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CONSENSUS UPDATE

# HEMOTHERAPY SUPPORT IN HSCT

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## ABSTRACT

Hemotherapy support is essential for Hematopoietic Stem Cell Transplantation (HSCT). In this article, we highlight the main points published in the 2020 SBTMO consensus and provide a brief update on the topic.

## KEY POINTS

### MOBILIZATION AND COLLECTION OF PERIPHERAL HEMATOPOIETIC PROGENITOR CELL (HPC)

**Standard mobilization:** filgrastim (G-CSF) 10 to 20µg/kg/day in one or two administrations for 5 days, with the first collection on day 5.[1]

**Alternative mobilization (chemotherapy and G-CSF association):** vinorelbine 35 mg/m$^2$; cyclophosphamide (Cy) 2 to 4 grams/m$^2$ or etoposide 375 mg.[1]

**Rescue mobilization:** plerixafor (0.24 mg/kg, 9 to 12 hours before collection) with G-CSF or chemotherapy + G-CSF.[1]

**CD34$^+$ cells minimum dose:** 2 x 10$^6$/kg per transplant (target dose of 4 to 5 x 10$^6$/kg).[1]

**High volume apheresis** (total blood volume processed more than 4 times patient's blood volume) increases the CD34+ collection.[1]

**Pediatric patients with less than 20 kg:** prime the apheresis kit with red blood cells and process at least three blood volume.[1]

### BONE MARROW HARVEST

**Collection target:** 10-15 ml/kg of recipient, not exceeding 20 ml/kg of donor.

**Recommended cell dose:** ≥ 3x10$^8$/kg of total nucleated cell (TNC) with minimum of 2 x 10$^8$ TCN/kg.[1]

### PROCESSING AND CRYOPRESERVATION OF HPC-A

**Cryoprotective solutions:** Dimethyl sulfoxide (DMSO) 10% or DMSO 5% + hydroxylamine (HES) 6%, both associated with a protein source.[1]

**Final nucleated cell (NC) concentration:** 100 to 500 x 10$^6$ NC/mL.[1, 2]

**Freezing ideal rate:** temperature reduction from 1 to 2° C per minute in a programmed freezing equipment or mechanical freezer.[1]

**Storage:** vapor phase or liquid nitrogen tank or mechanical freezer (-80 or -150° C).[1]

### TRANSPORT, THAWING AND INFUSION OF HPC

**Transport of fresh products** kept the temperature between 2 and 24ºC (preferably close to 4ºC).[1]

**Transport of cryopreserved products:** if the cells were stored in -80° C mechanical freezer kept the temperature at or below - 65°C (dry ice); if the cells were stored in temperature below - 150°C, kept the temperature below -130°C.[1]

**Premedication:** hydration, diphenhydramine, dipyrone and/or hydrocortisone to prevent allergic, febrile types and/or DMSO-related reactions.[1]

**Maximum DMSO volume:** 1ml DMSO/Kg patient weight/day to reduce risk of adverse event. In lower weight pediatric patients consider removal of DMSO.[1]

**Infusion:** Do not use transfusion set device with leukocytes filter. Rate: 10 mL/minute for thawed products and 6mL/Kg of patient weight/hour for fresh products (maximum 4h).[1]

## TRANSFUSION SUPPORT

**Red blood cells (RBC), platelet and granulocyte concentrates** intended for HSCT patients should be **leukoreduced and irradiated**.[1]

**Platelet refractoriness:** relative common in HSCT. Causes: non-immune (> 80%) or immune (< 20%). Calculation of platelet increment is important to confirm the platelet refractoriness diagnosis.[1]

**Granulocyte transfusion** is used to prevent (patients with neutropenia or neutrophil function disorders) or treat infections in severe neutropenia (granulocytes < 500/µL) patients. There are no randomized studies that prove its clinical efficacy.[1]

