# Screening of related donors and peripheral blood stem cell collection practices at different Italian apheresis centres

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**Background.** Recommendations on eligibility criteria for donation of haematopoietic stem cells, management of collection of the cells and follow-up mainly concern unrelated donors. The aim of this study was to analyse the screening of related donors and collection practices at different Italian apheresis centres.

**Materials and methods.** A questionnaire regarding eligibility criteria for related haematopoietic stem cell donors, their peripheral blood collections and early follow-up was sent to several apheresis units. Data from the full charts of 500 candidates, screened between May 2005 and December 2009, were retrospectively evaluated.

**Results.** The donors' records, eligibility criteria, collections and follow-up are managed differently in each centre. Of the 500 evaluable candidates (51.2% male, 49.8% female; median age 47 years, range 13-77), 26.4% underwent thorough screening according to Italian Bone Marrow Donor Registry standards, while local protocols were applied to 73.6%; 91 candidates (18.2%) proved ineligible for donation. In the end, 352 donors (53.4% male, 46.6% female; median age 45 years, range 16-76) underwent 508 leukaphereses. Central venous catheters were used in 8.0% of donors, mainly in one centre. Unsuitable pre-apheresis peripheral blood parameters were reported in 38.7% of the aphereses. Leukapheresis-related adverse events were recorded in 23.0% of the procedures, with a drop-out rate of 0.2% for severe events. No donation-related fatalities occurred. The CD34+ cell yield was $<2x10^6$/kg of recipient's body weight from 1.1% of donors ≥70 years old.

**Discussion.** More uniformity in donor screening procedures, management of peripheral blood collection and follow-up should be planned at a national level to maximise the safety of related donors.

**Keywords**: related donors; donation eligibility criteria; PBSC collection; donation-related adverse events.

## Introduction

Unrelated haematopoietic stem cell donors benefit from restrictive recommendations on recruitment, eligibility criteria, work-up, management and follow-up based on unrelated donor registry reports, such as the World Marrow Donor Association (WMDA)[1,2] and national registries (for example, the Italian Bone Marrow Donor Registry, IBMDR). Although the European Group for Bone Marrow Transplantation (EBMT) survey in 2009 found that a substantial


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proportion of allogeneic haematopoietic stem cell transplants (HSCT) still involve identical sibling donors and other family members (43% and 6%, respectively, versus 51% of unrelated donors)[3], real standardised criteria for stem cell collection from related donors are still lacking. Principles and recommendations for related donors have been suggested by the WMDA Ethics and Clinical working groups[4] and by other authors[5,6]. The Italian Decree on Blood Donation 2005[7] contains rather vague suggestions for haematopoietic stem cell donation and the mobilisation of cells by granulocyte colony-stimulating factor (G-CSF) and only recently have new and updated recommendations on the topic been published by the Società Italiana di Medicina Trasfusionale (SIMTI) and Gruppo Italiano Trapianto Midollo Osseo (GITMO)[8]. Although the Joint Accreditation Committee ISCT & EBMT (JACIE) and/or the Foundation for the Accreditation of Cellular Therapy (FACT) demand that institutions adopt written local guidelines for managing related donors too, only few transplant centres have done this so far. Recent publications point out the previously underestimated risks of allogeneic haematopoietic stem cell donations, including peripheral blood stem cell (PBSC) donations from related donors[9]. Unlike bone marrow (BM) donation, which is a well-established procedure whose related adverse events have been amply studied[10], such data on related PBSC donations are scarce.

The aim of our retrospective study was to investigate any differences in the eligibility criteria adopted and management of related donors and subsequent PBSC collections at different apheresis centres, and any collection-related early adverse events.

## Materials and methods

### Study design and participating teams

This was a retrospective analysis of data collected at several apheresis units affiliated to the Italian Society of Haemapheresis and Cell Manipulation (SIdEM) in Lombardy and Piedmont. A data collection form was sent to physicians at the units to ascertain how closely their practices for related donors followed the IBMDR donor safety guidelines, and to record: (i) general adult HSCT activities; (ii) family donor screening criteria and reasons for deferral; (iii) G-CSF mobilisation; (iv) PBSC collection management; (v) early adverse events related to PBSC donations; and (vi) follow-up policy.

