American Society of Hematology

Carrier Advisory Committee Virtual Meeting

June 25, 2021

Virtual Annual Meeting
Zoom Teleconference
10:00 a.m. – 1:00 p.m. ET

American Society of Hematology

Helping hematologists conquer blood diseases worldwide

Hematology Carrier Advisory Committee
Virtual Annual Meeting Agenda

June 25, 2021

10:00 am	Welcome & Introductions	
	• Speaker List • ASH Staff • Contractor Medical Director (CMD) List • Jurisdiction Map	Steve Allen, MD Harriet Bering, MD
10:15 am	Removal of Coverage with Evidence Development (CED) for Stem Cell Transplantation for Myelodysplastic Syndromes (MDS)	
	• Biologic Assignment Trial of Reduced-Intensity Hematopoietic Cell Transplantation Based on Donor Availability in Patients 50-75 Years of Age With Advanced Myelodysplastic Syndrome	Corey Cutler, MD, MPH Doug Rizzo, MD, MS
11:15 am	Coverage for Hematopoietic Stem Cell Transplantation for Certain Patients with Lymphoma	
	• ASH / ASTCT Letter to Medical Directors	Dianna Howard, MD Gary Oakes, MD
11:45 am	BREAK	
12:00 pm	Overview of New ASH Guidelines as it Relates to Evidence Needed for Local Coverage Decisions	
	• ASH Clinical Practice Guidelines	Lisa Hicks, MD Barbara Konkle, MD
12:30 pm	Open Discussion: Coverage Issues	
12:50 pm	Closing Remarks	
	• Centers for Medicare & Medicaid Services (CMS) Resources • ASH Practice Resources	Dr. Allen Dr. Bering
1:00 pm	Adjourn	

Speaker List

Corey Cutler, MD, MPH
Corey Cutler, MD, MPH received his medical doctor degree from McGill University, Montreal, Canada. He subsequently received his Master of Public Health degree from the Harvard school of Public Health. He completed postgraduate training in Internal Medicine at Royal Victoria Hospital, Montreal, followed by a fellowship in Hematology/Oncology at DFCI. In 2002, he joined DFCI, where he is currently Medical Directory of the Adult Stem Cell Transplantation Program. Dr. Cutler co-chaired the national BMT CTN trial comparing transplantation with non-transplant therapy for MDS.

Doug Rizzo, MD, MS
Doug Rizzo, MD, MS received his medical doctor degree from Johns Hopkins University School of Medicine in 1990. From 1994-1998 he was Senior Clinical Fellow, Johns Hopkins University School of Medicine, in the departments of oncology and hematology. Dr. Rizzo completed a Robert Wood Johnson fellowship in epidemiology and cost-effectiveness research at Johns Hopkins University in 1998. He received an MS in epidemiology from the Medical College of Wisconsin in 2005. He joined the Medical College of Wisconsin and CIBMTR in 1998 and has been the Project Director of the Stem Cell Therapeutic Outcomes Database since 2008. Dr. Rizzo serves as the Associate Director for Cancer Services for the Froedtert and MCW Cancer Center.

Dianna Howard, MD
Dianna Howard, MD has been the director of a bone marrow transplant (BMT) program for 15 years, first at the University of Kentucky, and now at Wake Forest. Both programs provide care to a swath of the Appalachian region and a subset of patients for whom barriers to access either because of co-morbidities, distance, or delay in referral remain a challenge. Dr. Howard has a special interest in the adolescent and young adult (AYA) population as she is trained in both pediatric and internal medicine. When Dr. Howard joined Wake Forest, her priorities included improving data management and quality reporting to Center for International Blood and Marrow Transplant Research (CIBMTR); transitioning autologous transplant care to outpatient; starting a transplant survivorship program; and positioning Wake as a center of excellence with insurers so patients would have access to transplant without having to travel. BMT programs are evaluated on volume and outcomes - accomplishing both at the same time is an imperative with greater challenges in modest sized transplant programs. Dr. Howard has been involved in efforts focused on expanding regional access for patients who need transplant. Her team was awarded an ASHP Best Practice Award in 2017 for our Autologous SCT outpatient program, recognizing our inclusion of clinical practice pharmacists. Consistent with her interest in patient access to health care, she has participated in advocacy campaigns with LLS, ACP, ASH and ASTCT. Dr. Howard completed the ASH Advocacy Leadership Institute and serves on ASH Committee of Government Affairs. Dr. Howard also serves on ASTCT Outcomes Committee, as faculty for the inaugural ASTCT Leadership Course, Co-Chair the ASTCT Leadership course for 2020, Chair ASTCT Government Relations Committee, and represents ASTCT on ASH Committee on Practice and ACP Council of Subspecialists, where she has co-chaired a health policy subcommittee. Through this level of committee engagement Dr. Howard has been able to work with colleagues to advocate for access to transplant and cell therapy - advancing health policy that impacts patient barriers. At Wake Forest she has worked with the government policy office to respond to the call for comments to CMS on issues important to our transplant program and led a regional effort to influence insurer policy with regard to transplant reimbursement practices.

Gary Oakes, MD
Gary Oakes, MD is currently one of the Contractor Medical Directors at Noridian HealthCare solutions with oversight of Medicare Jurisdictions E and F. He is a graduate of the University of Tennessee College of Medicine. He completed his residency in Family Medicine in the United States Navy where he later served as one of the Senior Medical Officers during the Operations Desert Shield/Desert Storm, where he was awarded the Navy Commendation Medal. He is board certified and a Fellow with the American Board of Family Medicine. He participates as a physician with the National Disaster Medical System serving with TN-1 DMAT.

Lisa Hicks, MD
Dr. Lisa Hicks is a malignant hematologist at St. Michael's Hospital in Toronto, Canada. She has a clinical focus in lymphoproliferative disease and an academic focus in health services research and quality improvement. Dr. Hicks is the Chair of the Committee on Quality for the American Society of Hematology and was a panel member on the ASH VTE Guidelines: Prevention and Treatment in Patients with Cancer.

Barbara Konkle, MD
Barbara Konkle, MD is the Chief Scientific Officer and Associate Director for the Washington Center for Bleeding Disorders at Bloodworks Northwest and a Professor of Medicine at the University of Washington. Dr. Konkle received her MD at Vanderbilt University and completed her residency at Rush Presbyterian-St. Luke's in Chicago and her residency in Hematology/Oncology at the University of Michigan, Ann Arbor. She currently sees patients with bleeding disorders in the Washington Center for Bleeding Disorders and patients with disorders of hemostasis at Seattle Cancer Care Alliance.

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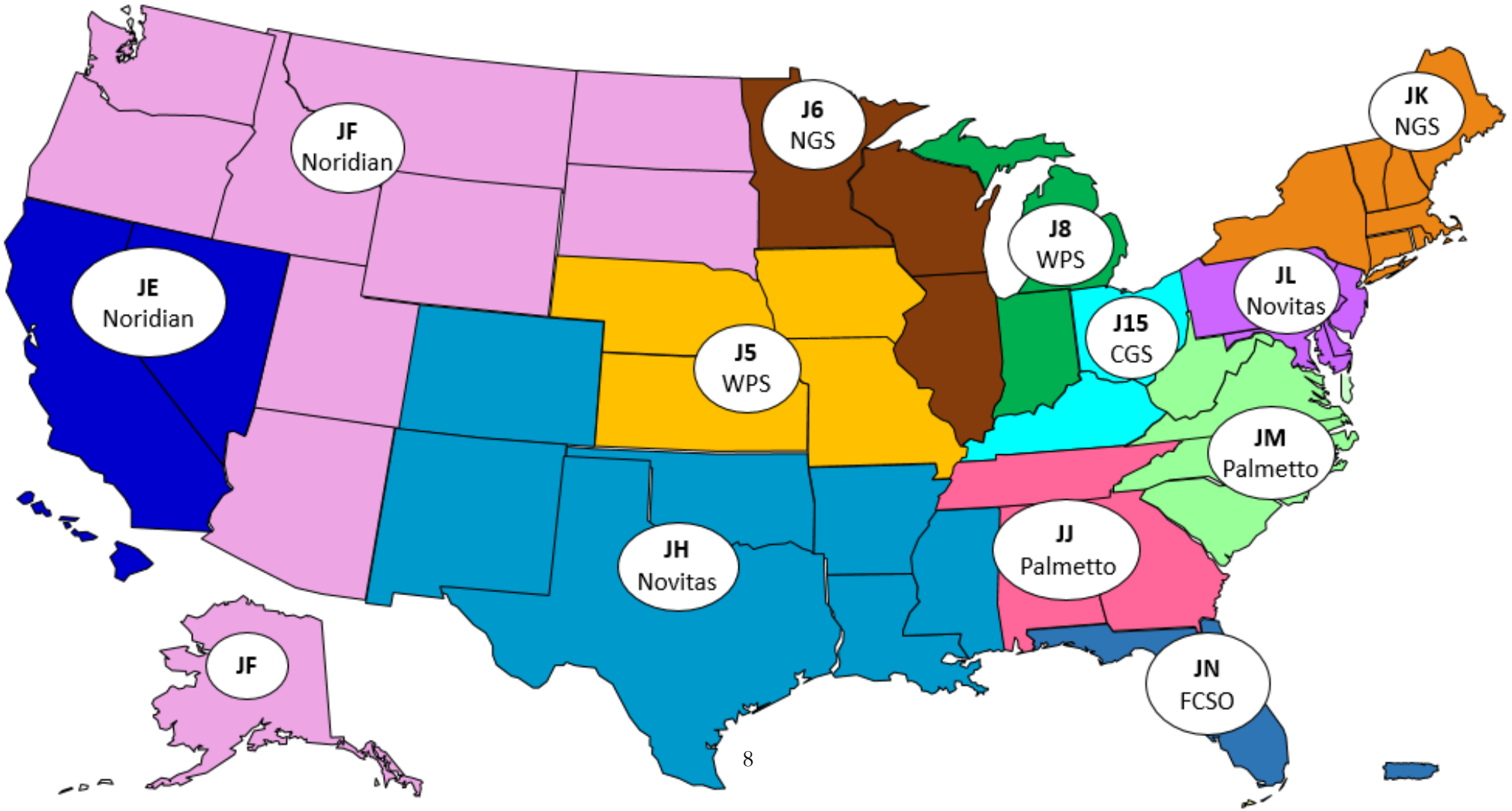
as of June 2019



