Emerging Considerations for Cord Blood Transplantation

Juliet Barker, MBBS
Joanne Kurtzberg, MD
Koen van Besien, MD, PhD

Moderators:
Janelle Olson, PhD, CHTC
Elizabeth Beduhn, CHTC

Cord Blood Unit Panel Discussion

Juliet Barker
Overview of CD34+ as a consideration in cord blood transplantation

Joanne Kurtzberg
Emerging uses of cords in non-malignant diseases

Koen van Besien
Use of dual haplo/cord blood transplants
Using CD34+ Cell Dose in Cord Blood Unit Selection

Juliet N. Barker, MBBS (Hons), FRACP
Associate Attending
Director, Cord Blood Transplant Program
Memorial Sloan-Kettering Cancer Center

Acknowledgements

Laboratory Medicine
Katherine Smith
Richard Meagher
Joann Tonon
Adult & Pediatric BMT
Duncan Purtill
Cladd Stevens
Doris Ponce
Parastoo Dahi
Andromachi Scaradavou
Sergio Giralt
CBT Program Research
Marissa Lubin
Emily Lauer
Biostatistics
Sean Devlin

Search Coordinators
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Eric Davis
Jen Paulson
Melissa Sideroff
Debbie Wells
3-yr DFS 8/8 & 7/8 URD-T or dCBT

N = 175.
Adults 16-60 yrs.
Acute leukemia or CML.

**dCBT:** higher 3-year DFS than 7/8 URD-T.

**dCBT:** Inf. CD34+ dose 1.3 + 0.7 x 10^5/kg.
11% 7-8/8, 48% 5-6/8, 41% 2-4/8.

Ponce et al, ASBMT 2014

**Distribution of URD, CB & No URD / CB by Patient Ancestry (n = 884)**

Image unavailable due to copyright restrictions
Relevance of CB?
(beyond extending access if no 7-8/8 URD)

- Decreases need to allograft with mismatched 7/8 URD.
- Extends transplant access if no haplo.

Only one quarter of Non-Europeans received 8/8 URD. Access for African ancestry patients most challenging.

Dahi et al, ASBMT 2015
CB: Approaches to Reduce TRM

- Unit selection
- Conditioning
- Immune suppression & GVHD
- Speeding engraftment (*beyond unit selection*)
- Preventing infections

How to Select Units?

- Dose (TNC, CD34+) & quality
- HLA-match
- RBC content (thaw & infusion)
% Viable CD34+s Post-Thaw by Bank (n = 366 units)

- **NYBC** (n=149):
  - Median: 94% (68-99)

- **Other US** (n=123):
  - Median: 89% (34-98)

- **International** (n=94):
  - Median: 92% (34-98)

Variability in viability by unit & by bank: introduces unit quality as important variable in unit selection.

**PROBLEM:**
Delayed or failed engraftment → increased TRM

**SOLUTIONS**
- Ex vivō expansion
- 3rd party cells
- Facilitate homing

Improved unit selection*
Cell Dose

Is infused viable CD34+ dose better than TNC dose?

Analysis of dCBT Neutrophil Engraftment
N = 129: Engraftment 95%

<table>
<thead>
<tr>
<th>Univariate Variable*</th>
<th>HR</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Recipient Age (continuous, per decade)</td>
<td>0.90</td>
<td>0.031</td>
</tr>
<tr>
<td>Dominant Unit Dose: Bank</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Pre-freeze TNC</td>
<td>1.19</td>
</tr>
<tr>
<td></td>
<td>Pre-freeze CD34+</td>
<td>1.39</td>
</tr>
<tr>
<td>Dominant Unit Dose: Post-thaw</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Inf. TNC</td>
<td>1.28</td>
<td></td>
</tr>
<tr>
<td>Inf. Viable CD34+</td>
<td>1.88</td>
<td>0.001</td>
</tr>
<tr>
<td>Inf. CFU</td>
<td>1.08</td>
<td></td>
</tr>
<tr>
<td>Inf. Viable CD3+</td>
<td>1.09</td>
<td>0.006</td>
</tr>
</tbody>
</table>

Multivariate analysis: only significant factor infused viable CD34+ cell dose of dominant unit: HR 1.95 (95% CI: 1.30-2.90), p < 0.001.