Since the Italian Decree on Blood Donation[7], which includes haematopoietic stem cell donation, was issued in March 2005, the centres were asked to review their candidates' records and subsequent donations from May 2005 to December 2009. In March 2010, 15 teams were contacted and seven of them responded promptly; the remaining centres were sent a reminder and two more answered; a third request had no effect.

Only seven centres could collect a complete data set from their donor charts, while these were only available from 2008 for one centre; one institution was unable to provide details on candidates, reasons for deferral and follow-up; another did not report the pre-apheresis peripheral blood parameters. In the end, data from 500 candidate related donors and 508 PBSC collections performed in 352 donors were analysed.

### Adverse events

Centres were asked to report adverse events occurring within 7 days of PBSC donations regarding G-CSF mobilisation, leukapheresis, central venous catheter (CVC) placement and transfusion needs. Leukapheresis-related adverse events were classified into three groups[11]; (i) symptomatic hypocalcaemia, blood clotting, haematoma at the venipuncture site, insufficient blood flow; (ii) allergic reactions, nausea/vomiting, fever with shivering; (iii) arrhythmias, vaso-vagal reactions, haemolysis.

Any adverse events requiring interruption of the mobilisation and/or leukapheresis and/or admission to hospital were noted and classified as severe. No clinical grading of G-CSF administration, symptoms or quantification of pain was retrospectively requested, as there was no uniformitity between centres in recording these data.

### Follow-up

The centres were asked whether donors were followed up for at least 1 week after PBSC collection and how many donors had haemoglobin (Hb) <11.5 g/dL in females or <12.5 g/dL in males; a platelet count $<50x10^6/\mu L$, leucocytosis $>15x10^6/\mu L$ or leucopenia (lymphocytes $<1.0x10^3/\mu L$ and polymorphonuclear cells $<2.0x10^3/\mu L$). Every centre was also asked to

specify its policy concerning later follow-up (at 1, 6 and 12 months and beyond); no data about this longer follow-up were analysed in this study.

### Statistical analysis

Only descriptive statistics were used. All statistical analyses were conducted using SAS 8 software (SAS Institute Inc., Cary, NC, USA; 1999).