original reports

Biologic Assignment Trial of Reduced-Intensity Hematopoietic Cell Transplantation Based on Donor Availability in Patients 50-75 Years of Age With Advanced Myelodysplastic Syndrome

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abstract

PURPOSE Allogeneic hematopoietic cell transplantation (HCT) is the only potentially curative therapy for myelodysplastic syndromes (MDS), although it is infrequently offered to older patients. The relative benefits of HCT over non-HCT therapy in older patients with higher-risk MDS have not been defined.

METHODS We conducted a multicenter biologic assignment trial comparing reduced-intensity HCT to hypomethylating therapy or best supportive care in subjects 50-75 years of age with intermediate-2 or high-risk de novo MDS. The primary outcome was overall survival probability at 3 years. Between January 2014 and November 2018, we enrolled 384 subjects at 34 centers. Subjects were assigned to the Donor or No-Donor arms according to the availability of a matched donor within 90 days of study registration.

RESULTS The median follow-up time for surviving subjects was 34.2 months (range: 2.3-38 months) in the Donor arm and 26.9 months (range: 2.4-37.2 months) in the No-Donor arm. In an intention-to-treat analysis, the adjusted overall survival rate at 3 years in the Donor arm was 47.9% (95% CI, 41.3 to 54.1) compared with 26.6% (95% CI, 18.4 to 35.6) in the No-Donor arm ($P = .0001$) with an absolute difference of 21.3% (95% CI, 10.2 to 31.8). Leukemia-free survival at 3 years was greater in the Donor arm (35.8%; 95% CI, 29.8 to 41.8) compared with the No-Donor arm (20.6%; 95% CI, 13.3 to 29.1; $P = .003$). The survival benefit was seen across all subgroups examined.

CONCLUSION We observed a significant survival advantage in older subjects with higher-risk MDS who have a matched donor identified and underwent reduced-intensity HCT, when compared with those without a donor. HCT should be included as an integral part of MDS management plans in fit older adults with higher-risk MDS.

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INTRODUCTION

Myelodysplastic syndrome (MDS) is predominantly a disease of older adults, with a median age at onset of 76 years.[1] Although there are few available therapeutic options, DNA hypomethylating agents (HMA) can improve hematologic parameters, reduce transfusion requirements, delay transformation to acute myelomonocytic leukemia (AML), and prolong progression-free survival and overall survival (OS) in individuals with higher-risk disease.[2-5] However, fewer than half of the patients with MDS achieve objective responses to hypomethylating therapy, and these responses are usually of limited duration. When patients develop HMA resistance, prognosis is dismal with few treatment options.[6,7] Allogeneic hematopoietic cell transplantation (HCT) is the only curative therapy for MDS and an established therapy for younger patients with MDS.[8-10] Although transplantation outcomes among selected older individuals with MDS are similar to those in younger patients with MDS,[11,12] early transplantation for older individuals is not broadly accepted. Statistical modeling analyses demonstrate the benefits of early HCT in older populations,[13,14] and two prospective studies from European groups showed a benefit of HCT over non-HCT therapy when a suitable donor is available.[15,16]

We designed a clinical trial to address the research question regarding the appropriateness of allogeneic HCT in this older population within the guidelines set forth by Centers for Medicare and Medicaid Services' (CMS) decision memo.[17,18] Although a randomized study comparing transplantation to nontransplant

ASSOCIATED CONTENT

Data Supplement

Protocol

Author affiliations and support information (if applicable) appear at the end of this article.

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CONTEXT

Key Objective

To determine whether having a suitable HLA-matched donor improves outcomes for older patients with higher-risk myelodysplastic syndrome (MDS) who are candidates for reduced-intensity allogeneic stem-cell transplantation.

Knowledge Generated

Overall survival and leukemia-free survival were statistically significantly and clinically meaningfully prolonged in individuals who had donors in comparison with those who did not. Quality of life was not impaired with transplantation.

Relevance

MDS is common among older individuals, and allogeneic stem-cell transplantation is underutilized in this age group. This study demonstrates that having a suitable donor for allogeneic stem-cell transplantation is associated with improved survival. Consultation for allogeneic stem-cell transplantation should occur early in the disease course for older individuals with higher-risk MDS to identify donors. Allogeneic transplantation should be used in this older age-group with MDS.

therapies would be optimal, this design was considered impractical.[19-21] We, therefore, conducted a multicenter, biologic assignment trial in subjects 50-75 years of age with advanced de novo MDS (defined as intermediate-2 or high-risk MDS risk score per the International Prognostic Scoring System [IPSS])[22] considered eligible for a reduced-intensity conditioning (RIC)[23] allogeneic HCT, comparing outcomes of those with a suitable donor to those without a suitable donor.

METHODS

Study Design

The study was an open-label, multicenter, biologic assignment trial conducted by the Blood and Marrow Transplant Clinical Trials Network (BMT CTN 1102).[19] Biologic assignment was to a Donor or No-Donor arm based on high-resolution HLA typing of eligible family members and a 90-day search of the unrelated donor registry through the National Marrow Donor Program. Subjects assigned to the Donor arm were expected to undergo RIC HCT within 6 months of enrollment, whereas those assigned to the No-Donor arm were expected to receive non-HCT therapy or best supportive care. The target enrollment was 338-400 subjects, dependent on the ratio of Donor vs. No-Donor assignment, where 60%-70% of subjects were expected to have a donor identified within 90 days. The primary end point was 3-year OS from registration in an intention-to-treat analysis. Prespecified secondary end points included 3-year leukemia-free survival (LFS), quality-of-life (QOL) measures, and cost effectiveness. Enrollment began in January 2014 and ended in November 2018. In February 2020, an independent Data and Safety Monitoring Board released the study data for analysis. Information regarding Study Oversight can be found in the Data Supplement (online only).

Subjects and Treatment

Eligible subjects were between 50 and 75 years of age and were considered to be candidates for RIC HCT from an HLA-matched related or 8/8 HLA-matched unrelated donor (HLA-A, B, C, and DR using high-resolution typing) by the treating hematologist. All subjects were required to have been diagnosed with de novo intermediate-2 or high-risk MDS by IPSS criteria. Individuals for whom a myeloablative transplant or an alternative donor transplant (mismatched unrelated, haploidentical, or umbilical cord blood) was planned were ineligible. The definition of RIC HCT regimens was based on the Center for International Blood and Marrow Transplant Research criteria.[23] All subjects provided written informed consent before enrollment. Subjects received RIC HCT or non-HCT therapy according to institutional standards. Subjects not undergoing transplantation were eligible to receive HMA therapy or supportive care at referring institutions, whereas HCT was performed at the enrolling site. More details are available in the full Protocol (online only), available on the BMT CTN website.[24]

Statistical Analysis

The primary analysis was an intention-to-treat analysis of all enrolled subjects. Subjects were initially assigned to the No-Donor arm at the time of consent; subjects were immediately reassigned to the Donor arm when a suitable donor was identified, whereas those whose 90-day donor search ended without a donor identified or who died before the search ended remained in the No-Donor arm. Subjects who died or withdrew without finding a donor during the search period could potentially bias this analysis, but this was expected to occur infrequently and additional sensitivity analyses removed these cases to examine their impact. The primary analysis compared 3-year OS between arms using adjusted survival estimates[25] to account for the potential bias resulting from biologic assignment,[26] adjusting for prespecified characteristics: age, race or ethnicity, performance status, disease status, comorbidity index, IPSS score, MDS disease duration, and response to HMA therapy. Deaths from any cause were considered failures for OS; subjects followed for < 3 years were censored at their last contact date. A point-wise comparison

of three-year survival was used rather than the Cox proportional hazards model because of the potential for non–proportional hazards because of early mortality after HCT.

