Between 2001 and 2012, the number of unrelated donors registered worldwide increased from 7 to 21 million, and the number of public cord blood units increased to over 500,000. We addressed the question of whether this expansion resulted in higher percentages of patients reaching transplantation. Unrelated donor searches were evaluated for 3,124 eligible patients in the Netherlands in two cohorts (2001-2006, n=995; 2007-2012, n=2129), comparing results for patients of Northwestern European and non-Northwestern European origin. Endpoints were ‘donor found’ and ‘transplantation reached’. The substantial growth of the donor inventory over the period studied did not increase the median number of potential unrelated donors (n=7) for non-Northwestern European patients, but almost doubled the number for Northwestern European patients from 42 to 71. Before and after 2007, an unrelated donor or cord blood was identified for 91% and 95%, respectively, of Northwestern European patients and for 65% and 82% of non-Northwestern European patients (P<0.0001). Non-Northwestern European patients more often needed a cord blood transplant. The degree of HLA matching was significantly lower for non-Northwestern European patients (P<0.0006). The time needed to identify a donor decreased for both populations. The percentage of Northwestern European patients reaching transplantation increased from 77% to 83% and for non-Northwestern European patients from 57% to 72% (P=0.0003). The increase of the global inventory resulted in more transplants for patients lacking a family donor, although the quality and quantity of (potential) haematopoietic cell grafts for patients of a non-Northwestern European descent remained inferior, indicating the need for adaptation of recruitment.
Introduction

Allogeneic hematopoietic progenitor cell transplantation plays an important role in treatment of hematological diseases. For patients lacking a matched related donor, an unrelated donor (UD) or cord blood unit (CBU) may provide a valuable alternative. Alternative donors are identified through registries of volunteer unrelated donors or public cord blood banks. In the past decade, the identification and availability of UD and UCB have improved. Bone Marrow Donors Worldwide (BMDW), the file of registered unrelated donors, almost tripled (from 7.4 million donors in 2001 to over 21 million in December 2012), while the inventory of unrelated CBU grew from 87,000 in 2001 to over 500,000. To date (2016) the number of registered donors has increased to over 27 million, and currently over 650,000 CBU are registered. Increased knowledge of the HLA system, more well-typed donors, and the availability of several search-related software tools have facilitated and speeded up the efficiency of the search process. Simultaneously searching for a back-up donor can minimize the delay if a donor is unexpectedly not fit or unavailable to donate. Given these recent improvements, we set out to address the questions of whether a higher percentage of patients in need of an UD/CBU may actually reach transplantation nowadays, whether the time needed to identify an UD/CBU has decreased, and whether possible factors can be identified for potential improvement. We addressed the questions in a large cohort of 3,365 consecutive UD searches performed between 2001-2012 in the Netherlands, including searches for Dutch patients of Northwestern European (NWE) and non-Northwestern European (non-NWE) descent.

Methods

The patients and donor searches

Europodonor Foundation, the Dutch Stem cell donor registry, coordinates the UD searches in the Netherlands, serving a population of 16.8 million inhabitants. There were eight adult and two pediatric stem cell transplantation units in 2012 in the Netherlands, and the number of new searches increased to approximately 500 annually. All UD and CBU searches performed from 2001 until 2012 for the patients of all Dutch transplantation centers were included (n=3,365, Figure 1) for the initial ‘donor found’ analysis, and divided into two periods: cohort I, 2001-2006 (n=1,093) and cohort II, 2007-2012 (n=2,272). Patients for whom a search was cancelled in less time than the median search time for the given year, and for whom no donor was yet identified were excluded for the ‘donor found’ analysis (cohort I, n=75; cohort II, n=131), leaving 3,124 evaluable search cases. Each cohort was split according to NWE and non-NWE descent. Patients were assigned to NWE or non-NWE background based upon self-identified descent. Descendants from the Netherlands, Germany, Belgium, Luxembourg, Great Britain, Ireland, and Scandinavia were considered NWE. The non-NWE group consisted of patients with self-reported genetic ancestry in Northern Africa (n=51), Sub-Saharan Africa (n=22), Turkey (n=87), Asia (n=54), Eastern Europe (n=4), Hispanic (n=9), or mixed (n=125). Patients with unknown ethnic background (n=35, of whom 14 reached
transplantation) were excluded. Searches for combined donor/CBU and CBU-only and searches for NWE and non-NWE patients were analyzed separately.

