Relationship between Changes in Hemoglobin Level and Quality of Life During Chemotherapy in Anemic Cancer Patients Receiving Epoetin Alfa Therapy

Jeffrey Crawford, M.D.[1]
David Cella, Ph.D.[2]
Charles S. Cleeland, Ph.D.[3]
Pierre-Yves Cremieux, Ph.D.[4,5]
George D. Demetri, M.D.[6]
Brenda J. Sarokhan, M.P.H.[7]
Mitchell B. Slavin, Pharm.D., M.B.A.[7]
John A. Glaspy, M.D.[8]

[1] Duke Comprehensive Cancer Center, Duke University Medical Center, Durham, North Carolina.

[2] Center on Outcomes, Research and Education, Evanston Northwestern Healthcare, Evanston, Illinois.

[3] University of Texas M.D. Anderson Cancer Center, Houston, Texas.

[4] Analysis Group/Economics, Cambridge, Massachusetts.

[5] Université du Québec à Montréal, Montreal, Canada.

[6] Dana-Farber Cancer Institute, Boston, Massachusetts.

[7] Ortho Biotech Products, L.P., Raritan, New Jersey.

[8] Division of Hematology-Oncology, Department of Medicine, University of California, Los Angeles, California.

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Address for reprints: John Glaspy, M.D., Suite 202, 200 Medical Plaza, Los Angeles, CA 90095-6926; Fax: (310) 794-1699; E-mail: jglaspy@mednet.ucla.edu

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BACKGROUND. Hemoglobin increases have been associated with quality of life (QOL) improvements in anemic cancer patients treated with epoetin alfa, but intervention generally has been reserved for symptomatic anemia or hemoglobin < 10 g/dL. Relationships among hemoglobin, functional status, and patient reported QOL have not been well characterized.

METHODS. Data from two open-label, community-based trials of epoetin alfa therapy that enrolled 4382 anemic cancer patients undergoing chemotherapy were used to evaluate the relationship between hemoglobin changes and QOL changes. The authors measured QOL using the Linear Analog Scale Assessment (LASA) and the more detailed, disease-specific Functional Assessment of Cancer Therapy-Anemia (FACT-An) instrument. Analyses were performed to determine the incremental change in QOL associated with hemoglobin increases (1 g/dL increments).

RESULTS. Cross-sectional analyses showed a nonlinear relationship and significant positive correlation between high hemoglobin levels and high LASA and FACT-An scores ($r = 0.25$ and 0.29, respectively, $P < 0.01$). Patients with hemoglobin increases of ≥ 2 g/dL reported statistically significant improvements in five FACT-An items selected a priori specifically to reflect functional capacity. An incremental analysis used regression methods to identify the longitudinal relationship between incremental changes in hemoglobin and QOL scores. This relationship was found to be nonlinear, with the maximum QOL gain occurring at a hemoglobin level of 12 g/dL (range, 11–13 g/dL). Patients with low baseline QOL scores and longer time periods between baseline and final QOL assessments experienced significantly ($P < 0.05$) greater increases in overall QOL. Progressive disease at baseline, change in disease status from baseline to end of study, and increase in self-reported pain or nausea all had significant ($P < 0.05$) negative effects on QOL scores.

CONCLUSIONS. A direct relationship exists between hemoglobin increases during epoetin alfa therapy and corresponding QOL improvements in cancer patients receiving chemotherapy across the clinically relevant hemoglobin range of 8–14 g/dL. These data suggest that the maximal incremental gain in QOL occurs when hemoglobin is in the range of 11–13 g/dL. ***Cancer*** **2002;95:888–95.**

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Quality of life (QOL) is important even when survival is the primary objective in patients with cancer. Supportive or palliative therapies that do not directly impact survival can have important positive effects on day-to-day physical, mental, and social functioning and self-perceived overall QOL.[1–4] Functional impairment, often associated with fatigue,[5,6] is experienced by most cancer patients and can be due to multiple factors, including underlying disease progression,

treatment-induced side effects, psychological disorders (e.g., depression, anxiety), and other comorbidities.[7,8] Chronic anemia is a well-recognized complication of both cancer and cytotoxic treatments[9] and is associated with symptoms (e.g., fatigue, dyspnea) that may induce or exacerbate functional deterioration.

