study is provided by Western Institutional Review Board; the IRB determined that additional informed consent for the clinical evaluation reported in this manuscript was not required. This study was supported in part by research funding from Otsuka Pharmaceutical Development and Commercialization Inc (J.D.B.).

The project described was supported by grant award no. UL1RR024143 from the National Center for Research Resources (NCRR), a component of the National Institutes of Health (NIH) and NIH Roadmap for Medical Research, and its contents are solely the responsibility of the authors and do not necessarily represent the official view of NCRR or NIH.

**Conflict-of-interest disclosure:** J.D.B. designed research and performed research, collected, analyzed, and interpreted data, and wrote the manuscript; J.T. and A.M. performed research, collected, analyzed, and interpreted data, and wrote the manuscript; B.C. analyzed and interpreted data and wrote the manuscript; D.G.B. participated in the design of the research protocol; and B.S. wrote the manuscript.

**Correspondence:** J.D.B. is a co-Executive Editor of the American Journal of Hypertension, for which he receives compensation by American Journal of Hypertension, Ltd. He is participating in ongoing clinical trials of tolvaptan for the treatment of autosomal dominant polycystic kidney disease sponsored by Otsuka Pharmaceutical Development and Commercialization Inc, and is a consultant to Forest Research Institute Inc and Primrose Therapeutics Inc. A.M. has received honoraria from CSL Behring. B.C. is an inventor of abciximab (Cenocror) and, in accord with Federal law and the policies of the Research Foundation of the State University of New York, receives royalties based on the sales of abciximab; is an inventor of the VerifyNow assays (Accumetrics) and, in accord with Federal law and the policies of the Mount Sinai School of Medicine, receives royalties based on the sales of the VerifyNow assays; is an inventor of small molecule αIIbβ3 antagonists (RUC-1 and RUC-2) and Rockefeller University has applied for patents on these molecules. D.G.B. has received grant/research support from Otsuka Pharmaceuticals for treatment of polycystic kidney disease with tolvaptan, a vasopressin V2 receptor antagonist. The remaining authors declare no competing financial interests.

**References**


**To the editor:**

Successful mobilization and engraftment of PBSCs derived from donor cord blood cells after a previous allogeneic RIC single unrelated cord blood transplantation

We describe a successful salvage treatment with intensive chemotherapy and stem cell transplantation for a relapse of Hodgkin lymphoma (HL) after single umbilical cord blood transplantation with a reduced intensity-conditioning regimen (RIC).1,2 The originality of this observation is the source of cells for the second transplantation; the grafted cells were obtained by the mobilization in the blood of stem cells (PBSCs) originating from the cord blood unit (CBU) used for the previous transplantation.

A 24-year-old patient was diagnosed with a nodular sclerosis classic HL (stage II Bb according to the Ann Arbor classification) in May 2007. A primary refractory disease was observed after 4 courses of adriamycin, bleomycin, vinblastine, and decarbazine (ABVD); 2 courses of mitoguazone, ifosfamide, vinorelbine, and etoposide plus rituximab (MINE-R); 2 courses of high-dose cytarabine (ARA-C), cisplatin, and dexamethasone (DHAP); and cervical irradiation (supplemental Table 1, available on the Blood Web site; see the Supplemental Materials link at the top of the online article). In August 2008, despite the availability of autologous stem cells and because of the chemotherapy refractoriness, we performed an allogeneic transplantation with RIC and a single unrelated CBU (6/6 HLA compatibility, 2.1 x 10^7 nucleated cells [NC]/kg, and 0.5 x 10^7 CD34+ cells/kg). RIC consisted of fludarabine (40 mg/m²/d on day −6 to day −2), cyclophosphamide (50 mg/kg/d on day −6), and a total body irradiation (2 Gy on day −1). Graft-versus-host disease (GVHD) prophylaxis associating oral mycophenolate mofetil (MMF; 1 g 3 times a day) and cyclosporine A (CsA; 4.5 mg/kg twice a day) was started on day −3. After thawing and washing, the viability of cells was 55%, the patient received 0.9 x 10^7 NC/kg and 0.3 x 10^7 CD34/kg. No grade > 2 conditioning-related toxicity was observed; the patient received G-CSF from day +22 to day +25 and was discharged at day +25 after the graft. Neutrophils were > 1000/L at day +40 and platelets > 50 000/µL at day +52 after transplantation. Grade IIa acute (day +29) and chronic GVHD (eyes and mouth) were treated with appropriate doses of corticosteroids. MMF was stopped at day +30 and CsA at day +240. Complete remission (CR) was confirmed at 3 and 9 months after CBU transplantation. Full donor chimerism was documented by quantitative PCR3 on day +40 and sustained until relapse at 16 months. A relapse occurred in January 2010; the patient received 3 cycles of salvage chemotherapy (GVD) between April and July 2010 (supplemental Table 1).