* Diagnosis, CMV serostatus, prep. regimen intensity & HLA match: NS

Purtill et al, Blood 2014
**What Determines Infused Viable CD34+ Cell Dose & Can it be Predicted at Unit Selection?**

Analysis of 3 Factors in 402 Units

<table>
<thead>
<tr>
<th>Pre-freeze</th>
<th>CD34+ count</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td>Post-thaw</td>
<td>CD34+ recovery</td>
</tr>
<tr>
<td></td>
<td>CD34+ viability*</td>
</tr>
</tbody>
</table>

*Tested at MSKCC by flow cytometry & 7-AAD exclusion*
Pre- vs Post-Thaw CD34+ Cell Recovery (n = 402)

Overall correlation: $r^2 = 0.73$
Median recovery: 101% (range 12-1480)

Low recovery (< 65%): 39 CB units (11%)
- Netcord-FACT accredited: 8%
- Non-Netcord-FACT accredited: 29%

$p < 0.001$
**Post-thaw CD34+ Cell Recovery & Viability**

Median viability: 92% (range 34-99%)  
< 75% viability: n = 33 (8%)

---

**Factors Associated with Low CD34+ Cell Viability**

<table>
<thead>
<tr>
<th>Variable (N)</th>
<th>N (%) &lt; 75% CD34+ Viability</th>
<th>OR* (95% CI)</th>
<th>Multivariate p value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Netcord-FACT accreditation</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes (n = 350)</td>
<td>15 (4%)</td>
<td>Reference</td>
<td>0.002</td>
</tr>
<tr>
<td>No (n = 52)</td>
<td>18 (35%)</td>
<td>4.9 (1.8-13.3)</td>
<td></td>
</tr>
<tr>
<td><strong>Cryopreservation year</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1997 – 2004 (n = 119)</td>
<td>17 (14%)</td>
<td>1.47 (0.6-3.7)</td>
<td>0.408</td>
</tr>
<tr>
<td>2005 – 2012 (n = 283)</td>
<td>16 (6%)</td>
<td>Reference</td>
<td></td>
</tr>
<tr>
<td><strong>Cryopreservation volume per bag (ml)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt; 24.5 (n = 14)</td>
<td>5 (36%)</td>
<td>8.8 (1.9-41.7)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>24.5 – 26.0 (n = 298)</td>
<td>8 (3%)</td>
<td>Reference</td>
<td></td>
</tr>
<tr>
<td>26.1 – 30.0 (n = 45)</td>
<td>7 (16%)</td>
<td>8.5 (2.6-28.0)</td>
<td></td>
</tr>
<tr>
<td>&gt; 30.0 (n = 45)</td>
<td>13 (29%)</td>
<td>7.5 (2.5-22.0)</td>
<td></td>
</tr>
<tr>
<td><strong>Processing method</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Manual (n = 187)</td>
<td>24 (13%)</td>
<td>2.3 (0.8-6.5)</td>
<td>0.131</td>
</tr>
<tr>
<td>Automated + semi-automated (n = 215)</td>
<td>9 (7%)</td>
<td>Reference</td>
<td></td>
</tr>
</tbody>
</table>
**CD34+ Conclusions:**

**Engraftment & Unit Quality Analysis**

- **Infused viable CD34+ cell dose** of dominant unit is critical determinant of engraftment after dCBT.

- **Post-thaw CD34+ recovery** is Bank-dependent:
  - Non-Netcord-FACT Banks associated with lower recovery.

- **Post-thaw CD34+ viability** is dependent on Banking practices:
  - Non-FACT accredited
  - $< 24.5 \text{ ml or } > 26 \text{ ml}$ lower post-thaw viability

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**CD34+ Conclusions:**

**Relevance in Unit Selection**

- **Pre-freeze CD34+ cell dose** can be used for unit selection: more reliable than TNC. Ideally $> 1 \times 10^5$/kg.

