Hemoglobin Trends and Anemia Treatment Resulting From Concomitant Chemotherapy in Community Oncology Clinics

By Bruce A. Feinberg, DO, Amanda S. Bruno, MPH, PhD, Sally Haislip, RPh, James Gilmore, PharmD, Gagan Jain, MBA, PhD, and Joanna L. Whyte, MS, MSPH

Georgia Cancer Specialists, Atlanta, GA; Xcenda, Palm Harbor, FL; and Amgen, Thousand Oaks, CA

Abstract

Purpose: This study describes changes in hemoglobin (Hb) levels in patients during chemotherapy before anemia treatment and in those who received no treatment, measuring time from chemotherapy initiation to Hb less than 10 g/dL and anemia treatment initiation.

Patients and Methods: This retrospective longitudinal cohort study used a database of outpatient oncology practice electronic medical records from January 1, 2006, to August 6, 2009. Unit of analysis was episode of chemotherapy care, beginning at initiation and including consecutive administrations within the next 60 days. Patients received two or more administrations of conventional chemotherapeutic agents, had a cancer diagnosis with at least 60 days of follow-up, and had no myelodysplastic syndrome. A total of 4,864 episodes (4,021 patients) met selection criteria, 73% with baseline Hb of 11 g/dL or greater and 60% receiving no anemia treatment.

Results: Episodes without anemia treatment increased from 44.6% (2006) to 77.8% (2009). Erythropoiesis-stimulating agent (ESA) use decreased from 45.4% (2006) to 11.5% (2009). Patients receiving transfusions increased from 3.4% to 8.7% (2006 to 2009; all $P < .001$). Total proportion of episodes with Hb less than 10 g/dL at anemia treatment increased from 16.2% to 93.1% during the same period ($P < .001$). Mean Hb values before anemia treatment decreased over time from 10.8 to 8.9 g/dL (2006 to 2009; $P < .001$). Overall, time from chemotherapy initiation to first anemia treatment increased from 24.7 to 36.9 days (2006 to 2009; $P < .01$).

Conclusion: Results suggest increased restrictions were associated with decreased use of ESAs and increased use of transfusions as well as delays in anemia treatment and lower Hb levels before anemia treatment. Additional investigation of the overall impact of delayed treatments on long-term patient outcomes is warranted.

Introduction

Cancer is associated with an elevated risk of anemia that may be caused by the disease itself and by its treatment. Anemia resulting from concomitant chemotherapy is one of the most common adverse effects directly associated with the administration of chemotherapy for the treatment of cancer. Anemia resulting from concomitant therapy affects up to 60% of patients with cancer receiving chemotherapy.¹⁻³ The development of anemia in patients with cancer predicts shorter survival times⁴ and may lead to fatigue, which has a negative impact on patient-reported quality of life.^{5,6} Compounding the problem of anemia that occurs with cancer is a high frequency of anemia caused by myelosuppressive chemotherapy.⁷ Management of anemia resulting from concomitant therapy may include RBC transfusions or erythropoiesis-stimulating agents (ESAs). Although both transfusions and ESAs increase hemoglobin (Hb) levels, the increase in Hb level is transient, and ESAs are indicated for the treatment of anemia resulting from concomitant chemotherapy based on studies demonstrating reduced need of transfusions in patients with metastatic nonmyeloid malignancies.

Several regulatory and reimbursement changes have significantly affected ESA use patterns over the last 3 years. Key among these are the National Coverage Determination (NCD)⁸ and the new product label. On July 30, 2007, the Centers for Medicare and Medicaid Services (CMS) issued the NCD limiting the use of ESAs among patients with anemia resulting from concomitant therapy. CMS ruled to restrict ESA use for the treatment of anemia secondary to myelosuppressive anticancer chemotherapy in certain cancer conditions, such as

