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ORIGINAL REPORT

Autologous Stem-Cell Transplantation Without Hematopoietic Support for the Treatment of Hematologic Malignancies in Jehovah's Witnesses

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ABSTRACT

Purpose
Autologous stem-cell transplantation (ASCT) has shown to provide curative benefit in patients with relapsed lymphoma and multiple myeloma (MM), often requiring hematopoietic support until marrow engraftment. Because of Jehovah's Witnesses' (JW) refusal of blood products, treatment challenges arise. This study represents 125 JWs with lymphoma (n = 55), MM (n = 68), or amyloidosis (n = 2), treated with high-dose chemotherapy (HDC) and ASCT without transfusions.

Patients and Methods
Priming with intravenous iron and erythropoietin occurred to increase hemoglobin (Hb) pretransplantation. Cytokine mobilization of stem-cells was used. Delay to HDC was done to allow Hb and platelets to approach 11 g/dL and 100 $\times$ $10^3/\mu$L, respectively. Patients with MM received a standard dose of melphalan 200 mg/m^2, with dose reduction for severe kidney dysfunction. Patients with lymphoma received carmustine 300 mg/m^2, cyclophosphamide 1,500 mg/m^2 on days 2 through 5 (total 6 g/m^2), and etoposide 700 mg/m^2 per day on days 2 through 4 (total 2,100 mg/m^2). Post-transplantation, a combination of granulocyte colony-stimulating factor, erythropoietin, aminocaproic acid, and phytonadione was administered.

Results
There were two major and 15 minor bleeding complications, none occurring at platelets less than 5.0 $\times$ $10^3/\mu$L, with six (4.8%) treatment-related mortalities. The median decrease in Hb was 5.0 g/dL, with median Hb nadir of 7.0 g/dL. The median number of days with platelet count less than 10 $\times$ $10^3/\mu$L was 3, with median platelet nadir of 5.0 $\times$ $10^3/\mu$L. Cardiac complications occurred in 40 patients (32%).

Conclusion
ASCT can safely be performed without transfusion support. A platelet transfusion trigger of $\leq$ 5 $\times$ $10^3/\mu$L may be appropriate in select patients. Pharmacotherapy and cardiac monitoring are effective in the management of cardiac complications.

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INTRODUCTION

High-dose chemotherapy (HDC) followed by autologous stem-cell transplantation (ASCT) offers the best option for disease-free and/or long-term survival in patients with high-risk or relapsed lymphoma and multiple myeloma (MM).[1-5] This treatment modality invariably will require hematopoietic support until marrow engraftment has occurred. A requirement key to approximately 6.5 million worldwide members of the Jehovah's Witnesses (JW) population, who refuse blood product transfusions, a refusal which results in denial of transplantation for hematologic malignancies at major medical centers because of presumed fear of increased morbidity and mortality from bleeding and profound anemia.

While JW do not accept major blood products, defined as WBCs, RBCs (including autologous), platelets, and plasma, the decision to accept derivatives such as peripheral blood stem-cells and albumin is of individual choice. To date, at Pennsylvania Hospital we have successfully treated hematologic malignancies using HDC and ASCT in 243 patients, of which 125 were JW with low rates of bleeding and mortality.

PATIENTS AND METHODS

All JW diagnosed with lymphoma or MM deemed otherwise as transplantation candidates were considered for eligibility. Patients were enrolled if the following criteria were met: evidence of chemosensitive disease, ejection fraction (EF) $\geq$ 50%, diffusion lung capacity of carbon

monoxide ≥ 50% predicted, creatinine clearance ≥ 60 mL/min, Eastern Cooperative Oncology Group performance status ≤ 2, and age ≥ 18 years. Patients were considered eligible irrespective of the number of prior treatment regimens or complete remissions. Before treatment initiation, patients met with Pennsylvania Hospital's Center for Bloodless Medicine's transplantation team, and were informed of risks, benefits, and alternatives to bloodless ASCT before signing informed consent as stipulated by the institution's review board. Between May 1996 and March 2014, 125 patients were enrolled and treated with HDC and ASCT.

