## *Incompatible red cells in HPC products*

**Question:** What is a safe volume of ABO-incompatible red cells to have in an allogeneic hematopoietic progenitor cell (HPC) product?

**Response:** Preventing the transfusion of ABO-incompatible Red Blood Cell (RBC) units is perhaps the main reason why so many blood bank processes are in place. Avoiding such a transfusion can literally save life and limb, as these incompatible transfusions almost always result in acute hemolytic transfusion reactions that occur in the intravascular space. Although such an incompatibility is obligatorily avoided in routine RBC unit transfusion, the infusion of ABO-incompatible red cells permissibly occurs in other settings, notably platelet transfusion and HPC products.

In transfusion of ABO-incompatible platelet units, up to 2 mL of incompatible red cells in these units are hemolyzed asymptomatically. HPC products, however, can contain significantly greater quantities of red cells. For example, there may be almost 20 mL in an HPC, Apheresis product. Up to 35% of the volume of an HPC, Marrow product may be red cells. In patients who receive fewer than 15 mL of ABO-incompatible red cells, hemolysis is found to be clinically insignificant, and red cell volumes up to 30 mL are usually well tolerated by adult recipients. Most centers limit ABO-incompatible red cells to 10-40 mL.

HPC yields can decrease with any manipulation, and this includes red cell reduction. Thus, while it may be possible to decrease red cell volumes below institutional thresholds, the decision to do so should always be made with the final HPC dose in mind. In cases where red cell reduction could reduce HPC yields below desirable levels, alternative strategies may be considered. These options include permissible hemolysis with aggressive hydration or infusing the transplant dose over two sessions, or even plasma exchange of the recipient to remove incompatible isohemagglutinins may be considered.

### References

1. Staley EM, Schwartz J, Pham HP. An update on ABO incompatible hematopoietic progenitor cell transplantation. Transfus Apher Sci 2016;54:337-44.

2. Daniel-Johnson J, Schwartz J. How do I approach ABO-incompatible hematopoietic progenitor cell transplantation? Transfusion 2011;51:1143-9.
3. Rowley SD, Liang PS, Ulz L. Transplantation of ABO incompatible bone marrow and peripheral blood stem cell components. Bone Marrow Transplant 2000;26:749-57.

## *Is there compensation for marrow donation?*

**Question:** Are marrow donors paid?

**Response:** Donors are never paid to donate marrow (or other sources of hematopoietic cells or blood). Typically, travel costs are reimbursed and reimbursement for other costs are made on a case-by-case basis. All medical costs for the donation procedure are covered by the marrow registry or by the patient's medical insurance. Total cost to add a new donor to a registry is about $100.

This is in contrast to some other donations, for which payments are made.

**Compensation for Donations***

| Source | Payment per Donation |
|---|---|
| Eggs | $5000-10,000 |
| Sperm | $30-200 |
| Fecal matter | Approx. $40 |
| Plasma | $20-50 |
| Blood | Zero |
| Marrow | Zero |

*Amounts change with time and geographic location.

### References

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2. Spector D, Brueck H. 9 ways to make money by selling your body to science. Business Insider March 13, 2018. [Available at http://www.businessinsider.com/ways-to-make-money-from-medical-research-and-donations-2013-12 (accessed July 6, 2018).]

## *Cell expansion in vivo?*

**Question:** Cord cell transplants are often limited by small numbers of pluripotential stem cells, which can lead to delayed or failed engraftment. Is there any way to expand these stem cells in vivo before the transplant procedure?

**Response:** There are currently several approaches under active investigation. These include:

MGTA-456: This is an aryl hydrocarbon receptor (AHR) antagonist being developed by the startup Magenta Therapeutics company (licensed from Novartis AG). This compound has been studied in two Phase II clinical studies. The studies demonstrated a median expansion of CD34-positive cord cells of 327-fold (range: 67-fold to 848-fold). Clinical engraftment was seen in all patients (with either myeloablative or nonmyeloablative conditioning). The observed low rates of graft-vs-host disease (GVHD), disease relapse, and 2-year survival were comparable to historical cohorts.

NiCord: This treatment is currently under development by the Israeli company Gamida Cell. In this ex-vivo expansion, stem cells are cultured for 3 weeks in the presence of nicotinamide (a form of vitamin B3). An expansion of approximately 100-fold has been observed along with low rates of GVHD following transplantation. The Food and Drug Administration (FDA) has granted this technique a breakthrough therapy designation, which might accelerate subsequent approval at the FDA. A multinational Phase III study evaluating NiCord in patients with leukemia and lymphoma is currently under way.

ECT-001: Developed at the University of Montreal. This treatment has been associated with a 35-fold increase in stem cells in just 7 days.