Characteristics of US Patients with Myelodysplastic Syndromes: Results of Six Cross-sectional Physician Surveys

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Background Myelodysplastic syndromes (MDS) comprise a group of pathologically and cytogenetically distinct bone marrow disorders. Little is known about the characteristics of MDS patients, including their pathological and prognostic classifications, cytopenias, transfusion and supportive care needs, and treatment regimens. We describe these characteristics in a large group of recently diagnosed and existing (ie, established) MDS patients.

Methods We conducted six consecutive cross-sectional surveys among US hematology and medical oncology specialists (identified from an American Medical Association [AMA] database of physicians who administer chemotherapy) between June 2005 and January 2007. A questionnaire collected data on the characteristics and treatment patterns of the 4–10 most recently seen MDS patients for each physician, including demographic data, transfusion needs, treatment approaches, and consideration for clinical trials or bone marrow transplantation.

Results A panel of 101 physicians who were geographically representative of physicians registered with the AMA characterized 614–827 patients per survey, for a total of 4514 responses. Among recently diagnosed patients, 55% were male (95% confidence interval [CI] = 52% to 59%), the median age at diagnosis was 71 years (range = 65–80 years), and 10% (95% CI = 8% to 12%) had MDS secondary to chemotherapy, radiation therapy, or environmental exposure. The median duration of MDS in established patients ranged from 13 to 16 months over the six surveys. Among recently diagnosed MDS patients, fewer patients with lower-risk disease than with higher-risk disease were dependent on either red blood cell transfusions (22% vs 68%) or platelet transfusions (6% vs 33%). More than 50% of all newly diagnosed and established patients used erythropoiesis-stimulating agents. A small percentage of all patients either had had or were being considered for bone marrow transplantation (recently diagnosed: 4%; established: 4% or less) or were being treated on clinical trials (recently diagnosed: 1%; established: 4% or less).

Conclusions MDS patients in the United States have substantial transfusion needs, and use of erythropoiesis-stimulating agents and are seldom considered for bone marrow transplantation or clinical trials. These data may be useful in characterizing the health care resource use and pharmacoeconomic impact of MDS in the United States.

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Myelodysplastic syndromes (MDS) are a collection of pathologically and cytogenetically distinct bone marrow disorders that have become widely recognized only over the past three decades (1–4). MDS are characterized by peripheral blood cytopenias, which result in an increased risk of bleeding and infectious complications, and MDS patients have a propensity to develop acute myeloid leukemia (AML), particularly those with more advanced MDS subtypes (5–8). Treatments for MDS focus on improving blood counts, minimizing the need for blood transfusions, delaying the progression to AML, improving survival, and maximizing patient quality of life (9–15). The only known curative therapy is bone marrow transplantation (16–18).

The epidemiology of MDS has only recently become clear. MDS is a disease of older adults; the median age of MDS patients at diagnosis is 70 years (6,19). Only a limited number of studies have investigated the descriptive epidemiology of MDS, the majority of

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which were carried out in Europe (19,20). Primary or de novo MDS arise spontaneously, whereas secondary MDS are caused by previous exposure to chemotherapy (particularly alkylating agents and topoisomerase inhibitors), radiation therapy, and/or environmental factors, such as benzene and its derivatives. In the United States, MDS have only in the past 7 years been included as a cancer diagnosis in the Surveillance, Epidemiology, and End Results (SEER) program database of the National Cancer Institute and the Centers for Disease Control and Prevention. Based on SEER data, the estimated age-adjusted incidence rate of MDS in the United States is 3.4 cases per 100 000 people, which translates to approximately 10 000 new cases per year (21). However, because SEER data derive from cancer registries, they lack detailed patient information other than the patient's age at diagnosis, sex, and race; the French–American–British (FAB) classification of disease at diagnosis; and survival rates among newly diagnosed MDS patients. Data on treatment, supportive care requirements, blood product transfusion needs, and specific cytogenetic abnormalities are lacking, as are data on the composition and health care needs of existing (ie, established) MDS patients.

Here, we report the results of six consecutive surveys that we conducted among hematologists and/or medical oncologists to obtain information on the characteristics of newly diagnosed and established MDS patients in the United States, including demographics, pathological and prognostic classifications, cytopenias, transfusion and supportive care needs, and treatment regimens. Through this information, we have gained insight into the impact of MDS on health care resource use.

CONTEXT AND CAVEATS

Prior knowledge

Myelodysplastic syndromes (MDS) comprise a group of pathologically and cytogenetically distinct bone marrow disorders. Recent changes in the therapeutic options for MDS support the need to characterize MDS patients, including their pathological and prognostic classifications, transfusion and supportive care needs, and treatment regimens.

Study design

Six consecutive cross-sectional surveys of 101 hematology and medical oncology specialists in the United States were conducted between June 2005 and January 2007 via questionnaires to ascertain the characteristics and treatment patterns of the 4–10 most recently seen MDS patients for each physician.

Contribution

The physicians characterized 614–827 patients per survey, for a total of 4514 responses. A high proportion of MDS patients were dependent on red blood cell or platelet transfusions. Among recently diagnosed MDS patients, fewer patients with lower-risk disease than with higher-risk disease were dependent on transfusions. More than half of MDS patients were treated with erythropoiesis-stimulating agents. Only a small percentage of MDS patients either had had or were being considered for bone marrow transplantation or were being treated on clinical trials.

Implications

These data may be useful in characterizing the health care resource use and pharmacoeconomic impact of MDS in the United States.