solid tumors, multiple myeloma, lymphoma, and lymphocytic leukemia. The NCD limited reimbursement of ESAs to patients with Hb levels lower than 10 g/dL, limited ESA treatment duration to a maximum of 8 weeks after completion of chemotherapy, and provided ESA dosing restrictions.⁸ In August 2008, a new product label was issued that among other changes, restricted initiation of ESAs to Hb less than 10 g/dL, restricted maintenance administrations to the lowest dose required to avoid transfusions, and identified ESAs as not indicated for chemotherapy treatment with curative intent. Recent analyses have found that after these limitations on ESAs, transfusion frequency increased from 2006 to mid 2008, and ESAs have been initiated at lower Hb levels and later in chemotherapy.^{9,10} Additionally, Feinberg et al¹¹ found that in a Medicare population of patients with cancer who were also receiving ESAs in 2007 to early 2008, patients received ESAs at significantly lower Hb levels after the NCD, and the percentage of the population transfused nearly doubled.¹¹ Thus, this study was proposed to assess Hb levels in patients receiving anemia treatment (ESAs or transfusions) in the time period from 2006 through the beginning of 2009 to determine if this trend of initiating anemia treatment at lower Hb levels and at a later time was continuing in both the Medicare and non-Medicare population and into 2009.

The objective of this study was to describe changes in Hb levels in patients during chemotherapy before anemia treatment and in those who received no treatment. Time from chemotherapy initiation to Hb less than 10 g/dL and anemia treatment initiation were also measured.

Patients and Methods

Patient Selection

Patients with a diagnosis of cancer between January 1, 2006, and August 6, 2009, were assessed for eligibility. Eligibility

Table 1. Characteristics of Patients and Episodes of Chemotherapy Accounting for All Episodes of Chemotherapy Care (January 2006 to July 31, 2009)

Factor	Frequency	%
Patient characteristics		
Total No.	4,021	
Sex		
Female	2,588	64.4
Male	1,433	35.6
Age, years		
18-64	2,382	59.2
≥ 65	1,639	40.8
Cancer type		
Breast	1,353	33.6
Colorectal	732	18.2
Lung	1,077	26.8
Other single	542	13.5
Other multiple	317	7.9
Episodes of chemotherapy		
Baseline Hb, g/dL*		
Total No.	4,654	
≥ 11	3,552	76.3
< 11	1,102	23.7
Any anemia treatment		
Total No.	4,864	
Yes	1,956	40.2
No	2,908	59.8

Abbreviation: Hb, hemoglobin.

* A total of 210 episodes of chemotherapy (4,864 – 4,654) did not have Hb recording at baseline.

criteria included receipt of two or more administrations of conventional chemotherapeutic agents (Appendix Table A1, online only) on two different dates, with the first administration occurring during the prespecified study period, allowing for a 60-day follow-up period. Patients with incomplete records (sex, year of birth), age younger than 18 years on the date of first conventional chemotherapeutic agent, or with a diagnosis of myelodysplastic syndrome were excluded.

Study Design

The study employed a retrospective, observational, multicenter design. Data sources included electronic medical records (EMRs) and patient management system applications from a large oncology/hematology private practice located in the southeastern part of the United States, providing approximately 160,000 outpatient visits annually. The database included information from nearly 30 physician offices with 40 practicing oncologists. EMR data included a relational database with

demographics, diagnoses, visit information, medication administrations, and laboratory results. Variables collected and analyzed included Hb level, patient demographics, tumor type, and anemia treatment. Baseline Hb level had to occur within 7 days before chemotherapy initiation. For patients with multiple Hb levels during the 7-day timeframe, the closest value to chemotherapy initiation was used. Hb trend was assessed at baseline and during chemotherapy, within 7 days before ESA treatment or RBC transfusion. Hb values at time of anemia treatment and for 6 weeks before and after initiation were analyzed, and those at time of anemia treatment were stratified per the 10 g/dL threshold for ESA initiation. Time from chemotherapy initiation to Hb less than 10 g/dL and to anemia treatment initiation was also measured. All results were reported for four patient cohorts: first, ESA treatment only; second, transfusion only; third, both ESA and transfusion; and fourth, no anemia treatment within the predetermined episode of chemotherapy care. No transfusion guidelines were in place during the study period; thus, each patient received care determined by the physician to meet the individual patient's needs.

