Guideline Page and Request	Panel Discussion/References	Institution Vote			
		YES	NO	ABSTAIN	ABSENT
ASTR-1 BRAIN-D (1 of 15) Internal request: Comment to consider the addition of BRAF/MEK inhibitors for adjuvant treatment of BRAF V600E mutant pilocytic astrocytoma, PXA, ganglioglioma.	The panel consensus was to include BRAF/MEK inhibitors for adjuvant treatment of BRAF V600E mutant pilocytic astrocytoma, PXA, gangliogliomas: dabrafenib/trametinib and vemurafenib/cobimetinib. This is a category 2A, useful in certain circumstances, recommendation.	24	0	0	4
BRAIN-D (5 of 15) Internal request: Comment to consider ibrutinib, TMZ, rituximab, rituximab + TMZ, lenalidomide, lenalidomide with rituximab, high-dose cytarabine, pemetrexed, and pomalidomide as induction therapy for patients who are unsuitable for or intolerant to high-dose methotrexate.	The panel consensus was to include ibrutinib, TMZ, rituximab, rituximab + TMZ, lenalidomide, lenalidomide with rituximab, high-dose cytarabine, pemetrexed, and pomalidomide as induction treatment options for patients who are unsuitable for or intolerant to high-dose methotrexate. This is a category 2A, useful in certain circumstances, recommendation.	19	0	5	4

Guideline Page and Request	Panel Discussion/References	YES	NO	ABSTAIN	ABSENT
BRAIN-D (8 of 15) External request: Submission from Puma Biotechnology, Inc (04/05/19 and 06/10/19) requesting that the recommendation for neratinib + capecitabine be changed from a 2B to 2A option for breast cancer with brain metastases for recurrent disease. BRAIN-D (8 of 15) Internal request: Comment to consider if the following regimens should be included in the NCCN Guidelines for CNS as treatment options for select patients (eg, patients with small asymptomatic brain metastases) with limited or extensive brain metastases from **HER2-positive breast cancer** with newly diagnosed disease, or patients with **HER2-positive breast cancer** who have recurrent brain metastases.	See submission Based on the data in the noted references, the panel re-evaluated the regimens and consensus was to include the following options for select patients (eg, patients with small asymptomatic brain metastases) with limited or extensive brain metastases from **HER2-positive breast cancer** with newly diagnosed disease, or patients with **HER2-positive breast cancer** who have recurrent brain metastases. • Capecitabine (category 2B) ➢ Rivera E, Meyers C, Groves M, et al. Phase I study of capecitabine in combination with temozolomide in the treatment of patients with brain metastases from breast carcinoma. Cancer 2006;107:1348-1354. ➢ Fabi A, Vidiri A, Ferretti G, et al. Dramatic regression of multiple brain metastases from breast cancer with capecitabine: another arrow at the bow? Cancer Invest 2006;24:466-468. ➢ Siegelmann-Danieli N, Stein M, Bar-Ziv J. Complete response of brain metastases originating in breast cancer to capecitabine therapy. Isr Med Assoc J 2003;5:833-834. ➢ Wang ML, Yung WK, Royce ME, et al. Capecitabine for 5-fluorouracil-resistant brain metastases from breast cancer. Am J Clin Oncol 2001;24:421-424. ➢ Hikino H, Yamada T, Johbara K, et al. Potential role of chemo-radiation with oral capecitabine in a breast cancer patient with central nervous system relapse. Breast 2006;15:97-99.	15	4	4	4

