



Memorial Sloan Kettering
Cancer Center

Overview of Cord Blood Searches: the Clinician's perspective

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Stem Cell Transplantation and Cellular Therapies

MSK Kids

Advisory Council on Blood Stem Cell Transplantation October 2024

Why is this important?

- **Selection of high-quality CB grafts leads to improved patient outcomes**

Barker et al, BBMT 2017; Purtill et al, Blood 2014; Scaradavou et al, BBMT 2010

- **There are many clinical scenarios when looking for a CB graft, and transplant centers need to have a process, which includes workflow and guidelines, that will work for all patients, efficiently and in real time**

- Female patient of mixed ethnic background with acute leukemia, needs a transplant in 4-6 weeks; has many high titer HLA antibodies
- Young boy with acute leukemia whose related donor fell through the last minute (and no back-up donor had been organized)
- Infant with inherited metabolic disease, needs a transplant very urgently
- Female child of Asian ancestry with AML in MRD positive CR
- Male patient of African/American ancestry, weight 100 kg, high risk acute leukemia, no related or haplo-identical donors

- **Many TC find CB transplants challenging, including the search/selection; so, they will not even look at CB options!**

**Completely eliminating CB options can compromise patient care and access to transplant
It also decreases utilization of CB as a graft source**

- **Unmet medical need**

NMDP/CIBMTR Cord Blood Unit Selection Guidelines (Dehn et al, Blood. 2019)



Table 2. Unrelated CB unit selection guidelines

	Guidelines
Bank practices Attached segment identity testing Use of RBC-replete units*† Cryovolume‡ Year of cryopreservation Bank location Bank accreditation and/or licensure	Mandatory Not recommended Should be considered, especially if the unit is to be diluted post thaw More recent units may be linked to optimal banking practices depending on the bank Domestic or international units fulfilling selection criteria Should be considered
HLA match Resolution of HLA typing Donor–recipient HLA match Unit–unit HLA match for double unit CBT Avoidance of units against which recipient has DSA§	Minimum of 8 high-resolution (HLA-A, HLA-B, HLA-C, and HLA-DRB1) for both patient and CB unit ≥4/6 HLA-A and HLA-B antigen, HLA-DRB1 high-resolution (traditional match), and ≥4/8 high-resolution match (some centers investigating use of 4/6 and 3/8 units if adequate dose) Not required Conflicting results in hematological malignancies; avoid if nonmalignant diagnosis
Cryopreserved cell dose ¶# Single-unit CBT: minimum dose/kg Double-unit CBT: minimum dose/kg per unit	TNC ≥2.5 × 10 ⁷ /kg and CD34 ⁺ cells ≥1.5 × 10 ⁵ /kg (some centers recommend higher CD34 ⁺ dose as minimum) TNC 1.5 × 10 ⁷ /kg for each unit and CD34 ⁺ cells ≥1.0 × 10 ⁵ /kg for each unit (some centers recommend higher CD34 ⁺ doses for each unit as minimum)

**Recommendations by
the NMDP and CB
transplant physicians**

NMDP: National Marrow Donor Program / Be the Match
CIBMTR: Center for International Blood and Marrow Transplant Research
HLA: Human Leukocyte Antigen

Dehn J, Spellman S, Hurley CK, et al. Selection of unrelated donors and cord blood units for hematopoietic cell transplantation: guidelines from the NMDP/CIBMTR. Blood. 2019;134(12):924-934. doi:10.1182/blood.2019001212

ASTCT Cord Blood Special Interest Group: Guidelines for CBU Selection



Biology of Blood and
Marrow Transplantation

journal homepage: www.bbmt.org



Guidelines for Cord Blood Unit Selection

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Evidence-based Guidelines and detailed, practical instructions by CB transplant physicians and search coordinators for the ASTCT

ASTCT: American Society for Transplantation and Cellular Therapy

Politikos I, Davis E, Nhaissi M, et al. Guidelines for Cord Blood Unit Selection. *Biology of Blood and Marrow Transplantation*. 2020;26(12):2190-2196. doi:10.1016/j.bbmt.2020.07.030

National Cord Blood Network

Consortium of collaborating new & existing CBT centers to increase transplant access - especially to under-served patients



<https://www.cordbloodnetwork.org>



Steering Committee

J. Barker (WCM), A. Scaradavou (MSKCC) & M. Finney (CCBC)

Administration:
Infrastructure, IT & oversight

10 Participating Centers/ Programs:
National distribution

Collaborations with Stakeholders

*HRSA, CBA, NMDP, CIBMTR, Anthony Nolan, patient advocates & social media/ press.
Future: ASTCT, FACT, WMDA, ISCT, AABB.*

Goals: Optimize CB transplant activities

Create, post & disseminate optimized guidelines / webinars / protocols
Create search coordinator consortium & health equity initiatives
Engage stakeholders & pursue multiple funding sources
Create infrastructure to perform research & advance the field



Consideration for all alternative donor options

Patient Considerations: **Who should get a CB search?**



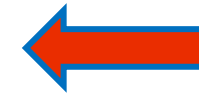
Transplant centers need to have **donor hierarchy algorithms** indicating who of the patients with malignant or non-malignant diseases will get a CB search.

CB transplant eligibility criteria include patient age, disease and disease status (e.g., presence of MRD), comorbidities/organ function and urgency of transplant.

