Stem cell transplantation for lymphoma

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- Verastem
- Seattle Genetics
- Merck
Presentation Outline

• Basics of bone marrow transplantation
• HCT utilization trends in ‘blood cancer’
• Role of BMT in follicular lymphoma & DLBCL
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• Role of BMT in follicular lymphoma & DLBCL
• New donor options in FL & DLBCL
Bone Marrow Transplantation (BMT): Confusing Terminology

- Autologous vs. Allogeneic transplantation
- Stem cell transplant vs. blood transplant vs. bone marrow transplant
- Sibling vs. Unrelated donor vs. Cord blood transplant vs. half matched family members
What is Bone Marrow?

Soft tissue inside the bones that produces all blood cells
Autologous Transplantation – No Donor Required

Auto (Greek autós) = Self
Effects of Increasing Chemotherapy Dose

High doses can cure Lymphomas

Lethal for Bone Marrow

Drug Concentration in Log scale

Response

High doses can cure Lymphomas
Autologous Transplantation – Basic Process

- SC Mobilizing Drugs
- "Freezing" Stem Cells
- "Thawing" Stem Cells
- Stem Cell Collection
Autologous Transplant: Advantages

• No need to find a donor

• Relatively low cost

• Low transplant mortality (~2-3%)

• Feasible in older patients

• Cure for some lymphomas (more on that later)
Allogeneic (Donor) Transplantation – Donor Required

Healthy Donor

Blood forming “Stem” Cells

Patient

Immune cells from Donor

Damage patient’s organs (Bad thing)

Eliminate Cancer (Good thing)
Allogeneic Transplant: Who can be a donor?

• A “matched” sibling (brother or sister)
Allogeneic Transplant: Who can be a donor?

- A “matched” sibling (brother or sister)
Allogeneic Transplant: Who can be a donor?

- A “matched” sibling (brothers or sisters)

- Adult matched, volunteer donor
## US Ethnic Minorities and Probabilities of Finding a Matched Donor

<table>
<thead>
<tr>
<th></th>
<th>Likelihood of Identifying an Unrelated Donor (%)</th>
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<tbody>
<tr>
<td></td>
<td>8/8 HLA match</td>
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<tr>
<td>White European</td>
<td>75</td>
</tr>
<tr>
<td>African-Americans</td>
<td>16</td>
</tr>
<tr>
<td>Chinese</td>
<td>41</td>
</tr>
<tr>
<td>Hispanics</td>
<td>34</td>
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</tbody>
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Alternative Donor Options in Lymphoma?

Matched Sibling or URD Available?

NO

Umbilical Cord Blood

≤7/8 Unrelated Donor

Haploidentical Related Donor

Half Matched Sibling
Allogeneic Transplant: Limitations

• Requires a donor

• Patients need anti-rejection medications

• Higher transplant mortality (~10-20%)

• Morbidity (infections and graft-vs-host disease)
Things to consider before: A Multidisciplinary Approach

- Selecting a Transplant Center
- Financial Considerations
- Caregiver Support
- Steep Learning Curve

Considerations before Transplant

- Lymphoma in remission?
- Autologous vs Allogeneic?
- Medical Fitness
- Compliance Assessment
- Medical Factors

- Patients
- Family
- Physician
- PA/NP
- Nurses
- Social Workers
- Pharmacists
- BMT-Psych
- Financial

CIBMTR
CENTER FOR INTERNATIONAL BLOOD & MARROW TRANSPLANT RESEARCH
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Annual Number of Transplant Recipients in the US by Transplant Type (All Indications)
Trends in Allogeneic Transplants by Recipient Age

Transplants, %

- <60 years
- ≥60 years

1993-1999: <60 years dominates
2000-2006: Transition period
2007-2013: ≥60 years increase

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Non-Hodgkin and Hodgkin Lymphoma Patients Undergoing Matched Donor AlloHCT from 2000-2013

- Matched Sibling
- Matched Unrelated
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Role of Transplant in Specific Lymphomas

Indolent Lymphoma

Follicular Lymphoma

Transplant and Lymphoma

Aggressive Lymphoma

Diffuse Large B-cell Lymphoma

In RELAPSED patients

Autologous vs Allogeneic vs No transplant

Autologous HCT in patients relapsing after Frist Line Treatment (e.g. R CHOP)

Early Autologous HCT (e.g. without R CHOP failure)

Allogeneic HCT
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**Allogeneic HCT**
Autologous HCT for relapsed DLBCL

PARMA Study

In *relapsed* DLBCL, responding to salvage chemotherapy, autologous HCT remains **Standard-of-Care**

Philip T, et al. NEJM 1995;333:1540-1545
AutoHCT after early R-CHOP failure?

CORAL Trial

Relapse \( \leq 12\) months after diagnosis

Relapse >12 months after diagnosis

Role of Transplant in Specific Lymphomas

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Transplant and Lymphoma

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Transplant and Lymphoma

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In RELAPSED patients
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Autologous HCT in patients relapsing after First Line Treatment (e.g. R CHOP)

Early Autologous HCT (e.g. without R CHOP failure)

Allogeneic HCT
Upfront AutoHCT for DLBCL

- New DLBCL
- Intermed-high or
- High IPI

Randomize

R-CHOP14 x8

Intention-to-treat results

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Allogeneic HCT for DLBCL

CIBMTR DATA

Patients Responding to treatment

Probability, %

Years


Patients NOT responding to treatment

Probability, %

Years

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- Transplant and Lymphoma

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**Autologous HCT in patients** **relapsing** after First Line Treatment (e.g. R CHOP)

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**Allogeneic HCT**
Auto-HCT for Relapsed FL – CUP Trial

- Relapsed FL
- Age 18-65 yrs
  (N=140 patients)

Randomization

Chemotherapy x3 (n=24)

Purged-Autograft (n=32)

Unpurged-Autograft (n=33)

PFS: Chemo vs. Auto
26% vs. ~55%

OS: Chemo vs. Auto
46% vs. ~71%

Auto-HCT for Relapsed FL – CUP Trial

- Conducted before rituximab was available
- Small number of patients
- Study questioned benefit of ‘purging’
Is Auto-HCT Curative for Relapsed FL?

FL: Autologous vs. Allogeneic BMT? Million $ Question

Autologous BMT:
- Low risk
- Disease control
- Second cancers
- Higher relapse

Allogeneic BMT:
- Relapse risk low
- Disease control
- Higher risk
- GVHD & QOL
Conclusions

• In chemotherapy-responsive DLBCL autologous HCT curative role remains cemented

• Autologous HCT is an underutilized option for follicular lymphoma

• Allogeneic HCT remains an integral therapeutic option for advanced lymphomas