



# **Glioblastoma**

## **Clinical Practice Guideline**

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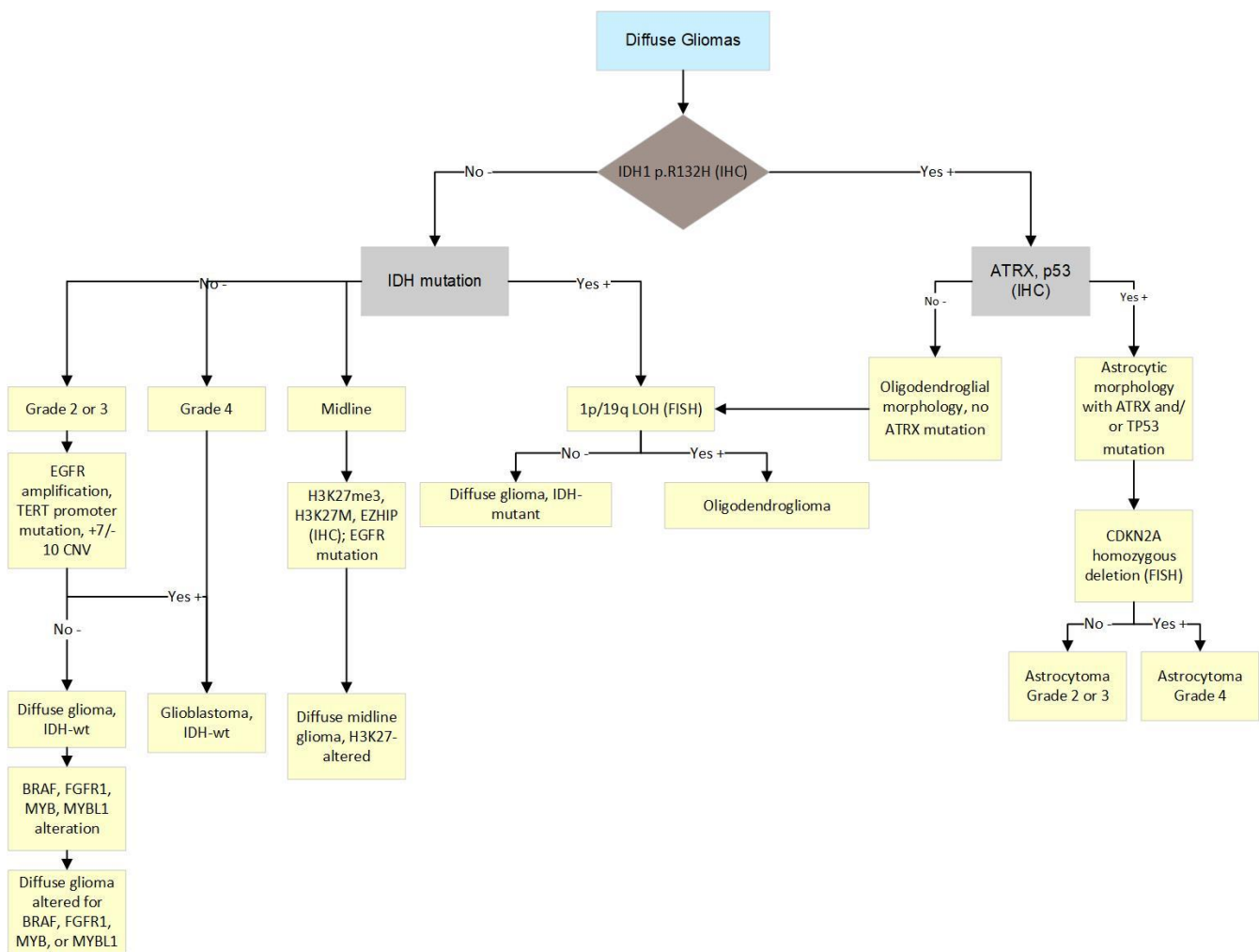
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*Disclaimer: Clinicians applying these guidelines should, in consultation with the patient, use independent medical judgment in the context of individual clinical circumstances to direct care. Visit the [Outpatient Cancer Drug Benefit Program](#) for up-to-date information on approved drugs for cancer patients in Alberta.*

