

Guideline Page and Request	Panel Discussion/References	Institution Vote			
		YES	NO	ABSTAIN	ABSENT
ASTR-2 Internal request: Institutional Review comment to reassess the inclusion of two regimens for low grade, high-risk resected glioma: 1) RT followed by TMZ and 2) RT with concurrent and adjuvant TMZ	1) The panel consensus supported RT followed by TMZ for low-grade, high-risk resected glioma. This remains a category 2B recommendation. (see references below)	12	6	0	8
	2) Based on the discussion (and noted references), the panel consensus supported the continued listing of RT with concurrent and adjuvant TMZ as an option for patients with low-grade, high-risk resected glioma, and the category was changed from category 2B to category 2A. <ul style="list-style-type: none"> • Pouratian N, Gasco J, Sherman JH, et al. Toxicity and efficacy of protracted low dose temozolomide for the treatment of low grade gliomas. J Neurooncol 2007;82:281-288. • Kesari S, Schiff D, Drappatz J, et al. Phase II study of protracted daily temozolomide for low-grade gliomas in adults. Clin Cancer Res 2009;15:330-337. • Fisher BJ, Hu C, Macdonald DR, et al. Phase 2 study of temozolomide-based chemoradiation therapy for high-risk low-grade gliomas: preliminary results of Radiation Therapy Oncology Group 0424. Int J Radiat Oncol Biol Phys 2015;91:497-504. 	16	2	0	8
ASTR-3 Internal request: Institutional Review comment, “For recurrent disease and no prior radiation, option of chemotherapy alone should be qualified.”	Based on a review of data and discussion, the panel consensus did not support the treatment options chemotherapy alone or external beam radiation therapy alone for patients with recurrent or progressive unresectable disease with no prior radiation therapy and poor performance status. No change was made to the treatment recommendations for patients with recurrent or progressive unresectable disease with no prior radiation therapy.	5	13	0	8

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<p>GLIO-2 Internal Request:</p> <p>Institutional Review comment, “Anaplastic oligodendroglioma should include RT with <i>adjuvant</i> TMZ.”</p>	<p>Based on the data in the noted references and discussion, the panel consensus was to include RT with adjuvant TMZ as a category 2A recommendation as an adjuvant treatment option for patients with anaplastic oligodendroglioma (1p19q co-deleted, KPS ≥60).</p> <ul style="list-style-type: none"> • Panageas KS, Iwamoto FM, Cloughesy TF, et al. Initial treatment patterns over time for anaplastic oligodendroglial tumors. <i>Neuro Oncol</i> 2012;14:761-767. • Shin JY, Diaz AZ. Utilization and impact of adjuvant therapy in anaplastic oligodendroglioma: an analysis on 1692 patients. <i>J Neurooncol</i> 2016;129:567-575. 	16	2	0	8
<p>BRAIN-D 2 of 13 Internal Request:</p> <p>Institutional Review comment, “We should reassess the use of irinotecan, etoposide, cyclophosphamide, and platinum containing regimens for recurrent high-grade glioma.”</p>	<p>Based on the discussion and noted references, the panel consensus follows:</p> <ul style="list-style-type: none"> • Remove irinotecan in combination with bevacizumab • Remove irinotecan alone • Remove cyclophosphamide • Include etoposide (as a category 2B option for recurrent glioblastoma) See references below: <ul style="list-style-type: none"> ➤ Fulton D, Urtasun R, Forsyth P. Phase II study of prolonged oral therapy with etoposide (VP16) for patients with recurrent malignant glioma. <i>J Neurooncol</i> 1996;27:149-155. ➤ Leonard A, Wolff JE. Etoposide improves survival in high-grade glioma: a meta-analysis. <i>Anticancer Res</i> 2013;33:3307-3315. • Category change for etoposide (category changed from 2A to 2B) for recurrent anaplastic glioma • Platinum-based regimens (category changed from 2A to category 3) See references below: <ul style="list-style-type: none"> ➤ Field KM, Simes J, Nowak AK, et al. Randomized phase 2 study of carboplatin and bevacizumab in recurrent glioblastoma. <i>Neuro Oncol</i> 2015;17:1504-1513. ➤ Kaloshi G, Diamandi P, Cakani B, et al. The added value of bevacizumab concomitantly administered with carboplatin versus carboplatin alone in patients with recurrent glioblastomas. <i>Tumori</i> 2015;101:41-45. ➤ Murray LJ, Bridgewater CH, Levy D. Carboplatin chemotherapy in patients with recurrent high-grade glioma. <i>Clin Oncol (R Coll Radiol)</i> 2011;23:55-61. ➤ Roci E, Cakani B, Brace G, et al. Platinum-based chemotherapy in recurrent high-grade glioma patients: retrospective study. <i>Med Arch</i> 2014;68:140-143. 	14 14 16	3 3 1	1 1 2	8 8 7
		11	6	2	7
		11	6	2	7
		7	11	0	8

