

Therapy for Diffuse Astrocytic and Oligodendroglial Tumors in Adults: ASCO-SNO Guideline Rapid Recommendation Update

Jaishri Blakeley, MD¹ ; Nimish A. Mohile, MD²; Hans Messersmith, MPH³ ; Andrew B. Lassman, MD⁴ ; and David Schiff, MD⁵ ; for the Therapy for Diffuse Astrocytic and Oligodendroglial Tumors in Adults Guideline Expert Panel

DOI <https://doi.org/10.1200/JCO-25-00250>

ASCO Rapid Recommendation Updates highlight revisions to select ASCO guideline recommendations as a response to the emergence of new and practice-changing data. The rapid updates are supported by an evidence review and follow the guideline development processes outlined in the [ASCO Guideline Methodology Manual](#). The goal of these articles is to disseminate updated recommendations, in a timely manner, to better inform health practitioners and the public on the best available cancer care options. Guidelines and updates are not intended to substitute for independent professional judgment of the treating clinician and do not account for individual variation among patients. See appendix for disclaimers and other important information ([Appendix 1](#) and [Appendix 2](#), online only).

ACCOMPANYING CONTENT

 Listen to the podcast by Dr Blakeley, Dr Mohile, and Brittany Harvey at <https://ascopubs.org/doi/therapy-diffuse-astrocytic-and-oligodendroglial-tumors-adults-asco-sno-rapid-update>

 Article, February 1, 2022 issue on p. 403

 Appendix

 Data Supplement

Accepted March 5, 2025

Published April 29, 2025

Evidence-Based Medicine

Committee approval:

January 24, 2025

SNO Guidelines and Reported

Outcomes Committee approval:

January 24, 2025

J Clin Oncol 43:2129-2133

© 2025 by American Society of
Clinical Oncology



[View Online
Article](#)

BACKGROUND

In 2021, ASCO and the Society for Neuro-Oncology (SNO) jointly published a guideline regarding gliomas in adults.¹ Recommendations 1.2 and 1.5 of that guideline stated that initial therapy with radiation and chemotherapy may be deferred in select patients with *IDH*-mutant WHO CNS grade 2 oligodendroglioma and astrocytoma.

On August 6, 2024, the US Food and Drug Administration (FDA) approved² vorasidenib based on results of the Investigating Vorasidenib In Glioma (INDIGO) trial³ for patients age ≥12 years with grade 2 astrocytoma or

oligodendroglioma with a susceptible *IDH1* or *IDH2* mutation following surgery including biopsy, subtotal resection, or gross total resection. INDIGO data and the regulatory approval prompted consideration of a rapid recommendation update to answer the following question: can any other intervention be recommended in patients who have had initial radio-chemotherapy deferred?

METHODS

A literature search was conducted for randomized controlled trials that met the selection criteria of the original guideline¹ published between January 1, 2020, and October 15, 2024,

TABLE 1. Evidence Profile for INDIGO Trial

Population: Patients With WHO Grade 2 <i>IDH</i> -Mutant Glioma Deferred for Radiation and Chemotherapy Intervention: Vorasidenib Comparator: Placebo					
Outcome Time Frame	Study Result and Measurement	Absolute Effect Estimate		Quality of Evidence	Summary
		Placebo	Vorasidenib		
Disease progression or death ^a 12 months after last surgery	Hazard ratio: 0.39 (95% CI, 0.27 to 0.56) Based on data from 331 participants in one study ^b Follow-up: median 14.2 months	570 per 1,000 Difference: 290 fewer per 1,000 (95% CI, 366 fewer to 193 fewer)	280 per 1,000	High	Vorasidenib improves PFS compared with placebo
Receipt of next intervention or death ^c 12 months after last surgery	Hazard ratio: 0.26 (95% CI, 0.15 to 0.43) Based on data from 331 participants in one study ^d Follow-up: median 14.2 months	270 per 1,000 Difference: 191 fewer per 1,000 (95% CI, 224 fewer to 143 fewer)	79 per 1,000	High	Patients are able to postpone the receipt of the next intervention longer with vorasidenib v placebo
Grade 3 or higher adverse events ^e during deferral period	Relative risk: 1.69 (95% CI, 1.04 to 2.72) Based on data from 331 participants in one study	135 per 1,000 Difference: 93 more per 1,000 (95% CI, 5 more to 232 more)	228 per 1,000	Moderate Due to serious risk of bias ^f	Patients probably experience more grade 3 or higher adverse events on vorasidenib than placebo
Treatment-related serious adverse events ^g during and after therapy	Based on data from 331 participants in one study ^h	1.8% (3 participants out of 167) with vorasidenib. No events reported with placebo		Very low Due to very serious imprecision and serious risk of bias ⁱ	Too few treatment-related serious adverse events occurred to determine whether vorasidenib made a difference

Abbreviation: PFS, progression-free survival.