## Background

Glioblastoma is the most common and aggressive primary malignant brain tumour.<sup>1</sup> It accounts for approximately 40% of all malignant central nervous system (CNS) tumours and 12–15% of all intracranial tumours, including both benign and malignant types. GBM represents 50–60% of astrocytic tumours, with a median age of onset between 55 and 60 years.<sup>2</sup> Its incidence increases significantly with age, particularly in patients over 60, and it is more common in men than women. According to the Brain Tumour Registry of Canada, the incidence of glioblastoma is approximately 4 per 100,000 people. Despite recent advances in treatment, the prognosis remains poor. The 2021 World Health Organization (WHO) classification of CNS tumours incorporates molecular features along with histology and traditional grading to provide a comprehensive diagnostic framework.<sup>3</sup> In its 5th edition, glioblastoma is classified as a distinct entity—IDH-wildtype, CNS WHO grade 4—based on its unique molecular and histopathologic characteristics.<sup>4</sup> Table 1 outlines the associated grades and histologic features of diffuse gliomas.

**Table 1. Molecular classification of Diffuse Gliomas<sup>3,4</sup>**



## Guideline Questions

1. Is resection better than biopsy for patients with glioblastoma?
2. Is adjuvant chemotherapy beneficial for patients with glioblastoma?
3. Is adjuvant chemotherapy of benefit to elderly patients with glioblastoma?
4. What is the optimal radiation therapy plan for patients with glioblastoma?
5. Is adjuvant radiation of benefit to elderly patients with glioblastoma?

## Target Population

The following recommendations apply to adult cancer patients with Glioblastoma cancer. Different principles may apply to pediatric patients.

## Recommendations

1. Surgery is the initial recommended approach for both debulking and obtaining tissue for diagnosis. Whenever possible, maximal safe resection is preferred in the management of GBM. A larger resection after initial biopsy is left to the discretion of the surgeon depending on the location of tumour and other factors. *(Level of evidence: I, Strength of recommendation: A)*<sup>9-12</sup>
2. To avoid interpretation of postoperative changes as residual enhancing disease, a baseline MRI scan should ideally be obtained within 24-48 hours of surgery and no later than 72 hours after surgery. *(Level of evidence: I, Strength of recommendation: A)*<sup>6,9</sup>
3. Adjuvant chemo-radiation therapy is considered the standard of care following surgery for patients with newly diagnosed GBM who are fit and up to 65 years old. Whenever possible, surgery should be followed by radiotherapy and concurrent temozolomide chemotherapy, followed by six cycles of adjuvant temozolomide. *(Level of evidence: I, Strength of recommendation: B)*<sup>6,8,9</sup>
4. External beam radiation therapy should be given in standard fractionation to a maximum total dose of 60Gy using 3D conformal planning techniques for patients under the age of 65 years. There is no strong evidence to recommend a total dose greater than 60 Gy in standard fractionation, and alternative fractionation schedules have not proven to improve survival outcomes. *(Level of evidence: I, Strength of recommendation: B)*<sup>5-8</sup>
5. For non-elderly fit patients with MGMT promoter-methylated tumors, an alternative treatment option is the combination of lomustine and temozolomide with radiotherapy, as evaluated in the CeTeG/NOA-09 trial. However, treatment options at recurrence remain limited following failure of this regimen. *(Level of evidence: III, Strength of recommendation: D)*<sup>6,9,13</sup>
6. For older patients (≥65 years old) with a good performance status (ECOG 0 to 2) and without serious comorbidity, short-course radiation (40 Gy in 15 fractions) with concurrent and adjuvant temozolomide is recommended. Patients with a methylated MGMT promoter will likely derive the most benefit from this treatment. *(Level of evidence: II, Strength of recommendation: C)*<sup>5,7,14</sup>

7. For patients over the age of 70 being treated without temozolomide, lower-dose radiation therapy regimens such as 25 Gy in 5 fractions or 40 Gy in 15 fractions are appropriate.<sup>8</sup> For those aged 65 to 70, either standard dosing (60 Gy) or hypofractionated schedules may be considered, depending on performance status. *(Level of evidence: I, Strength of recommendation: A)*<sup>7,9</sup>
8. Determination of MGMT promoter methylation status may assist in determination of prognosis. MGMT promoter methylation is both predictive of response to temozolomide and prognostic.<sup>5,7</sup>
9. For elderly patients and/or those with poor performance status, consideration may be given to adjuvant radiation therapy alone (MGMT unmethylated), temozolomide alone (MGMT methylated) or best supportive care. *(Level of evidence: II, Strength of recommendation: C)*<sup>5,7</sup>
10. Tumor Treating Fields (TTFields) is a form of non-invasive, non-ionizing treatment modality that may be offered to patients with newly diagnosed glioblastoma in combination with monthly cycle of temozolomides following maximal surgical resection and completion of radiation therapy. Patients with MGMT methylated glioblastoma may derive greater benefit from TTFields therapy. *While it is Health Canada-approved, it is currently not funded or in use within the province. (Level of evidence: II, Strength of recommendation: B)*<sup>15,16</sup>

