Central Nervous System Cancers

Overall management of Central Nervous System Cancers is described in the full NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Central Nervous System Cancers. Visit NCCN.org to view the complete library of NCCN Guidelines®.

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Central Nervous System Cancers | NCCN Guidelines®
Adult Glioma: IDH-Mutant Astrocytoma

**PATHOLOGY**

**WHO grade 2** (good PS, KPS ≥60)
- **Low risk**
  - Consider clinical trial (preferred for eligible patients)
  - Observe

**WHO grade 3** (good PS, KPS ≥60)
- **High risk**
  - Consider clinical trial (preferred for eligible patients)
  - Standard RT + adjuvant TMZ
  - Standard RT + concurrent and adjuvant TMZ
  - Standard RT + adjuvant PCV (procarbazine/lomustine/vincristine)
  - Observe in highly select patients

**WHO grade 4s** (good PS, KPS ≥60)
- Consider clinical trial (preferred for eligible patients)
- Standard RT with concurrent and adjuvant TMZ

**ADJUVANT TREATMENT**

**FOLLOW-UP**

**Brain MRI**
- every 3–6 mo for 5 y then at least every 6 mo or as clinically indicated
- every 2–4 mo for 3 y, then every 3–6 mo indefinitely

**Recurrence**

**Note:** All recommendations are category 2A unless otherwise indicated.
Clinical Trials: NCCN believes that the best management of any patient with cancer is in a clinical trial. Participation in clinical trials is especially encouraged.
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Adult Glioma: Glioblastoma

Version 1.2023
March 24, 2023

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Adult Glioma: Glioblastoma
Version 1.2023
March 24, 2023

**Central Nervous System Cancers**

**Adult Glioma: Glioblastoma**

**GLIOBLASTOMA PATHOLOGY**

**MGMT PROMOTER STATUS**

- Methylated or indeterminate
- Unmethylated

**ADJUVANT TREATMENT**

- Consider clinical trial (preferred for eligible patients)
- Hypofractionated RT\textsuperscript{m} + concurrent and adjuvant TMZ (category 1)\textsuperscript{g,ff,gg,ill}
- Standard RT\textsuperscript{m} + concurrent TMZ and adjuvant TMZ + alternating electric field therapy (category 1)\textsuperscript{g,ff,gg,hh}
- Standard RT\textsuperscript{m} + concurrent TMZ and adjuvant TMZ\textsuperscript{g,ff,gg}
- TMZ\textsuperscript{g}
- Hypofractionated RT alone\textsuperscript{m} (category 2B)

**PRIMARY TREATMENT FOLLOW-UP**

- Brain MRI 2–8 wks after RT, then every 2–4 mo for 3 y, then every 3–6 mo indefinitely

**FOLLOW-UP**

- Recurrence (GLIO-10)

**GLIO-8**

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\textsuperscript{a} Principles of Brain and Spine Tumor Imaging (BRAIN-A).

\textsuperscript{c} Principles of Brain Tumor Pathology (BRAIN-E).

\textsuperscript{g} Systemic Therapy Options (GLIO-A).

\textsuperscript{m} Principles of Radiation Therapy for Brain and Spinal Cord (BRAIN-C 1 of 9).

\textsuperscript{q} Consider TMZ if tumor is MGMT promoter methylated.

\textsuperscript{r} Within the first 3 months after completion of RT and concomitant TMZ, diagnosis of recurrence can be indistinguishable from pseudoprogression on neuroimaging.

\textsuperscript{dd} This pathway also includes gliosarcoma.


\textsuperscript{ff} Combination of modalities may lead to increased toxicity or radiographic changes.

\textsuperscript{gg} There are no clear data that treatment with TMZ beyond 6 months is beneficial, even in patients with MGMT-methylated disease.

\textsuperscript{hh} Alternating electric field therapy is only an option for patients with supratentorial disease.

\textsuperscript{jj} Clinical benefit from TMZ is likely to be lower in patients whose tumors lack MGMT promoter methylation.

