Review of Stem-Cell Transplantation for Myelodysplastic Syndromes in Older Patients in the Context of the Decision Memo for Allogeneic Hematopoietic Stem Cell Transplantation for Myelodysplastic Syndrome Emanating From the Centers for Medicare and Medicaid Services

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ABSTRACT

Myelodysplastic syndromes (MDS) comprise a heterogeneous group of clonal hematopoietic stem-cell disorders that result in varying degrees of cytopenia and risk of transformation into acute leukemia. Allogeneic stem-cell transplantation (SCT) is the only known cure for this disease. The treatment is routinely used for younger patients, but only a minority of patients older than the age of 60 undergo this procedure. The overall MDS incidence is 3.3 per 100,000, but the incidence in patients older than age 70 is between 15 and 50 per 100,000. The median age at presentation is 76 years. Medicare-age patients 65 or older represent 80% of the total population receiving an MDS diagnosis. In the United States, one of the obstacles to SCT for older patients with MDS has been lack of third party reimbursement. On August 4, 2010, the Centers for Medicare and Medicaid Services released their Decision Memo for Allogeneic Hematopoietic Stem Cell Transplantation (HSCT) for Myelodysplastic Syndrome. This memo states: "Allogeneic HSCT for MDS is covered by Medicare only for beneficiaries with MDS participating in an approved clinical study that meets the criteria below. . . ." In this review, we will summarize what is known regarding the role of allogeneic SCT in older patients as well as other elements that should be included within clinical trials that can provide the evidence necessary to demonstrate that allogeneic SCT should be a covered benefit for Medicare beneficiaries.

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INTRODUCTION

Myelodysplastic syndromes (MDS) comprise a heterogeneous group of hematologic disorders characterized by a clonal abnormality of hematopoietic stem cells that results in a varying degree of cytopenias and risk of transformation into acute leukemia.¹ The incidence and prevalence of MDS has increased significantly over the past 20 years as a result of increasing longevity of the population and increasing physician awareness.²⁻⁴ New therapeutic options, such as hypomethylating agents, immunomodulatory drugs, and differentiation induction agents, improve hematologic parameters and reduce transfusion requirements,⁵⁻⁹ but only 5-azacytidine has been shown in randomized trials to prolong survival.^{5,6} Allogeneic stem-cell transplantation (SCT) is the only known therapeutic option that has been demonstrated to cure this disease, leading to the current National Comprehensive Cancer Network (NCCN) recommendation that patients eligible for a transplan-

tion procedure based on age and donor availability be considered for this therapy.¹⁰⁻²¹

The role of allogeneic SCT as therapy for MDS in younger patients is well-established and has been a subject of a recent comprehensive review.²² However, the efficacy of this strategy in older patients, particularly those older than 60 years, has not been well-established since until only recently these patients were not considered eligible for an allogeneic SCT.²³⁻²⁵ The advent of reduced intensity conditioning (RIC) has resulted in significant increases in the number of patients older than 60 years who undergo transplantation for a number of diseases, such as acute myeloid leukemia (AML).²⁶ This procedure is considered routine for patients with AML and is a covered benefit by most insurance companies and Medicare beneficiaries in North America.

In the United States, one of the obstacles to SCT for older patients with MDS has been lack of third-party reimbursement. Until recently the Centers for Medicare and Medicaid Services (CMS) did not have a national policy addressing the issue of

coverage for allogeneic transplantation for patients with MDS. This lack of policy precluded hospitals from providing this service for most Medicare beneficiaries since there was no assurance that services rendered would be covered. On November 10, 2009, CMS opened a National Coverage Analysis based on a request from many interested groups (ie, The National Marrow Donor Program, American Society for Blood and Marrow Transplantation, American Cancer Society, American Cancer Society Cancer Action Network, AABB, American Society of Hematology, American Society of Clinical Oncology, Aplastic Anemia and MDS International Foundation, Blood and Marrow Transplant Information Network, National Bone Marrow Transplant Link, The Bone Marrow Foundation and The Leukemia and Lymphoma Society). The official request asked for “national coverage of allogeneic HSCT for Medicare beneficiaries who would either be at high risk for progression to leukemia or be at risk for MDS complications that place them at high risk for death or prevent the future possibility of a transplant.”²⁷

On August 4, 2010, CMS released their Decision Memo for Allogeneic Hematopoietic Stem Cell Transplantation (HSCT) for Myelodysplastic Syndrome (CAG-00415N). This memo states: “Allogeneic HSCT for MDS is covered by Medicare only for beneficiaries with MDS participating in an approved clinical study that meets the criteria below. A clinical study seeking Medicare payment for allogeneic hematopoietic stem-cell transplantation for myelodysplastic syndrome pursuant to Coverage with Evidence Development must address one or more aspects of the following questions. . . .”²⁷ In this review we will summarize what is known regarding the role of allogeneic SCT in older patients as well as other elements that should be included within the clinical trials that can provide the evidence necessary to demonstrate that allogeneic SCT should be a covered benefit for Medicare beneficiaries.