The targeted sample size was selected to provide at least 80% power to detect a 15% difference in the 3-year OS rate between the two study groups, assuming survival of 35%-40% in the Donor arm and 20%-25% in the No-Donor arm and 10% loss to follow-up. Since the required sample size depended also on the true, unknown proportion of donor availability, treatment assignment was monitored during the study. This study used a group sequential design with a maximum of four efficacy analyses planned, three interim and one final, the first occurring at study enrollment closure and yearly thereafter. A Bonferroni correction was used to control the overall type I error rate for multiplicity, with a Haybittle-Peto boundary of 3.00 used for interim analyses and 2.03 for the final analysis. Confidence intervals and *P* values for the OS primary analysis are adjusted for multiple interim analyses.

A prespecified, as-treated analyses was also performed for OS and LFS at 3 years, adjusting for the above-mentioned variables, with death and transformation to AML considered LFS failures. QOL was measured by the Functional Assessment of Cancer Therapy—General, the Medical Outcomes Study 36-Item Short Form Survey Physical Component Score and Mental Component Score, and the EuroQol-5D utility score,[27-29] and changes in scores from enrollment were compared between arms using analysis of covariance models adjusted for enrollment score. *P* values $< .05$ were considered statistically significant and QOL score differences greater than half a standard deviation were considered clinically meaningful. Prespecified subgroup analyses by response to HMA, age, disease duration, and IPSS were conducted using treatment interaction terms in pseudovalue regression models for 3-year OS and LFS.[30]

In Donor arm subjects who underwent HCT within 6 months of biologic assignment, post-transplant outcomes of OS, disease-free survival (DFS, defined as freedom from death, MDS recurrence, and AML transformation), relapse, treatment-related mortality (TRM), and acute and chronic graft-versus-host disease (GVHD) were described using the Kaplan-Meier and Aalen-Johansen estimators. These outcomes are described through 27 months post-HCT to coincide with the primary end point's 3-year time point and the 9-month window during which Donor arm subjects are expected to undergo transplant. For these outcomes, multivariable models were constructed using stepwise variable selection to assess the potential influence of response to HMA, age, disease duration, IPSS, and Revised International Prognostic Scoring System.

RESULTS

Enrollment and Subject Characteristics

Enrollment occurred between January 2014 and November 2018, with 384 subjects (median age 66.7 years; 235 [62.1%] > 65) registered at 34 transplantation centers and biologically assigned to the Donor (n = 260) or No-Donor (n = 124) arms (Fig 1). Subject and donor characteristics are shown in Table 1. The Donor and No-Donor arms were well balanced with respect to age, sex, Karnofsky performance status, IPSS disease risk, MDS disease duration, and in their use of, and responsiveness to, HMA. The Data and Safety Monitoring Board permitted early release of the study data for publication following an efficacy finding at the second interim analysis. At the time of analysis, 287 (74.7%) subjects had complete 3-year data for analysis, with an additional 47 (12.2%) followed for at least 2 years from registration. Follow-up was similar between study arms (completeness index: 94.4% in the Donor arm and 93.9% in the No-Donor arm).[31] Three subjects (1%) withdrew consent. Seven subjects died during the 90-day search period without finding a donor and were analyzed in the No-Donor arm. Five subjects died in the Donor arm before the 90-day search window ended and were analyzed in the Donor arm.

Overall Survival

At the time of the analysis, 211 subjects had died (125 Donor and 86 No-Donor). The median follow-up time for surviving subjects was 34.2 months (range: 2.3-38 months) in the Donor arm and 26.9 months (range: 2.4-37.2 months) in the No-Donor arm. Adjusted OS at 3 years was significantly higher in the Donor arm when compared with the No-Donor arm: 47.9% (95% CI, 41.3 to 54.1) versus 26.6% (95% CI, 18.4 to 35.6, absolute improvement 21.3% [95% CI, 10.2 to 31.8], $P = .0001$; Fig 2A, Data Supplement). High IPSS risk score significantly affected OS outcomes (reference: intermediate-2 risk: hazard ratio [HR] 1.75, $P < .0001$), as did no response to HMA before HCT (reference: no exposure to HMA, HR 1.64, $P = .0097$; Data Supplement). In a sensitivity analysis, excluding the eight subjects assigned to the No-Donor arm who died (n = 7) or withdrew (n = 1) before the end of the 90-day search window had no effect on outcomes (adjusted OS: 48.0% *v* 28.1%, $P = .0004$). Subgroup analyses of OS found no evidence of interactions between treatment assignment and age group (older than or younger than 65 years, $P = .73$), HMA response type ($P = .33$), or other factors considered (Fig 2B).

Leukemia-Free Survival

LFS was significantly higher in the Donor arm when compared with the No-Donor arm at 3 years: 35.8% (95% CI, 29.8 to 41.8) versus 20.6% (95% CI, 13.3 to 29.1, absolute improvement: 15.2% [95% CI, 13.3 to 29.1], $P = .003$; Fig 2C, Data Supplement). Significant predictors of LFS included high-risk IPSS score (HR 1.541, $P = .0011$) and unresponsiveness to HMA (HR 1.643, $P = .0037$; Data Supplement). Excluding subjects in the No-Donor arm who died or withdrew during the 90-day donor search window had no effect on outcomes (35.9% *v*

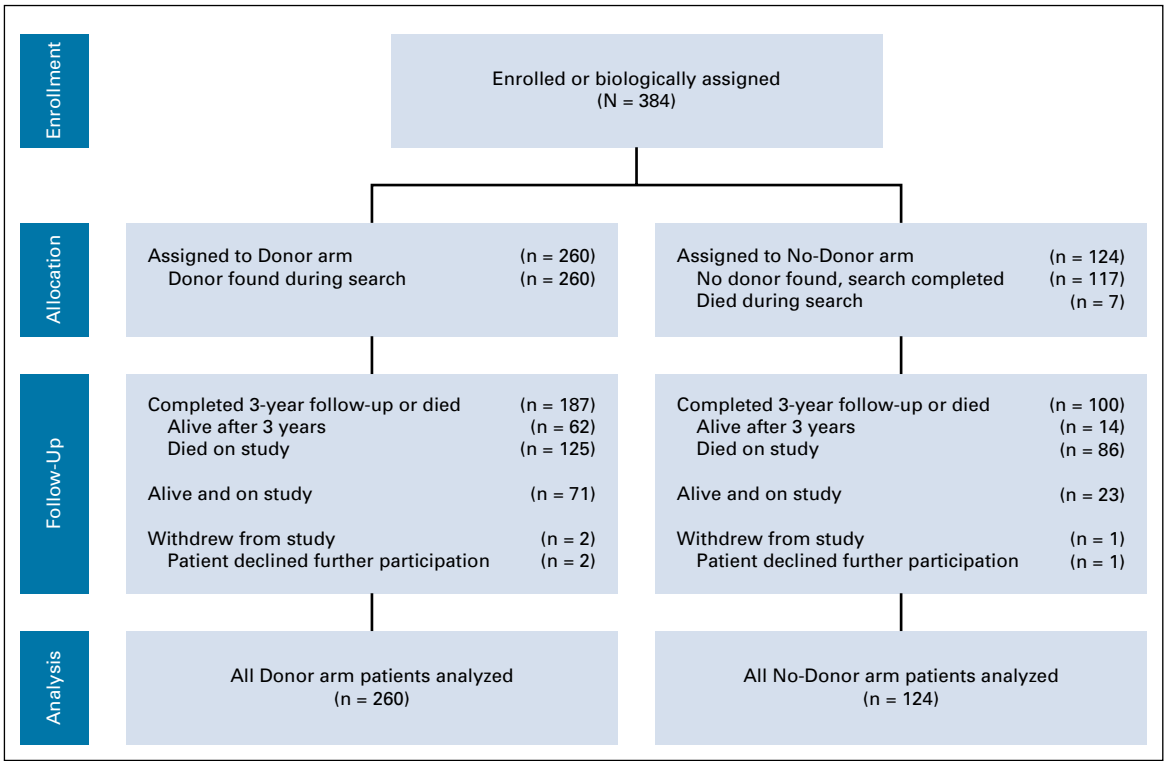

FIG 1. CONSORT diagram for BMT CTN 1102. Two hundred sixty (67.7%) of the enrolled subjects were biologically assigned to the Donor arm and 124 (32.3%) assigned to the No-Donor arm. On the Donor arm, 187 (71.9%) of the participants have completed the 3-year follow-up period, with 62 surviving until 3 years and 125 dying. Of the No-Donor arm participants, 100 (80.6%) have completed the follow-up period, 14 surviving until the 3 years and 86 dying. Three subjects withdrew from study, two on the Donor arm and one on the Non-Donor arm, each declining to participate further in completing study visits and quality-of-life assessments. The remaining 71 subjects on the Donor arm and 23 on the Non-Donor arm are still being followed until the 3-year mark.

21.8%, $P = .0074$). Subgroup analysis of LFS detected no interactions of treatment assignment with age group (older than or younger than 65 years, $P = .90$), HMA response type ($P = .99$), or any other factor (Fig 2D).

