Patient and physician characteristics associated with erythropoiesis-stimulating agent use in patients with myelodysplastic syndromes

Amy J. Davidoff,[1,2] Sheila Weiss Smith,[1,2,3] Maria R. Baer,[2] Xuehua Ke,[1] Jason M. Bierenbaum,[2] Franklin Hendrick,[1] Diane L. McNally,[4] and Steven D. Gore[5]

[1]Department of Pharmaceutical Health Services Research, University of Maryland School of Pharmacy, Baltimore, MD; [2]Greenebaum Cancer Center, University of Maryland School of Medicine, Baltimore, MD; [3]Center for Drug Safety, University of Maryland School of Pharmacy, Baltimore, MD; [4]Pharmaceutical Research Computing, University of Maryland School of Pharmacy, Baltimore, MD; and [5]Sidney Kimmel Comprehensive Cancer Center, Johns Hopkins University, Baltimore, MD, USA

ABSTRACT

Patient and physician characteristics associated with use of erythropoiesis-stimulating agents in myelodysplastic syndrome patients have not yet been described. Myelodysplastic syndrome patients diagnosed from 2001 to 2005 were identified from the Surveillance Epidemiology and End Results-Medicare database. Multivariate regressions examined the association between patient and physician characteristics and the probability of receiving any erythropoiesis-stimulating agents, and of receiving therapeutic-length (≥8 week) treatment episodes.

Among the 6,588 myelodysplastic syndrome patients studied, 65% received erythropoiesis-stimulating agents. Use of erythropoiesis-stimulating agents was lower for blacks compared to whites (OR 0.78; 95% CI:0.61-0.99), single persons compared to married (OR 0.77; 95% CI:0.62-0.97), Medicaid recipients (OR 0.66; 95% CI:0.55-0.79), and those living in census tracts with lower educational attainment. Patients who did not consult a hematology-oncology specialist were less likely to receive erythropoiesis-stimulating agents. Specialist access, financial resources and mobility are key determinants of receipt of erythropoiesis-stimulating agents among myelodysplastic syndrome patients.

Key words: erythropoiesis-stimulating agent, myelodysplastic syndromes, patient, physician, characteristics.

Citation: Davidoff AJ, Weiss Smith S, Baer MR, Ke X, Bierenbaum JM, Hendrick F, McNally DL, and Gore SD. Patient and physician characteristics associated with erythropoiesis-stimulating agent use in patients with myelodysplastic syndromes. Haematologica 2012;97(1):128-132. doi:10.3324/haematol.2011.049130

Introduction

Myelodysplastic syndromes (MDS) are a group of hematopoietic stem cell neoplasms characterized by ineffective hematopoiesis. Approximately 80% of MDS patients experience symptomatic anemia, which dramatically diminishes quality of life. Supportive care is an important component of clinical management of MDS patients. Erythropoiesis-stimulating agents (ESAs) are recommended to reduce the need for red blood cell transfusions in patients with low-risk MDS.[1] Recombinant erythropoietin-alfa is administered by subcutaneous injection once to three times weekly, most often in a doctor's surgery. The introduction in 2002 of longer-acting darbepoetin-alfa, administered every one to three weeks, offered an alternative treatment approach with less frequent injections and surgery visits, but at a higher weekly drug cost.[2,3] Approximately 20% of unselected, and 40% of low-risk patients have a clinically meaningful hemoglobin response to ESAs; median response duration is two years.[4-6] Predictors of ESA response include a low endogeneous serum erythropoietin (EPO) level, and a low transfusion requirement.[7]

While recent evidence suggests that ESAs are used by approximately 60% of MDS patients, there is little information concerning determinants of treatment.[8] Given the cost of treatment and administration, and the burden associated with repeated visits to the surgery over extended periods, there may be significant barriers to receiving and continuing ESA therapy. In this study, we examine determinants of the receipt of ESA and the receipt of ESA for a period of sufficient length to enable clinicians to assess therapeutic effect (therapeutic-length treatment episode, TTE). TTE assessment is important, as the need for persistent use over time may create an additional challenge to patients.