In the absence of a Matched Related Donor (MRD), most patients with malignancy need to have a **simultaneous search** for Unrelated Donors (URD) and CB units.

For patients who need an **urgent transplant** and those that the preliminary search results* and/or the haplogenic predictions indicate few/no suitable URDs, **a formal CB search should be initiated.**

Avoid prolonged URD searches – Move promptly to mismatched donor options such as MMUD, CB or haplo-identical



CB grafts can also be **backup option** for patients with URD or even MRD, in case problems with the donor occur.

Training Tool for Optimizing CB graft selection

Best Practices in Cord Blood Unit Selection for Allogeneic Transplant: Step-by-Step Instructions



Aim: to increase TC search coordinator proficiency and “ease” with CBU search and optimize CB graft selection

Detailed steps for CBU search/selection following the ASTCT Guideline, in order to create a customized CBU list for each patient, that can be shared and reviewed

- Search Coordinator Review
- Physician Review of CBU list
- Final CB graft and back-up Selection

National Cord Blood Network
www.cordbloodnetwork.org

Date: 10/15/2024; v. 1.0

Physician Review of the Customized CBU list for selection



CBU Selection – Level 2 (Cord Physician Review and Selection)



Table 1
Step-by-Step CB Unit Selection Guide in the United States

Step	Action	Comments
9	<p>Review and select units for confirmatory typing.</p> <p>Units already typed or high resolution can be placed on hold. Will need 1 to 2 units for the graft and 1 to 2 domestic units as backups.</p>	<p>Must consider cell dose, HLA match, and unit quality.</p> <p>1) Select 4 to 6 (if possible) units with adequate TNC and CD34+ cell dose/kg and acceptable HLA match.</p> <p>2) Assess specificities and titers of DSA (if present).</p> <p>Notes:</p> <p>- Minimum cell dose thresholds capture all potentially acceptable units.</p> <p>- Selection of units with higher cell doses is now recommended: Single units: TNC cell dose $\geq 3.0 \times 10^7$/kg and CD34+ cell dose $\geq 2.0 \times 10^5$/kg Double units: CD34+ cell dose $\sim 1.5 \times 10^5$/kg for each unit</p> <p>- If the CD34+ TNC content ratio is unexpectedly high ($\geq 1.5\%$ to 2%) the listed CD34+ cell dose should be verified.</p> <p>- How to trade off dose versus HLA match is not well established. If all units have a low cell dose, selection of highly HLA-mismatched units may be necessary to achieve acceptable dose. HLA match can be optimized if multiple high cell dose units are available.</p> <p>- For patients with hematologic malignancies, units that are very well HLA matched (ie, B/B HLA-allele matched) may be avoided to reduce the risk of relapse.</p> <p>- For patients with nonmalignant diseases, both cell dose and HLA match need to be optimized.</p> <p>- Units targeted by high DSA titers should be avoided if possible.</p> <p>- Additional center-specific criteria may be applied in final CB unit selection.</p>

Selection of CBUs to Pursue for HLA Confirmatory Typing (CT) or HOLD (HE) if CBU was previously CT'ed

Recommendations based on the ASTCT guideline

Summary

- Need to consider both TNC/kg and CD34+/kg of the CBU
 Consider double unit graft if no CBUs of adequate cell content – avoid using CBUs with only “minimal” cell doses
- Need to consider patient’s diagnosis:
 For patients with hematologic malignancies, avoid very well HLA matched CBU, to enhance anti-leukemic effect
 For patients with nonmalignant diseases, select very well HLA matched CBU with high cell doses
- Need to consider CBU quality and CB Bank of origin - Be familiar with the CB Banks your center has used, and the results
- Need to consider DSA
- Apply same selection criteria for each unit of the graft and for backups
Always have a backup: CBU from domestic bank, ready to ship, in case there are problems
- Additional considerations may apply depending on study

Final CB graft Selection

CBU Selection – Level 3 (Final Selection: Graft & Backup)



Final Cord Blood Summary

Selection	Cord Blood Bank	HLA Match Out of 6	HLA Match Out of 8 (Mismatch Locations)	TNC/kg x 10 ⁷	CD34/kg x 10 ⁵	Final Total Volume (mL)	Collection Date	ABO/Rh	Sex	Comments
Unit 1A	Domestic #1 FACT	4/6	5/8 (B,C,DR)	3.23	4.96	25.5	04/2023	O-	M	CT completed Licensed No HLA abs against CBU
Unit 1B	Domestic #2 FACT	4/6	5/8 (A,b,dr)	2.11	4.95	25	05/2017	O+	F	CT completed Pt has HLA abs against A1 (MFI 2084)
Backup	Domestic #3 FACT	4/6	4/8 (A,b,C,dr)	4.37	4.32	26.4	10/2021	O+	M	CT completed No HLA abs against CBU
Backup	Domestic #4 FACT	4/6	4/8 (A,B,C,c)	3.81	4.15	26	11/2015	AB+	M	CT completed Licensed No HLA abs against CBU

A final Summary with the pertinent information for each CBU needs to be saved.

Back-up CBU remains at the CB Bank, ready to ship in case of an emergency.

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Next steps:

- Network of Search Coordinators for dissemination of training – apply metrics to training
- Webinar for the NCBN website

National Cord Blood Network
www.cordbloodnetwork.org

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