

An Open-Label, Randomized Study to Develop a Screening Tool for Functional Capacity in Anemic Subjects With Nonmyeloid Malignancies Receiving Chemotherapy and Darbepoetin Alfa

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Origin of Study	USA
Type of Study	PHASE II, RANDOMIZED, OPEN-LABEL CLINICAL TRIAL
Objectives	<p>Develop a screening tool for functional capacity (as measured by maximal oxygen-carrying capacity) in anemic patients with nonmyeloid malignancies receiving darbepoetin alfa and multiple cycles of chemotherapy</p> <p>Evaluate the relationship between hemoglobin response and change in functional capacity</p> <p>Analyze the effect of darbepoetin alfa on hemoglobin and fatigue and energy levels, by baseline hemoglobin levels and sex</p>
Study Design	<p>Eligible patients were ≥ 18 years of age, anemic (hemoglobin level ≤ 11.0 g/dL), receiving chemotherapy for a nonmyeloid malignancy, and had adequate renal and liver function.</p> <p>Darbepoetin alfa 3.0 $\mu\text{g}/\text{kg}$ was administered every 2 weeks for 16 weeks.</p> <p>Hemoglobin was collected at baseline (week 1) and every 2 weeks during treatment.</p> <p>The Modified Harvard Step Test (MHST) and patient-reported functional quality-of-life questionnaires, including the Functional Assessment of Cancer Therapy-Fatigue (FACT-Fatigue) subscale and Energy Numerical Rating Grade (ENRG), were administered at baseline and at weeks 9 and 17.</p> <p>Data reported here were analyzed using an intent-to treat (ITT) approach; missing values were imputed by carrying forward the last observed value, and hemoglobin values within 28 days of a transfusion were excluded and considered missing for analyses of hemoglobin endpoints.</p>
Patients	<p>Mean age ($n = 1,558$) was 60.1 ± 13.0 (SD) years; 66% of the patients were women.</p> <p>Mean (\pm SD) baseline hemoglobin value ($n = 1,462$) was 10.4 ± 1.0 g/dL. Mean baseline FACT-Fatigue ($n = 1,505$) and ENRG ($n = 1,501$) scores were 26.1 (95% CI: 25.5%–26.8%) and 45.8 (95% CI: 44.7%–46.9%), respectively.</p>
Observations	<p>Although 96% of patients started the MHST, only 35% completed the test.</p> <p>Seventy percent of patients achieved a hematopoietic response (hemoglobin level increase ≥ 2 g/dL or a hemoglobin value ≥ 12 g/dL), independent of their baseline hemoglobin level or sex.</p> <p>Transfusions decreased by 64% from month 1 to month 4 of treatment.</p> <p>Over the 16 weeks of the study, the FACT-Fatigue score increased by an average of 6.7 points (95% CI: 6.0–7.5), and the mean ENRG score increased by 11.6 points (95% CI: 10.1–13.2).</p> <p>Darbepoetin alfa was well tolerated; serious adverse effects possibly or probably related to the study drug occurred in only 1% of patients.</p>

Functional Capacity in Anemic Subjects With Nonmyeloid Malignancies Receiving Chemotherapy and Darbepoetin Alfa

Conclusions

Treatment with darbepoetin alfa 3.0 µg/kg every 2 weeks leads to clinically significant improvements in hemoglobin level and quality of life (increased energy and decreased fatigue) in anemic patients undergoing chemotherapy, independent of baseline hemoglobin level or sex.

Less-frequent dosing of darbepoetin alfa may provide an additional benefit to both patients and their caregivers.

Discussion

Patients undergoing chemotherapy frequently develop anemia, resulting in impaired functional capacity and decreased quality of life. In this 17-week randomized, open-label study on 1,558 anemic patients receiving chemotherapy, those who took darbepoetin alfa (Aranesp) had a mean increase in hemoglobin level of 2.1 g/dL, a mean change in FACT-Fatigue score of 6.7, and a mean change in energy level of 11.6 at the end of the study.

Seventy percent of patients in the study achieved a hemoglobin increase ≥ 2 g/dL or a hemoglobin value ≥ 12 g/dL. Red blood cell transfusions decreased by 64% from the first to fourth month of the study after treatment with the drug.

In the study, researchers developed a screening tool for functional capacity, the MHST, in which maximal oxygen-carrying capacity in cancer patients undergoing chemotherapy could be measured. This test was administered at baseline and at weeks 9 and 17. Hemoglobin was collected at baseline and every 2 weeks throughout the study. Patients also completed the FACT-Fatigue questionnaire and ENRG at baseline and at 9 and 17 weeks.

A high percentage of patients attempted the step test, but only a third were able to complete it. Thus, the primary endpoint of the study could not be assessed due to the small proportion of patients with two measurements on the test.

Factors that had significant impact on the change in hemoglobin, fatigue, and energy included the patients' baseline hemoglobin level and type of tumor. Those who had a baseline hemoglobin value < 10 g/dL experienced less improvement with darbepoetin alfa than those with a baseline hemoglobin value > 10 g/dL. Likewise, those with gynecological and breast cancers had a greater reduction in fatigue than those with lung, gastrointestinal, or lymphoid malignancies who took darbepoetin alfa.

The most common adverse event related to treatment with darbepoetin alfa was injection-site pain. Eighteen patients reported serious adverse events that might have been related to treatment.

The authors concluded that the MHST is not an effective tool for measuring functional capacity in anemic patients with cancer. They also noted that using darbepoetin alfa to treat cancer patients with anemia results in clinically meaningful improvements. The less-frequent dosing required by darbepoetin alfa "may benefit patients and caregivers and improve compliance," the researchers noted.

Key Points

- The Modified Harvard Step Test cannot be applied in oncology practice to assess functional capacity in anemic cancer patients.
- Darbepoetin alfa is safe and effective in a significant proportion of patients with anemia receiving chemotherapy.

References

- Vadhan-Raj S, Hong JJ, Gregory SA, Terry D, Tomita D, Colowick A. An open-label, randomized study to develop a screening tool for functional capacity in anemic subjects with nonmyeloid malignancies receiving chemotherapy and darbepoetin alfa. Poster presented at the 45th Annual Meeting of the American Society of Hematology; December 6–9, 2003; San Diego, Calif. Abstract 1814.
- Vadhan-Raj S, Mirtsching B, Charu V, et al. Assessment of hematological effects and fatigue in cancer patients with chemotherapy-induced anemia given darbepoetin alfa every two weeks. *J Support Oncol* 2003;1:131–138.