Central Nervous System Cancers

Overall management of Central Nervous System Cancers from diagnosis through recurrence is described in the full NCCN Guidelines® for Central Nervous System Cancers. Visit NCCN.org to view the complete library of NCCN Guidelines.

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Anaplastic Gliomas\(^a\)/Glioblastoma

**GLIOBLASTOMA PATHOLOGY\(^d\)**

**MGMT\(^p\) PROMOTER STATUS**

- **Good performance status (KPS \(\geq 60\))**
  - Methylated
  - **Methylation**
  - Unmethylated or indeterminate

- **Age \(\leq 70\) y**
  - Glioblastoma ± carmustine (BCNU) wafer\(^q\)

- **Poor performance status (KPS <60)**

- **Age >70 y**
  - See GLIO-4

**ADJUVANT TREATMENT**

- Standard brain RT\(^l\) + concurrent temozolomide and adjuvant temozolomide + alternating electric field therapy\(^n, r, s, t\)
  - or
  - Standard brain RT\(^l\) + concurrent temozolomide and adjuvant temozolomide (category 1)\(^{n, r, s}\)

- Standard brain RT\(^l\) + concurrent temozolomide\(^u\) and adjuvant temozolomide\(^u\) + alternating electric field therapy\(^n, r, s, t\)
  - or
  - Standard brain RT\(^l\) + concurrent temozolomide\(^u\) and adjuvant temozolomide (category 1)\(^{n, r, s, u}\)
  - or
  - Standard brain RT alone\(^l\)

**FOLLOW-UP\(^b\)**

- Brain MRI 2–6 wk after RT, then every 2–4 mo for 3 y, then every 6 mo indefinitely\(^o\)
  - See Recurrence (GLIO-5)

**MGMT PROMOTER STATUS**

- **Methylated**
- **Unmethylated**
- **Indeterminate**

- **Standard or hypofractionated brain RT\(^l\)**
  - **Temozolomide\(^v\)**
  - **Palliative/Best supportive care**

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\(^a\)This pathway includes the classification of mixed anaplastic oligoastrocytoma (AOA), anaplastic astrocytoma (AA), anaplastic oligodendroglioma (AO), and other rare anaplastic gliomas.

\(^b\)See Principles of Brain and Spine Tumor Imaging (BRAIN-A).

\(^c\)See Principles of Brain Tumor Pathology (BRAIN-F).

\(^d\)This pathway also includes gliosarcoma.

\(^e\)See Principles of Brain and Spinal Cord Tumor Radiation Therapy (BRAIN-C).

\(^f\)See Principles of Brain and Spinal Cord Tumor Systemic Therapy (BRAIN-D).

\(^g\)Within the first 3 months after completion of RT and concomitant temozolomide, diagnosis of recurrence can be indistinguishable from pseudoprogression on neuroimaging.

\(^h\)MGMT = O\(^6\)-methylguanine-DNA methyltransferase.

\(^i\)Treatment with carmustine wafer, reirradiation, or multiple prior systemic therapies may impact enrollment in some adjuvant clinical trials.

\(^j\)Combination of agents may lead to increased toxicity or radiographic changes.

\(^k\)Benefit of treatment with temozolomide for glioblastomas beyond 6 months is unknown.

\(^l\)The optimal duration of treatment with temozolomide for anaplastic astrocytoma is unknown.

\(^m\)Alternating electric field therapy is only an option for patients with supratentorial disease.

\(^n\)Clinical benefit from temozolomide is likely to be lower in patients whose tumors lack MGMT promoter methylation.

\(^o\)Temozolomide monotherapy is only recommended if tumor is MGMT promoter methylated.

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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.
## Anaplastic Gliomas\(^a\)/Glioblastoma

<table>
<thead>
<tr>
<th>Glioblastoma Pathology(^d)</th>
<th>MGMT Promoter Status(^p)</th>
<th>Adjuvant Treatment</th>
<th>Follow-up(^b)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age &gt;70 y (Glioblastoma(^j) ± carmustine [BCNU] wafer(^q))</td>
<td>Methylated</td>
<td>Hypofractionated brain RT(^l) + concurrent and adjuvant temozolomide(^h,r,s) or Temozolomide or Hypofractionated brain RT alone(^l) (category 1)</td>
<td>Brain MRI 2–6 wk after RT, then every 2–4 mo for 3 y, then every 6 mo through 5 y post-treatment, then yearly indefinitely(^o)</td>
</tr>
<tr>
<td>Good performance status (KPS ≥60)</td>
<td>Unmethylated or indeterminate</td>
<td>Standard RT(^l) + concurrent temozolomide and adjuvant temozolomide + alternating electric field therapy(^n,r,s,t) or Standard RT(^l) + concurrent temozolomide and adjuvant temozolomide(^h,r,s)</td>
<td></td>
</tr>
<tr>
<td>Poor performance status (KPS &lt;60)</td>
<td></td>
<td>Hypofractionated brain RT alone(^l) (category 1) or Standard RT(^l) + concurrent temozolomide(^u) and adjuvant temozolomide(^u) + alternating electric field therapy(^n,r,s,t) or Standard RT(^l) + concurrent temozolomide(^u) and adjuvant temozolomide(^h,r,s,u)</td>
<td></td>
</tr>
</tbody>
</table>

