Licensing of Cord Blood Units for Indications other than currently approved

Joanne Kurtzberg
Cord Blood Association
January 30, 2018
Background and Rationale

• Treatments using umbilical cord blood for indications other than HSCT are undergoing evaluation in clinical trials around the world. Over 300 trials with UCB in regenerative applications are listed on clinicaltrials.gov.

• At Duke, we are conducting trials under INDs in babies with HIE, children with cerebral palsy and autism, and adults with acute ischemic stroke.

• Results of phase I and II studies in children with autism and CP, respectively have shown favorable safety profiles and encouraging efficacy results.

• Both autologous, related and unrelated cord blood units are being utilized.

• The mechanism of action using cord blood in these patients is that cord blood acts through paracrine signaling to instruct endogenous cells to repair damaged tissue and to build new connections in the brain.
Feasibility and Safety

- Cord blood is administered after thawing and washing, as an IV infusion in the outpatient clinic.
- Patients are pre-medicated with a single dose of IV diphenhydramine (0.5mg/kg) and solumedrol (0.5mg/kg).
- The cells are infused over 15 minutes.
- The patient is hydrated with standard IV fluids for 1-2 hours post infusion.
- In over 800 infusions over the past 10 years, the infusion reaction rate is <1%.
- Reactions were characterized as urticarial +/- cough or wheezing. All were self limited and deemed not serious.
- There have been no late ADEs.
Additional safety precautions

• Eligibility limited to patients without genetic causes of their disease
• Patients must have normal ALC
• Patients with a PMH of cancer, immune deficiency, autoimmune disease, immunosuppressive or chemotherapy are ineligible
• Patients treated with other cell therapies are excluded
Efficacy – Completed studies

- Safety
- CP
- Autism
- HIE
- Speech Apraxia
- Congenital Hydrocephalus
- Stroke
Safety

NIH Public Access

Author Manuscript

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Differences in quality between privately and publicly banked umbilical cord blood units: a pilot study of autologous cord blood infusion in children with acquired neurologic disorders

Jessica Sun, June Allison, Colleen McLaughlin, Linda Sledge, Barbara Waters-Pick, Stephen Wease, and Joanne Kurtzberg

Pediatric Blood and Marrow Transplant Program and the Carolinas Cord Blood Bank, Duke University, Durham, North Carolina; and the EMMES Corporation, Rockville, Maryland

Autism

Autologous Cord Blood Infusions Are Safe and Feasible in Young Children with Autism Spectrum Disorder: Results of a Single-Center Phase I Open-Label Trial

Gerardine Dawson, Jessica M. Sun, Katherine S. Davlantis, Michael Murias, Lauren Franz, Jesse Troy, Ryan Simmons, Maura Sabatino-DiVito, Rebecca Durahan, Joanne Kurtzberg

Key Words: Autism spectrum disorder • Autologous umbilical cord blood • Cell therapy

HIE

Effect of Autologous Cord Blood Infusion on Motor Function and Brain Connectivity in Young Children with Cerebral Palsy: A Randomized, Placebo-Controlled Trial

Jessica M. Sun, Allen W. Song, Laura R. Char, Mohamad A. Missi, Katherine E. Gustafson, Ryan Simmons, Rick Goldstein, Josi Petris, Colleen McLaughlin, Barbara Waters-Pick, Leon W. Cheng, Stephen Wease, Beth Blackwell, Gordon Worek, Jesse Troy, Joanne Kurtzberg

Key Words: Autologous cord cell transplantation • Cellular therapy • Clinical Trials • Cord blood • Human cord blood • Nervous system • Umbilical cord blood

Feasibility of Autologous Cord Blood Cells for Infants with Hypoxic-Ischemic Encephalopathy

