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Neoadjuvant clinical trials in adults with newly diagnosed high-grade glioma: A systematic review

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Abstract

Background: High-grade gliomas are devastating cancers that remain incurable with standard surgical resection and radiochemotherapy. Although beneficial against neoplasms, radiation lowers lymphocyte counts, weakens immune activation, and recruits suppressive myeloid cells impairing immune responses. Tumor environments treated with radiation experience long-term immunosuppression, reducing immunotherapy effectiveness and contributing to recurrence. Investigating pre-radiation treatments in newly diagnosed patients could identify active agents, assess immunotherapy impact, and enable multiomic analyses without radiation-induced confounding factors. This literature review was conducted to describe the feasibility, safety, and outcomes of postsurgical, pre-radiation clinical trials for adults with newly diagnosed high-grade glioma.

Methods: A systematic review was performed of the English-language literature reporting results of clinical trials for adults with newly diagnosed high-grade glioma administered postsurgical treatment prior to radiation therapy. A search was conducted in PubMed and references cited in research and review articles were also considered.

Results: From 1991 to 2024, 52 clinical trials were identified: 3 phase I, 38 phase II, 4 phase III, and 7 of unknown phase. Nine trials were randomized, 24 were multicenter trials, 21 investigated temozolomide-containing regimens, and 12 focused on inoperable tumors, involving a total of 2737 patients.

Conclusion: Pre-radiation neoadjuvant studies are feasible and may identify active drugs. This is particularly relevant in the era of personalized medicine with brain-penetrant drugs, targeted therapy, and immuno-oncology advancements. Investigating pre-radiation treatments in newly diagnosed high-grade glioma is a viable approach to rapidly identify active and inactive regimens while the immune system and tumor microenvironment remain intact.

Keywords: Clinical trial; Glioma; Neoadjuvant; Preradiation.