## Recurrent Disease

11. There is no established standard of care for patients with recurrent disease; treatment options such as resection, radiation therapy, or chemotherapy should be considered on a case-by-case basis, ideally through discussion at a multidisciplinary tumour board to determine the most appropriate approach for each patient.
12. Whenever possible, patients with IDH wild-type glioblastoma should be encouraged to participate in ongoing clinical trials. Up-to-date information on trials offered in Alberta is available on the Alberta Cancer Clinical Trials website.

## Discussion

### Surgical Resection

Although prospective, randomized trials addressing surgery for GBM are lacking, there is a consensus among the published clinical practice guidelines that surgical resection is the main treatment for alleviation of symptoms and prolongation of life in patients with GBM. Members of the Alberta Provincial CNS Tumour Team therefore recommend surgery as the initial approach for both debulking and obtaining of tissue for diagnosis. Several small studies and retrospective analyses have addressed the impact of biopsy versus surgical resection on overall survival in patients with high grade gliomas. *Hart et al.* recently conducted a comprehensive and systematic search of the literature to address whether surgical resection was superior to biopsy for high-grade gliomas.<sup>12</sup> They identified only one randomized phase III trial, published by *Vuorinen et al.*,<sup>11</sup> which met their search criteria. Although many of the other studies they identified did report a survival advantage for resection over biopsy, *Hart et al.* suggested that these studies be interpreted with caution as most were not designed to answer this question, were underpowered, and had methodological flaws.

### Postoperative Imaging

Prognosis, evaluation of response to treatment, and decisions about further therapy depend on a correct assessment of the extent of residual tumour after resection. Benign enhancement following surgery (due to hypervascularization and disruption of the blood-brain barrier during scar formation) can make it more difficult to detect residual tumour in post-operative imaging. *Albert et al.* were first to establish a diagnostic window of 72 hours where any contrast enhancement should reflect residual glioma only.<sup>17</sup> This time frame has since been supported by multiple MRI studies, with several suggesting a shorter window if possible. *Bette et al.* found 34.1% of cases imaged more than 45 hours after surgery showed reactive enhancement, while 17.9% of cases imaged within 45 hours showed reactive enhancement ( $p=0.02$ ). Current guidelines recommend a post-operative brain MRI within 24-72 hours of surgery to determine avoid interpretation of postoperative changes as residual enhancing disease and to be used as a baseline for future therapeutic efficacy and tumour progression.<sup>5,9</sup> Consistent with these guidelines, the Alberta Provincial CNS Tumour Team recommends that a baseline MRI scan should ideally be obtained within 24-48 hours of surgery and no later than 72 hours after surgery.

### Adjuvant Treatment

Adjuvant chemo-radiation therapy is considered the standard of care following surgery for patients with newly diagnosed GBM.

**Radiation Therapy:** Radiation therapy has remained a standard-of-care adjuvant treatment for patients with glioblastoma. Even in the elderly, radiation therapy has demonstrated a modest improvement in survival without a detriment in quality of life or neurocognition. The use of external-beam radiotherapy is a well-established recommendation for patients with newly diagnosed GBM following surgical resection.<sup>5</sup> More recent trials of radiotherapy in GBM have focused on varying techniques and dosing of radiation

following surgical resection, as well as comparisons between post-operative radiotherapy alone and in combination with chemotherapy.<sup>18,19</sup>

Based on the published results of radiotherapy for patients with newly diagnosed GBM to date, the Alberta Provincial CNS Tumour Team members recommend that external beam radiation therapy should be given in standard fractionation to a maximum total dose of 59.4 to 60 Gy using 3D conformal planning techniques. The volume treated should be partial brain irradiation and not whole brain irradiation. There is no strong evidence to recommend a total dose greater than 60 Gy in standard fractionation, and alternative fractionation schedules have not proven to be more beneficial.

