Updated 2012 guidelines for selecting unrelated donors and CBUs for HCT

Dr. Dennis Confer
Chief Medical Officer, NMDP
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Financial disclosure

The following in control of content had no relevant financial relationships to disclose.

- Dennis L. Confer, MD  Presenter
- Darlene Haven  Planning Committee
- Ellyce Hayes, RD  Planning Committee
- Mary Horowitz, MD  Planning Committee
- Craig Malmberg, CHS  Planning Committee
- Michelle Setterholm, CHS  Planning Committee
- Stephen Spellman, PhD  Planning Committee
Learning objectives

• Identify pre/post-transplant factors that contribute to improved HCT survival

• Apply updated matching criteria for selecting marrow, PBSC, and cord blood cell sources for transplant recipients

• Identify strategies for selection between mismatched loci with consideration for decision-making based on strength of supporting research
Recent Update to Matching Guidelines

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2012 120: 259-265
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A perspective on the selection of unrelated donors and cord blood units for transplantation

Stephen R. Spellman, Mary Eapen, Brent R. Logan, Carlheinz Mueller, Pablo Rubinstein, Michelle I. Setterholm, Ann E. Woolfrey, Mary M. Horowitz, Dennis L. Confer and Carolyn K. Hurley

Factors that Affect Transplant Outcomes

Pre-transplant
- HLA matching
- Patient CMV seropositivity
- Performance score
- Disease
- Disease status
- Graft cell dose

Post-transplant
- Infections
- aGVHD and cGVHD
- Organ toxicity
- Recurrent/2nd malignant neoplasms
Questions to Answer

• Which loci should be evaluated for HLA matching?
• How do antigen mismatches compare to allele mismatches?
• Are some loci more important than others?
• Is bone marrow the same as PBSC?
• What about HLA-DP?
• What about anti-HLA antibodies?
• What about cord blood unit transplants?
• Anything about KIR?
High-resolution donor-recipient HLA matching contributes to the success of unrelated donor marrow transplantation

BLOOD (2007) 110: 4576-83

Study Population

- AML, ALL, CML, MDS
- Myeloablative conditioning
- Calcineurin inhibitor-based GVHD prophylaxis, T replete grafts (79%)
- Bone marrow (94%)
- Median follow-up 6 years
## Any Single Locus Mismatch

9/10 associated with worse survival, DFS, TRM, acute GVHD

<table>
<thead>
<tr>
<th></th>
<th>n</th>
<th>RR (95% CI)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Survival</td>
<td>952</td>
<td>1.17 (1.06-1.329)</td>
<td>0.002</td>
</tr>
<tr>
<td>DFS</td>
<td>945</td>
<td>1.16 (1.05-1.28)</td>
<td>0.003</td>
</tr>
<tr>
<td>TRM</td>
<td>945</td>
<td>1.31 (1.16-1.47)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Relapse</td>
<td>945</td>
<td>0.90 (0.81-1.00)</td>
<td>0.04</td>
</tr>
<tr>
<td>Engraftment</td>
<td>956</td>
<td>OR 0.90 (0.80-1.01)</td>
<td>0.06</td>
</tr>
<tr>
<td>Acute GVHD</td>
<td>957</td>
<td>1.35 (1.19-1.56)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Chronic GVHD</td>
<td>910</td>
<td>0.96 (0.91-1.03)</td>
<td>0.25</td>
</tr>
</tbody>
</table>
### Single Antigen vs. Allele MM

<table>
<thead>
<tr>
<th></th>
<th>Antigen</th>
<th>Allele</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Survival</td>
<td>1.16</td>
<td>1.19</td>
<td>0.69</td>
</tr>
<tr>
<td>DFS</td>
<td>1.16</td>
<td>1.17</td>
<td>0.92</td>
</tr>
<tr>
<td>TRM</td>
<td>1.34</td>
<td>1.32</td>
<td>0.86</td>
</tr>
<tr>
<td>Relapse</td>
<td>0.80</td>
<td>0.93</td>
<td>0.31</td>
</tr>
<tr>
<td>Engraftment</td>
<td>0.74</td>
<td>1.08</td>
<td>0.07</td>
</tr>
<tr>
<td>Acute GVHD</td>
<td>1.52</td>
<td>1.24</td>
<td>0.06</td>
</tr>
<tr>
<td>Chronic GVHD</td>
<td>0.95</td>
<td>0.97</td>
<td>0.84</td>
</tr>
</tbody>
</table>