Limitations

The data were collected retrospectively by asking physicians to report on their 4–10 most recently seen MDS patients. Because of the lack of unique identifiers for patients and their physicians, it was not possible to identify a cohort of MDS patients who could be followed over time.

From the Editors

Methods

Physician Sample

We conducted six cross-sectional surveys, at 3- to 5-month intervals, between June 2005 and January 2007; the surveys were mailed to eligible physicians in June and October of 2005; in January, April, and September of 2006; and in January of 2007. Physicians who were eligible to participate in the surveys (eligibility criteria defined below) were identified from an American Medical Association (AMA) database that includes 22 033 medical oncologists, hematologists/oncologists, hematologists, internal medicine physicians with a secondary specialty in oncology, gynecologic oncologists, and urologists who practice in the United States (22). From this database, we identified a sample of 426 physicians who administer chemotherapy and who take part in a regular oncology patient record audit that collects information about the patients seen in their treatment practice (conducted by the US Tandem Oncology Monitor, Synovate Healthcare [Mahwah, NJ] in exchange for remuneration of 30 US dollars for each patient record completed). Data from this sample of 426 physicians were compared by this company with their internal data from more than 50 pharmaceutical and biotechnology companies and were found to be representative in terms of the geographic distribution of the patients who were treated, the tumor types seen in cancer patients, and patient treatment patterns in the United States (C. Humphries, personal communication, Account Manager, US Tandem Oncology Monitor). From this sample of 426 physicians, we identified 101 physicians who treated 10 or more MDS patients per month and who agreed to participate in this series of surveys of patient-specific questionnaires (Figure 1). These 101 specialists were asked to fill out one questionnaire for each of the 4–10 MDS patients they had most recently seen.

Data Collection

We developed a questionnaire that was to be completed by the treating physicians to assess MDS patient characteristics and therapeutic modalities in the United States. The questionnaire included sections on the patient's demographics; current laboratory values; MDS classification [including FAB and World Health Organization (WHO) designations (1,4)]; International Prognostic Scoring System (IPSS) score (6); cytogenetic information (including an item requesting a list of specific abnormalities and cytogenetic risk group category according to the IPSS [good, intermediate, and poor]); current blood product transfusion requirements (dependent, not dependent, or never needed); what therapy the patient was currently receiving; and whether the patient was being considered for participation in a clinical trial or for bone marrow transplantation. The questionnaire was slightly modified

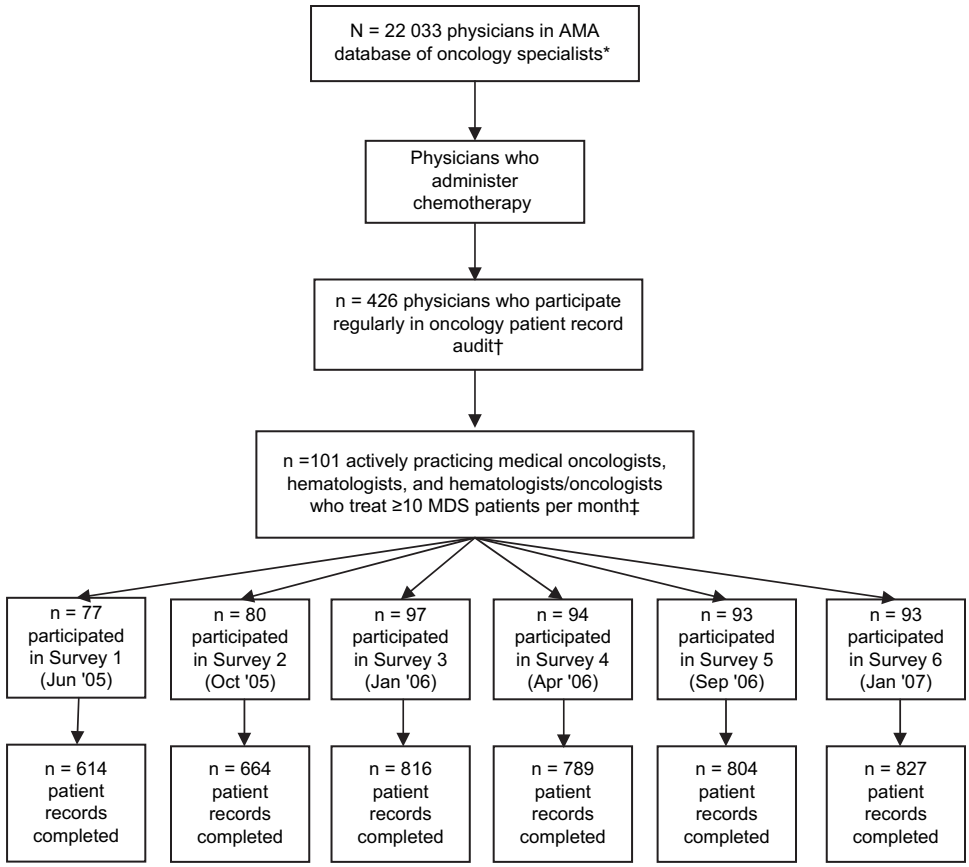

Figure 1. Flow diagram of the administration of six cross-sectional surveys completed by physicians treating patients with myelodysplastic syndrome (MDS) in the United States. *Includes medical oncologists, hematologists/oncologists, hematologists, internal medicine physicians with a secondary specialty in oncology, gynecological oncologists, and urologists. †Sample of 426 physicians was compared with internal data from more than 50 pharmaceutical and biotechnology companies and was found to be representative in terms of tumor types seen and treatment patterns in the United States. ‡Considered to be representative of the larger group of 426 physicians. AMA = American Medical Association.

in surveys 2, 4, and 5 to include information about the reasons for choosing a specific therapy. Information was also collected on all surveys on the physicians who completed the questionnaires, including their subspecialty, type of clinical practice, and patient volume.