\(^a\)This pathway includes the classification of mixed anaplastic oligoastrocytoma (AOA), anaplastic astrocytoma (AA), anaplastic oligodendroglioma (AO), and other rare anaplastic gliomas.

\(^b\)See Principles of Brain and Spine Tumor Imaging (BRAIN-A).

\(^d\)See Principles of Brain Tumor Pathology (BRAIN-F).

\(^j\)This pathway also includes gliosarcoma.

\(^q\)Combination of agents may lead to increased toxicity or radiographic changes.

\(^u\)Within the first 3 months after completion of RT and concomitant temozolomide, diagnosis of recurrence can be indistinguishable from pseudoprogression on neuroimaging.

\(^r\)Benefit of treatment with temozolomide for glioblastomas beyond 6 months is unknown.

\(^t\)The optimal duration of treatment with temozolomide for anaplastic astrocytoma is unknown.

\(^v\)Methylated

\(^o\)Treatment with carmustine wafer, reirradiation, or multiple prior systemic therapies may impact enrollment in some adjuvant clinical trials.

\(^p\)Within the first 3 months after completion of RT and concomitant temozolomide, diagnosis of recurrence can be indistinguishable from pseudoprogression on neuroimaging.

\(^s\)Benefit of treatment with temozolomide for glioblastomas beyond 6 months is unknown.

\(^h\)Alternating electric field therapy is only an option for patients with supratentorial disease.

\(^n\)Clinical benefit from temozolomide is likely to be lower in patients whose tumors lack MGMT promoter methylation.

\(^s\)Temozolomide monotherapy is only recommended if tumor is MGMT promoter methylated.

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Anaplastic Gliomas\textsuperscript{a}/Glioblastoma

### Recurrence

<table>
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<tr>
<th>Diffuse or multiple</th>
<th>Resectable</th>
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<tbody>
<tr>
<td>Resection + carmustine (BCNU) wafer\textsuperscript{m}</td>
<td>Resection without carmustine (BCNU) wafer</td>
</tr>
</tbody>
</table>

### Treatment

- Clinical trials (preferred for eligible patients)\textsuperscript{k} or
- Palliative/Best supportive care if poor performance status or
- Systemic chemotherapy\textsuperscript{n,y} or
- Surgery for symptomatic, large lesion or
- Consider alternating electric field therapy for glioblastoma (category 2B) Clinical trials (preferred for eligible patients)\textsuperscript{k} or
- Palliative/Best supportive care if poor performance status or
- Systemic chemotherapy\textsuperscript{n,y} or
- Consider reirradiation (category 2B)\textsuperscript{l,z} or
- Consider alternating electric field therapy for glioblastoma (category 2B)

\textsuperscript{a}This pathway includes the classification of mixed anaplastic oligoastrocytoma (AOA), anaplastic astrocytoma (AA), anaplastic oligodendroglioma (AO), and other rare anaplastic gliomas.
\textsuperscript{b}See Principles of Brain and Spine Tumor Imaging (BRAIN-A).
\textsuperscript{c}Postoperative brain MRI within 24–72 hours after surgery.
\textsuperscript{d}NOS WHO 2016 has deleted this category, although it may continue to be used for some patients.
\textsuperscript{e}See Principles of Brain and Spinal Cord Tumor Radiation Therapy (BRAIN-C).
\textsuperscript{f}Within the first 3 months after completion of RT and concomitant temozolomide, diagnosis of recurrence can be indistinguishable from pseudoprogression on neuroimaging.
\textsuperscript{g}The efficacy of standard-of-care treatment for recurrent glioblastoma is suboptimal, so for eligible patients consideration of clinical trials is highly encouraged. Prior treatment may impact enrollment in the majority of clinical trial options.
\textsuperscript{h}Consider biopsy, MR spectroscopy, MR perfusion, brain PET/CT or brain PET/MRI, or re-image to follow changes that may be due to progression versus radionecrosis.
\textsuperscript{i}Anaplastic oligodendrogliomas have been reported to be especially sensitive to chemotherapy. Chemotherapy using temozolomide or nitrosourea-based regimens may be appropriate.
\textsuperscript{j}Especially if long interval since prior RT and/or if there was a good response to prior RT.

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