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REVIEW ARTICLE

EPOETIN ALFA CORRECTS ANEMIA AND IMPROVES QUALITY OF LIFE IN PATIENTS WITH HEMATOLOGIC MALIGNANCIES RECEIVING NON-PLATINUM CHEMOTHERAPY

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SUMMARY

Anemia, a commonly occurring morbidity in patients with cancer, often leads to diminished quality of life (QOL). Numerous clinical trials have shown that epoetin alfa treatment improves hematologic and QOL variables in cancer patients. The clinical trial analysis reported here was performed to assess response to epoetin alfa in patients with hematologic malignancies. Cancer patients with anemia undergoing non-platinum-based chemotherapy who were enrolled in a multinational, randomized (2:1), double-blind, placebo-controlled trial were prospectively stratified by tumor type (hematologic, solid). Efficacy endpoints included proportion of patients transfused after day 28; change in hemoglobin (Hb) level from baseline to last assessment; proportion of treatment responders (increase in Hb $\geq$2 g/dl unrelated to transfusion) and correctors (patients whose Hb levels reached $\geq$12 g/dl during the study); and QOL. The protocol was amended before unblinding to prospectively collect and assess survival data 12 months after the last patient completed the study, and survival for the full study cohort was estimated using Kaplan–Meier techniques. Efficacy analyses of hematologic and QOL variables, as well as Kaplan–Meier estimates of survival, were performed *post hoc* for the hematologic tumor stratum. Among patients with hematologic malignancies, the mean increase in Hb levels was greater with epoetin alfa than with placebo treatment (2.2 vs. 0.3 g/dl). Transfusion requirements were lower in patients who received epoetin alfa versus placebo (25.2 vs. 43.1%), and the proportion of responders and correctors was higher with epoetin alfa than with placebo (75.2 vs. 16.7% and 72.6 vs. 14.8%, respectively). Patients who received epoetin alfa had improved QOL while patients who received placebo had decreased QOL. These results are similar to those seen in the full study cohort, where differences between epoetin alfa and placebo were significant ($P < 0.05$) for all five primary cancer- and anemia-specific QOL domains evaluated. Although the study was not powered for survival, Kaplan–Meier estimates showed a trend in overall survival favoring epoetin alfa in both the full study cohort and the hematologic subgroup. Epoetin alfa treatment was well tolerated. Epoetin alfa therapy increased Hb levels, reduced transfusion requirements, and improved QOL in patients with anemia undergoing non-platinum chemotherapy for hematologic malignancies. Copyright © 2004 John Wiley & Sons, Ltd.

KEY WORDS: epoetin alfa; hematologic malignancies; anemia; hemoglobin; quality of life

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INTRODUCTION

Anemia is a common complication of cancer and its treatment. Anemia has been reported to occur in 15 to 90% of patients with hematologic malignancies, the incidence varying by cancer type, duration and progression of disease, and treatment administered.[1–11] Kyle[1] for example, reported a 62% incidence of anemia in patients presenting with multiple myeloma, and Rai *et al.*[7] reported a 20% incidence of anemia at diagnosis in patients with chronic lymphocytic leukemia (CLL). In a 2-year retrospective chart survey of patients with a variety of solid or non-myeloid hematologic malignancies, Coiffier *et al.* found that the prevalence of moderate anemia (8.0 to $<$10.5 g/dL) in patients with Hodgkin's disease or non-Hodgkin's lymphoma increased from 16.1 and 18.9%, respectively at baseline to 25.7 and 34.9%, respectively at the start of the fourth chemotherapy cycle.[11]

The significance of cancer-related anemia with respect to outcomes is only now being recognized. Cancer-related anemia may cause such symptoms as weakness, fatigue, exhaustion, impaired concentration, respiratory distress and chest pain, resulting in decreased functional capacity and quality of life (QOL)[12–15] as well as the necessity for red blood cell transfusions, with their associated risks and costs.[16] In addition to contributing to significant morbidity, cancer-related anemia may be associated with poorer prognosis and may contribute to mortality.[17–20]