- **Quality**: another factor in unit selection: Netcord-FACT accreditation, processing & cryovolume.

- Applies to both units of double unit graft.

- Post-thaw testing (with back-up) warranted if low unit - esp. if single unit CBT.
If units can be selected based on likely post-thaw viable CD34+ dose are 2 units needed?

What is an adequate single?

MSKCC dCBT: Role of Non-Dominant Unit
(n = 129 myeloablative dCBT)

Winner determines speed & success of engraftment, but non-dominant unit may have facilitation effect- role in overcoming allogeneic barrier to engraftment ???

Purtill / Barker, ASH 2014
Recognition of HLA-Allele Mismatch

Selection based on high resolution typing now standard & selection of better matched units possible.

Dahi et al, BMT 2014
Novel Applications of Cord Blood Therapies

Joanne Kurtzberg, MD
Jerome Harris Distinguished Professor of Pediatrics
Professor of Pathology
Pediatric Blood and Marrow Transplant Program
Carolinas Cord Blood Bank
Julian Robertson Cell and Translational Therapy Program
Early Observations

- Cord blood could substitute for bone marrow as a donor for HSCT for all standard allogeneic indications
  - Hematological malignancies, marrow failure, immunodeficiencies, hemoglobinopathies, certain inherited metabolic diseases
- Cell dose matters and single cord blood unit may be on the cusp or too small for larger individuals
- HLA matching also matters, but lesser matches can be utilized when higher cell doses are administered
- Immune reconstitution is delayed
- GvHD is decreased as compared to adult HSCT sources
- Relapse may be lower post CBT versus other HSCT sources
**0501 Treatment Schema**

- **UCB 1**: HLA ≤ 2 ag mm, TNC > 2.5 x 10^7/kg
- **UCB 2**: HLA ≤ 2 ag mm, TNC > 3.5 x 10^7/kg

Flu 25 mg/m2 daily
TBI 165 cGy twice daily
Cy 60 mg/kg daily

**Overall Survival**
- **Intent-to-Treat**

<table>
<thead>
<tr>
<th>Months</th>
<th>Number at risk</th>
<th>Double UCB</th>
<th>Single UCB</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>111</td>
<td>95</td>
<td>95</td>
</tr>
<tr>
<td>3</td>
<td>102</td>
<td>88</td>
<td>88</td>
</tr>
<tr>
<td>6</td>
<td>68</td>
<td>77</td>
<td>77</td>
</tr>
<tr>
<td>9</td>
<td>62</td>
<td>62</td>
<td>62</td>
</tr>
<tr>
<td>12</td>
<td>61</td>
<td>61</td>
<td>61</td>
</tr>
</tbody>
</table>

Single UCB: 71% (62 - 79)
Double UCB: 65% (55 - 73)

P=0.13
**Engraftment (ANC 500)**

- Partially Matched, Cryopreserved (med = 19 days)
- NON-matched, Cryopreserved (med = 19 days)
- Conventional CBT (med = 25 days)

**Expanded Unit CD34 Cell Dose**
- Average: 12.5 million/kg
- Median: 8.3 million/kg
- Range: 0.9 to 49 million/kg

**Expanded Unit CD34 Cell Dose**
- Average: 6.8 million/kg
- Median: 6 million/kg
- Range: 3.1 to 11.6 million/kg

---

**NiCord® Product for BMT**

1. **NiCord®**
   - Cord Blood Unit

2. **CliniMACS separation:**
   - Enrichment of CD133⁺ cells

3. **Cultured fraction (CF):**
   - The CD133 positive cell fraction - Cultured for 3 weeks using NAM technology

4. **Non-cultured fraction (NF):**
   - The CD133 negative cell fraction - Kept frozen till the day of transplantation
NiCord® Graft Processing and Transplantation Schema

