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## Adjuvant Systemic Chemotherapy, Following Surgery and External Beam Radiotherapy, for Adults with Newly Diagnosed Malignant Glioma Practice Guideline Report #9-2

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ORIGINAL GUIDELINE: March 10, 2004  
MOST RECENT LITERATURE SEARCH: June 2004  
NEW EVIDENCE ADDED TO GUIDELINE REPORT: June 2004  
RECOMMENDATIONS MODIFIED: June 2004

Based on new evidence that has emerged since completion of the original guideline, the Neuro-oncology Disease Site Group has modified this practice guideline report. The revised recommendations and supporting evidence are labelled **Update**.

### SUMMARY

#### Guideline Question

Should chemotherapy be recommended, following surgery and external beam radiotherapy, to adults with newly diagnosed malignant glioma in order to improve overall survival and/or quality of life?

#### Target Population

These recommendations apply to adults with newly diagnosed malignant glioma who have undergone surgery and external beam radiotherapy.

#### Recommendations

- **Update**  
The use of concurrent temozolomide during radiation therapy and postradiation adjuvant temozolomide is recommended for all patients with newly diagnosed glioblastoma multiforme who are fit for radical therapy. Temozolomide should be considered in patients with malignant gliomas.
- Younger patients, patients with anaplastic (grade 3) astrocytoma, and patients with pure or mixed oligodendroglioma, are more likely to harbour chemosensitive tumours, and adjuvant chemotherapy may be an option in these cases. However, there is no evidence of a survival advantage from adjuvant chemotherapy in these patients, and treatment-related adverse effects and their impact upon quality of life are poorly studied.
- Patients should be provided with information about the controversies surrounding the benefit and optimal timing of such treatment.

## Qualifying Statements

- This guideline considers chemotherapy in the adjuvant setting only and should not discourage the consideration of chemotherapy for selected patients at the time of tumour progression or in the context of clinical trials evaluating new treatment regimens at any point in the disease.
- **Update**  
The recommendation regarding the use of adjuvant temozolomide is based on abstract data from one randomized trial. There may be subgroups of patients who will benefit more or less from adjuvant temozolomide; thus the Neuro-oncology Disease Site Group will revise their recommendations as necessary as subgroup data emerges.

## Methods

Entries to MEDLINE (1966 to June 2004), EMBASE (1980 to week 25, 2004), CANCERLIT (1983 to October 2002), and the Cochrane Library (2004, Issue 2) databases and abstracts published in the proceedings of the annual meetings of the American Society of Clinical Oncology (1997 to 2004) were systematically searched for evidence relevant to this practice guideline report.

Evidence was selected and reviewed by members of the Practice Guidelines Initiative's Neuro-oncology Disease Site Group and methodologists. This practice guideline report has been reviewed and approved by the Neuro-oncology Disease Site Group, which is comprised of neuro-oncologists, neurosurgeons, radiation oncologists, medical oncologists, an oncology nurse, and a patient representative.

External review by Ontario practitioners is obtained for all practice guidelines through a mailed survey. Final approval of the practice guideline report is obtained from the Practice Guidelines Coordinating Committee.

The Practice Guidelines Initiative has a formal standardized process to ensure the currency of each guideline report. This process consists of the periodic review and evaluation of the scientific literature and, where appropriate, integration of this literature with the original guideline information.

## Key Evidence

- Twenty-four heterogeneous randomized controlled trials, and two meta-analyses incorporating some of these trials, variably detected either no advantage or a small survival advantage in favour of adjuvant chemotherapy. These studies often did not consider quality of life as an outcome variable. The most contemporary and largest trial reported a slight survival advantage in favour of adjuvant chemotherapy compared with no-chemotherapy controls in patients with anaplastic astrocytoma or glioblastoma.
- **Update**  
One randomized controlled trial (abstract) randomized 573 patients with newly diagnosed glioblastoma multiforme to receive either temozolomide and radiation therapy or radiation therapy alone. The trial reported a significant improvement in median progression-free survival, overall survival, and two-year survival in the patients receiving temozolomide with radiation therapy compared to those receiving radiation therapy alone ( $p < 0.001$ ). There was a three month difference in median overall survival between the treatment arms (15 months for patients treated with temozolomide and radiation therapy versus 12 months for patients treated with radiation therapy alone).

## **Future Research**

- Planned and ongoing therapeutic and clinical-molecular correlative studies with quality-of-life outcomes may clarify the role of chemotherapy in the subgroups of patients most likely to benefit from treatment. Participation in these trials is encouraged.

*For further information about this evidence summary report, please contact*

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## **PREAMBLE: About Our Practice Guideline Reports**

The Practice Guidelines Initiative (PGI) is a project supported by Cancer Care Ontario (CCO) and the Ontario Ministry of Health and Long-Term Care, as part of the Program in Evidence-based Care. The purpose of the Program is to improve outcomes for cancer patients, to assist practitioners to apply the best available research evidence to clinical decisions, and to promote responsible use of health care resources. The core activity of the Program is the development of practice guidelines by multidisciplinary Disease Site Groups of the PGI using the methodology of the Practice Guidelines Development Cycle.<sup>1</sup> The resulting practice guideline reports are convenient and up-to-date sources of the best available evidence on clinical topics, developed through systematic reviews, evidence synthesis, and input from a broad community of practitioners. They are intended to promote evidence-based practice.

This practice guideline report has been formally approved by the Practice Guidelines Coordinating Committee, whose membership includes oncologists, other health providers, patient representatives, and CCO executives. Formal approval of a practice guideline by the Coordinating Committee does not necessarily mean that the practice guideline has been adopted as a practice policy of CCO. The decision to adopt a practice guideline as a practice policy rests with each regional cancer network that is expected to consult with relevant stakeholders, including CCO.

### Reference:

<sup>1</sup> Browman GP, Levine MN, Mohide EA, Hayward RSA, Pritchard KI, Gafni A, et al. The practice guidelines development cycle: a conceptual tool for practice guidelines development and implementation. *J Clin Oncol* 1995;13(2):502-12.

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