CORD BLOOD UNIT (CBU) SELECTION CRITERIA

MARCH 15, 2019

For successful engraftment, optimal CB graft selection and the patient's rejection risk must be considered.

BANK PRACTICES	GUIDELINES*
Attached segment identity testing	Mandatory
Use of RBC-replete units[a,b]	Not Recommended
Cryovolume[c]	Should be considered, especially if the unit is to be diluted post thaw
Year of cryopreservation	More recent units may be linked to optimal banking practices depending on the bank
Bank location	Domestic or international units fulfilling selection criteria
Bank accreditation	Should be considered
HLA-MATCH	**GUIDELINES***
Resolution of HLA-typing	Minimum of 8 allele (HLA-A,-B,-C,-DRB1) for both patient & CBU
Donor-recipient HLA-match	>/= 4/6 HLA-A,-B antigen, -DRB1 allele (Traditional Match) & >/= 4/8 allele match *(Some centers investigating use of 4/6 & 3/8 units if adequate dose)*
Unit-unit HLA-match for double unit CBT	Not required
Avoidance of units against which recipient has DSA[d]	Conflicting results in hematological malignancies; Avoid if non-malignant diagnosis
CRYOPRESERVED CELL DOSE[e,f,g]	**GUIDELINES***
Single unit CBT: Minimum dose/ kg	TNC >/= 2.5 x 10^7/kg & CD34+ cells >/= 1.5 x 10^5/kg *(Some centers recommend higher CD34+ dose as minimum)*
Double unit CBT: Minimum dose/ kg/ unit	TNC 1.5 x 10^7/kg for **each** unit & CD34+ cells >/= 1.0 x 10^5/kg for **each** unit *(Some centers recommend higher CD34+ doses for each unit as minimum)*

Abbreviations: HLA, human leukocyte antigen; TNC, total nucleated cell; RBC, red blood cell; DSA, donor specific antibodies; CBT, cord blood transplant.

[a] **RBC replete units:** RBC-replete units have been associated with life-threatening infusion reactions. Washing is difficult due to the lack of a clear interface after centrifugation; washing also risks cell loss. Therefore, RBC-replete units should be used with caution. They should only be considered in the absence of RBC-depleted CBUs meeting acceptable criteria.

[b] **Nucleated red cell content:** Incorporation of nucleated red cell content in unit selection is not recommended at this time.

[c] **Cryovolume:** Expert centers prefer to use an RBC depleted unit that has a post-cryopreservation volume of approximately 25 ml/bag. If a unit was divided into two bags for storage, each bag should contain approximately 25 ml.

[d] **Significance of HLA antibodies:** DSA must be considered on a case-by-case basis based on diagnosis and prior immunosuppressive therapy that determine rejection risk, the intensity of planned conditioning, and the number/ titer/ specificity/ complement fixation of donor-specific antibodies. DSA targeted units should be avoided in non-malignant diagnoses. In patients with malignancies, avoid if possible but use caution if avoidance of units against which the patient has antibodies compromises the selected CBU dose and HLA-match.

[e] **Single vs double unit CBT:** If no adequate single unit, a double unit graft is recommended. Clinical trials investigating addition of other cellular products to a single unit graft can also be investigated.

[f] **Prioritization of cell dose vs HLA-match (applies to single and double unit transplants):** Cell dose frequently needs to take priority over HLA-match for adult and larger pediatric patients. HLA-match can take priority in children/ smaller adults or those with common HLA typing who have units with high cell dose. Optimizing HLA-match is very important in CBT for non-malignant diagnoses. In children with non-malignant diagnoses higher cell doses (>/= 5 x10^7/kg) should be sought. Further data is required as to how to balance cell dose against HLA-match. A current guidance for consideration is:

- If high doses (e.g. TNC >/= 3 x 10^7/kg and CD34+ >/= 2 x 10^5/kg) consider optimizing allele match over cell dose.
- If lower TNC and CD34+ doses, optimize dose first and allele match second.
- If units have similar cell doses, optimize allele match.

[g] **Viability Testing:** Reporting of unit viability testing is not fully standardized. Flow based assays of CD34+ cell viability on a segment can be informative but have not been validated in multiple banks/ centers. The NMDP will facilitate discussion between centers and the Bank if questions concerning viability testing arise.

[*] *Barker JN, Kurtzberg J, Ballen K, Boo M, Brunstein C, Cutler C, Horwitz M, Milano F, Olson A, Spellman S, Wagner JE, Delaney C, Shpall E. Optimal Practices in Unrelated Donor Cord Blood Transplantation for Hematologic Malignancies. Biol Blood Marrow Transplant. 2017; 23(6): 882-896.*