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<p>BRAIN-D 4 of 13 Internal Request:</p> <p>Institutional Review comment, “Is there any indication for vismodegib/SHH inhibitors for recurrent adult medulloblastoma?”</p>	<p>Based on the data in the noted reference and panel discussion, consensus was to include vismodegib (for mutations in the sonic hedgehog pathway and if prior chemotherapy) as an option for recurrent adult medulloblastoma. This is a category 2A recommendation.</p> <ul style="list-style-type: none"> Robinson GW, Orr BA, Wu G, et al. Vismodegib exerts targeted efficacy against recurrent sonic hedgehog-subgroup medulloblastoma: results from phase II Pediatric Brain Tumor Consortium Studies PBTC-025B and PBTC-032. J Clin Oncol 2015;33:2646-2654. 	14	1	2	9
<p>BRAIN-D 5 of 13 Internal Request:</p> <p>Institutional Review comment to add pomalidomide to PCNSL for relapsed or refractory disease.</p>	<p>Based on the data in the noted reference and panel discussion, consensus was to include pomalidomide as an option for relapsed or refractory disease PCNSL. This is a category 2A recommendation.</p> <ul style="list-style-type: none"> Tun HW, Johnston PB, DeAngelis LM, et al. Phase 1 study of pomalidomide and dexamethasone for relapsed/refractory primary CNS or vitreoretinal lymphoma. Blood 2018;132:2240-2248. 	15	0	3	8
<p>BRAIN-D 5 of 13, 7 of 13 and 8 of 13 External Request:</p> <p>Submission request from BTG International Inc.: Consider support for revision to the footnote recommendation on use of glucarpidase for patients with primary CNS lymphoma who are treated with methotrexate, “Glucarpidase is strongly recommended in the context of a rising serum creatinine if the 36-hour plasma methotrexate level is above 30 µM, 42-hour level is above 10 µM, or 48-hour level is above 5 µM. Optimal administration of glucarpidase is within 48 to 60 hours from the start of methotrexate infusion.”</p>	<p>Based on a review of data and discussion, the panel did not use the language proposed in the submission. However, the panel supported adding the following reference to the footnote already on this page:</p> <ul style="list-style-type: none"> Ramsey LB, Balis FM, O'Brien MM, et al. Consensus guideline for use of glucarpidase in patients with high-dose methotrexate induced acute kidney injury and delayed methotrexate clearance. Oncologist 2018;23:52-61. 	15	0	3	8

<p>BRAIN-D 6 of 13 Internal Request:</p> <p>Institutional Review comment to consider adding bevacizumab alone as an option for recurrent meningioma.</p>	<p>Based on the data in the noted references and discussion, the panel consensus was to include bevacizumab monotherapy as an option for recurrent meningioma. This is a category 2A recommendation.</p> <ul style="list-style-type: none"> • Lou E, Sumrall AL, Turner S, et al. Bevacizumab therapy for adults with recurrent/progressive meningioma: a retrospective series. J Neurooncol 2012;109:63-70. • Nayak L, Iwamoto FM, Rudnick JD, et al. Atypical and anaplastic meningiomas treated with bevacizumab. J Neurooncol 2012;109:187-193. 	13	1	4	8
<p>BRAIN-D 7 of 13 External Request:</p> <p>Submission request from AstraZeneca: 1) “Consider including osimertinib as an option for <i>newly diagnosed</i> brain metastases for EGFR mutation-positive NSCLC.</p>	<p>1) Based on a review of data and discussion, the panel consensus supported inclusion of osimertinib for newly diagnosed brain metastasis for EGFR mutation-positive NSCLC. This is a category 2A recommendation.</p> <ul style="list-style-type: none"> • Soria JC, Ohe Y, Vansteenkiste J, et al. Osimertinib in untreated EGFR-mutated advanced non-small-cell lung cancer. N Engl J Med 2018;378:113-125. 	17	0	1	8
<p>2) Request that the reference cited to support the use of osimertinib for <i>recurrent disease</i>, EGFR T790M mutation positive NSCLC be updated.</p>	<p>2) Based on a review of data and discussion, the panel consensus supported to update the reference for osimertinib for recurrent disease EGFR T790M mutation-positive NSCLC. This is a category 2A recommendation.</p> <ul style="list-style-type: none"> • Goss G, Tsai CM, Shepherd FA, et al. CNS response to osimertinib in patients with T790M-positive advanced NSCLC: pooled data from two phase II trials. Ann Oncol 2018;29:687-693. 	17	0	1	8
<p>3) Request that osimertinib be considered as an option for patients with leptomeningeal metastases and EGFR mutation-positive NSCLC.</p>	<p>3) Based on a review of data and discussion, the panel consensus supported osimertinib as an option for patients with leptomeningeal metastasis from EGFR mutation-positive NSCLC. This is a category 2A recommendation.</p> <ul style="list-style-type: none"> • Yang JCH, Cho BC, Kim DW, et al. Osimertinib for patients (pts) with leptomeningeal metastases (LM) from EGFR-mutant non-small cell lung cancer (NSCLC): updated results from the BLOOM study. 2017 ASCO Annual Meeting. Vol. 35: J Clin Oncol; 2017:2020. 	17	0	1	8

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<p>BRAIN-D External Request:</p> <p>Submission request from Munson Medical Oncology: Consider listing bevacizumab as a treatment for radiation necrosis in patients with metastatic disease to the brain who have undergone radiation.</p>	<p><u>Change not made</u> The panel consensus did not support the inclusion of bevacizumab as a treatment for radiation necrosis in patients with metastatic disease to the brain who have undergone radiation. Radiation necrosis is covered in the NCCN CNS Guidelines on BRAIN-E 2 of 3 under Medical Management.</p>	0	18	0	8
<p>BRAIN-E External Request:</p> <p>Submission request from Jazz Pharmaceuticals: Consider inclusion of defibrotide sodium (defibrotide) as the treatment of hepatic veno-occlusive disease (VOD).</p>	<p><u>Change not made</u> The panel consensus was this request was outside of the scope of the Guidelines recommendations.</p>	0	18	0	8