USE OF ALLOGENEIC SCT IN OLDER PATIENTS WITH MDS

The median age of diagnosis for patients with MDS is 76 years of age according to the Surveillance, Epidemiology and End Results database with 86% of patients older than 60 years.²⁻⁴ The NCCN Practice Guidelines, as well as recent expert reviews, recommend allogeneic SCT for patients with high-risk MDS without making any age restrictions.^{21,28,29} However, registry analysis show that few patients older than 65 years are actually undergoing this procedure. Even with the advent of RIC regimens, the number of patients undergoing SCT older than 65 years reported to the Center for International Blood and Marrow Transplant increased from 16 during the years of 1995 through 2002 to 39 from 2003 to 2005.³⁰ Thus, factors other than availability of well-tolerated conditioning regimens have determined the use of this procedure in this patient population. The current decision memorandum from CMS will allow patients, physicians, and institutions to offer allogeneic SCT for this patient population as long as the CMS guidelines are met, thus eliminating one potential barrier to the use of this procedure.

USE OF INTERNATIONAL PROGNOSTIC STAGING SYSTEM SCORE FOR RISK STRATIFICATION

Since introduced in 1998, the International Prognostic Staging System (IPSS) is an invaluable and frequently utilized instrument to categorize

risk of patients with MDS and decide treatment strategy. The IPSS score separates patient into four distinct risk categories (ie, low, intermediate 1, intermediate 2, and high risk) based on the degree of cytopenias, percentage of bone marrow blasts, and presence or absence of specific cytogenetic abnormalities.³¹ With supportive care, the median survival expectations are longer than 5 years for patients with low-risk disease, but shorter than 1 year for patients with high-risk disease. Likewise, the risk of progression to AML is fewer than 10% for patients with low-risk disease and is 25% for patients with high-risk disease. This difference in prognosis has led to the current NCCN guidelines recommending that patients with low or intermediate 1 risk IPSS scores not be considered for aggressive therapies such as intensive chemotherapy or allogeneic SCT.²¹

The IPSS score was developed at a time when MDS was classified according to the French-American-British classification and the only therapeutic options for most patients was supportive care or intensive chemotherapy.³² The role of IPSS scoring in treatment decisions needs to be readdressed in the context of the new WHO classification of myeloproliferative disorders and the known survival benefits that treatment with hypomethylating agents confer.^{5-7,33}

The CMS proposal suggests that risk stratification using the IPSS scoring system during the Coverage with Development of Evidence be evaluated. In addition to evaluating the IPSS, it will be important to consider other, potentially more discriminating, prognostic scores. Malcovati et al³⁴ have proposed the WHO prognostic scoring system (WPSS), which takes into account the impact of RBC transfusion dependency on overall survival and progression to AML. In this analysis, the investigators looked at the relevance of the WHO classification and transfusion requirement among different IPSS groups. For patients with low and intermediate 1 risk IPSS scores, the WHO histologic classification scheme was able to significantly differentiate survival among the different histologic subtypes within each IPSS range. Patients in higher IPSS risk categories did not have significantly different survival outcomes when stratified by WHO histology. The authors also demonstrated a significant effect on survival based on the requirement for transfusion support, particularly in patients in the lower risk categories. Based on this a newer WPSS was proposed.³⁵ In the WPSS, the impact of regular transfusion requirement (defined as requiring at least one transfusion every 8 weeks in a 4-month period) was given the same regression weight as progressing to a higher cytogenetic risk group. The model was shown to be time adaptable, such that patients could be continually re-evaluated and a prognostically useful updated score generated.³⁶