The etiology of cancer-related anemia is multifactorial.[21–23] One proposed etiology is a blunted erythropoietin response to low hemoglobin (Hb) levels, since erythropoietin levels in patients with cancer-related anemia are lower than those in patients with a similar degree of anemia due to iron deficiency.[24,25] Several clinical studies have demonstrated that administration of epoetin alfa, a recombinant human erythropoietin, increases Hb levels, decreases transfusion requirements, and improves QOL in anemic patients with a broad range of non-myeloid malignancies receiving platinum- or non-platinum-based chemotherapy.[26–33] The benefits of epoetin alfa administration were shown not only in large studies conducted in community-based oncology practices in the United States[29,32,34] but also in randomized, placebo-controlled trials.[27,31,33]

The present report describes a subgroup analysis of the efficacy of epoetin alfa in 173 patients with hematologic malignancies who were part of a full study cohort of 375 patients enrolled in a multicenter, multinational (14 European, one African), double-blind, placebo-controlled trial.[33] The trial was designed to evaluate the efficacy and safety of epoetin alfa therapy in patients with solid or non-myeloid hematologic malignancies who were receiving non-platinum chemotherapy.

MATERIALS AND METHODS

The methods have been reported in detail previously.[33] In brief, male and female patients at least 18 years of age with solid or non-myeloid hematologic malignancies were eligible for enrollment if non-platinum chemotherapy was underway or imminent and if they had a life expectancy of at least 6 months. Patients were required to have anemia, defined as an Hb level $\leq$10.5 g/dl or a decrease in Hb of $\geq$1.5 g/dl per previous cycle or month since beginning chemotherapy resulting in an Hb level $>$10.5 g/dl but $\leq$12.0 g/dl. Patients were excluded from enrollment if they had uncontrolled hypertension; untreated iron, folate or vitamin B_{12} deficiency; or severe illness or surgery within 1 week, blood transfusion or radiotherapy within 2 weeks, or major blood loss or infection within 4 weeks of study entry. All patients gave written informed consent before study entry and the study protocol and amendments were reviewed by an independent ethics committee.

Study design and treatment

Patients were randomized 2:1 to receive epoetin alfa 150 IU/kg or a matching volume of placebo subcutaneously three times weekly for up to 28 weeks. Randomization to study treatment was stratified prospectively according to baseline Hb level ($\leq$10.5 or $>$10.5 g/dl but $\leq$12.0 g/dl) and tumor type (hematologic or solid). If after 4 weeks the Hb level had increased by $\geq$1 g/dl or the reticulocyte count by $\geq$40 000/μl above baseline, study treatment was continued at the same dose. If the Hb level or reticulocyte count had not increased by the above levels, the dose of epoetin alfa was doubled to 300 IU/kg (or matching volume of placebo) administered three times weekly. An oral daily dose of 200 mg of elemental iron was recommended to maintain appropriate iron availability and stores. Red blood cell transfusions were permitted during the study at the discretion of the physician but were to be avoided in patients with Hb levels $>$8 g/dl unless clinically indicated. Outside of the United States, epoetin alfa is manufactured by Ortho Biologics, LLC and distributed and marketed as EPREX® or ERYPO® by Ortho Biotech and Janssen-Cilag. In the United States, PROCRIT® (epoetin alfa) is manufactured by Amgen Inc. and distributed and marketed by Ortho Biotech Products, L.P.

Efficacy analyses

The primary endpoint of the trial was the proportion of patients transfused after day 28. Secondary endpoints included the change in Hb level from baseline to last value, the proportion of treatment responders (defined as patients with an increase in Hb level $\geq$2 g/dl unrelated to transfusion) and correctors (patients who achieved an Hb level $\geq$12 g/dl during the study), and the change in QOL scores from baseline to last value for five cancer-specific, Hb-sensitive scales. The QOL instruments designated *a priori* included the Functional Assessment of Cancer Therapy-Anemia (FACT-An), for which the FACT-General (FACT-G Total) scale (measuring social/family, functional, emotional, and physical well-being) and the fatigue (FACT-An Fatigue) subscale were assessed, and the Cancer Linear Analog Scale (CLAS, also known as the Linear Analog Scale Assessment (LASA)), for which energy level, ability to do daily activities, and overall QOL items were assessed.