No statistical difference if mismatched at antigen or allele level, except for C – Antigen worse than Allele
## HLA DQ Lacked Impact: As a Single Mismatch

<table>
<thead>
<tr>
<th>Survival</th>
<th>TRM</th>
<th>Acute GVHD</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>RR</td>
<td>p</td>
</tr>
<tr>
<td>10/10</td>
<td>1.00</td>
<td></td>
</tr>
<tr>
<td>DQ MM</td>
<td>0.97</td>
<td>0.77</td>
</tr>
</tbody>
</table>

## As a Second Mismatch

<table>
<thead>
<tr>
<th></th>
<th>8/10</th>
<th>9/10</th>
<th>RR (95% CI)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>DQ MM</td>
<td>191</td>
<td>797</td>
<td>1.14 (0.94-1.38)</td>
<td>0.17</td>
</tr>
</tbody>
</table>
## Specific Single Locus Mismatches

**Considering 8/8 as “fully matched”**

<table>
<thead>
<tr>
<th></th>
<th>Survival</th>
<th>TRM</th>
<th>Acute GVHD</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>RR p</td>
<td>RR p</td>
<td>RR p</td>
</tr>
<tr>
<td>8/8</td>
<td>1.00 1.00</td>
<td>1.00 1.00</td>
<td>1.00</td>
</tr>
<tr>
<td>A MM</td>
<td>1.36 &lt;0.0001</td>
<td>1.47 &lt;0.0001</td>
<td>1.57 &lt;0.0001</td>
</tr>
<tr>
<td>B MM</td>
<td>1.16 0.20</td>
<td>1.32 0.03</td>
<td>1.63 0.001</td>
</tr>
<tr>
<td>C MM</td>
<td>1.19 0.006</td>
<td>1.32 0.0002</td>
<td>1.43 &lt;0.0001</td>
</tr>
<tr>
<td>DR MM</td>
<td>1.48 0.0005</td>
<td>1.56 0.0007</td>
<td>1.27 0.16</td>
</tr>
</tbody>
</table>

**Survival:** Mismatch at A or DRB1 vs. B or C, RR 1.18 (1.10-1.38), p=0.04
Survival

9-10% lower overall survival with each additional mismatch

<table>
<thead>
<tr>
<th>Match</th>
<th>n</th>
<th>Survival (CI)</th>
<th>RR (CI)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>8/8</td>
<td>1840</td>
<td>52 (50-54)</td>
<td>1.00</td>
<td></td>
</tr>
<tr>
<td>7/8</td>
<td>988</td>
<td>43 (40-46)</td>
<td>1.25 (1.13-1.37)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>6/8</td>
<td>633</td>
<td>33 (30-37)</td>
<td>1.65 (1.48-1.84)</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>
Early stage disease

Log-rank p-value = < 0.0001


8/8 HLA Matched (n=835)
7/8 HLA Matched (n=378)
6/8 HLA Matched (n=241)
Intermediate stage disease

8/8 HLA Matched (n=674)
7/8 HLA Matched (n=410)
6/8 HLA Matched (n=268)

Log-rank p-value < 0.0001

Advanced stage disease

Log-rank p-value = 0.02

8/8 HLA Matched (n=327)
7/8 HLA Matched (n=195)
6/8 HLA Matched (n=123)

Lee Study Conclusions

- High resolution matching of HLA-A, -B, -C, and DRB1 alleles is associated with the best survival.
- The adverse effects of allele and antigen mismatches appear equivalent (except at C).
- HLA-DQ matching is not important for survival, TRM or acute GvHD.
Lee Study Conclusions, cont.

- Single mismatches HLA-A or DRB1 may be more poorly tolerated than at HLA-B and HLA-C
- Each mismatch is associated with a 9-10% decrease in survival, and the absolute decrement in survival is most pronounced in the early stage patients
Questions to Answer

• Which loci should be evaluated for HLA matching?
• How do antigen mismatches compare to allele mismatches?
• Are some loci more important than others?
• Is bone marrow the same as PBSC?
• What about HLA-DP?
• What about anti-HLA antibodies?
• What about cord blood unit transplants?
• Anything about KIR?
Evaluation of HLA Matching Requirements for Unrelated PBSC Transplantation

