AUTOLOGOUS TRANSPLANTATION IN MULTIPLE MYELOMA

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BACKGROUND OF MULTIPLE MYELOMA

- Accounts for 1% of all cancers, and 10% of hematological malignancies

- The American Cancer Society estimates for 2017:
  - 30,280 new cases (17,490 men and 12,790 women)
  - 12,590 expected deaths (6,660 men and 5,930 women)

- Median age 66 years

- Occurs in all races;
  - African-American more than Caucasian
HISTORY OF MYELOMA THERAPY

- Oral Melphalan & Prednisone
- High dose Melphalan
- ABMT
- VAD
- High dose Dexamethasone
- HDT/ASCT
- Thalidomide
- PI IMiDS Immunotherapy

ALL THESE HAVE IMPROVED SURVIVAL TO ~8-10 YEARS
HIGH DOSE THERAPY AND STEM CELL RESCUE - CONCEPTS
An Auto Transplant is Like Lawn Care

Weeds = malignancy

Weed killer = chemotherapy

MELPHALAN

Courtesy: Dr. Fenske
Ablated Marrow

Seeds = Stem Cells
Waiting for count recovery
Days 1-8

Initial count recovery
Days 10-30
Lawn restored, and no weeds
Indications for Hematopoietic Cell Transplant in the US, 2014

- **Allogeneic (Total N=8,211)**
- **Autologous (Total N=12,831)**

<table>
<thead>
<tr>
<th>Condition</th>
<th>Number of Transplants</th>
</tr>
</thead>
<tbody>
<tr>
<td>Myeloma / PCD</td>
<td>8000</td>
</tr>
<tr>
<td>NHL</td>
<td>7000</td>
</tr>
<tr>
<td>AML</td>
<td>4000</td>
</tr>
<tr>
<td>HD</td>
<td>3000</td>
</tr>
<tr>
<td>ALL</td>
<td>3000</td>
</tr>
<tr>
<td>MDS / MPN</td>
<td>3000</td>
</tr>
<tr>
<td>CLL</td>
<td>2000</td>
</tr>
<tr>
<td>Other Cancer</td>
<td>1000</td>
</tr>
<tr>
<td>CML</td>
<td>1000</td>
</tr>
<tr>
<td>Aplastic Anemia</td>
<td>1000</td>
</tr>
<tr>
<td>Other Non-Malign Dis</td>
<td>1000</td>
</tr>
</tbody>
</table>
Selected Disease Trends for Autologous HCT in the US

![Graph showing the number of transplants for Myeloma / PCD and NHL / HL from 2000 to 2015.](image)

**Number of Transplants**


**Legend:**
- Blue line: Myeloma / PCD
- Orange line: NHL / HL
THE ROLE OF AUTO TRANSPLANT IN MYELOMA
### BEFORE NOVEL AGENTS:

<table>
<thead>
<tr>
<th>Study</th>
<th>HDT regimen</th>
<th>EFS/PFS CC vs. HDT</th>
<th>OS CC vs. HDT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Attal</td>
<td>Mel 140 mg/m² + TBI 8 Gy</td>
<td>Median EFS 18 vs. 27</td>
<td>5-year OS 12 vs. 52%</td>
</tr>
<tr>
<td>Child</td>
<td>Mel 200 mg/m² (Mel140 mg/m² + TBI allowed)</td>
<td>Median PFS 19.6 vs. 31.6</td>
<td>Median OS 42.3 vs. 52.1</td>
</tr>
<tr>
<td>Barlogie</td>
<td>Mel 140 mg/m² + TBI 12Gy</td>
<td>7-year PFS 14 vs. 17%</td>
<td>7-year OS 38%</td>
</tr>
<tr>
<td>Blade</td>
<td>Mel 200 mg/m² (Mel140 mg/m² + TBI allowed)</td>
<td>Median PFS 33 vs. 42</td>
<td>Median OS 66 vs. 61</td>
</tr>
<tr>
<td>Fermand</td>
<td>Mel 200 mg/m² or Mel140 mg/m²+ busulfan16 mg/kg</td>
<td>Median EFS 19 vs. 29</td>
<td>Median OS 47.6 vs. 47.8</td>
</tr>
</tbody>
</table>
## AFTER NOVEL AGENTS