\textsuperscript{kk} NCCN Guidelines for Older Adult Oncology.

\textsuperscript{ll} Hypofractionated RT and TMZ have not been formally compared with standard RT and TMZ in patients aged >70 y.
## GLIOBLASTOMA: SYSTEMIC THERAPY OPTIONS

<table>
<thead>
<tr>
<th>Stage/Circumstance</th>
<th>Preferred Regimens</th>
<th>Other Recommended Regimens</th>
<th>Useful in Certain Circumstances</th>
</tr>
</thead>
</table>
| Adjuvant Treatment, KPS ≥60 | • RT + concurrent and adjuvant TMZ<sup>44,45</sup> ± tumor treating fields (TTF)<sup>0,46</sup> | • None | - TMZ (for patients with MGMT promoter-methylated or indeterminate tumors and age >70 years)<sup>44,64</sup>
- Standard RT + concurrent and adjuvant lomustine and TMZ (for patients with MGMT promoter-methylated or indeterminate tumors and age ≤70 years) (category 2B)<sup>65</sup> |
| Adjuvant Treatment, KPS <60 | • None | • None | - Hypofractionated RT + concurrent or adjuvant TMZ (for patients aged ≤70 years)<sup>63</sup>
- TMZ (for patients with MGMT promoter-methylated tumors)<sup>64</sup> |
| Recurrent or Progressive Disease<sup>e,m,n</sup> | • Bevacizumab<sup>g,h,47-50</sup>
• TMZ<sup>2,24,51,52</sup>
• Carmustine or carmustine<sup>53-56</sup>
• PCV<sup>0,57,58</sup>
• Regorafenib<sup>59</sup> | • Systemic therapy<sup>m</sup> + bevacizumab<sup>g,h</sup>
- Carmustine or lomustine + bevacizumab<sup>g,h,60</sup>
- TMZ + bevacizumab<sup>g,h,61,62</sup> | - If failure or intolerance to the preferred or other recommended regimens
- Etoposide (category 2B)<sup>37</sup>
- Platinum-based regimens<sup>r,39-41</sup> (category 3)
- NTRK gene fusion tumors
- Larotrectinib<sup>10</sup>
- Entrectinib<sup>11</sup>
- BRAF V600E activation mutation
- BRAF/MEK inhibitors:
  - Dabrafenib/trametinib<sup>4,5</sup>
  - Vemurafenib/cobimetinib<sup>6,7</sup> |

<sup>b</sup> When PCV is recommended, carmustine may be substituted for lomustine.<br>
<sup>e</sup> Strongly suggest consideration of clinical trials prior to treating recurrent disease with standard systemic therapy, as additional therapies may eliminate the majority of clinical trial options.<br>
<sup>g</sup> Patients who have evidence of radiographic progression may benefit from continuation of bevacizumab to prevent rapid neurologic deterioration.<br>
<sup>h</sup> An FDA-approved biosimilar is an appropriate substitute for bevacizumab.<br>
<sup>i</sup> Hypofractionated RT preferred.<br>
<sup>m</sup> Bevacizumab + systemic therapy can be considered if bevacizumab monotherapy fails and it is desirable to continue the steroid-sparing effects of bevacizumab.<br>
<sup>q</sup> There are no identified targeted agents with demonstrated efficacy in glioblastoma. However, the panel encourages molecular testing of tumor because if a driver mutation is detected, it may be reasonable to treat with a targeted therapy on a compassionate use basis and/or the patient may have more treatment options in the context of a clinical trial. Molecular testing also has a valuable role in improving diagnostic accuracy and prognostic stratification that may inform treatment selection.<br>
<sup>p</sup> Alternating electric field therapy is only an option for patients with supratentorial disease.<br>
<sup>r</sup> Moderate to significant myelosuppression was observed, but the toxicity profile for this regimen is not yet fully defined.<br>
<sup>s</sup> Platinum-based regimens include cisplatin or carboplatin.

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