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NCCN Guidelines Insights: Central Nervous System Cancers, Version 1.2017

Louis Burt Nabors, MD; Jana Portnow, MD; Mario Ammirati, MD, MBA; Joachim Baehring, MD; Henry Brem, MD; Nicholas Butowski, MD; Robert A. Fenstermaker, MD; Peter Forsyth, MD; Jona Hattangadi-Gluth, MD; Matthias Holdhoff, MD, PhD; Steven Howard, MD; Larry Junck, MD; Thomas Kaley, MD; Priya Kumthekar, MD; Jay S. Loeffler, MD; Paul L. Moots, MD; Maciej M. Mrugala, MD, PhD, MPH; Seema Nagpal, MD; Manjari Pandey, MD; Ian Parney, MD, PhD; Katherine Peters, MD, PhD; Vinay K. Puduvalli, MD; John Ragsdale III, MD; Jason Rockhill, MD, PhD; Lisa Rogers, MD; Chad Rusthoven, MD; Nicole Shonka, MD; Dennis C. Shrieve, MD, PhD; Allen K. Sills Jr, MD; Lode J. Swinnen, MB, ChB; Christina Tsien, MD; Stephanie Weiss, MD; Patrick Yung Wen, MD; Nicole Willmarth, PhD; Mary Anne Bergman; and Anita Engh, PhD

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eTable 1. Histologic and Molecular Subgrouping of Grade II/III Gliomas

WHO Classification System[a]			NCCN Guidelines, Version 1.2017[45,b]	
Grade	**WHO 2007[3]**	**WHO 2016[26]**	**Label**	**Relevant Algorithm Pages[d]**
II	Diffuse astrocytoma	• Diffuse astrocytoma, *IDH*-mut • Diffuse astrocytoma, *IDH*-wt • Diffuse astrocytoma, NOS	Low-grade infiltrative astrocytoma[c]	Newly diagnosed: ASTR-1 Recurrent/Progressive: ASTR-2[c]
II	Oligodendroglioma	• Oligodendroglioma, *IDH*-mut and 1p19q-codel • Oligodendroglioma, NOS	Low-grade infiltrative oligodendroglioma[c]	
II	Oligoastrocytoma	• Oligoastrocytoma, NOS[e]	Low-grade infiltrative oligoastrocytoma[c,e]	
III	Anaplastic astrocytoma	• Anaplastic astrocytoma, *IDH*-mut • Anaplastic astrocytoma, *IDH*-wt • Anaplastic astrocytoma, NOS	Anaplastic astrocytoma	Newly diagnosed: GLIO-1 and GLIO-2 Recurrent: GLIO-5
III	Anaplastic oligodendroglioma	• Anaplastic oligodendroglioma, *IDH*-mut and 1p19q-codel • Anaplastic oligodendroglioma, NOS	Anaplastic oligodendroglioma, 1p19q-codel	
III	Anaplastic oligoastrocytoma	• Anaplastic oligoastrocytoma, NOS[e]	Anaplastic oligoastrocytoma[e]	

Abbreviations: 1p19q-codel, codeletion of 1p and 19q; *IDH*-mut, mutation present in either *IDH1* or *IDH2*; *IDH*-wt, tumors with wild-type *IDH1* codon 132 and *IDH2* codon 172 by sequencing; NOS, not otherwise specified (lesions that cannot be classified due to insufficient genetic, pathologic, or clinical data).

[a]Categories listed are limited to those covered in the NCCN Guidelines for Central Nervous System Cancers. Highlighted entries represent new categories added in the 2016 WHO classification system.

[b]Table shows histologic category and molecular features used to determine the recommended treatment pathway. Each pathway has several recommended adjuvant treatment options. The recommended treatment pathway is also determined by performance status. The "Principles of Brain Tumor Pathology" appendix (see BRAIN-F, pages 1334 and 1335) comments on how *IDH* mutation status may be used to select among recommended treatment options, but *IDH* genotype is not used to determine which treatment options are recommended.

[c]The recommendations on ASTR-1[d] and ASTR-2[d] apply only to supratentorial tumors in adult patients.

[d]Available in the full version of these guidelines at NCCN.org.

[e]2016 WHO has deleted oligoastrocytoma as a category, although "oligoastrocytoma, NOS" and "anaplastic oligoastrocytoma, NOS" may continue to be used for lesions that cannot be classified as astrocytoma or oligodendroglioma due to the absence of appropriate diagnostic molecular testing.

eTable 2. Molecular Subtypes of Grade II/III Gliomas[4,5,7,9,11,28,31,34,35,37,40]

IDH Status:	**IDH-mut**	**IDH-mut**	**IDH-wt**
1p19q Status:	**1p19q-codel**	**1p19q Intact or Deletion of Only 1p or 19q**	**1p19q Intact or Deletion of Only 1p or 19q**
Phenotype characteristics	• Location: more frontal than temporal	• Location: more frontal than temporal	• Location: more temporal than frontal
Notable patient characteristics	• Younger than *IDH*-wt[a]	• Younger than *IDH*-wt[a]	• Older than *IDH*-mut[a]
Associated molecular features[b]	• Inactivating: *CIC*, *NOTCH1*, *FUBP1* • Activating: *PIK3CA*, *TERT*	• Inactivating: *TP53*, *ATRX*	• Inactivating[c]: *PTEN*, *NF1*, *CDKN2A/B* • Activating[c]: *EGFR*, *TERT* • Frequent copy number changes (especially chr 7 & 10)[c]
Prognosis[d]	Good	Medium	Poor

Abbreviations: 1p19q-codel, codeletion of 1p and 19q; chr, chromosome; GBM, glioblastoma; *IDH*-mut, mutation present in either *IDH1* or *IDH2; IDH*-wt, both *IDH1* and *IDH2* are wild-type.
[a]Age increases with grade for all subtypes.
[b]Molecular features that have been observed in some fraction of tumors within the subgroup defined by *IDH* mutation and 1p19q codeletion status. These associated molecular markers are not necessarily found in all tumors in a subgroup.
[c]The molecular profile shown here accounts for the vast majority of *IDH*-wt grade II/III gliomas. However, some studies indicate that there are one or more small subgroups within the grade II/III *IDH*-wt subgroup that have distinct molecular profiles and lack all of the "classic" GBM markers listed here. One such subgroup may be similar to a subgroup of less-common GBMs with even poorer prognosis that have mutations in *H3F3A* and often *ATRX* loss. Another subgroup appears to lack all abovementioned GBM markers, may be localized in the midline, and has far better prognosis than most GBMs, more similar to *IDH*-mut grade II/III gliomas.[9,40]
[d]See data in Table 1.