Although the study was not designed or powered to detect differences in survival, the protocol was amended before the study was unblinded and completed to permit prospective analysis of survival. Information regarding date and cause of death was collected 12 months after the last patient completed the study. Survival distributions were estimated with Kaplan–Meier curves. For the full study cohort, the Kaplan–Meier curves were compared by means of log-rank tests. To compensate for the variable survival times associated with different malignancies, Kaplan–Meier estimates of survival were performed by tumor stratum.

Efficacy analyses were performed on three populations: intent-to-treat, which included all randomized patients; efficacy, which included all randomized patients on study $>$28 days; and QOL, which was defined as all patients who had been randomized, received the study drug and had a baseline and at least one follow-up QOL assessment. Statistical analyses of efficacy parameters were not performed for tumor subgroup populations since the overall trial was not powered to discriminate treatment differences within subgroups. Therefore, no *P* values are reported herein for the hematologic malignancy subgroup.

RESULTS

The epoetin alfa ($n = 251$) and placebo ($n = 124$) treatment groups of the full study cohort and of the hematologic subgroup ($n = 115$ and $n = 58$, respectively) were generally well-matched with respect to baseline demographic and clinical characteristics (Table 1). Overall, the majority of patients enrolled

Table 1. Baseline demographic and clinical characteristics of the intent-to-treat population of the full study cohort and the hematologic subgroup. Adapted with permission from Littlewood *et al.*[33]

	Full study cohort		Hematologic subgroup	
Characteristic	Epoetin alfa ($n = 251$)	Placebo ($n = 124$)	Epoetin alfa ($n = 115$)	Placebo ($n = 58$)
Sex, *n* (%)				
Female	166 (66)	85 (68)	56 (49)	26 (45)
Male	85 (34)	39 (31)	59 (51)	32 (55)
Mean age (years)	58.3	59.5	59.4	63.9
Months since diagnosis				
Mean ± SD	35.3 ± 47.39	31.1 ± 40.34	27.8 ± 45.75	23.2 ± 36.27
Hemoglobin (g/dl)				
Mean ± SD	9.9 ± 1.13	9.7 ± 1.13	9.9 ± 1.22	9.7 ± 1.21
Prestudy transfusion,* *n* (%)	71 (28)	44 (36)	41 (36)	20 (34)

*Within 3 months prior to study entry.
SD, standard deviation.

Table 2. Tumor diagnoses within hematologic subgroup

Diagnosis	Epoetin alfa ($n = 115$)	Placebo ($n = 58$)
Non-Hodgkin's lymphoma	41 (36%)	21 (36%)
Myeloma	37 (32%)	25 (43%)
Hodgkin's lymphoma	19 (16%)	6 (10%)
Chronic lymphocytic leukemia	16 (14%)	5 (9%)
Other	2 (2%)	1 (2%)

in the trial were white (96%), had late stages of disease (stages III and IV), and had received chemotherapy within the 3 months prior to enrollment (92%). The median Eastern Cooperative Oncology Group (ECOG) performance status was 1.0. Hematologic malignancies were present in 46% of patients (Table 2). Major tumor types in the overall population included breast (30%), non-Hodgkin's lymphoma (17%), and myeloma (17%). Major tumor types in the hematologic subgroup included non-Hodgkin's lymphoma (36%), myeloma (36%), and Hodgkin's disease (14%).

Efficacy

Results of the efficacy analyses for both the full study cohort and the hematologic subgroup are presented for comparative purposes. Except for the analysis of transfusion variables, which was based on the intent-to-treat population, all efficacy analyses were based on the efficacy population.