Design and Methods

Data and cohort selection

MDS patients were identified from the National Cancer Institute's

The online version of this article has a Supplementary Appendix.

Acknowledgments: the authors wish to thank the Pharmaceutical Research Computing Center (PRC) for data management and analytic support. This study used the linked SEER-Medicare database. The interpretation and reporting of these data are the sole responsibility of the authors. The authors acknowledge the efforts of the Applied Research Program, NCI; the Office of Research, Development and Information, CMS; Information Management Services (IMS), Inc.; and the Surveillance, Epidemiology, and End Results (SEER) Program tumor registries in the creation of the SEER-Medicare database.

Funding: this work was supported by the National Institutes of Health (NIH 1RC1CA145831-01; ARRA Challenge Grant with AJD and 2K24CA111717-06A1 with STG).

Manuscript received on June 7, 2011. Revised version arrived on September 22, 2011. Manuscript accepted on September 23, 2011.

Correspondence: Amy J. Davidoff, Ph.D., Associate Professor, Department of Pharmaceutical Health Services Research, University of Maryland School of Pharmacy, 220 Arch Street, 12th floor, Room 214, Baltimore, Maryland 21201, USA. Phone: international +410.7065397. Fax: international +410.7065394. E-mail: adavidof@rx.umaryland.edu

Surveillance Epidemiology and End Results (SEER) database, which aggregates data from 16 regional cancer registries, including cancer site, histology, diagnosis month, date and cause of death, and demographic characteristics. For Medicare beneficiaries, SEER data are linked to Medicare enrollment and claims files. Medicare Parts A and B claims data provide detailed medical care information for all types of covered services. Part B claims data capture drugs administered by infusion or injection in a doctor's surgery or other outpatient setting, including ESAs. Census tract-level measures of income and education supplement patient information.

The study sample included MDS cases newly diagnosed between 2001 and 2005, with linked Medicare claims from 2000 through 2007. SEER reports MDS diagnoses using the World Health Organization (WHO) classification system. Because ESAs are indicated for treatment of dialysis-associated anemia, we excluded patients with a history of chronic renal failure and those receiving renal dialysis. Patients were followed from their initial MDS diagnosis until death or the end of the study period. The 12-month period prior to MDS diagnosis was used to characterize past medical history and ESA use. Patients were excluded if they had incomplete information concerning dates of diagnosis or death, a period without Medicare Parts A and B coverage, or if enrolled in Medicare Advantage during the observation period.

ESA use

Patients were classified as ESA users if they had at least one claim for an ESA during follow up. Among ESA users, we also determined if the patient received a therapeutic-length treatment episode (TTE), defined as eight weeks or over. This is the minimum duration suggested by the NCCN treatment guideline[9] and it has been used as an assessment cut-off point in several trials.[10,11] Episodes were counted separately for epoetin alfa and darbepoetin alfa. The first treatment episode began at the first week there was a claim for an ESA and continued weekly until there was a gap in treatment of three weeks for epoetin alfa or six weeks for darbepoetin alfa. Additional treatment episodes began at the week of the first prescription claim following a gap in treatment. One week was added to the episode length of each darbepoetin episode to account for the extended half-life of darbepoetin. Each treatment episode was then classified by length as TTE or not TTE.

Measurement of key study variables

Sociodemographic characteristics included patient age, race, sex, marital status, pre-diagnosis enrollment in Medicaid or a Medicare Savings Program (MSP; where state Medicaid programs pay for Medicare Part B premiums), census track-level median household income and proportion of adults with less than a high school education (quartile ranges), whether less than 5% of households reported difficulty speaking English, size of metropolitan area, region and year of diagnosis.