^aProgressive disease or death (based on reported PFS).

^bPrimary study. Baseline/comparator control arm of reference used for intervention. PFS rate estimated as 43% for the control arm at 12 months from the Kaplan-Meier curve in the publication, Figure 2A, yielding 570 progressions or deaths per 1,000.³

^cPatient has received further therapy or has died.

^dPrimary study. Baseline/comparator Control arm of reference used for intervention. Estimated 73% of patients had not received the next intervention or died at 12 months, yielding 270 per 1,000 control arm event rate.³

^ePatient experiences at least one grade 3 or higher adverse event during the period where radiation and chemotherapy were deferred.

^fRisk of bias: serious. No blinded assessment of adverse events.

^gSerious adverse events assessed by the investigators to be related to vorasidenib or placebo.

^hPrimary study.³

ⁱRisk of bias: serious. No blinded assessment of adverse events; imprecision: very serious. Very low number of serious adverse events.

that were not previously identified. The original guideline Expert Panel was reconvened to review new evidence from this search, including the INDIGO trial, and to review and approve the revised recommendation.

EVIDENCE REVIEW

The new literature search identified 688 potential articles, of which 62 were reviewed in full text. Sixteen new publications for previously identified trials and 27 new publications of 26 previously unknown trials were located. Of these, only one trial was identified that was relevant to the specific subpopulation addressed in this rapid update: the INDIGO trial.³ The remaining trials are briefly summarized in the Supplement. None of the other trials were considered to require a rapid recommendation update to the original guideline recommendations.

The published INDIGO trial outcomes are summarized in the Evidence Profile (Table 1). Vorasidenib was associated with significantly improved progression-free survival (PFS) and prolonged time to next intervention, but increased frequency of grade 3 or higher adverse events (mainly reversible and asymptomatic transaminitis) versus placebo. Patients were required to have at least one previous surgery with the most recent surgery occurring between 1 year and 5 years before random assignment, no other anticancer treatment for glioma, and be considered an appropriate candidate for a watch-and-wait approach. In addition, measurable non-enhancing disease (≥ 1 target lesion measuring ≥ 1 cm²) was required and any contrast enhancement had to be minimal, non-nodular, and nonmeasurable.

The panel updated Recommendations 1.2 and 1.5 to clarify that they speak to the deferral of radiation therapy and chemotherapy and added new Recommendations 1.2.1 and 1.5.1 addressing therapy with vorasidenib. Recommendations 1.1 and 1.4 are reprinted here for clarity. Note that based on current ASCO definitions, all Weak recommendations here and in the Table of Recommendations have been changed to Conditional.

UPDATED AND NEW RECOMMENDATIONS

Recommendation 1.1 (reprinted here for clarity)

People with oligodendroglioma, *IDH*-mutant, 1p19q codeleted, CNS WHO grade 2 should be offered radiation in combination with procarbazine, lomustine, and vincristine (PCV) (Evidence quality: Moderate; Strength of recommendation: Strong). Temozolomide is a reasonable alternative to PCV when toxicity is a concern (Evidence quality: Low; Strength of recommendation: Conditional).

Updated Recommendation 1.2

Within the group of people with oligodendroglioma, *IDH*-mutant, 1p19q codeleted, CNS WHO grade 2, initial radiation

therapy and chemotherapy (with PCV or temozolomide) may be deferred until radiographic or symptomatic progression in some people with favorable prognostic factors (eg, complete resection and younger age) or concerns about toxicity. See the Clinical Interpretation section (in the original publication) for more details (Evidence quality: Low; Strength of recommendation: Conditional).

New Recommendation 1.2.1

Vorasidenib may be offered to people with oligodendroglioma, *IDH*-mutant, 1p19q codeleted, CNS WHO grade 2, where, after one or more surgeries, further treatment with radiation and chemotherapy has been or can be deferred (Evidence quality: High; Strength of recommendation: Conditional).