Treatment Plan

Before stem-cell mobilization and collection, patients were primed with intravenous iron and erythropoietin at a standard dose of 60,000 units weekly to target Hb ≥ 11g/dL. Menstruating women were treated with oral contraceptives or Depo-Provera (Pfizer Pharmaceuticals Group, New York, NY) for menses cessation, to reduce sources of blood loss. Cytokine mobilization of stem-cells was used preferentially over chemo-mobilization, to avoid pretransplantation pancytopenia. Granulocyte colony-stimulating factor was given at a dose of 20 mg/kg/d in addition to plerixafor at a dose of 0.24 mg/kg/dose, to achieve a target minimum collection of 2.5×10^6 CD34+ cells/kg. Patients underwent a second mobilization with granulocyte colony-stimulating factor if the target was not met. Stem-cells were collected and processed in 5% albumin and saline in lieu of fresh frozen plasma. After treatment of the second JW patient, undergoing transplantation with an initial Hb of 9 g/dL and subsequently dying as a result of profound anemia, the protocol was amended to delay transplantation after apheresis to obtain approximate targets of Hb ≥ 11 g/dL and platelets ≥ $100 \times 10^3/\mu$L. The decision to enroll patients outside these parameters was based on relapsed patients with lymphoma being offered ASCT as the best option for long-term survival, in addition to patients with MM having less of a decline in Hb post-transplantation.

Patients with MM received a standard dose of melphalan 200 mg/m^2, with dose adjustment to 140 to 150 mg/m^2 for severe kidney dysfunction. Patients with lymphoma received carmustine 300 mg/m^2 day 1 (total 300 mg/m^2), cyclophosphamide 1,500 mg/m^2 day 2 to 5(total 6 g/m^2), and VP16 700 mg/m^2/d days 2 through 4 (total 2,100 mg/m^2).

Blood conservation techniques included use of pediatric tubes for phlebotomy, minimization of unnecessary phlebotomy for stable labs, or repetitive blood cultures concomitant with each febrile episode. Limitation of potential sources of blood loss from the GI and genitourinary tract was done by use of proton pump inhibitors, stool softeners, and progestational agents in menstruating women. Mechanical thromboembolism prophylaxis was used to avoid heparin-based therapies, with avoidance of antiplatelet agents. Patients received aminocaproic acid as an alternative to platelet transfusion to enhance hemostasis at a dose of 1 g every 4 hours prophylactically for platelet counts less than $30 \times 10^3/\mu$L. Titration to 4 g every 4 hours intravenously was required for platelet counts less than $10 \times 10^3/\mu$L or clinical bleeding. Rarely, desmopressin was used at an intravenous dose of 0.3 μg/kg with repeat doses as required. Cryoprecipitate, though rarely used, was used for refractory bleeding. All patients received prophylactic phytonadione. Interleukin-11(IL-11) was initially used in the immediate post-transplantation period to decrease the duration of thrombocytopenia; however, it was discontinued as a result of inability to demonstrate benefit in the time to platelet engraftment post–stem-cell reinfusion, in addition to concerns for its role in the development of cardiac toxicities.

Statistical Analysis

Days to engraftment (ie, days to ANC ≥ 1,000, hemoglobin ≥ 8, and platelets ≥ 20,000) were calculated from the day of reinfusion, which was designated as day 0. Median time to engraftment was estimated by the Kaplan-Meier method. Patients who died because of transplantation-related mortality (TRM) before engraftment were censored at the date of their death. The days to engraftment range was based on the minimum and maximum observed engraftment dates. Fisher's exact test was employed to test the association between cardiac complications and baseline factors. All analyses were produced in SPSS (SPSS Inc, Chicago, IL).

Table 1. Patient Demographic and Clinical Characteristics

	No.	%
Total No. of patients	125	
Age, years		
Median	52	
Range	21-71	
Sex		
Male	57	45.6
Female	68	54.4
Diagnosis		
Multiple myeloma	68	54.4
Hodgkin lymphoma	19	15.2
Non-Hodgkin lymphoma	36	28.8
Amyloidosis	2	1.6
30-day follow-up status		
Complete 30-day follow-up	99	79.2
Incomplete 30-day follow-up	20	16.0
Median follow-up, days*	19	
Range, days	13-27	
100-day follow-up status		
Alive at 100 days	115	92
Dead at 100 days	10	8

*Follow-up calculated for 20 patients who left the study before day 30.

RESULTS

Patient Characteristics

From May 1996 to March 2014, 125 patients met the eligibility criteria and were enrolled. Patient characteristics are summarized in Table 1. The median age at enrollment was 52 years (range, 21 to 71years). Diagnoses included non-Hodgkin lymphoma (n = 36), Hodgkin lymphoma (n = 19), multiple myeloma (n = 68), and amyloidosis (n = 2).