Patient health status indicators included MDS diagnostic category, history of a different primary cancer within five years prior to MDS diagnosis, transfusions prior to MDS diagnosis, acute or chronic medical conditions, indicators of poor performance status, and an indicator for end-stage renal disease (ESRD) or disability as reason for initial Medicare eligibility. SEER data were used to classify patients into lower-risk [refractory anemia (RA), refractory anemia with ringed sideroblasts (RARS), refractory cytopenia with multilineage dysplasia (RCMD), and MDS with 5q deletion], refractory anemia with excess blasts (RAEB), therapy-related MDS, and MDS not otherwise specified (NOS). We used selected claims-based indicators associated with poor baseline performance status, including prior hospitalization period, skilled nursing facility stay, nursing home admission, home oxygen, walking aids, and wheelchair use.[12]

The physician responsible for initial treatment management was identified based on an algorithm which took into account the most relevant and frequent provider on insurance claims for "evaluation and management" visits in the two months prior through the three months following the month of MDS diagnosis. Speciality codes on the claims (when available) identified the type of specialist or subspecialist seen. We applied a hierarchy to identify a managing physician, giving preference to hematologists or oncologists, primary care physicians (family practice and general internal medicine), and, finally, physicians in other specialities or subspecialities. Type of practice was identified by linking to data provided by the American Medical Association.

Statistical analysis

ESA use was summarized overall and by patients' characteristics. Multivariate logistic regression analyses examined the association between patient and physician characteristics and ESA use.[13] Analyses were completed using SAS 9.2 (SAS, Cary, NC, USA) or Stata 10 (Statacorp. College Station, TX, USA). The project was approved by the University of Maryland Baltimore Institutional Review Board.

Results and Discussion

The cohort consisted of 6,588 patients with MDS; 34.6% lower-risk, 13.7% RAEB, 1.4% therapy-related and 50.4% NOS. Almost two-thirds of MDS patients (64.6%) received ESAs at some point during the observation period. ESA use rates were higher for the lower-risk (68.5%) and RAEB (67.9%) subgroups, compared to 61.2% of patients in the NOS group (Table 1). Among those who received an ESA, 73% had at least one TTE. TTEs were more frequent in lower-risk MDS than in RAEB patients (77.9% *vs.* 66.8%, $P<0.001$), possibly due to early disease progression. *Online Supplementary Table S1* describes characteristics of the study cohort.

In the multivariate models, patient mobility, access to care, and characteristics of the treating physician were the most significant determinants of ESA use (Table 2). A recent history of blood transfusion (OR 1.84; 95% CI: 1.58-2.14) was also associated with ESA use. However, the presence of most co-morbid conditions did not affect the probability of ESA use; only patients with dementia were less likely to receive ESAs (OR 0.63; 95% CI: 0.51-0.77). Several indicators of poor PS, such as history of wheelchair use and nursing home stays, were also associated with a lower likelihood of ESA use.

Rates of ESA use were lower for blacks compared to

Table 1. ESA use among MDS patients, overall and by MDS type.

Variables	Overall %	Lower risk %	Higher risk %	Risk not specified %	*P* value
Full sample (N)	6,588	2,276	904	3,408	
Any ESA use (pre or post MDS dxdt)	64.6	68.5	67.9	61.2	<0.0001
ESA users (N)	4,112	1,514	600	1,998	
Receipt of therapeutic length ESA episode	72.7	77.9	66.8	70.5	<0.0001

ESA: erythropoiesis stimulating agents; MDS: myelodysplastic syndromes; Dxdt: diagnosis date. Source: Surveillance, Epidemiology and End Results (SEER)-Medicare, 2001-2005; linked American Medical Association data on physicians' characteristics.

Table 2. Determinants of ESA use and therapeutic length ESA episode for MDS patients.