I. NiCord® cultured fraction (CF)
   Day -21: Cultured with cytokines (FLT3, SCF, TPO, IL-6) + Nicotinamide in cultured bags for 21 days
   Day 0: Cells harvested, safety and quality tested
   Hand delivery to clinical site (18hr stability)

NiCord® Graft Processing and Transplantation Schema

- ARRIVAL OF NiCord® CF TO CLINICAL SITE
- ARRIVAL OF NiCord® NF TO CLINICAL SITE
- TRANSPLANTATION
  I. NiCord® CF
  II. NiCord® NF
  III. Unmanipulated CBU

- CD133+CD34+ Fraction
- NiCord® non-cultured Fraction (NF)
- Day -21: cryopreserved CD133-CD34-Fraction

CONDITIONING:
Day -9 to 0
FOLLOW UP

- MMF
- Tacrolimus

Patients engrafted with NiCord®:
23.5 (Day 14 post transplant discharge)

Patients engrafted with the UM CBU:
40 (Day 31 post transplant discharge)

Duke control cohort (n=17) average 36 (Day 24 post transplant discharge)

Avg. hospitalization days

Rapid PB WBC Reconstitution in Patients Engrafted with NiCord®

NiCord® (n=8)
UM (n=2)
Cont. (n=17)

0.00 0.50 1.00 1.50 2.00 2.50 3.00 3.50 4.00 4.50 5.00
0 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15
ANC>500 (median)
ANC>500 (average)

WBC NiCord® Rapid Engraftment Shortens Hospitalization


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Stable Donor Derived Chimerism, Over Three Years, Provided by NiCord® HSC’s

Image unavailable due to copyright restrictions

NiCord Single Expanded Cord Blood Transplantation

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How does SCT correct inborn errors of metabolism?

- Marrow and immunoablation
- Replacement with donor cells
- Donor leukocytes produce enzyme
- Enzyme distributed through blood circulation
- Cells migrate to brain, cross blood brain barrier, replace enzyme in brain “Cellular Enzyme Replacement Therapy”
- Non-hematopoietic cell engraftment
Differentiation of Donor Cells into Cardiac Myocytes

Engraftment of donor-derived insulin-expressing beta cells in a recipient of UCBT

Donor-derived islet in a 1.5 year old, MPS 1, female recipient of a male UCBT surviving 161 days post transplant

Huang et al. Diabetologia (2011) 54:1066-74
SCT for Krabbe Disease:
Early transplantation is critical!

Newborn Screening:
New York State 2008
Now 7 other states

Some newborns with Krabbe Disease have sustained prenatal damage to their cortical spinal tracks

M Escolar, CDL, NFRD, UNC-CH
All 2-3 days of age

Tierney, Borrassa, Degan Miles;
Cerebral pudgeone - k4 and k6 are normal (yellow is myelination) Middle - Bourassa - less fibres, no myelin; the outcome of the motor function worse in the middle child.

Vinod Prasad, 4/12/2007
Donor Cells engraft in the brain after IV UCBT

DUOC-01

DUOC-01 – Initial Description


- Completed preclinical toxicology, biodistribution, animal toxicology, validation of manufacturing, stability, development of release criteria, clinical protocol for IND submission
Robertson CT²

100 employees

GMP Cell Manufacturing Facility

- **Flexible** manufacturing spaces.
- Three class 10,000 (ISO class 7) suites available
- Aseptic processing, fill, and finish for cellular product
- cGMP sample storage
- Controlled receipt, storage and release of raw materials and supplies
- Environmental monitoring using industry standard equipment with quality audit and trending

www.DukeGMP.org
DUOC-01-Manufacturing (GMP)
More than Minimally Manipulated

• Thaw 20% fraction of licensed CBU, wash
• Deplete RBC
• Culture, NCS proliferation conditions, demi-depleting non-adherent cells in feeding
• Differentiation medium d14-17
• Trypsinize, wash d21
• Formulate for IT injection in syringe
• Release: viability, sterility, endotoxin, flow