In the full study cohort, significantly fewer patients treated with epoetin alfa required transfusion after day 28 compared with those treated with placebo (24.7 vs. 39.5%, $P = 0.006$). In the hematologic subgroup, 25.2% of patients treated with epoetin alfa were transfused after day 28 compared with 43.1% of placebo-treated patients (Table 3). Mean Hb at transfusion was 7.9 g/dl for epoetin alfa-treated patients and 7.8 g/dl for placebo patients for the transfused population (ITT).

The mean increase in Hb levels from baseline to last value was significantly greater for patients in the full study cohort who were treated with epoetin alfa compared with placebo, 2.2 g/dl vs. 0.5 g/dl ($P < 0.001$). Differences in Hb levels between patients given epoetin alfa and placebo were evident at week 2 and continued throughout the treatment period (Figure 1). In the hematologic subgroup, the mean increases in Hb levels from baseline were also markedly greater for patients treated with epoetin

Table 3. Summary of efficacy parameters, hematologic subgroup

Parameter	Epoetin alfa	Placebo
Patients transfused after day 28*	25.2% (29/115)	43.1% (25/58)
Hemoglobin† (g/dl), mean change ± SEM	2.2 ± 0.21	0.3 ± 0.25
Hematocrit† (%), mean change ± SEM	6.8 ± 0.63	0.4 ± 0.76
Proportion of responders†,‡	75.2% (85/113)	16.7% (9/54)
Proportion of correctors†,§	72.6% (82/113)	14.8% (8/54)

*Intent-to-treat population.
†Efficacy population.
‡Responders, patients with an increase in Hb of ≥2 g/dl unrelated to transfusion.
§Correctors, patients whose Hb levels reached ≥12 g/dl during the study.
SEM, standard error of the mean.

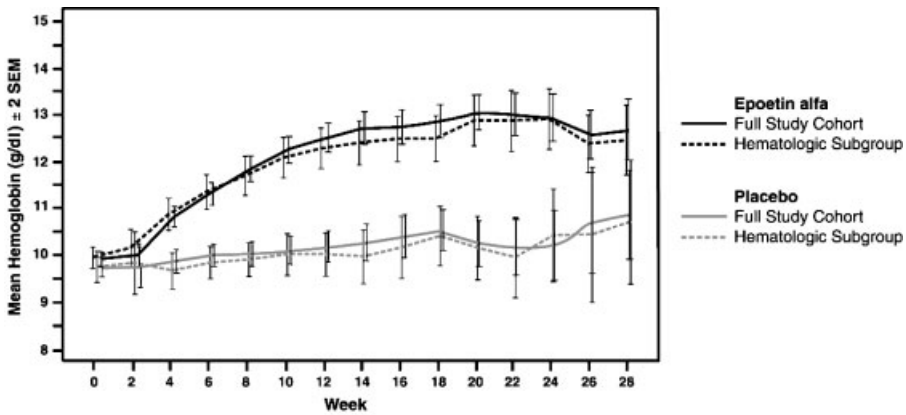

Figure 1. Comparison of the mean bi-weekly hemoglobin (Hb) values for patients treated with epoetin alfa or placebo. Missing values at any evaluation point are replaced by the last value carried forward. Mean increases in Hb levels from baseline to last value were substantially higher in patients treated with epoetin alfa compared with placebo for the efficacy population of the full study cohort (2.2 vs. 0.5 g/dl, $P < 0.001$), as well as the hematologic malignancy stratum (2.2 vs. 0.3 g/dl). Adapted with permission from Littlewood *et al.*[33]

alfa compared with placebo: 2.2 vs. 0.3 g/dl, respectively (Table 3; Figure 1). As with the full study cohort, differences between epoetin alfa and placebo were already evident after 2 weeks. In the epoetin alfa group, mean Hb levels progressively increased from 9.93 g/dl at baseline to 10.14 g/dl at week 2, 10.86 g/dl at week 4, and 12.08 g/dl or greater from week 10 onward. In contrast, Hb levels in the placebo group ranged from 9.73 g/dl at baseline to 9.82 g/dl at week 2, 9.65 g/dl at week 4, and then 10.00 g/dl at week 10 (peak, 10.7 g/dl at week 28, $n = 8$). In addition, the mean increases in hematocrit from baseline to last value for patients in the hematologic subgroup were greater for patients in the epoetin alfa treatment group (Table 3).

