Combination Therapy for the Treatment of Central Nervous System Malignancies: Clinical Effectiveness and Guidelines
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About CADTH: CADTH is an independent, not-for-profit organization responsible for providing Canada’s health care decision-makers with objective evidence to help make informed decisions about the optimal use of drugs, medical devices, diagnostics, and procedures in our health care system.

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Research Questions

1. What is the clinical effectiveness of combination therapy for the treatment of patients with central nervous system malignancies?

2. What are the evidence-based guidelines associated with the use of combination therapy for the treatment of patients with central nervous system malignancies?

Key Findings

Three non-randomized studies were identified regarding combination therapy for the treatment of central nervous system malignancies.

Methods

A limited literature search was conducted on key resources including PubMed, the Cochrane Library, University of York Centre for Reviews and Dissemination (CRD) databases, Canadian and major international health technology agencies, as well as a focused Internet search. No filters were applied to limit the retrieval by study type. Where possible, retrieval was limited to the human population. The search was also limited to English language documents published between January 1, 2014 and January 25, 2019. Internet links were provided, where available.

Selection Criteria

One reviewer screened citations and selected studies based on the inclusion criteria presented in Table 1.

Table 1: Selection Criteria

<table>
<thead>
<tr>
<th>Population</th>
<th>Patients (adults and children) with a CNS malignancy (e.g., gliomatosis cerebri, meningioma, glioblastoma, glioma, astrocytoma, neuroblastoma)</th>
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</thead>
<tbody>
<tr>
<td>Intervention</td>
<td>Either combined with each other (in groups of two or more) or with standard of care (e.g., conventional chemotherapy).</td>
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<td>- Dimethyl sulfoxide (DMSO);</td>
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<td>- Hyperthermia (any variant, including electric and magnetic);</td>
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<td>- Sonodynamic therapy;</td>
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<td></td>
<td>- Laser therapy;</td>
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<td>- Rife therapy;</td>
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<td>- Biomagnetic therapy</td>
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<tr>
<td>Comparator</td>
<td>Q1: Any comparator; No comparator</td>
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<td></td>
<td>Q2: No comparator</td>
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<tr>
<td>Outcomes</td>
<td>Q1: Clinical effectiveness (e.g., progression-free survival, response rate, change in tumour size, overall survival, quality of life) and safety (e.g., toxicity, adverse events, discontinuation)</td>
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<td>Q2: Guidelines</td>
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<tr>
<td>Study Designs</td>
<td>Health technology assessments, systematic reviews, meta-analyses, randomized controlled trials, non-randomized studies, evidence-based guidelines</td>
</tr>
</tbody>
</table>
Results

Rapid Response reports are organized so that the higher quality evidence is presented first. Therefore, health technology assessment reports, systematic reviews, and meta-analyses are presented first. These are followed by randomized controlled trials, non-randomized studies, and evidence-based guidelines.

Three non-randomized studies were identified regarding combination therapies for central nervous system malignancies. No relevant health technology assessments, systematic reviews, meta-analyses, randomized controlled trials, or evidence-based guidelines were identified.

Additional references of potential interest are provided in the appendix.

Overall Summary of Findings

Three non-randomized studies were identified regarding combination therapies for central nervous system (CNS) malignancies.\(^1\)\(^-\)\(^3\) Each study utilized a varying combination of therapies for CNS cancers. The authors of the first study investigated the safety of using radiation and laser therapy in patients with brain tumours.\(^1\) They observed that laser interstitial thermal therapy in combination with radiation therapy can induce cerebral edema (a safety issue) and thus prolong cancer treatment.\(^3\) In a minority of cases, patients may require more aggressive treatment such as drug therapy.\(^1\) The authors of the second study\(^2\) investigated the efficacy of radiation therapy with hyperthermia for patients with high grade gliomas and observed that combination therapy of radiation and hyperthermia was safe and well-tolerated. In the third study\(^3\) the authors investigated the efficacy and cost-effectiveness of modulated electrohyperthermia in combination with chemotherapy treatment. Their effect-to-treatment analysis found that patient survival significantly improved after receiving the combination therapy in a regimen of 21 out of 28 days.\(^3\)

No evidence-based guidelines were identified; therefore, no summary can be provided.

References Summarized

Health Technology Assessments

No literature identified.

Systematic Reviews and Meta-analyses

No literature identified.

Randomized Controlled Trials

No literature identified.
Non-Randomized Studies

Radiation and Laser Therapy


Radiation and Hyperthermia


Chemotherapy and Hyperthermia


Guidelines and Recommendations

No literature identified.
Appendix — Further Information

Previous CADTH Reports


Non-Randomized Studies

*Radiation and Hyperthermia*

**Case Series**

PubMed: PM30506500

*Chemotherapy and Laser Therapy*

**Case Series**

PubMed: PM29933086

*High Intensity Focused Ultrasound – Uncertain if Combined with Another Therapy*

**Alternative Population – Mixture of Cancer Types**

PubMed: PM27199087

**Alternative Outcome**

PubMed: PM26910903

**Review Articles**


Additional References

**Laser Therapy – Uncertain if Combined with Another Therapy Modality**


**Radiation and Hyperthermia**

**Mathematical Models**