Recombinant human erythropoietin (epoetin alfa) can mitigate anemia associated with inappropriately low serum levels of endogenous erythropoietin, such as that seen in chronic renal failure and cancer patients.[10] In patients with chronic renal failure (including those on hemodialysis), overwhelming evidence indicates that correcting anemia with epoetin alfa contributes to improvements in physical and social activity, neurologic status (e.g., mood, cognitive function), and other symptoms (e.g., abnormalities in appetite and sleep).[11–25] Similarly, both placebo-controlled and nonrandomized studies of epoetin alfa therapy in cancer patients undergoing chemotherapy have shown significant increases in both hematologic and QOL parameters, even in patients with advanced or progressive disease and a short life expectancy.[26–34]

In patients with cancer, it has been difficult to characterize precisely the QOL benefits of epoetin alfa therapy because of the broad range of cancers and the wide variety of treatment. Unfortunately, most studies of epoetin alfa that have used QOL as an end point included small numbers of patients and lacked reliable multivariate regression models. Thus, conclusive evidence has not been generated previously to identify the hemoglobin levels that optimize QOL in cancer patients. However, in patients with chronic renal failure, recent studies support a target level of 12 g/dL or higher.[14,18,23,35]

Two recently published clinical trials of three times weekly epoetin alfa (Procrit®; Ortho Biotech Products, L.P., Raritan, NJ) in anemic cancer patients receiving chemotherapy have shown its efficacy in improving hemoglobin levels and QOL and in reducing transfusion requirements in the community practice setting.[28,29] These studies enrolled 4382 anemic cancer patients with baseline hemoglobin levels across the range of 8 to 14 g/dL, permitting a closer look at the relationship between hemoglobin and QOL in cancer patients using comprehensive statistical methods.[28,29] The current analyses of data from these previously published Phase IV epoetin alfa trials were performed to examine the relationships among: 1) baseline hemoglobin levels and QOL; 2) change in hemoglobin levels during epoetin alfa therapy and change in QOL; and 3) incremental change in hemoglobin levels during epoetin alfa therapy and incremental change in QOL. In addition, we sought to determine whether the magnitude of QOL improvement during epoetin alfa therapy for incremental change in hemoglobin level depends on the patient's hemoglobin level at the onset of treatment.

PATIENTS AND METHODS

Patient Database

Statistical analyses were performed using the database of cancer patients who participated in either of two Phase IV epoetin alfa clinical trials described below.[28,29]

Design of Original Studies

Two large scale, open-label, nonrandomized, multicenter clinical trials evaluated the efficacy, tolerability, and QOL effects of epoetin alfa as an adjunct to chemotherapy in community-based practices.[28,29] These similarly designed studies prospectively evaluated 16 weeks of three times weekly epoetin alfa therapy in patients with anemia who were undergoing chemotherapy for treatment of nonmyeloid malignancy. Patient enrollment requirements were a life expectancy $\geq$ 6 months and no evidence of uncontrolled hypertension or anemia attributable to other factors (e.g., hemolysis or iron, folate, or B_{12} deficiency). Stage of disease was not a criterion for entry.

In the first study (Community Study-1 [CS-1]), "anemic" (unspecified degree) patients were to receive epoetin alfa 150 U/kg subcutaneously three times weekly, with an increase to 300 U/kg three times weekly after eight weeks if hematopoietic response was judged inadequate (undefined). For the second study (Community Study-2 [CS-2]), anemic (hemoglobin level $\leq$ 11 g/dL) patients were to receive epoetin alfa 10,000 U three times weekly; epoetin alfa dosing was increased to 20,000 U three times weekly after four weeks if the increase in hemoglobin level was $<$ 1.0 g/dL.

Patients were seen and evaluated each month in the clinic. Hematopoietic response to epoetin alfa was assessed by hemoglobin levels and transfusion utilization over time. To evaluate the impact of epoetin alfa on self-perceived QOL, patients in both studies rated their energy levels, abilities to perform daily activities, and overall QOL using the 100-mm Linear Analog Scale Assessment (LASA) at baseline and Month 4 or at the time of study completion for early terminators, with 0 representing the least favorable self-perception of these parameters and 100 the greatest. In CS-2, the same LASA scale was administered at baseline, Month 2, and Month 4 (or study termination) along with the more detailed Functional Assessment of Cancer Therapy-Anemia (FACT-An) questionnaire. The FACT-An questionnaire is a validated and sensitive instrument for monitoring QOL in cancer patients, provid-