All data were collected anonymously (ie, there were no unique identifiers for either the patient or the treating physicians). Patients who were diagnosed during the 2 months before a survey was conducted were considered to be newly diagnosed. All other patients were considered to be established MDS patients. It was not possible to assess which established patients were included in more than one survey. By contrast, each newly diagnosed patient was included as such in only one survey (although he or she may have been included as an established patient in subsequent surveys). Patients with lower-risk MDS were defined as belonging to FAB categories of refractory anemia (RA) and refractory anemia with ringed sideroblasts (RARS); WHO categories of RARS, refractory cytopenia with multilineage dysplasia (RCMD), refractory cytopenia with multilineage dysplasia with ringed sideroblasts (RCMD-RS), MDS with deletion of chromosome 5q (del(5q)), and MDS unclassified; and IPSS categories of low and intermediate-1. Patients with higher-risk MDS were defined as belonging to FAB categories of refractory anemia with excess blasts (RAEB) and refractory anemia with excess of blasts in transformation (RAEBt); WHO categories of RAEB-1 and RAEB-2; and IPSS categories of intermediate-2 and high.

Statistical Analyses

All statistical analyses were descriptive in nature. The prevalent patient population was stratified by recently diagnosed MDS patients (ie, those diagnosed during the 2 months before an incident survey) and established MDS patients. To describe the characteristics for the recently diagnosed patients, we collated the results for such patients from all six surveys and calculated overall median values and percentages, along with 95% confidence intervals (CIs). It was not appropriate to use the same approach to describe the characteristics of the established MDS patients, however, because these patients were potentially included in more than one survey. Instead, for established MDS patients, we calculated median values and percentages for each of the six surveys. For the purpose of this analysis, "supportive care" was defined as therapy with growth factors (including erythropoiesis-stimulating agents [eg, erythropoietin, darbepoetin], granulocyte colony-stimulating factor [G-CSF], granulocyte–macrophage colony-stimulating factor [GM-CSF], and pegfilgrastim); vitamins and/or vitamin supplements; glucocorticoids; cytokines (ie, interleukin 11); immunoglobulins; bisphosphonates; and red blood cell and/or platelet transfusions. "Other treatments" (ie, therapies that did not include growth factors) included differentiation agents, such as azacitidine, decitabine, arsenic trioxide, and all-*trans*-retinoic acid; immunomodulators, such as lenalidomide, thalidomide, CellCept, cyclosporine; and nonablative cytotoxic agents, such as 6-thioguanine, alemtuzumab, amifostine trihydrate, bortezomib, busulfan, cladribine, cyclophosphamide, cytarabine, daunorubicin, etoposide, fludarabine, gemtuzumab, hydroxyurea, idarubicin, melphalan, methotrexate, mitoxantrone, and topotecan.

Results

Characteristics of Responding Physicians

The response rates from the 101 physicians for each of the six surveys ranged from 77% to 97% (Figure 1). These 101 physicians were similar to the total group of physicians in the AMA database with respect to the frequency distributions of practice type and geographic region (Table 1). The regional distribution of their practice sites across surveys are as follows: New England (3%–6%); Mid-Atlantic (20%–26%); North Central (18%–24%); South Atlantic (20%–28%); South Central (20%–28%); Mountain (3%–4%); and Pacific (8%–13%). Among the participating physicians, 68%–76% had an office-based practice, 7%–13% had a university hospital–based practice, 7%–12% had a community hospital–based practice, 3%–8% had a Veterans Affairs hospital–based practice, and 3%–7% had a practice based at a comprehensive cancer center.

We received 4514 completed patient questionnaires from the physicians; the number of completed questionnaires received per survey ranged from 614 to 827.

Table 1. Characteristics of physicians who participated in the six surveys and of all internal medicine physicians registered with the American Medical Association (AMA)

Characteristic	Participating physicians (N = 101), range per survey, %	AMA physicians* (N = 139 090), %
Practice type		
Office based	68 to 76	73
Hospital based	24 to 32	28
Community	7 to 12	—
University	7 to 13	—
Veterans Affairs or military	3 to 8	—
Comprehensive cancer center	3 to 7	—
Geographical location		
North Central	18 to 24	21
South Atlantic	20 to 28	18
Mid-Atlantic	20 to 26	21
South Central	13 to 16	13
Pacific	8 to 13	15
New England	3 to 6	8
Mountain	3 to 4	5

* Internal medicine physicians who were registered with the AMA and actively involved in patient care during the year 2004 (23). No information was provided regarding the type of hospital physicians worked in. Some percentages do not total 100% due to rounding. — = not applicable.

Patient Characteristics

Of the 4514 returned questionnaires, 670 were obtained from recently diagnosed patients, of whom 55% were male (Table 2). Among the recently diagnosed patients, the median age at diagnosis was 71 years (range = 65–80 years) and did not differ markedly between men and women (data not shown). Secondary MDS due to chemotherapy, radiation therapy, or chemical exposure was seen in 10% (95% CI = 8% to 12%) of recently diagnosed patients, mostly (76%) following treatment with chemotherapy. The characteristics of established MDS patients were similar to those of recently diagnosed patients (Table 2). Disease duration among the established MDS patients varied widely; the minimum and maximum disease durations were 3 and 250 months, respectively; the median disease duration was less variable, ranging from 13 to 16 months across the six surveys.

