NEW & APPROVED

Ontak Solution for IV Injection

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Ontak Solution for IV Injection
(denileukin diftitox, Eisai Inc.)

A genetically engineered cytotoxin converted to full approval by the Food and Drug Administration for treatment of persistent or recurrent cutaneous T-cell lymphoma (CTCL) with malignant cells that express the CD25 component of the interleukin-2 receptor.

► **Recommended Dosage:** An intravenous infusion of 9 mcg/kg or 18 mcg/kg per day over 30-60 minutes, for 5 consecutive days every 21 days for 8 cycles, with acetaminophen or an antihistamine used as premedication.

► **Special Considerations:** In the study that was the basis of the full approval, the following adverse events affected at least 20% of patients on the 18-mcg/kg dose and occurred more often than among patients who received placebo: fever, nausea, rigors, fatigue, vomiting, headache, peripheral edema, diarrhea, anorexia, rash, and myalgia. Serious adverse events associated with Ontak included infusion reactions, capillary leak syndrome, and loss of visual acuity, including loss of color vision. Hypoalbuminemia and hepatic transaminitis were among the laboratory abnormalities reported.

► **Comment:** In 1999, accelerated approval of Ontak was based on "durable, objective responses" in an open-label study comparing two doses. Full approval was based on a multinational, placebo-controlled dose-ranging study of 144 patients with CD25-positive cutaneous T-cell lymphoma (stages Ia-III), who had received three or fewer treatments previously, and whose mean age was 59 years; 65% had less than IIa disease. Patients received 18 mcg/kg or 9 mcg/kg of Ontak in an intravenous infusion daily, for the first 5 days of a 21-day cycle, for a maximum of 8 cycles, or a placebo saline infusion.

The overall response rate was 46% on the higher dose and 37% on the lower dose, compared with 15% among those on placebo; the differences between both doses and placebo were significant. The median duration of response was 220, 277, and 81 days, respectively. ■

Leukemia May Relapse to Skin In Rare Cases

SAN FRANCISCO — A rare case of relapsing leukemia cutis appeared only in the skin, in a patient with no evidence of circulating leukemia whose bone marrow appeared to have responded completely to previous treatment.

A 45-year-old patient had undergone chemotherapy in 2007 for myeloid leukemia, Dr. George Elgart and his associates wrote in a poster presented at the annual meeting of the American Society of Dermatopathology. Although he responded initially, he was lost to follow-up before completing therapy. After he returned to care and resumed chemotherapy, remission was confirmed by peripheral blood and bone marrow analyses.

He subsequently developed multiple skin lesions that were nonspecific on clinical exam but that suggested a systemic process. The lesions increased rapidly in number and size. Because of the patient's history, "the diagnosis was not challenging," reported Dr. Elgart, professor of dermatology and cutaneous surgery at the University of Miami.

The lesions first presented as subcutaneous nodules, some in bizarre shapes, such as a plaque shaped like a question mark. Many of the lesions eventually ulcerated or developed an adherent thick crust. A punch biopsy of one of the lesions showed a dramatic infiltrate to all margins of the specimen.

Immunopathology can be helpful but is highly variable in the skin manifestations of hematologic processes and is complicated by the inconsistency of myeloid leukemia immunohistochemistry, Dr. Elgart noted. In this case, review of the primary histology helped to direct the immunohistochemical evaluation.

The punch biopsy specimen was positive on immunostaining for CD56 and CD177 but negative for myeloperoxidase and CD34. The cells had a decidedly geometric configuration and appreciable cytoplasm. They appeared unconstrained by the surrounding dermal anatomy and extended to track among the collagen bundles in a manner parallel to that of metastatic carcinoma. In contrast, a recent review by other investigators reported the most sensitive markers to be lysozyme and CD68.

—Sherry Boschert