E. Tracy, T. Gentry, GMP Lab

Tissue distribution of DUOC-01 cells

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LSD enzyme production

Image unavailable due to copyright restrictions

Cytokines secreted by DUOC-01 in response to TNF-α

Image unavailable due to copyright restrictions
Myelin basic protein expression one week after return to normal diet and treatment with DUOC-01 or Ringer’s solution

Ringers

DUOC-01

Anti-MBP

72 tiled images of representative section

A. Saha RP2 Lab

DUOC-01 First in Humans Trial Design

80%

20%

CBT

21 days

IT 1-5 X10⁶ cells

DUOC-01

Assess: Safety, Motor function, Cognitive function, long term

Period DUOC-01 will provide benefit

IND 9/2014

Cells from CBT in CNS

CBT provides enzyme permanently
Our Roadmap

- Allo UCBT in IMD
- Donor cells engraft in brain
- Further injury prevented, some repair
- What about auto cells for brain injury?
- What about an allo cord-derived product for brain injury?

Autologous UCBT at Duke

- Safety
- HIE Study “Babybac”
  - Cooling +/- UCB infusion
  - Auto UCB infusion (volume reduced, fresh CB)
- Congenital Hydrocephalus
- HLHS/ECMO
  - Cryopreserved cord blood
- CP ages 1-6
  - Cryopreserved cord blood
- Autism
HIE (babybac) Pilot Study
Mike Cotten, Ron Goldberg, Amy Murtha, STCL, CCBB

- Term Newborns with HIE meeting diagnostic criteria for moderate to severe encephalopathy
- Eligible for cooling
- Collected autologous cord blood
- Cooled per SOC
- Informed consent
- Given autologous CB infusions at <24 and <48 hours of age
- Followed for infusional toxicity, survival and functional outcomes at 1 and 2 years of age

Cotton et al, J Peds, 2014

Survival with 1 yr Bayley III scores ≥ 85 in 3 domains

<table>
<thead>
<tr>
<th></th>
<th>Cells N = 18</th>
<th>Cooled only N = 46</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>*Survived to 15 months</td>
<td>16 (89)</td>
<td>35 (76)</td>
<td>0.25</td>
</tr>
<tr>
<td>Survival with all 3 Bayley domain scores ≥ 85</td>
<td>13 (72)</td>
<td>19 (41)</td>
<td>0.05</td>
</tr>
</tbody>
</table>

NEXT STEPS: PHASE II RANDOMIZED TRIAL:
- 240 patients, 8-10 centers
- ~$5-6M
- ? Standard Rx vs Placebo (RBC pellet)
  or 1 versus multiple (and later) infusions
“CP-AC” (IND)
Jessica Sun, Allen Song, Anne Fitzgerald, Colleen McLaughlin

- Randomized, placebo-controlled trial of autologous CB in children with spastic CP
  - Ages 1-6 yrs
  - Eligible cord blood
  - GMFM level (II-IV)
- Blinded/cross-over design
  - Baseline, 1 yr, 2yrs
- Evaluations by exam, neurocog/fxnl testing, MRI (functional in older pts), TMS, CB microarrays, QOL
- Primary Endpoint: >30% increase in predicted GMFM score at 1 year
- Activated 7/2010; completed accrual 2/2013
- First analysis planned 3/2015

4.2 Study Flow Chart

*Placebo = TC199 + 1% DMSO
Assessing Change in Changing Subjects

Assumptions:
- Mean increase of 6 points/year without intervention
- ~30% additional increase (7.8 total points/year) would be clinically significant

GMFM-66 Percentiles by Age


Longitudinal Assessment

(Left Hemiplegia)

A Song BIAC

Year 0

GMFM change < 10

Increased normalized connection volume

Decreased normalized connection volume

GMFM change >= 10

0 < change < 0

Increased normalized connection volume

0 > change > 0

Decreased normalized connection volume

Right (R)