Table 2. Clinical and demographic characteristics of recently diagnosed and established myelodysplastic syndrome (MDS) patients*

Characteristic†	Recently diagnosed patients (N = 670)	Established patients % per survey (N = 4570)					
		Survey 1 (n = 614)	Survey 2 (n = 664)	Survey 3 (n = 816)	Survey 4 (n = 789)	Survey 5 (n = 804)	Survey 6 (n = 827)
Patients per survey, n							
Median (IQR)	112 (66 to 149)	—	—	—	—	—	—
Median age at diagnosis, y (IQR)	71 (65 to 80)	72 (65 to 80)	74 (67 to 80)	74 (67 to 80)	75 (68 to 81)	74 (68 to 81)	74 (67 to 80)
Male‡, % (95% CI)	55 (52 to 59)	57	51	51	54	54	55
Duration of disease, mo							
Median (IQR)	—	16 (7 to 36)	16 (8 to 37)	13 (7 to 31)	16 (7 to 36)	16 (8 to 33)	15 (7 to 34)
Minimum; maximum		3; 240	3; 220	3; 169	3; 194	3; 172	3; 250
Secondary MDS§, % (95% CI)	10 (8 to 12)	12	12	9	8	7	7
Suspected reason for secondary MDS‖, % (95% CI)							
Chemotherapy only	76 (66 to 86)	58	67	55	60	80	74
Radiation only	7 (1 to 14)	11	12	15	21	8	6
Chemotherapy and radiation	7 (1 to 14)	11	4	8	0	0	2
Chemical exposure	3 (0 to 7)	5	6	2	4	6	9
Other	6 (0 to 12)	15	12	20	15	6	9

* The total "n" listed at the heading of each established patients survey column includes recently diagnosed (ie, diagnosed in the previous 2 months) and established patients for whom this information was collected in that survey. Results for recently diagnosed patients were combined from across all six surveys and reported along with 95% CIs. IQR = interquartile range; — = not applicable; CI = confidence interval.

† Characteristic at the time of the survey, excluding 14 patients with unknown duration of disease.

‡ Excludes 1 recently diagnosed patient and 10 established patients with missing information on sex.

§ Excludes one recently diagnosed patient and three established patients with missing information on primary vs secondary MDS disease status.

‖ Reported for patients with secondary MDS only (N = 68 recently diagnosed and N = 344 established patients). Excludes one recently diagnosed patient and two established patients with secondary MDS who had missing information on the suspected cause of disease.

The distributions of MDS subtypes for recently diagnosed and established patients according to FAB and WHO pathological classifications and IPSS risk category are presented in Table 3. Lower-risk MDS (FAB categories of refractory anemia RA and RARS; WHO categories of RARS, RCMD, RCMD-RS, MDS with deletion of chromosome 5q, and MDS unclassified; and IPSS scores of low and intermediate-1) was more common in established MDS patients than in recently diagnosed patients (percentage of lower-risk MDS among established vs recently diagnosed patients: by FAB criteria, 60%–69% across the six surveys vs 50% [95% CI = 46% to 53%]; by WHO criteria: 56%–66% vs 51% [95% CI = 47% to 54%]; and by IPSS criteria 75%–79% vs 64% [95% CI = 61% to 68%]).

Cytogenetic data were available for approximately 90% of the patients for whom a questionnaire was completed (Table 4). Among the recently diagnosed patients, 51% had an IPSS cytogenetic risk classification of "good," 20% had a risk classification of "intermediate," and 17% had a risk classification of "poor." A higher proportion of recently diagnosed MDS patients than established MDS patients had an IPSS cytogenetic risk classification of either intermediate or poor (range 17%–20% vs 7%–18%, respectively). The most commonly reported cytogenetic abnormality was del(5q), which occurred in 11% (95% CI = 9% to 14%) of recently diagnosed patients and 7%–8% of established patients.

Among the recently diagnosed MDS patients, the majority were anemic and had mild thrombocytopenia and neutropenia: the median hemoglobin value was 9.1 g/dL (interquartile range [IQR] = 8–10 g/dL), the median platelet count was 100 000/mm^3 (IQR = 56 000–150 500/mm^3), and the median absolute neutrophil count was 1780/mm^3 (IQR = 1070–2800/mm^3). A minority of recently diagnosed patients had circulating blasts: 16% of patients (95% CI = 13% to 19%) had 1%–5% blasts in their circulation and 10% of patients (95% CI = 8% to 12%) had more than 5% blasts in their circulation.

Transfusion and Supportive Care Requirements

Among the recently diagnosed MDS patients, those with lower-risk disease were less likely to have received a transfusion than those with higher-risk disease (17% vs 54%) (Table 5). Moreover, fewer recently diagnosed patients with lower-risk disease than with higher-risk disease were dependent on either red blood cell transfusions (22% vs 68%) or platelet transfusions (6% vs 33%) (Figure 2).

Erythropoiesis-stimulating agents (ie, erythropoietin and/or darbepoetin) were used by the majority (58%) of recently diagnosed patients and by 55%–63% of established patients (Figure 3). When we further subdivided recently diagnosed and established patients into those with lower-risk and higher-risk disease, we observed no clear difference in the proportion of patients in these risk groups who received erythropoiesis-stimulating agents (Table 5). Other growth factors (ie, G-CSF, GM-CSF, or pegfilgrastim) were used by only 10% of recently diagnosed patients and 8%–11% of established patients (Figure 3).