C. Michael Cotter, MD, Amy P. Murtha, MD, Ronald N. Goldberg, MD, Chad A. Grotegut, MD, P. Brian Smith, MD, Ricki F. Goldstein, MD, Kimberley A. Fisher, PhD, Kathryn E. Gustafson, PhD, Barbara Waters-Pick, BS, MT(ASCP), Geeta K. Swamy, MD, Benjamin Rattray, MD, Siddhartha Tan, MD, and Joanne Kurtzberg, MD
Allogeneic Umbilical Cord Blood Infusion for Adults with Ischemic Stroke (CoBIS): Clinical Outcomes from a Phase 1 Safety Study

Repeated autologous umbilical cord blood infusions are feasible and had no acute safety issues in young babies with congenital hydrocephalus

Treatment of Childhood Apraxia with Autologous Cord Blood Infusions
Ongoing Studies

- **CP**
  - Phase II randomized trial comparing allogeneic unrelated donor cord blood infusions and third party cord tissue MSCs in young children with CP
    - 100 children, 1:1:1 randomization, 6 and 12 month endpoints, change in GMFM level
    - Completion July 2019

- **Autism**
  - Duke ACT: Phase II, Placebo-Controlled, Cross-over, Randomized Trial Comparing autologous or unrelated donor allogeneic cord blood infusion to placebo in young children with ASD
    - 177 children, 2:1 randomization, 6 month endpoint, Vineland Socialization Scale
    - Completion August 2018

- **Adults with acute ischemic Stroke**
  - COBIS II: Phase II randomized, placebo-controlled trial of infusion of unmatched, unrelated donor umbilical cord blood in adults with acute stroke, 3-10 days post stroke
    - 110 patients, 1:1 randomization, 5 sites
    - Completion Q1 2019

- **HIE**
  - Babybac II: Phase II, randomized, placebo-controlled trial of fresh, volume and RBC reduced UCB infusion in newborn babies with moderate-severe encephalopathy treated with SOC hypothermia.
    - 120-160 babies, 2:1 randomization, 12 sites
    - Completion 2020
Effect of Autologous Cord Blood Infusion on Motor Function and Brain Connectivity in Young Children with Cerebral Palsy: A Randomized, Placebo-Controlled Trial


Key Words: Autologous stem cell transplantation • Cellular therapy • Clinical Trials • Cord blood • Human cord blood • Nervous system • Umbilical cord blood
CPAC - Study Overview

• 63 patients
• Ages 1-6 years
• Qualified autologous cord blood unit
  – 16 Banks
• CP with spasticity, GMFCS levels I-IV
• Randomized, placebo controlled cross over design
• Placebo = TC199 + 1% DMSO
• Primary endpoint: Change in GMFM score
• Follow up at 1 and 2 years
Table 1. Qualifying characteristics of autologous umbilical cord blood units

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Specification</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Precryopreservation characteristics</strong></td>
<td></td>
</tr>
<tr>
<td>Total nucleated cell count (TNCC)</td>
<td>$\geq 1 \times 10^7$/kg</td>
</tr>
<tr>
<td>Viability (total or CD34)</td>
<td>$\geq 80%$</td>
</tr>
<tr>
<td>Sterility culture</td>
<td>Negative</td>
</tr>
<tr>
<td>Maternal infectious disease screening&lt;sup&gt;a&lt;/sup&gt;</td>
<td>Negative</td>
</tr>
<tr>
<td>Test sample available for confirmatory HLA typing</td>
<td>Yes</td>
</tr>
<tr>
<td><strong>Cord blood test sample characteristics</strong></td>
<td></td>
</tr>
<tr>
<td>Identity confirmation via HLA testing of subject and cord blood sample</td>
<td>Confirmed</td>
</tr>
<tr>
<td>CD34 viability</td>
<td>$\geq 60%$</td>
</tr>
<tr>
<td>Colony forming units</td>
<td>Growth</td>
</tr>
</tbody>
</table>

<sup>a</sup>All mothers/units were tested for Hepatitis B, Hepatitis C, HIV, and syphilis. Most were also tested for HTLV I/II.