Characteristics	Receipt of Any ESA Pre or Post MDS Dxdt among All MDS Sample (N=6314) OR	95% Confidence Interval		*P* value	Receipt of Therapeutic Length ESA Episode among All ESA Users from MDS Dxdt (N=4007) OR	95% Confidence Interval		*P* value
Modified FAB group at diagnosis* &								
9980 - RA	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
9982 - RARS	1.35	1.08	1.68	0.01	1.46	1.10	1.94	0.01
9983 - RAEB	0.99	0.81	1.21	0.92	0.63	0.49	0.81	0.00
9985 - RCMD	1.08	0.80	1.47	0.61	1.03	0.69	1.52	0.90
9986 - 5q deletion	0.86	0.56	1.32	0.48	1.18	0.64	2.18	0.59
9987 - Therapy-related MDS, NOS	0.74	0.45	1.20	0.22	0.43	0.23	0.81	0.01
9989 - MDS, NOS	0.86	0.73	1.01	0.06	0.84	0.69	1.03	0.10
Blood transfusion (12 months before MDS dxdt)	1.84	1.58	2.14	<0.0001	1.17	0.97	1.40	0.10
Other primary cancer (within 5 years prior to MDS dxdt)	1.14	0.94	1.37	0.18	0.93	0.74	1.17	0.53
History of comorbidities								
Acute myocardial infarction (AMI)	0.86	0.62	1.20	0.37	1.12	0.71	1.77	0.63
Congestive heart failure (CHF) or ischemic heart disease (IHD)	1.08	0.96	1.23	0.21	0.95	0.81	1.11	0.50
Conduction disorder	0.94	0.82	1.07	0.34	0.94	0.79	1.12	0.48
Deep-vein thrombosis (DVT) and pulmonary embolism (PE)	0.93	0.68	1.28	0.67	0.90	0.59	1.37	0.61
Hepatitis or other liver diseases	0.82	0.63	1.07	0.14	0.90	0.63	1.29	0.57
Renal disease	0.97	0.78	1.20	0.77	1.05	0.78	1.40	0.76
Stroke	0.89	0.72	1.08	0.24	0.94	0.72	1.23	0.66
Dementia	0.63	0.51	0.77	<0.0001	0.63	0.46	0.85	0.00
Bipolar or depression or schizophrenia	0.83	0.68	1.02	0.07	0.77	0.59	1.02	0.07
Healthcare use - prior 12 months								
Hospital use	0.93	0.81	1.07	0.30	0.79	0.66	0.94	0.01
Oxygen and related supplies	0.80	0.64	1.00	0.05	0.94	0.68	1.28	0.68
SNF use	1.02	0.74	1.40	0.93	0.76	0.46	1.23	0.26
Walking aids	1.08	0.86	1.35	0.52	0.88	0.66	1.19	0.41
Wheelchair claims	0.68	0.54	0.86	<0.0001	0.71	0.51	1.00	0.05
Nursing home stay	0.37	0.28	0.51	<0.0001	1.14	0.69	1.88	0.60
Age at diagnosis* &								
<65	0.72	0.51	1.02	0.06	0.56	0.35	0.91	0.02
65-69	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
70-74	1.15	0.91	1.45	0.25	0.94	0.69	1.27	0.68
75-79	1.11	0.89	1.39	0.34	1.06	0.79	1.43	0.69
80-84	1.23	0.98	1.53	0.08	0.99	0.74	1.32	0.93
85+	0.94	0.75	1.19	0.61	0.79	0.58	1.08	0.14
Race/ethnicity								
White, non-Hispanic	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
Black, non-Hispanic	0.78	0.61	0.99	0.04	1.03	0.74	1.45	0.85
Hispanic	1.31	0.80	2.16	0.28	0.62	0.34	1.12	0.11
Other	1.09	0.81	1.48	0.56	0.82	0.56	1.19	0.29
Sex								
Male	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
Female	1.04	0.92	1.17	0.52	1.02	0.87	1.20	0.79
Marital Status								
Single, never married	0.77	0.62	0.97	0.03	1.24	0.89	1.73	0.20
Married	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
Divorced, separated, widowed, or unknown	0.99	0.87	1.13	0.91	1.01	0.86	1.19	0.90
Disabled or ESRD for original Medicare entitlement & > =65 years at MDS dxdt	0.87	0.71	1.07	0.19	0.87	0.66	1.14	0.30
Prior year Medicaid/MSPs								
No Medicaid	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
Medicaid	0.66	0.55	0.79	<0.0001	0.70	0.54	0.89	0.00
Median household income quartiles								
Lowest (<=$35268.5)	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
Second ($35268.6-$46257.0)	0.95	0.80	1.13	0.54	1.03	0.82	1.30	0.81
Third ($46257.1-$61038.0)	1.06	0.87	1.29	0.58	1.10	0.85	1.42	0.49
Highest (>$61038.0)	1.02	0.81	1.27	0.90	1.08	0.81	1.44	0.62