**Chemotherapy:** For patients with a good KPS, a high level of evidence supports the use of daily temozolomide administered with postoperative radiotherapy and followed by six cycles of adjuvant temozolomide. Three phase II clinical trials conducted by *Stupp et al.*,<sup>20,21</sup> *Lanzetta et al.*,<sup>22</sup> and *Athanassiou et al.*<sup>23</sup> all reported better one-year survival rates with the addition of temozolomide compared to radiotherapy alone (58%, 58%, 56.3%, respectively). *Stupp et al.* published the results of a large, randomized, multicentre phase III trial that included 573 patients with newly diagnosed GBM from 85 European and Canadian centres. Following surgical resection, patients were randomized to receive radiotherapy alone or in combination with chemotherapy. In the chemotherapy arm, patients received radiotherapy with concurrent low dose temozolomide (75 mg/m<sup>2</sup> po daily) for six weeks, followed by a four-week break and then six cycles of temozolomide (150 – 200 mg/m<sup>2</sup>/day on days 1-5 of a 28-day cycle). The median overall survival was 14.6 months (95% CI 13.2 – 16.8) for the radiotherapy plus temozolomide group versus 12.1 months (95% CI 11.2 – 13.0) for the radiotherapy alone group.<sup>21</sup> In addition, the two-year survival rate was 26.4 percent for the radiotherapy plus temozolomide group versus 10.4 percent for the radiotherapy alone group ( $p < 0.001$ ). At five years, the overall survival was 9.8 percent for the group treated with temozolomide versus 1.9 percent for the group treated with radiotherapy alone (HR 0.6, 95% CI 0.5 – 0.7;  $p < 0.0001$ ).

## MGMT Promoter Methylation Status

In a companion to the 2005 *Stupp et al.* publication, *Hegi et al.* reported an analysis of 206 patients who were treated as part of the clinical trial.<sup>24</sup> The authors examined the relationship between the occurrence of epigenetic silencing of the O<sup>6</sup>- methylguanine – DNA methyltransferase (MGMT) gene by promoter methylation and overall survival. Among patients with MGMT promoter methylation, the median survival was 21.7 months for those treated with temozolomide versus 15.3 months for those treated with radiotherapy alone ( $p = 0.007$ ). In patients with tumours without a methylated MGMT promoter, the administration of concurrent and monthly temozolomide only marginally improved median survival when compared to radiotherapy alone (12.7 months versus 11.8 months,  $p = 0.06$ ). The authors also reported that, irrespective of treatment, MGMT promoter methylation was an independent favourable prognostic factor for patients with GBM (HR=0.45, 95% CI 0.32 – 0.61;  $p < 0.001$ ). A phase III trial, CE.6 led by the Canadian Cancer Trials Group (CCTG) and published in 2017 found that among elderly patients with methylated MGMT status ( $n = 165$ ), the median OS was 13.5 months with radiotherapy plus temozolomide versus 7.7 months with radiotherapy alone (HR for death, 0.53; 95% CI, 0.38 to 0.73;  $p < 0.001$ ).<sup>25</sup> Among elderly patients with unmethylated MGMT status ( $n = 189$ ), the median OS was 10.0 months with radiotherapy plus

temozolomide and 7.9 months with radiotherapy alone (HR for death, 0.75; 95% CI, 0.56 to 1.01;  $p=0.055$ ;  $p=0.08$  for interaction).

The Canadian GBM Recommendations Committee states that since MGMT status appears to be a prognostic factor for increased survival and for better response to temozolomide treatment, sufficient tissue should be obtained during surgery for molecular analysis and tumour banking.<sup>26</sup> On the basis of this recommendation, the members of the Alberta Provincial CNS Tumour Team agree that, whenever possible, determination of MGMT promoter methylation status should be conducted, as it can support assessment of prognosis and inform treatment decisions.

Based on the CeTeG/NOA-09 trial, an alternative treatment option for younger fit patients with newly diagnosed MGMT promoter-methylated glioblastoma is the combination of lomustine and temozolomide administered with radiotherapy. However, treatment options at recurrence following failure of this regimen remain limited.<sup>13</sup>

The open-label, randomized, phase 3 trial compared lomustine plus temozolomide with the current standard of temozolomide-based chemoradiotherapy in adults aged 18–70 years with newly diagnosed MGMT promoter-methylated glioblastoma. The combination regimen was associated with a longer median overall survival (48.1 vs. 31.4 months) and an approximately 40% reduction in the risk of death as compared with standard therapy (HR 0.60, 95% CI 0.35–1.03; log-rank  $p = 0.0492$ ).<sup>13</sup> Although these findings suggest a survival benefit with the lomustine-temozolomide combination, the statistical significance was marginal, and the relatively small sample size limits the strength of the results. The findings should be interpreted cautiously and require confirmation in larger studies.