Engraftment Data

A median of 4.7×10^6 CD34+/kg (range, 0.6 to 24.6×10^6 CD34+/kg) cells were reinfused post HDC. In a select few unable to achieve the target collection, proceeding to transplantation after explanation of higher risks involved was of individual choice. Engraftment data of all patients are outlined in Table 2. The median Hb at the onset of therapy was 11.8 g/dL. There was an average delay of 7 days between stem-cell collection and HDC initiation, to allow approximate Hb and platelet targets to be attained. Despite patients with lymphoma experiencing a significantly greater drop in Hb postcytotoxic therapy than patients with MM (mean ± SE, 5.9 ± 0.20 g/dL for lymphoma; 4.2 ± 0.16 g/dL for MM; $P < .001$, t test), and although their rate of TRM was higher, it was not statistically significant (TRM rate, 7.3% [four of 55] for lymphoma; 2.9% [two of 68] for MM; $P = .41$, Fisher's exact test).

Bleeding Complications

Bleeding complications were classified using the WHO grading system, and summarized in Table 3. No bleeding complications occurred at platelet counts more than $5 \times 10^3/\mu$L, and no bleeding associated mortalities resulted. There were 18 bleeding episodes, including one grade 4 hemorrhagic temporal infarction with associated

Table 2. Engraftment Parameters

	No.	Median	Range
Neutrophils			
Days to ANC ≥ 1,000 μL	125	10	4-19
Hemoglobin, g/dL			
Hemoglobin at onset of conditioning	125	11.8	7.0-11.8
Hemoglobin decrease to nadir	124	4.9	0.5-10.2
Hemoglobin nadir	123	7.0	2.0-11.6
Duration of grade 3/4 anemia hemoglobin < 8 g/dL, days	125	9	1-28
Hemoglobin at day +30	98	10.9	3.5-14.9
Platelets, $\times 10^3/\mu L$			
Platelets at onset of conditioning	124	148	65-502
Platelet nadir	123	5	1-50
Duration of grade 4 thrombocytopenia platelets $< 10 \times 10^3/\mu L$, days	125	3	0-14
Duration of grade 3 thrombocytopenia platelets $< 20 \times 10^3/\mu L$, days	125	4	0-20
Days to platelets > 20, $\times 10^3/\mu L$	125	11	0-23
Platelet count at day + 30, $\times 10^3/\mu L$	97	137	17-557

Abbreviation: ANC, absolute neutrophil count.

Table 4. Cardiac Complications

	No.	%
Total No. of patients	40	
Deaths	3	7.5
Fatal myocardial infarction	1	2.5
Tachyarrhythmia most commonly atrial fibrillation	20	50
CHF	15	37.5
Hypotension	17	42.5
Bradyarrythmia	3	7.5

Abbreviation: CHF, congestive heart failure.

retinal hemorrhages, resulting in temporary vision loss and confusion, one grade 3 GI bleed, one grade 2 retinal bleed, and one grade 2 vaginal bleed requiring administration of a progestational agent. Fifteen patients (83.3%) experienced grade 1 bleeding episodes consisting of conjunctival hemorrhage (n = 7), epistaxis (n = 5), minor vaginal bleeding (n = 1), oral bleeding (n = 1), a thigh hematoma (n = 1), and petechiae (n = 3). Four patients experienced at least two bleeding episodes of varying severities.

Cardiac Complications

Forty patients (32%) experienced cardiac complications (median age, 56; range, 21 to 71 years) as outlined in Table 4 and Table 5. These were classified using the National Cancer Institute toxicity grading system. The most commonly encountered complications were arrhythmias. One patient experience an acute myocardial infarction resulting in fatality (n = 1). Congestive heart failure (CHF) was more frequent in nine patients who received IL-11 (6/9; 67%) compared with 31 patients who had not received it (67% *v* 29%), an association that approached statistical significance ($P = .06$). The median Hb at the onset of a cardiac complication was 8.9 g/dL (range, 4.2 to 12.5g/dL; n = 37). The median number of days from reinfusion of stem-cells to the onset of a cardiac complication was 4.5 days (range, 1 to 17 days). CHF was significantly more frequent in 15 patients with Hb less than 8 g/dL (9/15; 60%) compared with 22 patients whose Hb did not fall below 8 g/dL (60% *v* 23%; $P = .04$). Twenty-six of the 40 patients (65%) who experienced cardiac complications had ≥ 1 risk factor for cardiovascular disease pretreatment, including hypertension, hyperlipidemia, diabetes mellitus, preexisting arrhythmias, known history of coronary artery disease (CAD), or stroke. There were no thrombotic events as a result of aminocaproic acid use.