Recommendation 1.4 (reprinted here for clarity)

People with astrocytoma, *IDH*-mutant, 1p19q non-codeleted, CNS WHO grade 2 (low grade diffuse glioma) should be offered radiation therapy with adjuvant chemotherapy (temozolomide or PCV) (Evidence quality: Moderate; Strength of recommendation: Strong).

Updated Recommendation 1.5

In astrocytoma, *IDH*-mutant, 1p19q non-codeleted, CNS WHO grade 2, initial radiation therapy and chemotherapy (with temozolomide or PCV) may be deferred until radiographic or symptomatic progression in some people with favorable prognostic factors (eg, complete resection, younger age) or concerns about short- and long-term toxicity given the natural history of the disease. See the Clinical Interpretation section (in the original publication) for more details (Evidence quality: Low; Strength of recommendation: Conditional).

New Recommendation 1.5.1

Vorasidenib may be offered to people with astrocytoma, *IDH*-mutant, 1p19q non-codeleted, CNS WHO grade 2, where, after one or more surgeries, further treatment with radiation and chemotherapy has been or can be deferred (Evidence quality: High; Strength of recommendation: Conditional).

For all guideline recommendations, a complete summary table is available in Appendix Table A1 (online only).

DISCUSSION

The benefits in terms of PFS and time to next intervention with vorasidenib versus observation outweigh the increased frequency of adverse events for many patients. Regular monitoring for liver function is necessary every 2 weeks in the first 2 months of treatment and monthly thereafter. People who are seeking pregnancy as either father or mother

and people who are pregnant or breast feeding should not be offered vorasidenib. The Panel notes that the FDA approval and the INDIGO trial itself included patients as young as age 12 years; the ASCO-SNO guideline and this update only address adult patients.

The regulatory approval of vorasidenib in the United States has several differences to the trial inclusion and exclusion criteria that warrant discussion.

- The trial required measurable disease assessed by magnetic resonance imaging (MRI) to determine the effect of vorasidenib on measurable tumor size; the approval allows patients to have had gross total resection. Patients without measurable tumor and their clinicians should carefully weigh the potential but uncertain benefits of beginning vorasidenib immediately versus continued observation until there is documented measurable tumor to allow for monitoring for response.
- The trial required patients to wait at least 1 year and no more than 5 years after surgery to determine the effect of vorasidenib on tumor growth rate before and then during treatment; the approval does not include this restriction. The panel believes this time window is arbitrary, and that it is reasonable to discuss vorasidenib at any time point after postoperative recovery.
- The trial only included patients with residual or recurrent disease who had received no previous nonsurgical therapy.

AFFILIATIONS

¹ Johns Hopkins University School of Medicine, Baltimore, MD

²Department of Neurology and Wilmot Cancer Institute, University of Rochester Medical Center, Rochester, NY

³ASCO, Alexandria, VA

⁴Columbia University Vagelos College of Physicians and Surgeons, Herbert Irving Comprehensive Cancer Center, and NewYork-Presbyterian, New York, NY

⁵University of Virginia Medical Center, Charlottesville, VA

CORRESPONDING AUTHOR

American Society of Clinical Oncology; e-mail: guidelines@asco.org.

DISCLAIMER

The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health or National Cancer Institute.

EDITOR'S NOTE

This ASCO Clinical Practice Guideline Recommendation Update provides a recommendation update, with review and analysis of the relevant literature for the recommendation. Additional information, including links to patient information at www.cancer.org, is available at www.asco.org/neurooncology-guidelines.

This Guideline was jointly developed by the American Society of Clinical Oncology, and the Society for NeuroOncology and has been co-published with permission in *Journal of Clinical Oncology* and in *Neuro-Oncology*. All rights reserved. The articles are identical except for minor stylistic and spelling differences in keeping with each journal's style.

This restriction on previous nonsurgical therapy is not mentioned in the approval. There are currently no randomized data from INDIGO or any other trial on the use of vorasidenib in patients who have received previous radiation and/or chemotherapy. The panel cannot make a recommendation about vorasidenib in those patients.

- The trial excluded patients based on criteria that may increase the patient's risk of progression or recurrence, such as measurable or nodular contrast enhancement on brain computed tomography and/or MRI, uncontrolled seizures, and brain-stem involvement. None of these factors are mentioned in the approval. There are currently inadequate data on the use of vorasidenib in these patients, and the panel cannot make a recommendation about vorasidenib in those patients.