Treatment Compliance and As-Treated Analysis

The overall noncompliance rate for the trial was 26.3% (Data Supplement). Overall, 44 subjects (16.7%) in the Donor arm did not undergo HCT because of disease progression to AML (18), subject preference (16), progressive comorbidity (7), donor or insurance issues (2), and death (1). In addition, 26 subjects (10%) in the Donor arm received a myeloablative HCT because of physician or subject preference (14), or disease-related issues (12). In the No-Donor arm, 31 subjects (25%) underwent HCT, including nine who found a matched donor after the 90-day search period (one related and eight unrelated). All others received alternative donor transplant, including six who received myeloablative conditioning.

In the as-treated analysis, OS comparing the HCT and No HCT arms demonstrated a significant advantage in 3-year OS (47.4% *v* 16.4%, $P < .0001$) and LFS (39.3% *v* 10.9%, $P < .0001$) for subjects who underwent HCT (Figs 3A and 3B). Among subjects in the No-Donor arm who underwent alternative donor HCT within 6 months of assignment in the absence of disease progression to AML (n = 25), 3-year OS and LFS were both 58.5%.

Transplantation Outcomes

Among the 216 Donor arm subjects who underwent HCT within 6 months of biologic assignment, OS was 55.7% (95% CI, 48.4 to 62.4) and DFS was 49.7% (95% CI, 42.6 to 56.5) at 27 months post-HCT. The estimated median DFS is 26.1 months; median OS has not been reached, with a median follow-up post-HCT among survivors of 28.4 months (interquartile range: 18.0-32.0 months). One hundred-day and 1-year TRM were 7.4% and 15.5%, respectively. In multivariable models, higher IPSS risk score was a significant predictor of both OS (HR 1.85; 95% CI, 1.21 to 2.83; $P = .004$) and DFS (HR 2.17; 95% CI, 1.47 to 3.20; $P < .0001$), whereas response to HMA only predicted OS (baseline: no treatment, HR 2.42 for any response, 2.17 for no response, $P = .005$ and .01, respectively; Data Supplement). At 27 months post-HCT, the cumulative incidence of relapse following HCT was 29.6% (95% CI, 23.5 to 35.9), and TRM was 20.6% (95% CI, 15.3 to 26.5).

TABLE 1. Baseline Clinical Characteristics of Enrolled Subjects

Subject Characteristic	Donor Arm (n = 260), No. (%)	No-Donor Arm (n = 124), No. (%)	Total (N = 384), No. (%)
Age, years			
Mean (SD)	65.6 (5.6)	66.0 (5.9)	65.7 (5.7)
Median (range)	66.3 (50.1-75.3)	67.3 (50.7-75.1)	66.7 (50.1-75.3)
65 or older	155 (59.6)	80 (64.5)	235 (61.2)
Sex			
Female	95 (36.5)	48 (38.7)	143 (37.2)
Male	165 (63.5)	76 (61.3)	241 (62.8)
Ethnicity			
Hispanic or Latino	11 (4.2)	9 (7.3)	20 (5.2)
Not Hispanic or Latino	233 (89.6)	108 (87.1)	341 (88.8)
Unknown	9 (3.5)	7 (5.6)	16 (4.2)
NA	7 (2.7)	0 (0.0)	7 (1.8)
Race			
American Indian or Alaskan	1 (0.4)	1 (0.8)	2 (0.5)
Asian	8 (3.1)	2 (1.6)	10 (2.6)
Hawaiian or Pacific Islander	0 (0.0)	0 (0.0)	0 (0.0)
Black or African American	6 (2.3)	9 (7.3)	15 (3.9)
White	234 (90.0)	105 (84.7)	339 (88.3)
More than one race	0 (0.0)	0 (0.0)	0 (0.0)
Other, specify	1 (0.4)	0 (0.0)	1 (0.3)
Unknown	6 (2.3)	4 (3.2)	10 (2.6)
NA	4 (1.5)	3 (2.4)	7 (1.8)
KPS[a]			
90–100	99 (55.0)	35 (41.7)	134 (50.8)
< 90	81 (45.0)	49 (58.3)	130 (49.2)
ECOG performance status[a]			
0	24 (30.0)	16 (40.0)	40 (33.3)
> 0	56 (70.0)	24 (60.0)	80 (66.7)
MDS subtype			
RCUD	5 (1.9)	1 (0.8)	6 (1.6)
RARS	5 (1.9)	2 (1.6)	7 (1.8)
RAEB-1	61 (23.5)	31 (25.0)	92 (24.0)
RAEB-2	132 (50.8)	63 (50.8)	195 (50.8)
RCMD	36 (13.8)	14 (11.3)	50 (13.0)
Isolated del(5q)	6 (2.3)	7 (5.6)	13 (3.4)
Unclassifiable	15 (5.8)	6 (4.8)	21 (5.5)
MDS duration from diagnosis to enrollment, months			
Mean (SD)	8.4 (21.6)	11.0 (27.1)	9.2 (23.5)
Median (range)	2.5 (0.2-182.3)	2.2 (0.3-211.6)	2.3 (0.2-211.6)
Highest IPSS score			
Intermediate-2 (1.5-2.0)	173 (66.5)	81 (65.3)	254 (66.1)
High risk (≥ 2.5)	87 (33.5)	43 (34.7)	130 (33.9)

(continued on following page)

TABLE 1. Baseline Clinical Characteristics of Enrolled Subjects (continued)

Subject Characteristic	Donor Arm (n = 260), No. (%)	No-Donor Arm (n = 124), No. (%)	Total (N = 384), No. (%)
Highest IPSS-R score			
Very low	4 (1.5)	0 (0.0)	4 (1.0)
Low	2 (0.8)	0 (0.0)	2 (0.5)
Intermediate	79 (30.4)	34 (27.4)	113 (29.4)
High	82 (31.5)	51 (41.1)	133 (34.6)
Very high	93 (35.8)	39 (31.5)	132 (34.4)
Response to hypomethylating therapy			
Complete response	10 (3.8)	7 (5.6)	17 (4.4)
Partial response	46 (17.7)	23 (18.5)	69 (18.0)
No response	79 (30.4)	42 (33.9)	121 (31.5)
Never had therapy	88 (33.8)	33 (26.6)	121 (31.5)
Unknown	37 (14.2)	19 (15.3)	56 (14.6)
Results of cytogenetics test			
Abnormalities identified	151 (58.1)	81 (65.3)	232 (60.4)
No evaluable metaphases	4 (1.5)	0 (0.0)	4 (1.0)
No abnormalities	84 (32.3)	31 (25.0)	115 (3.0)
Not done or missing	21 (8.1)	12 (9.7)	33 (8.6)
No. of distinct cytogenetic abnormalities			
1	43 (28.5)	28 (34.6)	71 (30.6)
2	31 (20.5)	19 (23.5)	50 (21.6)
3	20 (13.2)	14 (17.3)	34 (14.7)
≥ 4	52 (34.4)	20 (24.7)	72 (31.0)
Missing	5 (3.3)	0 (0.0)	5 (2.2)
Donor type			
Matched related	80 (30.8)	NA	80 (30.8)
Matched unrelated	180 (69.2)	NA	180 (69.2)
HCT-CI			
0	41 (15.8)	NA	41 (15.8)
1	31 (11.9)	NA	31 (11.9)
2	35 (13.5)	NA	35 (13.5)
3+	98 (37.7)	NA	98 (37.7)
Missing	55 (21.2)	NA	55 (21.2)

Abbreviations: ECOG, Eastern Cooperative Oncology Group; HCT, hematopoietic cell transplantation; HCT-CI, Hematopoietic Cell Transplant-Comorbidity Index; IPSS, International Prognostic Scoring System; IPSS-R, Revised International Prognostic Scoring System; KPS, Karnofsky performance score; MDS, myelodysplastic syndrome; NA, no answer; RAEB, refractory anemia with excess blasts; RARS, refractory anemia with ringed sideroblasts; RCMD, refractory cytopenia with multilineage dysplasia; RCUD, refractory cytopenia with unilineage dysplasia; SD, standard deviation.

[a]Either KPS or ECOG was collected from participants at enrollment.

Only high IPSS score predicted relapse in multivariable models (HR 2.85; 95% CI, 1.74 to 4.68; $P < .0001$). Grades II-IV and III-IV acute GVHD occurred in 43.1% (95% CI, 36.1 to 49.9) and 17.1% (95% CI, 12.2 to 22.7) by day 100, respectively, whereas chronic GVHD was reported in 55.5% (95% CI, 47.8 to 62.5) of subjects by 27 months post-HCT. Among 63 subjects with chronic GVHD severity scores, 40 were classified as moderate and 23 had severe chronic GVHD. Conditioning regimens used before HCT are listed in the Data Supplement.