TRM

Ninety-two percent of patients (n = 115) were alive at 100 days post-transplantation, and 10 patients had died before 100 days. Six patients (4.8%) died before day 30 and were considered TRMs. The

Table 3. Bleeding Complications

JW	Sex	Age (years)	Diagnosis	WHO Grade	Event
31	Female	42	Non-Hodgkin lymphoma	1	Epistaxis requiring nasal packing
41	Female	40	Multiple myeloma	2	Vaginal bleeding requiring progestational agents administration
45	Male	34	Non-Hodgkin lymphoma	1,1,1	Epistaxis requiring nasal packing, petechiae, conjunctival hemorrhage
46	Male	25	Non-Hodgkin lymphoma	3,1	GI bleeding, epistaxis
64	Female	29	Hodgkin lymphoma	1	Conjunctival hemorrhage
84	Female	47	Non-Hodgkin lymphoma	1,1	Conjunctival hemorrhage, vaginal bleeding
97	Male	61	Non-Hodgkin lymphoma	1	Petechiae
113	Male	59	Non-Hodgkin lymphoma	1	Conjunctival hemorrhage
131	Female	53	Hodgkin lymphoma	4	Temporal hemorrhagic infarct and vision loss
138	Female	52	Non-Hodgkin lymphoma	1	Conjunctival hemorrhage
150	Female	26	Non-Hodgkin lymphoma	1	Thigh hematoma
152	Male	28	Hodgkin lymphoma	1	Conjunctival hemorrhage
177	Male	48	Multiple myeloma	1	Oral bleeding
178	Female	28	Hodgkin disease	1	Epistaxis
193	Female	56	Non-Hodgkin lymphoma	1	Conjunctival hemorrhage
183	Male	61	Amyloidosis	1	Petechiae lower extremities
216	Female	47	Multiple myeloma	2	Retinal bleed
233	Male	48	Non-Hodgkin lymphoma	1	Epistaxis

Abbreviation: JW, Jehovah's Witness.

Table 5. Details of Cardiac Deaths

JW	Sex	Age (years)	Diagnosis	Chemotherapy	Cause of Death	Days Post-Transplantation
89	Female	59	Amyloidosis	Melphalan	Ventricular fibrillation/tachycardia arrest precipitated by cardiac amyloidosis	5
75	Female	60	Hodgkin lymphoma	BCNU, cytoxan, VP16	Fatal myocardial infarction NSTEMI: day 2 HDC with proven CAD	2
66	Male	49	Multiple myeloma	Melphalan 200 mg/m^2	Hypertrophic obstructive cardiomyopathy	10

Abbreviations: BCNU, carmustine; CAD, coronary artery disease; HDC, high-dose chemotherapy; NSTEMI, non-ST segment elevation myocardial infarction; VP16, etoposide.

etiologies were as follows: profound anemia (n = 1), severe sepsis (n = 1), multiorgan failure due to pancytopenia (n = 1), or cardiac events (n = 3). Since March 2010, there have been no additional TRMs.