Patients with grade 3 or 4 disease are outside the scope of this rapid update and were not included in the INDIGO trial.

Evidence supporting unchanged recommendations and sections on patient-clinician communication, health equity, cost implications, and more are found in the full guideline publication and apply to this Rapid Update.¹ Additionally, for guideline tools and resources, visit www.asco.org/neurooncology-guidelines.

Either citation can be used when citing this article. For permissions, please email permissions@LWW.com.

EQUAL CONTRIBUTION

J.B. and N.A.M. were Expert Panel Co-Chairs. A.B.L. and D.S. were Society for Neuro-Oncology formal representatives.

SUPPORT

Supported in part by Herbert Irving Comprehensive Cancer Center National Cancer Institute Support Grant P30CA013696 (to A.B.L.); William Rhodes and Louise Tilzer-Rhodes Center for Glioblastoma at NewYork-Presbyterian Hospital, Hearst Foundations; and the Michael Weiner Glioblastoma Research into Treatment Fund.

AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

Disclosures provided by the authors are available with this article at DOI <https://doi.org/10.1200/JCO-25-00250>.

AUTHOR CONTRIBUTIONS

Conception and design: All authors

Collection and assembly of data: All authors

Data analysis and interpretation: All authors

Manuscript writing: All authors

Final approval of manuscript: All authors

Accountable for all aspects of the work: All authors

ACKNOWLEDGMENT

The authors wish to thank Priscilla Brastianos, MD (co-chair of the Multi-Site Guideline Advisory Group), Susan Chang, MD and Lauren Singer, MD (EBMC reviewers), the Society for Neuro-Oncology Guidelines and Reported Outcomes Committee, and the ASCO Evidence

Based Medicine Committee for their thoughtful reviews and insightful comments on this guideline update.

Members of the Therapy for Diffuse Astrocytic and Oligodendroglial Tumors in Adults Guideline Expert Panel are listed in [Appendix 3](#).

REFERENCES

1. Mohile NA, Messersmith H, Gatson NT, et al: Therapy for diffuse astrocytic and oligodendroglial tumors in adults: ASCO-SNO guideline. *J Clin Oncol* 40:403-426, 2022
 2. VORANIGO® Prescribing Information. Silver Springs, MD, US Food and Drug Administration, 2024
 3. Mellinghoff IK, van den Bent MJ, Blumenthal DT, et al: Vorasidenib in IDH1- or IDH2-mutant low-grade glioma. *N Engl J Med* 389:589-601, 2023
-

AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

Therapy for Diffuse Astrocytic and Oligodendroglial Tumors in Adults: ASCO-SNO Guideline Rapid Recommendation Update

The following represents disclosure information provided by authors of this manuscript. All relationships are considered compensated unless otherwise noted. Relationships are self-held unless noted. I = Immediate Family Member, Inst = My Institution. Relationships may not relate to the subject matter of this manuscript. For more information about ASCO's conflict of interest policy, please refer to www.asco.org/rwc or ascopubs.org/jco/authors/author-center.

Open Payments is a public database containing information reported by companies about payments made to US-licensed physicians (Open Payments).

Jaishri Blakeley

Consulting or Advisory Role: SpringWorks Therapeutics, Alexion Pharmaceuticals

Research Funding: Bristol Myers Squibb (Inst)

Uncompensated Relationships: SpringWorks Therapeutics (Inst)

Open Payments Link: <https://openpaymentsdata.cms.gov/physician/747718>

Nimish A. Mohile

Research Funding: Novocure (Inst)

Andrew B. Lassman

Consulting or Advisory Role: Sapience Therapeutics, Global Coalition for Adaptive Research, Orbus Therapeutics, Servier, Fore Biotherapeutics, Curio Science, Alpha Detail, Bluestar Bioadvisors, Gerson Lehrman Group, Reach Market Research, Guidepoint Global, Modifi Bio

Research Funding: AbbVie (Inst), Genentech/Roche (Inst), Aeterna Zentaris (Inst), VBI Vaccines (Inst), Pfizer (Inst), Karyopharm