TABLE 1
Time Varying Factors Included in Multivariate Longitudinal Regression Models

Variable	Study	
	CS-1	CS-2
Change in the following:		
Tumor response		√
No. of CT treatments administered	√	√
No. of CT cycles administered	√	√
No. of RT cycles administered		√
No. of days elapsed between CT and QOL evaluation	√	√
No. of days elapsed between RT and QOL evaluation		√
No. of transfusions	√	√
Self-reported feeling of nausea		√
Self-reported feeling of pain		√
Elapsed time between baseline and final QOL evaluations	√	√
Progressive disease recorded at baseline		√
Baseline QOL evaluation scores	√	√

CS: Community Study; CT: chemotherapy; RT: radiation therapy; QOL: quality of life.

ing a measure of the four general domains of day-to-day functioning (physical, emotional/mental, social/family, and functional well-being).[36,37] The results of CS-2 showed that QOL changes derived from the FACT-An questionnaire correlated well ($r = 0.72$) with those derived from LASA.[28] A retrospective collection and analysis of disease response data was performed on a subset (40%) of patients who participated in CS-1.[29] This analysis was done prospectively in CS-2 to better evaluate the influence of tumor response on QOL parameters and to help separate the QOL effects of disease response from those of response to epoetin alfa.[28]

Statistical Analyses

Longitudinal analyses were used to examine the relationship between incremental change in hemoglobin levels and incremental change in QOL scores. Patients' baseline and final QOL scores were paired with their closest hemoglobin levels and other laboratory/clinical measures.

Multivariate regression models were constructed based on longitudinal data and variables that changed over time (with potential influence on self-perceived QOL during the studies), including transfusion use, number of chemotherapy treatments/cycles administered, and length of time between baseline and final QOL evaluations (Table 1). The short term negative effects of chemotherapy and radiation on QOL scores were controlled for by calculating 1) the difference between the number of cycles received before and during the studies and 2) the difference in elapsed days between the cycle immediately preceding baseline and final QOL evaluations. Changes in self-perceived pain and nausea (assessed by FACT-An) also were control variables, ensuring that parameter estimates reflected the impact of hemoglobin levels on QOL scores independent of any simultaneous increase or decrease in these commonly reported symptoms. The effect of pain and nausea on the relationship between hemoglobin and QOL was further examined using interaction terms between pain and hemoglobin and between nausea and hemoglobin. The effect of disease and treatment characteristics likely to vary over the course of the study on each patient's change in QOL score was evaluated using a longitudinal design. Thus, the parameter estimates measure a given patient's QOL response to a change in hemoglobin (rather than an estimation of differences in QOL improvements among patients with different hemoglobin levels).

The relative difference in QOL scores between successive 1 g/dL hemoglobin level increases was further examined via a marginal (or incremental) analysis, a widely used measure in economic decision making.[38] In economics, marginal benefit (profit) represents the change in total benefit (profit) resulting from a single unit increase in output or activity.[38] Examining the form (or shape) of the relationship between incremental change in hemoglobin levels and incremental change in QOL scores during epoetin alfa therapy determined the target hemoglobin range within which the greatest gain in QOL might be obtained in response to a unit hemoglobin change.

A two stage Heckman procedure,[39] commonly used to address the problems of missing data and sample selection bias in clinical trials,[40] was performed to correct for potential bias resulting from patients who were clinically evaluated at least twice but failed or declined to complete a second QOL evaluation. This procedure identified systematic characteristics of patients whose second QOL measurement is missing and included a variable that embodies these characteristics in the analysis of patients with complete data, thereby reducing the likelihood of bias resulting from nonrandomly missing data.

All statistical analyses were performed using SAS release 6.12 (SAS Institute, Cary, NC) and TSP version 4.2 (TSP International, Inc., Palo Alto, CA). For graphic presentation of all statistical analyses, a hemoglobin level of 7 g/dL refers to levels below 7.50 g/dL; 8 g/dL refers to levels from 7.50 to 8.49 g/dL; and so forth.