Abbreviation: HLA, Human Leukocyte Antigen.
CP-AC Study Design

Phone Screen → CBU Screen & Ship to Duke

Qualifying Visit

Enrolled on Study → RANDOMIZE

Visit 1 (time 0)
- Arm 1: UCB
- Arm 2: Placebo

Visit 2 (1st year)
- Evaluation
- 1° Endpoint
- Placebo
- UCB

Visit 3 (2nd year)
- Evaluation

1° Endpoint
GMFM-66 Assessing Change in Study Subjects
Assessing Change in Changing Subjects

GMFM-66 Score

Level I
Level II
Level III
Level IV
Level V

Age, y

0 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15
Figure 3: GMFM-66 Scores from Baseline to Year 1 by Randomized Treatment Assignment and Cell Dose
Analysis One Year after CB Infusion

1. Enrolled on Study (n=63)
   - Phone Screen
   - Qualifying Visit

2. Randomize
   - Arm 1
   - Arm 2

3. CBU Screen & Ship to Duke

4. Visit 1 (time 0)
   - Evaluation
     - UCB (n=32)
     - Placebo (n=31)

5. Visit 2 (1st year)
   - Evaluation
     - UCB (n=31)

6. Visit 3 (2nd year)
   - Evaluation
**Dose Group Characteristics**

<table>
<thead>
<tr>
<th>Comparison</th>
<th>High $&gt;2 \times 10^7$/kg</th>
<th>Low $&lt;2 \times 10^7$/kg</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (median, range)</td>
<td>2.6 (1.1-6.3)</td>
<td>2.9 (1.2-8.0)</td>
<td>0.47</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td>0.79</td>
</tr>
<tr>
<td>Male</td>
<td>22 (68.8%)</td>
<td>20 (64.5%)</td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>10 (31.3%)</td>
<td>11 (35.5%)</td>
<td></td>
</tr>
<tr>
<td>Type of CP</td>
<td></td>
<td></td>
<td>0.53</td>
</tr>
<tr>
<td>Hypotonic Quadriplegia</td>
<td>2 (6.3%)</td>
<td>2 (6.5%)</td>
<td></td>
</tr>
<tr>
<td>Spastic Diplegia</td>
<td>5 (15.6%)</td>
<td>7 (22.6%)</td>
<td></td>
</tr>
<tr>
<td>Spastic Hemiplegia</td>
<td>18 (56.3%)</td>
<td>12 (38.7%)</td>
<td></td>
</tr>
<tr>
<td>Spastic Quadriplegia</td>
<td>7 (21.9%)</td>
<td>10 (32.3%)</td>
<td></td>
</tr>
<tr>
<td>Baseline GMFCS level</td>
<td></td>
<td></td>
<td>0.19</td>
</tr>
<tr>
<td>I/II</td>
<td>24 (75%)</td>
<td>18 (58.1%)</td>
<td></td>
</tr>
<tr>
<td>III/IV</td>
<td>8 (25%)</td>
<td>13 (41.9%)</td>
<td></td>
</tr>
<tr>
<td>Infused TNC $x10^7$/kg (median, range)</td>
<td>3.1 (2.0-5.0)</td>
<td>1.5 (0.4-1.9)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>
One year outcomes post UCB infusion
GMFM-66 Change and Peabody GM Scale

- $N = 38$
- $\geq 2$ years old at the time of infusion

- $N = 47$
- $\leq 72$ months at time of follow-up
• N = 38 with analyzable images
UCB infusions in children with CP

- Appropriately dosed autologous CB infusions increase motor function in children with CP. The regulatory pathway for approval of this therapy is being explored.
- Infusions of partially or fully-HLA matched sibling cord blood infusion are also safe and feasible in young children with cerebral palsy.
- There was no evidence of immune activation or persistence of donor cells in this cohort of patients treated with sibling cord blood.
- The efficacy of allogeneic, partially matched cord blood infusion should be studied in a Phase II clinical trial. A trial with allogeneic unrelated cord blood and cord tissue MSCs is planned.
Autologous Cord Blood Infusions Are Safe and Feasible in Young Children with Autism Spectrum Disorder: Results of a Single-Center Phase I Open-Label Trial

