

Every-2-Week Dosing of Darbepoetin Alfa in Patients With Anemia of Cancer: Interim Analysis of a Randomized, Controlled Study

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Origin of Study	USA
Type of Study	RANDOMIZED, OPEN-LABEL, CONTROLLED STUDY
Study Design	<p>Patients were randomized (4:1) to receive darbepoetin alfa 3 µg/kg every 2 weeks for 21 weeks or to join a control group (12-week observation period followed by 9 weeks of darbepoetin alfa therapy).</p> <p>During weeks 1–13, hemoglobin levels were measured every 2 weeks, transfusions were recorded, and a Subject Outcomes Questionnaire, including the Functional Assessment of Cancer Therapy-Fatigue (FACT-Fatigue) subscale, was administered at weeks 1, 5, 9, and 13.</p> <p>No chemotherapy or radiotherapy was given within 4 weeks of screening or during the 25-week study period.</p> <p>An intent-to-treat approach was used to analyze the change in hemoglobin level, with missing hemoglobin values and values obtained within 28 days of a red blood cell transfusion imputed using the last value carried forward method.</p>
Patients	<p>Enrolled patients were ≥ 18 years of age and anemic (hemoglobin value ≤ 11 g/dL) due to cancer or previous chemotherapy or radiotherapy, had a current diagnosis or history of a nonmyeloid malignancy (including lymphocytic leukemia), and had adequate renal and liver function.</p> <p>The majority of patients were women (59% in the darbepoetin alfa group, 71% in the control group). Mean age was 71.1 ± 10.5 (SD) years and 68.0 ± 10.8 years for the darbepoetin alfa and control groups, respectively. Most patients in both groups were white (85% for the darbepoetin alfa group and 83% for the control group). The most common tumor types were lymphoid malignancy (30%), breast cancer (22%), and genitourinary or lung cancers (14% each).</p>
Observations	<p>Data for the first 170 patients randomized (darbepoetin alfa, 135; control, 35) were evaluated through week 13 (1 patient randomized to the darbepoetin alfa treatment arm did not receive the study drug and was excluded from the analysis).</p> <p>Baseline hemoglobin values were 10.2 ± 0.9 and 10.3 ± 0.9 g/dL for the darbepoetin alfa and control (no treatment) groups, respectively.</p> <p>After 12 weeks of treatment, the mean change in hemoglobin value was 2.1 ± 1.9 g/dL in the darbepoetin alfa group and 0.3 ± 1.0 g/dL in the control group.</p> <p>Kaplan-Meier estimates of hemoglobin and hematopoietic response were 72% and 81%, respectively, in the darbepoetin alfa group and 12% and 27% in the control group.</p>
Conclusions	<p>Darbepoetin alfa 3 µg/kg every 2 weeks is highly effective in increasing hemoglobin levels and providing a robust hematopoietic response in patients with anemia of cancer.</p> <p>The less-frequent dosing of darbepoetin alfa may provide additional benefits to patients and their caregivers in this setting.</p>

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Discussion

Darbepoetin alfa (Aranesp) and epoetin alfa (Epogen, Procrit) have been shown to reduce the need for transfusions and increase hemoglobin levels in anemic patients with cancer who are not receiving concurrent chemotherapy. Questions remain, however, regarding the use of an erythropoietic agent in this population. To address these issues, Veena Charu, MD, of Pacific Medical Center in Anaheim, Calif., and colleagues designed a randomized, open-label, comparative study to evaluate the effect of darbepoetin alfa therapy on hospitalization, hemoglobin levels, and health-related quality of life (HRQOL) in patients with anemia of cancer. This interim analysis assesses the efficacy of darbepoetin alfa on hemoglobin and HRQOL endpoints.

Anemia of cancer is an underdiagnosed side effect of cancer thought to affect as many as 475,000 people in the United States. "Oncologists are beginning to focus not only on chemotherapy-induced anemia, but anemia of cancer as well," said Dr. Charu. "Building on the findings of previous studies, we designed this study to examine the efficacy of Aranesp in treating cancer patients with anemia not receiving chemotherapy."

Patients in the trial were randomized in a 4:1 ratio to receive 21 weeks of treatment with darbepoetin alfa or 12 weeks of observation followed by 9 weeks of treatment with darbepoetin alfa. The study included patients who suffered from a wide range of nonmyeloid malignancies, including breast, lung, gastrointestinal, and gynecological cancers. All patients had an ECOG performance status of 0–2.

Patients filled out a Subject Outcomes Questionnaire every 4 weeks, providing information about their healthcare utilization, ability to work, productivity, and HRQOL.

In the study, those who took darbepoetin alfa for the first 12 weeks experienced a 2.1 g/dL mean change in hemoglobin, whereas those who underwent only observation for the first 12 weeks experienced only a 0.3 g/dL mean change in hemoglobin.

The number of patients receiving red blood cell transfusions was significantly fewer in the darbepoetin alfa group than in the control group (30% vs 10%). Eighty-one percent of patients in the darbepoetin alfa group experienced a hematopoietic response, and 72% had a hemoglobin response. In the control group, only 27% of patients achieved a hematopoietic response and 12% a hemoglobin response.

The patients who received darbepoetin alfa for the first 12 weeks also had a significantly greater reduction of fatigue (6 points in FACT-Fatigue score) than the control group (2 points). "A six-point reduction in fatigue is very significant for a cancer patient," said Dr. Charu. "That's quite an improvement in energy."

The most common serious adverse event was pneumonia, experienced by 4% of patients in the darbepoetin alfa group and 6% of patients in the control group.

Key Points

- Darbepoetin alfa can increase hemoglobin values and reduce the need for red blood cell transfusions among patients with anemia of cancer.
- Treatment with darbepoetin alfa also significantly reduces the level of fatigue in these patients.

References

Charu V, Belani CP, Gill AN, et al. Every-2-week (Q2W) dosing of darbepoetin alfa in patients with anemia of cancer (AOC): interim analysis of a randomized, controlled study. Poster presented at the 45th Annual Meeting of the American Society of Hematology; December 6–9, 2003; San Diego, Calif. Abstract 1816.

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