Investigators at the MD Anderson Cancer Center proposed a more comprehensive risk stratification system based on a retrospective analysis of 1,915 patients with MDS (including chronic myelomonocytic leukemia, secondary MDS, and MDS with prior therapy). The multivariate analysis of prognostic factors in the study group identified the following adverse prognostic factors: poor performance status, older age, thrombocytopenia, anemia, increased bone marrow blasts, leukocytosis, chromosome 7 or complex cytogenetic abnormalities, and prior transfusions. The proposed MDS prognostic model divided patients into four groups with significantly different outcomes. The model was validated in a test group. The model was predictive within all four traditional IPSS groups, in patients with primary and secondary MDS and with or without prior therapy.³⁷ The model was further refined in 865 patients with low or intermediate-1 IPSS risk disease; these patients could be further divided into three

distinct risk categories using information on degree of thrombocytopenia, patient age, cytogenetics, and marrow blast count divided patients into three distinct risk categories: low risk disease representing 21% of patients with a median survival of 80 months; intermediate risk diseases representing 48% of patients with a median survival of 26.6 months; and, high risk disease comprising 31% of the patients with a median survival of 14 months.³⁸ Of note, higher ferritin and beta-2-microglobulin levels were also associated with worse prognosis but were not included in the prognostic model because they added limited additional predictive value after adjustment for the other factors.

Although the IPSS was developed in a population of patients receiving nontransplant therapy, it has also been shown to predict transplant outcomes in several retrospective analyses.^{12,13,39,40} Other prognostic scoring systems have also been used, but are less well studied in the SCT setting. Platzbecker et al⁴¹ compared the outcomes of patients who were and were not transfusion dependent at the time of transplantation. Three-year overall survival was inferior in the transfusion dependent group when compared to the transfusion independent group (49% v 60%) despite the fact that the latter group included more patients with lower-risk disease. The prognostic impact of WPSS on transplant outcome was also documented in at least one retrospective analysis performed by Alessandrino et al.⁴²

The new proposed prognostic systems demonstrate that patients with low or intermediate 1 risk disease are a heterogeneous group of patients in which MDS can be a leading cause of death.⁴³ During the Coverage with Evidence Development phase, it will be important to identify the best system or systems for categorizing risk so that transplant and nontransplant outcomes can be compared in equivalent patients. It will also be important to determine whether there are specific individual factors that identify patients better served by specific therapies such as SCT. For example, none of the current prognostic scoring systems take into account the potential survival impact of specific cytogenetic abnormalities, serum ferritin levels, and/or gene expression profiles which have all been reported to be of prognostic significance.⁴⁴⁻⁴⁷

TIMING OF SCT IN OLDER PATIENTS

The optimal timing of transplantation for patients with MDS is controversial due to the uncertainty of transplant outcomes, but the certainty of eventual MDS disease progression. Many transplant physicians encourage early transplantation since an increasing number of single and multi-institution studies demonstrate good outcomes in this setting. There is inherent bias in these studies, since the patients included in these analyses are generally selected based on a variety of clinical parameters and often represent the best transplant candidates, by virtue of disease status, overall health, and ability to comply with complex medical therapy or other unmeasured factors.

The majority of analyses examining the timing of transplantation for MDS included patients who underwent myeloablative procedures. Deeg et al³⁹ reported on transplant outcomes of patients with MDS undergoing related or unrelated donor SCT and stratified outcomes based on the pretransplant IPSS risk score. There were no post-SCT relapses among the patients in the lowest IPSS score group, whereas the relapse rate was 42% for patients in the highest IPSS category. As a consequence, three-year survival was 80% in the lowest IPSS risk

group, but was lower 30% for patients in the high IPSS category. De Witte et al⁴⁰ also reported that earlier transplantation was associated with an absolute increase in overall survival of 10% at 4 years (57% v 47%; $P = .02$), and was associated with improved relapse-free survival in multivariable analysis.

Neither of these studies formally considered the results of non-SCT therapy in similar patients. To address this shortcoming, a Markov decision model was developed by Cutler et al⁴⁸ to understand how treatment decisions would affect overall outcome in large cohorts of patients with newly diagnosed MDS. The decision model was designed to determine if transplantation at the time of initial diagnosis, transplantation delayed for a fixed number of years, or transplantation delayed until the time of leukemic transformation was the optimal usage strategy for transplantation. Using data from several large, non-overlapping databases, it was demonstrated that the optimal treatment strategy for patients with low and intermediate-1 IPSS disease categories was to delay transplantation until the time of leukemic progression and immediate transplantation was recommended for patients with intermediate-2 and high-risk IPSS scores.