Statistical Analyses

The unit of analysis for this evaluation was the episode of chemotherapy care, which began on the patient's first date of chemotherapy administration. Subsequent chemotherapy administrations occurring within 60 days were considered part of the same episode. If a gap in chemotherapy was greater than 60 days, then the first episode concluded at the end of the chemotherapy administration. Any new chemotherapy initiation after 60 days was considered the beginning of a new episode. Study variables, including patient characteristics, ESA and transfusion use, and outcome measures, were analyzed using descriptive statistics, including mean, standard deviation, frequency, and percentages. Results were calculated by year over the study period based on year of episode initiation. The differences from 2006 to 2009 in baseline characteristics based on age and sex along with cancer type distribution, Hb levels, and transfusion rates were compared using χ^2 and *t*-tests. In addition, *P* values were provided for these descriptive statistics, and all data management and analyses were conducted using SAS software, version 9.1 (SAS Institute, Cary, NC).

Results

Patient Characteristics

A total of 4,864 episodes (for 4,021 patients) met study selection criteria in the 3.5-year study period from January 1, 2006, through July 31, 2009. The majority of patients had only one episode (83%); however, the maximum number of episodes for a single patient during the entire study period was five. Women comprised 64% of patients, and 41% of the total population was older than age 65 years, with a mean age of 61 years. Breast cancer was the most common type of cancer (34%), followed by lung (27%), colorectal (18%), other single cancers (13%), and multiple cancer diagnoses (8%). Of the 4,654 episodes with baseline Hb values (ie, before chemotherapy initiation), 76%

Table 2. Anemia Treatment During Episodes of Chemotherapy Care by Year and Tumor Type

Episode	Overall*							
	2006		2007		2008		2009†	
	No.	%	No.	%	No.	%	No.	%
Total	1,200	24.67	1,552	31.91‡	1,711	35.18‡	401	8.24‡
No anemia treatment	535	44.58	910	58.63‡	1,151	67.27‡	312	77.81‡
Transfusion only	41	3.42	117	7.54‡	164	9.59‡	35	8.73‡
ESA only	545	45.42	446	28.74‡	316	18.47‡	46	11.47‡
Both ESA and transfusion	79	6.58	79	5.09	80	4.68§	8	2.00‡

Episode	Breast							
	2006		2007		2008		2009†	
	No.	%	No.	%	No.	%	No.	%
Total	286	19.13	470	31.44‡	569	38.06‡	170	11.37‡
No anemia treatment	110	38.46	268	57.02‡	405	71.18‡	141	82.94‡
Transfusion only	6	2.10	19	4.04	24	4.22	8	4.71
ESA only	157	54.90	168	35.74‡	132	23.20‡	19	11.18‡
Both ESA and transfusion	13	4.55	15	3.19	8	1.41	2	1.18

Episode	Lung							
	2006		2007		2008		2009†	
	No.	%	No.	%	No.	%	No.	%
Total	373	27.69	444	32.96§	436	32.37§	94	6.98‡
No anemia treatment	143	38.34	228	51.35‡	248	56.88‡	64	68.09‡
Transfusion only	14	3.75	54	12.16‡	75	17.20‡	14	14.89‡
ESA only	175	46.92	122	27.48‡	70	16.06‡	13	13.83‡
Both ESA and transfusion	41	10.99	40	9.01	43	9.86	3	3.19§

NOTE. Year 2006 used as comparator for descriptive, between-year comparisons. Abbreviation: ESA, erythropoietin-stimulating agent.

* Year-to-year comparisons for all tumor types were statistically significant ($P < .05$), except transfusion-only episodes from 2008 to 2009 and ESA-plus-transfusion episodes between 2007 and 2008.

† January 1, 2009, to July 31, 2009.

‡ $P < .001$.

§ $P < .05$.

had Hb of 11 g/dL or greater. Overall, 60% of episodes involved no ESA treatment or RBC transfusions, as shown in Table 1.

Hematologic Outcomes

Hematologic outcomes were reported for episodes that involved no anemia treatment, only ESAs, only transfusion, or treatment with both ESAs and transfusion. Episodes without anemia treatment increased from 44.6% (2006) to 77.8% (2009), ESA use decreased from 45.4% (2006) to 11.5% (2009), and rates of transfusion increased from 3.4% (2006) to

Table 2. Anemia Treatment During Episodes of Chemotherapy Care by Year and Tumor Type (continued)

	Colorectal Cancer							
	2006		2007		2008		2009†	
	No.	%	No.	%	No.	%	No.	%
	257	27.81	288	31.17	323	34.96‡	56	6.06‡
	157	61.09	198	68.75	264	81.73‡	47	83.93‡
	5	1.95	7	2.43	12	3.72	2	3.57
	90	35.02	76	26.39§	41	12.69‡	7	12.50§
	5	1.95	7	2.43	6	1.86	0	0.00

