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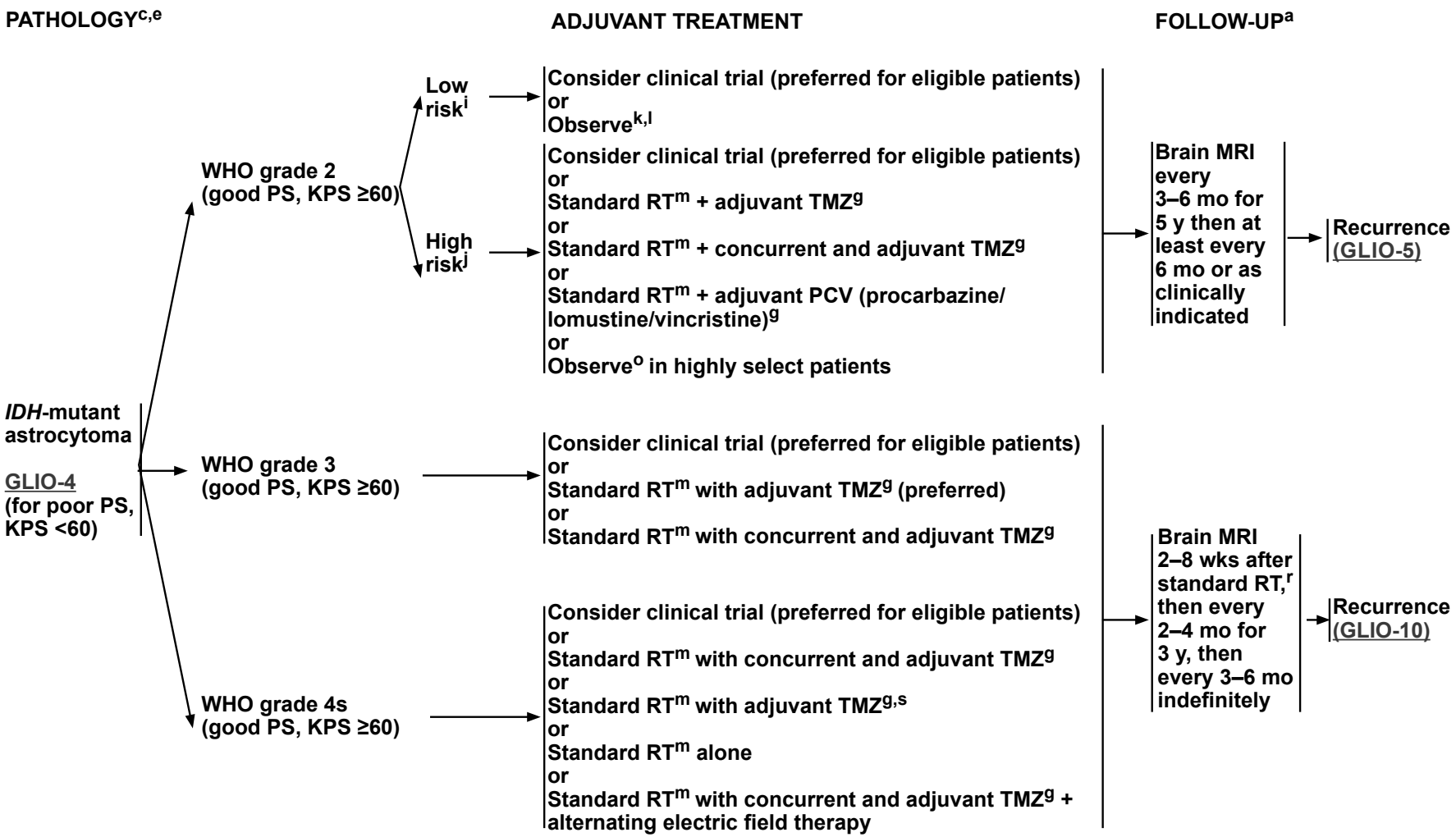
NCCN Clinical Practice Guidelines in Oncology
(NCCN Guidelines®)