Therapeutics (Inst), Bayer (Inst), QED Therapeutics (Inst), Orbus Therapeutics (Inst), BMS (Inst), Chimerix (Inst), NextSource (Inst), DelMar Pharmaceuticals (Inst), Corden (Inst), Kazia Therapeutics (Inst), Servier (Inst), Biohaven Pharmaceuticals (Inst), Vigeo Therapeutics (Inst), Incyte (Inst), Abbott Laboratories (Inst), Polaris (Inst), Kintara Therapeutics (Inst), Novartis (Inst), Global Coalition for Adaptive Research (Inst), AstraZeneca (Inst)

Travel, Accommodations, Expenses: AbbVie, Foundation Medicine, Servier, Anheart Therapeutics, Global Coalition for Adaptive Research, Gilead Sciences, Sapience Therapeutics, Orbus Therapeutics, Incyte, Moving Innovation and Technology, Modifi Bio, VBI Vaccines

David Schiff

Consulting or Advisory Role: Orbus Therapeutics, PRA, Anheart Therapeutics, Servier (I), SymBio Pharmaceuticals

Patents, Royalties, Other Intellectual Property: Receive royalties for submissions to UpToDate

No other potential conflicts of interest were reported.

APPENDIX 1. GUIDELINE DISCLAIMER

The Clinical Practice Guidelines and other guidance published herein are provided by ASCO, Inc to assist clinicians in clinical decision making. The information herein should not be relied upon as being complete or accurate, nor should it be considered as inclusive of all proper treatments or methods of care or as a statement of the standard of care. With the rapid development of scientific knowledge, new evidence may emerge between the time information is developed and when it is published or read. The information is not continually updated and may not reflect the most recent evidence. The information addresses only the topics specifically identified therein and is not applicable to other interventions, diseases, or stages of diseases. This information does not mandate any particular course of medical care. Furthermore, the information is not intended to substitute for the independent professional judgment of the treating clinician, as the information does not account for individual variation among patients. Recommendations specify the level of confidence that the recommendation reflects the net effect of a given course of action. The use of words like must, must not, should, and should not indicates that a course of action is recommended or not recommended for either most or many patients, but there is latitude for the treating physician to select other courses of action in individual cases. In all cases, the selected course of action should be considered by the treating clinician in the context of treating the individual patient. Use of the information is voluntary. ASCO does not endorse third party drugs, devices, services, or therapies used to diagnose, treat, monitor, manage, or alleviate health conditions. Any use of a brand or trade name is for identification purposes only. ASCO provides this information on an as is basis and makes no warranty, express or implied, regarding the information. ASCO specifically disclaims any warranties of merchantability or fitness for a particular use or purpose. ASCO assumes no responsibility for any injury or damage to persons or property arising out of or related to any use of this information or for any errors or omissions.

APPENDIX 2. GUIDELINE AND CONFLICTS OF INTEREST

The Expert Panel was assembled in accordance with ASCO's Conflict of Interest Policy Implementation for Clinical Practice Guidelines ("Policy," found at <http://www.asco.org/guideline-methodology>). All members of the Expert Panel completed ASCO's disclosure form, which requires disclosure of financial and other interests, including relationships with commercial entities that are reasonably likely to experience direct regulatory or commercial impact as a result of promulgation of the guideline. Categories for disclosure include employment; leadership; stock or other ownership; honoraria, consulting, or advisory role; speaker's bureau; research funding; patents, royalties, other intellectual property; expert testimony; travel, accommodations, expenses; and other relationships. In accordance with the Policy, the majority of the members of the Expert Panel did not disclose any relationships constituting a conflict under the Policy.

APPENDIX 3. THERAPY FOR DIFFUSE ASTROCYTIC AND OLIGODENDROGLIAL TUMORS IN ADULTS GUIDELINE EXPERT PANEL

The following are members of the Therapy for Diffuse Astrocytic and Oligodendroglial Tumors in Adults Guideline Expert Panel: Jaishri Blakeley, MD; Na Tosha Gatson, MD, PhD; Andreas F. Hottinger, MD, PhD; Andrew Lassman, MD; Nimish A. Mohile, MD; Jordan Morton, MD; Douglas Ney, MD; Phioanh Leia Nghiemphu, MD; James Perry, MD; David Schiff, MD; Anne Shannon, MA; Helen A. Shih, MD, MS; Roy Stowd, MD, MEd, MS; Martin van den Bent, MD, PhD; Mateo Ziu, MD, MBA.