This model was developed in 2003 and included only younger patients (≤ 60 years) who had undergone SCT primarily in the 1990s. Consequently, it did not incorporate the impact of hypomethylating agents both before and after SCT as well as the potential impact of RIC regimens, and a variety of supportive care measure which have caused transplant-related mortality to decrease over time.⁴⁹⁻⁵⁴ Thus, in the context of the Coverage with Evidence Development phase currently being proposed by CMS, it may be timely to re-evaluate the decision model developed in 2003 for patients older than and younger than 65 years and incorporate newer prognostic schema as well as the results of hypomethylating agents and RIC regimens into the model. These analyses are currently underway.

All transplant series for MDS indicate that patients in remission or with low burden of disease have lower relapse rates and improved outcomes.^{22,39-41} However, studies evaluating whether reducing disease burden by administration of induction therapy before transplantation do not indicate improved results.^{22,30,55-58} These studies were done using traditional cytotoxic chemotherapy; results may differ if less intensive induction regimens incorporating 5-azacytidine, decitabine, lenalidomide, or clofarabine are used. So far, the data suggests no effect but the number of patients reported is too small to draw definitive conclusion. The Center for International Blood and Marrow Transplant is embarking on a registry analysis to examine this question in a larger cohort of patients.

CURRENT RESULTS OF ALLOGENEIC SCT IN THE MEDICARE BENEFICIARY POPULATION

The vast number of reports related to transplant outcomes for MDS include only a minority of patients older than 65 years. The largest studies to date come from registry analysis (Table 1). Lim et al⁵⁸ recently published the transplant outcomes of 1,333 patients with MDS older than 50 years reported to the European Group for Bone Marrow Transplant. The median age was 56 (range, 50 to 74) with 34% of patients being older than 60 years, 52% having advanced disease at the time of transplant and 62% receiving a RIC regimen. Overall survival for the whole group was 31% at 4 years, with 63% of patients dying of nonrelapse causes. The nonrelapse mortality rate was

Table 1. Largest Transplantation Series for Patients With MDS Older Than 60 Years of Age

Reference	No. of Patients	Age (years)		Percentage of Patients			OS/DFS at X Years (%)	NRM/RR at X Years (%)
		Median	Range	Age Older Than 60 Years	RIC	Advanced Disease		
McClune et al ³⁰	181	62 (patients age 60-64)		NA	68	60	45/35 at 2 years (patients age 60-64 years)	35/29 at 2 years (patients age 60-64 years)
		67 (patients age > 65)					38/36 at 2 years (patients age > 65 years)	39/25 at 2 years (patients age > 65 years)
Lim et al ⁵⁸	1,333	56	50-74	34	62	52	31 at 4 years	39/36 at 4 years

Abbreviations: MDS, myelodysplastic syndromes; RIC, reduced intensity conditioning; OS, overall survival; DFS, disease-free survival; NRM, nonrelapse mortality; RR, relapse risk; NA, not available.

36% at 4 years with no significant difference demonstrated in patients older or younger than 60 years. Patients receiving a myeloablative conditioning regimen had a higher risk of transplant-related mortality than those receiving an RIC regimen (44% v 32%). Relapse rates were higher in patients receiving RIC regimens than those receiving myeloablative conditioning (41% v 33%). On multivariate analysis, only advanced disease stage at transplantation emerged as a major predictor of overall survival.⁵⁸ McClune et al³⁰ reported on the outcomes of 181 patients with MDS older than 60 years (of which, 55 were older than 65 years). One hundred twenty-three patients (68%) received RIC regimens and 108 (60%) had advanced disease at the time of transplantation. Overall survival at 2 years was 45% for those 60 to 65 years and 38% for those older than 65 years. On multivariate analysis, transplant-related mortality was associated with donor-recipient HLA disparity, increasing donor age, and cytogenetic risk group. Relapse risk was associated with advanced disease, cytogenetic risk category, and use of nonmyeloablative conditioning versus RIC. Only Karnofsky performance score and degree of HLA matching predicted survival and disease-free survival.³⁰ Laport et al⁵⁹ reported on outcomes of 148 patients with AML or MDS who underwent transplantation with low intensity conditioning regimen incorporating fludarabine and 2.0 Gy of TBI. Half of the patients were older than 60 years. Overall survival for patients with MDS was 27% with nonrelapse mortality of 31% at 3 years.⁵⁹ These positive results provided the rationale for the request for National Coverage Analysis submitted by the National Marrow Donor Program and other interested parties.

