Brain Metastases

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KEYWORDS

- Brain metastases • Breast cancer • Lung cancer • Melanoma
- Whole brain radiation • Stereotactic radiosurgery

KEY POINTS

- Which treatment(s) to offer a patient with brain metastases depends on the primary cancer, the number and location of the metastases, the extent of systemic disease, functional status, age, and prognosis.
- The 2 main local therapies available to patients with brain metastases are neurosurgical resection and radiation therapy.
- Stereotactic radiation is an approach frequently used in patients with 1 to 4 brain metastases. Trials exploring the benefit with more than 4 brain metastases are underway.

INTRODUCTION

Brain metastases (BM) from solid tumors are associated with increased morbidity and mortality. Patients can present with focal neurologic deficits, seizures, neurocognitive impairments, or symptoms of increased intracranial pressure depending on the number, size, and location of the BMs. Standard treatment to date is local therapy with surgery and/or radiation therapy, although there is increasing interest in systemic therapies that can control both intracranial and extracranial disease. Unfortunately, few available systemic agents sufficiently control disease inside the central nervous system (CNS).[1]

The decision on which treatment(s) to offer a BM patient depends on several factors, including the primary cancer, the molecular subtype, the number and location of BMs, the extent of systemic disease, functional status, age, and prognosis. Although survival is generally poor, subsets of patients with BM can live longer than expected. The Diagnosis-Specific Graded Prognostic Assessment is a prognostic index for

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patients with BM refined according to diagnosis, for example, breast carcinoma, small cell lung cancer (SCLC), non-SCLC (NSCLC), gastrointestinal cancers, melanoma, or renal cell carcinoma (**Table 1**).[2] The median overall survival for a patient with a low GPA of 0.0 to 1.0 is approximately 3 to 7 months regardless of primary cancer, whereas the median overall survival for a patient with a high GPA varies according to primary cancer. The Diagnosis-Specific Graded Prognostic Assessment has been further updated in lung adenocarcinoma by incorporating the presence or absence of epidermal growth factor receptor (EGFR) or anaplastic lymphoma kinase (ALK) alterations as a prognostic factor.[3] The median overall survival for a patient with lung adenocarcinoma and high GPA score of 4.0 (age <70, Karnofsky performance status 90–100, absence of extracranial metastases, ≤4 BM, and EGFR positive or ALK

Table 1
Summary of diagnosis-specific GPA indices, which estimates survival from brain metastases

| Diagnosis | Prognostic Factors | Median Survival (mo) | | | |
		GPA 0.0–1.0	GPA 1.5–2.0	GPA 2.5–3.0	GPA 3.5–4.0
Breast cancer	KPS Subtype (triple negative, HR+, HER2+, HR/HER2+) Age (y)	3.4	7.7	15.1	25.3
GI cancers	KPS	3.1	4.4	6.9	13.5
Melanoma	KPS Number of BM	3.4	4.7	8.8	13.2
NSCLC (adenocarcinoma)	Age (y) KPS Presence/absence of extracranial metastases Number of BM EGFR or ALK positive	6.9	13.7	26.5	46.8
NSCLC (nonadenocarcinoma)	Age (y) KPS Presence/absence of extracranial metastases Number of BM	5.3	9.8	12.8	N/A
Renal cell carcinoma	KPS Number of BM	3.3	7.3	11.3	14.8
SCLC	Age (y) KPS Presence/absence of extracranial metastases Number of BM	3.0	5.5	9.4	14.8

Points are added for each prognostic factor according to primary cancer to calculate a GPA score.

Abbreviations: ALK, anaplastic lymphoma kinase; BM, brain metastases; EGFR, epidermal growth factor receptor; GI, gastrointestinal; GPA, graded prognostic assessment; HER2, human epidermal growth factor receptor 2; HR, hormone receptor; KPS, Karnofsky performance status; NSCLS, non-small cell lung cancer; SCLC, small cell lung cancer.

Adapted from Sperduto PW, Kased N, Roberge D, et al. Summary report on the graded prognostic assessment: an accurate and facile diagnosis-specific tool to estimate survival for patients with brain metastases. J Clin Oncol 2012;30(4):421; and Sperduto PW, Yang TJ, Beal K, et al. Estimating survival in patients with lung cancer and brain metastases: an update of the graded prognostic assessment for lung cancer using molecular markers (lung-molGPA). JAMA Oncol 2017;3(6):829; with permission.