Table 3. Disease characteristics of recently diagnosed and established MDS patients*

Characteristic	Recently diagnosed patients, % (95% CI) (N = 670)	Established patients, % per survey (N = 4514)					
		Survey 1 (n = 614)	Survey 2 (n = 664)	Survey 3 (n = 816)	Survey 4 (n = 789)	Survey 5 (n = 804)	Survey 6 (n = 827)
FAB classification							
RA	38 (34 to 41)	45	44	46	44	49	52
RARS	12 (9 to 14)	16	19	14	18	16	17
RAEB	16 (14 to 19)	16	13	14	12	14	12
RAEBt	10 (7 to 12)	6	5	4	3	3	4
CMML	5 (4 to 7)	7	6	3	4	4	4
Unclassifiable	5 (3 to 7)	7	8	6	6	5	3
Missing FAB	14 (12 to 17)	4	5	14	12	8	10
WHO classification							
RARS	13 (10 to 15)	13	13	14	15	13	14
RCMD	20 (17 to 23)	24	21	24	19	22	21
RCMD-RS	1 (0 to 2)	2	2	3	2	3	3
RAEB-1	11 (8 to 13)	11	8	9	8	9	9
RAEB-2	12 (10 to 15)	10	7	5	6	4	3
MDS-U	13 (11 to 16)	4	3	3	3	4	4
MDS, isolated del(5q)	4 (2 to 5)	23	19	16	19	15	17
Missing WHO	27 (23 to 30)	13	28	25	28	30	29
IPSS risk score							
Low	30 (27 to 33)	37	40	38	44	41	40
Intermediate-1	34 (31 to 38)	38	38	39	34	38	39
Intermediate-2	16 (13 to 19)	12	13	13	8	12	15
High	13 (11 to 16)	13	5	5	7	7	5
Missing IPSS	6 (4 to 8)	0	4	5	7	3	2

* The total "n" listed at the heading of each established patients survey column includes recently diagnosed (ie, diagnosed in the previous 2 months) and established patients for whom this information was collected in that survey. Results for recently diagnosed patients were combined from across all six surveys and reported along with 95% CIs. MDS = myelodysplastic syndrome; CI = confidence interval; FAB = French–American–British; RA = refractory anemia; RARS = refractory anemia with ringed sideroblasts; RAEB = refractory anemia with excess of blasts; RAEBt = refractory anemia with excess of blasts in transformation; CMML = chronic myelomonocytic leukemia; WHO = World Health Organization; RCMD = refractory cytopenia with multilineage dysplasia; RCMD-RS = refractory cytopenia with multilineage dysplasia with ringed sideroblasts; MDS-U = myelodysplastic syndrome unclassified; IPSS = International Prognostic Scoring System.

Table 4. Cytogenetic findings and specified abnormalities among recently diagnosed and established MDS patients*

Finding or abnormality	Recently diagnosed patients (N = 670)		Established patients, % per survey (N = 4514)					
	n	% (95% CI)	Survey 1 (n = 614)	Survey 2 (n = 664)	Survey 3 (n = 816)	Survey 4 (n = 789)	Survey 5 (n = 804)	Survey 6 (n = 827)
Cytogenetic findings†								
Good	339	51 (47 to 54)	66	63	63	64	62	67
Intermediate	135	20 (17 to 23)	12	18	17	15	18	16
Poor	114	17 (14 to 20)	13	11	11	9	10	7
Missing	82	12 (10 to 15)	8	8	9	12	11	9
Specified abnormalities‡								
Normal set/none§	123	18 (15 to 21)	18	15	20	15	24	44
Uninformative cytogenetics/no data§	294	44 (40 to 48)	55	58	49	59	51	29
BMA not conducted	80	12 9 to 14)	54	26	9	9	7	7
del(5q)	75	11 (9 to 14)	7	7	8	8	7	8
−7 or 7q−	41	6 (4 to 8)	2	4	4	5	4	4
Trisomy 8	34	5 (3 to 7)	5	4	5	5	3	3
Multiple/complex abnormalities	31	5 (3 to 6)	3	1	2	2	1	2
Loss of Y chromosome	19	3 (2 to 4)	2	1	1	1	2	2
del(20q)	16	2 (1 to 4)	2	1	1	2	2	2
Monosomy 7	10	1 (1 to 2)	4	1	2	2	1	1
11q23	7	1 (0 to 2)	1	1	1	1	1	1
6	4	‖	0	0	0	0	0	0
1q	2	‖	1	0	0	0	0	0
Trisomy 19	2	‖	0	0	0	0	0	0
Trisomy 14	1	‖	1	0	0	0	0	0
17p−/−17	1	‖	0	0	0	0	0	0
21	1	‖	0	0	0	0	0	0
Other 12p	1	‖	0	0	0	0	0	0
X	0	‖	1	0	0	0	0	0
13	0	‖	0	0	0	0	0	0
t(5;12)(q33;p13)	0	‖	0	0	0	0	0	0
inv(3)(q21p26)	0	‖	0	0	0	0	0	0
t(3;5)(q25;p34)	0	‖	0	0	0	0	0	0
Other abnormalities not specified	38	6 (4 to 7)	1	9	15	5	8	8

* The total "n" listed at the heading of each established patients survey column includes recently diagnosed (ie, diagnosed in the previous 2 months) and established patients for whom this information was collected in that survey. Results for recently diagnosed patients were combined from across all six surveys and reported along with 95% CIs. MDS = myelodysplastic syndrome; CI = confidence interval; BMA = bone marrow analysis.