Response to treatment was assessed in terms of responders, defined as patients who achieved a ≥2 g/dl increase in Hb levels unrelated to transfusion. In the full study cohort, there were significantly more responders in the epoetin alfa treatment group than in the placebo group (70.5 vs. 19.1%, $P < 0.001$). The response of the hematologic subgroup paralleled that of the full study cohort, with a substantially higher proportion of epoetin alfa-treated than placebo-treated patients responding to anemia treatment (75.2 vs. 16.7%, respectively; Table 3).

Table 4. Mean QOL changes scores in hematologic subgroup

		Epoetin alfa		Placebo	
Scale/subscale	Range	*n*	Change score	*n*	Change score
FACT-G total	0–108	92	5.78	38	1.08
FACT-An: Fatigue	0–52	94	4.30	41	−0.16
CLAS: Energy levels	0–100	107	10.14	49	−2.53
CLAS: Ability to do daily activities	0–100	107	11.57	49	−2.92
CLAS: Overall QOL	0–100	107	8.96	48	−5.23

Treatment response was also assessed in terms of correctors, defined as patients who attained an Hb level of $\geq$12 g/dl during the study. In the full study cohort, there were significantly more correctors in the epoetin alfa group than in the placebo group (67.6 vs. 15.7%, $P < 0.001$). Treatment response in the hematologic subgroup again paralleled that observed in the full study cohort, with 72.6% of patients in the epoetin alfa group categorized as correctors, compared with 14.8% in the placebo group (Table 3).

Timing of QOL assessments and reasons for missing patient QOL data have been detailed previously.[35] Differences in change scores between the epoetin alfa and placebo groups for each QOL parameter greatly favored epoetin alfa for the hematologic subgroup (Table 4). Results were comparable with the full study cohort for which the between-group differences in the FACT-An and CLAS scores were significant ($P < 0.01$).[33] By most scales, QOL worsened in placebo-treated patients in the hematologic subgroup despite maintenance of baseline Hb levels with transfusion.

At the time of the 12-month assessment of survival (median follow-up, 26 months), 94 (38%) patients treated with epoetin alfa and 41 (33%) treated with placebo in the full study cohort were alive. Median survival times were 17 months with epoetin alfa and 11 months with placebo, and the Kaplan–Meier 12-month estimates of survival were 60 and 49% for the epoetin alfa and placebo treatment groups, respectively. There was a trend in overall survival favouring epoetin alfa ($P = 0.13$, log-rank test).[33] For the hematologic subgroup the estimated median survival times were approximately 32 months with epoetin alfa group and 19 months with placebo. At the 12-month assessment, 61 patients (53%) and 28 patients (48%) treated with epoetin alfa and placebo respectively, in the hematologic tumor stratum were alive.

Because this study was not designed or powered to evaluate survival, these data must be interpreted with caution. Moreover, the interpretive value of the data regarding survival is limited because variables that influence survival such as disease stage, bone marrow involvement, chemotherapy intensity, and disease progression were not controlled for or stratified in the study or collected during follow-up.

Safety

Safety was assessed by study treatment for the full study cohort ($n = 251$, epoetin alfa; $n = 124$, placebo). Epoetin alfa treatment was well tolerated. The overall incidence of adverse events was similar for the epoetin alfa (86%) and placebo (81%) treatment groups, and the incidences of individual adverse events generally were similar for both treatment groups. The most common adverse events in both treatment groups were fever (22% epoetin alfa vs. 17% placebo), granulocytopenia (20 vs. 13%), disease progression (18 vs. 22%) and nausea (18 vs. 14%). Fever, granulocytopenia, and nausea were more likely to be induced by chemotherapy than by epoetin alfa therapy. A thrombotic or possible thrombotic event was experienced by 17 patients (7%) in the epoetin alfa group and by eight patients (6%) in the placebo group, and the incidence of deep vein thrombosis was the same in both treatment groups.[33] Adverse events were not analyzed separately for the treatment groups in the hematologic stratum.

