Version 1.2022
June 2, 2022

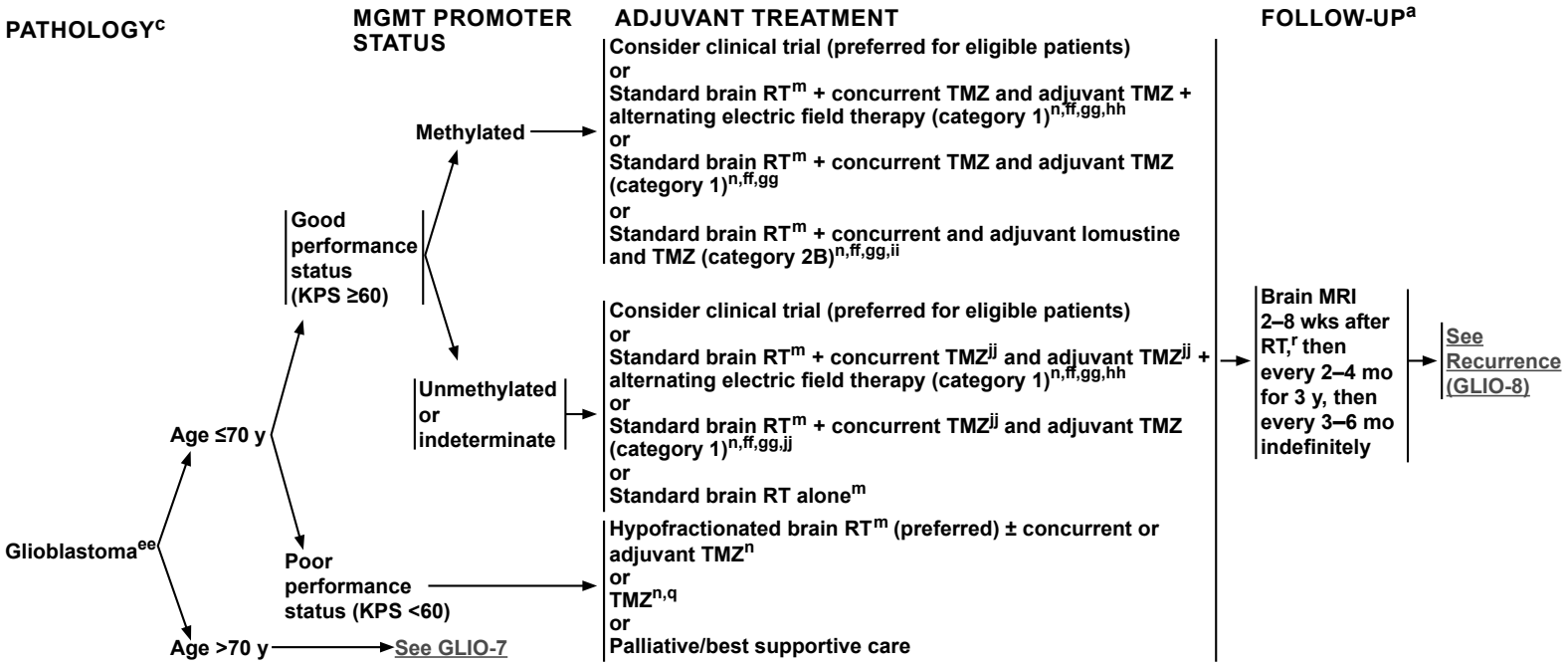
NCCN Clinical Practice Guidelines in Oncology
(NCCN Guidelines®)

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®.