Central Nervous System Cancers

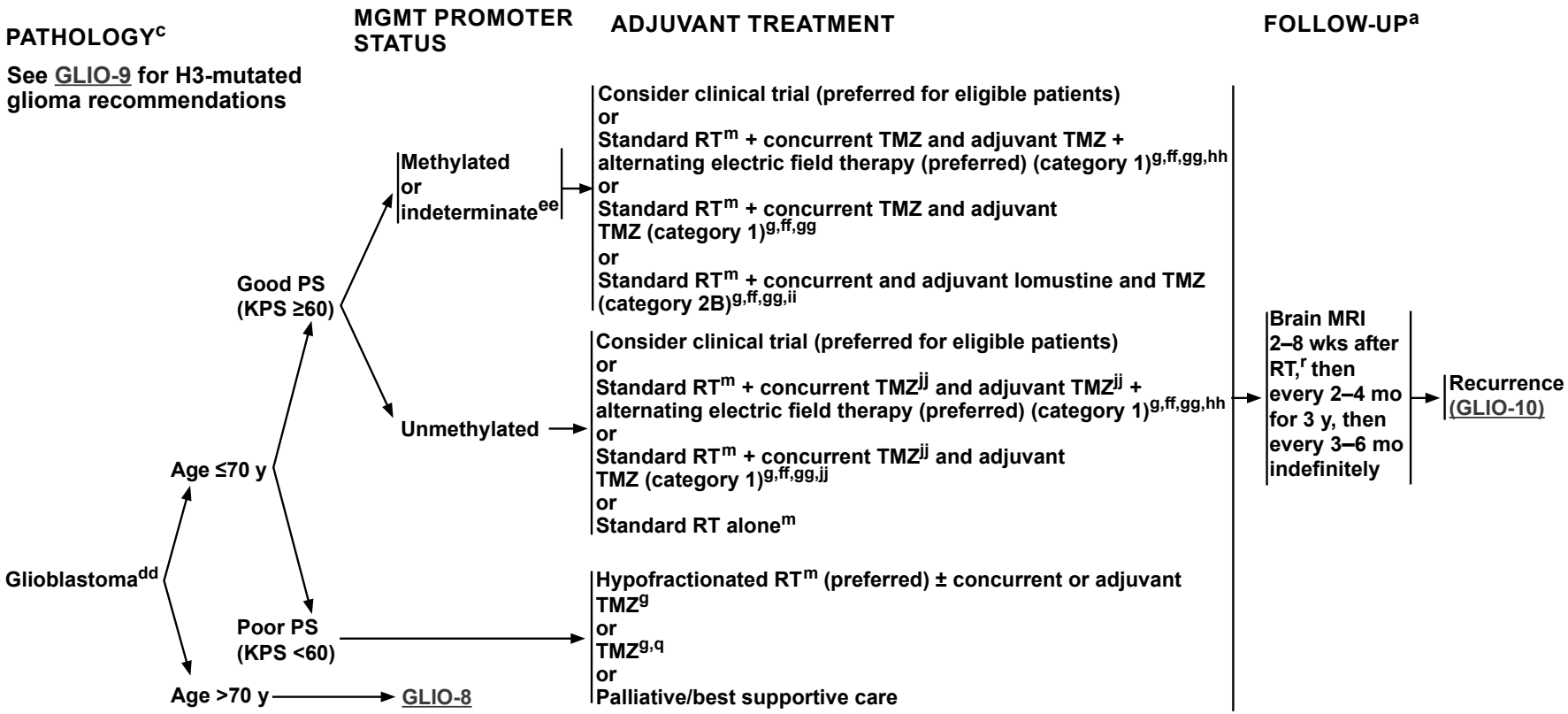
Overall management of Central Nervous System Cancers is described in the full NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Central Nervous System Cancers. Visit NCCN.org to view the complete library of NCCN Guidelines®.