Ann Woolfrey, John Klein, Michael Haagenson, Stephen Spellman, Effie Petersdorf, Machteld Oudshoorn, James Gajewski, Gregory Hale, John Horan, Minoo Battiwalla, Susana Marino, Michelle Setterholm, Craig Kollman, Stephanie Lee

On behalf of the CIBMTR Immunobiology Working Committee

## Patient Characteristics (N=1933)

<table>
<thead>
<tr>
<th>Variable</th>
<th>N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, yrs</td>
<td>Median (range)</td>
</tr>
<tr>
<td>Male</td>
<td></td>
</tr>
<tr>
<td>KPS ≥ 90</td>
<td></td>
</tr>
<tr>
<td>Disease</td>
<td></td>
</tr>
<tr>
<td>AML</td>
<td></td>
</tr>
<tr>
<td>ALL</td>
<td></td>
</tr>
<tr>
<td>CML</td>
<td></td>
</tr>
<tr>
<td>MDS</td>
<td></td>
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</tbody>
</table>
### Does DQ Matter?

<table>
<thead>
<tr>
<th>8/8 Match with</th>
<th>N</th>
<th>RR</th>
<th>95% CI</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>DQB1 match</td>
<td>1125</td>
<td>1.00</td>
<td></td>
<td></td>
</tr>
<tr>
<td>DQB1 allele MM</td>
<td>68</td>
<td>0.97</td>
<td>0.71-1.34</td>
<td>0.87</td>
</tr>
<tr>
<td>DQB1 antigen MM</td>
<td>46</td>
<td>1.36</td>
<td>0.95-1.96</td>
<td>0.10</td>
</tr>
</tbody>
</table>

No Significant Effect of DQ Mismatch
## Mortality

<table>
<thead>
<tr>
<th></th>
<th>N</th>
<th>RR</th>
<th>95% CI</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>8/8 match</td>
<td>1243</td>
<td>1.00</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 allele MM</td>
<td>208</td>
<td>1.11</td>
<td>0.91-1.35</td>
<td>0.30</td>
</tr>
<tr>
<td>1 antigen MM</td>
<td>293</td>
<td>1.32</td>
<td>1.12-1.55</td>
<td>&lt;0.0007</td>
</tr>
<tr>
<td>2 allele MM</td>
<td>29</td>
<td>1.21</td>
<td>0.77-1.90</td>
<td>0.42</td>
</tr>
<tr>
<td>2 antigen MM</td>
<td>31</td>
<td>2.27</td>
<td>1.55-3.34</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>2 mixed MM</td>
<td>68</td>
<td>2.32</td>
<td>1.78-3.02</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

Mismatch for 1 antigen or >1 allele/antigen increases risk of **mortality**
# Locus-Specific Analysis — Mortality

<table>
<thead>
<tr>
<th></th>
<th>N</th>
<th>RR</th>
<th>95% CI</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>8/8 match</strong></td>
<td>1243</td>
<td>1.00</td>
<td></td>
<td></td>
</tr>
<tr>
<td>A allele MM</td>
<td>51</td>
<td>1.16</td>
<td>0.80-1.67</td>
<td>0.43</td>
</tr>
<tr>
<td>A antigen MM</td>
<td>85</td>
<td>1.17</td>
<td>0.88-1.55</td>
<td>0.29</td>
</tr>
<tr>
<td>B allele MM</td>
<td>57</td>
<td>1.29</td>
<td>0.92-1.28</td>
<td>0.14</td>
</tr>
<tr>
<td>B antigen MM</td>
<td>16</td>
<td>1.01</td>
<td>0.50-2.04</td>
<td>0.97</td>
</tr>
<tr>
<td>C allele MM</td>
<td>61</td>
<td>0.82</td>
<td>0.57-1.19</td>
<td>0.30</td>
</tr>
<tr>
<td><strong>C antigen MM</strong></td>
<td>187</td>
<td>1.41</td>
<td><strong>1.16-1.70</strong></td>
<td><strong>0.0005</strong></td>
</tr>
<tr>
<td>DRB1 MM</td>
<td>39</td>
<td>1.30</td>
<td>0.87-1.94</td>
<td>0.20</td>
</tr>
<tr>
<td><strong>C allele vs. antigen</strong></td>
<td>0.58</td>
<td>0.39-0.88</td>
<td><strong>0.009</strong></td>
<td></td>
</tr>
</tbody>
</table>

C antigen mismatch increases risk for mortality, DFS, TRM & GVHD III-IV
Unrelated Donor PBSC Transplantation Conclusions

- C antigen mismatch confers the greatest risk for poor outcome
- C antigen mismatch is important in both ablative & non-myeloablative HCT
- A larger sample size may reveal additional associations
Lee data (marrow) vs. Woolfrey (PBSC)

• Similar findings
  – One antigen level mismatch at A, B, C, or DRB1 caused worse OS
  – Survival not affected by isolated DQ or DP mismatches

• Woolfrey differs
  – Allele mismatches, no significant effect on survival
    • Far fewer patients to evaluate for comparisons than Lee
Can’t avoid C antigen mismatch?