Quality of Life

Preliminary analyses of patient-reported QOL outcomes demonstrated no differences between Donor and No-Donor arms in any of the QOL scores at any time points evaluated (enrollment, 6, 12, 18, 24, and 36 months) that

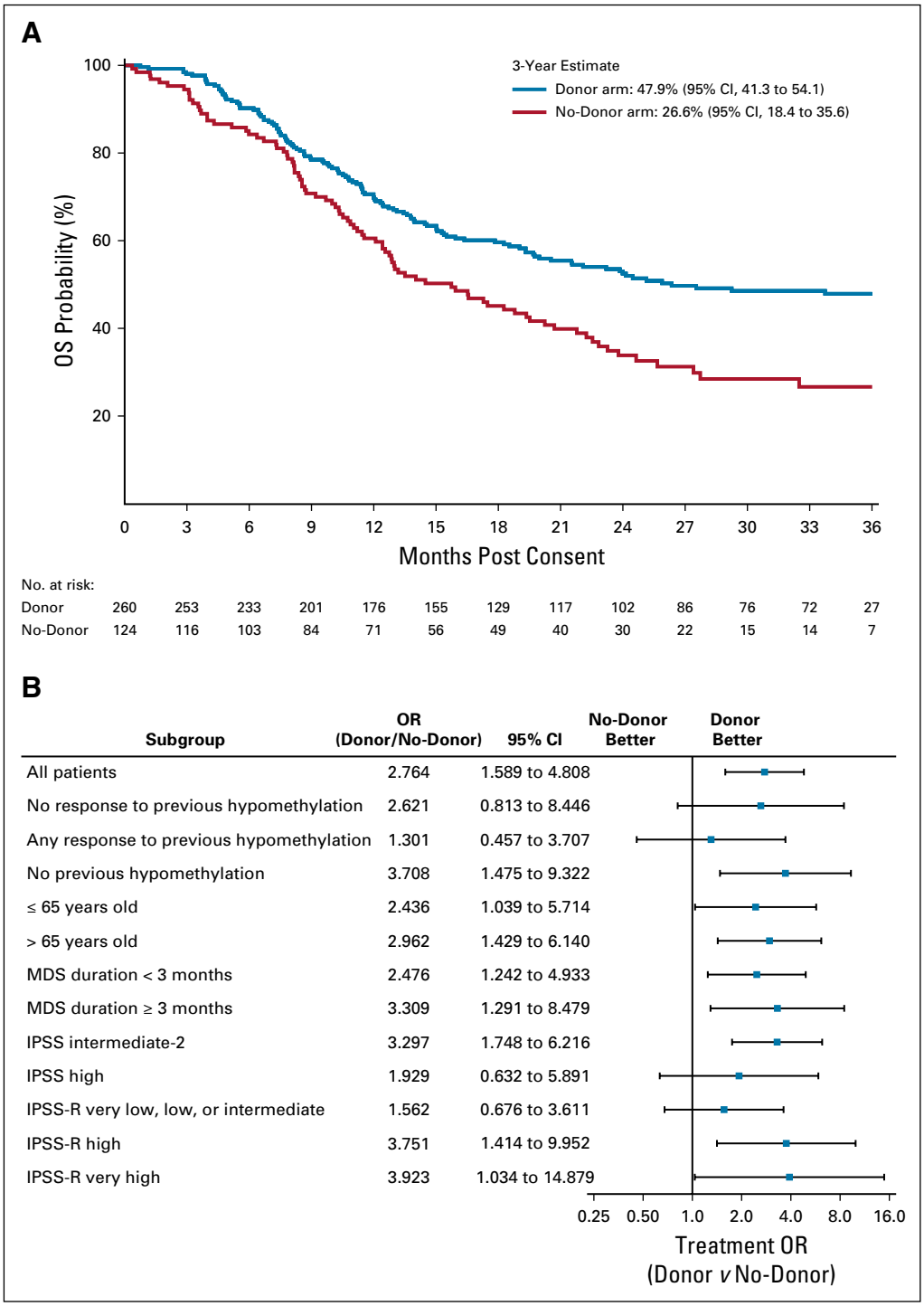

FIG 2. (A) Estimates of OS after registration. OS curves are adjusted for age, race or ethnicity, performance status, IPSS score, duration of disease, and response to HMA in an intention-to-treat analysis. (B) Forest plot of subgroup analyses for OS. The forest plot shows the OR of OS at 3 years for Donor versus No-Donor arm subjects in subgroups determined by age, race or ethnicity, performance status, IPSS score, duration of disease, and response to HMA. NOTE. x-axis has a logarithmic scale. (C) Estimates of LFS after registration. LFS curves are adjusted for age, race or ethnicity, performance status, IPSS score, duration of disease, and response to HMA in an intention-to-treat analysis. (D) Forest plot of subgroup analyses for LFS. The forest plot shows the OR for LFS at 3 years after consent for Donor versus No-Donor arm subjects in subgroups determined by age, race or ethnicity, performance status, IPSS score, duration of disease, and response to HMA. NOTE. x-axis has a logarithmic scale. HMA, hypomethylating agent; IPSS, International Prognostic Scoring System; IPSS-R, Revised International Prognostic Scoring System; LFS, leukemia-free survival; MDS, myelodysplastic syndromes; OR, odds ratio; OS, overall survival.

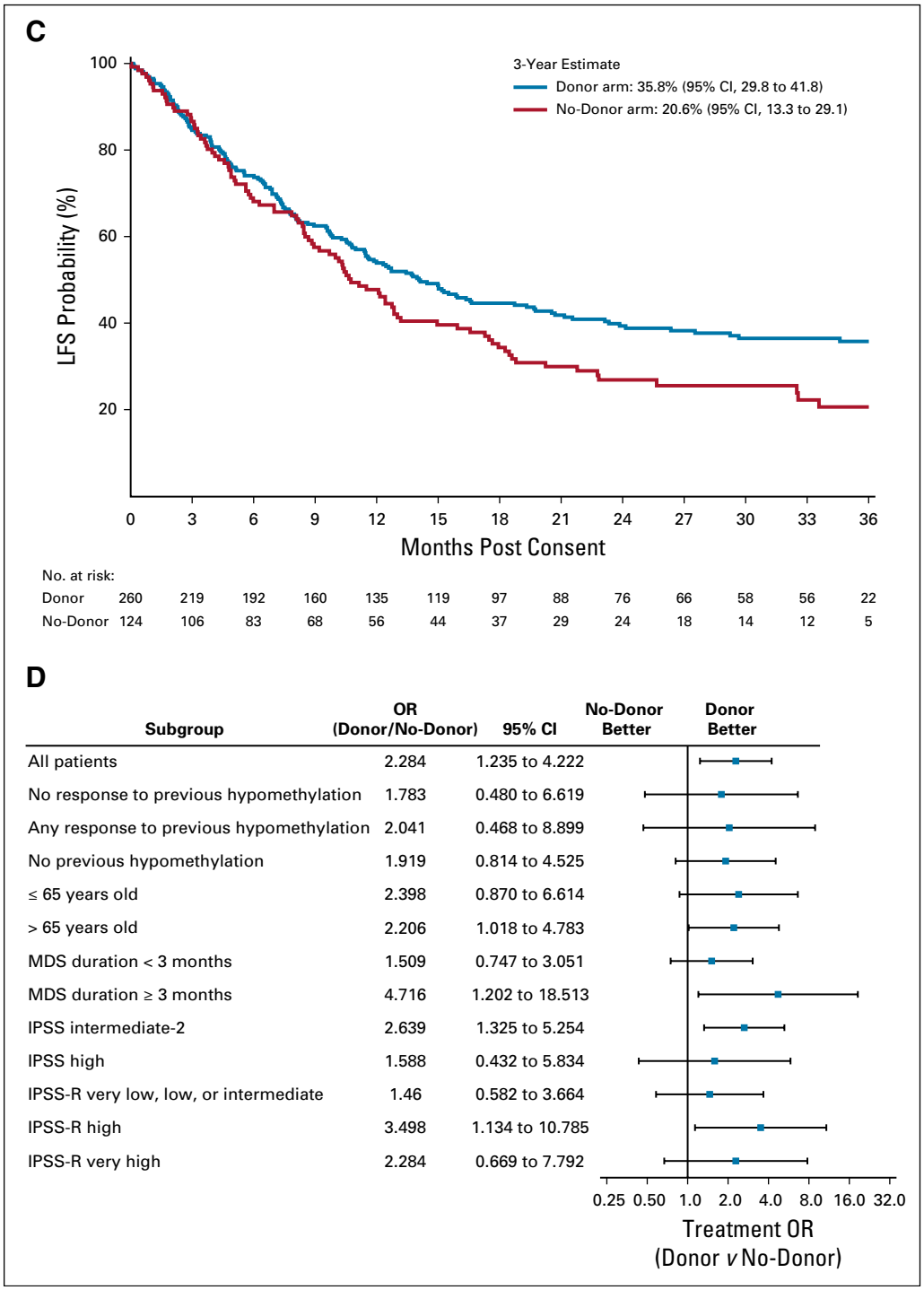

FIG 2. (Continued).

were both statistically significant and clinically meaningful (Data Supplement).

