

## Darbepoetin Alfa 3.0 µg/kg Every 2 Weeks Improves Hemoglobin and Quality of Life in a Subset of Breast Cancer Patients in a Community-Based Trial of Patients With Chemotherapy-Induced Anemia

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<b>Origin of Study</b>	USA
<b>Type of Study</b>	MULTICENTER, OPEN-LABEL CLINICAL TRIAL
<b>Objectives</b>	<p>Assess hemoglobin outcomes and related changes in quality of life (fatigue and energy levels) in patients with breast cancer</p> <p>Compare these results with outcomes in the entire group</p>
<b>Study Design</b>	<p>Patients who completed one or more post-baseline quality-of-life questionnaires (including both the Functional Assessment of Cancer Therapy-Fatigue [FACT-F] subscale [scored 0–52] and Energy Numerical Rating Grade [ENRG; scored 0–100]) were included in the analysis of fatigue endpoints.</p> <p>Available data and intent-to-treat (ITT) approaches were used. For ITT, missing hemoglobin values and hemoglobin concentrations obtained within 28 days of a transfusion were imputed using the last value carried forward approach; for available data, no imputation was used, and hemoglobin values obtained within 28 days of transfusion were excluded.</p>
<b>Patients</b>	<p>Eligible patients were anemic (hemoglobin value <math>\leq 11</math> g/dL), had nonmyeloid tumors receiving multicycle chemotherapy, an ECOG score of 0–1, adequate renal and liver function, and were to receive cytotoxic chemotherapy for up to 16 weeks.</p> <p>Of the first 1,173 patients enrolled in this study, 320 (27%) had breast cancer.</p> <p>At study entry, 181 patients (56%) had stage I (9%), II (35%), or III (12%) disease.</p>
<b>Observations</b>	<p>Mean baseline hemoglobin level in breast cancer patients was <math>10.5 \pm 0.9</math> (SD) g/dL, compared with <math>10.4 \pm 1.0</math> g/dL for all patients.</p> <p>Mean change in hemoglobin from baseline after 16 weeks of therapy was 2.2 g/dL (95% CL: 2.0, 2.4) (available data) and 1.9 g/dL (95% CL: 1.8, 2.1) (ITT approach) in breast cancer patients, comparable to the mean hemoglobin change (available, 2.1 g/dL [1.9, 2.2]; ITT, 1.7 g/dL [1.6, 1.8]) for all patients.</p> <p>The Kaplan-Meier estimate of the proportion of breast cancer patients with a hematopoietic response (hemoglobin level increase <math>\geq 2</math> g/dL or hemoglobin level <math>\geq 12</math> g/dL) after 16 weeks of therapy was 88% (95% CL: 84%, 93%).</p> <p>Incidence of red blood cell (RBC) transfusions in breast cancer patients declined from 7% at month 1 to 1% at month 4.</p> <p>FACT-F scores in breast cancer patients increased by a mean of 8.6 (95% CL: 6.9, 10.2) points (a 3-point improvement is considered clinically meaningful). ENRG scores also improved by a mean of 15.5 (95% CL: 12.5, 18.5) points.</p> <p>Adverse events were as expected for this patient population. Similar findings were observed in all patients.</p>

## Darbepoetin Alfa Improves Hemoglobin and Quality of Life in Breast Cancer Patients With Chemotherapy-Induced Anemia

### Conclusions

In patients with breast cancer, as well as in all patients, darbepoetin alfa 3.0 µg/kg every 2 weeks appears to be effective in producing a hematopoietic response and in improving quality of life.

Darbepoetin has the added benefit of less-frequent dosing relative to that of epoetin alfa.

### Discussion

Darbepoetin alfa 3.0 µg/kg every 2 weeks improved not only hemoglobin levels but also quality of life in patients with chemotherapy-induced anemia in this large study of 1,558 patients.

The study measured functional capacity in anemic patients with nonmyeloid malignancies and related hemoglobin response to changes from baseline. This was the final report on all 1,558 patients in the study, with a final subset report on the 424 breast cancer patients.

Nearly all breast cancer patients (80%) had a hematopoietic response, as did 70% of the whole study population. By the ITT analysis, mean change in hemoglobin from baseline to week 17 was 1.9 g/dL in the breast cancer subset and 1.7 g/dL for the whole population. Changes in hemoglobin levels in the available data cohort were 2.2 and 2.1 g/dL, respectively.

Reductions in RBC transfusions were seen from month 1 to month 4 of treatment, similarly for the whole population and the breast cancer subset. RBC counts were reduced from 14% to 5% in the whole population, and from 7% to 2% in the breast cancer population, reported Douglas Blayney, MD, of Wilshire Oncology Group, Pomona, California.

Dr. Blayney noted that darbepoetin alfa seems to work more rapidly in patients with breast cancer than in those with other tumors. "This may be because these [breast cancer patients] are mostly stage I and II patients whose tumors have been resected, so many [of them] are without active cancer. Also, the other tumor types were largely treated with cisplatin, which may have additional hematopoietic suppressive effects," he explained.

Clinically meaningful improvements in fatigue and energy level were observed at week 17 with darbepoetin alfa. The mean change in the FACT-Fatigue subscale was 8.2 for breast cancer patients and 6.7 for all patients (a 3-point change is considered clinically meaningful). Only 18 patients (1%) reported serious adverse events that might have been related to treatment.

Due to an approximately threefold longer half-life, darbepoetin alfa can be given less frequently. Dr. Blayney added, "Convenience is an advantage with darbepoetin alfa, since it is not given weekly. This is especially relevant in breast cancer, since many adjuvant [dose-dense] regimens are now being given every 2 weeks."

### Key Points

- Nearly all cancer patients with chemotherapy-induced anemia achieved a hematopoietic response to darbepoetin alfa therapy, as well as clinically meaningful improvements in fatigue and energy.
- Breast cancer patients derived even more benefit from treatment with darbepoetin alfa than the overall study population.
- Dosing every 2 weeks is convenient to patients and their caregivers.

### References

Blayney DW, Vadhan-Raj S, Mirtsching BC, Tomita D, Colowick A. Darbepoetin alfa 3.0 mcg/kg every 2 weeks improves hemoglobin and quality of life in a subset of breast cancer patients in a community-based trial of patients with chemotherapy-induced anemia. Poster presented at the 26th Annual San Antonio Breast Cancer Symposium; December 3–6, 2003; San Antonio, Tex. Abstract 640.

Vadhan-Raj S, Mirtsching B, Charu V, et al. Assessment of hematologic effects and fatigue in cancer patients with chemotherapy-induced anemia given darbepoetin alfa every two weeks. *J Support Oncol* 2003;1:131–138.