† Excludes 82 recently diagnosed patients and 367 established patients missing information on cytogenetic findings.

‡ Abnormalities not mutually exclusive. However, those with "bone marrow analysis not conducted," "normal," or "other abnormalities" did not have any of the other specified abnormalities.

§ Combined 46XX and 46XY into "Normal."

‖ Too few case patients to present percentages. The total number with the specified abnormality is presented.

MDS Therapy

The basis on which physicians chose a particular therapy was similar for recently diagnosed and established MDS patients, with the exception that hemoglobin values were more likely to be used to make therapy decisions for established patients than for recently diagnosed patients (Table 6).

Among recently diagnosed MDS patients, those with lower-risk disease were more likely to be monitored without treatment (a "watch and wait" approach) than those with higher-risk disease (24% vs 5%) (Table 5). Among established patients who were being monitored without treatment, the average duration of follow-up at the time of the six surveys ranged from 13 to 20 months.

Among recently diagnosed patients, those with higher-risk disease were more likely to use non–growth factor therapies (ie, chemotherapy or biologic or immunologic approaches) than those with lower-risk disease (69% vs 22%) (Table 5). Similar proportions of recently diagnosed and established patients were treated with the non–growth factor therapies azacitidine (16% vs 11%–15%), lenalidomide (8% vs 1%–9%), and decitabine (2% vs 0%–4%) (Figure 3). The use of other non–growth factor drugs was comparatively small. Use of vitamins and/or vitamin supplements was similar between recently diagnosed and established patients and between patients with lower-risk and higher-risk disease (Table 5).

In each of the six surveys, only a small minority of MDS patients was described as having had or being considered for bone marrow transplantation (4% of recently diagnosed patients and 0%–4% of established patients). More than half of bone marrow transplants that were performed or being considered were full myeloablative transplants (as opposed to nonmyeloablative or peripheral blood stem cell transplants, which were performed less commonly [data not shown]). The proportion of MDS patients in clinical trials was similarly low (1% of recently diagnosed patients and 1%–4% of established patients).

Table 5. Current treatment information for recently diagnosed and established MDS patients, by IPSS risk score*

	IPSS Low/Int-1							IPSS Int-2/High						
	Recently diagnosed patients, % (95% CI) (N = 432)	Established patients, % per survey (N = 4514)						Recently diagnosed patients, % (95% CI) (N = 198)	Established patients, % per survey (N = 4514)					
Treatment		Survey 1 (n = 614)	Survey 2 (n = 664)	Survey 3 (n = 816)	Survey 4 (n = 789)	Survey 5 (n = 804)	Survey 6 (n = 827)		Survey 1 (n = 614)	Survey 2 (n = 664)	Survey 3 (n = 816)	Survey 4 (n = 789)	Survey 5 (n = 804)	Survey 6 (n = 827)
Monitoring†	24 (20 to 28)	19	15	16	19	17	18	5 (2 to 7)	12	6	9	9	5	10
Supportive care‡, with or without other treatments	70 (66 to 74)	77	82	80	74	78	77	83 (78 to 89)	84	85	80	68	88	79
Transfusion§	17 (14 to 21)	31	24	24	3	25	18	54 (47 to 61)	70	52	50	3	66	48
ESA	59 (54 to 64)	58	63	62	64	65	64	58 (51 to 65)	48	63	57	54	55	56
G(M)-CSF	5 (3 to 7)	7	6	8	5	8	7	19 (14 to 25)	20	21	15	21	21	28
Vitamins and supplements	22 (18 to 26)	10	22	21	20	23	20	16 (11 to 21)	4	19	17	21	17	15
Supportive care‡ without other treatments	53 (49 to 58)	58	67	61	60	60	61	27 (21 to 33)	37	49	33	24	31	33
Transfusion§	2 (1 to 3)	4	5	4	3	2	3	4 (1 to 6)	9	7	5	3	9	4
ESA	27 (23 to 31)	29	32	29	38	28	34	6 (3 to 9)	5	9	10	11	6	7
G(M)-CSF	0 (0 to 1)	1	1	1	1	0	0	0	0	0	1	0	0	0
Vitamins and supplements	4 (2 to 6)	4	5	5	3	3	4	0	1	4	0	4	2	2
Other treatments‖, with or without supportive care	22 (18 to 26)	23	18	23	22	23	21	69 (62 to 75)	51	45	59	66	64	57
Other treatments‖ without supportive care	6 (4 to 9)	6	4	5	8	5	5	12 (8 to 17)	4	9	11	22	8	11

* The total "n" listed at the heading of each established patients survey column includes recently diagnosed (ie, diagnosed in the previous 2 months) and established patients for whom this information was collected in that survey. Results for recently diagnosed patients were combined from across all six surveys and reported along with 95% CIs. Excludes 40 recently diagnosed patients and 133 established patients with missing values for IPSS risk score. MDS = myelodysplastic syndrome; IPSS = International Prognostic Scoring System; Low/Int-1 = low and intermediate-1 risk classification; Int-2/High = intermediate-2 and high risk classification; CI = confidence interval; ESA = erythropoiesis-stimulating agents; G(M)-CSF = granulocyte–macrophage colony-stimulating factor.

† Patients who were being monitored without receiving any form of therapy ("watch and wait" patients).