Diagnoses were described in broad groups (Table 1). Overall, a donor was found for 2,861 (91%) of the patients (Table 2). For the subsequent analysis of ‘reaching transplantation’ we excluded 288 patients from the original cohorts I (n=89/995) and II (n=199/2,129) for whom a donor was found but transplantation was cancelled for reasons not related to the search process (Figure 1). These reasons included never having reached remission/refractory disease (n=100), alternative therapy chosen (e.g. anti-thymocyte globulin for severe aplastic anemia, or randomized to a non-transplant arm in a study, n=88), autologous hematopoietic stem cell transplant (n=5), (extended) family donor available (n=23), indication changed/good clinical condition (n=27), and patient withdrawal (n=45). This left 2,836 patients for whom a successful search was performed (788 NWE and 118 non-NWE patients in cohort I, and 1,720 NWE and 210 non-NWE patients in cohort II).

Search strategies

The basis for the UD/CBU search has been described elsewhere,[11,12] and was adjusted to new insights and better quality of the donor pool. Each new search, irrespectively of whether it was for an UD or CBU, started with estimation of the likelihood of finding an acceptable donor, taking into consideration the match-grade or haematopoietic cell source preferences of a center. These results were communicated to the center so that, in cases for which it was unlikely that an acceptable donor would be found, search strategies or treatment options could be adjusted to avoid unnecessary delay.

The search profile for an UD was based upon confirmed HLA-typing of the patient (HLA-A, B, C, DRB1, DQB1 high resolution), including a review of family typing, haplotype frequencies, allele frequencies, HLA-B/C-associations, and HLA-DRB1/DQB1 associations. Ethnic background and results of the BMDW regular exchange from all patients referred for UD searches. Additional informed consent for (anonymized) data analysis and data exchange from all patients referred for UD searches. Additional Institutional Review Board approval to perform this study was not necessary. Dutch Transplant Centers are responsible for obtaining informed consent for (anonymized) data analysis and data exchange from all patients referred for UD searches. Additional Institutional Review Board approval to perform this study was not necessary.

Table 1. Baseline characteristics of 2772 NWE and 352 non-NWE patients in the two search periods.

<table>
<thead>
<tr>
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</tr>
</thead>
<tbody>
<tr>
<td>Acute leukemia</td>
<td>341 (39.2)</td>
<td>885 (46.6)</td>
<td>P=0.0003</td>
<td>50 (40.3)</td>
<td>85 (37.3)</td>
<td>n.s.</td>
</tr>
<tr>
<td>Chronic leukemia</td>
<td>123 (14.1)</td>
<td>165 (18.8)</td>
<td>P=0.0038</td>
<td>16 (8.1)</td>
<td>16 (7.0)</td>
<td>n.s.</td>
</tr>
<tr>
<td>Myelodysplastic syndrome</td>
<td>124 (14.2)</td>
<td>241 (21.7)</td>
<td>P=0.0038</td>
<td>11 (6.8)</td>
<td>19 (8.1)</td>
<td>n.s.</td>
</tr>
<tr>
<td>Lymphoma</td>
<td>109 (12.5)</td>
<td>227 (11.9)</td>
<td>n.s.</td>
<td>4 (3.2)</td>
<td>19 (8.1)</td>
<td>n.s.</td>
</tr>
<tr>
<td>Other malignant diseases</td>
<td>57 (6.5)</td>
<td>190 (16.0)</td>
<td>P=0.0032</td>
<td>2 (1.6)</td>
<td>8 (3.5)</td>
<td>n.s.</td>
</tr>
<tr>
<td>Non-malignant disease</td>
<td>117 (13.4)</td>
<td>163 (8.6)</td>
<td>P=0.0001</td>
<td>47 (37.9)</td>
<td>81 (35.5)</td>
<td>n.s.</td>
</tr>
</tbody>
</table>

Acute leukemia includes acute lymphoblastic leukemia and acute myeloid leukemia; chronic leukemia includes chronic lymphocytic leukemia and chronic myeloid leukemia. Other malignant diseases include plasma cell disorders, Non-malignant diseases include bone marrow failure and inborn errors. *Fisher exact test; **Wilcoxon rank sum test; ***chi square test.
Results

The baseline characteristics of NWE (n=2,772) and non-NWE (n=352) patients are presented in Table 1. The distribution of NWE and non-NWE patients did not differ significantly over time between the two cohorts (13% non-NWE in cohort I, and 11% non-NWE in cohort II). Data for non-NWE and mixed background patients were also analyzed separately, but showed similar outcome results and no significant differences between groups. The medi-

Table 2. Characteristics of the search process and reaching transplantation for NWE and non-NWE patients in the two periods.