	Other Single Tumor							
	2006		2007		2008		2009†	
	No.	%	No.	%	No.	%	No.	%
	142	21.29	211	31.63‡	255	38.23‡	59	8.85‡
	62	43.66	130	61.61‡	150	58.82§	41	69.49‡
	5	3.52	24	11.37§	36	14.12‡	8	13.56§
	63	44.37	48	22.75‡	50	19.61‡	7	11.86‡
	12	8.45	9	4.27	19	7.45	3	5.08

	Other Multiple Tumors							
	2006		2007		2008		2009†	
	No.	%	No.	%	No.	%	No.	%
	142	32.95	139	32.25	128	29.70	22	5.10‡
	63	44.37	86	61.87§	84	65.63‡	19	86.36‡
	11	7.75	13	9.35	17	13.28	3	13.64
	60	42.25	32	23.02‡	23	17.97‡	0	0.00‡
	8	5.63	8	5.76	4	3.13	0	0.00

8.7% (2009; all $P < .001$), as shown in Table 2. Additionally, all year-to-year trends were statistically significant ($P < .05$), with the exception of transfusion-only episodes between 2008 and 2009 and episodes with ESA and transfusion between 2007 and 2008. Only 246 episodes overall involved both ESAs and transfusion; however, a decreasing trend was observed over the 3.5-year study period from 6.6% in 2006 to 2% in 2009 ($P < .001$). Because breast, lung, and colorectal cancers account for the majority of cancer cases in the United States, we evaluated trends by tumor type in a post hoc analysis. The use of ESAs as the only form of anemia treatment decreased significantly

across all tumor types between 2006 and 2009, whereas the proportion of episodes with no anemia treatment significantly increased across all tumor types in the same time period. Also, the use of ESAs and transfusion decreased among lung cancer episodes, whereas use of transfusion as the only form of anemia treatment increased in episodes of lung cancer and other single tumor types.

Mean Hb values at initiation of anemia treatment decreased over time from 10.8 g/dL (2006) to 8.9 g/dL (2009; $P < .001$), and Hb levels were generally lower up to 6 weeks before and 6 weeks after anemia treatment for episodes involving treatment with ESAs only (Figure 1). Similar trends were observed in episodes for elderly (age ≥ 65 years) and nonelderly patients across years, with lower Hb values in later years relative to 2006 (10.6 g/dL in 2006 *v* 8.8 g/dL in 2009 for episodes occurring in elderly patients). Patients with baseline Hb of 11 g/dL or greater retained higher mean Hb values (11.6 g/dL in 2006 and 12.1 g/dL in 2008) during the 6 weeks after treatment compared with mean Hb values (10.1 g/dL in 2006 and 9.2 g/dL in 2008) for patients with Hb less than 11 g/dL at baseline during the same time. However, both groups experienced a decreased trend in Hb value at anemia treatment initiation over the study period.

The total proportion of episodes with Hb less than 10 g/dL at anemia treatment initiation increased from 16.2% to 93.1% during the study period ($P < .001$). Of those episodes with Hb less than 10 g/dL at anemia treatment, treatment with transfusion comprised a larger proportion in 2009 (49%) than in 2006 (27%; $P < .001$).

Overall, the average number of days between chemotherapy initiation and first anemia treatment increased for episodes treated with ESAs during each year after 2006 (29.4 days in 2007, 39.7 days in 2008, and 39.0 days in 2009; all mean values [$P < .001$] relative to 21.2 days in 2006). The increased time interval was observed for both age strata (elderly and nonelderly) during each year after 2006. The average number of days between chemotherapy initiation and anemia treatment in 2008 and 2009 was also significantly greater (relative to 2006) in episodes with both ESAs and transfusion. Additionally, the time interval was longer (mean, 21 days) in episodes with baseline Hb of 11 g/dL or greater compared with those episodes with lower baseline Hb values less than 11 g/dL (mean, 12.8 days).

