

# Interferon Is an 'Imperfect Standard' for Melanoma

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SAN DIEGO — For patients with regionally advanced melanoma, the current standard of care is high-dose interferon.

"It's an imperfect standard, but nonetheless it is the standard," Dr. Michael P. Kosty said at a melanoma update sponsored by the Scripps Clinic.

To date, five randomized trials of high-dose interferon have shown a recurrence-

free survival advantage, but an overall survival advantage "has been harder to demonstrate," said Dr. Kosty, program director of the hematology/oncology fellowship training program at the Scripps Clinic.

"One of the things about survival as an end point is that if you have a patient population and you treat them with your experimental therapy and they progress or recur, a lot of patients will go on standard therapy, which will impact your ability to assess their survival," he said.

Two studies have shown a survival advantage for high-dose interferon. In one study, patients were randomized to either 52 weeks of observation or to an induction phase of 20 megaunits/m<sup>2</sup> IV five times per week for 4 weeks, followed by a maintenance phase of 10 megaunits/m<sup>2</sup> administered subcutaneously three times a week for 48 weeks. Median overall survival was 3.8 years in the treatment group and 2.8 years in the observation group (J. Clin. Oncol. 1996;14:7-17).

A more recent study assessed the impact of low-dose and high-dose interferon on overall survival compared with no treatment. It found that only high-dose interferon conferred a survival advantage: a median of 20 months, compared with a median of 9.6 months among those who did not receive treatment (J. Clin. Oncol. 2000; 18: 2444-58). A similar association was seen in the rates of recurrence-free survival.

"There is a dose-response relationship between the higher doses of interferon and the higher likelihood of recurrence-free benefit," said Dr. Kosty, who had no relevant conflicts of interest to disclose.

At this time, patients with stage III or stage IV disease are ideal candidates for systemic therapy. "If you look at the current data, there is no evidence in stage II disease of efficacy of adjuvant therapy, either in terms of progression free or overall survival," he noted.

The most common adverse events from high-dose interferon treatment include fatigue and depressive symptoms. Despite aggressive antidepressive therapy, "this im-

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**Recurrence-free survival has been shown, but overall survival 'has been harder to demonstrate.'**

DR. KOSTY

pacts the function of many patients. Some are unable to work, particularly if they have physically demanding jobs or mentally challenging jobs," said Dr. Kosty.

In an effort to find a better alternative, a trial of 400 patients to compare standard high-dose interferon treatment to a chemoimmunotherapy combination has completed accrual. Results are expected in the coming year.

So far, no vaccine trial has shown improvement in overall survival, although some trials have shown an improvement in relapse-free survival. "There is about a 20% reduction in relapse rate and perhaps as high as a 10% reduction in death rate, although that 10% is probably the most optimistic number," he said. "Vaccines will probably have their ultimate utility in patients who have a very high risk of either developing melanoma or developing recurrence from their surgically treated melanoma, as opposed to patients with more advanced disease."

Effective treatment options for metastatic melanoma remain a challenge for researchers. Current therapies have little impact on median survival, although the combination of chemotherapy, interleukin-2, and interferon has "a fairly high response rate," Dr. Kosty said.

"That therapy might be useful if you have somebody with metastatic disease that is significantly symptomatic from the disease, such as somebody with bony metastasis and pain or somebody with liver metastasis and diminished appetite. They may benefit symptomatically but will not benefit from that therapy in terms of survival," he noted. ■