OPTIMAL TRANSPLANTATION STRATEGY IN THE MEDICARE BENEFICIARY POPULATION

Recently the American Society for Blood and Marrow Transplantation published an evidence-based review addressing some of the issues that will be important to consider when the role of SCT in the Medicare beneficiary population is analyzed. Table 2 summarizes the most important conclusions found within the American Society for Blood and Marrow Transplantation document.²²

Of all the transplant-related variables relevant to outcomes in the Medicare beneficiary population, regimen intensity is probably the most controversial. RIC regimens began to be explored in the mid-1990s for older patients with MDS or AML.²³⁻²⁵ The rationale for reducing regimen intensity was the premise that the graft-versus-malignancy effect could be effective without myeloablative therapy, as seen in some situation with donor lymphocyte infusions.^{60,61} Since RIC regimens allow engraftment of donor stem cells without many of

the toxicities of myeloablative therapies, it was also postulated that reduction in tissue damage and associated lessening of inflammatory cytokines, would also lower the risk of acute GVHD.⁶⁰

The issue of optimal dose intensity for MDS patients has not been resolved. De Lima et al⁶² reported that patients receiving a truly nonablative regimen with fludarabine and cytarabine had a higher relapse rate and inferior outcomes than patients receiving a more intense regimen of fludarabine and melphalan. Luger et al⁶³ reported on transplant outcomes of 3,731 patients with AML or MDS who underwent an allogeneic SCT and compared them to the results of 1,500 patients who received either a RIC or nonmyeloablative regimen. Patients receiving a nonmyeloablative regimen had a higher relapse rate and lower probability of long-term disease control when compared to patients receiving a conventional ablative regimen.

Currently, busulfan-based regimens are being used with increasing frequency for transplant conditioning for MDS.⁶⁴ Both oral busulfan with pharmacologic targeting and intravenous busulfan are shown to reduce the incidence of serious transplant complications and are reported to improve transplant outcomes in MDS.^{39,64-67} The substitution of fludarabine for cyclophosphamide as part of the conditioning regimen is also associated with good tolerance and low NRM rates in both the ablative and reduced intensity setting.^{66,67} Thus, the issue of dose intensity becomes more complex since advances in chemotherapy preparations and pharmacokinetic monitoring now allow myeloablative doses to be safely given to selected patients older than 60 years.⁶⁸

Comorbidity scoring and performance status have been suggested as strategies to guide dose adjustment and to identify fit 65- to 70-year-old patients who can tolerate myeloablative conditioning while those with comorbidities receive less intense regimens.^{69,70}

SUMMARY AND FUTURE DIRECTIONS

The situation in the United States for Medicare beneficiaries with MDS before August 4, 2010, depended on the geographical location chosen for their SCT evaluation since CMS did not have a national policy addressing the issue of coverage for allogeneic transplantation for patients with MDS and hospitals were uncertain whether services rendered would be covered. This situation was difficult for patients and physicians alike since the presence of more than 20% peripheral blood or bone marrow blasts would allow the same patient to undergo SCT as a covered benefit with the diagnosis of AML.

The proposed Coverage with Evidence Development that CMS has recommended is a helpful and thoughtful step forward since it

Table 2. Issues to be Addressed During the CED Phase of Allogeneic SCT for Older Patients With MDS (adapted from Oliansky et al²²)

