

## SECOND DONATION

### 1 GENERAL

This SOP is primarily based on the recommendation by the WMDA (World Marrow Donor Association) [1] concerning the second donation.

A second donation refers to a situation in which the same donor donates cells for the second time for the same or a different patient. 5–10% of the donors might be asked to donate cells for a second time. The most common second donation is a lymphocyte donation (DLI, donor lymphocyte infusion), but bone marrow cells and peripheral blood stem cells might be needed. A second donation might be asked soon after the first donation in cases where a transplant collected from blood (PBSC) does not contain enough cells or the collection procedure has been discontinued due to e.g. a decline in the donor's thrombocyte levels. The transplant centre might also send a request for a second donation for the same patient, if the first transplant has not taken root in the patient, the transplant is rejected, or the patient's disease recurs.

The number of second donations might increase as RIC transplantations become more common. The donation of other cell types might also be necessary as the stem cell therapies develop. If the donor remains in the registry after the donation, he/she might be asked to donate to another patient. It is important that the donor is told about the possibility for a second donation even when he/she is considering his/her consent to the first donation.

According to the studies published so far, the donor's experiences and subsequent problems associated with the second donation of stem cells from the bone marrow or peripheral blood are not significantly different from the first donation [2-6]. In a fairly small study consisting of 16 donors, the cell quantity in bone marrow collected the second time was as good as in the first collection [2]. In some studies, the CD34+ cell quantity of a PBSC transplant has been equally good [3-4], but other studies [5] have found the quantity to be poorer in the second collection than in the first collection.

The donor candidate is informed that he/she is requested to donate again. The donor does not have to commit to a new donation. The donor must have enough time to consider whether to give his/her consent or not. The request for a second donation must never use a pressing tone.

After the donation, the donor remains reserved for the patient for 24 months (status TU). If the patient dies, the donor can be released after 4 weeks from the donation (status AV).

### 2 HOW MANY TIMES CAN A PERSON DONATE STEM CELLS

There is no research data on the safety of more than two stem cell donations. On the other hand, there is no reason to assume, for example, that a third time would entail a higher risk than the second time. Therefore, a third donation may be approved in exceptional cases when the matter has been discussed thoroughly with the donor, with an emphasis on the voluntariness of the donation. The donations can be collections of stem cells from the bone marrow or blood circulation. A member of the registry who has donated once may remain as the member of the registry. If a donor has already donated stem cells twice for the same patient, he/she should be deleted from the registry.

### 3 REQUEST FOR A SECOND DONATION FOR THE SAME PATIENT

The transplant centre requests Stem Cell Registry for a second donation using on a WMDA form WMDA/DRWG/PrevTxInfo.

The transplant centre must pay particular attention to the justifications of the second transplant. The patient's current status must also be described carefully, and an objective assessment on the probability of the success of a second transplant is required. The Medical Director of the Registry evaluates the request and, if necessary, may consult the medical group of experts of the Registry. The consultation must be done quickly and the goal is to send a reply to the transplant centre in 72 hours.

As a rule, the second collection can be performed only after a minimum of four (4) weeks have passed from the first donation. A collection taking place earlier can be approved in exceptional cases (for example if the transplant is destroyed before the transplantation has been performed), which the Medical Director evaluates after a careful discussion with the donor.

If the request is approved, a Coordinator of the Stem Cell Registry contacts the donor by phone.

If the donor is not mobilised sufficiently during the growth factor therapy (the transplant collected from blood circulation does not contain enough cells) or if the donor's condition changes significantly during collection and the collection has to be discontinued as a result (e.g. the donor's thrombocyte level falls markedly), the donor can be asked to give his/her consent to the collection of stem cells from the bone marrow. In these cases, the consent is always asked for by an independent physician.

