

## Early Results of a Head-To-Head Comparison of Darbepoetin Alfa 200 µg Given Every 2 Weeks and Epoetin Alfa 40,000 U Given Weekly

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| <b>Origin of Study</b> | USA   |
| <b>Type of Study</b>   | PHASE II, RANDOMIZED, OPEN-LABEL, CLINICAL TRIAL  |
| <b>Objectives</b>      | Compare the efficacy of darbepoetin alfa 200 µg every 2 weeks with that of epoetin alfa 40,000 U once weekly within three specific populations of cancer patients: those with breast, lung, or gynecologic cancers  |
| <b>Study Design</b>    | <p>Patients were randomized 1:1 to receive either darbepoetin alfa 200 µg every 2 weeks or epoetin alfa 40,000 U once weekly.</p> <p>In patients who did not achieve at least a 1 g/dL increase in hemoglobin after 4 weeks, doses were increased at week 5 to 300 µg every 2 weeks for darbepoetin alfa or to 60,000 U once weekly for epoetin alfa.</p> <p>If the hemoglobin value was &gt; 13.0 g/dL, doses of either agent were withheld until the hemoglobin level fell to ≤ 13.0 g/dL, at which time therapy was restarted at the previous dose.</p> <p>A sample size of approximately 100 patients was planned per study, for a total of 300 patients across the three studies. Endpoints included hematologic outcomes. Exploratory endpoints were based on achieving a targeted hemoglobin range of 11–12 g/dL (NCCN Clinical Practice Guidelines in Oncology, 2004). Kaplan-Meier methodology was used to calculate proportion endpoints.</p> |
| <b>Patients</b>        | <p>Patients were ≥ 18 years of age, were anemic (hemoglobin value ≤ 11.0 g/dL) due to chemotherapy, were expected to receive ≥ 8 additional weeks of multicycle chemotherapy for nonmyeloid malignancies, and had adequate renal and liver function and a Karnofsky performance status ≥ 50%.</p> <p>Most patients were women (85% in each treatment group). Mean age of the first 210 patients enrolled was 57.3 ± 11.3 (SD) years in the darbepoetin alfa group (n = 105) and 61.8 ± 12.9 years in the epoetin alfa group (n = 105).</p>  |
| <b>Observations</b>    | <p>Mean baseline hemoglobin level was 10.4 ± 0.8 g/dL and 10.5 ± 0.8 g/dL for the darbepoetin alfa and epoetin alfa groups, respectively.</p> <p>Mean change in hemoglobin value after 17 weeks of treatment was 1.4 g/dL (95% CI: 1.1–1.8) for the darbepoetin alfa group and 1.5 g/dL (95% CI: 1.2–1.8) for the epoetin alfa group, using the intent-to-treat approach (missing values or values within 28 days of a transfusion were imputed using the last value carried forward method).</p> <p>Cumulative incidence of red blood cell (RBC) transfusions from week 1 to week 17 was 21% (95% CI: 11%–29%) in the darbepoetin alfa group and 19% (95% CI: 11%–28%) in the epoetin alfa group.</p> <p>A similar proportion of patients in the two treatment groups achieved the NCCN hemoglobin target range of 11–12 g/dL and maintained this level after reaching this target.</p>  |
| <b>Conclusions</b>     | <p>Based on this interim analysis at 17 weeks, darbepoetin alfa 200 µg every 2 weeks and epoetin alfa 40,000 U once weekly appear to achieve comparable outcomes with respect to improvement in hemoglobin levels and reduction in number of RBC transfusions.</p> <p>Less-frequent dosing of darbepoetin alfa may provide added benefits to patients with chemotherapy-induced anemia and their caregivers, compared with the more frequent dosing required by epoetin alfa.</p>   |

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### Discussion

Because the relative efficacy of darbepoetin alfa (Aranesp) and epoetin alfa (Epogen, Procrit) for the treatment of chemotherapy-induced anemia is still an important question, researchers used three identical clinical trials to compare the most commonly used doses of darbepoetin alfa and epoetin alfa within tumor-specific populations of patients with breast, lung, or gynecologic cancers. In all three trials, the patients were at least 18 years old, receiving multicycle chemotherapy, anemic due to chemotherapy, expected to receive more than 8 additional weeks of chemotherapy, and had adequate renal and liver function and a Karnofsky performance status  $\geq 50\%$ . The planned sample size was 100 patients per trial, for a total of 300 patients.

In each trial, patients were randomly assigned to receive darbepoetin alfa 200 µg every 2 weeks or epoetin alfa 40,000 U once weekly for up to 16 weeks. In patients who did not achieve at least a 1 g/dL increase in hemoglobin after 4 weeks, doses were increased at week 5 to 300 µg every 2 weeks for darbepoetin alfa or 60,000 U epoetin alfa once weekly. If the hemoglobin concentration exceeded 13.0 g/dL, doses of either agent were withheld until the hemoglobin value was less than or equal to 13.0 g/dL, at which time therapy was restarted at the previous dose.

This interim analysis included data through week 17 for the first 210 patients enrolled, including 105 randomized to receive darbepoetin alfa therapy and an equal number to receive epoetin alfa. The mean hemoglobin value at baseline was 10.4 and 10.5 g/dL for the darbepoetin alfa and epoetin alfa groups, respectively. The estimated proportion of patients needing RBC transfusions up to week 17 was 21% in the darbepoetin alfa arm and 19% in the epoetin alfa arm. After 17 weeks of treatment, both groups showed a similar change in hemoglobin values: 1.4 g/dL in patients receiving darbepoetin alfa and 1.5 g/dL in those receiving epoetin alfa (intent-to-treat population).

Researchers observed no difference in the incidence or severity of adverse events between the two groups, and only two events were reported as related to erythropoietic therapy: one incident of pneumonitis in the darbepoetin alfa group and one case of pulmonary embolism in the epoetin alfa group.

### Key Points

- The most commonly used doses of darbepoetin alfa and epoetin alfa appear to be comparable with respect to changing hemoglobin values and reducing the need for transfusions.
- The less-frequent dosing of darbepoetin alfa may provide added benefits to patients with chemotherapy-induced anemia and their caregivers, compared with the more frequent dosing required by epoetin alfa.
- Time to achieve the NCCN target hemoglobin range of 11–12 g/dL and maintenance of these target hemoglobin levels after they are reached are similar for epoetin alfa and darbepoetin alfa.

### References

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