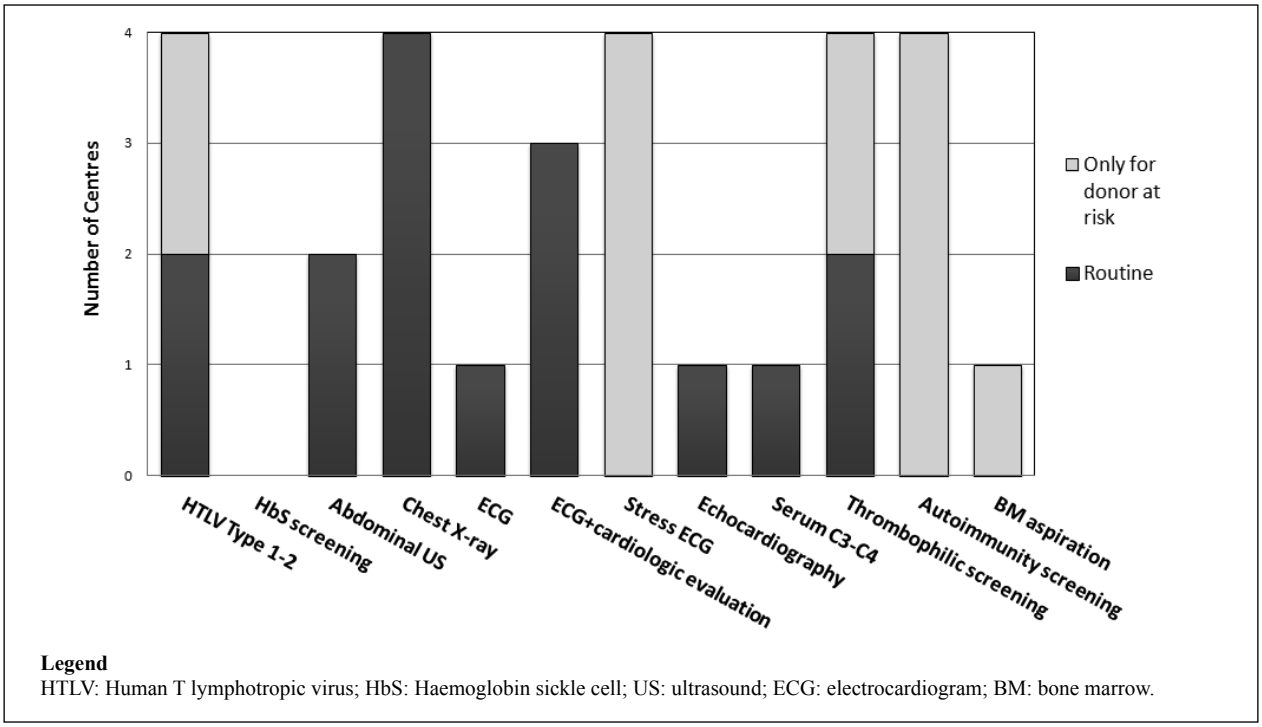
## Results

All participating centres mainly collected PBSC for adult HSCT, except for one centre that considered BM as the principal source. Haplo-identical HSCT was performed at two out of the nine centres. Five of the nine centres, accounting for 328 (65.6%) of the 500 candidates considered, were certified by JACIE. Donors (or the guardians of minors) always signed a written informed consent form, according to each hospital's policy, before the donation. Information and informed consent were provided on both kinds of possible donation (PBSC and BM) to 453 candidates (90.6%) at seven out of the nine centres. Two centres, in which 23.4% of all screening took place, offered candidates the support of a psychologist. When a second donation was required, re-mobilisation occurred 1 to 12 months (median, 6 months) after the first donation, but no fixed timing of second donations was established at four centres. Lymphocytes for donor lymphocyte infusions were collected a median of 7 days before starting mobilisation in the two centres performing haplo-identical HSCT.

### Donor screening and reasons for deferral

Candidate donors first underwent HLA testing. A team including an attending physician from the transplant centre and a physician from the apheresis unit screened 299 candidates at five out of the nine centres, while in the other four at least 201 candidates (one centre gave no information about number of candidates) were checked by an apheresis physician only for the suitability of their peripheral venous access.

IBMDR standards and the Italian Decree on Blood Donations were applied at two out of the nine centres, which assessed 68 candidates (13.6%). Only the national criteria were used at four centres (for 368 candidates, 73.6%), and only the IBMDR standards in the remaining three (for 64 candidates, 12.8%). Overall, 132 (26.4%) of the 500 candidates were evaluated using the IBMDR standards, and 368 (73.6%) according to local protocols (Figure 1). Screening tests for infectious diseases and blood chemistry were not analysed, since this was not an aim of the current study. Pre-mobilisation BM aspiration




**Legend**
HTLV: Human T lymphotropic virus; HbS: Haemoglobin sickle cell; US: ultrasound; ECG: electrocardiogram; BM: bone marrow.

**Figure 1 -** Related-donor assessment criteria used at four centres not following IBMDR standards to evaluate 368 candidates.

was performed in elderly donors (>60 years old) at one institution.

Among the 500 evaluable candidates, whose characteristics are given in Table I, 91 (18.2%) were judged ineligible, while 402 (80.4%) donated either PBSC or BM. Donations were not obtained from seven suitable candidates (1.4%) because HSCT was no longer needed. Personal refusal was the cause of deferral for six candidates (1.2%). The main causes of ineligibility were "various diseases/dubious test findings" (30 candidates, 6.0%), followed by high cardiovascular risk (13 candidates, 2.6%) and autoimmune problems (11 candidates, 2.2%). Other reasons for deferral are given in Table II.