Variable or Issue	Observation	Evidence Available	Current Recommendations	Issues for Medicare Beneficiaries	Recommendations for CED Phase
Timing of transplantation	Transplant outcomes improve when patients undergo transplantation earlier in the course of the disease	Retrospective review and expert panel	Early SCT for patients with an IPSS score of INT-2 or high risk at diagnosis, who have a suitable donor	Limited data for older patients with low-risk or INT-1 disease; retrospective data do not include role of hypomethylating agents	Define patient populations to be studied with both transplant and nontransplant strategies that have comparable natural histories
Pre-SCT chemo	Transplant outcome not improved by pre SCT induction therapy	Retrospective analysis and expert panel	The decision to use pre-SCT induction therapy should be made on an individual basis	No data regarding the impact of pre-SCT hypomethylating agent induction impacting transplant outcomes	Registry analysis of potential impact of hypomethylating use before SCT as a predictor of transplant outcome; collect data on pre-SCT therapy and response to therapy on all patients
Donor selection	With current HLA typing techniques outcomes for siblings and unrelated donors are similar; limited data on cord blood grafting are available	Retrospective review and expert panel	Fully matched related sibling if available; if not fully matched unrelated donor	Older patients usually have older donors; impact of donor age on transplant outcomes uncertain (particularly because outcomes for patients receiving cells from donors older than 60 years of age are uncertain)	Registry analysis of transplant outcomes for patients older than 65 according to donor age and relationship
Cell source BM v PB	PBSCT associated with higher rates of chronic GVHD but lower rates of relapse in patients with high-risk malignancies	Prospective and retrospective studies in sibling donors; retrospective analysis and expert panel in unrelated donor transplantation	For low-risk disease, PBSCT and BMT from related donors have similar outcomes; for high-risk disease PBSCT may have a survival benefit; uncertain in unrelated donors	The risk/benefit ratio of PB v BM may be different in older patients with MDS and may differ using RIC regimens	Limited data from the BMT-CTN trial comparing outcomes of unrelated donor PB v BM should be available for subset analysis with emphasis on patients older than the age of 65; registry analysis of patients older than the age of 65
Conditioning regimen	No evidence for benefit of any specific conditioning regimen although high dose TBI felt to be more toxic	Retrospective analysis	No specific recommendations given	Limited data for Medicare beneficiaries; most receive NMA or RIC conditioning; in selected patients fully ablative fludarabine and busulfan has been given	Prospective trials are required to determine whether optimal conditioning regimens exist for patients older than the age of 65

Abbreviations: CED, Coverage with Evidence Development; SCT, stem-cell transplantation; MDS, myelodysplastic syndromes; IPSS, International Prognostic Scoring System; INT-2, intermediate risk 2; BM, bone marrow; PB, peripheral blood; GVHD, graft-versus-host disease; BMT, bone marrow transplant; RIC, reduced intensity conditioning; BMT-CTN, Blood and Marrow Transplant Clinical Trials Network; TBI, total body irradiation; NMA, nonmyeloablative.

now allows all Medicare beneficiaries to undergo allogeneic transplantation if they are deemed adequate candidates and participate in a clinical study addressing one of the following issues: prospective comparison of outcomes between Medicare beneficiaries with MDS who did and did not receive a SCT; prospective determination of the prognostic significance of IPSS score, patient age, cytopenias, and comorbidities on transplant outcomes of Medicare beneficiaries; or prospective determination of what treatment facility characteristics impact transplant outcomes in Medicare beneficiaries with MDS who receive a SCT.

What is yet to be determined are the details and specifics behind this recommendation and whether these trials need to be cleared by CMS in addition to local institutional review boards.

A prospective randomized trial of transplant versus nontransplant therapy for Medicare beneficiaries with MDS who have HLA compatible donors would provide the definitive answer to this question, however, such an approach would have many limitations. First, it would take many years to plan and execute and would likely enroll only a small proportion of the ultimate target population for this therapy. Second, it would likely not be large enough or inclusive enough (of either patients or transplant and nontransplant approaches) to address the many issues addressed in the preceding

paragraphs, such as best staging system, best pretransplant therapy, and best conditioning regimens.

Ideally, one would like a protocol that could be implemented across the country in all or most transplant centers with minimal delay and that would ensure that patients receive the best possible care based on currently available knowledge. A large, multicenter prospective cohort study that would gather the necessary information regarding patient, disease, and transplant characteristics to validate risk factors and scoring systems and perform comparative effectiveness analyses is probably the most appropriate approach to addressing the issues raised in the Coverage with Evidence Development. Using the existing infrastructures for SCT data collection available through the United States Stem Cell Outcome Database may allow such a study to be activated quickly and in the most cost-efficient way. However, the Stem Cell Outcome Database has not previously collected data on non-SCT patients; collaboration with clinical trials networks and others with experience in evaluation of non-SCT MDS therapy will be necessary. In fact, to ensure that patients receive appropriate care while advancing knowledge essential to understanding the appropriate role of SCT in treating MDS in the Medicare population will require cooperation of individuals with a broad ranges of expertise including,

among others, transplanters, hematologists, oncologists, statisticians, and patient advocates.

AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

The author(s) indicated no potential conflicts of interest.

AUTHOR CONTRIBUTIONS

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