RESULTS

Database Characteristics

Demographic data were available for 2030 patients in CS-1 and 2352 patients in CS-2 (Table 2). In both

TABLE 2
Patient Baseline Demographics and Clinical Characteristics

	Study	
Characteristic	**CS-1**	**CS-2**
Mean age (yr)	62.7	63.3
Gender (%)		
Male	38	40
Female	62	60
Tumor type (%)		
Solid tumors	81	78
Hematologic	19	22
Mean hemoglobin level (g/dL)	9.27	9.29
Mean FACT-An score ± SD	—	113 ± 29.7
Mean LASA overall QOL score[a] ± SD	45.0 ± 23.8	45.4 ± 24.1
Mean change in hemoglobin level (g/dL)	1.70	1.93

CS: Community Study; FACT-An: Functional Assessment in Cancer Therapy-Anemia; SD: standard deviation; LASA: Linear Analog Scale Assessment; QOL: quality of life.

[a] Expressed as a 100 mm scale, with 0 representing the lowest self-perception of each parameter and 100 representing the highest.

studies, the mean age was approximately 63 years, approximately 61% of participants were female, and most patients (about 80%) had solid tumors. Non-Hodgkin lymphoma accounted for nearly one half of the hematologic malignancies, whereas the solid tumor diagnoses were distributed relatively evenly among lung, breast, gynecologic, and all other tumor types. The mean baseline hemoglobin level was 9.3 g/dL (range, 4.6 to 11.0 g/dL) for both studies, and the mean baseline LASA overall QOL (45 mm of a possible 100 mm maximum) and FACT-An (113 points of a possible 196 maximum) scores suggested substantial functional impairment.[28,29] In a healthy population (i.e., without cancer or serious comorbidities), expected mean LASA scores would be at least 85 mm for individuals 21–50 years of age and 70–80 mm for those 51 years or older.[41] These "normal" values for a 100-mm LASA were derived from data collected for the EuroQOL instrument (which is a 200-mm scale, with each point represented by 2 mm).[41]

Characteristics of the CS-1 and CS-2 databases are summarized in Table 3. Of the 2030 patients who participated in CS-1 and 2352 in CS-2, 1990 and 2114, respectively, were available for the cross-sectional analysis, since they had at least a baseline QOL and hemoglobin measurement. Of the 2114 patients in CS-2, 1642 had at least two QOL measurements and complete clinical data. These 1642 patients are included in the longitudinal analysis. However, the Heckman sample selection correction addressed sample selection bias that might result form nonrandomly missing data.

TABLE 3
Database Characteristics of CS-1 and CS-2

	Study		
	CS-1	**CS-2**	
Data set	**LASA**	**LASA**	**FACT-An**
No. of patients	2030	2352	2352
Patients with baseline QOL measurements	2004	2182	2135
Patients with baseline QOL and hemoglobin measurements	1990	2114	2080
Patients with all variables included in regression analysis and two QOL observations	1474	1642	1580

CS: Community Study; LASA: Linear Analog Scale Assessment; FACT-An: Functional Assessment of Cancer Therapy-Anemia; QOL: quality of life.

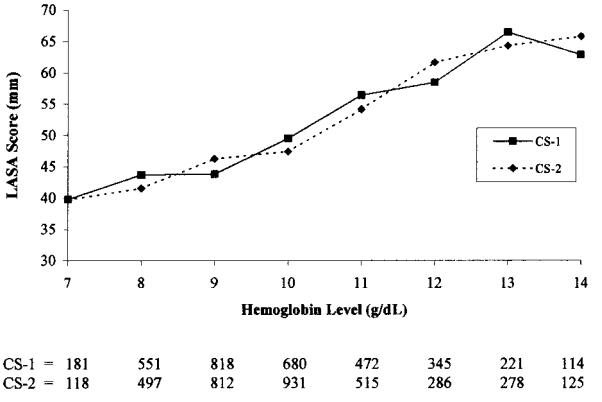

FIGURE 1. Changes in Linear Analog Scale Assessment (LASA), overall quality-of-life scores, and associated hemoglobin level changes, based on cross-sectional analyses of Community Study (CS) 1 and CS-2. Data collected at baseline, Week 8 (CS-2 only), and Week 16 were included in the analyses.