The first TRM occurred in the second JW treated, a 21-year-old female with Hodgkin lymphoma with a pretransplantation Hb of 7 g/dL. An Hb of 2.0 g/dL lasted 7 days post-transplantation; she subsequently died 15 days postreinfusion as a result of respiratory failure. After this patient, the protocol was amended to delay transplantation after apheresis to target Hb close to 11 g/dL. The second TRM occurred because of sepsis resulting from hospital-acquired pneumonia, and the third resulted from pancytopenia. There were three additional TRMs as a result of cardiac events: the first occurred in a male who developed severe symptomatic refractory hypotension and CHF during stem-cell reinfusion. His repeat echocardiogram (ECHO) supported severe hypertrophic obstructive cardiomyopathy physiology not previously detected on pre-eligibility multigated acquisition scan. The second occurred as a result of a fatal MI on day 2 post–stem-cell reinfusion. This patient underwent urgent cardiac catheterization on day 1 of HDC administration, subsequently revealing severe triple-vessel CAD. Medical management was implemented; however, on day 1 post–stem-cell reinfusion, the patient developed cardiac arrest as a result of acute myocardial infarction and ventricular free wall rupture. After this patient, all candidates for bloodless ASCT age older than 50 years or at risk for cardiac disease were required to have pretransplantation cardiac consultation. The third cardiac mortality, a 59 year old female with amyloidosis, was found on eligibility testing to have severe tricuspid regurgitation and bi-atrial enlargement, findings which may indicate cardiac amyloidosis. On day 3 post reinfusion, she developed recurrent cardiac dysrhythmic arrests and subsequent death 2 days later. The other four deaths before day 100 occurred due to disease recurrence and progression in three patients with diagnoses of lymphoma; for the fourth patient, the cause of death could not be ascertained as a result of the lack of availability of medical records. The median number of days of hospitalization was 19 days (range, 5 to 35 days), in comparison to 17 days (range, 6 to 76 days) for our non-JW population undergoing HDC followed by ASCT for similar malignancies.

DISCUSSION

The Center for Bloodless Medicine and Surgery at Pennsylvania Hospital receives an average of 1,000 referrals annually, for the management of various surgical and medical conditions. Patients referred to our center for ASCT have been evaluated prior at major transplantation centers but declined solely on the basis of their refusal to accept blood products. The three most important basic blood management techniques utilized, include priming the Hb pretransplantation with erythropoiesis stimulating agents (ESAs) and intravenous iron, limiting iatrogenic blood loss by minimizing phlebotomy, and controlling and/or preventing bleeding with hemostatic agents.

Though our mortality rate was higher than the national mortality rate of 1 to 3.5% for lymphoma and MM,[6,7] it may be acceptable for JWs because of this population's unique characteristics; this, however, remains unsupported as a result of little published data on JW undergoing HDC administration and ASCT, therefore limiting the ability to determine an acceptable mortality rate. Our improved TRM observed has been attributed to the earlier recognition and intervention of the critically ill patient in the immediate transplantation period, involvement of cardiologists in the management of common cardiac complications, and more frequent monitoring of patients in critical care units (CCUs).

The unexpected rate of, and mortality as a result of, cardiac complications in our population was likely multifactorial in etiology. The majority of cardiac toxicities were grade 4 in severity as classified by the National Cancer Institute toxicity system. These toxicities required interventions such as telemetry monitoring, antiarrhythmics or atrioventricular nodal blocking agents, and less commonly, transfer to CCUs. Cardiovascular toxicities may occur at any time during transplantation and may be dependent on the following factors: age, pretransplantation patient performance status, pre-existing cardiac comorbidity, conditioning regimen, and the direct cardiovascular involvement by diseases such as amyloidosis.[8]

Horacek et al[9] observed a statistically significant change in systolic and diastolic blood pressure in 133 patients receiving stem-cell infusions cryopreserved with dimethyl sulfoxide in comparison to the control group. This finding may have a crucial impact on the development of clinically significant cardiovascular events in those with pre-existing cardiovascular disease. Older age has also been associated with a higher risk of cardiovascular events, with patients $\geq$ 60 years old experiencing increased incidence of supraventricular tachycardia and atrial fibrillation post HDC and SCT than patients younger than 60 years old,[10-12] a trend similar to our patient population. The intensity and duration of the conditioning regimen has been related to the development of cardiotoxicity. Melphalan for MM or carmustine, cyclophosphamide, and etoposide (BCV) for lymphoma have been shown to be cardiotoxic in high doses, whereas at lower doses subclinical damage may occur.[10,13-14] Multiple classes of chemotherapeutic agents, including the alkylating agents and anthracyclines, have been associated with cardiac toxicity. Among stem-cell transplant recipients, history of long-term or high-dose anthracyline administration or use within 60 days before HDC/ASCT were especially associated with higher incidences of cardiac complications.[15]

Thirty-six patients (65%) had ≥ 1 risk factor; 27.5% had ≥ 2 for cardiovascular disease at pretreatment, including hypertension, hyperlipidemia, diabetes mellitus, preexisting arrhythmias, and known history of CAD or stroke. Damage to the cardiovascular system as a result of these diseases may have occurred before treatment, a finding which has been supported in the literature, where cardiovascular comorbidities have been associated with increased risk for cardiotoxicity in patients undergoing transplantation.[10,16]

Initially IL-11, was used in the immediate post-transplantation period; after its discontinuation, the number of CHF events were reduced. However, all other cardiac events remained unchanged.