Geraldine Dawson, a Jessica M. Sun, b Katherine S. Davlantis, a Michael Murias, a,e Lauren Franz, a Jesse Troy, b Ryan Simmons, b Maura Sabatos-Devito, a Rebecca Durham, a Joanne Kurtzberg b

Key Words: Autism spectrum disorder • Autologous umbilical cord blood • Cell therapy
Duke ABCs
Open-label clinical trial of autologous cord blood in young children with autism spectrum disorder

Hypothesis: Cord blood cells, acting through paracrine signaling, will modulate inflammation and suppress microglial activation in children with autism.

- Open label trial with 25 children with autism, age 2-6 yrs (avg = 4.5), followed for 1 year
- Assess tolerability/safety of autologous CB infused IV x 1 with 6 and 12 month follow-up
- Evaluate the feasibility of the evaluation protocol
- Define primary and secondary endpoints for subsequent larger clinical trials
- Define optimal length of trial
**Open label clinical trial of autologous cord blood in young children with autism spectrum disorder**

(Joanne Kurtzberg and Geraldine Dawson, Co-PIs)

<table>
<thead>
<tr>
<th>Participant Characteristics (N = 25)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age</strong></td>
</tr>
<tr>
<td><strong>Sex</strong></td>
</tr>
<tr>
<td><strong>Diagnosis</strong></td>
</tr>
<tr>
<td><strong>IQ</strong></td>
</tr>
</tbody>
</table>
Autism Phase I - Safety results

• No serious adverse events reported
• 3 children had mild allergic reactions
  • Cough and hives during infusion (1 child)
  • Cough post-infusion (2 children)
• 1 parent reported that their child was more irritable for 2 days post-infusion
• Conclusion: Preliminary safety/tolerability appears to be very good
• Endpoints were defined
Improvements in social behavior
Primary endpoint: Vineland Adaptive Behavior Scale – Socialization Standard Score

- Significant increase in socialization standard score (p = 0.02)
- Scores expected to decrease over time.
- 13/25 participants showed stable or increasing scores.
- Increase was not correlated with number of hours of behavioral intervention received.
- Children with higher baseline IQ had greater response.
Secondary Outcome Measures

- **PDD-BI Total Autism Symptoms**: Autism symptom composite T-score; median change = 7 point decrease (p = 0.01)

- **CGI – Severity Ratings**: The median change score is significantly different from zero (p=0.01, Wilcoxon signed rank test)

- **Expressive Vocabulary**: Statistically significant increase in expressive vocabulary (p < .001); 15 of the 25 patients improved, 7 exhibited no change, 1 declined
Phase II Study Design: DukeACT

• 180 Children with ASD 2-7 years of age
• Children evaluated at baseline and 6 months later and assessed remotely via parent questionnaire at 12 months
• **Primary endpoint:** Social communication skills assessed by Vineland Adaptive Behavior Scales Interview
• **Secondary endpoints:** Pervasive Developmental Disorder Behavior Inventory (parent report), Clinical Global Impression (clinician), Expressive One-Word Vocabulary (clinician), Safety and Tolerability
• **Exploratory:** GI symptoms, Eye-tracking, EEG, and MRI
Autism CBU “Best Donor” Trial Design
Expanded Access Protocol

• For infusions of autologous and haplo or fully matched qualified sibling cord blood in children with CP, ASD, HIE, and other related brain injuries.
• IND/IRB, parental informed consent
• Cost of care, not product, charged to third party payers
• 3 day visit: Outpatient
• IV infusion of washed cord blood cells on day 2 in the Duke CHC VDH
• Follow up remotely per diagnosis
• Data reported to the CIBMTR
• Hundreds of patients have approached Duke for enrollment on this protocol. Capacity is limiting.
What are the next steps?

• End of Phase 2 meeting with the FDA
  ✓ Is this the appropriate meeting to have?