‡ Supportive care includes growth factors (erythropoietin, darbepoetin, G-CSF, GM-CSF, pegfilgrastim), vitamins and supplements, red blood cell transfusions, platelet transfusions, glucocorticoids, cytokines (IL11), immunoglobulins and bisphosphonates.

§ Red blood cell and/or platelet transfusions.

‖ Other treatments include 6-thioguanine, alemtuzumab, all-*trans*-retonic acid, amifostine trihydrate, anagrelide, androgens, arsenic trioxide, azacitidine, bortezomib, busulfan, CellCept, cladribine, cyclophosphamide, cyclosporine, cytarabine, daunorubicin, decitabine, etoposide, fludarabine, gemtuzumab, hydroxyurea, idarubicin, imatinib mesylate, lenalidomide, leuprolide, melphalan, methotrexate, mitoxantrone, pentostatin, rituximab, strontium 89, thalidomide, tipifarnib, topotecan, and other chemotherapy, biologics, immunotherapy, and DNA therapy.

Discussion

The range of therapeutic options for the management of MDS has changed dramatically over the past 3 years due to the approval by the US Food and Drug Administration (FDA) of three drugs—azacitidine, lenalidomide, and decitabine—to treat the disease (11,12,15). In addition to these FDA-approved drug options, erythropoiesis-stimulating agents have been used for decades in the supportive setting, either as stand-alone therapy or as adjunctive therapy with non–growth factor approaches (10,13,23,24). With this change in therapeutic landscape came the need to characterize the composition of MDS patients in the United States and the treatments they are receiving.

In this study, we describe the characteristics of a large sample of MDS patients in the United States, including their transfusion and supportive care needs and treatment approaches for a 19-month period that ended in January 2007. The patients included in this study derive mainly from office-based practices, and thus represent a "real-world" glimpse of the makeup of this disease. To our knowledge, this is the first study to describe the characteristics and treatment patterns of established MDS patients.

The proportions of recently diagnosed MDS patients with lower-risk and higher-risk disease were consistent with those reported in a previous study (6). In addition, the signs and symptoms at presentation, baseline laboratory values, and cytogenetic risk distributions among both recently diagnosed and established patients were similar to those reported earlier (2,6,8,25). The majority of lower-risk patients had fewer transfusion needs and was more likely to be followed by a "watch and wait" approach than higher-risk patients, as would be predicted by their longer survival and more indolent disease course. To our knowledge, this is the first report describing the length of time that patients are monitored with a "watch and wait approach" prior to initiating therapy (ie, 13–20 months). These data may be useful in supporting decision models for treating MDS and for describing transfusion, supportive, and therapeutic needs over the entire disease course (15).

It is surprising that despite the high proportion of lower-risk MDS subtypes among recently diagnosed and established patients, a large percentage of patients were reported to currently receive blood and/or platelet transfusions. The majority of the patients with higher-risk disease were dependent on red blood cell transfusions, and a substantial minority was dependent on platelet transfusions. Up to 20% of recently diagnosed lower-risk MDS patients and up to 67% of higher-risk patients were dependent on red blood cell transfusions, and up to 6% of recently diagnosed lower-risk and 33% of higher-risk patients were dependent on platelet transfusions. Among patients with established MDS, the percentages of those requiring red blood cell or platelet transfusions were higher: up to 25% of established lower-risk patients and up to 67% of established higher-risk patients required blood products. Given the estimated 10 000 incident and 50 000 prevalent cases of MDS in the United States each year (21), the public health impact of these transfusion needs may be greater than previously thought, because ultimately the majority of MDS patients may, as they transition from lower-risk disease to higher-risk disease, require blood product transfusions over the rest of their lifetimes. The use

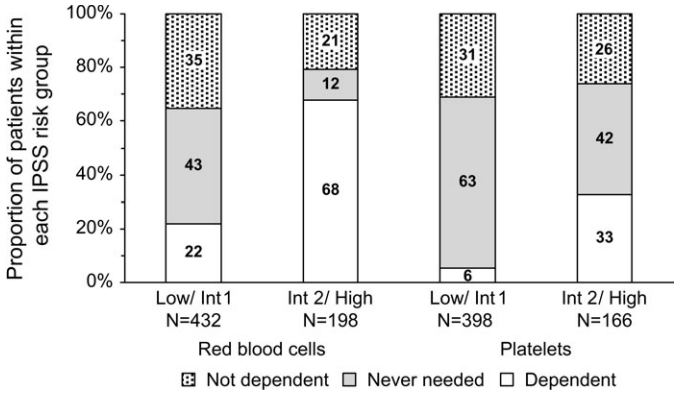

Figure 2. Transfusion dependency among recently diagnosed patients. IPSS = International Prognostic Scoring System; Low/Int-1 = low and intermediate-1 risk classification; Int-2/High = intermediate-2 and high risk classification.

of erythropoiesis-stimulating agents was also high: the majority of recently diagnosed and established patients were receiving such agents at the time of survey, either alone or in combination with other therapies. We were surprised to discover that physicians were treating patients with erythropoiesis-stimulating agents in combination with non–growth factor therapy off-study, because combination therapy is just now being explored in phase 1 and phase 2 clinical trials. One caveat to the interpretation of these erythropoiesis-stimulating agent results is that, by design, surveyed physicians demonstrated at least some familiarity with treating MDS patients and thus may have preferentially been referred MDS patients with transfusion or erythropoiesis-stimulating agent needs. Thus, although every attempt was made to demonstrate that physician responders were geographically representative of practices across the country, this potential for a referral bias may mean that their ESA treatment practices do not apply to the full spectrum of MDS patients in the United States.