TABLE A1. Summary of All Recommendations

Patient Population		Recommendation
<i>General Note.</i> The following recommendations (strong or conditional/weak) and terminology (see Data Supplement) represent reasonable options for patients depending on clinical circumstances and in the context of individual patient preferences. Recommended care should be accessible to patients whenever possible.		
<i>IDH</i> -Mutant Astrocytic and Oligodendroglial Tumors	Oligodendroglioma, <i>IDH</i> -mutant, 1p19q co-deleted, CNS WHO grade 2	1.1. People with oligodendroglioma, <i>IDH</i> -mutant, 1p19q co-deleted, CNS WHO grade 2 should be offered radiation in combination with PCV (Evidence quality: Moderate; Strength of recommendation: Strong). Temozolomide is a reasonable alternative to PCV when toxicity is a concern (Evidence quality: Low; Strength of recommendation: Conditional) 1.2. (Updated) Within the group of people with oligodendroglioma, <i>IDH</i> -mutant, 1p19q codeleted, CNS WHO grade 2, initial radiation therapy and chemotherapy (with PCV or temozolomide) may be deferred until radiographic or symptomatic progression in some people with favorable prognostic factors (eg, complete resection and younger age) or concerns about toxicity. See the Clinical Interpretation section (in the original publication) for more details (Evidence quality: Low; Strength of recommendation: Conditional) 1.2.1. (New) Vorasidenib may be offered to people with oligodendroglioma, <i>IDH</i> -mutant, 1p19q codeleted, CNS WHO grade 2, where, after one or more surgeries, further treatment with radiation and chemotherapy has been or can be deferred (Evidence quality: High; Strength of recommendation: Conditional)
	Oligodendroglioma, <i>IDH</i> -mutant, 1p19q co-deleted, CNS WHO grade 3 (formerly anaplastic oligodendroglioma)	1.3. People with oligodendroglioma, <i>IDH</i> -mutant, 1p19q co-deleted, CNS WHO grade 3 should be offered radiation therapy in combination with PCV (Evidence quality: Moderate; Strength of recommendation: Strong). Temozolomide is a reasonable alternative to PCV when toxicity is a concern (Evidence quality: Low; Strength of recommendation: Conditional)
	Astrocytoma, <i>IDH</i> -mutant, 1p19q non-codeleted, CNS WHO grade 2 (formerly diffuse astrocytoma)	1.4. People with astrocytoma, <i>IDH</i> -mutant, 1p19q non-codeleted, CNS WHO grade 2 (low grade diffuse glioma) should be offered radiation therapy with adjuvant chemotherapy (temozolomide or PCV) (Evidence quality: Moderate; Strength of recommendation: Strong) 1.5. (Updated) In astrocytoma, <i>IDH</i> -mutant, 1p19q non-codeleted, CNS WHO grade 2, initial radiation therapy and chemotherapy (with temozolomide or PCV) may be deferred until radiographic or symptomatic progression in some people with favorable prognostic factors (eg, complete resection, younger age) or concerns about short- and long-term toxicity given the natural history of the disease. See the Clinical Interpretation section (in the original publication) for more details (Evidence quality: Low; Strength of recommendation: Conditional) 1.5.1. (New) Vorasidenib may be offered to people with astrocytoma, <i>IDH</i> -mutant, 1p19q non-codeleted, CNS WHO grade 2, where, after one or more surgeries, further treatment with radiation and chemotherapy has been or can be deferred (Evidence quality: High; Strength of recommendation: Conditional)
	Astrocytoma, <i>IDH</i> -mutant, 1p19q non-codeleted, CNS WHO grade 3 (formerly anaplastic astrocytoma)	1.6. People with astrocytoma, <i>IDH</i> -mutant, 1p19q non-codeleted CNS WHO grade 3 should be offered radiation therapy with adjuvant temozolomide (Evidence quality: Moderate; Strength of recommendation: Strong)
	Astrocytoma, <i>IDH</i> -mutant, CNS WHO grade 4 (formerly <i>IDH</i> -mutant glioblastoma)	1.7. People with astrocytoma, <i>IDH</i> -mutant CNS WHO grade 4 may be treated like an astrocytoma, <i>IDH</i> -mutant, non-codeleted, CNS WHO grade 3 (formerly anaplastic astrocytoma; see Recommendation 1.6) or like a glioblastoma, <i>IDH</i> -wild-type, CNS WHO grade 4 (formerly <i>IDH</i> -wildtype glioblastoma; see Recommendation 2.2) (Evidence quality: Very low; Strength of recommendation: Conditional)

