

## **Title: Combinatorial Study of Vorapaxar and Phenyl Derivative Targeting GPR17 Receptor in Glioblastoma Multiforme Cells**

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### **Abstract**

Glioblastoma is a highly aggressive 4th grade brain tumor characterized by poor prognosis and limited treatment options. This study investigates the combinatorial effects of Vorapaxar, an FDA-approved selective antagonist of the protease-activated receptor-1 (PAR-1), and phenyl derivative (T0), a novel compound targeting the GPR17 receptor, on glioblastoma multiforme (GBM) cells. The objective of this research is to evaluate the synergistic potential of Vorapaxar and T0 in inhibiting progression and inducing apoptosis in GBM cell lines. We assessed the cytotoxic effects of the drug combination at various concentrations by using cell death assay and determined the Combination Index (CI) and Drug Resistance Index (DRI) to evaluate the nature of their interaction and the minimum effective dose to minimize any possible adverse effect of the both drugs. Our findings demonstrate that the Vorapaxar and T0 combination exhibits significant synergistic effects, particularly at higher concentrations. This study highlights the potential of targeting GPR17 in conjunction with PAR-1 inhibition as a promising therapeutic strategy for enhancing the efficacy of glioblastoma treatment.