## Management of Glioblastoma in Older Patients

The incidence of Glioblastoma greatly increases in patients over the age of sixty, and thus accounts for the majority of primary brain tumours in this population. Advanced age has also been repeatedly identified as one of the most powerful predictors of a poor prognosis in patients with high-grade gliomas, and therefore becomes an important factor in planning treatment strategies.<sup>27-30</sup> However, the causal relationship between age and poor prognosis is not fully understood; since survival time and quality of life are often poor in older patients, many are offered only supportive care with no further interventions, and this itself may have a negative impact on disease outcome.

**Combination therapy:** The Alberta Provincial CNS Tumour Team members recommend that older patients ( $\geq 65$  years old) with a good performance status (ECOG 0 to 2) and without serious comorbidity, be offered short-course radiation (40 Gy in 15 fractions) with concurrent and adjuvant temozolomide. For those with a poor performance status, consideration may be given to adjuvant radiation therapy alone, adjuvant temozolomide alone or best supportive care. These recommendations are based on the results from a few key studies, including from Perry et al. reported the results of CE.6 in which 562 patients 65 years of age or older with newly diagnosed GBM were randomized to receive either radiotherapy alone (40 Gy in 15 fractions) or radiotherapy with concurrent and adjuvant temozolomide (75 mg/m<sup>2</sup> po daily for three weeks, followed by a four-week break and then six cycles of temozolomide (150 – 200 mg/m<sup>2</sup>/day on days 1-5 of a 28-day cycle).<sup>25</sup> Eligible patients had an ECOG score of 0 to 2. The median overall survival was longer with radiotherapy plus temozolomide than with radiotherapy alone (9.3 months vs. 7.6 months; HR, 0.67; 95%

CI, 0.56 to 0.80;  $p < 0.001$ ). Quality of life was similar in the two trial groups.

*Roa et al.* randomized 100 patients over the age of 60 to receive either standard radiotherapy (60 Gy in 30 fractions) or an abbreviated course (40 Gy in 15 fractions) within six weeks of surgery. The authors reported similar median survival times for the two groups of patients (5.1 months standard versus 5.6 months abbreviated,  $p=0.57$ ).<sup>31</sup> *Roa et al.* also compared a lower dose regimen of 25 Gy in 5 fractions with 40 Gy in 15 fractions and reported similar progression-free survival between the two groups.<sup>14</sup>

In addition, they did not report any significant differences in KPS over time between the two groups. They concluded that a shorter course of radiotherapy is a reasonable treatment option for older patients with GBM and may be considered in patients with a poor performance status.

The management of GBM in elderly patients with poor performance status is not well established. In a phase III trial by Malmstrom et al compared the standard RT, hypofractionated RT, and temozolomide monotherapy (200 mg/m<sup>2</sup> on days 1-5 of every 28 days for up to six cycles) in elderly patients. The study was performed on elder patients ( $\geq 60$  years) with newly diagnosed GBM and concluded that MGMT promoter methylation significantly prolonged survival in patients treated with temozolomide. The other study by NOA-08 Study<sup>32</sup> performed the long-term analysis comparing temozolomide vs. RT monotherapy in patients  $>65$  years with MGMT-methylated and unmethylated GBM. MGMT-methylated patients showed temozolomide significantly improved median overall survival (OS: 18.4 months) compared to RT (OS: 9.6 months). However, the patients with MGMT-unmethylated, RT led to better outcomes than temozolomide (OS: 10.2 vs. 6.7 months).

**Optune Device:** Tumour Treating Fields (TTFields) are Health Canada approved for the treatment of newly diagnosed patients in the adjuvant setting.<sup>15</sup> These are low-intensity electric fields which are delivered via device called Optune. The EF-14 phase-III unblinded trial assigned the newly diagnosed glioblastoma patients in a 2:1 ratio to TTFields plus TMZ versus TMZ alone to identify the survival benefits of TTFields. The median PFS was 3.9 months in TMZ alone group as compared to 7.1 months in TTFields with TMZ. The median survival times were 15.6 in TMZ alone and 20.5 months in TMZ+ TTFields group respectively.<sup>16</sup>

## Methodology

*A detailed description of the methodology followed during the guideline development process can be found in the [Guidance & Resource Unit Handbook](#).*

