Phase II study of tivozanib, an oral VEGFR inhibitor, in patients with recurrent glioblastoma.

BACKGROUND: Tivozanib, an oral, pure VEGFR tyrosine kinase inhibitor is an anti-angiogenesis drug which aims to modulate the tumor blood supply. This phase II study was designed to test the effectiveness of oral tivozanib in patients with recurrent glioblastoma.

METHODS: Ten adult patients with recurrent glioblastoma, median age of 62 (range 51-73), were enrolled and treated with tivozanib 1.5mg daily, 3 weeks on/1 week off in 28 day cycles. Brain MRI was done at baseline and after each cycle. The enhancing tumor and surrounding area of abnormal FLAIR hyperintensity were outlined and median tumor CBF and CBV were derived from dynamic susceptibility contrast MRI to assess the performance of tivozanib. Vessel architectural imaging (VAI) was used to measure tissue oxygen saturation. A t-test was used to compare baseline MRI parameters to the pre-cycle 3 visit. A univariate Cox model was used to test the association of each MRI parameter with time to progression.

RESULTS: Best MacDonald criteria responses were: CR (1), PR (1), SD (4), PD (4) and the median duration of response was only 3.6 mo (1.7-3.8mo). One patient was taken off study for unacceptable skin toxicity and nine patients were taken off study for progressive disease. Given the dropout rate, only data up to cycle 3 was included in this analysis. There was no statistically significant change in enhancing tumor volume (p=0.70), FLAIR volume (p=0.31), or median CBV (p=0.13) or median CBF (p=0.54) within the enhancing tumor. Within the FLAIR hyperintensity, median CBV (p=0.12) and median CBF (p=0.41) also did not change significantly. No parameter was associated with time to tumor progression. VAI showed no change in tissue oxygenation.

CONCLUSION: Tivozanib was well tolerated but most patients progressed rapidly. The majority of patients had little change in tumor enhancement and perfusion imaging demonstrated insignificant changes in tumor and peritumoral blood volume, flow, and oxygenation suggesting that this anti-angiogenic agent had limited impact on brain tumor vasculature.

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