

Resident Scholarly Project

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Title of Project:

Meta-analysis on the overall survival rate of pediatric patients when using various chemotherapeutic regimens compared to radiotherapy alone when treating high-grade gliomas (HGG).

Study Purpose and Rationale:

In the pediatric population, HGG comprises approximately 8–12% of all primary CNS tumors. However, HGG in children are due to an aggressive clinical behavior profile and are classified as either grade III or IV and they account for a significant amount of morbidity and mortality among children with brain tumors. Despite numerous treatment approaches, outcomes have remained dismal, with most series showing 5-year survival outcomes ranging from 15 to 35% and the far majority of children unfortunately succumb to their disease. Most oncologists agree that a gross total resection (GTR) followed by focal irradiation to the tumor bed plus additional chemotherapy is an appropriate treatment approach. In the CCG-943 trial, children with newly diagnosed HGG were randomized to receive either focal radiation therapy alone or the same radiotherapy with a combination of concomitant and maintenance chemotherapy. Five-year survival was 46% in the chemotherapy treated group versus 17% in the radiation-only group which was a statistically significant difference ($p < 0.05$); however, a central pathology review performed many years later revealed that many of the patients included in this study harbored low-grade gliomas (LGG). Despite a few publications reporting the additional benefit of chemotherapy to survival as compared to radiation therapy alone, its exact role and true survival benefit remain disputed. The aim of this study is to perform a meta-analysis on the overall survival rate of the various chemotherapeutic regimens when compared to radiotherapy alone.

Methodology:

Performed a literature review in PubMed using phrases ‘pediatric high grade gliomas’, ‘anaplastic astrocytoma’ and ‘glioblastoma’ to compile a list of randomized control trials comparing radiotherapy alone to the various chemotherapy regimens. Compared the overall survival rate and the event free rate between the various chemotherapy regimens.

Inclusion Criteria:

Study is focused on the pediatric population with participants ages ranging 0 – 25. Additionally pathology should be performed after gross total resection to confirm the presence of high-grade glioma (HGG) vs low-grade glioma.

Statistical Analysis

Power Analysis

The 5-year overall survival rate (SR) was 17% in the radiotherapy-only group as found in the CCG-943 trial. A power analysis was conducted setting the N for group 1 as 30, with 30 being the number of subjects randomized to radiotherapy alone, and the group 1 proportion was set as 0.17. Coupled with the knowledge that N2 will be at least 3 times greater than N1, the power analysis reflects that a 5-year SR of $\geq 45\%$ in the chemotherapy regimens will be statistically significant assuming a p value of < 0.05 .

Statistical Methods

Statistical analysis will be conducted using Microsoft Excel and R. We will compare the overall survival rate between various chemotherapy regimens by reconstructing Kaplan Meier Curves and Cox Proportional Hazards Modeling from data used in the studies. We will assume a p value of < 0.05 for statistical significance.

Study Drugs: Not Applicable

Medical Device: Not Applicable

Confidentiality of Study Data: The participants in the various studies are anonymous to the data collectors.

Potential Conflict of Interest: No conflict of interest to declare

Potential Risks: None identified.

Potential Benefits:

Information collected could guide oncologists about the risk and benefits of various chemotherapy regimens when treating high-grade glioma (HGG).

References:

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2. Broniscer A., Gajjar A. (2004). Supratentorial high-grade astrocytoma and diffuse brainstem glioma: two challenges for the pediatric oncologist. *Oncologist* 9 197–206
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