- Further Lee and Woolfrey data analysis
- *No* significant advantage to using marrow over PBSC as graft source with isolated C antigen mismatch
Questions to Answer

• Which loci should be evaluated for HLA matching?
• How do antigen mismatches compare to allele mismatches?
• Are some loci more important than others?
• Is bone marrow the same as PBSC?
• What about HLA-DP?
• What about anti-HLA antibodies?
• What about cord blood unit transplants?
• Anything about KIR?
DPB1 Matching

Studies have suggested that a DPB1 matching does not impact overall survival

- DPB1 match increases relapse risk
- DPB1 mismatch increases acute GVHD and TRM

Lack of tight DPB1 linkage with other loci decreases the ease of finding a DPB1 match

- Only ~20% of 10 of 10 matched transplants will be matched for DPB1
DPB1 Permissive Mismatching

  - Grouped DPB1 alleles into groups based on cross-reactive T-cell epitopes
- Created the concept of permissive and non-permissive mismatches
- DPB1 matches and permissive mismatches are present in ~70% of 10 of 10 matched transplants
DPB1 and 10/10 donors, NRM

10 of 10 HLA-matched with DPB1 Assessment

DPB1 Permissive Mismatches May Benefit 9 of 10 Matched Transplant

<table>
<thead>
<tr>
<th></th>
<th>HLA 10/10 match, non-permissive DPB1 mismatch (n=1654)</th>
<th>HLA 9/10 match, permissive DPB1 mismatch (n=1595)</th>
<th>HLA 9/10 match, DPB1 match (n=500)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>HR or OR</td>
<td>p value</td>
<td>HR or OR</td>
</tr>
<tr>
<td>Overall mortality</td>
<td>1 (ref)</td>
<td></td>
<td>1.04 (0.94-1.14)</td>
</tr>
<tr>
<td>Non-relapse mortality</td>
<td>1 (ref)</td>
<td></td>
<td>1.01 (0.90-1.13)</td>
</tr>
<tr>
<td>Relapse*</td>
<td>1 (ref)</td>
<td></td>
<td>1.12 (0.96-1.31)</td>
</tr>
<tr>
<td>Grade 3–4 aGvHD</td>
<td>1 (ref)</td>
<td></td>
<td>1.00 (0.84-1.19)</td>
</tr>
</tbody>
</table>

### DPB1 Permissive Mismatches May Benefit 9 of 10 Matched Transplant

<table>
<thead>
<tr>
<th></th>
<th>HLA 10/10 match, non-permissive DPB1 mismatch (n=1654)</th>
<th>HLA 9/10 match, non-permissive DPB1 mismatch (n=1001)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall mortality</td>
<td>1 (ref)</td>
<td>1.13 (1.02–1.26)</td>
</tr>
<tr>
<td>Non-relapse mortality</td>
<td>1 (ref)</td>
<td>1.19 (1.05–1.35)</td>
</tr>
<tr>
<td>Relapse*</td>
<td>1 (ref)</td>
<td>1.04 (0.87–1.24)</td>
</tr>
<tr>
<td>Grade 3–4 aGvHD</td>
<td>1 (ref)</td>
<td>1.36 (1.13–1.65)</td>
</tr>
</tbody>
</table>

Questions to Answer

• Which loci should be evaluated for HLA matching?
• How do antigen mismatches compare to allele mismatches?
• Are some loci more important than others?
• Is bone marrow the same as PBSC?
• What about HLA-DP?
• What about anti-HLA antibodies?
• What about cord blood unit transplants?
• Anything about KIR?
THE DETECTION OF DONOR-DIRECTED, HLA-SPECIFIC ALLOANTIBODIES IN RECIPIENTS OF UNRELATED HEMATOPOIETIC CELL TRANSPLANTATION IS PREDICTIVE OF GRAFT FAILURE

Stephen Spellman, Robert Bray, Sandra Rosen-Bronson, Michael Haagenson, John Klein, Susan Flesch, Cynthia Vierra-Green, and Claudio Anasetti

Background

- Alloantibodies directed against mismatched HLA antigens are well established as a significant risk factor in solid organ transplantation (renal, cardiac and pancreas).