• Potential pathways to approval:
  ✓ 361 product
    • Homologous use
    • NMMM
    • Autologous or sibling
  ✓ 351 product
    • Conduct a single arm, open label phase III study to confirm observations in Phase II
    • Conduct a randomized, phase III study, multicenter
? About a BLA

• If a BLA is required
  ✓ Who obtains the BLA?
    • No guidance for private/family banks
    • Highly unlikely the private banks will do so.
    • Not practical for each bank to get its own BLA
  ✓ Could treatment facility(ies) obtain a treatment BLA?
    • Consider the CBU from the private bank as source material
    • Use qualification specifications per IND
    • Is there a role for a shared BLA?
• For products with heterogeneous populations, can multiple homologous uses be identified?
• Will the FDA accept this approach for cord blood where there are many different types of therapeutic cells?
  ✓ HSCs
  ✓ T-cells
  ✓ NK cells
  ✓ Monocytes
    • CD14 cells
Types of Cells in Cord Blood

- Multipotent hematopoietic stem cell (Hemocytoblast)
- Common myeloid progenitor
  - Erythrocyte
  - Mast cell
  - Myeloblast
- Common lymphoid progenitor
  - Small lymphocyte
  - Natural killer cell (Large granular lymphocyte)
  - B lymphocyte
  - T lymphocyte
  - Plasma cell
- Megakaryocyte
  - Thrombocytes
- Monocyte
- Macrophage

CD14
Hypoxic Injury

DUOC-01
Remyelination
Effects of CB CD14+ monocytes on OGD in brain slice cultures

GFAP, NeuN, Iba1
Identification of CB populations that protect brain cells from OGD in cortical slice cultures
Human Umbilical Cord Blood Cells Ameliorate Motor Deficits in Rabbits in a Cerebral Palsy Model

Alexander Drobychevsky\textsuperscript{a} C. Michael Cotten\textsuperscript{b} Zhongjie Shi\textsuperscript{a} Kehuan Luo\textsuperscript{a} Rugang Jiang\textsuperscript{a} Matthew Derrick\textsuperscript{a} Elizabeth T. Tracy\textsuperscript{b} Tracy Gentry\textsuperscript{b} Ronald N. Goldberg\textsuperscript{b} Joanne Kurtzberg\textsuperscript{c} Sidhartha Tan\textsuperscript{a}

\textsuperscript{a}Department of Pediatrics, NorthShore University HealthSystem, Evanston, Ill, and \textsuperscript{b}Department of Pediatrics and \textsuperscript{c}Robertson Cell and Translational Therapy Program, Duke University, Durham, N.C., USA
Intrauterine hypoxia e22
C/S e31
Severe phenotype
4 hours postnatal
2.5.0x10⁶/ml saline IV

HUCB Cells improve Motor Function in rabbit CP model.

Replication
• same volume (1 ml)
• lower dose (2.5 x 10⁶)
• Compared cells to media+saline
• Improved outcome
• No increase in mortality

UCBT for EIKD: Functional Outcomes vary with best outcomes in babies transplanted in the first month of life.
Donor Cells engraft in the brain after IV UCBT
DUOC-01 treatment accelerates remyelination of corpus collosum
Potential mechanisms of DUOC-01 action

- Enzyme replacement
- “Clean up”
- Cytokine secretion:
  - Modulate inflammation
    - [IL10, IL6, TGF-beta]
  - Drives oligodendrocyte proliferation
  - Promotes myelination

<table>
<thead>
<tr>
<th>Gene name</th>
<th>Fold change Mean ±SEM</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>PDGF-α</td>
<td>32.3±8.3</td>
<td>≤0.01</td>
</tr>
<tr>
<td>IGF-1</td>
<td>799±294</td>
<td>≤0.05</td>
</tr>
<tr>
<td>SCF-1</td>
<td>26.7±4.8</td>
<td>≤0.033</td>
</tr>
<tr>
<td>MMP9</td>
<td>632±109</td>
<td>≤0.002</td>
</tr>
<tr>
<td>MMP12</td>
<td>2057±460</td>
<td>≤0.006</td>
</tr>
<tr>
<td>TREM2</td>
<td>1634±368</td>
<td>≤0.011</td>
</tr>
</tbody>
</table>