	• Capecitabine + lapatinib (category 2A) ➢ Bachelot T, Romieu G, Campone M, et al. Lapatinib plus capecitabine in patients with previously untreated brain metastases from HER2-positive metastatic breast cancer (LANDSCAPE): a single-group phase 2 study. Lancet Oncol 2013;14:64-71. ➢ Petrelli F, Ghidini M, Lonati V, et al. The efficacy of lapatinib and capecitabine in HER-2 positive breast cancer with brain metastases: A systematic review and pooled analysis. Eur J Cancer 2017;84:141-148.	18	3	2	4
	• Capecitabine + neratinib (category 2A) ➢ Freedman RA, Gelman RS, Anders CK, et al. TBCRC 022: a phase II trial of neratinib and capecitabine for patients with human epidermal growth factor receptor 2-positive breast cancer and brain metastases. J Clin Oncol 2019;37:1081-1089. ➢ Saura C, Oliveira M, Feng Y, et al. Neratinib + capecitabine versus lapatinib + capecitabine in patients with HER2+ metastatic breast cancer previously treated with ≥ 2 HER2-directed regimens: findings from the multinational, randomized, phase III NALA trial. J Clin Oncol 2019;37:1002-1002.	17	3	2	4
	• Paclitaxel + neratinib (category 2B) ➢ Awada A, Colomer R, Inoue K, et al. Neratinib plus paclitaxel vs trastuzumab plus paclitaxel in previously untreated metastatic ERBB2-positive breast cancer: the NEfERT-T randomized clinical trial. JAMA Oncol 2016;2:1557-1564.	13	7	3	4

Guideline Page and Request	Panel Discussion/References	YES	NO	ABSTAIN	ABSENT
BRAIN-D (8 of 15) Internal request: Comment to consider if the following regimens should be included in the NCCN Guidelines for CNS as treatment options for select patients (eg, patients with small asymptomatic brain metastases) with limited or extensive brain metastases from **HER2-non-specific breast cancer** with newly diagnosed disease, or patients with **HER2-non-specific breast cancer** who have recurrent brain metastases.	Based on the data in the noted references, the panel re-evaluated the regimens and consensus was to include the following options for select patients (eg, patients with small asymptomatic brain metastases) with limited or extensive brain metastases from **HER2-non-specific breast cancer** with newly diagnosed disease, or patients with **HER2-non-specific breast cancer** who have recurrent brain metastases:				
	• Cisplatin (category 2B) ➢ Cocconi G, Lottici R, Bisagni G, et al. Combination therapy with platinum and etoposide of brain metastases from breast carcinoma. Cancer Invest 1990;8:327-334. ➢ Franciosi V, Cocconi G, Michiara M, et al. Front-line chemotherapy with cisplatin and etoposide for patients with brain metastases from breast carcinoma, nonsmall cell lung carcinoma, or malignant melanoma: a prospective study. Cancer 1999;85:1599-1605.	11	7	6	4
	• Etoposide (category 2B) ➢ Cocconi G, Lottici R, Bisagni G, et al. Combination therapy with platinum and etoposide of brain metastases from breast carcinoma. Cancer Invest 1990;8:327-334. ➢ Franciosi V, Cocconi G, Michiara M, et al. Front-line chemotherapy with cisplatin and etoposide for patients with brain metastases from breast carcinoma, nonsmall cell lung carcinoma, or malignant melanoma: a prospective study. Cancer 1999;85:1599-1605.	12	7	5	4
	• Cisplatin + etoposide (category 2B) ➢ Franciosi V, Cocconi G, Michiara M, et al. Front-line chemotherapy with cisplatin and etoposide for patients with brain metastases from breast carcinoma, nonsmall cell lung carcinoma, or malignant melanoma: a prospective study. Cancer 1999;85:1599-1605. ➢ Vinolas N, Graus F, Mellado B, et al. Phase II trial of cisplatinum and etoposide in brain metastases of solid tumors. J Neurooncol 1997;35:145-148.	15	5	4	4
	• High-dose methotrexate (category 2B) ➢ Lassman AB, Abrey LE, Shah GD, et al. Systemic high-dose intravenous methotrexate for central nervous system metastases. J Neurooncol 2006;78:255.	14	7	3	4