DISCUSSION

This large, multicenter, biologic assignment trial demonstrated a significant 3-year OS and LFS advantage in older MDS subjects who were RIC HCT candidates with matched donors identified when compared with those without a donor. The benefit of having a matched donor was seen across subgroups, including those who were of Medicare age (> 65 years) and younger. Our prospective data are consistent with the survival outcomes observed in cohort studies,[6,16,32,33] retrospective comparative analyses,[13,14] and confirmed the findings from similarly designed

Agend

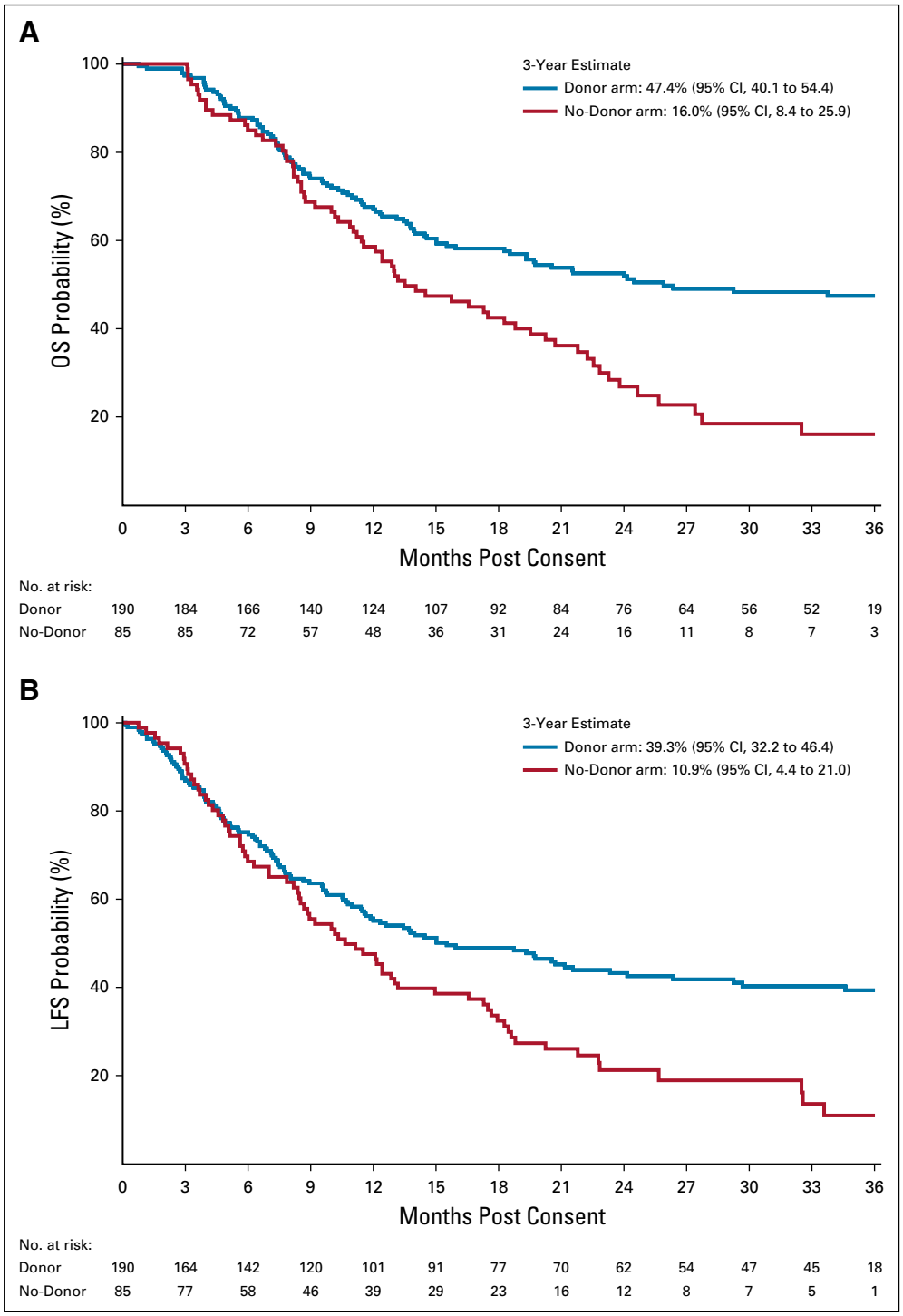

FIG 3. (A) Estimates of OS after registration, as-treated analysis. OS curves are adjusted for age, race or ethnicity, performance status, IPSS score, duration of disease, and response to HMA in an as-treated analysis. (B) Estimates of LFS after registration, as-treated analysis. LFS curves are adjusted for age, race or ethnicity, performance status, IPSS score, duration of disease, and response to HMA in an as-treated analysis. HMA, hypomethylating agent; IPSS, International Prognostic Scoring System; LFS, leukemia-free survival; OS, overall survival.

prospective studies conducted in Europe.[15,16] The French HCT-MDS study group reported trial results on 162 patients with MDS (age: 50-70 years; donor: n = 112, no-donor: n = 50) demonstrating better 4-year OS in patients with an HLA-matched donor (37%) compared with those without a donor (15%, $P = .002$).[15] The German cooperative group also conducted a trial comparing continued azacytidine versus HCT in patients with higher-risk MDS (age, 55-70

years) after azacytidine induction (four to six cycles).[18] This trial showed an improved the 3-year OS of 49% versus 22% (95% CI, 36 to 61, 6 to 44) with HCT (n = 83) versus continuous treatment with 5-Aza (n = 26; P = .027).

Our trial was approved by the CMS to prospectively address their question posed in 2010: compare(d) to Medicare beneficiaries with MDS who do not receive hematopoietic stem-cell transplantation, do Medicare beneficiaries with MDS who receive hematopoietic stem-cell transplantation have improved outcomes as indicated by relapse-free mortality, progression-free survival, relapse, and OS? A recently reported prospective CIBMTR study (NCT01166009) compared outcomes from 688 patients with MDS (age ≥ 65 years) with 592 patients 55-64 years of age. The study demonstrated no significant difference in 3-year OS.[11] Together, the data from these two trials provide strong evidence that the use of HCT improves health outcomes in Medicare beneficiaries with MDS. Furthermore, the QOL measures between the two groups in our trial were similar, indicating that the observed survival benefit with RIC HCT was achieved without an early decrement in QOL.

Although randomized controlled trials represent the gold-standard design to compare two therapies, a study that randomly assigns subjects to transplantation is difficult to perform and poses ethical challenges, particularly when one therapy has curative potential.[26] Our approach to conduct a biologic assignment trial has been successfully used to evaluate the role of HCT in multiple scenarios.[34-36] Although selection bias can still arise with biologic assignment, this design was considered the most feasible for this research question.[19] To reduce bias, we enrolled subjects without knowledge of donor status and adjusted survival estimates.[25,26] Excessive early deaths before the end of the 90-day search period could have potentially biased the study in favor of the Donor arm, but there were few early deaths and excluding those subjects had no effect on outcomes. Noncompliance with prescribed therapy occurred at the predicted rate (26.3% *v* 25% anticipated). Noncompliance is expected in a real-world scenario, where the timing and conditioning regimen for HCT may differ from original intent because of disease progression, donor availability, and evolving comorbidity. Noncompliance in this trial was clinically appropriate, reflected best clinical care, and did not favor the Donor arm. Donor arm subjects who did not undergo HCT had worse outcomes than those who did, and subjects on the No-Donor arm who underwent HCT had better outcomes than those who did not.

Our trial excluded subjects who were considered for alternative donor HCT. No prospective study has been done to compare outcomes of alternative donor transplant to HLA-matched transplantation in MDS, although registry analyses suggest that alternative donor outcomes are either similar or only minimally inferior to HLA-matched transplantation,[37-39] particularly with the adoption of post-transplant cyclophosphamide as GVHD prophylaxis.[40] Although not designed to specifically evaluate this end point, the favorable outcomes seen with alternative donor transplantation in the No-Donor arm support these assertions.

We designed this trial with a focus on RIC HCT candidates to ensure enrollment of the intended age group (median of 66.7 years). The RIC regimen was left to participating centers according to their institutional guidelines; however, the two most commonly used regimens were fludarabine combined with busulfan or melphalan. Although recent registry studies suggested superior outcomes with fludarabine or melphalan in AML or MDS,[41,42] our study was not designed to address this question. Similarly, our study was not designed to address the issue of the optimal pre-transplant therapeutic strategy, as the majority of subjects received HMA before the registration, reflecting current practice.

Next-generation sequencing–based mutation analysis was not initially performed as part of this trial, despite accumulating evidence that specific somatic mutations in MDS are associated with prognosis and HCT outcomes.[43-46] Future studies are warranted to better define the benefit of HCT according to molecularly informed prognosis toward personalized medicine. Additionally, better assessment tools for older patients with MDS incorporating frailty and resiliency may enhance risk-stratification for HCT (NCT03992352).[47]

Despite the safety of RIC HCT, older patients with hematologic malignant diseases are not routinely offered HCT. In a large trial for older patients with high-risk MDS, only 13% of patients proceeded to HCT,[48] and in a cross-sectional survey of 101 physicians responsible for 4,154 patients with MDS, fewer than 5% of patients were evaluated for HCT.[49] Our study demonstrated a significant survival advantage in older patients with MDS who are RIC HCT candidates and have a matched donor identified when compared with those without a donor. Based on these data, HCT should be included as an integral part of MDS management plans in fit older adults with higher-risk MDS. Early referral to a transplant center and coverage of HCT by CMS are strongly recommended.