NCCN National Comprehensive Cancer Network®



Continued
Footnotes (GLIO-4)

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.



[a] Principles of Brain and Spine Tumor Imaging (BRAIN-A).
[c] For recommended molecular diagnostics, see Principles of Brain Tumor Pathology (BRAIN-E).
[g] Systemic Therapy Options (GLIO-A).
[m] Principles of Radiation Therapy for Brain and Spinal Cord (BRAIN-C 1 of 9).
[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.
[dd] This pathway also includes gliosarcoma.
[ee] Consider pyrosequencing if not done (Mansouri A, et al. Neuro Oncol 2019;21:167-178).
[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 TMZ is likely to be lower in patients whose tumors lack MGMT promoter methylation.

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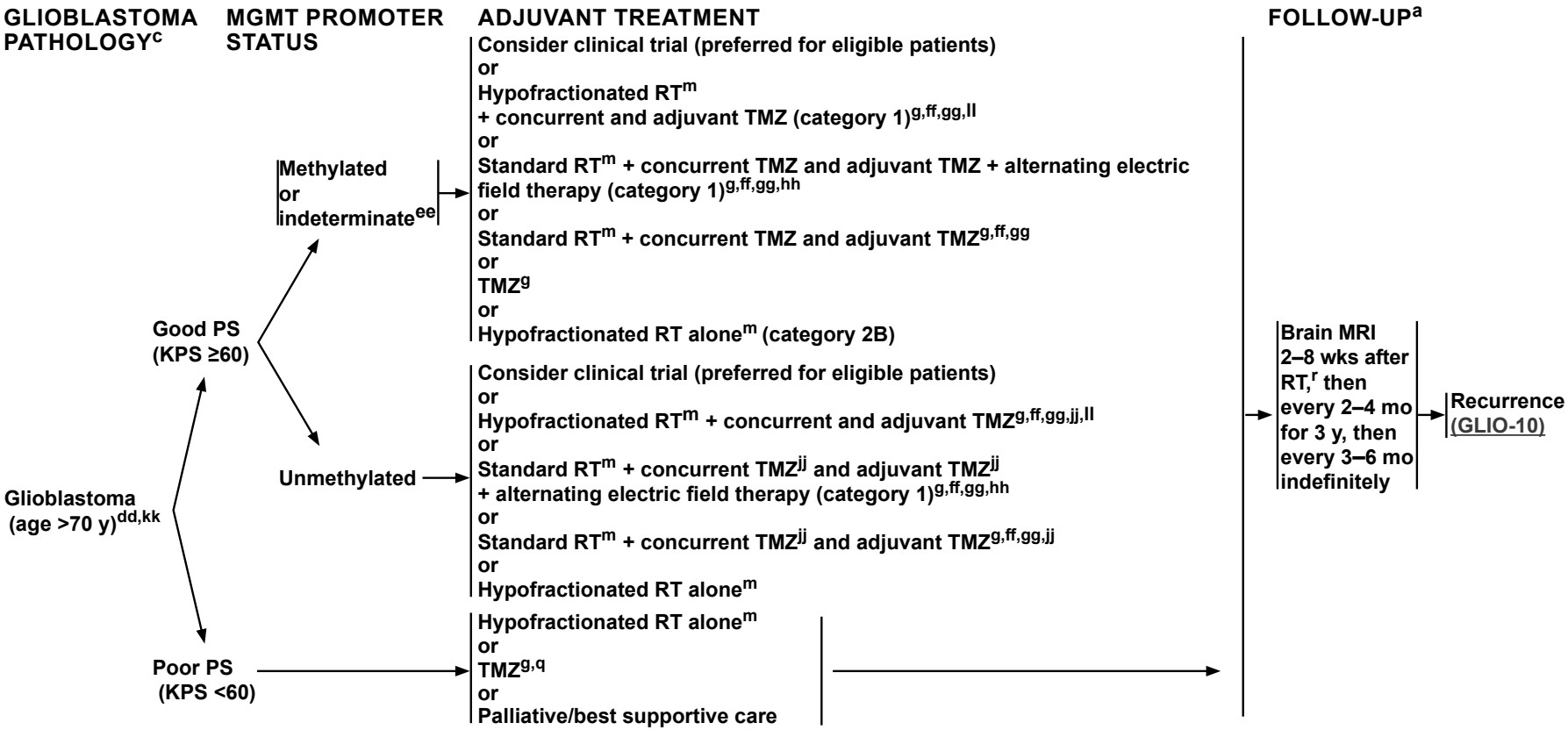

