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Management of patients suffering from metastatic malignant melanoma and brain metastasis remains challenging in routine clinical practice. The inhibitory anti-CTLA-4 antibody ipilimumab has recently been approved as second-line therapeutic option for melanoma patients. Increasing evidence suggests distinct therapeutic activity on central nervous system metastases, although this continues to be actively debated. Here, we present the case of a patient suffering from metastatic melanoma, including symptomatic brain metastasis, who showed a partial response to ipilimumab in extracranial tumor manifestations, while the disease was progressing intracranially. Subsequently, intracranial disease progression could be managed by local irradiation. An overview of currently available literature on the efficacy of ipilimumab in melanoma patients with central nervous system metastases is provided.