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STUDY GROUPS

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DISCLAIMER

The views expressed in this article are those of the authors and do not reflect the views or the official policy or position of the National Heart, Lung, and Blood Institute, the National Cancer Institute, or the National Marrow Donor Program.

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AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

Biologic Assignment Trial of Reduced-Intensity Hematopoietic Cell Transplantation Based on Donor Availability in Patients 50-75 Years of Age With Advanced Myelodysplastic Syndrome

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Ryotaro Nakamura
Consulting or Advisory Role: Viracor Eurofins, Magenta Therapeutics, Kadmon, Napajen Pharma
Research Funding: Helocyte, Miyarisan Pharmaceutical
Travel, Accommodations, Expenses: Kyowa Hakko Kirin, Alexion Pharmaceuticals

Bart Scott
Honoraria: Bristol Myers Squibb
Consulting or Advisory Role: Celgene, Acceleron Pharma, Astex Pharmaceuticals, Novartis
Speakers' Bureau: Alexion Pharmaceuticals, Celgene, Jazz Pharmaceuticals, Novartis
Research Funding: Celgene

Betul Oran
Research Funding: AROG Phamarceuticals, Astex Pharmaceuticals

Asmita Mishra
Research Funding: Novartis

Richard T. Maziarz
Honoraria: Novartis, Omeros, PACT Pharmaceuticals
Consulting or Advisory Role: Novartis, Incyte, Kite, a Gilead company, Bristol Myers Squibb, Intellia Therapeutics, Artiva
Patents, Royalties, Other Intellectual Property: Athersys Inc shared patent re: use of mesenchymal stromal cells for treatment of GVHD
Travel, Accommodations, Expenses: Novartis, Incyte, Kite, a Gilead company

Joseph McGuirk
Honoraria: Kite, a Gilead company, AlloVir, Juno Therapeutics, Magenta Therapeutics
Consulting or Advisory Role: Kite, a Gilead company, Juno Therapeutics, AlloVir, Magenta Therapeutics, EcoR1 Capital
Speakers' Bureau: Kite/Gilead
Research Funding: Novartis, Fresenius Biotech, Astellas Pharma, Bellicum Pharmaceuticals, Gamida Cell, Pluristem Therapeutics, Kite, a Gilead company, AlloVir
Travel, Accommodations, Expenses: Kite, a Gilead company

Peter Westervelt
Consulting or Advisory Role: Pfizer

Sumithira Vasu
Consulting or Advisory Role: Omeros, Johnson & Johnson
Patents, Royalties, Other Intellectual Property: The Ohio State University has entered into an exclusive licensing agreement with Kiadis Inc

Mrinal Patnaik
Honoraria: Kura Oncology
Consulting or Advisory Role: Kura Oncology
Research Funding: Stemline Therapeutics

Stephen J. Forman
Stock and Other Ownership Interests: MustangBio, Lixte Biotechnology
Consulting or Advisory Role: Alimera Sciences, Lixte Biotechnology, MustangBio
Research Funding: MustangBio
Patents, Royalties, Other Intellectual Property: MustangBio

Mikkael A. Sekeres
Consulting or Advisory Role: Celgene, Millennium, Pfizer, Novartis
Research Funding: Takeda, Pfizer, Bristol Myers Squibb

Frederick Appelbaum
Stock and Other Ownership Interests: Jasper Therapeutics

Brent Logan
Consulting or Advisory Role: Daiichi Sankyo, Enlivex Therapeutics Ltd, Gamida Cell

Mary Horowitz
Consulting or Advisory Role: Magenta Therapeutics, Janssen Research & Development, Medac
Research Funding: Biovitrum, Jazz Pharmaceuticals, Magenta Therapeutics, Novartis, Kite/Gilead, Actinium Pharmaceuticals, Amgen, Amneal Pharmaceuticals, Anthem, Bluebird Bio, Bristol Myers Squibb, Chimerix, CSL Behring, Cyto-Sen Therapeutics, Daiichi Sankyo, Gamida Cell, GlaxoSmithKline, Mesoblast, Miltenyi Biotec, Neovii, Oncoimmune, Pfizer, Pharmacyclics, Regeneron, Sanofi, Seattle Genetics, Shire

Corey Cutler
Stock and Other Ownership Interests: Bluebird Bio, Idera, Verastem, Northwest Biotherapeutics, Actinium Pharmaceuticals
Honoraria: Omeros, Pfizer
Consulting or Advisory Role: Incyte, Jazz Pharmaceuticals, CareDX, Mesoblast, Syndax, Medsenic

No other potential conflicts of interest were reported.

Agend

April 2, 2021

Dear Medical Director,

On behalf of the American Society of Hematology (ASH) and the American Society for Transplantation and Cellular Therapy (ASTCT), we write to you today to support the timely creation of a Local Coverage Determination (LCD) to allow Medicare beneficiaries to receive allogeneic hematopoietic cell transplantation (allo-HCT) for primary refractory or relapsed Hodgkin's lymphoma and Non-Hodgkin's lymphoma of B-cell or T-cell origin for whom there are no other curative intent options. Our organizations offer our assistance in developing a policy that could be used in all Medicare Administrative Contractor (MAC) jurisdictions.

As you know, lymphoma is not included in the National Coverage Determination (NCD) for Allogeneic Stem Cell Transplantation (110.23). This gap in coverage means that Medicare beneficiaries with lymphoma across the country can be denied access to this potentially curative treatment and are subjected to a different standard of care than patients with commercial insurance. Thanks to recent advances in science and treatments, such as chimeric antigen receptor (CAR) T-cell therapy, the subset of lymphoma patients who are in need of allo-HCT has gotten smaller, but for these patients it is their only option for curative intent therapy.

ASH and ASTCT strongly support Medicare coverage for allo-HCT for individuals with lymphoma. The procedure is widely covered for patients with private insurance and is considered a cost-effective means to treat patients. An abundance of clinical experience exists and has been published demonstrating both effectiveness in general and the comparable success regardless of age. Included in this letter are references to the most recent literature outlining the current evidence for allo-HCT. For example, in 2015 members of ASTCT published evidence graded guidelines for indications for autologous and allogeneic transplant. Our Societies would also be happy to help identify lymphoma experts to participate in your Carrier Advisory Council meetings on this topic.

Should you have any questions or if you are in need of lymphoma experts, please contact Katherine Stark (kstark@hematology.org), ASH's Policy and Practice Specialist or Alycia Maloney (amaloney@astct.org), ASTCT's Director of Government Relations.

Sincerely,

Martin S. Tallman, MD
President
ASH

Stella Davies, MBBS, PhD, MRCP
President
ASTCT

1. Blood Adv. 2018 Apr 24;2(8):933-940. doi: 10.1182/bloodadvances.2018018531. Outcomes of Medicare-age eligible NHL patients receiving RIC allogeneic transplantation: a CIBMTR analysis. Primary author is Nirav Shah.
2. Biol Blood Marrow Transplant. 2015 Nov;21(11):1863-1869. doi: 10.1016/j.bbmt.2015.07.032. Epub 2015 Aug 7.PMID: 26256941.
   Indications for Autologous and Allogeneic Hematopoietic Cell Transplantation: Guidelines fr om the American Society for Blood and Marrow Transplantation. Majhail NS, Farnia SH, Carpenter PA, Champlin RE, Crawford S, Marks DI, Omel JL, Orchard PJ, Palmer J, Saber W, Savani BN, Veys PA, Bredeson CN, Giralt SA, LeMaistre CF.
3. Biol Blood Marrow Transplant. 2017 Nov;23(11):1826-1838. doi: 10.1016/j.bbmt.2017.07.027. Epub 2017 Aug 7. Clinical Practice Recommendations on Indication and Timing of Hematopoietic Cell Transplantation in Mature T Cell and NK/T Cell Lymphomas: An International Collaborative Effort on Behalf of the Guidelines Committee of the American Society for Blood and Marrow Transplantation. First author is Mohamed A Kharfan-Dabaja.
4. Indications for Hematopoietic Cell Transplantation and Immune Effector Cell Therapy: Guidelines from the American Society for Transplantation and Cellular Therapy. Kanate AS, Majhail NS, Savani BN, Bredeson C, Champlin RE, Crawford S, Giralt SA, LeMaistre CF, Marks DI, Omel JL, Orchard PJ, Palmer J, Saber W, Veys PA, Carpenter PA, Hamadani M.Biol Blood Marrow Transplant. 2020 Jul;26(7):1247-1256. doi: 10.1016/j.bbmt.2020.03.002. Epub 2020 Mar 9.PMID: 32165328

CMS Resources

- Medicare's Program Integrity Manual, Chapter 13 (*Revised 2/12/19: outlines the local coverage determinations the Carrier Advisory Committee (CAC) and contractor responsibilities surrounding CACs*)
- General Information on CMS' Contracting Reform
- Medicare Administrative Contractors (MAC) Regions and Updates
- Map of Current Jurisdictions
- Map of Consolidated Regions (*what CMS is moving toward*)
- Durable Medical Equipment MACs
- Medicare Coverage
- Medicare Coverage Centers
- Patients over Paperwork: 9th Issue - Modernization Update: Local Coverage Determination (LCD)

American Society of Hematology Practice-Related Resources

ASH offers a wide range of practice-related resources on its website . Below, please find a list of resources that may be of interest to you.

