Integration of chemotherapy into current treatment strategies for brain metastases from solid tumors.

ABSTRACT: Patients with brain metastases represent a heterogeneous group where selection of the most appropriate treatment depends on many patient- and disease-related factors. Eventually, a considerable proportion of patients are treated with palliative approaches such as whole-brain radiotherapy. Whole-brain radiotherapy in combination with chemotherapy has recently gained increasing attention and is hoped to augment the palliative effect of whole-brain radiotherapy alone and to extend survival in certain subsets of patients with controlled extracranial disease and good performance status. The randomized trials of whole-brain radiotherapy vs. whole-brain radiotherapy plus chemotherapy suggest that this concept deserves further study, although they failed to improve survival. However, survival might not be the most relevant endpoint in a condition, where most patients die from extracranial progression. Sometimes, the question arises whether patients with newly detected brain metastases and the indication for systemic treatment of extracranial disease can undergo standard systemic chemotherapy with the option of deferred rather than immediate radiotherapy to the brain. The literature contains numerous small reports on this issue, mainly in malignant melanoma, breast cancer, lung cancer and ovarian cancer, but very few sufficiently powered randomized trials. With chemotherapy
alone, response rates were mostly in the order of 20-40%. The choice of chemotherapy regimen is often complicated by previous systemic treatment and takes into account the activity of the drugs in extracranial metastatic disease. Because the blood-brain barrier is partially disrupted in most macroscopic metastases, systemically administered agents can gain access to such tumor sites. Our systematic literature review suggests that both chemotherapy and radiochemotherapy for newly diagnosed brain metastases need further critical evaluation before standard clinical implementation. A potential chemotherapy indication might exist as palliative option for patients who have progressive disease after radiotherapy.