**Table I -** Characteristics of related donors and collections.

| | Candidates | PBSC Donors |
|---|---|---|
| *Donors* | | |
| Number of centres evaluated | 8[1] | 9 |
| Total number of donors | 500[2] | 352 |
| Median donors/centre (range) | 54.5 (2-182) | 42 (2-69) |
| Median age (years) (range) | 47 (13-77) | 45 (16-76) |
| *Gender* | | |
| Male (%) | 256 (51.2) | 188 (53.4) |
| Female (%) | 244 (48.8) | 164 (46.6) |
| *Collections* | | |
| Total | | 508[3] |
| Median (range) | | 46 (2-113) |

**Legend:** [1]one centre out of nine did not provide data about candidates; [2]evaluation performed in 495 candidates for a first donation and in five for a second donation. Fifty candidates donated bone marrow, 91 were ineligible and seven were eligible but their donations were no longer needed; [3]including 32 haplo-identical PBSC collections in two centres.

**Table II -** Reasons for deferral in 500 candidate related donors.

| Reason | N. of candidates (%) |
|---|---|
| Candidate's refusal | 6 (1.2) |
| Uncooperative candidates | 2 (0.4) |
| Pregnancy | 1 (0.2) |
| Old age | 4 (0.8) |
| Infections | 8 (1.6) |
| Drugs/dangerous behaviour | 3 (0.6) |
| Haematological disease | 4 (0.8) |
| Congenital disorders | 1 (0.2)[1] |
| Autoimmunity[2] | 11 (2.2) |
| High cardiovascular risk | 13 (2.6) |
| Other diseases/dubious test findings[3] | 30 (6.0) |
| Transplant problems[4] | 8 (1.6) |

**Legend:** [1]G-6-PD deficiency;[2]autoimmunity (serological findings and/or autoimmune disease); [3]history of malignant diseases; pulmonary pathology and infections; neurological diseases; [4]donor's anti-HLA antibodies against recipient's platelets in haplo-identical HSCT; no NK alloreactivity in haplo-identical HSCT for myeloid disease.

### Granulocyte colony-stimulating factor mobilisation schedule

Overall mobilisation was performed in 352 donors and handled by the apheresis physician at three of the nine centres (for 254 mobilisations, 72.2%) and by the transplant centre physician at six centres (for 97 mobilisations, 27.6%). Filgrastim was the only agent used at three centres, filgrastim or lenograstim at three, filgrastim and pegfilgrastim at one and lenograstim at two. For HLA-identical transplant protocols the median dose of G-CSF was 10 μg/kg recipient's body weight daily at eight of the nine centres and 9 μg/kg daily at one centre. Leukapheresis was performed on day +4 after G-CSF at six centres and on day +5 at the three others. For haplo-identical HSCT, PBSC were always collected on day +4 after G-CSF 15 μg/kg daily at one centre, and 16 μg/kg daily at the other. A single dose of 12 μg/kg recipient's body weight of pegfilgrastim was reported for the mobilisation protocol as already described by other authors[12] in a single-centre experience.

### Peripheral blood stem cell collection

Pre-leukapheresis peripheral blood parameters were available for 506 PBSC collections at eight centres as shown in Table III. Unsuitable parameters were reported in 38.7% of apheresis with the most common problem being pre-leukaphereses platelet counts because 90 collections (17.8%) started with a platelet count $<150x10^6/\mu L$ and in six more cases the count was $<80x10^6/\mu L$ (1.2%). No blood components were used, apart from autologous platelet reinfusions at three of the nine centres when the post-apheresis peripheral platelet count was $<150x10^6/\mu L$ at one centre and $<100x10^6/\mu L$ at the other two.

Anti-thrombotic prophylaxis was used for high-risk donors at five out of eight centres (low-molecular-weight heparin was used at 4 centres, acetylsalicylic acid at 1). ACE-inhibitors were withdrawn during leukapheresis in all centres.

Differences in the centres' management of PBSC collection are shown in Table IV. Six centres placed

**Table III -** Pre-apheresis peripheral blood parameters for 506 PBSC collections.

| Blood counts[1] | N. of apheresis (%) |
|---|---|
| *Haemoglobin* | |
| <12.5 g/dL in females or <13.5 g/dL in males | 84 (16.6) |
| *Platelets* | |
| <150x10$^6$/μL | 90 (17.8) |
| <80x10$^6$/μL | 6 (1.2) |
| *White blood cell count* | |
| >70x10$^6$/μL | 10 (1.9) |
| *CD34+ cells* | |
| <10/μL | 6 (1.2) |

**Legend:** Data from eight centres (506 leukaphereses). [1]Parameters recorded mainly after the first day of collection. For only three donors was the harvest <10 CD34+ cells/μL on the first day.