BRAIN-D (8 of 15) Internal request: Comment to consider if the following regimens should be included in the NCCN Guidelines for CNS as treatment options for select patients (eg, patients with small asymptomatic brain metastases) with limited or extensive brain metastases from **EGFR sensitizing mutation positive non-small cell lung cancer** with newly diagnosed disease, or patients with **EGFR sensitizing mutation positive non-small cell lung cancer** who have recurrent brain metastases	Based on the data in the noted references, the panel re-evaluated the regimens and consensus was to include the following options for select patients (eg, patients with small asymptomatic brain metastases) with limited or extensive brain metastases from **EGFR sensitizing mutation positive non-small cell lung cancer** with newly diagnosed disease, or patients with **EGFR sensitizing mutation positive non-small cell lung cancer** who have recurrent brain metastases: • Osimertinib (EGFR T790M mutation positive) (category 2A) ➢ 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. ➢ 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. ➢ Mok TS, Wu YL, Ahn MJ, et al. Osimertinib or platinum-pemetrexed in EGFR T790M-positive lung cancer. N Engl J Med 2017;376:629-640. • Pulsatile erlotinib (category 2A) ➢ Grommes C, Oxnard GR, Kris MG, et al. "Pulsatile" high-dose weekly erlotinib for CNS metastases from EGFR mutant non-small cell lung cancer. Neuro Oncol 2011;13:1364-1369. ➢ Katayama T, Shimizu J, Suda K, et al. Efficacy of erlotinib for brain and leptomeningeal metastases in patients with lung adenocarcinoma who showed initial good response to gefitinib. J Thorac Oncol 2009;4:1415-1419. ➢ Arbour KC, Kris MG, Riely GJ, et al. Twice weekly pulse and daily continuous-dose erlotinib as initial treatment for patients with epidermal growth factor receptor-mutant lung cancers and brain metastases. Cancer 2018;124:105-109. • Afatinib (category 2B) ➢ Hoffknecht P, Tufman A, Wehler T, et al. Efficacy of the irreversible ErbB family blocker afatinib in epidermal growth factor receptor (EGFR) tyrosine kinase inhibitor (TKI)-pretreated non-small-cell lung cancer patients with brain metastases or leptomeningeal disease. J Thorac Oncol 2015;10:156-163. Gefitinib (category 2B) ➢ Ceresoli GL, Cappuzzo F, Gregorc V, et al. Gefitinib in patients with brain metastases from non-small-cell lung cancer: a prospective trial. Ann Oncol 2004;15:1042-1047 ➢ Wu C, Li YL, Wang ZM, et al. Gefitinib as palliative therapy for lung adenocarcinoma metastatic to the brain. Lung Cancer 2007;57:359-364.	23 21 20 16	1 2 4 7	0 1 0 1	4 4 4 4

Guideline Page and Request	Panel Discussion/References	YES	NO	ABSTAIN	ABSENT
BRAIN-D (8 of 15) Internal request: Comment to consider if the following regimens should be included in the NCCN Guidelines for CNS as treatment options for select patients (eg, patients with small asymptomatic brain metastases) with limited or extensive brain metastases from **non-small cell lung cancer** with newly diagnosed disease, or patients with **non-small cell lung cancer** who have recurrent brain metastases.	Based on the data in the noted references, the panel re-evaluated the regimens and consensus was to include the following options for select patients (eg, patients with small asymptomatic brain metastases) with limited or extensive brain metastases from **non-small cell lung cancer** with newly diagnosed disease, or patients with **non-small cell lung cancer** who have recurrent brain metastases: • Certinib (ALK rearrangement positive) (category 2A) ➢ Kim DW, Mehra R, Tan DSW, et al. Activity and safety of ceritinib in patients with ALK-rearranged non-small-cell lung cancer (ASCEND-1): updated results from the multicentre, open-label, phase 1 trial. Lancet Oncol 2016;17:452-463. • Crizotinib (ALK rearrangement positive and ROS1 positive (category 2B) ➢ Costa DB, Shaw AT, Ou SH, et al. Clinical experience with crizotinib in patients with advanced ALK-rearranged non-small-cell lung cancer and brain metastases. J Clin Oncol 2015;33:1881-1888. • Nivolumab (PD-L1 positive) (category 2A) ➢ Gauvain C, Vauleon E, Chouaid C, et al. Intracerebral efficacy and tolerance of nivolumab in non-small-cell lung cancer patients with brain metastases. Lung Cancer 2018;116:62-66. ➢ Goldman JW, Crino L, Vokes EE, et al. P2.36: Nivolumab (nivo) in patients (pts) with advanced (adv) NSCLC and central nervous system (CNS) metastases (mets). J Thorac Oncol 2016;11:S238-S239. ➢ Rizvi NA, Mazieres J, Planchard D, et al. Activity and safety of nivolumab, an anti-PD-1 immune checkpoint inhibitor, for patients with advanced, refractory squamous non-small-cell lung cancer (CheckMate 063): a phase 2, single-arm trial. Lancet Oncol 2015;16:257-265.	22 18 20	1 5 2	1 1 1	4 4 4