to be continued on next page

continued from previous page

Quartiles for percent of persons 25+ with<12 yrs education (race specific)*								
Lowest (<=7.92)	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
Second (7.93-13.86)	0.83	0.70	0.98	0.03	0.93	0.75	1.16	0.52
Third (13.87-23.01)	0.80	0.65	0.97	0.02	0.97	0.76	1.25	0.82
Highest (>23.01)	0.73	0.58	0.92	0.01	0.77	0.58	1.04	0.08
> 5% households with difficulty speaking English								
No	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
Yes	1.08	0.91	1.28	0.36	1.11	0.89	1.38	0.34
Residence								
Large, small MSA	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
Urban, non MSA	0.96	0.75	1.23	0.75	1.12	0.80	1.55	0.52
Less urban, rural	0.87	0.71	1.07	0.20	1.26	0.94	1.67	0.12
Region* &								
Midwest	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
Northeast	0.92	0.76	1.10	0.35	0.83	0.65	1.05	0.12
South	1.29	1.07	1.56	0.01	1.27	0.99	1.62	0.06
West	1.25	1.05	1.48	0.01	1.25	1.00	1.55	0.05
Diagnosis year								
2001	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
2002	1.03	0.85	1.23	0.79	1.34	1.05	1.71	0.02
2003	1.05	0.88	1.26	0.57	1.19	0.94	1.50	0.15
2004	1.12	0.94	1.34	0.21	1.32	1.05	1.66	0.02
2005	1.15	0.96	1.38	0.13	1.28	1.01	1.62	0.04
Physicians' characteristics								
Speciality*								
Heme-onc	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
Primary care	0.47	0.40	0.56	<0.0001	0.87	0.67	1.13	0.30
Other	0.27	0.20	0.38	<0.0001	0.68	0.40	1.13	0.14
Years from final medical school graduation year to diagnosis year of MDS								
< 10	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
10-19	1.28	1.00	1.63	0.05	1.16	0.84	1.62	0.36
20-29	1.13	0.89	1.43	0.33	1.06	0.77	1.47	0.71
30+	1.07	0.83	1.37	0.62	1.03	0.74	1.43	0.88
Type of practice*								
Office based	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
Medical teaching or research	0.71	0.55	0.91	0.01	0.91	0.64	1.30	0.60
Residency/fellowship or hospital based	0.89	0.70	1.12	0.32	1.04	0.76	1.41	0.83
Other or inactive	1.43	0.97	2.08	0.07	0.98	0.62	1.54	0.92
Model Fit Statistics								
R-Square	0.10				0.04			
Max-rescaled R-Square	0.14				0.06			
	χ^2	DF	*P* value		χ^2	DF	*P* value	
Likelihood Ratio Test	672.06	60.00	<0.0001		183.45	60.00	<0.0001	

*ESA: erythropoiesis stimulating agents; MDS: myelodysplastic syndromes; Dxdt: diagnosis date; FAB: French-American-British; RA: refractory anemia; RARS: refractory anemia with ringed sideroblasts; RAEB: refractory anemia with excess blasts; RCMD: refractory cytopenia with multilineage dysplasia; NOS: not otherwise specified; SNF: skilled nursing facility; MSPs: Medicare Savings Programs; MSA: metropolitan statistical area. Note: *, & means a categorical variable with three or over categories is jointly significant at* P *value<0.05 in the model of Receipt of Any ESA Pre or Post MDS Dxdt among All MDS Sample and the model of Receipt of Therapeutic Length ESA Episode among All ESA Users from MDS Dxdt, respectively.*

whites (OR 0.78; 95% CI:0.61-0.99), never-married compared to married persons (OR 0.77; 95% CI:0.62-0.97), Medicaid/MSP recipients (OR 0.66; 95% CI:0.55-0.79), and those living in census tracts with lower educational attainment. Patients who did not consult with a hematology or oncology specialist were much less likely to receive ESAs. There were no trends associated with year of diagnosis.