[a] Principles of Brain and Spine Tumor Imaging (BRAIN-A).
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[g] Systemic Therapy Options (GLIO-A).
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[jj] Clinical benefit from TMZ is likely to be lower in patients whose tumors lack MGMT promoter methylation.
[kk] NCCN Guidelines for Older Adult Oncology.
[ll] Hypofractionated RT and TMZ have not been formally compared with standard RT and TMZ in patients aged >70 y.

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GLIOBLASTOMA: SYSTEMIC THERAPY OPTIONS

	Preferred Regimens	Other Recommended Regimens	Useful in Certain Circumstances
Adjuvant Treatment, KPS ≥60	• RT + concurrent and adjuvant TMZ[44,45] ± tumor treating fields (TTF)[p,46]	• None	• TMZ (for patients with MGMT promoter-methylated or indeterminate tumors and age >70 years)[44,64] • Standard RT + concurrent and adjuvant lomustine and TMZ (for patients with MGMT promoter-methylated or indeterminate tumors and age ≤70 years) (category 2B[q,65]
Adjuvant Treatment, KPS <60	• None	• None	• Hypofractionated RT + concurrent or adjuvant TMZ (for patients aged ≤70 years)[j,63] • TMZ (for patients with MGMT promoter-methylated tumors)[64]
Recurrent or Progressive Disease[e,m,n]	• Bevacizumab[g,h,47-50] • TMZ[2,24,51,52] • Lomustine or carmustine[53-56] • PCV[b,57,58] • Regorafenib[59]	• Systemic therapy[m] + bevacizumab[g,h] ▸ Carmustine or lomustine + bevacizumab[g,h,60] ▸ TMZ + bevacizumab[g,h,61,62]	• If failure or intolerance to the preferred or other recommended regimens ▸ Etoposide (category 2B)[37] ▸ Platinum-based regimens[r,39-41] (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.
[m] Bevacizumab + systemic therapy can be considered if bevacizumab monotherapy fails and it is desirable to continue the steroid-sparing effects of bevacizumab.
[n] Systemic therapy options also apply for *H3*-mutated high-grade glioma. Crowell C, et al. Neurooncol Adv 2022;4:1-10 and Gojo J, et al. Front Oncol 2020;9:1436.
[o] 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.
[p] Alternating electric field therapy is only an option for patients with supratentorial disease.
[q] Moderate to significant myelosuppression was observed, but the toxicity profile for this regimen is not yet fully defined.
[r] Platinum-based regimens include cisplatin or carboplatin.

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Continued

NCCN Categories of Evidence and Consensus	
Category 1	Based upon high-level evidence, there is uniform NCCN consensus that the intervention is appropriate.
Category 2A	Based upon lower-level evidence, there is uniform NCCN consensus that the intervention is appropriate.
Category 2B	Based upon lower-level evidence, there is NCCN consensus that the intervention is appropriate.
Category 3	Based upon any level of evidence, there is major NCCN disagreement that the intervention is appropriate.

All recommendations are category 2A unless otherwise indicated.

NCCN Categories of Preference	
Preferred intervention	Interventions that are based on superior efficacy, safety, and evidence; and, when appropriate, affordability.
Other recommended intervention	Other interventions that may be somewhat less efficacious, more toxic, or based on less mature data; or significantly less affordable for similar outcomes.
Useful in certain circumstances	Other interventions that may be used for selected patient populations (defined with recommendation).

All recommendations are considered appropriate.

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