DISCUSSION

Although anemia is a common problem in patients with cancer, its clinical importance has been largely underappreciated. In addition to affecting virtually all organ and tissue systems, cancer-related anemia is now known to have an adverse impact on patients' QOL.[13,36,37] Moreover, it is suggested that cancer-related anemia also may be associated with poorer prognosis and may contribute to mortality.[17–20,38] Therefore, prevention and/or treatment of cancer-related anemia may improve not only morbidity and QOL, but also prognosis and, potentially survival.

One cause of cancer-related anemia is inadequate levels of serum erythropoietin for the degree of anemia.[24,25] Numerous clinical studies have established that epoetin alfa administration effectively and safely treats anemia in cancer patients undergoing either platinum- or non-platinum-based chemotherapy.[26–33] In these studies, epoetin alfa treatment significantly increased Hb levels and reduced the need for transfusions. Several studies have demonstrated an improvement in QOL related to the increase in Hb level.[29,30,32,33]

The present report of a subgroup analysis of the efficacy of epoetin alfa in 375 patients stratified by tumor type in a multicenter, double-blind, controlled trial[33] indicates that epoetin alfa administration is effective in patients with non-myeloid hematologic malignancies who are receiving non-platinum chemotherapy. Substantially fewer epoetin alfa- than placebo-treated patients in the hematologic subgroup required transfusions after 28 days of treatment: 25.2% compared with 43.1%. Also, epoetin alfa-treated patients in this subgroup had greater increases in Hb levels overall (2.2 g/dl) than did placebo-treated patients (0.3 g/dl). Improvement in Hb levels occurred rapidly, i.e. differences between epoetin alfa and placebo patients were already apparent after the first 2 weeks of treatment, with epoetin alfa patients demonstrating Hb-level increases of approximately 1 g/dl after 1 month and 2 g/dl after 2 months. In addition, substantially more patients in the hematologic subgroup responded to epoetin alfa treatment (defined as achieving a $\geq$2 g/dl increase in Hb level unrelated to transfusion) than did patients in the placebo group (75.2 vs. 16.7%).

These findings are consistent with those of previously published studies. An early study that evaluated epoetin alfa for the treatment of chronic anemia in patients with multiple myeloma and squamous cell carcinoma reported respective response rates of 75 and 79% as well as improvements in iron metabolism.[39] Pooled data from a series of three controlled trials showed that epoetin alfa was effective in correcting anemia in a wide variety of tumor types and that response rates were equivalent in patients with hematologic and solid tumors.[40] In addition, there was no difference in response rates between patients with and without tumor infiltration of the bone marrow. More recently, results of a large ($N = 2964$), single-arm, community-based study that evaluated once-weekly epoetin alfa dosing showed an overall response rate of 68% and a significant ($P < 0.001$) increase of 1.8 g/dl in Hb levels across all tumor types over the 16-week course of study treatment.[32] Analyses of data for the hematologic subgroup in the same study showed similar results, i.e. a response rate of 65% and a significant ($P < 0.001$) increase in Hb level of 2.2 g/dl from baseline to week 16.[41] As in the present study, mean Hb levels for the full study cohort and the hematologic subgroup in this community-based study were increased by approximately 1 g/dl after 1 month, and 2 g/dl after 2 months of treatment; Hb values for the hematologic subgroup were 9.4 g/dl at baseline, 10.4 g/dl at month 1, and 11.2 g/dl at month 2. Reported complete response rates to epoetin alfa in anemic patients with B-chronic lymphocytic leukemia (B-CLL) and multiple myeloma were 55 and 58%, respectively.[10,31]