**Table IV -** Management of PBSC collection.

| | N. of cases (%) |
|---|---|
| Central venous access/donor | 28 (8.0)[1] |
| Hospitalisation for mobilisation | 59 (17.0)[2] |
| Hospitalisation for leukapheresis | 214 (43.0)[3] |
| Leukapheresis in an ICU | 3 (0.6)[3] |

**Legend:** ICU=intensive care unit, for monitoring donors at cardiovascular risk; [1]Range 1-21. One centre adopted a double lumen jugular catheter in 50% of its donors (21 subjects); [2]n= 352 mobilisation procedures; [3]n= 508 leukaphereses.

CVC for leukapheresis in 8.0% of donors; three centres, accounting for 117 donors (33.2%), never used CVC during the study period. Donors were mainly treated as outpatients, while hospitalisation for donor safety and CVC implantation was used for mobilisation and/or leukapheresis according to local protocols. Only one centre hospitalised donors for the whole period of donation (mobilisation and leukapheresis), partly because donors came from far away.

Data on the results of PBSC collection were available from all centres (352 mobilisations and 508 collections). The CD34+ yield from four donors (1.1%) aged ≥70 years was <2x10$^6$/kg and two of them had to donate BM (total collection of 1.4x10$^6$ CD34+ cells/kg prior to selection in one 75-year old haplo-identical donor and 0.84x10$^6$/kg in one 70-year old). The target dose required by the different protocols was obtained with a median 1.8 collections per donor (range, 1-4), processing the donors' total blood volume a median of 2.5 times (range, 1.5-3.0). Only one donor underwent four collections due to poor mobilisation (total collection of 4.51x10$^6$ CD34+ cells/kg).

**Early adverse events**

Information on early leukapheresis-related adverse events was available from all nine centres. These events occurred in 117 (23.0%) of 508 collections. They were mainly group 1 events (n=113), while there were no group 2 adverse events and group 3 events occurred during four collections. Leukapheresis could not be completed due to a severe adverse event in one donor (0.2%), who developed bronchospasm, hypotension and sporadic extrasystoles 45 minutes after leukapheresis was started. The PBSC collection was interrupted and, after adequate treatment, the donor recovered and donated BM. No CVC-related adverse events were reported. Among 352 evaluable mobilisation procedures, the incidence of G-CSF-related toxicity was 93.2% (328 adverse events). No mobilisation-related deaths or severe events were recorded. Bone pain was the most frequent symptom (60.0%), followed by myalgia without rhabdomyolysis (13.3%), headache (7.5%), asthenia/insomnia (5.6%), fever (2.8%), nausea (1.9%), sweating (1.1%) and abdominal/back pain (0.5%). Splenomegaly, without splenic rupture, was documented by ultrasound during two mobilisation procedures at the same centre (0.5%). No allergic reactions or pulmonary, cardiac, thromboembolic or haemorrhagic problems were reported. The frequency of adverse events in pegfilgrastim-mobilised donors was not different from that reported after conventional G-CSF in a single centre experience.

**Donor follow-up**

All centres offered a follow-up 1 week after PBSC donation, but one was unable to provide data on this follow-up. Among 309 evaluable donors, Hb was <11.5 g/dL in females or <12.5 g/dL in males in 30 donors (9.7%) a week after collection; no cases of relevant thrombocytopenia, leucocytosis, or leucopenia were reported. Eight centres offered a follow-up at 1 month after the donation; follow-up was also offered at 6 months by five centres, at 1 year by six and more than a year after the donation by five centres.

## Discussion

Efforts made by the JACIE organisation to standardise procedures aim to improve the safety of PBSC donations, but -unlike the case of unrelated donors coordinated by the WMDA and national registries- there is still a paucity of information on related donors. A retrospective analysis conducted by the EBMT[9] reported on five fatalities among family donors and a two-fold higher risk of severe adverse events after PBSC collection that after BM donation. In the light of this information, we investigated differences in related donor screening methods among several Italian centres, focusing on how PBSC are collected and early adverse events. The limitation of our study is that it is a retrospective analysis, relying on the team members' ability to collect the data. Only 60% of the centres contacted in the present study answered our questionnaire, because their policy included keeping donor files. Some centres were not able to provide their own data at all or in a complete manner, despite being certified by JACIE, because they did not have them promptly available. In the end, data on 500 candidates and 508 PBSC collections from 352 donors were analysed.