<table>
<thead>
<tr>
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<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Total n. of patients</td>
<td>871</td>
<td>1901</td>
<td></td>
<td>124</td>
<td>228</td>
<td></td>
</tr>
<tr>
<td>HLA-A/B/DR- matches in BMDW*</td>
<td>(0-17651)</td>
<td>(0-37618)</td>
<td>P=0.0002</td>
<td>7</td>
<td>7</td>
<td>n.s.</td>
</tr>
<tr>
<td>median number (range)</td>
<td>42</td>
<td>71</td>
<td></td>
<td>115</td>
<td>187</td>
<td></td>
</tr>
</tbody>
</table>

Search performed, n (%)**

Donor/CBU search, n          | 862       | 1819      |       | 9 (1)     | 82 (4.5)  | P<0.0001  |
CBU only search, n (%)       | 3869      | 8450      |       | 77 (1-17) | 4 (1-17)  | n.s.    |
Median (range)               | 4         | 3         | P<0.0001 | 3         | 2         | n.s.    |

Donor/CBU found, n (%)**

Donor, n (%)                 | 788 (90.5)| 1807 (96.1)| P<0.0001 | 80 (64.5)| 186 (91.6)| P=0.0007 |
CBU, n (%)                   | 756 (88.5)| 1624 (85.4)| n.s.    | 58 (46.8)| 112 (48)  | n.s.    |

No donor found, n            | 83        | 94        | P<0.0001 | 44        | 42        | P=0.0007 |
Donor not acceptable, n      | 7         | 26        |         | 2         | 1         |         |

Match-grade donors if, **

10/10, n (%)                 | 460 (64.2)| 1153 (68.8)| P=0.03  | 23 (38.8)| 46 (25.6)| n.s.    |
9/10, n (%)                  | 193 (26.9)| 326 (19.4)| P=0.0003 | 28 (35.0)| 59 (32.8)| n.s.    |
<9/10, n (%)                 | 32 (4.5)  | 17 (1.0)  | P<0.0001 | 7 (8.8)  | 1 (0.6)   | n.s.    |

CMV status known, n. of pairs | 381       | 1126      |       | 31        | 70        |       |
Matched (%)                  | 237 (62.2)| 817 (72.5)| P<0.0001 | 21 (67.7)| 49 (70.0)| n.s.    |
CMV mismatched, n (%)**      | 144 (37.8)| 309 (27.5)| P=0.0002 | 10 (32.3)| 21 (30.0)| n.s.    |
Pat. negative – donor positive, n (%) | 51 (13.4)| 122 (9.9)| P=0.02  | 1 (3.2)  | 6 (8.6)  | n.s.    |
Pat. positive – donor negative, n (%) | 93 (24.4)| 187 (16.6)| P=0.0001 | 9 (29.1)| 15 (21.4)| n.s.    |

Length of search in days*

Start-donor found, median (range) | 43 (2-393)| 34 (1-276)| P<0.0001 | 56 (7-123)| 36 (1-290)| P=0.0005 |
Excluded, n**                 | 83        | 181       | n.s.    | 6         | 18        | n.s.    |
Included for reaching transplant analysis, n | 788 | 1720 | 118 | 210 |     |

Reaching transplant, n (%)**

UD BM/PBSC, n (%)             | 571 (93.8)| 1248 (87.6)| P<0.0001 | 43 (64.2)| 82 (54.3)| n.s.    |
CBU, n (%)                    | 28 (4.6)  | 169 (11.6)| P<0.0001 | 19 (28.4)| 62 (41.1)| n.s.    |
Alternative family donor, n (%) | 10 (1.6)| 8 (0.8)  | P<0.03   | 5 (7.4)  | 7 (4.6)  | n.s.    |
With back-up donor/CBU, n (%) | 68 (10.8)| 157 (11.1)| n.s.    | 2 (3.0)  | 13 (9.0) | n.s.    |

Time to transplantation in days

Donor found – infusion        | 68        | 54        | P<0.0001 | 48        | 53        | P=0.0001 |
Start – infusion              | 113       | 91        | P<0.0001 | 109       | 92        | P=0.0008 |
If CBU                       | 102       | 85        | P<0.0001 | 91        | 81        | P=0.0001 |
Transplant with back-up donor (%) | 68 (11.4)| 157 (11.1)| n.s.    | 2 (3.3)  | 13 (9.0) | P=0.01  |

CMV: cytomegalovirus; BM: bone marrow; PBSC: peripheral blood stem cells. *Fisher exact test; **Wilcoxon rank sum test; ***chi square test. #Match-grade for 71 patient donor pairs in cohort I and 129 in cohort II were considered unknown due to incomplete typing.


