

Adjuvant therapy for resected stage III melanoma patients: high-dose interferon-alpha versus ipilimumab combined with kinases inhibitors

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ABSTRACT

High-dose interferon-alpha remains the first-line treatment in the adjuvant therapy of metastatic melanoma. More recently, high-dose pegylated interferon-alpha-2b has been approved by the US Food and Drug Administration. Actually, an adjuvant therapy alternative to high-dose interferon-alpha is represented by ipilimumab. Moreover, combination therapy of IFN-alpha or ipilimumab with tyrosine kinase inhibitors has been proved in patients with specific mutations. It is mandatory to understand what the best adjuvant treatment is for resected metastatic melanoma patients, particularly at stage III-N1, in terms of overall survival rather than recurrence-free survival. The ECOG 1609 clinical trial compared high-dose interferon-alpha and ipilimumab alone or combined with tyrosine kinase inhibitors for the treatment of early metastatic melanoma. In the past, ECOG 1684, 1690 and 1694 trials showed improvement in recurrence-free survival more than overall survival for high-risk melanoma patients (stage IIB-III) treated with high-dose interferon-alpha, whereas more recently the EORTC 18991 trial reported successful therapeutic results in terms of recurrence-free survival rather than overall survival for stage III-N1 melanoma patients treated with high-dose pegylated interferon-alpha-2b. Toxicity was more acceptable within one year of treatment. Randomized trials have demonstrated that ipilimumab as second-line therapy is able to increase dose-dependent overall survival rates in advanced melanoma patients despite severe but reversible immune-related adverse events. Old tyrosine kinase inhibitors have been used in combination with interferon for the treatment of advanced melanoma patients with moderate benefits and increased toxicity, but new selective drugs seem to be more efficacious. Early metastatic melanoma patients (stage III-N1) should be the principal subset to be treated with the most suitable adjuvant therapy to achieve the best overall survival. New schedules have to be tested with high-dose interferon-alpha and ipilimumab alone or combined with tyrosine kinase inhibitors while waiting for results from ECOG 1609.

Key words: high-dose interferon-alpha, ipilimumab, metastatic melanoma, sentinel node biopsy, tyrosine kinase inhibitors.

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