Discussion

Study Findings

This study sought to assess the impact of regulatory and reimbursement changes, including NCD guidance and US Food and Drug Administration product labeling, over the last 3 years on the use of therapeutic interventions in the management of patients with anemia resulting from concomitant therapy in community oncology clinics. Results generated for these patients indicated that prescribing restrictions, particularly the recommendation for the initiation of ESAs in patients with Hb less than 10 g/dL only and cessation of ESA for subsequent Hb

greater than 10 g/dL, have resulted in significant changes in the severity and duration of anemia in patients receiving concomitant myelosuppressive chemotherapy. Our results reveal both a decreased use of ESAs as well as increased rates of transfusion. In patients who received anemia treatment, initiation occurred later in the episode and at a lower starting Hb. Finally, throughout the entire post-NCD evaluation period, we observed an average 1 to 1.9 g/dL lower Hb. The clinical significance of deferred anemia treatment, increased frequency and number of transfusions, and lower mean Hb levels has not yet been elucidated. Additional investigation in quality of life and adverse reactions to transfusions is warranted.

Further research is required to determine if these trends are persistent and generalizable to a majority of oncology practice sites. Additional evaluation is also required to assess compliance with ESA use in selected cancer populations, such as incurable patients with prespecified maximum dosing recommendation, capped 8-week treatment duration after anticancer therapy, and restriction of maintenance administration to the lowest dose required to avoid transfusion.

Supporting Investigations

An initial evaluation of the impact of NCD guidelines on treatment of anemia resulting from concomitant therapy in Medicare patients has been previously published.¹¹ The study found that in the 6-month period after the NCD, patients with anemia resulting from concomitant chemotherapy had lower Hb levels at time of treatment and higher transfusion rates than patients treated in the 3 months before the policy change. Additionally, since the initiation of this study, other investigators have evaluated the amended ESA use patterns after the NCD for ESA therapies and have provided additional data on this topic. However, even in light of the results from these investigations, data assessing prescribing patterns pre- and post-NCD for anemia resulting from concomitant therapy are still scarce.

Several studies were presented at the 2009 American Society of Hematology Annual Meeting in New Orleans, Louisiana. Burton et al¹² published an investigation from a single oncology clinic involving 359 patients. The post-NCD group had a significantly lower proportion of patients treated with ESAs; however, the number of transfused patients remained unchanged. The difference in transfusion rates between this study and our investigation may be the result of the small sample size in the Burton et al study. Furthermore, there was a trend toward shorter ESA treatment duration and lower transfusion-independent Hb levels in the post-NCD group at each evaluable time point (baseline, week 8, and week 12). These two conclusions are in accordance with our results. The utilization of clinic visits remained constant in the two periods, whereas the number of hospital admissions was higher in the post-NCD period. This evaluation of health care resource utilization was not addressed in our study.

In a second study, Henry et al¹³ compared the transfusion rates in patients with breast, colon, or lung cancer who developed anemia resulting from concomitant therapy before and after the NCD, regardless of treatment with ESAs. This study

Figure 1. Mean hemoglobin (Hb) from 6 weeks before to 6 weeks after treatment initiation in patients receiving (A) only erythropoiesis-stimulating agents and (B) only transfusions.

included 1,794 Medicare patients from 49 community oncology clinics. Hb levels were lower at time of treatment in the post-NCD period. There was also a decrease in the number of ESA-treated patients and ESA treatment duration. The transfusion rates were significantly higher in the post-NCD arm, further aligning these findings with our results.

In a still larger study of more than 22,000 episodes of chemotherapy care with ESA treatment, Hill et al¹⁰ found that from 2005 through 2008, time from chemotherapy start to ESA initiation increased (44 to 66 days from 2006 to 2008), and ESA initiation was at lower baseline Hb levels over time (0.3 g/dL lower in 2007 [$P < .001$] and 1.0 g/dL lower in 2008 [$P < .001$]). This analysis, however, did not include transfusions.

Both Apgar et al¹⁴ and Baribeault¹⁵ investigated clinical practices based on ESA dosing per the NCD. Apgar et al analyzed data from 836 patients from 54 sites. ESA treatment duration was 10 days shorter in the post-NCD group than in the pre-NCD group, and this difference was statistically significant. The percentage of patients treated with RBC transfusions was also statistically different in the post-NCD group (pre-NCD, 15.6% *v* post-NCD, 26.7%; $P < .001$), as was the percentage of patients with any blood utilization, which is uniform with our results. Similarly, Baribeault analyzed transfusion rate, ESA dose, and length of therapy in patient medical records from 6 months before to 6 months after the CMS NCD (July 2007) and found that RBC transfusions increased more than 36%, ESA therapy duration decreased by nearly 25%, and cumulative ESA dose decreased by 10%, although average dose increased by 20% after the NCD.