In the present study, the results of the efficacy analysis based on the hematologic subgroup additionally favored epoetin alfa over placebo for improvements in the five primary measures of QOL. These findings are consistent with an analysis of data from the hematologic subgroups of three large, community-based studies with over 7000 overall enrolled patients, which showed significant

($P < 0.001$) improvement in all three LASA variables.[34] Interestingly, numerous studies that evaluated QOL in patients with chemotherapy-related anemia treated with epoetin alfa, demonstrated that the improvement in QOL observed in both the full study cohort[29,30,32–34] and hematologic subgroup[34] were associated with increases in Hb level. Importantly, the increases in Hb levels in patients treated with epoetin alfa occurred despite lower transfusion rates in this group than in the placebo group. In the placebo-treated patients, stabilization of Hb levels by transfusion was not adequate for maintaining QOL in anemic cancer patients receiving chemotherapy; in fact, placebo-treated patients experienced substantial decreases in QOL.[33]

Two potential biases associated with QOL results in clinical trials are effects of disease response and other confounding factors and missing data. Of importance to note, multivariate regression analysis of the data obtained from this trial, taking into account the effects of disease response and other confounding factors, confirmed significant ($P < 0.05$) QOL improvements in epoetin alfa-treated patients versus placebo-treated patients.[35] In addition, sensitivity analysis conducted to account for the effects of missing data on QOL results in this trial confirmed significant ($P < 0.05$) between-group QOL differences favoring epoetin alfa-treated patients for four of the five scales reported here.[42]

A growing body of evidence suggests that low Hb levels are associated with poorer prognosis in patients with cancer who are treated with chemotherapy and/or radiotherapy.[17,43–46] In addition, associations have been demonstrated between anemia and reduced survival in patients with solid tumors, as well as in patients with non-Hodgkin's lymphoma, Hodgkin's disease, mantle cell lymphoma or Waldenstrom's macroglobulinemia, and in previously treated patients with CLL.[18–20,47–51] A recent meta-analysis of 60 papers that reported survival of cancer patients according to either Hb levels or presence of anemia showed that the overall estimated relative risk of death in anemic cancer patients was increased by 65% (54 to 77%, 95% confidence interval).[52]

After noticing in a small study that some epoetin alfa-treated patients with multiple myeloma showed a survival time that was longer than expected, Mittelman *et al*. evaluated the potential effects of this agent on the course of tumor progression in a murine myeloma model.[53] The investigators found that daily administration of epoetin alfa for several weeks induced complete tumor regression in 30 to 60% of the mice. The effects of epoetin alfa were ascribed to a T cell-mediated mechanism. Further study in a murine model of myeloma bone disease showed that epoetin alfa treatment significantly ($P < 0.0001$) prolonged survival in tumor-bearing mice.[53] These findings in animal models suggest that epoetin alfa may have intrinsic anti-tumor activity in addition to a stimulatory effect on red blood cell production.

Against this background and the results observed in the full study cohort of the trial considered here, in which Kaplan–Meier estimates showed a trend in survival favoring epoetin alfa over placebo,[33] survival was evaluated in the hematologic subgroup. At the 12-month assessment, a higher proportion of hematologic subgroup patients treated with epoetin alfa were alive than were those treated with placebo (53 vs. 48%). However, the trial was not powered with respect to survival and did not control for or stratify patients based on variables that influence survival, such as disease stage, bone marrow involvement, chemotherapy intensity, and disease progression. Thus, the observed effect of epoetin alfa on survival and the relationship of Hb level to survival, although interesting, require confirmation in additional controlled trials specifically designed to assess survival in anemic cancer patients receiving chemotherapy.

In summary, epoetin alfa treatment was effective and safe for reducing transfusion requirements and rapidly and effectively correcting Hb levels in patients with hematologic malignancies who were receiving non-platinum-based chemotherapy. Importantly, epoetin alfa also improved or maintained QOL measures in these patients and epoetin alfa treatment was well tolerated. A possible survival benefit of epoetin alfa in patients with hematologic malignancies suggests that further study is necessary to explore the full potential of this novel treatment.

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APPENDIX

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