Relationship between Hemoglobin Levels and QOL

Based on data obtained at baseline, Week 8 (CS-2 only), and Week 16, direct correlations between hemoglobin levels and LASA overall QOL scores in CS-1 and CS-2 were modest but statistically significant ($r = 0.25$ and 0.29, respectively; $P < 0.01$; Fig. 1). Using a similar methodology, the direct correlation between hemoglobin levels and FACT-An scores ($r = 0.27$) was also significant ($P < 0.01$) and followed a pattern similar to that observed with LASA overall QOL scores. The statistically significant but modest correlation coefficients could have resulted in part from nonlinearity in the relationship between QOL and hemoglobin level or from the inadequacy of simple correlation coefficients to completely capture a relationship when confounding factors are present.

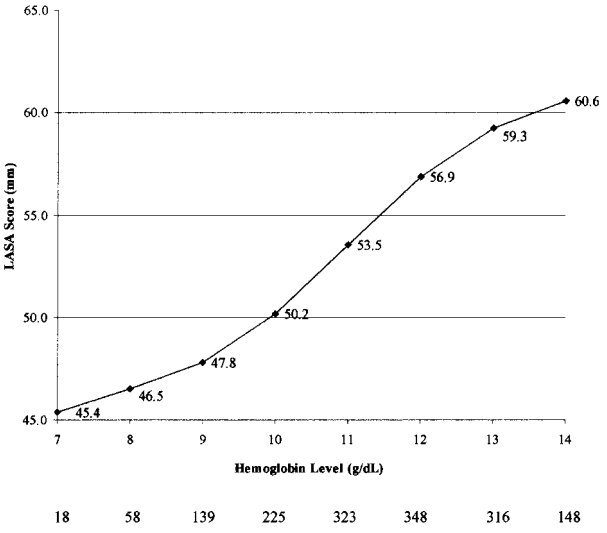

FIGURE 2. Hemoglobin levels and associated Linear Analog Scale Assessment (LASA) overall quality-of-life scores, based a longitudinal analysis of Community Study 2. Data collected at baseline, Week 8, and Week 16 were included in the analyses.

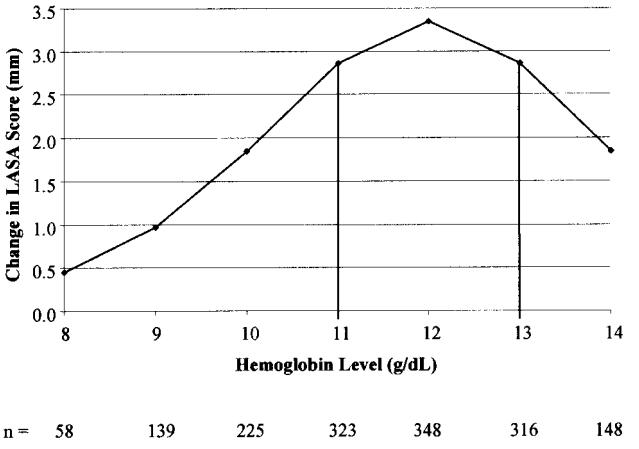

FIGURE 3. Incremental changes in Linear Analog Scale Assessment (LASA) overall quality-of-life scores and hemoglobin levels, based on a longitudinal analysis of Community Study 2. Data collected at baseline, Week 8, and Week 16 were included in the analyses.

Relationship between Changes in Hemoglobin Levels and Change in QOL Scores

The relationship between hemoglobin levels and QOL scores among patients suggests that patients with higher hemoglobin levels will also experience better QOL. Determining whether a patient will experience an increase in QOL in response to an increase in hemoglobin level, however, requires a longitudinal approach. This analysis was only possible for the CS-2 dataset because the absence of prospectively collected tumor response data in CS-1 precluded consideration of all relevant control variables, resulting in potential bias. Furthermore, the self-reported levels of pain and nausea were also included as predictor variables to control for the confounding effects of these two conditions on patients' QOL data. Because the FACT-An scale includes the pain and nausea metrics, the longitudinal analysis could only be performed on the LASA. The results of the multivariate longitudinal regression to assess the effect of an incremental change in hemoglobin levels on LASA overall QOL scores from CS-2 are shown in Figure 2. Successively positive changes in LASA overall QOL scores continued with increases in hemoglobin levels to 14 g/dL, where the estimated QOL was 15.2 mm higher than at a hemoglobin level below 7.5 g/dL ($P < 0.01$). When using a 100-mm LASA for QOL parameters, a change of 10 mm is considered clinically meaningful based on effect size comparisons to QOL studies in cancer patients treated for moderate-to-severe pain.[42] The relationship between a patient's change in hemoglobin level and change in LASA overall QOL scores up to a hemoglobin level of 14 g/dL was direct and significant ($P < 0.01$). Interactions between pain and hemoglobin and between nausea and hemoglobin were not significant, indicating that the relationship between hemoglobin and QOL was similar across patients reporting various levels of pain or nausea. This relationship also was maintained after correcting for potential sample selection bias using the Heckman correction method.