Characteristics associated with receipt of a TTE, among those who used an ESA, were similar to those associated with ESA use overall (Table 2). Receipt of a TTE was more common in RARS than in RA patients (OR 1.46; 95% CI: 1.10-1.94) and less common in RAEB (OR 0.63; 95% CI: 0.49-0.81), possibly due to early disease progression. TTEs were also less common in patients with dementia (OR 0.63; 95%CI: 0.46-0.85), prior hospital admission or wheelchair use, as well as disabled non-elderly persons and those Medicaid/MSP enrolled. Models estimating determinants of ESA use stratified by MDS risk group (lower, higher, NOS) are shown in the *Online Supplementary Tables S2 and S3*. Overall, the same factors were predictive of ESA use regardless of risk group, though because the sample sizes are smaller some of these associations are no longer statistically significant.

Information on factors associated with ESA use is critical in order to determine whether there are subgroups of patients with MDS who may not be receiving adequate

supportive care. Access issues are considered particularly critical, as MDS-related anemia is an off-label use and Medicare, which is an important payer, given the median age of MDS patients, has considerably restricted payments for ESAs in recent years. Factors that are typically related to access were associated with lower likelihood of receiving ESAs among MDS patients in this study. Race is often seen as an important determinant of cancer treatment generally,[14-16] with blacks less likely to receive a variety of treatments. The fact that our findings were consistent with this, despite all patients having Medicare insurance and despite adjustment for many clinical and socioeconomic factors, suggests residual differences in patient preferences or the potential for clinician bias. Even among patients with adequate access to clinicians, the cost of ESAs may be a barrier to access, and there can be important indirect costs associated with transportation and time. The 2007 weekly Medicare reimbursement for epoetin alfa ranged from $543 to $1,087 with estimates of $873 to $1,455 for darbepoetin.[17] Medicare covers only 80% of the approved amount of the treatment, with the remaining 20% being the responsibility of the patient. Historically, approximately 10% of Medicare beneficiaries have lacked a source of supplemental insurance, and hence would face full responsibility for the patient share.[18] We also found some evidence that patients are less likely to receive ESAs if they have mobility issues and/or lack social support that may be necessary to sustain a pattern of repeated surgery visits over time. There was no evidence that co-morbidities affected the probability of ESA use.

As with all observational studies that use administrative tumor registry and claims data, this study is subject to limitations. SEER registry data provide important information concerning WHO categorization of MDS type. While the International Prognostic Scoring System assignment was not available, the WHO classification system also has prognostic value, and can provide a useful structure to examine treatment patterns, although a large proportion of MDS patients in this study were reported under the category of MDS–NOS. Claims data provide a rich source of information with which to examine treatment, yet they do not provide information on clinical parameters, therapeutic intent or patient preferences that may drive observed care patterns. Also, there is no information on supplemental insurance coverage other than Medicaid and Medicare Advantage, and no information on perceived access to care. Despite these limitations, this study provides important insights into factors associated with ESA use in MDS.

ESAs are of particular interest from a public policy perspective because of their historic widespread use as supportive care for cancer patients, the high costs associated with their use, and the more recent recognition of safety risks in solid tumor patients, particularly when used to produce excessive increases in hemoglobin levels. The current study provides a critical baseline for analysis of the effects of regulatory and policy interventions designed to reduce inappropriate use.

Authorship and Disclosures

The information provided by the authors about contributions from persons listed as authors and in acknowledgments is available with the full text of this paper at www.haematologica.org.

Financial and other disclosures provided by the authors using the ICMJE (www.icmje.org) Uniform Format for Disclosure of Competing Interests are also available at www.haematologica.org.

