Long-Term Effects of a Transplant Using Your Own Stem Cells (Autologous Transplant)

Celebrating a Second Chance at Life Survivorship Symposium
April 29 – May 5, 2023

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Learning Objectives

• Brief review of autologous stem cell transplantation.

• Discuss major healthcare and health maintenance issues after autologous stem cell transplant.
Who are autologous stem cell transplant patients?

Number of HCTs in the US Reported to CIBMTR by Transplant Type

- Allogeneic HCT
- Autologous HCT

Who are autologous stem cell transplant patients?

Number of HCTs by Indications in the US, 2020

Abbreviations:
- MM: Multiple myeloma
- PCs: Plasma cell disorders
- AML: Acute myeloid leukemia
- MDS: Myelodysplastic syndromes
- MPN: Myeloproliferative neoplasms
- ALL: Acute lymphoblastic leukemia
- HL: Hodgkin lymphoma
- Aplastic anemia
- CML: Chronic myeloid leukemia
- Other malignancy
- Non-malignant disease

*excludes Aplastic anemia
Who are autologous stem cell transplant patients?

Relative Proportion of Autologous HCTs for Malignant Diseases* in the US by Recipient Age

Number of Autologous HCTs in the US by Selected Disease
What happens during an autologous stem cell transplant?

- High-dose chemotherapy
  - Multiple myeloma: melphalan
  - Lymphoma: BEAM, BCV, Busulfan + cyclophosphamide, TBI

- Re-infusion of your own stem cells

<table>
<thead>
<tr>
<th>BCNU (carmustine)</th>
<th>Etoposide</th>
<th>Ara-C (cytarabine)</th>
<th>Melphalan</th>
</tr>
</thead>
<tbody>
<tr>
<td>BCNU (carmustine)</td>
<td>Cyclophosphamide</td>
<td>VP-15 (Etoposide)</td>
<td>Total body irradiation</td>
</tr>
</tbody>
</table>

Autologous Transplants are different than Allogeneic (donor) Transplants

- Less transplant-related complications
  - No GVHD
  - No immunosuppressive meds

- More disease-related effects
  - For myeloma, maintenance therapy and expected disease progression and additional therapy.

- Increases in risk of normal health problems
  - Cardiovascular/lung disease (prior therapies + transplant)
  - Impaired “immune health” (infections and autoimmune disease).
  - Second cancers and reproductive/sexual health
Recovering from Autologous Stem Cell Transplant

• Early phase (first few months)
  o Recover blood counts
  o Food/fluid intake
  o Watch for “autologous GVHD”
  o Watch for infections
  o Gradually improving energy

• Late phase (months-years)
  o Continued physical recovery
  o Re-vaccination
  o Resume normal health maintenance routines

Most Patients are Expected to “Return to Normal”
Patient-reported quality of life (myeloma)

<table>
<thead>
<tr>
<th>Patients, N</th>
<th>Baseline</th>
<th>Cycle 2</th>
<th>Pre-mobilization</th>
<th>RVd cycle 5 / post-ASCT</th>
<th>RVd cycle 6 / RVd cycle 5</th>
<th>Maintenance</th>
<th>2 years</th>
<th>3 years</th>
</tr>
</thead>
<tbody>
<tr>
<td>p-value</td>
<td>0.108</td>
<td>0.441</td>
<td>&lt;0.0001</td>
<td>0.021</td>
<td>0.413</td>
<td>0.455</td>
<td>0.105</td>
<td></td>
</tr>
</tbody>
</table>

Richardson et al., N Engl J Med 2022; 387:132-147
Effects of Maintenance Therapy for Myeloma

• Lenalidomide (Revlimid) is the most commonly used drug
• Side effects include diarrhea, fatigue, and decreased cognition


Decrease in quality of life (Q)OL with disease progression

Commonly Reported Medical Problems
Late after Autologous Transplant

- Survey of 389 myeloma/lymphoma patients ≥5 years post transplant
- Problems reported with >10% incidence:
  - Sexual dysfunction
  - Shingles
  - Cataracts
  - Osteoporosis/osteopenia
  - Joint replacement
  - Skin cancer

Late pulmonary complications

- Idiopathic pulmonary syndrome: ~day 60, rare (<5%), treated with steroids
- Lung inflammation caused by chemotherapy (BCNU/carmustine):
  - Up to 20% of patients
  - Usually within 3 months of transplant
  - Risk factors: prior chest radiation, higher BCNU dose, prior bleomycin, younger age
  - Treated with steroids
  - Vast majority of patients recover
Cardiovascular complications

- Attributed to heart/lung radiation and/or doxorubicin (a.k.a. adriamycin) chemotherapy, which is part of lymphoma treatment (CHOP, EPOCH, ABVD).
- Increased long-term risk of congestive heart failure
  - NHL: ~200 extra cases of heart failure than would be expected per 1,000 patients over 10 years.
  - HL: ~twice the number of cardiovascular complications compared to controls.

