Overview of Stem Cell Transplant

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Blood Matters

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Disclosures

• Financial disclosures
  – None
• Advisory Boards
  – Novartis

Objective
Provide an overview of Bone Marrow Transplantation
Principles of SCT

• Allows the administration of high-dose therapy

• Takes advantage of graft-versus-leukemia effect
Principles of SCT

- Source of stem cells
  - Autologous
  - Allogeneic
    - HLA-matched sibling
    - Matched, unrelated donor
    - Umbilical cord blood
  - Cells
    - Bone marrow
    - Peripheral blood
Bone marrow

- 750-1500mL harvested from posterior iliac crests
  - general anesthesia
  - generally well tolerated

- NMDP
  - 6 deaths from normal donors
  - 1/10,000 risk
Peripheral Blood

- CD34+ cells circulate in the peripheral blood
  - Increase following administration of chemotherapy and/or growth factors

- NMDP
  - 3 deaths amongst PB donors
Indications for SCT

• Hematologic malignancies

• Other
  – Solid tumors
  – Immunodeficiencies
  – Autoimmune diseases
  – Hemoglobinopathies
<table>
<thead>
<tr>
<th>Condition</th>
<th>Type</th>
</tr>
</thead>
<tbody>
<tr>
<td>AML</td>
<td>Allogeneic</td>
</tr>
<tr>
<td>ALL</td>
<td>Allogeneic</td>
</tr>
<tr>
<td>CML</td>
<td>Allogeneic</td>
</tr>
<tr>
<td>MDS</td>
<td>Allogeneic</td>
</tr>
<tr>
<td>Aggressive lymphoma</td>
<td>Usually autologous</td>
</tr>
<tr>
<td>Hodgkin lymphoma</td>
<td>Usually autologous</td>
</tr>
<tr>
<td>Indolent lymphoma</td>
<td>Autologous/Allogeneic</td>
</tr>
<tr>
<td>CLL</td>
<td>Allogeneic</td>
</tr>
<tr>
<td>Myeloma</td>
<td>Autologous</td>
</tr>
<tr>
<td>Aplastic anemia</td>
<td>Allogeneic</td>
</tr>
</tbody>
</table>
Indications for Transplant

Indications for hematopoietic stem cell transplant in North America 2008

- Multiple Myeloma
- NHL
- AML
- HD
- ALL
- MDS/MPD
- Aplastic Anemia
- CML
- Other Leuk
- Other Cancer
- Non-Malignant Disease

Allogeneic (Total N=6,672)
Autologous (Total N=10,302)
Indications for Transplant

Indications for allogeneic hematopoietic stem cell transplantation in North America 2008

- Related Donor (Total N=3,282)
- Unrelated Donor (Total N=3,389)

- AML
- ALL
- MDS/MPD
- NHL
- Aplastic Anemia
- CML
- Non-Malignant Disease
- Leuk
- Other
- Cancer
What type of transplant?

<table>
<thead>
<tr>
<th>Type of transplant</th>
<th>Risk of TRM</th>
</tr>
</thead>
<tbody>
<tr>
<td>Autologous</td>
<td>5-10%</td>
</tr>
<tr>
<td>Sibling allogeneic</td>
<td>20%</td>
</tr>
<tr>
<td>MUD</td>
<td>30-40%</td>
</tr>
<tr>
<td>Non-myeloablative</td>
<td>5-10%</td>
</tr>
</tbody>
</table>
Transplant Complications

• Acute complications
  – Infections
  – Acute graft-versus-host disease
  – VOD
Timing of Likely Infections Among Allogeneic Stem Cell/Bone Marrow Recipients Receiving Antimicrobial Prophylaxis

**Viral**
- Herpes simplex
- Respiratory viruses
- Cytomegalovirus
- Human herpesvirus 6, 7
- Varicella zoster virus
- Epstein Barr virus
- BK/JC viruses

**Bacterial**
- Gram positives
- Gram negatives
- Encapsulated bacteria

**Fungal**
- Candida spp.
- Aspergillus spp.

**Parasitic**
- Toxoplasma gondii
- Pneumocystis carinii

**Risk factors**
- Acute graft-versus-host disease (GVHD) and therapy for this condition
- Chronic GVHD and therapy for this condition
- Mucocutaneous damage (GVHD)
- Cellular and humoral immune dysfunction
- Hypoplenism, decrease in opsonization
- Decrease in reticuloendothelial function

**Pre-engraftment**
- Mucositis
- Organ dysfunction
- Neutropenia
- Other immune defects

**Immediate post-engraftment**
- Acute graft-versus-host disease (GVHD) and therapy for this condition
- Mucocutaneous damage (GVHD)
- Cellular immune dysfunction
- Immunomodulating viruses

**Late post-engraftment**
- Chronic GVHD and therapy for this condition
- Mucocutaneous damage (GVHD)
- Cellular and humoral immune dysfunction
- Hypoplenism, decrease in opsonization
- Decrease in reticuloendothelial function

* Respiratory viruses are very common; morbidity associated with these infections is not fully defined.
△ Early incidence decreased with preemptive therapy; late CMV infections occur in patients with deficient CMV-specific T-cell immunity.
† Pseudomonas aeruginosa accounts for <1 percent of infections; pneumonia associated with GVHD occurs at a median time of 10 months post transplantation.
○ Incidence of Aspergillus depends upon the presence of acute GVHD and prednisone dose (associated with doses ≥1mg/kg per day).
Acute GVHD

- Clinical manifestations
  - Rash
  - Diarrhea
  - Hepatic dysfunction
VOD

- Clinical features
  - sudden weight gain
  - hepatomegaly (tender)
  - jaundice
  - peripheral edema and ascites
Long-term Complications

- Toxicities from treatment regimens
- Immune deficiency
- Autoimmune syndromes
- Infectious complications
- Endocrine disturbances
- Chronic GVHD
- Second malignancies
- Cognitive dysfunction
- Psychosocial adjustment
- Decreased quality of life
Causes of Death

Causes of death after transplantations done in 2003-2008

- Primary Disease (43%)
- IPn* (3%)
- Infection (14%)
- Organ Failure (8%)
- Other (22%)

Autoimmune

- Primary Disease (43%)
- IPn* (3%)
- Infection (14%)
- Organ Failure (8%)
- Other (22%)

Unrelated donor

- Primary Disease (35%)
- IPn* (5%)
- Infection (17%)
- Other Cause (19%)
- Organ Failure (12%)

Infection (14%)

Other Cause (22%)

*IPn = idiopathic pneumonia syndrome
Donor Selection

- HLA match
- Age
- Sex
- CMV status
- ABO group
Questions?