Donor found

A donor was found for 2,861 patients (91%). Significantly more UD/CBU were found in cohort II (P<0·0001) for both NWE and non-NWE patients (Table 2). In cohort I, an UD/CBU was identified for 91% of NWE patients and 65% of non-NWE patients. In cohort II, an UD/CBU was identified for 95% of NWE and 82% of non-NWE patients. Cord blood as an alternative haematopoietic cell source was needed more frequently for non-NWE patients in both cohorts (P<0·0001), although better matched (6/6) units were more often found for non-NWE patients in both cohorts (P<0·0001), as well as NWE patients almost doubled over time (18%-33%).

Grade of HLA-matching and aspects of non-HLA-matching

Major differences in match-grade were observed between NWE and non-NWE patients. As far as concerns non-NWE patients, fewer 10/10 HLA-matched or 9/10 HLA-matched donors were identified in cohort II than in cohort I. A 9/10 donor was found for at least 91% of NWE patients in cohort I and 88% in cohort II, compared to 64% of non-NWE patients in cohort I and 58% non-NWE patients in cohort II (Table 2).

The median time to identify a donor in a combined donor/CBU search for NWE patients was 43 days in cohort I and 34 days in cohort II. The same improvement was also seen for non-NWE patients (median of 56 and 36 days in cohort I and II, respectively, Table 3).

A CBU-only search was performed upon request of the centers for 18 patients in cohort I (2%) and 123 patients in cohort II (6%). Preferred CBU-only searches were performed significantly more often for non-NWE patients in both cohorts. A preferred CBU search, despite the availability of a fully matched UD, was performed for a few non-NWE patients (1 and 2 patients in cohort I and II, respectively) and some NWE patients (5 and 17 patients in cohort I and II, respectively).

Other characteristics that may affect transplant outcome, such as donor-recipient gender disparity, reduced over time for NWE patients but not for non-NWE patients in cohort II. Cytomegalovirus status mismatches between the recipient-donor pairs decreased significantly for NWE patients but not for non-NWE patients.

The donor searches for the patients excluded from the ‘reached transplantation’ analysis (89 in cohort I and 199 in cohort II, see Methods section) did not differ in length (median 42 days and 35 days, respectively). No acceptable UD/CBU was identified for 127/995 patients (13%) in cohort I and 136/2124 (6%) patients in cohort II. The median search time was longer for these patients than those in the ‘donor found’ group (P<0·0001, data not shown).

Reaching transplantation

Despite a successful donor search, Transplant Centers cancelled procedures for 89 patients in cohort I and 199 patients in cohort II, because the patients clinically deteriorated or died (Table 2). There was no correlation between length of search and whether or not a transplant was actually performed. The time from starting the search to transplantation was significantly shorter for patients receiving a cord blood graft in cohort II (P<0·0001). The percentage of transplanted patients increased significantly over time, with NWE patients more often reaching their

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**Table 3. Major differences between results for NWE and non-NWE patients in the two periods (I: 2001-2006, II: 2007-2012).**