The Medline and PubMed database was searched for relevant studies, guidelines and consensus documents published up to December 2025. The specific search strategy, search terms, and search results are available upon request. Online resources from oncology-based health organizations and guideline developers were also systematically searched, and relevant guidelines from the following organizations were considered in the development of our recommendations: American Society of Clinical Oncology (ASCO)<sup>5</sup>, European Association of Neuro-Oncology (EANO)<sup>6</sup>, American Society for Radiation Oncology (ASTRO)<sup>7</sup>, Society for Neuro-Oncology (SNO)<sup>8</sup>, and the National Comprehensive Cancer Network (NCCN)<sup>9</sup>.

Search Strategy- Medline & PubMed- glioblastoma (MeSH term), high grade glioma (keyword), limited to human studies published in English from 2013 to present, clinical trials, randomized controlled trials, meta-analyses, systematic reviews and practice guidelines, excluding recurrent neoplasms (MeSH term). Articles were excluded if they included less than 10 patients, involved pediatric patients, did not include survival outcomes or involved anaplastic astrocytoma or oligodendroglioma as the only high grade glioma.

## Appraisal and rating of recommendations

**Table 1. Levels of Evidence**

| Level | Description of Evidence                                                                                                                                                                                                                                                                                                               |
|-------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| I     | Evidence from at least one large randomized, controlled trial of good methodological quality (low potential for bias) or meta-analyses of well-conducted randomized trials without heterogeneity                                                                                                                                      |
| II    | Small randomized trials or large randomized trials with a suspicion of bias (lower methodological quality) or meta-analyses of such trials or of trials with demonstrated heterogeneity                                                                                                                                               |
| III   | Prospective cohort studies, post-hoc and ad-hoc analyses of randomized trials, or target trials                                                                                                                                                                                                                                       |
| IV    | Retrospective cohort studies, case-control studies, instrument validation studies (may be classified as Level III depending on population size, and methodology), or single-arm clinical trials (which may also be listed as Level III when randomized clinical trials are not feasible and the methodology is sufficiently rigorous) |
| V     | Case reports, interviews, focus groups, surveys, and expert opinion including narrative or non-systematic reviews and Delphi studies                                                                                                                                                                                                  |

**Table 2. Strength of Recommendations**

| Grade | Description of Recommendation Strength                                                               |
|-------|------------------------------------------------------------------------------------------------------|
| A     | Strongly recommended; strong evidence for efficacy with a substantial clinical benefit.              |
| B     | Generally recommended; strong or moderate evidence for efficacy but with a limited clinical benefit. |
| C     | Optional; insufficient evidence for efficacy or benefit does not outweigh the risks/disadvantages.   |
| D     | Generally not recommended; moderate evidence against efficacy or for adverse outcomes.               |
| E     | Never recommended; strong evidence against efficacy or for adverse outcomes.                         |

