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Report

Suitability Criteria for Adult Related Donors: A Consensus Statement from the Worldwide Network for Blood and Marrow Transplantation Standing Committee on Donor Issues

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A B S T R A C T

The number of allogeneic hematopoietic stem cell (HSC) transplants performed globally each year continues to increase. Advances in HLA typing, better supportive care, and administration of reduced-intensity conditioning regimens allow treatment of older patients with older sibling donors. Pretransplant donor assessment and testing are very important processes affecting the quality and safety of donation. For unrelated HSC donors detailed recommendations for health assessment have been published, allowing donation only if they are unrestrictedly healthy. Eligibility criteria for related donors are less strict and vary significantly between centers. In situations where a family donor does not meet the suitability criteria for unrelated donors, involved physicians often struggle with the decision whether the matched relative is suitable for donation or not. On behalf of the Worldwide Network for Blood and Marrow Transplantation Standing Committee on

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Donor Issues, we intended to develop a consensus document with recommendations for donor workup and final clearance of family donors who would not be able to serve as unrelated donors because of their age or pre-existing diseases. This article covers different topics intending to support decision-making, with the goal of minimizing medical risk to the donor and protection of the recipient from transmissible diseases.

INTRODUCTION

Over the last years the total number of allogeneic hematopoietic stem cell transplantations (HSCTs) performed annually has exceeded 30,000 a year. The observed continuous annual increase of around 10% is mainly because of a rise in allogeneic HSCT from unrelated stem cell donors (URDs) [1,2]. In 2013 the proportion of URDs was 53% in centers reporting to the European Group for Blood and Marrow Transplantation (EBMT) [3], and the stem cell source preferably used was granulocyte colony-stimulating factor (G-CSF)-mobilized peripheral blood stem cells (PBSCs) in 73% of HSCTs [2]. Furthermore, the number of donor lymphocyte infusions has also been increasing. Advances in HLA typing, the use of new immunosuppressive protocols, better supportive care, and the administration of reduced-intensity conditioning regimens contribute to the increased frequency of HSCT and allow treatment of older patients whose related donors usually are also older [4,5].

Pretransplant donor assessment and testing are very important issues affecting the quality and safety of donation. Several international regulatory bodies (eg, European Directives for Donation of Tissues and Cellular Therapy Products, US Food and Drug Administration) have detailed requirements on donor evaluation to ensure the safety of the product for the recipient but do not address donor safety issues. For HSC URDs, the World Marrow Donor Association (WMDA) has published detailed recommendations for donor assessment [6] and a donor suitability tool [7] open access file reflecting WMDA recommendations to ensure donor and recipient safety as well as the quality of the cellular product. In addition, the Worldwide Network for Blood and Marrow Transplantation (WBMT) has established a consensus statement for a standardized assessment of donor outcome data [8]. Donor eligibility criteria for related donors [9], who still comprise almost half of all donors, are less strict than for URDs [6], with few definite criteria and significant variation between HSCT centers. URDs are only eligible if they are unrestrictedly healthy, most often very similar to eligibility criteria for blood donation. Further differences between related donors and URDs may exist in mobilization and collection practices [8,10-12]. Published data suggest that the risks for serious adverse events and reactions might be higher for related donors than for URDs, but the amount of adequate prospective data in the related setting is still limited [13,14].

Involved physicians often struggle with the decision about whether a related donor not meeting suitability criteria for an URD can be regarded suitable for donation in the related HSCT setting. This article intends to give recommendations to support decision-making, with the goal of minimizing medical risk to the donor and protection of the recipient from transmissible diseases.

METHODS

On behalf of the WBMT Standing Committee on Donor Issues, a workshop with international representatives (Supplementary Table 1) involved in related and/or unrelated HSC donation from various member societies of WBMT took place in Vienna in September 2013. The purpose of this workshop was to develop a consensus document with recommendations for donor workup and final clearance of family donors who would not be able to serve as an URD because of their age (<18 or >60 years) or pre-existing diseases. In preparation for this workshop, different sections regarding organ system assessment, medical conditions, and pediatric donation were defined and assigned to experts in the field who served as group leaders for the particular sections (Supplementary Table 1). Group members performed a thorough review of the literature presented at the workshop and came to a consensus on recommendations for standardized related donor screening.

Sources of information included English-language articles extracted from PubMed (www.ncbi.nlm.nih.gov/pubmed) published until May 31, 2013, focusing on clinical studies of HSC mobilization and donation, guidelines for preoperative cardiac risk assessment and perioperative cardiac management in noncardiac surgery [15], and G-CSF application for other conditions than HSC mobilization [16], and the UK, Canadian, Italian, National Marrow Donor Program [17] and WMDA [18] recommendations for evaluation of URD were provided. In addition, group leaders received the S(P)EAR (Serious (Product) Events and Adverse Reactions) Committee Annual Report from 2011 provided by the WMDA (http://www.worldmarrow.org/fileadmin/Committees/SEAR/PRES/20110707-CLWG-SEAR_Summary_2003-2010.pdf) and the report of NOTIFY, a global consultation organized by the Italian National Transplant Centre and the European Union–funded Project "Vigilance and Surveillance of Substances of Human Origin" exploring vigilance notification for organs, tissues, and cells (published in February 2011; http://www.notifylibrary.org/sites/default/files/BOOK%20NOTIFY.pdf).

A consensus was achieved that a classification system for evaluating the physical status of a donor would be very useful to enable assessment by independent physicians or respective specialists for donors with disorders (eg, cardiologists, dermatologists, rheumatologists) who should preferably have knowledge of PBSC mobilization and/or PBSC and bone marrow (BM) donation modalities. Especially for related donor evaluation assigned to BM donation, the implementation of the American Society of Anesthesiologists Physical Status (ASA-PS) classification system [19] was discussed as a possibly useful tool because it records only the individual's preoperative physical status rather than the surgical risk. The ASA system consists of 5 categories that classify individuals according to the severity of their systemic disease and is used worldwide by anesthesia providers [20] (Supplementary Table 2).

The term "disorders" expresses all medical conditions that may affect the safety and efficacy of donation. The participants agreed that the term "generally not recommended" instead of "deferral" should be used to categorize certain medical conditions in the related donor setting.

RESULTS

General Considerations

During the process of donor selection and evaluation, the following general considerations need to be taken into account.

1. *A 10/10 HLA-identical URD should be preferred to a related donor with health disorders exposing himself or herself or the recipient to a higher risk for adverse events as described in the entire article.* For many diseases outcome after URD transplantation is comparable with HSCT with related donors [21]. For these situations an URD if available should be preferred to a related donor with health disorders.
2. *Suitability might be assessed also in donors below and above the age limits for URD.* No strict chronological age limit can be recommended for related donors, but experience is available up to a donor age of 75 years. However, physicians assessing the donor's suitability