Fold increase DUOC-01 relative to CB CD14+ by RTqPCR. N>3
THE DEVELOPMENTAL PATHWAY FOR DUOC-01
2007-2015

OUTCOMES

Day 0 IV
Day 28 IT
Begin D7
16 Patients treated with DUOC-01

17 and 18th patients pending

2 reversible reactions in 2/3 patients receiving different donor DUOC cells

Hard to assess efficacy in these diseases which have improvement and variable courses post transplant

Enhancing manufacturing using entire CBU

Planning clinical trials in adult demyelinating diseases
Conclusions

• Banked umbilical cord blood has great potential for use as a regenerative therapy.
• Results in children with ASD and CP are encouraging.
• There is a huge demand for use of 361 products at the current time.
• Pathways for regulatory approval for these products are unclear
  • If the homologous use premise is accepted by FDA, they can be utilized in the clinic under practice of medicine;
  • If not accepted, the entity obtaining a license is not clear and the pathway forward is also not clear.
• Consideration of a use license considering 361 cord blood products as source materials may be a possible solution.
• Would it be possible to have a broad license shared by multiple clinics?
BACK-UP SLIDES
Timelines

- 1988- 1st UCBT (MRD – 5 yo with FA)
- 1991- 1st US Public Bank (NYBC – Rubinstein)
- 1993- 1st URD UCBT (4yo T-ALL, Duke/Kurtzberg)
- 1996- Report of 1st 25 patients UCBT (Kurtzberg)
- 1998- Report of 562 UCBT (Rubinstein)
- 1999- COBLT Banking and Transplant Study (NIH)
  - Establishment of 3 additional CBBs
  - Multiple prospective, multicenter Phase II clinical trials
- 2005- COBLT publications
Timelines - 2005- Stem Cell ACT OF 2005

- Established **CW Bill Young Cell Transplantation Program**
- Mandate to FDA to regulate/license public CBBs
- Established the **NCBI** network of public CBBs with subsidized funding to increase accrual of minority donors to the registry
- **Single Point of Access Registry** for adult and cord blood donors – contract to NMDP
- Established the **Stem Cell Transplant Outcomes Database** – contract to CIBMTR
- Coordinating Centers for Adult and CB donors – contract to NMDP
- Advisory Council for Blood Stem Cell Transplantation
C.W. Bill Young Cell Transplantation Program*

US Department of Health and Human Services

Advisory Council on Blood Stem Cell Transplantation

HRSA/Division of Transplantation

National Cord Blood Inventory
Individually contracted and accredited cord blood banks

Cord Blood Coordinating Center
Bone Marrow Coordinating Center
Stem Cell Therapeutic Outcomes Database

Components of the C. W. Bill Young Cell Transplantation Program

Office of Patient Advocacy/Single Point of Access
Public Interface

Made reporting allogeneic transplant data mandatory in the US in 2005

= HRSA Contract Organizations
= Other New Organizations or Relationships

* Created by the Stem Cell Therapeutic and Research Act of 2005 and the Stem Cell Therapeutic and Research Reauthorization Act of 2010
Timelines

- 2005- Mandate to FDA to regulate public CBBs
- 2005- NMDP holds IND for public CBBs
  - Center for Cord Blood (17 banks)
- 2005- FDA Docket to report UCBT outcomes
  - Multiple TCs report to banks and CIBMTR
- 2011- FDA issues final guidance for CB licensure
- 2012- First licenses issued to the NYBC, Colorado, Duke
- 2017- Public inventory ~800K, Private inventory >5M
- 2017- ~100 public banks registered with WMDA; hundreds of private banks worldwide
Carolinas Cord Blood Bank - History

