Title

A RANDOMIZED PHASE II TRIAL TO COMPARE THE EFFICACY OF STANDARD VERSUS COMBINATION THERAPY (PERAMPANEL, MEMANTINE PLUS STANDARD) IN THE TREATMENT OF PATIENTS WITH NEWLY DIAGNOSED GBM-A STUDY DESIGN

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Abstracts

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BACKGROUND: Glioblastoma (GBM) is the most aggressive malignant brain tumor in adults with poor prognosis. Effective treatment is urgently needed. Recent studies demonstrated neurogliomal synaptic communication through AMPA and NMDA receptors promotes glioma invasion and progression in vitro and in vivo. Therefore, dual blocking AMPA and NMDA receptor therapy is a potential enhancing strategy to prevent and to treat GBM progression given the two blockers act through different anti-glioma mechanisms. OBJECTIVE/HYPOTHESIS: We hypothesize that adding AMPA blocker Perampanel (An anti-seizure medication) and NMDA blocker Memantine (An anti-dementia medication) to standard temozolomide plus radiation therapy (Stupp's regimen) for the treatment of newly diagnosed GBM may prevent tumor progression. It may also reduce the frequency of onset/recurrence of seizure episodes and possibly improve radiation related cognition impairment. STUDY DESIGN: This is a randomized, active controlled, open label, two arm phase II study of efficacy of treatment of GBM with combination therapy (dual AMPA and NMDA receptor blockers plus standard therapy) versus standard therapy. In the combination therapy arm, patients take Perampanel 2 mg daily and Memantine 5 mg bid, starting from -14 days to +14 days from initiation of concurrent chemo-radiation therapy. Titrating up at a 2 mg increment for Perampanel and 5 mg bid increment for Memantine until reaching MTD. If the patient has AE >= grade 2, then reduce doses at a decrement of 2 mg for Perampanel and decrement of 5 mg bid for Memantine. In the standard therapy arm, the patients are treated with Stupp's regimen. PRIMARY AND SECONDARY ENDPOINTS: PFS, 12, 24 month survival rates and response duration. Safety will be assessed by CTCAE V5. We will use Kaplan-Meier estimates for survival data and a stratified log-rank test for the randomization strata.