<table>
<thead>
<tr>
<th></th>
<th>NWE I</th>
<th>NWE II</th>
<th>P</th>
<th>non-NWE I</th>
<th>non-NWE II</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median age (years)*</td>
<td>38.5</td>
<td>13.8</td>
<td>P&lt;0·0001</td>
<td>51.5</td>
<td>19.9</td>
<td>P&lt;0·0001</td>
</tr>
<tr>
<td>Diagnosis (%)**</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Acute myeloid leukemia</td>
<td>23.8</td>
<td>20.2</td>
<td>n.s.</td>
<td>33.9</td>
<td>21.5</td>
<td>P&lt;0·0001</td>
</tr>
<tr>
<td>Plasma cell dyscrasias</td>
<td>5.9</td>
<td>0.8</td>
<td>P=0·0153</td>
<td>9.3</td>
<td>3.5</td>
<td>P=0·0018</td>
</tr>
<tr>
<td>Non-malignant disease</td>
<td>8.8</td>
<td>32.3</td>
<td>P&lt;0·0001</td>
<td>5.1</td>
<td>27.6</td>
<td>P=0·0001</td>
</tr>
<tr>
<td>Median donors in BMDW (n)*</td>
<td>42</td>
<td>7</td>
<td>P&lt;0·0001</td>
<td>71</td>
<td>7</td>
<td>P&lt;0·0006</td>
</tr>
<tr>
<td>CBU only search (%)***</td>
<td>1</td>
<td>7.3</td>
<td>P&lt;0·0001</td>
<td>4.4</td>
<td>41</td>
<td>P&lt;0·0001</td>
</tr>
<tr>
<td>Samples received for CT (%)*</td>
<td>63</td>
<td>53</td>
<td>P=0·05</td>
<td>65</td>
<td>49</td>
<td>P&lt;0·0001</td>
</tr>
<tr>
<td>Length of search (days)</td>
<td>43</td>
<td>56</td>
<td>P=0·013</td>
<td>34</td>
<td>36</td>
<td>P=0·02</td>
</tr>
<tr>
<td>Donor/CBU found (%)****</td>
<td>90.5</td>
<td>64.5</td>
<td>P&lt;0·0001</td>
<td>95.1</td>
<td>81.2</td>
<td>P&lt;0·0001</td>
</tr>
<tr>
<td>10/10 (%)</td>
<td>64.2</td>
<td>28.8</td>
<td>P&lt;0·0001</td>
<td>68.8</td>
<td>25.6</td>
<td>P&lt;0·0001</td>
</tr>
<tr>
<td>9/10 (%)</td>
<td>26.9</td>
<td>35</td>
<td>P=0·02</td>
<td>19.4</td>
<td>32.8</td>
<td>n.s.</td>
</tr>
<tr>
<td>CB as stem cell source (%)</td>
<td>4.7</td>
<td>27.6</td>
<td>P&lt;0·0001</td>
<td>10.1</td>
<td>39.8</td>
<td>P&lt;0·0001</td>
</tr>
</tbody>
</table>

*Wilcoxon rank-sum test; **Fisher exact test; CT-confirmatory typing; CB, cord blood.
intended transplantation. In total 77% (609/788) NWE and 57% (67/118) non-NWE eligible patients in cohort I and 82% (1,425/1,720) NWE and 72% (144/210) non-NWE eligible patients in cohort II reached transplantation. The increase in reaching transplantation was statistically significant for both NWE and non-NWE patients ($P=0.001$ and $P=0.007$, respectively) in the two cohorts, but not between NWE and non-NWE patients in cohort II. Overall NWE patients were transplanted with better matched donors (Figure 2), and cord blood as the source of hematopoietic cells was significantly more frequent in non-NWE patients. Fifteen patients in both cohorts were transplanted with a mismatched family donor (haplo-identical), because the chosen donor (and back-up donor if identified) was no longer available. Overall, 240 patients received hematopoietic cells from a back-up donor ($n=234$) or a back-up cord blood unit ($n=6$), because the initial chosen donor was no longer available: 70 patients in cohort I (9.3% of NWE and 5.5% of non-NWE patients) and 170 patients in cohort II (9.8% of NWE and 7.8% of non-NWE patients).

Discussion

In the last decade, substantial investments resulted in an increase of the worldwide hematopoietic progenitor cell donor pool and improvement of the quality of donor HLA typing. However, the availability of alternative donors, especially for patients of non-European descent remains concerning. Currently, for a Dutch NWE patient a median number of 71 potentially matched donors are listed, often allowing selection for non-HLA characteristics (e.g., age, gender, cytomegalovirus status) that may improve transplant outcome. In contrast, we found that the number of potentially matched donors for our non-NWE patients remained low: a median number of seven UD per patient. We addressed the question of whether the above-mentioned developments resulted in a higher percentage of transplants for Dutch patients. Overall, we observed that the percentages of patients reaching transplantation among both NWE and non-NWE patients in the period 2007-2012 were higher than those in the search period before 2007. However, the probability of identifying a 10/10 matched donor for non-NWE patients has not improved, while a significant advantage for NWE patients has become apparent (Table 3). The probability of finding a CBU with at least a 4/6 match increased over time for non-NWE patients, but here also the degree of matching appeared significantly less optimal than that for the NWE patients in our study. Thirty percent of non-NWE patients received cord blood grafts, compared to 10% of NWE patients. Cord blood is currently increasingly used in patients with very poor risk, acute leukemia, needing an immediate transplant after having obtained remission, or children with inborn errors, other than hemoglobinopathies. CBU are almost instantly available and require less stringent HLA matching criteria, but are associated with a higher rate of graft failure and delayed hematopoietic recovery. Studies have suggested that the outcome of cord blood grafting is better when the CBU contains higher numbers of cells, or when double CBU grafts, and/or better HLA-C matched grafts are used. While allele level matching was recently found to be associated with better transplant outcomes, high resolution typing for HLA-A-B-C and DRB1 would probably show 8/8 matching in only 10% of recipient/cord blood pairs. Requiring a higher level of matching for cord blood will result in fewer matching units, in particular for non-NWE patients.
Matching for HLA-DPB1 is currently not mandatory in Dutch transplant protocols. The likelihood of being DBP1-matched is approximately 20%, while approximately 50% permissive HLA-DPB1 mismatches would lower transplant mortality.28 DBP1 selection might be considered in the future, but will be less feasible for non-NWE patients given the restricted numbers of available donors allowing no choices.