- Established 1997 through COBLT/NHLBI contract (IND)
- Current inventory ~40,000 units
- 10 collection sites with access to >55,000 births/year
- Staff, hybrid and kit collection models
- Units listed and distributed through NMDP for HSCT
- NMDP Member bank 2004-present (IND)
- FACT accreditation 2005-present
- FDA Masterfile 3/2005-closed at licensure
- HRSA: NCBI Bank 2006-present (cohorts 1 and 5)
- Netcord Bank 2007-present
- CAP Accreditation/CLIA Certified 2010 - present
- BLA received October 4, 2012
# Routine Testing of Cord Blood

<table>
<thead>
<tr>
<th>Pre-Processing Sample (Whole Cord Blood + CPD)</th>
<th>Post-Processing Sample (HPC-C)</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Pre-processing TNCC</td>
<td>• Post-Processing TNCC</td>
</tr>
<tr>
<td>• ABO/Rh testing</td>
<td>• Viability</td>
</tr>
<tr>
<td>• Manual Diff (if applicable)</td>
<td>• Sterility (on CBU RBC/Plasma)</td>
</tr>
<tr>
<td></td>
<td>• CMV PCR (on CBU Plasma) for CMV + Moms</td>
</tr>
<tr>
<td><strong>Maternal IDMs</strong></td>
<td><strong>Stem Cell Lab</strong></td>
</tr>
<tr>
<td><strong>Maternal HLA</strong></td>
<td></td>
</tr>
<tr>
<td><strong>Baby NBS - hemoglobinopathies</strong></td>
<td></td>
</tr>
<tr>
<td><strong>Cord blood and maternal reference samples of whole blood, plasma, serum, FTA cards</strong></td>
<td></td>
</tr>
</tbody>
</table>
Current Criteria for Banking and Release to Donor Registry under the BLA

- ≥60ml / ≥80ml collection volumes (Minority / Caucasian)
- ≥1x10e9 TNCC pre processing
- ≥0.9x10e9 TNCC post processing
- ≥90% Viability post processing
- ≥ 1.25x10e6 viable CD34
- + CFU Growth
- Negative Sterility Testing
- Negative donor screening tests (except CMV) and donor screening questionnaires
- Negative Hemoglobinopathy screen for homozygous disease
SAE and AE Reporting

SAE

- Transplant Centers report directly through the web-based FormsNet system which distributes the report to the NMDP and to the CBB in realtime.

AE

- Transplant Centers report to the CIBMTR on a scheduled basis. Reports are downloaded to the cord blood bank monthly.

Investigations and Reporting

*By the NMDP if the unit was distributed under IND*
*By the CBB if the unit was distributed under BLA*
CCBB Information Systems

- CIBMTR Outcomes Database
  - CBC, diff
  - Viability
  - CFU
  - Viable CD34
  - Hemoglobinopathy
  - Sterility
  - ABO/Rh Typing

- CCBB Data Analyst

- NMDP CordSource

- HLA Data

- Other NMDP Systems

- IDM Data

- American Red Cross

- Department of Defense
Collected vs. Bankable CBUs

* FY defined as 7/1 – 6/30. Cumulative data for CCBB sites from EMMES data.
CCBB Total Units Banked by Licensure Status (1997-2017)
Source: CordSource as of 06/07/2017
Last units registered collected March 2017
CCBB Units Distributed to Patients

For Transplants

For BI clinical trials

FY defined as May-April

Duke Robertson Clinical and Translational Cell Therapy (CT²) Program
Applications of unrelated donor UCB

- Provide a source of hematopoietic stem and progenitor cells for hematopoietic reconstitution after myeloablative therapy.

- Can substitute for BM in all proven indications:
  - Hematological malignancies, hemoglobinopathies, bone marrow failure, congenital immunodeficiencies, certain inherited metabolic diseases.

- Can be utilized without full HLA matching increasing access to HSCT for patients of minority ancestry.
Applications of unrelated donor UCB

- Lower relapse rates in patients with high risk HM, especially those with MRD at the time of transplant.
- Superior outcomes in pediatric patients with certain inherited metabolic diseases compared to adult donor sources.
- Newer applications in regenerative therapies in clinical trials.