- Previous studies in humans and recent animal studies have indicated a role for donor-specific HLA antibodies (DSA) as a risk factor for rejection of hematopoietic stem cell transplants.
Study Design

- Retrospective, case-controlled study of recipients who received an unrelated stem cell transplant (SCTx) facilitated through the NMDP

- The study group was selected based on:
  - Preferred mismatched HCT (antigen or allele)
  - Survival past day 28
  - No sustained engraftment
  - Serum samples available in repository

- A total of 37 patients and 78 case-matched controls (2-3 to 1) were tested
Study Design

- Controls were matched for disease, disease status, graft type, age, sex and year of transplant (1990-2002)
- Diseases included AML, CML, ALL, and MDS
- 98% Myeloablative Conditioning
  97% Bone Marrow Stem cells
  97% Calcineurin-Based GvHD Prophylaxis
  100% T-Replete Grafts
Lack of Association Between the Presence of HLA Antibody and Graft Failure

<table>
<thead>
<tr>
<th>HLA Antibody (Class I and/or II)</th>
<th>Failed Engraftment</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>YES</td>
<td>YES</td>
<td>16  (43%)</td>
</tr>
<tr>
<td></td>
<td>NO</td>
<td>25  (32%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>21  (57%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>53  (68%)</td>
</tr>
</tbody>
</table>

N = 37
N = 78
Positive Association Between the Presence of DSA and Graft Failure

Donor Specific HLA Antibody (Class I or II)

<table>
<thead>
<tr>
<th></th>
<th>Failed Engraftment</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>YES</td>
<td>NO</td>
<td></td>
</tr>
<tr>
<td>YES</td>
<td>9 (24%)</td>
<td>1 (1%)</td>
<td>N = 10</td>
</tr>
<tr>
<td>NO</td>
<td>28 (76%)</td>
<td>77 (99%)</td>
<td>N = 105</td>
</tr>
</tbody>
</table>

N = 37            N = 78

*p = 0.0002*
Study Conclusions

- Approximately 35% of patients receiving unrelated stem cell transplants possess HLA antibodies.
- The presence of donor-specific HLA antibodies against HLA-A, B and/or DP as determined by solid-phase testing, associates with graft failure.
- HLA antibody evaluations should be a part of the routine workup for unrelated stem cell transplantation.
Questions to Answer

• Which loci should be evaluated for HLA matching?
• How do antigen mismatches compare to allele mismatches?
• Are some loci more important than others?
• Is bone marrow the same as PBSC?
• What about HLA-DP?
• What about anti-HLA antibodies?
• What about cord blood unit transplants?
• Anything about KIR?
Fewer cord data available

- Better HLA matching + higher cell dose are significant in UCB outcomes
  - > 1,000 recipients

UCB and mismatch location data

- **C antigen** mismatch associated with higher mortality
- If 2 locus mismatches among the 4 major HLA loci, **C/DRB1** combo had highest mortality

Transplant-related Mortality

Treatment-related Mortality

Overall Survival
- Mismatch at HLA-C + HLA A or DRB1 -

Double Cord Blood Unit Transplant

• Some centers use two unit to increase cell dose

• No studies evaluate cord to cord matching
  – Currently, no standard practice
    • Some protocols match ≥ 3/6 cord to cord
    • Others require ≥ 4/6
Non-Inherited Maternal Antigens (NIMA)

<table>
<thead>
<tr>
<th></th>
<th>HLA-A</th>
<th>HLA-B</th>
<th>HLA-DRB1</th>
</tr>
</thead>
<tbody>
<tr>
<td>NIMA matched *</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>UCB unit/donor</td>
<td>A*02, 32</td>
<td>B*18, 35</td>
<td>DRB1*01:01, 11:04</td>
</tr>
<tr>
<td>UCB donor mother</td>
<td>A*24, 32</td>
<td>B*07, 35</td>
<td>DRB1*01:01, 13:01</td>
</tr>
<tr>
<td>Recipient</td>
<td>A*02, 24</td>
<td>B*18, 35</td>
<td>DRB1*01:01, 11:04</td>
</tr>
</tbody>
</table>