## References

1. Pouyan A, Ghorbanlo M, Eslami M, et al. Glioblastoma multiforme: insights into pathogenesis, key signaling pathways, and therapeutic strategies. *Mol Cancer*. Feb 26 2025;24(1):58. doi:10.1186/s12943-025-02267-0
2. Cancer statistics at a glance. Canadian Cancer Society 2024.Cancer statistics at a glance | Canadian Cancer Society.
3. Louis DN, Perry A, Wesseling P, et al. The 2021 WHO Classification of Tumors of the Central Nervous System: a summary. *Neuro Oncol*. Aug 02 2021;23(8):1231-1251. doi:10.1093/neuonc/noab106
4. Torp SH, Solheim O, Skjulsvik AJ. The WHO 2021 Classification of Central Nervous System tumours: a practical update on what neurosurgeons need to know-a minireview. *Acta Neurochir (Wien)*. Sep 2022;164(9):2453-2464. doi:10.1007/s00701-022-05301-y
5. Sulman EP, Ismaila N, Armstrong TS, et al. Radiation Therapy for Glioblastoma: American Society of Clinical Oncology Clinical Practice Guideline Endorsement of the American Society for Radiation Oncology Guideline. *J Clin Oncol*. Jan 20 2017;35(3):361-369. doi:10.1200/JCO.2016.70.7562
6. Weller M, van den Bent M, Preusser M, et al. EANO guidelines on the diagnosis and treatment of diffuse gliomas of adulthood. *Nat Rev Clin Oncol*. Mar 2021;18(3):170-186. doi:10.1038/s41571-020-00447-z
7. Yeboa DN, Braunstein SE, Cabrera A, et al. Radiation Therapy for WHO Grade 4 Adult-Type Diffuse Glioma: An ASTRO Clinical Practice Guideline. *Pract Radiat Oncol*. Jun 25 2025;doi:10.1016/j.prro.2025.05.014
8. Mohile NA, Messersmith H, Gatson NT, et al. Therapy for Diffuse Astrocytic and Oligodendroglial Tumors in Adults: ASCO-SNO Guideline. *J Clin Oncol*. Feb 01 2022;40(4):403-426. doi:10.1200/JCO.21.02036
9. Central Nervous System Cancers: NCCN Guidelines Version 1.2025 Central Nervous System Cancers - Guidelines Detail,Central Nervous System Cancers - Guidelines Detail.
10. Bonosi L, Marrone S, Benigno UE, et al. Maximal Safe Resection in Glioblastoma Surgery: A Systematic Review of Advanced Intraoperative Image-Guided Techniques. *Brain Sci*. Jan 28 2023;13(2)doi:10.3390/brainsci13020216
11. Vuorinen V, Hinkka S, Färkkilä M, Jääskeläinen J. Debulking or biopsy of malignant glioma in elderly people - a randomised study. *Acta Neurochir (Wien)*. Jan 2003;145(1):5-10. doi:10.1007/s00701-002-1030-6
12. Hart MG, Grant GR, Solyom EF, Grant R. Biopsy versus resection for high-grade glioma. *Cochrane Database Syst Rev*. Jun 06 2019;6(6):CD002034. doi:10.1002/14651858.CD002034.pub2
13. Herrlinger U, Tzaridis T, Mack F, et al. Lomustine-temozolomide combination therapy versus standard temozolomide therapy in patients with newly diagnosed glioblastoma with methylated MGMT promoter (CeTeG/NOA-09): a randomised, open-label, phase 3 trial. *Lancet*. Feb 16 2019;393(10172):678-688. doi:10.1016/S0140-6736(18)31791-4
14. Roa W, Kepka L, Kumar N, et al. International Atomic Energy Agency Randomized Phase III Study of Radiation Therapy in Elderly and/or Frail Patients With Newly Diagnosed Glioblastoma Multiforme. *J Clin Oncol*. Dec 10 2015;33(35):4145-50. doi:10.1200/JCO.2015.62.6606
15. Stupp R, Wong ET, Kanner AA, et al. NovoTTF-100A versus physician's choice chemotherapy in recurrent glioblastoma: a randomised phase III trial of a novel treatment modality. *Eur J Cancer*. Sep 2012;48(14):2192-202. doi:10.1016/j.ejca.2012.04.011
16. Ram Z, Kim CY, Hottinger AF, Idbaih A, Nicholas G, Zhu JJ. Efficacy and Safety of Tumor Treating Fields (TTFields) in Elderly Patients with Newly Diagnosed Glioblastoma: Subgroup Analysis of the Phase 3 EF-14 Clinical Trial. *Front Oncol*. 2021;11:671972. doi:10.3389/fonc.2021.671972
17. Albert NL, Weller M, Suchorska B, et al. Response Assessment in Neuro-Oncology working group and European Association for Neuro-Oncology recommendations for the clinical use of PET imaging in gliomas. *Neuro Oncol*. Sep 2016;18(9):1199-208. doi:10.1093/neuonc/now058