This study showed that the management of related haematopoietic stem cell donors is heterogeneous. At four out of the nine centres donors were only assessed by transplant centre doctors, not by the apheresis team, unless they donated PBSC, so the transplant centre physicians were involved in the care of both the donor and recipient[13,14], although this is widely discouraged[4]. Refusal to donate was the reason for deferral in 1.2% of the candidates, but this could underestimate the phenomenon, since siblings unwilling to donate may have been kept confidential. Psychological support could be offered in the case of uncooperative candidates (0.4% of causes of deferral), but only few centres provided it (2 of the 9 evaluated centres). Although related donors cannot choose between different types of donation because the transplant team usually prefers a particular source of haematopoietic stem cell, counselling on PBSC and BM collections should still be offered, and written consent to both types of collection should be proposed. Anyway, the present study revealed that two centres responsible for the evaluation of 47 candidates (9.4%) omitted this issue. This topic is particularly important should PBSC donation fail, or if the yield of CD34+ cells harvested is insufficient and a BM donation is urgently needed, as reported in this study (0.8%).

While the screening tests for infections are clearly defined and similar to those used for blood donors, no other detailed tests for related haematopoietic stem cell donor work-up were specified by the Italian Decree on Blood Donation[7], and guidelines issued by Italian scientific societies[15] were not exhaustive, until the new, updated recommendations just published[8]. Hence the eligibility criteria and screening tests adopted by the centres analysed in the study period were diverse, with five centres (132 screenings, 26.4%) preferring to follow IBMDR criteria for related donors, while the remaining four centres (368 screenings 73.6%) developed their own criteria, which varied. Apart from chest X-ray and electrocardiography (ECG) (alone or with a cardiological evaluation), which were mandatory for all candidates, only two centres performed ultrasonography of the spleen. Testing for HTLV type 1-2 was mandatory, always or for donors at risk, while no screening for HbS was done, probably because physicians preferred to rely on family history and peripheral blood parameters, which may suggest sickle cell disease. Stress ECG was contemplated for donors at "high cardiovascular risk" (defined differently at different centres - for example, a positive cardiovascular history was the only criterion for prescribing this test at one centre, while at another it was simply age over 50 years). Echocardiography was part of the cardiological protocol at only one centre. Minimal thrombophilic screening as suggested by the IBMDR was always offered at two out of four centres, and for donors whose personal or family history suggested a risk at the others. Autoimmunity was assessed for donors at risk, while a C3-C4 assay was only reported by one centre, probably due to the difficulty of interpreting the potentially frequent borderline results in donors with no real history of autoimmune disease, as may happen for tests for thrombophilia. Standardisation of thrombophilic and autoimmune screenings is advisable, as a more uniform definition of cardiovascular risk: this could facilitate decisions on any need for antithrombotic prophylaxis, which was adopted at five centres, although the use of any drugs for prophylactic purposes remains

controversial. Better results following advances in HLA typing, new immunosuppressive protocols and improved supportive care, as well as the use of reduced conditioning protocols, have increased the transplantation rate and raised the age limits for patients and donors, especially in the related-donor transplantation setting. The main reasons for the permanent deferral of candidates considered in this study were "other diseases/dubious test findings", high cardiovascular risk and autoimmunity. As the age of donors increases, comorbidities are more frequent and a more accurate screening based on the donor's age should be offered[5,16]. The use of aspirated BM as a screening method is controversial. Some transplant centres -like one in our study, which was responsible for screening the largest number of candidates (36.4%)- use BM aspiration to rule out occult haematological malignancies and/or to ascertain BM quality in older donors (>65 years old), or in cases of an abnormal medical history or altered test results. Elderly donors should be carefully evaluated, also for possible higher incidence of complications of leukapheresis and worse mobilisation results[17], with a consequent risk of an insufficient CD34+ yield, as reported in our series (4 donors aged ≥70 years).

