Panel Backs Peginterferon for Stage III Melanoma

BY ELIZABETH MECHCATIE

GAITHERSBURG, MD. — Peginterferon alfa-2b has a favorable risk-benefit ratio as an adjuvant treatment for stage III melanoma, a Food and Drug Administration advisory panel said

The FDA's Oncologic Drugs Advisory Committee voted 6-4 after reviewing the data on the adjuvant use of peginterferon alfa-2b after complete lymphadenectomy, the indication up for approval. The panel did not vote specifically on whether to recommend approval of peginterferon for the indication.

Peginterferon alfa-2b (Peg-IFN), a long-acting formulation of interferon alfa-2b, is marketed by Schering-Plough Corp. as Pegintron and was approved as a treatment for chronic hepatitis C in 2001. Interferon alfa-2b (Intron A), also manufactured by Schering-Plough, was approved as an adjuvant treatment for melanoma in 1995, on the basis of a study that found it had a significant impact on overall survival, the primary end point.

Those voting positively generally agreed that although the substantial toxicity and the modest effect on relapse-free survival were concerns, the toxicity did not appear to be worse than that associated with high-dose interferon, and that it would be a reasonable alternative treatment option. Several said that the pegylated formulation would be more convenient, since it is administered subcutaneously once a week.

Peg IFN is administered subcutaneously once a week, with a higher dose during the 8-week induction period, and is recommended for 5 years.

The results of a multicenter, phase III study, of 1,256 patients (median age 50 years) with stage III melanoma were submitted for approval.

Subjects had either microscopic or palpable nodal involvement, and were randomized to either treatment with Peg-IFN or observation after undergoing regional lymph node dissection. Most of the patients were in Europe, but none was in the United States.

Median relapse-free survival was 34.8 months for patients on the long-acting interferon and 25.2 months among those in the observation arm, a statistically significant 18% reduction.

The primary endpoint was relapse-free survival (defined as the earliest detection of locoregional relapse, distant metastasis, or death). The rate of these events was 52.3% among those on Peg-IFN, compared with 58.5% in the observation group. The median relapse-free survival was 34.8 months, compared with 25.5 months among those in the observation arm, an 18% reduction in the risk of relapse or death associated with treatment, which was statistically significant. However, there were no significant differences in overall survival or distant metastasis-free survival between the two arms.

Fatigue was the most common serious adverse event associated with treatment. Depression was more than twice as high among patients on Peg-IFN, and severe depression was also higher among treated patients (7% vs. 0.5%). Of those on Peg-IFN, 44% stopped treatment because of adverse events. Only 13% of patients completed 5 years of treatment.

There were three deaths considered possibly related to peginterferon, which were cardiovascular related.

The FDA usually follows the recommendations of its advisory panels. ■

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'One of the fellows here said, "Wow, this is fantastic; now I will get time to know my metastatic melanoma patients." That's how bad the field was.'

Dr. Alexander Eggermont, discussing a new oral agent, p. 18