(continued on following page)

TABLE A1. Summary of All Recommendations (continued)

Patient Population	Recommendation
Glioblastoma and other <i>IDH</i> -Wildtype Diffuse Glioma	2.1. People with astrocytoma, <i>IDH</i> -wildtype, CNS WHO grade 2 or 3 may be treated according to recommendations for glioblastoma, <i>IDH</i> -wildtype, CNS WHO grade 4 found in this guideline (Evidence quality: Very low; Strength of recommendation: Conditional)
	2.2. Concurrent temozolomide and radiation therapy should be offered to people with newly diagnosed glioblastoma, <i>IDH</i> -wildtype, CNS WHO grade 4 (Evidence quality: Moderate; Strength of recommendation: Strong)
	<i>Qualifying Statement for Recommendation 2.2:</i> With the exception of studies addressing glioblastoma diagnosis in people of older age or poor performance status, no prospective, randomized evidence provides a sufficient basis to guide decision making based on MGMT promotor methylation status
	2.3. Six months of adjuvant temozolomide should be offered to people with newly diagnosed glioblastoma, <i>IDH</i> -wildtype, CNS WHO grade 4 who have received concurrent radiation therapy plus temozolomide (Evidence quality: Moderate; Strength of recommendation: Strong)
	2.4. Alternating electric field therapy may be added to adjuvant temozolomide in people with newly diagnosed supratentorial glioblastoma, <i>IDH</i> -wildtype, CNS WHO grade 4 who have completed chemoradiation therapy (Evidence quality: Moderate; Strength of recommendation: Conditional)
	2.5. Bevacizumab is not recommended for people with newly diagnosed glioblastoma, <i>IDH</i> -wildtype, CNS WHO grade 4 (Evidence quality: Moderate; Strength of recommendation: Conditional)
	2.6. In people with glioblastoma, <i>IDH</i> -wildtype, CNS WHO grade 4 where the expected survival benefits of a six-week radiation course combined with temozolomide may not outweigh the harms, hypofractionated radiation therapy combined with temozolomide is a reasonable alternative. See Clinical Interpretation for further explanation (Evidence quality: Moderate; Strength of recommendation: Conditional)
	2.7. In people with glioblastoma, <i>IDH</i> -wildtype, CNS WHO grade 4 with older age, poor performance status or with concerns about toxicity or prognosis, best supportive care alone, hypofractionated radiation therapy alone (for MGMT promotor unmethylated tumors) or temozolomide alone (for MGMT promotor methylated tumors) are reasonable options. See Clinical Interpretation for further explanation (Evidence quality: Low; Strength of recommendation: Conditional)
	2.8. No recommendation for or against any therapeutic strategy can be made for treatment of recurrent glioblastoma, <i>IDH</i> -wildtype, CNS WHO grade 4. (Evidence quality: Low; Strength of recommendation: No recommendation). People with recurrent glioblastoma should be referred for participation in a clinical trial where possible (Evidence quality: No evidence considered; Strength of recommendation: Strong)
	2.9. No recommendation for or against any therapeutic strategy can be made for treatment of diffuse midline glioma (Evidence quality: Low; Strength of recommendation: No recommendation). People with diffuse midline glioma should be referred for participation in a clinical trial when possible (Evidence quality: No evidence considered; Strength of recommendation: Strong)

NOTE. The strength of the recommendation is defined as follows: Strong: In recommendations for an intervention, the desirable effects of an intervention outweigh its undesirable effects. In recommendations against an intervention, the undesirable effects of an intervention outweigh its desirable effects. All or almost all informed people would make the recommended choice for or against an intervention. Conditional: In recommendations for an intervention, the desirable effects probably outweigh the undesirable effects, but appreciable uncertainty exists. In recommendations against an intervention, the undesirable effects probably outweigh the desirable effects, but appreciable uncertainty exists. Most informed people would choose the recommended course of action, but a substantial number would not.

Abbreviations: IDH, Isocitrate dehydrogenase; MGMT, O⁶-methylguanine-DNA methyltransferase; PCV, procarbazine, lomustine, and vincristine.