Gragert et al. described a theoretical model based on population genetics for calculating the likelihood of finding a well-matched UD or CBU for patients of different ethnic background in the USA.15 Donor availability, inconsistent typing results and donor medical eligibility were taken into account. Their model is based on donor and cord blood data in the BeTheMatch registry itself, representing approximately 50% of the global inventory. They calculated a more than 95% likelihood of identifying an UD/CBU for both white and African-American patients, which is possibly an overestimate. Using 100% of the UD/CBU for both white and African-American patients, calculated a more than 95% likelihood of identifying an UD/CBU for both white and African-American patients, respectively. In this light, preliminary results of recent and ongoing studies indicate that the role of extended family (or haploidentical) donors could become clearer in the future.

All patients for whom no donor was found in our study had one or more rare alleles, uncommon HLA-B-C/DRB1-DQB1 associations, or a combination of these, often originating from a mixed racial background. A similar observation was reported by Testi et al.,27 who identified a 9/10- or 10/10-matched donor for 75% of their 315 patients, who had a high frequency allele. In contrast Grubic et al.26 reported having found a 9/10- or 10/10-matched donor for 95% of 105 Croatian patients, but their cohort only consisted of patients who were actually transplanted. The genetic heterogeneity of a population apparently also plays a role.

A weakness of our study is that the proportions of non-NWE patients in both cohorts (13% and 11%) were small and so confounding factors are possible. However, we have no indication that the findings were influenced by factors such as relapse, untimely referral, more withdrawals, or financial aspects. Unfortunately, the proportion of donors from ethnic minorities in the various donor registries is not recorded.29

In more recent years, the significantly shorter search time, observed for both NWE and non-NWE patients, may be a reason for fewer cancellations. The cancellation rate, due to clinical deterioration of the patient after a donor had been found, preventing the patient from undergoing transplantation, was approximately 50% in the period 1991-2000,30 and only 10% in the years after 2007. This demonstrates the importance of time, in particular in adult patients with high-risk leukemia.30,31 Future complete, high-resolution HLA typing and provision of additional donor characteristics could theoretically minimize the length of a search to a single day,32,33 and probably further reduce the rate of transplant cancellations due to relapsed malignancies. This, however, may not help non-NWE patients, since the limited number of registered, available and suitable non-NWE donors in the national and international registries34-38 highlights the need for strategic recruitment of both UD and CBU,39 and for methods to prevent untimely opt-out of donors, in particular those from ethnic minorities.40 Targeted donor recruitment, with personal and written native speaker support, and through social media, is being increasingly practiced.41 Furthermore, addressing misconceptions about donation add to donor commitment, and improve chances for all patients, but in particular non-NWE patients, to receive optimal allogeneic stem cell grafts.42 The subject is on the agenda of registries united in the World Marrow Donor Association.

Conclusions

Improved efficiency of searches for hematopoietic stem cell donors is associated, overall, with more NWE and non-NWE patients reaching their intended transplantation. However, we conclude from this large retrospective study that the increase of the global inventory and the major efforts and investments to improve the search process have resulted in a strong benefit mainly for NWE patients. For non-NWE patients, the probability of identifying a well-matched UD has not increased over time and non-NWE patients more often rely on CBU as an alternative source of hematopoietic stem cells. In addition, the match-grade for both UD and CBU is less optimal for non-NWE patients. In concordance with others, our findings in successive cohorts of non-NWE patients are strong confirmation of the need to expand the global inventory, focusing on donors and grafts from underrepresented ethnicities.

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