransmitters like GABA and GABA-related endogenous metabolites β-hydroxybutyric acid (BHB) and γ-amino-β-hydroxybutyric acid (GABOB) [1].

The mutations in KV 7 potassium channels are involved in many neurological diseases like epilepsy, bipolar disorder, major depressive disorder, and rare diseases like neuromyelitis optica spectrum disorder (NMOSD), development and epileptic encephalopathy (DEE) etc [2]. Mutation in the gene KCNQ2 is linked with DEE and Benign Familial Neonatal Convulsions (BFNC) [3]. The selective activation mechanism of BHV-7000 is a novel therapy for such rare neurological disorders.

BHV-7000 is a selective activator of 7.2-7.3 members of KV7 channels. This drug has completed Phase 1 of clinical trial for epilepsy yielding the positive results minimal GABA receptor activation, no adverse CNS side effects, no impact on neurobehavior and motor behaviour. The results of the clinical trial have been summarized in table 1.

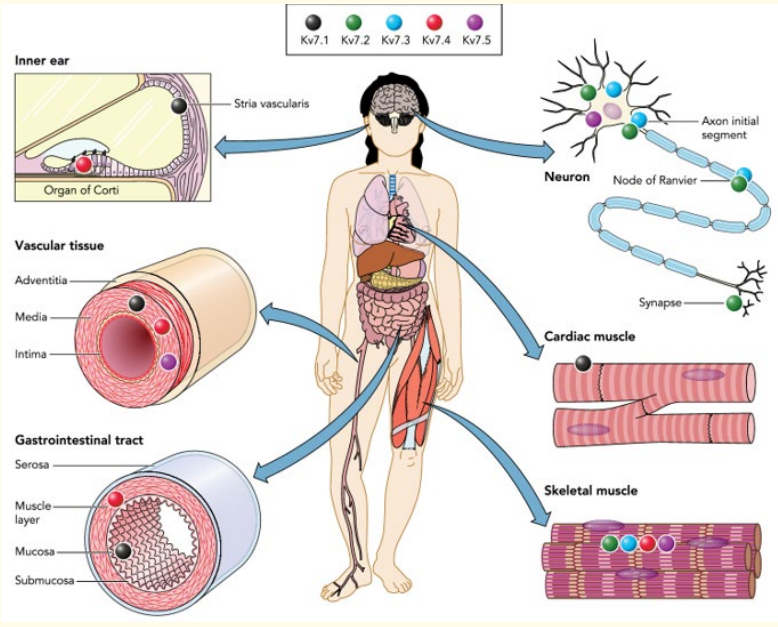

Figure 1: *Locations of KV7 channels in the body [Source: Soldovieri, Maria Virginia, Francesco Miceli and Maurizio Taglialatela. "Driving with no brakes: molecular pathophysiology of Kv7 potassium channels". Physiology 26 5 (2011): 365-76].*

Results of therapy BHV-7000 in Epilepsy Phase 1	Data assessment
Maximum efficacy	In children from 3-6 months to 5 years of age
Highest spectral power in EEG	Alpha, Beta and Gamma frequency bands
Major side effects	Headache, abdominal discomfort
Well tolerated single dose	100 mg for 15 days

Table 1: *Results of BHV7000 in clinical trial phase 1 for epilepsy.*

The results of the phase 1 clinical trial in epilepsy for BHV-7000 gives a hope for the treatment of multiple neurological disorders as KV7 channels are involved in multiple neurological disorders. The company has not yet given any idea for the cost which can be a limitation as this drug uses biotechnology and gene therapy. Nevertheless, this drug has potential to treat bipolar disorder, epilepsies, major depressive disorders, and other disorders that include the disrupted KV7 potassium channel.

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