Relationship between Incremental Changes in Hemoglobin Levels and QOL Scores

Based on the longitudinal results reported in the previous section, it is possible to identify the incremental effect of increases in hemoglobin levels on overall QOL, as measured by LASA. The sigmoid-like shape on Figure 2 implies that incremental increases in hemoglobin had differing effects on patient's QOL response depending on the level of hemoglobin from which that incremental increase was achieved.

Figure 3 indicates the effect of an incremental increase in hemoglobin level on LASA scores based on the average 2 g/dL increase observed among evaluable patients in the CS-2 trial. This 2 g/dL change translates into the gains in QOL shown in unit increments of hemoglobin in Figure 3. On average, increases in QOL resulting from incremental increases in hemoglobin at various hemoglobin levels rose until a hemoglobin level of 12 g/dL was reached. Beyond a hemoglobin level of 12 g/dL, subsequent incremental increases in hemoglobin continued to yield additional gains in QOL, but at a decreasing rate. Together, these two patterns imply that a 1 g/dL increase in hemoglobin

from 11 g/dL to 12 g/dL yields the greatest incremental gain in QOL as measured by the LASA. Because this finding is based on a longitudinal analysis of the data, it reflects the QOL response to a hemoglobin level change in a given patient rather than to differences in QOL reported by different patients.

Factors Other than Hemoglobin Level Influencing QOL

In CS-2, greater positive increases in QOL scores were experienced by patients with low baseline scores or longer intervals between baseline and final QOL evaluations ($P < 0.05$). In this same study, progressive disease at baseline or during the study, an increase in transfusion requirements, and an increase in self-reported pain or nausea had significant ($P < 0.05$) negative influence on QOL scores after controlling for changes in hemoglobin. Change in tumor status from stable or in remission to progressive disease was associated with a reduction of approximately 12 mm in overall QOL ($P < 0.05$) on the LASA scale. A 1 point increase in pain (derived from FACT-An) led to overall reductions (2.5-mm reduction) in overall QOL ($P < 0.05$); the reduction in overall QOL observed due to a 1 point increase in nausea was 3.8 mm. In contrast, the number of radiation treatments had no measurable statistically significant effect on the relationship between change in QOL and change in hemoglobin level, while the change in the number of chemotherapy administrations had a small but statistically significant positive effect ($P < 0.05$).

DISCUSSION

An extensive body of literature supports the existence of a relationship between anemia and self-perceived QOL in patients with cancer and other chronic illnesses. In the current study, we sought to understand the relationship between changes in hemoglobin levels and QOL in anemic cancer patients receiving epoetin alfa therapy during concomitant chemotherapy.

Our cross-sectional analysis revealed preliminary evidence of a relationship between anemia and QOL in cancer patients receiving chemotherapy, consistent with conclusions of prior studies of epoetin alfa therapy.[26–34] Of note, a recent retrospective subset analysis of the community based studies found that patients with lung carcinoma, a population with a high incidence of anemia and transfusion use, achieved hematopoietic and QOL benefits from epoetin alfa therapy.[34] We consider the findings of the current cross-sectional analyses to be clinically important despite the subjective and variable nature of patient-rated QOL instruments and the absence of controls for factors other than hemoglobin. The modest correlation coefficients could be explained in part by the apparent nonlinearity of the relationship and the presence of confounding factors. Cross-sectional correlation analyses indicated that there is a direct and positive relationship between hemoglobin and QOL; however, determining the relationship between incremental change in hemoglobin level and incremental change in QOL required multivariate longitudinal analyses. These analyses allowed for a more comprehensive examination of the dynamic relationship between hemoglobin change and its effect on self-perceived QOL within individual patient data.

