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NEO212: A new drug for Temozolomide resistant malignant gliomas

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Although the alkylating agent temozolomide (TMZ) has become the standard of care in the treatment of malignant gliomas, its overall efficacy is still limited by development of drug resistance, limited blood brain barrier (BBB) penetrance and myelotoxicity. Recently, we have synthesized a TMZ analog by covalently linking the monoterpene perillyl alcohol (POH) to TMZ via a carbamate bond. This new compound (NEO212) has been tested in TMZ resistant malignant gliomas. U251 and U87 TMZ resistant gliomas were tested and implanted intracranially for *in vivo* model. NEO212 was administered subcutaneously using 10 day treatment, 7 day rest cycles; no significant toxicity on normal astrocytes and brain endothelial cells were detected. NEO212 revealed considerably greater therapeutic efficacy than TMZ, where a single cycle of treatment (10 days) extended median survival benefit from 6 days (in the case of TMZ) to 24 days with good tolerance. Pharmacokinetic analysis demonstrated that NEO212 has at least three times the brain concentration compared to TMZ when both agents are administered subcutaneously. Formal toxicity studies conducted at Charles Rivers (Montreal, Canada) demonstrated that it can be safely tolerated in both acute and chronic administration studies (up to 250 mg/kg). Long term toxicity appears to be myelotoxicity. NEO212 appears to be a promising well tolerated new agent with similar mechanism of cytotoxicity to TMZ. Its increased potency is most likely multi-factorial increased DNA damage, involving a broader scope of DNA repair mechanisms, linkage with POH, resulting in longer biological half-life and stability, increased lipophilicity, allowing for better penetration of the BBB and possibly cell membrane. This talk will emphasize the bench to bedside development in taking this drug to IND status.

Biography

Thomas C Chen has founded NEONC Technologies, Inc., in 2008 and serves as its Chairman, Chief Executive Officer and Chief Scientific Officer. He is an Executive Director at Cognos Therapeutics Inc., Co-Founder of Pharmaco-Kinesis Corporation and serves as its Chief Oncology Officer. He serves as a Scientific Advisor, Scientific Collaborator at Tocagen Inc. He serves as an Associate Professor of Neurological Surgery and Pathology at the University of Southern California (USC), Principal Investigator of an Independent Laboratory and Head of the Glioma Research Group at USC. He also serves as the Director of Surgical Neuro-Oncology at USC. He is a Member of Neurological Board, Member of Clinical Advisory Board at Magnetecs Corporation. He is a Physician and a board certified Neurosurgeon. He holds an MD from the University of California San Francisco, completed his Neurological Surgery Residency and PhD in Pathobiology at the University of Southern California. He has obtained Fellowship training in Spinal Surgery from the Medical College of Wisconsin and was graduated from the University of Illinois at Urbana-Champaign. He holds a Bronze Tablet Honors from University of Illinois at Urbana-Champaign and was inducted into the Phi Beta Kappa national academic honor society.

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