Vekeman et al¹⁶ modeled the potential decrease in blood supply based on limiting ESA use to patients with concomitant

chemotherapy. On the basis of the Vekeman et al models, decreasing ESA use could potentially increase blood supply demand by 10% to more than 100%. Additionally, Shord et al¹⁷ pointed out the potential risks of transfusions, and although others have published on this,¹⁸⁻²⁰ our data were not linked to a claims database or the National Death Index and thus did not contain data on adverse events associated with transfusions or survival.

Limitations

Our study was carried out using EMR data from a large community oncology practice, which generally depict information on the diagnoses and treatments offered only in the oncology clinic. Therefore, our results may not be uniformly generalized to smaller oncology community practices and/or large academic institutions.

Data on therapeutic interventions in patients who developed significant symptoms of anemia requiring immediate transfusion outside these facilities were not included in our analysis. Even though this void in information may lead to underrepresentation of our results, these shortcomings would be uniformly present in both pre- and post-NCD periods and would be unlikely to influence our conclusions. Comorbidities that may have affected treatment selection in the oncology clinic were not available for analysis.

Despite the outlined limitations, our outcomes are consistent with our initial hypothesis, and their validity to a broader population has been confirmed by previously cited investigations reaffirming the significant impact of the NCD and US Food and Drug Administration prescribing revisions. Observed practice adjustments such as the diminished use of ESAs and

augmented transfusion rates are the direct representations of the ongoing change.

In conclusion, our study suggests that adoption of the NCD for ESA agents has resulted in decreased use of ESAs and increased use of transfusions as well as delays in anemia treatment and lower mean Hb levels at time of anemia treatment. Additional investigation is warranted to evaluate the overall impact of increases in frequency and number of RBC transfusions as well as lower mean Hb on long-term patient outcomes, including both clinical and quality of life.

Accepted for publication on June 22, 2011.

Acknowledgment

Supported by Amgen, Georgia Cancer Specialists, and Xcenda.

Authors' Disclosures of Potential Conflicts of Interest

Although all authors completed the disclosure declaration, the following author(s) indicated a financial or other interest that is relevant to the subject matter under consideration in this article. Certain relationships marked with a "U" are those for which no compensation was received; those relationships marked with a "C" were compensated. For a detailed description of the disclosure categories, or for more information about ASCO's conflict of interest policy, please refer to the Author

Disclosure Declaration and the Disclosures of Potential Conflicts of Interest section in Information for Contributors.

Employment or Leadership Position: Joanna L. Whyte, Amgen (C); Amanda S. Bruno, Xcenda (C); Gagan Jain, Xcenda (C) **Consultant or Advisory Role:** None **Stock Ownership:** Joanna L. Whyte, Amgen **Honoraria:** None **Research Funding:** None **Expert Testimony:** None **Other Remuneration:** None

Author Contributions

Conception and design: Amanda S. Bruno, Sally Haislip, James Gilmore, Joanna L. Whyte

Administrative support: Amanda S. Bruno, Sally Haislip

Provision of study materials or patients: Bruce Feinberg

Collection and assembly of data: Amanda S. Bruno, Sally Haislip, James Gilmore, Gagan Jain

Data analysis and interpretation: All authors

Manuscript writing: All authors

Final approval of manuscript: All authors

Corresponding author: Joanna L. Whyte, MS, MSPH, Senior Manager, Center for Observational Research, Amgen, One Amgen Center Dr, MS 24-1-C, Thousand Oaks, CA 91320-1799; e-mail: jwhyte@amgen.com.

