

## Randomized, open-label comparison of epoetin alfa extended dosing (80,000 U every two weeks) versus weekly dosing (40,000 U weekly) in anemic patients with cancer receiving chemotherapy

<b>Authors</b>	David H. Henry, Denise Williams, John Xie, and Francois Wilhelm
<b>Origin of Study</b>	USA
<b>Type of Study</b>	PROSPECTIVE, RANDOMIZED, OPEN-LABEL, MULTICENTER STUDY
<b>Objectives</b>	Examine extended-interval initial dosing with 80,000 U of epoetin alfa (Procrit) given every 2 weeks versus the standard regimen of 40,000 U given once weekly.
<b>Study Design</b>	<p>In this 13-week study, 145 patients were given 40,000 U of epoetin alfa subcutaneously (SC) once weekly, and 153 patients were given 80,000 U SC every 2 weeks. The drug was held if the hemoglobin level was &gt; 13 g/dL; the dose was reduced if the hemoglobin level was &gt; 12 g/dL or rose &gt; 1 g/dL over any 2-week period.</p> <p>If patients had an inadequate hemoglobin response, those given 80,000 U every 2 weeks were switched to 40,000 U once weekly, and those given 40,000 U once weekly were increased to 60,000 U once weekly.</p> <p>The primary analysis was a comparison of the mean change in hemoglobin level from baseline to end of study.</p>
<b>Patients</b>	<p>Patients were ≥ 18 years of age, diagnosed with a nonmyeloid malignancy, and had baseline hemoglobin levels ≤ 11 g/dL and chemotherapy planned for at least 12 weeks. Patients were ineligible if they had undergone stem cell harvest of bone marrow, high-dose chemotherapy with stem cell transplant, or nonpalliative radiation therapy during the study; had uncontrolled hypertension; or had a history of uncontrolled cardiac arrhythmia, pulmonary embolism, or thrombosis. They also could not have received a transfusion of packed red blood cells within 28 days of their first study dose or have been treated with any erythropoietic agent within the previous 3 months.</p> <p>Characteristics at baseline between the groups were comparable (overall mean age, 62 years; 66% female; mean baseline hemoglobin level = 10.0 g/dL). The most common tumor types were breast cancer (25%), lung cancer (22%), and colorectal cancer (14%).</p>
<b>Observations</b>	<p>Efficacy was analyzed in 153 patients using the 80,000 U twice weekly regimen and 145 patients using the 40,000 U once weekly regimen who had ≥ 1 g/dL postbaseline hemoglobin value.</p> <p>The mean hemoglobin change from baseline to end of study for the every-2-week group was <math>1.27 \pm 1.48</math> g/dL and for the once-weekly group was <math>1.28 \pm 1.60</math> g/dL. In the per protocol population, the difference in mean hemoglobin level change was similar. The mean hemoglobin values over time also were similar between the groups.</p> <p>Kaplan-Meier estimates of post-28-day transfusion rates were 11.2% in the every-2-week group versus 12.0% in the once-weekly group. Fewer patients in the every-2-week group than in the once-weekly group required dose holds (21% vs 42%) or dose reductions (41% vs 59%). Further, 13% of the patients in the every-2-week group were switched to once-weekly dosing, and 37% of patients in the once-weekly group required a dose increase.</p> <p>The incidences of clinically relevant thrombotic vascular events (7.8% vs 7.6%) and deaths (6.5% vs 6.2%) were similar in the every-2-week and once-weekly groups.</p>

**Final results of a randomized study comparing two dosing regimens of epoetin alfa****Conclusions**

Patients treated with 80,000 U of epoetin alfa given every 2 weeks demonstrated similar increases in hemoglobin level, transfusion rates, and safety outcomes as did those given 40,000 U once weekly.

**Discussion**

Every-2-week dosing of epoetin alfa has demonstrated changes in hemoglobin levels and safety in treating chemotherapy-related anemia in patients with nonmyeloid malignancies comparable to the current recommended once-weekly dosage. These data were the final results of a randomized, open-label, 13-week study, the first of its kind to evaluate an extended initiation dose of epoetin alfa in this patient population.

“The possibility of administering epoetin alfa every-2-weeks merits further investigation,” said Dr. Henry.

Patients with nonmyeloid malignancies who had a baseline hemoglobin level of  $\leq 11$  g/dL and who were scheduled to receive chemotherapy for at least 12 weeks were enrolled in the study. In all, 153 patients received 80,000 U of epoetin alfa SC every 2 weeks, and 145 patients received 40,000 U of epoetin alfa SC weekly.

The mean hemoglobin change from baseline to the end of therapy was  $1.27 \pm 1.48$  g/dL for the every-2-week group and  $1.28 \pm 1.60$  g/dL for the weekly epoetin group. Fewer patients receiving epoetin alfa every 2 weeks required doses to be withheld or reduced.

Diarrhea occurred in 20% of those given epoetin therapy every 2 weeks and 28% receiving weekly therapy, nausea occurred in 24% of both groups, and fatigue occurred in 25% and 20%, respectively. Thrombotic vascular events were similar in both groups. Furthermore, 10 patients receiving every-2-weeks therapy and 9 patients receiving weekly therapy died.

An initial extended-dose regimen of epoetin alfa is feasible, and these findings confirmed the results of previous studies using weekly epoetin use followed by every-2-week or every-3-week extended dosing, Dr. Henry concluded. The safety and efficacy results for this study consistently showed that 80,000 U of epoetin alfa every 2 weeks is comparable to 40,000 U of epoetin alfa weekly in cancer patients with chemotherapy-induced anemia. “The increased flexibility of the every-2-week regimen may improve patient compliance,” suggested Dr. Henry.

**Key Points**

- Dosing with 80,000 U given every other week is an effective regimen that may be more convenient when treating patients with chemotherapy-induced anemia and particularly for patients given dose-dense chemotherapy every 2 weeks.

**Reference**

Henry DH, Kamin M, Wilhelm F, Williams D, Xie J, Woodman RC. Final results of a randomized study comparing two dosing regimens of epoetin alfa in patients with chemotherapy-induced anemia: 80,000 U every two weeks vs 40,000 U weekly. Presented at the 42nd Annual Meeting of the American Society of Clinical Oncology; June 2–6, 2006; Atlanta, Georgia. Abstract 8624.