References

1. Melchert M, List AF. Management of RBC-transfusion dependence. Hematology Am Soc Hematol Educ Program. 2007:398-404.
2. Mannone L, Gardin C, Quarre MC, Bernard JF, Vassilieff D, Ades L, et al. High-dose darbepoetin alfa in the treatment of anaemia of lower risk myelodysplastic syndrome: results of a phase II study. Br J Haematol. 2006;133(5):513-9.
3. Gabrilove J, Paquette R, Lyons RM, Mushtaq C, Sekeres MA, Tomita D, et al. Phase 2, single-arm trial to evaluate the effectiveness of darbepoetin alfa for correcting anemia in patients with myelodysplastic syndromes. Br J Haematol. 2008;142 (3):379-93.
4. Hellstrom-Lindberg E, Ahlgren T, Beguin Y, Carlsson M, Carneskog J, Dahl IM, et al. Treatment of anemia in myelodysplastic syndromes with granulocyte colony-stimulating factor plus erythropoietin: results from a randomized phase II study and long-term follow-up of 71 patients. Blood. 1998(1);92:68-75.
5. Negrin R, Stein R, Doherty K, Cornwell J, Varidman J, Krantz S, et al. Maintenance treatment of the anemia of myelodysplastic syndromes with recombinant human granulocyte colony-stimulating factor and erythropoietin: evidence for in vivo synergy. Blood. 1996;87(10):4076-81.
6. Golshayan AR, Jin T, Maciejewski J, Fu AZ, Bershadsky B, Kattan MW, et al. Efficacy of growth factors compared to other therapies for low-risk myelodysplastic syndromes. Br J Haematol. 2007;137(2):125-32.
7. Hellström-Lindberg E, Gulbrandsen N, Lindberg G, Ahlgren T, Dahl IS, Dybedal I, et al. A validated decision model for treating the anaemia of myelodysplastic syndromes with erythropoietin + granulocyte colony-stimulating factor: significant effects on quality of life. Br J Haematol. 2003;120(6):1037-46.
8. Sekeres MA, Schoonen WM, Kantarjian H, List A, Fryzek J, Paquette R, et al. Characteristics of US patients with myelodysplastic syndromes: results of six cross-sectional physician surveys. J Natl Cancer Inst. 2008;100(21):1542-51.
9. National Comprehensive Cancer Network Myelodysplastic Syndromes Guidelines. [NCCN website] Available from http://guidelines.nccn.org/epc-guideline/guideline/id/0B60A42F-683E-6522-8648-4FDA3324FA47?jumpTo=false#;history=4_gls%40F12B7809-A151-672B-58A4-1CB8F75FF92D_empty_-1. Accessed April 11, 2011.
10. Casadevall N, Durieux P, Dubois S, Hemery F, Lepage E, Quarré MC, et al. Health, economic, and quality-of-life effects of erythropoietin and granulocyte colony-stimulating factor for the treatment of myelodysplastic syndromes: a randomized, controlled trial. Blood. 2004;104(2):321-7.
11. Hellström-Lindberg E, Ahlgren T, Beguin Y, Carlsson M, Carneskog J, Dahl IM, et al. Treatment of anemia in myelodysplastic syndromes with granulocyte colony-stimulating factor plus erythropoietin: results from a randomized phase II study and long-term follow-up of 71 patients. Blood. 1998;92(1):68-75.
12. Davidoff AJ, Tang M, Seal B, et al. Chemotherapy and survival benefit in elderly patients with advanced non–small-cell lung cancer. J Clin Oncol. 2010;28(13):2191-7.
13. Hosmer D, Lemeshow S. Applied Logistic Regression. 2nd ed. Hoboken, New Jersey: John Wiley and Sons; 2002.
14. Potosky AL, Harlan LC, Kaplan RS, Johnson KA, Lynch CF. Age, sex, and racial differences in the use of standard adjuvant therapy for colorectal cancer. J Clin Oncol. 2002;20(5):1192-202.
15. Mahoney T, Kuo YH, Topilow A, Mirhan DJ. Stage III colon cancers: why adjuvant chemotherapy is not offered to elderly patients. Arch Surg. 2000;135(2):182-5.
16. Roetzheim RG, Pal N, Gonzalez EC, Ferrante JM, Van Durme DJ, Krischer JP. Effects of health insurance and race on colorectal cancer treatments and outcomes. Am J Public Health. 2000;90(11):1746-54.
17. Greenberg PL, Cosler LE, Ferro SA, Lyman GH. The costs of drugs used to treat myelodysplastic syndromes following the National Comprehensive Cancer Network guidelines. J Natl Compr Canc Netw. 2008; 6(9):942-53.
18. Cubanski J, Huang J, Damico A, Jacobson G, Neuman T. Medicare Chartbook, Pub. n. 8103. 4th ed. Menlo Park, CA: Henry J. Kaiser Family Foundation; 2010.