Guideline Page and Request	Panel Discussion/References	YES	NO	ABSTAIN	ABSENT
BRAIN-D (8 of 15) Internal request: Should *topotecan* be included in the NCCN Guidelines for CNS as a treatment option for select patients (eg, patients with small asymptomatic brain metastases) with limited or extensive brain metastases from **small cell lung cancer** with newly diagnosed disease, or patients with **small cell lung cancer** who have recurrent brain metastases?	Based on the data in the noted references, the panel re-evaluated and consensus was to include topotecan as an option for select patients (eg, patients with small asymptomatic brain metastases) with limited or extensive brain metastases from **small cell lung cancer** with newly diagnosed disease, or patients with **small cell lung cancer** who have recurrent brain metastases. This is a category 2B recommendation. • Groves MD, Glantz MJ, Chamberlain MC, et al. A multicenter phase II trial of intrathecal topotecan in patients with meningeal malignancies. Neuro Oncol 2008;10:208-215.	11	6	5	4
BRAIN-D (8 of 15) Internal request: Should *high-dose methotrexate* be included in the NCCN Guidelines for CNS as a treatment option for select patients (eg, patients with small asymptomatic brain metastases) with limited or extensive brain metastases from **lymphoma** with newly diagnosed disease, or patients with **lymphoma** who have recurrent brain metastases?	Based on the data in the noted references, the panel consensus was to include high-dose methotrexate as an option for select patients (eg, patients with small asymptomatic brain metastases) with limited or extensive brain metastases from **lymphoma** with newly diagnosed disease, or patients with **lymphoma** who have recurrent brain metastases. This is a category 2A recommendation. • Bokstein F, Lossos A, Lossos IS, Siegal T. Central nervous system relapse of systemic non-Hodgkin's lymphoma: results of treatment based on high-dose methotrexate combination chemotherapy. Leuk Lymphoma 2002;43:587-593.	20	2	2	4

Guideline Page and Request	Panel Discussion/References	YES	NO	ABSTAIN	ABSENT
BRAIN-D (8 of 15) Internal request: Is *ipilimumab + nivolumab* a **preferred** treatment option for select patients (eg, patients with small asymptomatic brain metastases) with limited or extensive brain metastases from **BRAF/MEK non-specific melanoma** with newly diagnosed disease, or patients with **BRAF/MEK non-specific melanoma** who have recurrent brain metastases? External request: Submission from Bristol-Myers Squibb (06/18/19) to consider the clinical data that were presented at the 2019 American Society of Clinical Oncology (ASCO) annual meeting. A phase 2 open-label study evaluated the safety and efficacy of nivolumab in combination with ipilimumab followed by nivolumab monotherapy for the treatment of patients with melanoma metastatic to the brain.	Based on the data in the noted references, the panel re-evaluated and consensus was to include ipilimumab + nivolumab as an option for select patients (eg, patients with small asymptomatic brain metastases) with limited or extensive brain metastases from **BRAF/MEK non-specific melanoma** with newly diagnosed disease, or patients with **BRAF/MEK non-specific melanoma** who have recurrent brain metastases. This is a category 2A, preferred recommendation. • Tawbi HA, Forsyth PA, Algazi A, et al. Combined nivolumab and ipilimumab in melanoma metastatic to the brain. N Engl J Med 2018;379:722-730. • Long GV, Atkinson V, Lo S, et al. Combination nivolumab and ipilimumab or nivolumab alone in melanoma brain metastases: a multicentre randomised phase 2 study. Lancet Oncol 2018;19:672-681. • Long GV, Atkinson V, Lo S, et al. Long-term outcomes from the randomized phase II study of nivolumab or nivolumab + ipilumumab in patients with melanoma brain metastases: Anti-PD-1 Brain Collaboration (the ABC trial). ESMO 2019 Congress. See submission	20	3	0	4