## ALLOGENIC BMT WITH ABO INCOMPATIBILITY

**Major or bidirectional ABO incompatibility:** RBC removal if bone marrow. Measures to reduce the anti-donor circulation isohemagglutinins (donor ABO plasma infusion or therapeutic plasmapheresis) if isohemaglutinin anti-donor ≥ 1:32.[1]

**Minor ABO incompatibility:** Plasma removal if bone marrow or if HPC-A, isohemaglutinin anti-receptor ≥ 1:256.[1]

**ABO blood component support:** summarized in table 1.

## DONOR LYMPHOCYTE INFUSION (DLI)

Medical evaluation of the donor is mandatory, and the eligibility criteria are the same used for blood donors.[1]

There is no need for any medication to prepare the donor for the collection.[1]

Lymphocytes can be obtained from the buffy coat of whole blood, however, the collection through apheresis equipment can offer a greater amount of CD3+ cells and is the most used.[1]

Each apheresis session should process 2 to 2.5 total blood volumes and if the number of cells needed is not obtained, a second procedure can be performed. There is a linear correlation between the number of CD3+ cells collected and the processed blood volume up to 12L.[1, 3]

Dose scheme depends on the type of BMT and disease, but a stagged regimen is recommended.[1]

## ANTI-HLA DONOR DESENSITIZATION

The presence of donor-specific anti-HLA antibody with mean fluorescence intensity (MFI) above 2000 is indication of desensitization protocols.[1]

## INDICATION OF PHLEBOTOMY IN IRON OVERLOAD POS BMT

Phlebotomy is a therapeutic option to drug treatment in patients with sustained hematopoiesis to reduce liver damage and irreversible tissue damage. It is indicated in cases with ferritin above 2500µg/L and transferrin saturation close to 100%.[1]

During the revision of the chapter published in the SBTMO consensus in 2020[1], we noticed the lack of a guidance on choosing the blood component to be transfused in the recipient undergoing transplantation with ABO incompatibility, which is now summarized in Table 1.[4]

There were few updates on the literature. We emphasize the safe nucleated cells concentration for cryopreservation, which can be up to 500,000 cells/mL after the cryoprotective solution addition.[2]

On the other hand, there have been many advances in Cell Therapy. SBTMO has published a technical manual on the topic that contains specific chapters of lymphocytes collection of by apheresis,[5] cryopreservation and transportation of mononuclear cells,[6] thawing and infusion of CAR-T cells,[7] among others.

At the national level, the current health legislation was updated.[8].

**TABLE 1.** Recommendation for post-transplantation transfusion support in ABO-incompatible HPC recipients.(4)

| | | | Fase I | Fase II | | | | Fase III |
|---|---|---|---|---|---|---|---|---|
| Receptor | Donor | Incompatibility type | All blood components | RBC concentrate | Platelet concentrate | | Plasma | All blood components |
| | | | | | 1st choice | Other choice | | |
| A | O | Minor | A | O | A | AB; B; O | A; AB | O |
| B | O | Minor | B | O | B | AB; A; O | B; AB | O |
| AB | O | Minor | AB | O | AB | A; B; O | AB | O |
| AB | A | Minor | AB | A | AB | A; B; O | AB | A |
| AB | B | Minor | AB | B | AB | B; A; O | AB | B |
| O | A | Major | O | O | A | AB; B; O | A; AB | A |
| O | B | Major | O | O | B | AB; A; O | B; AB | B |
| O | AB | Major | O | O | AB | A; B;O | AB | AB |
| A | AB | Major | A | A | AB | A; B; O | AB | AB |
| B | AB | Major | B | B | AB | B; A; O | AB | AB |
| A | B | Bidirecional | A | O | AB | A; B; O | AB | B |
| B | A | Bidirecional | B | O | AB | B; A; O | AB | A |

**Phase I**: from the beginning of patient preparation to the beginning of conditioning; **Phase II:** from the beginning of conditioning until the direct antiglobulin test becomes negative and the direct typing of the patient becomes the same as the donor; **Phase III:** from the moment when the direct and reverse typing of the patient is the same as the donor.

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