

CANCER THERAPY AND ONCOLOGY

&

NEUROLOGY AND BRAIN DISORDERS

June 21 - 22, 2018 | Osaka, Japan

Allied J Med Res 2018, Volume 2

PHASE I/IIA TRIALS IN GBM PATIENTS USING A NEW DRUG (CEREBRACA WAFER) TARGETING AXL RECEPTOR TYROSINE KINASE

Shinn Zong (John) Lin

Hualien Tzu Chi Hospital, Taiwan

Malignant brain glioma is a highly invasive disease with a very high death rate. The effective treatment method for this disease is still an unmet medical need. In our previous reports, a pure compound EF-001 showed activities to arrest the growth and initiate apoptosis of malignant brain glioma. To overcome the limitation of the blood-brain barrier, a local-release system with EF-001 incorporated into a biodegradable polyanhydride material, p(CPP-SA), was developed and named "Cerebraca Wafer". Both the *in vitro* and the *in vivo* release kinetics of the Cerebraca Wafers have been characterized. The *in situ* therapeutic effects of the Cerebraca Wafer on brain gliomas were demonstrated by FGF-SV40 transgenic mice and orthotopic brain tumor F344 rat models. Significant effects on the inhibition of tumor growth and the increase of survival rate by Cerebraca Wafer implantations were observed, with no significant adverse effects on the rodents. Mechanisms involved in the antitumor effect of EF-001, downstream of AXL receptor tyrosine kinase, including the up-regulation of Nurr77 by PKC, the repression of human telomerase reverse transcriptase (hTERT) transcriptional activity via down-regulating Sp1 expression, and the down-regulation of the S-phase kinase-associated protein 2 (Skp2) which resulted in the brain tumor senescence, were also investigated in the study. The toxicity studies and the PIC/s GMP grade Cerebraca Wafer production for clinical trials were accomplished. IND (investigational New Drug) application for the Phase I/IIa clinical trials aiming to determine the safety and the efficacy of Cerebraca Wafer implantation on the recurrent GBM patients have been approved by USFDA and TFDA at 2016. The trial is now being performed at Hualien Tzu-Chi hospital and Tri-Service General hospital, with the first Wafer implantation surgery completed at the end of 2017. The preliminary results for the first three trial patients will be presented and discussed.

shinnzong@yahoo.com.tw