DOI: 10.1200/JOP.2011.000268

References

- Nissenson AR, Wade S, Goodnough T, et al: Economic burden of anemia in an insured population. *J Manag Care Pharm* 11:565-574, 2005
- Norum J, Moen MA: Practice and costs of red blood cell (RBC) transfusion in an oncological unit. *Anticancer Res* 28:459-464, 2008
- Schwartz RN: Anemia in patients with cancer: Incidence, causes, impact, management, and use of treatment guidelines and protocols. *Am J Health Syst Pharm* 64:S5-S13, 2007; quiz S28-S30 (suppl 2)
- Caro JJ, Salas M, Ward A, et al: Anemia as an independent prognostic factor for survival in patients with cancer: A systemic, quantitative review. *Cancer* 91:2214-2221, 2001
- Cella D: Factors influencing quality of life in cancer patients: Anemia and fatigue. *Semin Oncol* 25:43-46, 1998 (suppl 7)
- Curt GA: Impact of fatigue on quality of life in oncology patients. *Semin Hematol* 37:14-17, 2000 (suppl 6)
- Groomman JL, Itri L: Chemotherapy induced anemia in adults: Incidence and treatment. *J Natl Cancer Inst* 91:1616-1634, 1999
- Centers for Medicare and Medicaid Services: National Coverage Determination 110.21, 2007. <http://www.cms.hhs.gov/mcd/viewncd.asp?ncd>
- Hess G, Nordyke R, Piroli M, et al: Effect of changes in labeling and reimbursement on use of ESAs and transfusions. *J Clin Oncol* 26:731s, 2008 (suppl; abstr 20589)
- Hill J, Cong Z, Hess G, et al: Trajectory of hemoglobin (Hb) in patients receiving erythropoiesis-stimulating agents (ESAs) for anemia due to concomitantly administered myelosuppressive chemotherapy (CIA). *Blood* 114, 2009 (abstr 1399)
- Feinberg B, Gilmore J, Gondesens T, et al: Impact on NCD guidelines on Medicare patients with chemotherapy-induced anemia receiving erythropoiesis-stimulating agents: Results from a community oncology practice. *Community Oncol* 6:257-261, 2009
- Burton T, Boulanger L, Larholt K, et al: Blood and resource utilization in cancer patients with chemotherapy-induced anemia (CIA) in the pre- and post-

National Coverage Determination (NCD) timeframes: Results from an electronic medical record study. Presented at the 51st Annual Meeting of the American Hematology Society, New Orleans, LA, December 5-9, 2009

13. Henry DH, Langer CJ, McKenzie RS, et al: Pre- and post-National Coverage Determination (NCD) hematologic outcomes and blood utilization in cancer patients with chemotherapy-induced anemia (CIA): Results from a multicenter chart review. Presented at the 51st Annual Meeting of the American Hematology Society, New Orleans, LA, December 5-9, 2009

14. Apgar E, Burton TM, Larholt K, et al: Hematologic and hospitalization outcomes in patients with chemotherapy-induced anemia (CIA) treated with erythropoiesis-stimulating agents (ESAs) in the pre- and post-National Coverage Determination (NCD) time periods. Presented at the 51st Annual Meeting of the American Hematology Society, New Orleans, LA, December 5-9, 2009

15. Baribeault DM: Evaluation of a change in prescribing patterns of darbepoetin alfa on red blood cell transfusion requirements in patients with chemotherapy-induced anemia. *Pharmacotherapy* 28:161e, 2008 (abstr 156)

16. Vekeman F, Bookhart BK, White J, et al: Impact of limiting erythropoiesis-stimulating agent use for chemotherapy-induced anemia on the United States blood supply margin. *Transfusion* 49:895-902, 2009

17. Shord SS, Auerbach M: Treating chemotherapy-induced anemia following the revised labeling for ESAs. *Commun Oncol* 6:279-282, 2009

18. Panagopoulos ND, Karakantza M, Koletsis E, et al: Influence of blood transfusions and preoperative anemia on long-term survival in patients operated for non-small cell lung cancer. *Lung Cancer* 62:273-280, 2008

19. Upile T, Jerjes W, Sandison A, et al: The direct effects of stored blood products may worsen prognosis of cancer patients; shall we transfuse or not? an explanation of the adverse oncological consequences of blood product transfusion with a testable hypothesis driven experimental research protocol. *Med Hypotheses* 71:489-492, 2008

20. Koch CG, Li L, Sessler DI, et al: Duration of red-cell storage and complications after cardiac surgery. *N Engl J Med* 358:1229-1239, 2008