The longitudinal multivariate regressions (incremental analysis) showed that increased hemoglobin levels during epoetin alfa therapy are associated with corresponding improvements in QOL scores, after controlling for a wide array of patient, disease, and treatment related factors that also are likely to influence QOL over time. In this analysis, QOL scores successively rose up to a hemoglobin level of 14 g/dL (CS-2 LASA), although the rate of rise slowed after a hemoglobin level of 12 g/dL was reached. The longitudinal results were logical and provided evidence of a positive and nonlinear relationship between change in hemoglobin level and change in QOL. Closer examination revealed that the greatest QOL change for an incremental increase in hemoglobin level occurred at or around 12 g/dL. The magnitude of the incremental improvements in QOL scores leveled off within the hemoglobin range of 11–13 g/dL, as increases in QOL scores were similar among patient subsets with final hemoglobin levels of 11 g/dL, 12 g/dL, and 13 g/dL.

The Heckman correction approach was used to control for sample selection bias that may have resulted from the nonrandom dropout of less well patients, leaving healthier patients who experienced less tumor progression or fewer positive changes in hemoglobin levels and were likelier to have both baseline and final QOL evaluations. Based on diagnostic measures recommended in the literature, the test statistics (i.e., condition number, percent censored, and R-square of second stage regressors on the inverse Mills ratio) were well within the range for which the Heckman procedure has been shown to be an effective statistical approach for sample selection bias.[43]

Not surprisingly, self-perceptions of QOL were negatively influenced by adverse disease status and the presence of nausea or pain, whereas patients with low baseline QOL scores and longer intervals between evaluations achieved greater QOL improvements. Discrepancies between the timing of the QOL assessments and the clinical evaluations (including hemoglobin levels) were partially corrected by matching the QOL assessment to the closest available clinical visit;

8% of patients reported QOL and hemoglobin assessments on different days.

The current analysis was carried out on an open label, uncontrolled dataset; the link between increased QOL and intervention in anemic patients can only be definitively established in randomized, placebo-controlled clinical trials. In a recently published randomized, placebo-controlled trial by Littlewood et al.,[32] patients receiving epoetin alfa experienced increased QOL (measured by either LASA or the FACT instrument), whereas patients receiving placebo showed a decline in QOL, with a significant between-group difference based on intent-to-treat analysis. These investigators concluded that, from a QOL standpoint, intervention for anemia benefits cancer patients.[32] Elucidating the relationship between hemoglobin and QOL requires a very large data set with adequate statistical power, such as the one utilized here. Thus, the current incremental analysis complements the Littlewood et al. study, providing insight from a much larger dataset with the power to address the specific relationship between hemoglobin and QOL as hemoglobin changes through the clinically relevant range.

Appropriately, increasing emphasis has been placed on using the patient's perception of QOL to guide therapeutic decision-making in oncology practice. Several clinical implications for the management of chemotherapy related anemia have emerged from these statistical analyses. The traditional approach to managing chemotherapy related anemia has been to wait until hemoglobin levels drop to $\leq$ 10 g/dL before considering epoetin alfa supplementation or transfusions. These data support a change in these practice patterns to maximize QOL. The current analyses suggest that it would be optimal to utilize a more individualized approach that incorporates not only the monitoring of hemoglobin levels but also the presence and severity of anemia related symptoms and patient self-reported QOL. Symptomatic anemia or hemoglobin levels lower than 8–9 g/dL are considered triggers for transfusion based on the belief that the benefit of transfusion (e.g., increasing cardiopulmonary function) outweighs the associated risks (e.g., infection, immunosuppression). Whereas a hemoglobin level $\leq$ 8 g/dL is associated with an increased risk of cardiopulmonary compromise, our current findings indicate that hemoglobin levels $\leq$ 12 g/dL are associated with suboptimal (and potentially correctible) levels of functional ability and overall QOL in patients with cancer.

In conclusion, a direct and robust relationship exists between hemoglobin increases induced by epoetin alfa therapy and corresponding improvements in QOL reported by anemic cancer patients. This relationship was shown across the clinically relevant hemoglobin level range of 8–14 g/dL, with the greatest incremental change in QOL occurring when the hemoglobin level increased from 11 to 12 g/dL. This is not surprising, since extensive data for epoetin alfa treatment of the anemia of renal dysfunction show that functional status is optimized at a hemoglobin level of 12 g/dL. From a QOL standpoint, clinicians, therefore, should consider maintaining their anemic chemotherapy patients at a hemoglobin level of approximately 11–13 g/dL.

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