Unlike the situation for unrelated donors, the need for a CVC was not an exclusion criterion, as it was used in 8% of our related donors; this percentage is higher than reported in other studies[18], probably because it mainly concerned one centre. CVC were always inserted by anaesthetists, and no CVC-related adverse events were reported.

More harmonised G-CSF mobilisation procedures, hospital admissions and protocols for the timing of re-mobilisation procedures and subsequent donations[19] would be desirable. Greater uniformity in the peripheral blood parameters during leukapheresis should also be considered, since parameters normally deemed unsuitable for starting or continuing collections from blood apheresis donors were accepted in our related haematopoietic stem cell donors, even if mainly recorded after the first day of collection. For example in the studied centres 1.2% of leukaphereses started with peripheral platelet counts <80x10$^6$/μL. Care should nonetheless be taken in these borderline situations, as they may contribute to the occurrence of severe adverse events as already reported[9]. The risk of thrombocytopenia may be prevented by reinfusion of autologous platelets separated from the PBSC, as stipulated in three of the centres, albeit at different post-apheresis platelet counts. Leucocytosis with a white cell count >70x10$^6$/μL was reported in 1.9% of cases, fortunately on the last day of collection. It is to be hoped that recently published recommendations on PBSC mobilisation and collection in adults and children[20] will optimise the clinical practice in the field of allogeneic HSCT from related donors too.

The early adverse events related to PBSC collection in our study were similar to those described elsewhere[6,17,21-24]: 93.2% of the mobilisation procedures prompted some G-CSF-related toxicity, but there were no mobilisation-related deaths or severe events. Leukapheresis-related adverse events were reported in 23.0% of cases, with one severe complication (0.2%), which did not prevent subsequent BM donation. The Intensive Care Unit was used for 0.6% of collections, with cardiovascular monitoring for donors at risk, and no adverse events occurred. Changes in blood counts a week after apheresis mainly affected haemoglobin levels and required no transfusions.

Finally, most centres offered a follow-up for more than a year, but no information on this aspect was collected in this retrospective study. As for unrelated donors, long-term information from scheduled follow-up visits for up to 5 or 10 years would be advisable to safeguard related donors; this strategy has been suggested by recent recommendations[8].

In conclusion, our analysis of PBSC donation by related donors for adult recipients in a small number of Italian regions revealed no severe early adverse episodes related to G-CSF, CVC and leukaphereses, though severe events and mobilisation problems do occur on very rare occasions. While the acceptable risks may differ for related and unrelated donors, more uniform screening criteria and donation management, and a longer, more in-depth follow-up are called for.