18. Gorlia T, van den Bent MJ, Hegi ME, et al. Nomograms for predicting survival of patients with newly diagnosed glioblastoma: prognostic factor analysis of EORTC and NCIC trial 26981-22981/CE.3. *Lancet Oncol.* Jan 2008;9(1):29-38. doi:10.1016/S1470-2045(07)70384-4
19. Zhong L, Zhou P, Chen L, et al. Modified Target Delineation and Moderately Hypofractionated Radiotherapy for High-Grade Glioma: A Randomized Clinical Trial. *JAMA Netw Open.* Jul 01 2025;8(7):e2523053. doi:10.1001/jamanetworkopen.2025.23053
20. Stupp R, Mason WP, van den Bent MJ, et al. Radiotherapy plus concomitant and adjuvant temozolomide for glioblastoma. *N Engl J Med.* Mar 10 2005;352(10):987-96. doi:10.1056/NEJMoa043330
21. Stupp R, Hegi ME, Mason WP, et al. Effects of radiotherapy with concomitant and adjuvant temozolomide versus radiotherapy alone on survival in glioblastoma in a randomised phase III study: 5-year analysis of the EORTC-NCIC trial. *Lancet Oncol.* May 2009;10(5):459-66. doi:10.1016/S1470-2045(09)70025-7
22. Lanzetta G, Campanella C, Rozzi A, et al. Temozolomide in radio-chemotherapy combined treatment for newly-diagnosed glioblastoma multiforme: phase II clinical trial. *Anticancer Res.* 2003;23(6D):5159-64.
23. Athanassiou H, Synodinou M, Maragoudakis E, et al. Randomized phase II study of temozolomide and radiotherapy compared with radiotherapy alone in newly diagnosed glioblastoma multiforme. *J Clin Oncol.* Apr 01 2005;23(10):2372-7. doi:10.1200/JCO.2005.00.331
24. Hegi ME, Diserens AC, Gorlia T, et al. MGMT gene silencing and benefit from temozolomide in glioblastoma. *N Engl J Med.* Mar 10 2005;352(10):997-1003. doi:10.1056/NEJMoa043331
25. Perry JR, Laperriere N, O'Callaghan CJ, et al. Short-Course Radiation plus Temozolomide in Elderly Patients with Glioblastoma. *N Engl J Med.* Mar 16 2017;376(11):1027-1037. doi:10.1056/NEJMoa1611977
26. Mason WP, Harrison RA, Lapointe S, et al. Canadian Expert Consensus Recommendations for the Diagnosis and Management of Glioblastoma: Results of a Delphi Study. *Curr Oncol.* Apr 01 2025;32(4)doi:10.3390/curroncol32040207
27. Brandes AA, Monfardini S. The treatment of elderly patients with high-grade gliomas. *Semin Oncol.* Dec 2003;30(6 Suppl 19):58-62. doi:10.1053/j.seminoncol.2003.11.025
28. Iwamoto FM, Reiner AS, Nayak L, Panageas KS, Elkin EB, Abrey LE. Prognosis and patterns of care in elderly patients with glioma. *Cancer.* Dec 01 2009;115(23):5534-40. doi:10.1002/cncr.24612
29. Davis FG, Freels S, Grutsch J, Barlas S, Brem S. Survival rates in patients with primary malignant brain tumors stratified by patient age and tumor histological type: an analysis based on Surveillance, Epidemiology, and End Results (SEER) data, 1973-1991. *J Neurosurg.* Jan 1998;88(1):1-10. doi:10.3171/jns.1998.88.1.0001
30. Asmaa A, Dixit S, Rowland-Hill C, et al. Management of elderly patients with glioblastoma-multiforme-a systematic review. *Br J Radiol.* Jul 2018;91(1088):20170271. doi:10.1259/bjr.20170271
31. Roa W, Brasher PM, Bauman G, et al. Abbreviated course of radiation therapy in older patients with glioblastoma multiforme: a prospective randomized clinical trial. *J Clin Oncol.* May 01 2004;22(9):1583-8. doi:10.1200/JCO.2004.06.082
32. Wick A, Kessler T, Platten M, et al. Superiority of temozolomide over radiotherapy for elderly patients with RTK II methylation class, MGMT promoter methylated malignant astrocytoma. *Neuro Oncol.* Aug 17 2020;22(8):1162-1172. doi:10.1093/neuonc/noaa033

## About this Guideline

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### Prepared for and endorsed by

Members of the Alberta Provincial CNS Team  
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### Revision history and maintenance

This guideline was originally developed in 2012 and updated in 2026. A formal review will be conducted in 2031 unless critical new evidence is brought forward sooner.

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### Conflict of interest statements (in order of authorship)

Folkman Frances, pharmacist, has nothing to disclose.  
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### Abbreviations

ALA, 5-aminolevulinic acid; CCO, Cancer Care Ontario; CI, confidence interval; CT, computed tomography; GBM, glioblastoma; GTR, gross total resection; HR, hazard ratio; IMRT, intensity-modulated radiotherapy; KPS, Karnofsky performance status; MGMT, O6- methylguanine – DNA methyltransferase; MRI, magnetic resonance imaging; PCV, procarbazine + lomustine + vincristine; RCT, randomized controlled trial; RR, risk ratio; STR, subtotal resection; TMZ, Temozolomide; TTFields, Tumour Treating Field; WBRT, whole brain radiotherapy;



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