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## Letter-to-the-Editor

## Cryopreservation for All Is No Option in Unrelated Stem Cell Transplantation. Comment on Dholaria B, et al. Securing the Graft During Pandemic: Are We Ready for Cryopreservation for All? *Biol Blood Marrow Transplant.* 2020;26:e145-e146.



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Dholaria et al [1] discuss the implications of 2 recent studies [2,3] analyzing the outcome of allogeneic hematopoietic stem cell transplantation (HSCT) with cryopreserved products. The results are rather encouraging, with the exception of severe aplastic anemia, and the authors raise the question of whether we are “ready for cryopreservation for all.” The commentary largely overlooks the implications for unrelated donors and from the perspective of an unrelated stem cell donor registry, we would caution the transplantation community and answer this question with “no.” However, we point out a path that may in the future allow the interests of unrelated donors and patients with their physicians to be better reconciled.

DKMS is a leading stem cell donor registry, with more than 10 million registered donors in 6 countries, including more than 6.6 million donors registered with DKMS Germany [4]. Before the COVID-19 pandemic, cryopreservation of unrelated stem cell products from DKMS Germany donors occurred in only a relatively small number of cases: of the 5603 products collected in 2019, only 262 (4.7%) were cryopreserved (239 peripheral blood stem cell [PBSC] products and 23 bone marrow products). In each of these cases, requests were individually assessed and, for reasons of donor protection, approved only if there were sound reasons for cryopreservation. According to our information, 18 of the 262 products were not transfused. Eight of these have been discarded in the meantime, and at least some of the remaining 10 products likely will not

be transfused either, resulting in a nontransfusion rate between 3.1% and 6.9%.

Cryopreservation of stem cell products has been unavoidable at times during the COVID-19 pandemic owing to border closures, passenger flight cancellations, and other crisis-related uncertainties and remains a prudent approach in some cases. Accordingly, the number of cryopreserved stem cell products from DKMS Germany donors has increased significantly. Of the 2299 products collected between March 1, 2020, and July 31, 2020, 1629 (70.9%) were cryopreserved. Thirty-one of these products (1.9%) will definitely not be transfused, according to information received by August 3, 2020. Worsening of the patient’s health status and discontent with product characteristics (eg, cell count) are typical reasons for nontransfusion. For many other cases, we know that the originally planned transplantation date has passed without the product being transfused or have no information at this time. Based on our experience with the cases already closed, we assume that between 5% and 10% of the cryopreserved products will not be transfused eventually.

When a fresh stem cell product is being transplanted, patient conditioning begins before the product is even collected. When the product arrives at the transplantation center, a last-minute change in therapy would not be in the patient’s best interest in most cases. Cryopreservation changes the clinical scenario; the cryopreserved product once received at the transplantation center before the start of conditioning is now a therapeutic option, but no more. Of course, every transplantation physician should constantly reevaluate all therapeutic options. If for whatever reason the cryopreserved product of an unrelated donor no longer seems to be the best therapeutic option, it would be absurd to transfuse it anyway of course. Donor safety also must not play a role in this decision, because whether or not the product is transfused obviously does not alter the risks of previous stem cell donation.

From the perspective of an unrelated stem cell donor, the situation is different. The donor undergoes apheresis after

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several days of stem cell mobilization or bone marrow harvest under general anesthesia to help a stranger. Both procedures are fundamentally safe but not entirely without risks [5,6], and are both time-consuming and associated with inconvenience for the donor. Therefore, each unused stem cell product from an unrelated donor poses an ethical problem, which should be avoided wherever possible. As stated above, at DKMS Germany we had up to 18 such cases in 5603 collections (.32%) in 2019. The COVID-19 crisis taught us that the number of nontransfused products will increase significantly with a “cryopreservation for all,” which raises serious ethical questions regarding the use of unrelated donors.

Even before the COVID-19 crisis, DKMS has begun to set up an adult unrelated donor stem cell bank (SCB), the adult donor equivalent of a cord blood bank. The main goal of this SCB is to be able to provide cryopreserved stem cell products from adult unrelated donors with 100% availability within a few days in urgent cases. We plan to cryopreserve the first stem cell products before the end of this year. The DKMS SCB will include only PBSCs from stem cell collections that have been performed for a specific patient. Our goal is to minimize the additional donor burden. The donor will not be given an additional dose of G-CSF, nor will there be a second day of apheresis. We will focus on young male donors with frequent HLA genotypes and on collections with favorable donor-patient weight ratio. The stem cell products will be made available via the usual channels (ie, World Marrow Donor Association, national registries). To our knowledge, several other stem

cell donor registries are considering similar projects. We believe that this approach has the potential to address the interests of both unrelated donors, who should not be exposed to the risks of stem cell donation for an ultimately nontransfused product, and patients and their physicians, for whom the logistical advantages of a cryopreserved product sometimes take precedence.

#### DECLARATION OF COMPETING INTEREST

The authors have no conflicts of interest to report.

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