Moser et al., Blood 2006, 107(7): 2912-2919
Bhakta et al., Lancet Oncology 2016, 17(9): 1325-34

Immune Health

- Difficult to study/uncertainties:
  - effects of disease/therapy vs effects of transplant
- Large study in lymphoma survivors:
  - Lifelong increased risk of infection and autoimmune disease
  - Not much difference in risk between patients who did and did not receive a transplant

Shree et al., Journal of Clinical Oncology 38, no. 15 (May 20, 2020) 1664-1675.
Managing Infection Risk

• Early phase:
  o Preventative antibiotics
  o Early treatment of fever

• Late phase:
  o Vaccination
  o For some patients, antibody replacement therapy - (intravenous immune globulin, or IVIG)

Vaccination after Transplant

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>Recommended for use after HCT</th>
<th>Time post-HCT to initiate vaccine</th>
<th>No. of doses *</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pneumococcal conjugate (PCV)</td>
<td>Yes</td>
<td>3-6 months</td>
<td>3-4 b</td>
</tr>
<tr>
<td>Tetanus, diphtheria, acellular pertussis</td>
<td>Yes</td>
<td>6-12 months</td>
<td>5 d</td>
</tr>
<tr>
<td>Haemophilus influenzae conjugate</td>
<td>Yes</td>
<td>6-12 months</td>
<td>3</td>
</tr>
<tr>
<td>Meningococcal conjugate</td>
<td>Follow country recommendations for general population</td>
<td>6-12 months</td>
<td>1</td>
</tr>
<tr>
<td>Inactivated polio</td>
<td>Yes</td>
<td>6-12 months</td>
<td>3</td>
</tr>
<tr>
<td>Recombinant hepatitis B</td>
<td>Follow country recommendations for general population</td>
<td>6-12 months</td>
<td>3</td>
</tr>
<tr>
<td>Inactivated influenza</td>
<td>Yearly</td>
<td>4-6 months</td>
<td>1-2 a</td>
</tr>
<tr>
<td>Measles-mumps-rubella (live) a</td>
<td>Measles: All children and seronegative adults</td>
<td>24 months</td>
<td>1-2 b</td>
</tr>
</tbody>
</table>

• Additional recommendations:
  o Shingrix x 2 doses
  o Repeat COVID19 mRNA vaccine series + boosters (4 total doses)
Risks of Other Cancers

• Difficult to study/uncertainties:
  o effects of prior cancer/therapy vs effects of transplant vs maintenance therapy

• Follow normal cancer screening guidelines for your age:
  o Mammograms (start at age 25 if chest radiation)
  o Pap smears
  o Colon cancer screening
  o Skin exams
  o Oral cancer screening

• Avoid smoking and protect from sunburn

Other problems

• Thyroid gland dysfunction (low thyroid levels)
  • ~10% risk
  • Monitor thyroid levels; thyroid hormone replacement is safe and straightforward

• Peripheral neuropathy
  • Usually related to pre-transplant therapy (e.g., bortezomib or brentuximab)
  • Gabapentin often prescribed; consider duloxetine
Other problems

- Cataracts
  - Exacerbated by steroid use (myeloma therapy)
  - Maintain routine eye exams
- Fatigue
- Depression/anxiety
- Cognitive dysfunction

Routine Healthcare

- Close attention to cardiovascular risk factors
  - Cholesterol
  - Diabetes
  - Exercise and body weight
- Bone health
  - Vitamin D and calcium intake
  - Follow primary care guidelines for DEXA screening + treatment of osteoporosis
  - Treat osteoporosis if diagnosed
Fertility after Autologous Transplant

- Most female patients are post-menopausal after transplant
- Fertility **depends** on age and prior therapy
- Minority of younger female patients recover ovarian function
  - Absence of menses does not mean infertility
  - Seek ob/gyn consultation if you wish to become pregnant
  - There does not appear to be an increased risk to the health of the mother or baby after transplant
- Male fertility is variable

Fertility preservation

- Female
  - Egg harvesting or embryo storage prior to therapy
  - May not be feasible or safe prior to starting chemotherapy
- Male
  - Sperm banking is usually feasible prior to starting chemotherapy
Sexual Health

- Both men and women report less sexual activity after transplant than expected for age.
- Reported reasons for lower activity among sexually active patients were...
  - reduced sexual function:
    - erectile dysfunction for men (38%)
    - vaginal dryness for women (63%)
  - reduced interest (55% of women, 23% of men)

Emerging Effects of Diet on Late Post-Transplant Myeloma Control

Syrjala et al., TCT VOLUME 27, ISSUE 1, P80.E1-80.E12, JANUARY 2021

Shah et al., Leukemia (2023). https://doi.org/10.1038/s41375-023-01874-4
Summary

• Most patients return to prior quality-of-life after autologous SCT
• Patients may have long-term impairments in “immune health.”
• Common health problems include reduced sexual health, low bone density, and infections.
• Important interventions include vaccinations, returning to routine primary care including cancer screenings, and measures to address sexual health.
• Emerging role for plant-based diet to potentially improve long-term myeloma control.

QUESTIONS?

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