Other non–growth factor therapies appeared to be used in similar proportions of established and recently diagnosed lower-risk patients but were used more frequently in higher-risk MDS patients than lower-risk patients. It is interesting that among higher-risk patients, non–growth factor therapies appeared to be used in a

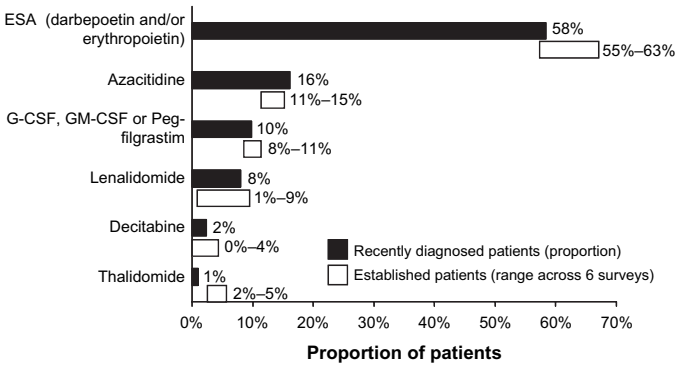

Figure 3. Mean proportion of recently diagnosed patients (N = 670) and range of percentages of established patients across six surveys (N = 3844) taking specific types of therapies at the time of the survey. ESA = erythropoiesis-stimulating agent; G-CSF = granulocyte colony-stimulating agent; GM-CSF = granulocyte–macrophage colony-stimulating agent.

Table 6. Reason for choice of current therapy for recently diagnosed and established MDS patients*

Reason†	Recently diagnosed patients, % (95% CI) (N = 549)	Established patients, % per survey (N = 4514)					
		Survey 1 (n = 614)	Survey 2 (n = 664)	Survey 3 (n = 816)	Survey 4 (n = 789)	Survey 5 (n = 804)	Survey 6 (n = 827)
FAB or WHO classification	30 (26 to 33)	30	16	19	24	21	29
IPSS score	18 (15 to 22)	19	18	23	25	21	20
Hemoglobin value	14 (10 to 19)	38	26	18	‡	‡	‡
Current symptoms	30 (26 to 34)	28	25	31	28	28	32
Patient choice	30 (27 to 34)	25	28	25	23	25	25
Other	78 (74 to 81)	73	78	78	80	78	77

* The total "n" listed at the heading of each established patients survey column includes recently diagnosed (ie, diagnosed in the previous 2 months) and established patients for whom this information was collected in that survey. Results for recently diagnosed patients were combined from across all six surveys and reported along with 95% CIs. Excludes 121 recently diagnosed patients and 594 established patients who were being monitored and were not receiving any form of therapy (ie, "watch and wait" patients). MDS = myelodysplastic syndrome; CI = confidence interval; FAB = French–American–British; WHO = World Health Organization; IPSS = International Prognostic Scoring System.

† Reason given at the time of the survey. Categories are not mutually exclusive (patients could be on a current therapy for more than one reason).

‡ Values for hemoglobin not recorded in surveys conducted in April and September of 2006 and in January of 2007.

higher proportion of recently diagnosed patients than of established patients; this difference may signify a greater awareness among treating physicians to initiate therapy quickly in higher-risk MDS patients and/or that established patients have already failed such therapy.

The only curative therapy for MDS is bone marrow transplantation. Despite the wider availability of reduced-intensity conditioning ("nonmyeloablative" or "mini") bone marrow transplants, the percentage of patients who were being considered for or had received these or other transplant modalities remains low. The low percentage of MDS patients being considered for transplantation may indicate a continued reluctance by physicians to pursue aggressive therapies in an older population and/or the recognized lack of available donors; in addition, older MDS patients have correspondingly aged siblings, who also may have substantial comorbidities that would preclude their participation as a donor. Another potential explanation for the low percentage of patients being considered for transplantation in this study is that patients being considered for transplantation would likely have been referred to transplant specialty centers, and thus might have been underrepresented in these survey data. However, it is still fair to conclude that transplantation was an underconsidered treatment modality within our physician sample, which we feel is representative of practice patterns in the Unites States. A similarly low percentage of MDS patients in our sample were enrolled in clinical trials. This finding is compatible with clinical trial enrollment patterns of adults with other types of cancer (26).

Our study has two potential limitations. One is that the data were collected retrospectively by asking physicians to report on the 4–10 most recently seen MDS patients. Although one could argue that physicians may have been more likely to remember the more severe cases of MDS, the heterogeneity of the data belies systematic recall bias. In addition, the sample of physician responders was also restricted to physicians who were familiar with MDS patients, thus lending more credence to the accuracy of the information collected. A second limitation is that because of a lack of unique identifiers for patients as well as their physicians, we were not able to identify a cohort of MDS patients who could be followed over time. In addition, because information on the same established patient may have been provided in more than one survey, it was not possible to pool results of all surveys to explore differences in therapies among established patients.

In conclusion, the majority of MDS patients have lower-risk disease, and 10% have secondary MDS. A high proportion of MDS patients are dependent on red blood cell and platelet transfusions, and the majority of recently diagnosed and established cases are treated with erythropoiesis-stimulating agents. Transplantation and clinical trial involvement continues to be an option for only a minority of MDS patients. These data may be useful for estimating the resource utility and pharmacoeconomic impact of MDS in the United States.

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