Left (L)
## Cell therapies for brain diseases

<table>
<thead>
<tr>
<th>Genetic Diseases</th>
<th>Acquired Brain Injuries</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Allogeneic cells</td>
<td>• Autologous cells</td>
</tr>
<tr>
<td>• Permanent engraftment</td>
<td>• Transient presence</td>
</tr>
<tr>
<td>– Including brain</td>
<td>• Paracrine/trophic effects</td>
</tr>
<tr>
<td>• Enzyme replacement</td>
<td>• Signaling of endogenous cells</td>
</tr>
<tr>
<td>• Requires chemotherapy</td>
<td>• No chemotherapy</td>
</tr>
</tbody>
</table>

### What about allogeneic cells for treatment of brain injuries?

### Allogeneic cells for Acquired brain injuries and other cellular therapies?

- Most patients do not have their cord blood banked.
- A donor derived, readily available product is needed:
  - Administration without chemotherapy.
  - Will immunosuppression be needed?
  - Should the product be HLA matched?
- Therapeutic effects through paracrine signaling
- Durable engraftment not necessary
The Marcus Foundation Grant  
JK and Geri Dawson

- Cord blood derived cellular therapies for treatment of autism, stroke, CP
- Autologous and allogeneic products  
  – Non homologous use
- Minimally manipulated and more than minimally manipulated cells
- Preclinical development, animal models, INDs, 11 clinical trials

FDA LICENSURE
‘hematopoietic reconstitution after myeloablative chemotherapy’
Acknowledgements

- Pediatric Blood and Marrow Transplant Team
  - MDs, APNs, NCs, SC, SW, FA, FSP
- Stem Cell Laboratory
- Carolinas Cord Blood Bank
- CT2: Andy Balber and team
- Allen Song and Jim Provenzale
- Jessica Sun/Mohamad Mikati/Gordon Worley
- Katie Gustafson/Laura Case and ND Team
- Amy Murtha, Haywood Brown
- Sid Tan, Mike Cotten, Ron Goldberg, Ricki Goldstein
- Geri Dawson and team
- NHLBI, HRSA, NMDP, The EMMES corp
- The Julian Robertson Foundation
- The Legacy of Angels Foundation
- The Katz Foundation
- The Marcus Foundation

Our Patients and their parents and families
Haplo-Cord Transplant – An update
Koen van Besien, MD, PhD
NYP-WCMC
New York, NY

Thanks to:
- U Chicago
  - Hong Tao Liu
  - Andy Artz
  - John Cunningham
  - Lucy Godley
  - Elizabeth Rich
  - Justin Kline
  - Richard Larson
  - Vu Nguyen
  - Toyosi Odenike
  - Wendy Stock
  - Amittha Wickrema

- WCMC
  - Tsiporah Shore
  - Usama Gergis
  - Sebastian Mayer
  - Melissa Cushing

- Transplant Unit Staff
- Research Coordinator
- RN, PA, Pharm D
- Rehab Medicine
- Biostatistics
- Chimerism
- HLA
8/8 Allele, Available-Match Rates in the Adult Donor Registry

HAPLO VS UCB (CTN PARALLEL TRIALS)

Neutrophilic Recovery

Outcome

Age <70 (med 58 UCB, 48 Haplo)
AL in CR
Chemores Agg Lymphoma
Fol Lymphoma ≥2 chemo

**FLUDARABINE MELPHALAN ATG**

- **Fludarabine** (30 mg/m²/day)
- **Melphalan** (140 mg/m²)
- *Thymo 1.5 mg/kg*
- Tacrolimus
- Mycophenolate
- TBI 2Gray

- Decrease ATG dose for patients over 50
- Decrease MMF
- TBI for selected patients

**CHIMERISM**

**UNFRACTIONATED**

**CD3**
PATIENT COURSE

- 66 YO WM
- Refractory AML
- ANC d10, Plt d30
- D50: Unfrac, 100% UCB
- D50: CD3, 100% UCB

- 65 YO WM
- Transformed Follicular
- ANC d10, Plt d14
- D50: CD33 100% Haplo
- D50: CD3 66% Haplo, 33% UCB