Resources for Clinicians

- COVID-19 Resources for Hematologists – In an effort to serve its members, ASH is maintaining this webpage as a medium to exchange information to assist hematologists in navigating the COVID-19 public health crisis.
    - COVID-19 Policy Resources – These resources, including practice webinars and reimbursement fact sheets, are intended to help navigate the complex and fast-changing COVID-19 policy landscape.
- ASH Practice Partnership – The ASH Practice Partnership (APP) is a group within the Society that was formed to better represent the interests of practicing hematologists. The APP is comprised of practicing hematologists from across the nation; participants must be board-certified in hematology and active members of ASH. Ideal candidates should be interested in malignant and nonmalignant hematology.
- Drug Resources - This page provides links to patient assistance programs and sample letters of appeal for high-cost drugs, links to Risk Evaluation and Mitigation Strategies (REMS) resources, an up-to-date list of hematologic drug shortages, resources for physicians dealing with shortages, and links to ASH/FDA webinars featuring an unbiased discussion of newly approved drugs and their uses.
- Consult a Colleague - A member service designed to help facilitate the exchange of information between hematologists and their peers.
- ASH Choosing Wisely List - Evidence-based recommendations about the necessity and potential harm of certain practices developed as part of Choosing Wisely®, an initiative of the ABIM Foundation.
- ASH Clinical Guidelines, ASH Pocket Guides, and Hematology Quality Metrics - Access guidelines on Venous Thromboembolism (VTE), Immune Thrombocytopenia (ITP), von Willebrand Disease, Sickle Cell Disease, Anticoagulation Therapy, and others. Access the full guidelines, along with other tools and resources, including pocket guides, apps, teaching slides, webinars, and podcasts.
- Well-Being and Resilience - Well-being is a critical factor in the strength of the workforce, and the Society is committed to helping hematologists address the myriad factors impacting well-being through interventions such as openly addressing burnout in live meetings and in publications, advocating on behalf of hematologists to streamline administrative work, and sharing approaches to building resilience among hematologists.

Advocacy Resources

ASH's Advocacy Center houses all of the Society's policy positions, advocacy efforts, and campaigns. Hematologists and their patients can follow the latest national policy news and directly influence their representatives through ASH Action Alerts. The Center also displays ASH's official policy statements along with Testimony and Correspondence related to federal regulation and private insurance developments.

- ASH's online advocacy toolkit provides members with the information and guidance necessary to communicate with elected officials in support of hematology. The toolkit clearly and concisely explains how members can undertake a number of actions to support ASH's advocacy efforts.

Clinical ASH Publications

- Practice Update – The Practice Update is the Society's bimonthly e-newsletter reporting on breaking news and activities of interest to the practice community.
- *ASH Clinical News* – *ASH Clinical News* is a magazine for ASH members and non-members alike – offering news and views for the broader hematology/oncology community.
- *The Hematologist*: ASH News and Reports - An award-winning, bimonthly publication that updates readers about important developments in the field of hematology and highlights what ASH is doing for its members.

Meeting Information for Clinicians

- ASH Annual Meeting and Exposition – Virtual Experience from December 5-8, 2020. The Society's Annual Meeting and Exposition is designed to provide hematologists from around the world a forum for discussing critical issues in the field. Abstracts presented at the meeting also contain the latest and most exciting developments in hematology research.
- Highlights of ASH - This meeting is designed to provide the highlights of the top presentations from ASH's annual meeting.

Other ASH Activities and Resources

- The ASH Academy on Demand – The ASH Academy on Demand provides hematologists with easy-to-use options for knowledge testing (for both MOC and CME purposes), completing practice improvement modules, as well as evaluating ASH meetings you attend and claiming CME credit for participating. The sixth edition of the ASH Self- Assessment Program (ASH-SAP) is also available on the ASH Academy on Demand.
- ASH FDA New Drug and Therapy Alerts – ASH partners with the Food and Drug Administration to alert members on newly approved hematologic therapies.
- ASH and the American Medical Association – ASH is an engaged participant and member of the American Medical Association's (AMA) House of Delegates (HOD), AMA Current Procedural Terminology (CPT) Committee, and Relative Value Scale Update Committee (RUC).
- ASH Committee on Practice - The Committee on Practice is concerned with all issues affecting the practice of hematology. The Committee communicates with other organizations that have programs and policies that affect hematology practice. With appropriate review and approval by the Executive Committee, the Committee on Practice responds to practice-related issues by formulating positions on pending federal legislation, regulatory issues, and private insurance developments. The Committee also responds to matters of importance at the regional, state, and local levels, and to Society member requests.

If you have any questions on this list or any of the programs, please contact Katherine Stark, Policy and Practice Specialist at kstark@hematology.org.

ASH Clinical Practice Guidelines

Venous Thromboembolism

- VTE: Treatment of Pediatric VTE (Published November 27 2018) American Society of Hematology 2018 Guidelines for management of venous thromboembolism: treatment of pediatric venous thromboembolism
- VTE: VTE in the Context of Pregnancy (Published November 27 2018) American Society of Hematology 2018 guidelines for management of venous thromboembolism: venous thromboembolism in the context of pregnancy
- VTE: Prophylaxis for Hospitalized and Non-hospitalized Medical Patients (Published November 27 2018) American Society of Hematology 2018 guidelines for management of venous thromboembolism: prophylaxis for hospitalized and nonhospitalized medical patients
- VTE: Optimal Management of Anticoagulation Therapy (Published November 27 2018) American Society of Hematology 2018 guidelines for management of venous thromboembolism: optimal management of anticoagulation therapy
- VTE: Heparin-induced Thrombocytopenia (Published November 27 2018) American Society of Hematology 2018 guidelines for management of venous thromboembolism: heparin-induced thrombocytopenia
- VTE: Diagnosis of VTE (Published November 27 2018) American Society of Hematology 2018 guidelines for management of venous thromboembolism: diagnosis of venous thromboembolism
- VTE: Prevention of VTE in Surgical Hospitalized Patients (Published December 3 2019) American Society of Hematology 2019 guidelines for management of venous thromboembolism: prevention of venous thromboembolism in surgical hospitalized patients
- VTE: Treatment of DVT and PE (Published October 2, 2020) American Society of Hematology 2020 guidelines for management of venous thromboembolism: treatment of deep vein thrombosis and pulmonary embolism
- VTE: Anticoagulation in COVID-19 (Published February 8, 2021) American Society of Hematology 2021 guidelines on the use of anticoagulation for thromboprophylaxis in patients with COVID-19
- VTE: Cancer-associated thrombosis (Published February 11, 2021) American Society of Hematology 2021 guidelines for management of venous thromboembolism: prevention and treatment in patients with cancer

Sickle Cell Disease

- SCD: Cardiopulmonary and Kidney Disease (Published December 3 2019) American Society of Hematology 2019 guidelines for sickle cell disease: cardiopulmonary and kidney disease
- SCD: Transfusion Support (Published January 27 2020) American Society of Hematology 2020 guidelines for sickle cell disease: transfusion support
- SCD: Cerebrovascular Disease (Published April 16 2020) American Society of Hematology 2020 guidelines for sickle cell disease: prevention, diagnosis, and treatment of cerebrovascular disease in children and adults
- SCD: Management of Acute and Chronic Pain (Published June 19 2020) American Society of Hematology 2020 guidelines for sickle cell disease: management of acute and chronic pain

Immune Thromboembolism

- ITP (Published December 3 2019) American Society of Hematology 2019 guidelines for immune thrombocytopenia

Acute Myeloid Leukemia

- AML: Treatment in Older Adults (Published August 6 2020) American Society of Hematology 2020 guidelines for treating newly diagnosed acute myeloid leukemia in older adults

Von Willebrand Disease

- VWD: Diagnosis (Published January 12, 2021) ASH ISTH NHF WFH 2021 guidelines on the diagnosis of von Willebrand disease
- VWD: Management (Published January 12, 2021) ASH ISTH NHF WFH 2021 guidelines on the management of von Willebrand disease

Learn More!
A user guide to the American Society of Hematology clinical practice guidelines

Coming Soon:

- VTE: Thrombophilia
- SCD: Stem Cell Transplant
- Ongoing, "living" updates to the Anticoagulation in COVID-19 Patients guideline