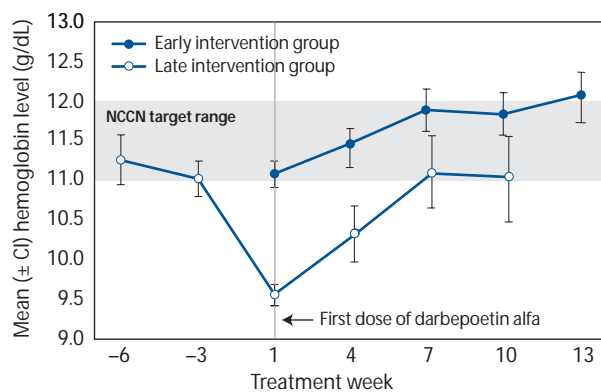


A Randomized Study of Darbepoetin Alfa Every 3 Weeks for Chemotherapy-Induced Anemia

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Origin of Study	USA
Type of Study	MULTICENTER, RANDOMIZED, OPEN-LABEL CLINICAL STUDY
Objectives	<p>Assess the ability of darbepoetin alfa to maintain a hemoglobin level ≥ 10 g/dL when administered every 3 weeks</p> <p>Compare the relative efficacy of early intervention (giving darbepoetin alfa when patients are mildly anemic) with late intervention (withholding darbepoetin alfa until patients are moderately anemic)</p>
Study Design	<p>Patients with a baseline hemoglobin level between 10.5 and 12 g/dL were assigned randomly (1:1) to undergo early (treatment started immediately) or late (treatment delayed until the hemoglobin level was < 10 g/dL) intervention with darbepoetin alfa 300 μg every 3 weeks for up to 23 weeks.</p> <p>The primary endpoint was the proportion in each group with hemoglobin values below 10 g/dL.</p> <p>Hemoglobin was measured and the Functional Assessment of Cancer Therapy-Fatigue (FACT-F) subscale questionnaire was administered at baseline and every 3 weeks. Kaplan-Meier methodology was used to calculate endpoints.</p>
Patients	A total of 201 patients were enrolled, 64% female. The most common tumors were breast (29%), lung (23%), gastrointestinal (21%), and lymphoid (9%) malignancies. Planned interim analysis included data through week 13, the first 56 patients per arm (112 total), as of March 4, 2003. Forty-nine percent of patients were ≥ 65 years of age and 17% ≥ 75 years of age.
Observations	<p>Baseline hemoglobin levels were 11.1 g/dL (95% CI: 10.9–11.2 g/dL) and 11.2 g/dL (95% CI: 11.0–11.3 g/dL) for the early- and late-intervention groups, respectively.</p> <p>By 13 weeks, 71% of patients in the early-intervention group were able to maintain a hemoglobin level ≥ 10 g/dL (mean: 12.0 g/dL), compared with 35% of patients in the late-intervention group (mean: 11.0 g/dL). This difference was highly significant ($P < 0.0001$).</p> <p>In the early-intervention group, 14% (95% CI: 7%–20%) of patients needed red blood cell (RBC) transfusions through week 13, compared with 22% (95% CI: 13%–30%) in the late-intervention group.</p> <p>Patients in the early-intervention group who maintained target hemoglobin levels (11–12 g/dL) performed better on standardized quality-of-life tests (FACT-F scores) at weeks 7, 10, and 13 than patients who received darbepoetin alfa later, after their hemoglobin level fell below 10 g/dL.</p>

Darbepoetin Alfa 300 μ g Every 3 Weeks Was Effective in Achieving and Maintaining Target Hemoglobin Levels in Both Early- and Late-Intervention Groups



Timing Intervention With Darbepoetin Alfa for Chemotherapy-Induced Anemia

Conclusions

Our early results suggest that darbepoetin alfa 300 µg every 3 weeks is effective for mild and moderate chemotherapy-induced anemia.

An erythropoietic therapy scheduled every 3 weeks simplifies anemia management and benefits patients and caregivers.

Discussion

Erythropoietic agents such as darbepoetin alfa (Aranesp) and epoetin alfa (Epogen, Procrit) have been shown to resolve chemotherapy-induced anemia, a condition that results in substantial fatigue. Current guidelines suggest that clinicians initiate therapy if the patient's hemoglobin level falls below 11 g/dL; the suggested hemoglobin target range is 11–12 g/dL.

However, comparatively little is known about the effects of these agents when administered earlier in patients undergoing myelosuppressive chemotherapy. Some studies suggest that these patients can have a substantial benefit when they receive early erythropoietic therapy. In one study, patients whose hemoglobin increased from 11 to 12 g/dL had optimal improvements in quality-of-life measures.

Accordingly, this randomized, open-label, multicenter study sought to assess whether darbepoetin alfa, administered every 3 weeks, could maintain hemoglobin concentrations at or above 10 g/dL in patients with nonmyeloid malignancies. In addition, investigators assessed quality of life using the FACT-F subscale questionnaire.

The study included patients with baseline hemoglobin levels between 10.5 and 12 g/dL randomized to receive darbepoetin alfa 300 µg given every 3 weeks (early intervention) or delayed until the hemoglobin level dropped below 10 g/dL (late intervention) for up to 23 weeks.

An interim analysis of the data showed that early darbepoetin alfa treatment significantly reduced the development of moderate-to-severe anemia. Patients in the early-treatment group whose hemoglobin concentration was maintained at the target level of 11–12 g/dL needed fewer transfusions. In addition, they had better scores on the FACT-F quality-of-life scale.

Based on these results, the investigators believe that maintaining the hemoglobin level in the range of 11–12 g/dL might be an effective strategy for reducing transfusion need and maximizing quality of life in patients undergoing chemotherapy. The results are consistent with National Comprehensive Cancer Network (NCCN) guidelines that specify a hemoglobin level of 11 g/dL as the threshold for intervening with erythropoietic therapy to achieve a 12 g/dL target.

Key Points

- Compared with late treatment, early treatment with darbepoetin alfa 300 µg every 3 weeks reduces the need for transfusions and improves quality of life in patients with chemotherapy-induced anemia.
- Early darbepoetin alfa treatment significantly reduces the development of moderate to severe anemia.
- In cancer patients receiving chemotherapy, maintaining a hemoglobin level in the 11–12 g/dL range may be an effective way to minimize transfusion needs and maximize quality of life.

References

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