<table>
<thead>
<tr>
<th>Study</th>
<th>HDT regimen</th>
<th>PFS SDT vs. HDT</th>
<th>OS SDT vs. HDT</th>
</tr>
</thead>
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<tr>
<td>Palumbo</td>
<td>Melphalan 200 x 2</td>
<td>22 vs. 43 months</td>
<td>65% vs. 83 % (4 yr. OS)</td>
</tr>
<tr>
<td>Gay</td>
<td>Melphalan 200 x 2</td>
<td>29 vs. 43 months</td>
<td>68% vs. 77% (4 yr. OS)</td>
</tr>
<tr>
<td>Attal</td>
<td>Melphalan 200</td>
<td>36 vs. 50 months</td>
<td>82% vs. 81% (4 yr. OS)</td>
</tr>
<tr>
<td>Cavo</td>
<td>Melphalan 100 or 200</td>
<td>57% vs. 65% (3 yr. PFS)</td>
<td>Not reported</td>
</tr>
</tbody>
</table>
EFFECT ON QUALITY OF LIFE?

Longer time without symptoms, treatment, and treatment toxicity (TwiSTT)

27.8 months for early HDT vs. 22.3 months for salvage HDT

There is no QOL data available in current era
CANDIDATE FOR AN AUTOLOGOUS STEM CELL TRANSPLANT

- Patient selection is the key!
- Age is not a limitation anymore (up to 80 years old!)
- No prohibitive comorbidities:
  - Organ function and infectious disease testing is evaluated prior to transplant
- Adequate **stem cell collection** (minimum 2 million CD34 cells/kg)
- No active infection and adequate performance status
- Transplant related mortality ~1-3% range (much lower at our center!)
STEM CELL MOBILIZATION AND HARVESTING

Mobilization: Movement of stem cells from the bone marrow into the peripheral blood

   Role of Neupogen and other agents

Stem Cell Harvesting

   Apheresis
   Venous access

Cryopreserving the Product

   DMSO
   Liquid nitrogen storage
STEM CELL TRANSPLANT

- Melphalan
  - Infusion
  - Side Effects
  - Cryotherapy
- Stem Cell Infusion
  - Timing of the infusion
  - Side effects
- Line Access
**TRANSPLANT HOSPITAL STAY**

- **Approximately 2 Weeks Stay**
  - HEPA air filtration
  - Activity/ Exercise
  - Nutrition

- **Visitors**
  - Risk of Infection
  - Children
  - Overnight stays

- **Items to Bring**
  - Comfortable clothes
  - Laptops/ iPad
  - Personal items

- **Items not to bring**
  - Medications from home
  - The kitchen sink
OUTPATIENT TRANSPLANTS

- Who is eligible
- Daily visits
- Average time 12-14 days
- Complications
- Possibility of Admission
- Care givers
- Staying within 45 minutes of the hospital
HOME PREPARATION

- Cleaning the House
  - Vacuuming/air filters
  - Bathrooms
  - Laundry
- Children
- Visitors
- Pets
  - Dogs and cats vs. Farm and cage animals
- Plants
  - Digging in dirt
  - House plant
- Outside Activity
  - Hunting/Fishing
  - Exposure to sun
POST TRANSPLANT CARE

- Care Giver
- Follow up Appointments
- Returning Home
- Returning to Your Primary Oncologist
- Food Safety
- Returning Back to The “Real World”
- Vaccinations
COMPLICATIONS:

Immediate Complications:
- Fever, chills, hives
- DMSO reactions (esp if unwashed)
- flushing/rash, n/v, chest tightness, wheezing, cough, HTN, garlic odor on breath

Early (prior to engraftment)
- Mucositis, bacterial infections

During Engraftment
- Auto GVHD (engraftment syndrome)

Later (after day 30)
- Delayed engraftment
- Infections (PJP, zoster)
- Idiopathic pneumonia syndrome
- Fatigue, depression, not returning to work

Very Late (> 1 yr. later)
- Secondary malignancies (MDS)
- Hypogammaglobulinemia
Causes of Death after Autologous HCT done in 2013-2014

- Primary Disease: 69%
- Infection: 24%
- Organ Failure: 2%
- Second Malignancy: 2%
- Other: 3%
CONCLUSION:

- Auto-transplant remains the preferred therapy for eligible patients.
- It is associated with significant **PFS** benefit.
- May be associated with **OS** benefit as well (?with longer follow up)
- It is associated with **deeper remissions** including the MRD negativity
- Toxicities and the death associated with procedure are very minimal
- May be associated with improved quality of life
QUESTIONS
THANK YOU!