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## References


1) Sacchi N, Costeas P, Hartwell L, et al. Haematopoietic stem cell donor registries: World Marrow Donor Association recommendations for evaluation of donor health. Bone Marrow Transplant 2008; **42**: 9-14.
2) Pulsisher MA, Chitphakdithai P, Miller JP, et al. Adverse events among 2408 unrelated donors of peripheral blood stem cells: results of a prospective trial from the National Marrow Donor Program. Blood 2009; **113**: 3604-11.
3) Baldomero H, Gratwohl M, Gratwohl A, et al. The EBMT activity survey 2009: trends over the past 5 years. Bone Marrow Transplant 2011; **46**: 485-501.
4) Van Walraven SM, Nicoloso-de Faveri G, Axdorph-Nygell UA, et al. Family donor care management: principles and recommendations. Bone Marrow Transplant 2010; **45**: 1269-73.
5) Niederwieser D, Gentilini C, Hegenbart U, et al. Transmission of donor illness by stem cell transplantation: should screening be different in older donors? Bone Marrow Transplant 2004; **34**: 657-65.
6) Mc Cullough J, Kahn J, Adamson J, et al. Hematopoietic growth factors - use in normal blood and stem cell donors; clinical and ethical issues. Transfusion 2008; **48**: 208-25.
7) Ministero della salute. Decreti 3 marzo 2005: Caratteristiche e modalità per la donazione del sangue e di emocomponenti; Protocolli per l'accertamento della idoneità del donatore di sangue e di emocomponenti. Gazzetta Ufficiale N. 85; 13 April 2005.
8) Raccomandazioni SIMTI-GITMO per la gestione donazione di cellule staminali ematopoietiche (CSE) nel donatore familiare e non familiare. Edizione 2011. Redatte e condivise da SIMTI e GITMO e approvate da CNS, CNT e IBMDR. Available at http://www.simti.it/cse/raccomandazioni_cse_online_bozza4.pdf. Accessed on 20/10/2011.
9) Halter J, Kodera Y, Ispizua AU, et al. Severe events in donors after allogeneic hematopoietic stem cell donation. Haematologica 2009; **94**: 94-101.
10) Bosi A, Bartolozzi B. Safety of bone marrow stem cell donation: a review. Transplant Proc 2010; **42**: 2192-4.
11) De Silvestro G, Bagatella P, Vicarioto M, et al. The Italian SidEM registry for apheresis: an overview of the 2005 statistics. Int J Artif Organs 2008; **31**: 354-62.
12) Kroschinsky F, Hölig K, Poppe-Thiede K, et al. Single-dose peg-filgrastim for the mobilization of allogeneic CD34+ peripheral blood progenitor cells in healthy family and unrelated donors. Haematologica 2005; **90**: 1665-71.
13) Clare S, Mank A, Stone R, et al. Management of related donor care: a European survey. Bone Marrow Transplant 2010; **45**: 97-101.
14) O' Donnell PV, Pedersen TL, Confer DL, et al. Practice patterns evaluation, consent and care of related donors and recipients at hematopoietic cell transplant centers in the United States. Blood 2010; **115**: 5097-101.
15) GITMO, IBMDR, SIdE, SIE. *Linee Guida per la raccolta delle cellule staminali ai fini di un trapianto allogenico di midollo osseo*. Milano: Edizioni SIMTI; 2001.
16) Jeger A, Favre G, Lutz J-M, et al. Tumor incidence in related hematopoietic stem cell donor. Bone Marrow Transplant 2011; **46**: 1240-4.
17) Lysák D, Kořístek Z, Gašová Z, et al. Efficacy and safety of peripheral blood stem cell collection in elderly donors: does age interfere? J Clin Apheresis 2011; **26**: 9-16.
18) Hölig K, Kramer M, Kroschinsky F, et al. Safety and efficacy of hematopoietic stem cell collection from mobilized peripheral blood in unrelated volunteers: 12 years of single-centre experience in 3928 donors. Blood 2009; **114**: 3757-63.
19) Confer DL, Shaw BE, Pamphilon DH, on behalf of the Clinical Working Group of the WMDA. WMDA guidelines for subsequent donations following initial BM or PBSCs. Bone Marrow Transplant 2011; **46**: 1409-12.
20) Pierelli L, Perseghin P, Marchetti M, et al. Best practice for peripheral blood progenitor cell mobilization and collection in adults and children: results of a Società Italiana Di Emafersi e Manipolazione Cellulare (SIDEM) and Gruppo Italiano Trapianto Midollo Osseo (GITMO) consensus process. Transfusion 2012; **52**: 893-905.
21) Anderlini P, Donato M, Chan KW, et al. Allogeneic blood progenitor cell collection in normal donors after mobilization with filgrastim: the M.D. Anderson Cancer Center experience. Transfusion 1999; **39**: 555-60.
22) Tassi C, Tazzari PL, Bonfazi F, et al. Short- and long-term haematological surveillance of healthy donors of allogeneic peripheral haematopoietic progenitors mobilized with G-CSF: a single institution prospective study. Bone Marrow Transplant 2005; **36**: 289-94.
23) Tigue CC, McKoy JM, Evens AM, et al. Granulocyte-colony stimulating factor administration to healthy individuals and persons with chronic neutropenia or cancer: an overview of safety and considerations from the research on adverse drug events and reports project. Bone Marrow Transplant 2009; **40**: 185-92.
24) De la Rubia J, de Arriba F, Arbona C, et al. Follow-up of healthy donors receiving granulocyte colony-stimulating factor for peripheral blood progenitor cell mobilization and collection. Results of Spanish Registry. Haematologica 2008; **93**: 735-40.


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