It is likely that the abovementioned risk factors for cardiotoxicity were exacerbated in patients with preexisting cardiac disease not detected on ECHO, as this in addition to EKG/ multigated acquisition are some of the major methods used in the evaluation of cardiovascular health. However, these methods may not be completely reliable in predicting cardiotoxic events in HDC and SCT patients.[15] The role of EFs as a predictor of cardiac events in HDC and ASCT remains unresolved in the literature.[10,13,17,18] Given the presence of cardiovascular risk factors in this population, in addition to noninvasive testing by ECHO, stress testing in patients with clear manifestations of CAD or underlying structural heart diseases should also be considered. In select patients, cardiac catheterization may prove to be of diagnostic and therapeutic value. Patients with preexisting comorbidities should be optimized medically before transplantation.

The low incidence of bleeding without prophylactic platelet transfusions observed in our series challenges current guidelines for prophylactic platelet administration. The American Society of Clinical Oncology recommends prophylactic platelet transfusions for platelet counts less than $10 \times 10^3/\mu L$.[19] However, the absence of major bleeding events observed at platelet counts greater than $5 \times 10^3/\mu L$ in patients with hematologic malignancies undergoing HDC and ASCT in our series suggests that a transfusion threshold trigger of $5 \times 10^3/\mu L$ may be appropriate in a select patient population.

Rebulla et al[20] in a randomized multicenter control trial challenged the prophylactic transfusion threshold of $20 \times 10^3/\mu L$ to the now accepted transfusion trigger of $10 \times 10^3/\mu L$. In this study of 255 patients with diagnoses of acute myeloid leukemia (AML), the rate of bleeding was similar in each group, either receiving platelet transfusion for platelets less than $10 \times 10^3/\mu L$ or less than $20 \times 10^3/\mu L$. In addition, the lower transfusion threshold group required fewer platelet transfusions.

Several studies have already demonstrated the safety of therapeutic platelet transfusions in clinically stable patients receiving ASCT for MM, lymphoma, and AML.[21,22] In a recently published article, Stanworth et al[23] compared the effectiveness of a no-prophylaxis platelet transfusion against a prophylactic platelet transfusion strategy in patients with a hematologic malignancy. This randomized, open labeled, noninferiority study of 600 patients measured primary end points of bleeding complications as graded by the WHO; the authors' results approached statistical significance ($P = .06$) in the rates of bleeding events between the treatment groups. More interestingly, in a subset analysis of patients treated with ASCT, the rate of bleeding was similar in both groups. Our study builds on these results, supporting the safety of therapeutic platelet transfusions in combination with patient blood management techniques in select patients with hematologic malignancies undergoing HDC and ASCT, as all bleeding incidents were readily managed in our population without transfusions, resulting in low morbidity rates and no fatalities. Adopting such a practice would not only be cost effective but reduce transfusion-associated risks and complications such as human error, platelet refractoriness, acute transfusion reactions, transfusion-transmitted infections, and transfusion-related acute lung injury. We believe the employment of basic blood management strategies are all that are needed to allow treatment of JW with HDC and ASCT. Though the high incidence of cardiac complications was unexpected, they were easily managed by pharmacologic agents, cardiology consultation, and escalation of the level of care to CCUs. In addition preexisting comorbidities, use of IL-11 before its discontinuation and use of cardiotoxic chemotherapy agents were likely contributory factors. No bleeding occurred at platelet counts greater than $5 \times 10^3/\mu L$, which supports lowering the prophylactic platelet transfusion threshold to $5 \times 10^3/\mu L$ and/or transfusing only on clinically significant bleeding in a select patient population undergoing ASCT for hematologic malignancies.

On the basis of low mortality and morbidities observed in this series, HDC followed by ASCT should be offered to JW with hematologic malignancies. These simple patient blood management strategies may be considered in select patients undergoing HDC and ASCT as an alternative to patients with platelet refractoriness or other medical contraindications to transfusions.

AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

Disclosures provided by the authors are available with this article at www.jco.org.

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AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

Autologous Stem-Cell Transplantation Without Hematopoietic Support for the Treatment of Hematologic Malignancies in Jehovah's Witnesses

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