* HLA-A*24 is not carried by UCB donor. HLA-A*24 is carried by the UCB donor’s mother and the recipient; thus, this is an NIMA-matched UCBT


**NIMA mismatch**

<table>
<thead>
<tr>
<th></th>
<th>HLA-A</th>
<th>HLA-B</th>
<th>HLA-DRB1</th>
</tr>
</thead>
<tbody>
<tr>
<td>NIMA matched *</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>UCB unit/donor</td>
<td>A*02, 32</td>
<td>B*18, 35</td>
<td>DRB1*01:01, 11:04</td>
</tr>
<tr>
<td>UCB donor mother</td>
<td>A*24, 32</td>
<td>B*07, 35</td>
<td>DRB1*01:01, 13:01</td>
</tr>
<tr>
<td>Recipient</td>
<td>A*01, 02</td>
<td>B*18, 35</td>
<td>DRB1*01:01, 11:04</td>
</tr>
</tbody>
</table>

* HLA-A*01 is not carried by UCB donor or the UCB donor’s mother; thus, this is an NIMA-mismatched UCBT.
NIMA Matching Survival Data

Why not insist on UCB NIMA matching?

- NIMA matches relatively rare
- In the Rocha and van Rood studies, only 7-10% of transplants were NIMA matched
- Relative frequency of the mismatched antigen(s) will strongly influence the ability to find a NIMA match
- Searching for NIMA match may delay transplant
Questions to Answer

• Which loci should be evaluated for HLA matching?
• How do antigen mismatches compare to allele mismatches?
• Are some loci more important than others?
• Is bone marrow the same as PBSC?
• What about HLA-DP?
• What about anti-HLA antibodies?
• What about cord blood unit transplants?
• Anything about KIR?
KIR – Insufficient Data

• KIR (natural killer cell immunoglobulin-like receptors) and KIR Ligands
  – Early studies showed survival advantage for AML
  – Subsequent studies, varied conclusions

• No current data to unequivocally indicate that class I mismatching in unrelated donor HCT should be preferred in any clinical circumstance
  – Donor selection based on KIR should only be considered within the context of a clinical trial
Recent Update to Matching Guidelines

A perspective on the selection of unrelated donors and cord blood units for transplantation

Stephen R. Spellman, Mary Eapen, Brent R. Logan, Carlheinz Mueller, Pablo Rubinstein, Michelle L. Setterholm, Ann E. Woolfrey, Mary M. Horowitz, Dennis L. Confer and Carolyn K. Hurley

Recap: Graft source selection chart

Unrelated Donor Search

8/8 A, B, C, DRB1 Matched Donor

No 8/8 donor

≥4/6 Cord Adequate cell dose
  Consider:
  HLA antibodies
  HLA-C
  NIMA

7/8 Donor
  Consider:
  HLA antibodies
  # mismatched secondary HLA loci
  (-DQB1, DRB3/4/5, DP)
Recap: Optimal donor matching, 8/8

- High likelihood of an 8/8 donor
  - Consider DQ, DP, and DRB3/4/5

- Consider nature of DPB1 mismatches
  - Favor DPB1 match or permissive mismatch
Recap: Optimal donor matching, 7/8

- **Marrow**
  - B or C mismatches *may* be less detrimental than A or DRB1
  - Favor donors with the lowest cumulative number of DP, DQ, and DRB3/4/5 mismatches when other matching criteria equal

- **PBSC**
  - Avoid C antigen mismatch when possible
  - Allele mismatch *may* be better tolerated than antigen mismatch
Recap: Optimal cord selection

- Favor extended HLA matching and higher cell dose
- C antigen mismatch associated with higher TRM
- C/DRB1, likely most detrimental pair of mismatches
- Can increase cell dose with double cords
- May consider NIMA matching as a tiebreaker among similarly mismatched units if no transplant delay
HLA expert advice

- Local or NMDP HLA expert
- search-strategies@nmdp.org
  - HLA search strategy team provides commentary and donor/cord recommendations for NMDP searches
  - Focus on donors/cords most likely to match
  - Guide you to optimal CT selections with efficient typing strategies
Acknowledgments

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Thank you for participating

- You may continue to listen to this recording to hear the question and answer session from our live event.
Q & A

- Thanks for your attention
- Questions?