ASCO® Guidelines

SNO The Society for NeuroOncology

ASTRO AMERICAN SOCIETY FOR RADIATION ONCOLOGY

Treatment for Brain Metastases: ASCO-SNO-ASTRO Guideline		
Clinical Question	**Recommendation**	**Evidence Rating**
Surgery		
What are the benefits and harms of surgery in adult patients with brain metastases?	**1.1.** Surgery may be offered for patients with brain metastases, considering the following factors: • Patients with suspected brain metastases without a primary cancer diagnosis may benefit from surgery to attain a diagnosis and undergo tumor removal. • Patients with large tumors with mass effect likely benefit from surgery. • Patients with multiple brain metastases and/or uncontrolled systemic disease are less likely to benefit from surgery unless the remaining disease is controllable via other measures.	Type: Informal consensus Evidence quality: Mixed Strength of recommendation: Moderate
	1.2. Where surgery is considered, no recommendation regarding the method of resection (piecemeal vs. en-bloc) can be made.	Type: Informal consensus Evidence quality: Low Strength of recommendation: None
What are the benefits and harms of LITT?	**1.3.** No recommendation can be made for or against LITT.	Type: Informal consensus Evidence quality: Low Strength of recommendation: None
Systemic Therapy		
What systemic therapy (chemotherapy, immunotherapy, targeted agents) options, alone or in combination, have demonstrated clinical benefits in adults with brain metastases?	**2.1.** Patients with symptomatic brain metastases should be offered local therapy (radiosurgery/radiation therapy and/or surgery) as recommended in this guideline regardless of the systemic therapy used for the systemic disease	Type: Evidence-based Evidence quality: High Strength of recommendation: Strong
	2.2. For patients with asymptomatic brain metastases, local therapy should not be deferred unless deferral is specifically recommended in Recommendations 2.3 through 2.7 of this guideline. The decision to defer local therapy should be based on a multi-disciplinary discussion (neuro or medical oncology, neuro-surgery, and radiation oncology) of the potential benefits and harms the patient may experience.	Type: Evidence-based Evidence quality: High Strength of recommendation: Strong

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Clinical Question	**Recommendation**	**Evidence Rating**
	Non-Small Cell Lung Cancer	
	2.3. Osimertinib or icotinib may be offered to patients with asymptomatic brain metastases from *EGFR*-mutant NSCLC. If these agents are used, local therapy may be delayed until there is evidence of intracranial progression.	Type: Informal consensus Evidence quality: Low Strength of recommendation: Weak
	Qualifying Statement: The expert panel recognizes that as of this publication, icotinib is not approved by the US Food & Drug Administration (FDA) or the European Medicines Agency.	
	2.4. Alectinib, brigatinib, or ceritinib may be offered to patients with asymptomatic brain metastases from *ALK*-rearranged NSCLC. If these agents are used, local therapy may be delayed until there is evidence of intracranial progression.	Type: Informal consensus Evidence quality: Low Strength of recommendation: Weak
	2.5. Pembrolizumab may be offered to patients with asymptomatic brain metastases from immunotherapy-naive PD-L1 expressing NSCLC who are also receiving pemetrexed and a platinum agent.	Type: Informal consensus Evidence quality: Low Strength of recommendation: Weak
	NOTE: See Recommendation 2.2. regarding local therapy.	
	Melanoma	
	2.6. Ipilimumab plus nivolumab (for all patients regardless of *BRAF* status) or dabrafenib plus trametinib (for patients with *BRAF-V600E* mutation) may be offered to patients with asymptomatic brain metastases from melanoma. If these agents are used, local therapy may be delayed until there is evidence of intracranial progression.	Type: Informal consensus Evidence quality: Low Strength of recommendation: Weak
	Breast Cancer	
	2.7. The combination of tucatinib, trastuzumab, and capecitabine may be offered to patients with *HER2*-positive metastatic breast cancer who have asymptomatic brain metastases and have progressed on previous trastuzumab, pertuzumab, and/or trastuzumab emtansine-based therapy. If these agents are used, local therapy may be delayed until there is evidence of intracranial progression.	Type: Evidence-based Evidence quality: Low Strength of recommendation: Weak

Radiation Therapy

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Clinical Question	**Recommendation**	**Evidence Rating**
What are the benefits and harms of whole brain radiation therapy in adults with brain metastases? What approaches have been found to mitigate the harms of whole brain radiation therapy (e.g. radio-protectants, memantine, hippocampal avoidance)? What are the benefits and harms of stereotactic radiosurgery/radiation therapy in adults with brain metastases? What are the relative benefits and harms of stereotactic radiosurgery/radiation therapy compared to whole brain radiation therapy? What are the benefits and harms of using radiation sensitizers?	**3.1.** Radiation therapy should not be offered to patients with asymptomatic brain metastases and who have either: • Performance status KPS ≤ 50, OR • Performance status KPS <70 and no systemic therapy options.	Type: Evidence-based Evidence quality: Low Strength of recommendation: Moderate
	3.2. SRS alone (as opposed to WBRT or combination of WBRT and SRS) should be offered to patients with 1 to 4 unresected brain metastases, excluding small cell carcinoma.	Type: Evidence-based Evidence quality: Intermediate Strength of recommendation: Moderate
	Qualifying Statement: The inclusion criteria of the randomized trials that underly this recommendation were generally tumors of less than 3 or 4 cm diameter and did not include radioprotectant strategies of memantine or hippocampal avoidance.	
	3.3. SRS alone should be offered to patients with 1 to 2 resected brain metastases if the surgical cavity can be safely treated and considering the extent of remaining intracranial disease.	Type: Evidence-based Evidence quality: Intermediate Strength of recommendation: Moderate
	Qualifying Statement: The randomized trials upon which this recommendation is based were of single-fraction SRS and conventional WBRT (without radioprotectant strategies of memantine or hippocampal avoidance).	
	3.4. SRS, WBRT, and the combination of SRS plus WBRT are all reasonable options for patients with more than 4 unresected or more than 2 resected brain metastases and better performance status (e.g. KPS ≥ 70). SRS may be preferred for patients with better prognosis or where systemic therapy that is known to be active in the central nervous system is available.	Type: Informal consensus Evidence quality: Low Strength of recommendation: Weak
	3.5. Memantine and hippocampal avoidance should be offered to patients who will receive WBRT and have no hippocampal lesions and 4 months or more expected survival.	Type: Evidence-based Evidence quality: High Strength of recommendation: Strong
	3.6. Radiation sensitizing agents should not be offered to patients.	Type: Evidence-based Evidence quality: Low Strength of recommendation: Strong

Timing and Interaction of Therapy

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Clinical Question	**Recommendation**	**Evidence Rating**
How does the relative timing of surgery, radiation therapy, and systemic therapy affect the benefits/harms of those therapies?	**4.1.** For patients who will receive both radiation therapy and surgery, no recommendation regarding the specific sequence of therapy can be made.	Type: Informal consensus Evidence quality: Low Strength of recommendation: None

Abbreviations. ALK, anaplastic lymphoma kinase; ASCO, American Society of Clinical Oncology; ASTRO, American Society for Radiation Oncology; EGFR, epidermal growth factor receptor; FDA, US Food & Drug Administration; HER2, human epidermal growth factor receptor 2; KPS, Karnofsky performance status; LITT, laser interstitial therapy therapy; NSCLC, non-small cell lung cancer; PD-L1, programmed death ligand 1; SNO, Society for Neuro-Oncology; SRS; stereotactic radiosurgery; WBRT, whole brain radiotherapy