NCCN National Comprehensive Cancer Network®

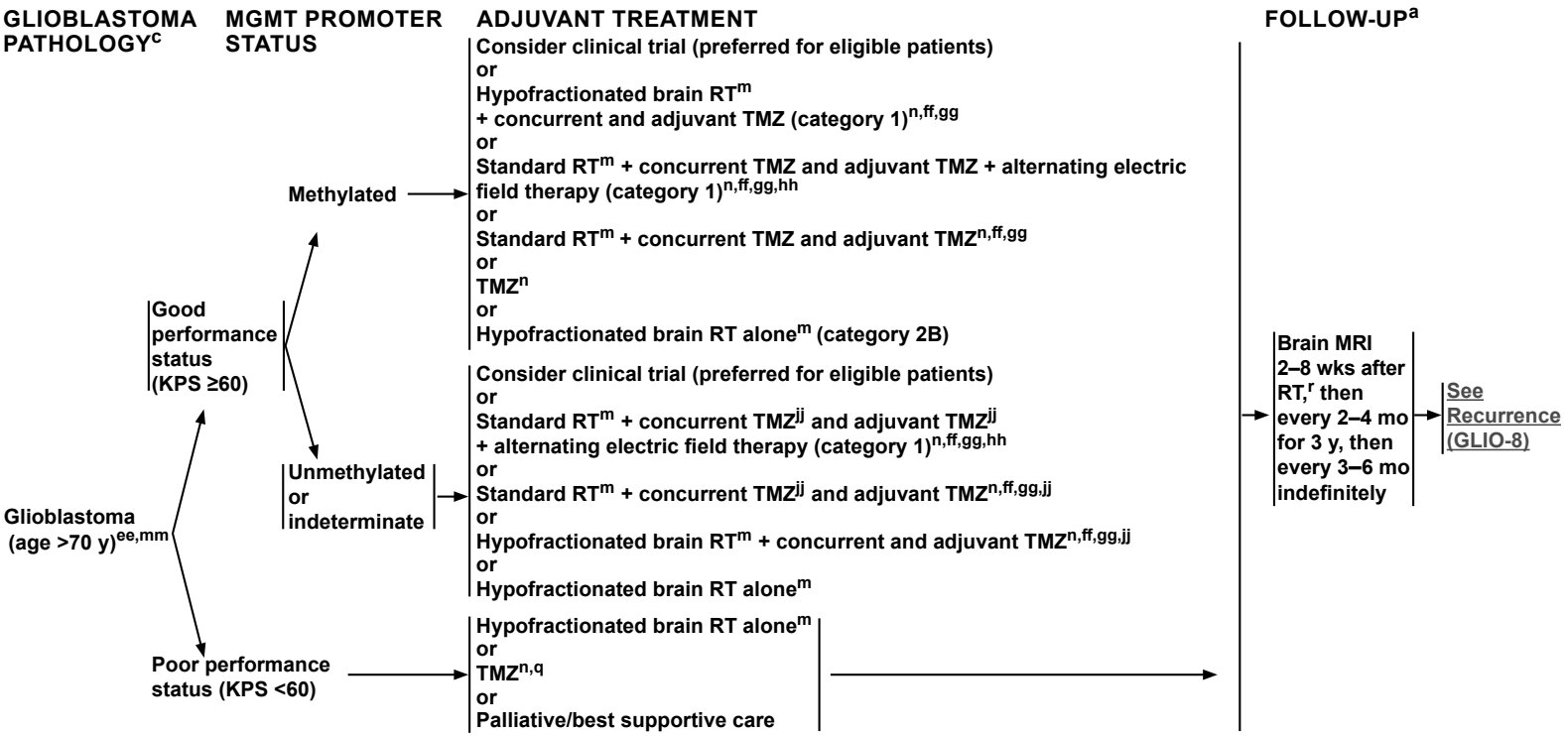
Adult Glioma: Glioblastoma



[a] See Principles of Brain and Spine Tumor Imaging (BRAIN-A).
[c] See Principles of Brain Tumor Pathology (BRAIN-F).
[m] See Principles of Brain and Spinal Cord Tumor Radiation Therapy (BRAIN-C).
[n] See Principles of Brain and Spinal Cord Tumor Systemic Therapy (BRAIN-D).
[q] Consider TMZ if tumor is MGMT promoter methylated.
[r] Within the first 3 months after completion of RT and concomitant TMZ, diagnosis of recurrence can be indistinguishable from pseudoprogression on neuroimaging.
[ee] This pathway also includes gliosarcoma.
[ff] Combination of modalities may lead to increased toxicity or radiographic changes.
[gg] There are no clear data that treatment with TMZ beyond 6 months is beneficial, even in patients with MGMT methylated disease.
[hh] Alternating electric field therapy is only an option for patients with supratentorial disease.
[ii] Moderate to significant myelosuppression was observed, but the toxicity profile for this regimen is not yet fully defined.
[jj] Clinical benefit from temozolomide is likely to be lower in patients whose tumors lack MGMT promoter methylation.

