

The following is a message from the FDA's Office of Oncology Drug Products Director, Dr. Richard Pazdur:

On March 20, 2008, the Food and Drug Administration (FDA) approved bendamustine hydrochloride (TREANDA®, Cephalon, Inc.), an intravenously administered alkylating agent, for the treatment of patients with chronic lymphocytic leukemia (CLL).

The safety and efficacy of bendamustine were evaluated in a randomized, controlled, multicenter trial comparing bendamustine to chlorambucil as first-line treatment for CLL patients. The trial was conducted in 301 patients (153 on bendamustine and 148 on chlorambucil) with Binet Stage B or C (Rai Stages I - IV) CLL requiring treatment. Need-to-treat criteria included hematopoietic insufficiency, B-symptoms, rapidly progressive disease, or risk of complications from bulky lymphadenopathy. Patients with autoimmune hemolytic anemia or autoimmune thrombocytopenia, Richter's syndrome, or transformation to prolymphocytic leukemia were excluded. Patients were randomized to receive either bendamustine, 100 mg/m² intravenously on days 1 and 2 every 28 days, or to receive chlorambucil, 0.8mg/kg/day orally on days 1 and 15 every 28 days. Up to 6 cycles were administered to each patient.

The efficacy analyses were based on National Cancer Institute-Sponsored Working Group criteria. The overall response rate was 59% for bendamustine versus 26% for chlorambucil ($p < 0.0001$) with 8% versus <1% complete responses on the bendamustine and chlorambucil arms, respectively. The median progression-free survival was 18 months for bendamustine versus 6 months for chlorambucil (hazard ratio 0.27, 95% CI 0.17, 0.43; $p < 0.0001$). Survival data are not mature.

Patients treated with bendamustine had a higher incidence of adverse reactions (89%) than those treated with chlorambucil (79%). The most common adverse reactions (frequency 15%) were neutropenia, pyrexia, thrombocytopenia, nausea, anemia, leucopenia, and vomiting. Neutropenic fever was more common in the bendamustine group compared to the chlorambucil group. Red blood cell transfusions were administered to 20% of the bendamustine-treated patients compared to 6% of those receiving chlorambucil. The most frequent adverse reactions leading to study withdrawal for patients receiving bendamustine were hypersensitivity and pyrexia. The number of deaths during the treatment period was similar in both treatment arms.

The recommended dose of TREANDA® is 100 mg/m² administered intravenously over 30 minutes on days 1 and 2 of a 28-day cycle, up to 6 cycles.

Full prescribing information, including clinical trial information, safety, dosing, drug-drug interactions and contraindications is available at
<http://www.fda.gov/cder/foi/label/2008/022249lbl.pdf>.