- 36 YO BF
- Hx Cadaveric Kidney Tx, CRF
- T- MDS
- ANC d10, Plt d42
- D50: CD33 100% UCB
- D50: CD3 100% UCB

HAPLOCORD VS DOUBLE UCB CASES REPORTED TO CIBMTR

<table>
<thead>
<tr>
<th></th>
<th>Haplo Cord</th>
<th>Double UCB</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>98</td>
<td>737</td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td>54</td>
<td>48</td>
<td>0.01</td>
</tr>
<tr>
<td>% Minority</td>
<td>34</td>
<td>24</td>
<td>0.001</td>
</tr>
<tr>
<td>Advanced Disease</td>
<td>44%</td>
<td>23%</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Year of Tx</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2007-2009</td>
<td>18%</td>
<td>50%</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>2010-2013</td>
<td>82%</td>
<td>50%</td>
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</tr>
</tbody>
</table>

Control Selection – (Propensky Score Matching)
Match 1 Case with up to four controls matched for: age, gender, race, disease type, disease stage pre-transplant, KPS and years within 2 years

Presented by: Koen van Besien, MD
### CASE CONTROL: HAPLOCORD VS DUCB MATCHED COHORT

<table>
<thead>
<tr>
<th></th>
<th>Haplo Cord</th>
<th>DUCB</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>98</td>
<td>340</td>
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</tr>
<tr>
<td>Median Age</td>
<td>54</td>
<td>52</td>
<td>0.57</td>
</tr>
<tr>
<td>Median Weight</td>
<td>80 (41-136)</td>
<td>78 (40-155)</td>
<td>0.32</td>
</tr>
<tr>
<td>% male</td>
<td>61</td>
<td>59</td>
<td>0.63</td>
</tr>
<tr>
<td>% Minority</td>
<td>34</td>
<td>33</td>
<td>0.89</td>
</tr>
<tr>
<td>% AML</td>
<td>55</td>
<td>56</td>
<td>0.96</td>
</tr>
<tr>
<td>% Advanced Disease</td>
<td>44</td>
<td>34</td>
<td>0.08</td>
</tr>
<tr>
<td>KPS ≤ 80</td>
<td>20</td>
<td>20</td>
<td>0.98</td>
</tr>
<tr>
<td>Year of Tx</td>
<td></td>
<td></td>
<td>0.33</td>
</tr>
<tr>
<td>2007-2009</td>
<td>18%</td>
<td>23%</td>
<td></td>
</tr>
<tr>
<td>2010-2013</td>
<td>82%</td>
<td>77%</td>
<td></td>
</tr>
<tr>
<td>Follow up of survivors (median)</td>
<td>14 mo</td>
<td>22 mo</td>
<td>0.19</td>
</tr>
</tbody>
</table>

### ENGRAFTMENT OUTCOMES

<table>
<thead>
<tr>
<th></th>
<th>Haplo Cord</th>
<th>DUCB</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neutrophil</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>d30</td>
<td>91%</td>
<td>72%</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>d60</td>
<td>96%</td>
<td>86%</td>
<td>0.0001</td>
</tr>
<tr>
<td>Platelets</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>d30</td>
<td>54%</td>
<td>6%</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>d60</td>
<td>78%</td>
<td>54%</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>
NEUTROPHIL AND PLATELET ENGRAFTMENT

Presented by: Koen van Besien, MD, PhD

HAPLOCORD VS DOUBLE UCB MATCHED COHORT

<table>
<thead>
<tr>
<th></th>
<th>Haplo Cord</th>
<th>Double UCB</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Conditioning Intensity</td>
<td></td>
<td></td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>RIC or NMA Conditioning</td>
<td>100%</td>
<td>55%</td>
<td></td>
</tr>
<tr>
<td>GVHD prophylaxis</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CNI+ MMF</td>
<td>100%</td>
<td>89%</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>ATG</td>
<td>100%</td>
<td>24%</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Total Nucleated Cell Doses (x10^7/kg) Median (range)</td>
<td>1.93 (0.78-20)</td>
<td>4.1 (0.03-21)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Degree of Mismatch*</td>
<td></td>
<td></td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>None (6/6)</td>
<td>10%</td>
<td>2% (4%)</td>
<td></td>
</tr>
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<td>41% (65%)</td>
<td></td>
</tr>
<tr>
<td>Three Mismatches (3/6)</td>
<td>0%</td>
<td>1% (2%)</td>
<td></td>
</tr>
<tr>
<td>Data not available</td>
<td>36%</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Patients who are missing CB match or cell dose data are excluded from Computation