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.

Adult Glioma: Glioblastoma



[a] See Principles of Brain and Spine Tumor Imaging (BRAIN-A).
[c] See Principles of Brain Tumor Pathology (BRAIN-F).
[m] See Principles of Brain and Spinal Cord Tumor Radiation Therapy (BRAIN-C).
[n] See Principles of Brain and Spinal Cord Tumor Systemic Therapy (BRAIN-D).
[q] Consider TMZ if tumor is MGMT promoter methylated.
[r] Within the first 3 months after completion of RT and concomitant TMZ, diagnosis of recurrence can be indistinguishable from pseudoprogression on neuroimaging.

[ee] This pathway also includes gliosarcoma.
[ff] Combination of modalities may lead to increased toxicity or radiographic changes.
[gg] There are no clear data that treatment with TMZ beyond 6 months is beneficial, even in patients with MGMT methylated disease.
[hh] Alternating electric field therapy is only an option for patients with supratentorial disease.
[jj] Clinical benefit from TMZ is likely to be lower in patients whose tumors lack MGMT promoter methylation.

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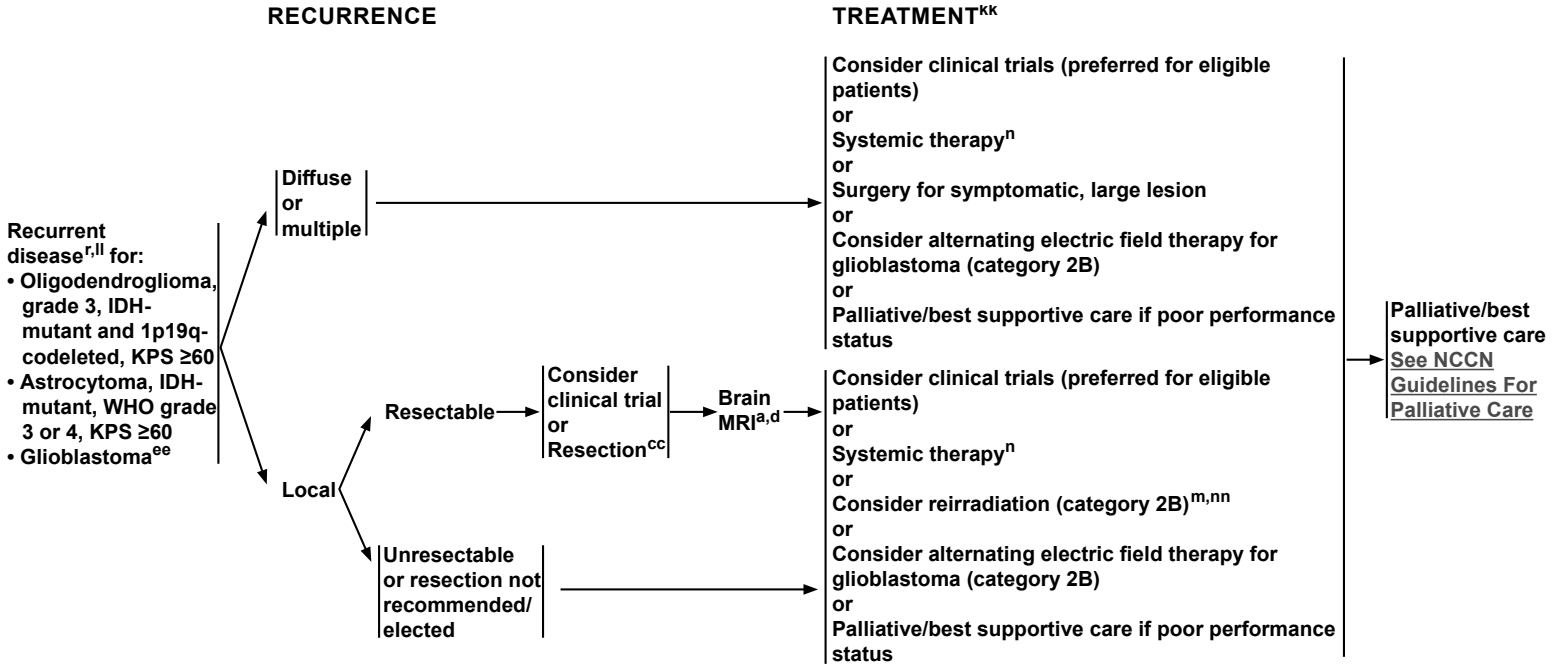
Adult Glioma: High-Grade