#### 4 REQUEST FOR A SECOND DONATION FOR A DIFFERENT PATIENT

A person who has donated once is not activated for confirmatory typing, if other good donor candidates are found for a patient. If, after the first donation, the donor is requested for confirmatory typing tests for another patient, the Registry checks first whether the patient who received the first transplant is alive. The donor is kept reserved for the patient for a possible second donation (for example DLI) for 24 months, during which the donor's status is: temporarily unavailable (TU).

If the patient who received the transplant has died or more than 24 months have passed since the transplantation, the donor can be offered for confirmatory typing for another patient. The transplant centre treating the patient must be informed of the fact that the donor has donated once before, and should the patient require a second transplant, the Registry's instructions allow a third donation only in exceptional cases.

#### 5 INFORMING THE DONOR AND A HEALTH CHECK-UP OF THE DONOR

If the donor is willing to donate again, an independent physician re-evaluates the donor's condition, physical and mental recovery from the previous donation and any risks.

An independent physician evaluates the need for a health check-up and laboratory tests on a case-by-case basis. For example, if the previous donation took place 3–4 months ago, a new thorough health check-up can be performed at the physician's discretion.

The donor must be re-informed about the risks of donation. The donor gives a signed confirmation stating that he/she has received sufficient information for a re-donation and that he/she is willing to donate again.

#### 6 COLLECTION OF LYMPHOCYTES

The collection of lymphocytes strains the donor much less than the donation of stem cells, and is rarely associated with significant complications [7]. A donor who has donated stem cells for two patients can be routinely asked to donate lymphocytes for both patients. It is recommended to arrange the lymphocyte collection in a way that enables the transplant centre to freeze the cells in several lots for dosing. If, in an exceptional case, another lymphocyte collection is requested for

the same patient, the responsible director of the Registry will decide on whether the request is approved or not. The time interval between lymphocyte collections must be at least four weeks.

## 7 LITERATURE

WMDA International Standards for Unrelated Hematopoietic Progenitor Cell Donor Registries, Version Effective January 1, 2014. 20140101-STDC-Standards.

1. Confer DL, Shaw BE, Pamphilon DH: WMDA guidelines for subsequent donations following initial BM or PBSCs. *Bone Marrow Transplant* 2011, 46(11):1409-1412.
2. Stroncek DF, McGlave P, Ramsay N, McCullough J: Effects on donors of second bone marrow collections. *Transfusion* 1991, 31(9):819-822.
3. Stroncek DF, Clay ME, Herr G, Smith J, Ilstrup S, McCullough J: Blood counts in healthy donors 1 year after the collection of granulocyte-colony-stimulating factor-mobilized progenitor cells and the results of a second mobilization and collection. *Transfusion* 1997, 37(3):304-308.
4. Anderlini P, Lauppe J, Przepiorka D, Seong D, Champlin R, Korbling M: Peripheral blood stem cell apheresis in normal donors: feasibility and yield of second collections. *Br J Haematol* 1997, 96(2):415-417.
5. De la Rubia J, Arbona C, Del Canizo C, Arrieta R, De Arriba F, Pascual MJ, Sanjuan I, Diaz MA, Brunet S, Alegre A, Insunza A, Espigado I, Zamora C, De la Serna J, Serrano D, Bargay J, Petit J, Martinez D, Verdeguer A, Ribera JM, Martinez C, Benlloch L, Sanz MA: Second mobilization and collection of peripheral blood progenitor cells in healthy donors is associated with lower CD34(+) cell yields. *J Hematother Stem Cell Res* 2002, 11(4):705-709.
6. Platzbecker U, Bornhauser M, Zimmer K, Lerche L, Rutt C, Ehninger G, Holig K: Second donation of granulocyte-colony-stimulating factor-mobilized peripheral blood progenitor cells: risk factors associated with a low yield of CD34+ cells. *Transfusion* 2005, 45(1):11-15.
7. McLeod BC, Price TH, Owen H, Ciavarella D, Sniecinski I, Randels MJ, Smith JW: Frequency of immediate adverse effects associated with apheresis donation. *Transfusion* 1998, 38(10):938-943.