Presented by: Koen van Besien, MD
### EXAMPLES

<table>
<thead>
<tr>
<th></th>
<th>x</th>
<th>Age</th>
<th>Weight</th>
<th>Comorb</th>
<th>UCB TNC/kg</th>
<th>Match Out of 8</th>
<th>ANC 500</th>
<th>PLT 20</th>
<th>AGVHD</th>
<th>CGVHD</th>
<th>Current Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>SC</td>
<td>HL Ref</td>
<td>24</td>
<td>136</td>
<td>ADD</td>
<td>1.2</td>
<td>5</td>
<td>14</td>
<td>20</td>
<td>0</td>
<td>NO</td>
<td>A&amp;W 17 Mo</td>
</tr>
<tr>
<td>SC</td>
<td>HL Ref</td>
<td>24</td>
<td>136</td>
<td>ADD</td>
<td>1.2</td>
<td>5</td>
<td>14</td>
<td>20</td>
<td>0</td>
<td>NO</td>
<td>A&amp;W 17 Mo</td>
</tr>
<tr>
<td>CS</td>
<td>Tr L SD</td>
<td>63</td>
<td>91</td>
<td>A fib Sleep apnea</td>
<td>1.1</td>
<td>8</td>
<td>10</td>
<td>15</td>
<td>0</td>
<td>NO</td>
<td>A&amp;W 10 Mo</td>
</tr>
</tbody>
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## EXAMPLES

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<td>10</td>
<td>15</td>
<td>0</td>
<td>NO</td>
<td>A&amp;W 10 Mo</td>
</tr>
<tr>
<td>DP</td>
<td>AML PIF</td>
<td>66</td>
<td>96</td>
<td>DM Arterial clot</td>
<td>1.2</td>
<td>7</td>
<td>9</td>
<td>13</td>
<td>0</td>
<td>NO</td>
<td>A&amp;W 12 Mo</td>
</tr>
<tr>
<td>MS</td>
<td>AML CR1 +PV +CLL</td>
<td>71</td>
<td>104</td>
<td>Prostate cancer TIA Glaucoma</td>
<td>2.5</td>
<td>7</td>
<td>25</td>
<td>38</td>
<td>0</td>
<td>A&amp;W 4 Mo</td>
<td></td>
</tr>
</tbody>
</table>

**Current Status**
- SC HL Ref: A&W 17 Mo
- CS Tr L SD: A&W 10 Mo
- DP AML PIF: A&W 12 Mo
- MS AML CR1 +PV +CLL: A&W 4 Mo
### Haplo Cord vs Double UCB Matched Cohort

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Presented by: Koen van Besien, MD

### Relation Between Minimal UCB Cell Dose and HR HLA Match

![Graph showing the relation between minimal UCB cell dose and HR HLA match](image)
## HAPLOCORD VS DOUBLE UCB MATCHED COHORT

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## INCIDENCE OF ACUTE AND CHRONIC GVHD

![Graphs showing incidence of acute and chronic GVHD](image-url)
PFS AND OS HAPLO CORD VS CONTROL GROUP

CONCLUSION: HAPLO CORD TRANSPLANT

- Reliable and fast Neutrophil and Platelet Recovery
- Ability to use smaller, better matched UCB grafts
- Low rates of acute and chronic GHVD without increases in relapse rates
  - Use of ATG?
  - Better HLA matching?
- Excellent option for
  - Patients with limited UCB options
  - Older patients
    - Rapid hematopoietic Recovery
    - Low rates of cGVHD
- Long term survival improved