Targeting Axl/EZH/Sox2 for glioblastoma multiform by novel biodegradable interstitial delivery system

The IND of Cerebraca® wafer has been approved by FDA for phase I/IIa. This clinical trial has been conducted at Tzu-Chi University Hospital in, Hualien, Taiwan

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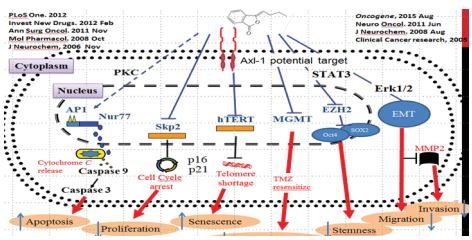
Targeting Cerebraca ® wafer, also known as BP/polymer wafer, is a biodegradable wafer for interstitial implantation comprises butylidenephthalide (BP; the active moiety; EF-001) and Carboxyphenoxypropane-Sebacic Acid Copolymer (CPPSA).



The anti-glioblastoma pharmacology effect of BP was identified in yellowish brown root of the plant Angelica sinensis, a well-known Chinese medicine. The antitumor effects of A. sinensis extracts were firstly evaluated in several human cancer cell lines, including a human glioblastoma multiform (GBM) cell line. These antitumor activity was suggested resulting from the effects of BP in suppression of telomerase level (Lin et al. 2011), up-regulation of nuclear receptor Nur77 (an apoptosis mediator) (Lin et al., 2008), reducing glioma migration and invasion mediated by Axl-1 tyrosine receptor (Yen et al., Oncogene, 2016) and tumor stem cell Sox-2 genes (unpublished data). More importantly, BP further showed the effects on reversing Temozolomide (TMZ) resistance by suppressing O6-methylguanine-DNA-methyltransferase (MGMT) mRNA and protein expression (Harn et al., 2013). Taken together, the targeting genes of BP are Axl/EZH2/SOX2, telomerase, DNA repair gene MGMT.

In order to overcome the limitation of blood-brain barrier, a local interstitial delivery system which BP incorporated into a biodegradable polyanhydride material CPPSA, namely, the BP/polymer wafer was applied. This novelty contributes the efficient effects on survival (2.44 time prolonged more than Gliadel® wafers).

At present, we have completed the project in a chemical manufacturing and control, preclinical efficacy and preclinical safety assessment and other tests. The IND of Cerebraca® wafer has been approved by FDA for phase I/IIa. This clinical trial will be conducted at Tzu-Chi University Hospital in, Hualien, Taiwan.

So far, we have finished cohort II six patients study. No safety issue is found. The first patient has been extending eleven months.

Biography

Horng-Jyh Harn, M.D. Ph.D current serves at the department of pathology at Tzu-Chi University as a professor and surgical pathologist and associate vice president, Bioinnovation Center, Tzu Chi foundation. He also owns PhD degree at pathology department of Duke University, Durham, USA (1987-1991). Previously, he was a professor in the Department of Pathology at the National Defense Medical Center, Taipei, Taiwan (1997-2002). He received his surgical pathology training at Tri-Service General Hospital, Taipei, Taiwan. He was appointed as a Director of Molecular Medicine, Tzu-Chi Buddhist General Hospital, Hualien, Taiwan; Chairman of Pathology, China medical university, Taichung, Taiwan. He is the author of over 120 original research articles and has been granted over 30 patents, both nationally and internationally. His main research interesting fields are molecular biology, tumor oncology, stem cell research and new drug development against neurological disease.

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