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Using a Pre-Radiation Window to Identify Potentially Active Cytotoxic Agents in Adults with Newly Diagnosed Glioblastoma

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Abstract

Background: Therapies shown to improve outcomes in patients with recurrent cancers are commonly used in the neoadjuvant setting to optimize surgery, reduce radiation fields, and treat micro-metastatic disease. While pre-radiation chemotherapy (PRC) use has flourished in systemic cancers, it has not in glioblastomas. This review documents these trajectories and highlights the potential of PRC to rapidly and safely screen cytotoxic drugs for efficacy in patients with newly diagnosed glioblastoma.

Methods: Prospective trials of adults with newly diagnosed systemic and brain cancers treated with PRC published between 1980 and 2023 were identified in PubMed. NCCN guidelines were used to document the standard use of PRC in patients with systemic and brain cancers.

Results: Over 5,000 prospective PRC trials in solid tumors were identified. These accrued >1 million patients and resulted in neoadjuvant therapies being standard-of-care in ~28 systemic cancers. Only 50 similar trials (2,206 patients) were identified in high grade gliomas. In 13 trials containing PRC temozolomide (n=846), radiographic responses ranged from 6-53% with a median survival of ~13 months. Glioblastoma PRC trials were not associated with unexpected toxicities or major negative impacts on survival.

Conclusions: PRC in patients with glioblastoma appears safe and feasible. The pre-radiation window is ideally suited to rapidly screen cytotoxic agents for efficacy. It permits radiographic response as a primary outcome, small sample sizes, and initiation of standard therapies a few months after diagnosis. PRC may be most appropriate in patients with glioblastoma who are unlikely to benefit from temozolomide.

Keywords: glioblastoma; high grade glioma; neoadjuvant chemotherapy; pre-radiation; solid tumors.