**Table 1. PBSC CD34+ cells collection**

<table>
<thead>
<tr>
<th>Separator</th>
<th>1st apheresis (July 2010)</th>
<th>2nd apheresis (August 2010)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Time collection, min</td>
<td>182</td>
<td>183</td>
</tr>
<tr>
<td>Volume treated, mL</td>
<td>9011</td>
<td>8001</td>
</tr>
<tr>
<td>Volume collected, mL</td>
<td>161</td>
<td>166</td>
</tr>
<tr>
<td>Circulating CD34+ cells, /µm³</td>
<td>44.1</td>
<td>28.8</td>
</tr>
<tr>
<td>Total collection, x 10^6/kg</td>
<td>2.46 (2 bags)</td>
<td>1.65 (2 bags)</td>
</tr>
</tbody>
</table>
PBSC CD34+ cells were stimulated with G-CSF (10 μg/kg/d for 5 days) after the second and third salvage cycles in July and August 2010 (Table 1). Apheresis collected 4.11 × 10^6 CD34+ cells/kg; these cells originated from the previous transplanted CBU as shown by PCR analyses in blood and on the collected product (Figure 1). A second SCT, conditioned with carmustine, cytarabine, etoposide, and melphalan (BEAM), was performed in September 2010 with the injection of 2.79 × 10^6 CD34+ cells/kg (viability of 92%). The patient experienced transient grade 4 mucositis without any documented infection and rapidly recovered from aplasia with G-CSF support started on day +7; neutrophils were >1G/L at day +11 and platelets >50 G/L at day +42 after the second transplantation. A sustained second CR has been maintained up to now and chimerism evaluations showed 100% derived-CBU cells at 1, 3, and 7 months.

This is the first report showing that, although CBUs contain 10 times fewer progenitor cells than bone marrow, CD34+ cell mobilization is feasible after CBU transplantation, allowing short- and long-term hematologic repopulation to occur by mobilized PBSCs issued from the original transplanted CBU.4

**Figure 1.** Chimerism analysis using STR (short tandem repeat) multiplex polymerase chain reaction. Genomic DNA, extracted from mononuclear, polynuclear, or PBSC CD34+ cells, was used as a template for amplification of 16 polymorphic STR markers (AmpFlSTR Profiler Plus Kit; Applied Biosystems). Full donor chimerism was detected in all informative STR markers (9 of 16) at time of relapse (January 2010), after salvage therapy in both PBSC CD34+ collections (July and August 2010) and 1 month after PBSC infusion (October 2010). Three representative STR markers (D2S1338, FGA, and D21S11) were depicted.

**CORRESPONDENCE** 477

BLOOD, 14 JULY 2011 • VOLUME 118, NUMBER 2

For personal use only.on April 12, 2017. By guest

From www.bloodjournal.org by guest on April 12, 2017. For personal use only.
To the editor:

Selection of unrelated cord blood grafts

We are concerned about statements in the article by Barker et al., who describe a factor of 0.75 \( \times \) TNC (total nucleated cell) to “correct” the TNC content of RBC-replete cord blood units. No data are provided to justify such an opinion, and the authors cite only “personal communication with multiple US investigators, 2004-2009.” Implementation of this policy, if incorrect, would underestimate the progenitor cell content of RBC-replete units resulting in the inappropriate rejection of some such units by transplant physicians in favor of RBC-reduced units. This would jeopardize the success of some such units by transplant physicians in favor of RBC-reduced units.

We are concerned about statements in the article by Barker et al., who propose 0.75 “correction factor,” and our data indicate that the expected 0.75 “correction factor” for RBC-replete units. This would jeopardize the success of these units by transplant physicians in favor of RBC-reduced units.

In Table 1, the average TNC of plasma-reduced units after processing was 124% of that in RBC-reduced units (81.56 \( \times 10^7 \) vs 65.77 \( \times 10^7 \), respectively [\( P = .002 \); 2-sample t test]). Of major importance is that plasma reduction caused virtually no loss of CD34+ cells, whereas there was a 16% loss of CD34+ cells in the RBC-reduced units, so that the postprocessing CD34+ cell count in plasma-reduced units was 121% of that in RBC-reduced units (1.415 \( \times 10^6 \) vs 1.165 \( \times 10^6 \), respectively, [\( P = .003 \)]). The recoveries of colony-forming units (CFU) were also higher for plasma-reduced products: 225% for CFU-GM (\( P = .05 \)) and 186% for total CFU (\( P = .01 \)). This indicates that the higher TNC value of RBC-replete units does not exaggerate the number of progenitor cells available and that a “correction factor” is inappropriate. The cell dose that is ultimately infused can be affected by washing cord blood units and that a “correction factor” is inappropriate. The cell dose that is ultimately infused can be affected by washing cord blood units.

Because there are no data to support the use of the authors’ proposed 0.75 “correction factor,” and our data indicate that the authors’ assertion that such correction should be applied to the TNC of RBC-replete units is incorrect, we submit that the authors’ important and potentially detrimental statement should not be accepted by the transplantation community at this time.
Successful mobilization and engraftment of PBSCs derived from donor cord blood cells after a previous allogeneic RIC single unrelated cord blood transplantation

Fabrice Larosa, Eric Deconinck, Philippe Helias, Jean Fontan, Marian Heczko, Annie Brion, Katell Ledu, Philippe Delaby, Jacqueline Vuiller, Christophe Ferrand, Philippe Saas, Fabienne Pouthier, Anne Dormoy, Jacqueline Chabod, Caroline Malugani, Pierre S. Rohrlich and Faezeh Legrand