[a] See Principles of Brain and Spine Tumor Imaging (BRAIN-A).
[d] Postoperative brain MRI within 48 hours after surgery.
[m] See Principles of Brain and Spinal Cord Tumor Radiation Therapy (BRAIN-C).
[n] See Principles of Brain and Spinal Cord Tumor Systemic Therapy (BRAIN-D).
[r] Within the first 3 months after completion of RT and concomitant TMZ, diagnosis of recurrence can be indistinguishable from pseudoprogression on neuroimaging.
[ee] This pathway also includes gliosarcoma.
[cc] Consider carmustine (BCNU) wafer implant during resection. Treatment with carmustine wafer may impact enrollment in clinical trials.
[kk] 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 clinical trials.
[ll] 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.
[nn] Especially if long interval since prior RT and/or if there was a good response to prior RT.

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PRINCIPLES OF BRAIN AND SPINAL CORD TUMOR SYSTEMIC THERAPY

ADULT GLIOMA: GLIOBLASTOMA

	Preferred Regimens	Other Recommended Regimens	Useful in Certain Circumstances
Adjuvant Treatment, KPS ≥60	• RT + concurrent and adjuvant TMZ[43,44] ± TTF[n,45]	• None	• TMZ (for patients with MGMT promoter-methylated tumors and age >70 years)[43,64] • RT + concurrent and adjuvant lomustine and TMZ (for patients with MGMT promoter-methylated tumors and age ≤70 years) (category 2B)[o,65]
Adjuvant Treatment, KPS <60	• None	• None	• RT + concurrent or adjuvant TMZ (for patients age 70 or younger)[j,63] • TMZ (for patients with MGMT promoter-methylated tumors)[64]
Recurrence Therapye[e,m]	• Bevacizumab[g,h,46-49] • TMZ[2,24,50,51] • Lomustine or carmustine[52-55] • PCV[b,56,57] • Regorafenib[58]	• Systemic therapy[l] + bevacizumab[g,h] ▸ Carmustine or lomustine + bevacizumab[g,h,59,60] ▸ TMZ + bevacizumab[g,h,61,62]	• If failure or intolerance to the preferred or other recommended regimens ▸ Etoposide (category 2B)[36] ▸ Platinum-based regimens[p,38-40] (category 3) • *NTRK* gene fusion tumors ▸ Larotrectinib[10] ▸ Entrectinib[11] • *BRAF* V600E activation mutation ▸ BRAF/MEK inhibitors: ◊ Dabrafenib/trametinib[4,5] ◊ Vemurafenib/cobimetinib[6,7]

[b] When PCV is recommended, carmustine may be substituted for lomustine.
[e] 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.
[g] Patients who have evidence of radiographic progression may benefit from continuation of bevacizumab to prevent rapid neurologic deterioration.
[h] An FDA-approved biosimilar is an appropriate substitute for bevacizumab.
[j] Hypofractionated RT preferred.
[l] Bevacizumab + systemic therapy can be considered if bevacizumab monotherapy fails and it is desirable to continue the steroid-sparing effects of bevacizumab.
[m] 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.
[n] Alternating electric field therapy is only an option for patients with supratentorial disease.
[o] Moderate to significant myelosuppression was observed, but the toxicity profile for this regimen is not yet fully defined.
[p] Platinum-based regimens include cisplatin or carboplatin.

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US-OPT-03660
FC-NOV-0069-0722