Bone Marrow Transplantation for Severe Congenital Neutropenia
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Transplant Definition

• Hematopoietic Stem Cell Transplant (HCT)
  – Infusion of blood “stem cells” into a recipient patient
Donor Source of Hematopoietic Stem Cells

• **Autologous**: Use patient’s own cells
  • Typically given in patients receiving high dose chemotherapy to “rescue” patients from toxic side effects

• **Allogeneic**: Use donor’s cells
  • Used in a variety of diseases (cancer, red cell disorders, bone marrow failure, metabolic disorders, **NEUTROPHIL DISORDERS**, immune deficiencies)
Donor Source of Hematopoietic Cells

- Donor sources include collection of stem cells from:
  - Bone Marrow
  - Peripheral Blood
  - Umbilical Cord

Types of donors include
- Fully matched sibling or other family member (matched related donor)
- Matched or partially matched unrelated donor
  - Includes both living donor and umbilical cords
- Parent (termed haplo-identical donor)
Hematopoietic Cell Transplant Process

Donor

Stem cells + Immune cells
Stem Cell Transplant Process

Recipient

Immune System

Bone Marrow

Neutrophil
Stem Cell Transplant Process

Recipient

Donor

Immune System

Bone Marrow

Neutrophil

Stem cells + Immune System
Stem Cell Transplant Process

Recipient

Donor

Immune System

Bone Marrow

Stem cells + Immune System

Neutrophil
Transplant Requirements: Conditioning

• Eliminates/weakens recipient bone marrow and immune system

• Myeloablative
  – Irradicates marrow and immune system
  – Increased toxicity to the patient

• Reduced Intensity
  – Less organ toxicity and therefore expands the use of transplant to sicker patients
  – Less conditioning therapy can result in increased risk of donor cells not growing in the patient recipient
Stem Cell Transplant Process

Recipient

Immune System

Bone Marrow

Neutrophil
Stem Cell Transplant Process

Recipient

Immune System

Bone Marrow

Conditioning Therapy

Neutrophil
Stem Cell Transplant Process

Recipient

Immune System

Bone Marrow

Neutrophil
Stem Cell Transplant Process

Recipient

Donor

Immune System

Bone Marrow

Stem cells + Immune System

Neutrophil
Stem Cell Transplant Process

Recipient

Immune System

Bone Marrow

Donor

Stem cells + Immune System

Neutrophil
Stem Cell Transplant Process

Recipient

Bone Marrow

Stem cells + Immune System

Fight Infection

Immune System

Prevent Cancer

Attack normal tissue?

Donor

Neutrophil
Finding an immune system match

Donor Immune Cell

Receptor

Recipient Skin Cell
Finding an immune system match

Donor Immune Cell  MATCH  Recipient Skin Cell
Finding an immune system match
Finding an immune system match

- Donor Immune Cell
- Recipient Skin Cell
Finding an immune system match

Donor Immune Cell

Recipient Skin Cell
Finding an immune system match

Donor Immune Cell

Recipient Skin Cell

Graft-versus-host-disease (GVHD)
Finding an immune system match

Immune Suppression

Donor Immune Cell

Recipient Skin Cell
GVHD prevention and treatment

• Patients are started on immune suppression shortly before stem cell infusion
  – Goal is to wean off immune suppression starting around 6 months after cells infused if no evidence of GVHD

• GVHD can occur early (in first couple months) and/or late (several months after transplant)
  – Treatment is additional immune suppression (typically steroid based)
What Determines a Successful SCN Transplant?

• The Availability of a Good Match
SCN Transplant Survival by Donor Type

Fioredda et al. Blood 2015
What Determines a Successful SCN Transplant?

- The Availability of a Good Match
  - Matched > Mismatched
What Determines a Successful SCN Transplant?

• The Availability of a Good Match
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• The Health of the Patient
SCN Transplant Survival by Age of Recipient

Fioredda et al. Blood 2015
What Determines a Successful SCN Transplant?

- The Availability of a Good Match
  - Matched > Mismatched

- The Health of the Patient
  - Healthy Patient > Unhealthy Patient
What Determines a Successful SCN Transplant?

• The Availability of a Good Match
  – Matched > Mismatched

• The Health of the Patient
  – Healthy Patient > Unhealthy Patient

• The presence of MDS or Leukemia
# Transplant Outcomes With and Without MDS/Leukemia

## Summary of Literature

<table>
<thead>
<tr>
<th>Case Reports/Series (^1)</th>
<th>Overall Survival Without MDS/Leukemia</th>
<th>Overall Survival With MDS/Leukemia</th>
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</thead>
<tbody>
<tr>
<td><strong>European Society for Blood and Marrow Transplantation</strong> (^2)</td>
<td>87%</td>
<td>79%</td>
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1. Connelly et al. COH 2013  
What Determines a Successful SCN Transplant?

• The Availability of a Good Match
  – Matched > Mismatched

• The Health of the Patient
  – Healthy Patient > Unhealthy Patient

• The presence of MDS or Leukemia
  – Without MDS/Leukemia > With MDS/Leukemia
  – Outcomes with MDS/Leukemia ARE improving in SCN
    • Avoidance of chemotherapy prior to conditioning therapy has decreased toxicity
What Determines a Successful SCN Transplant?

• The Availability of a Good Match
  – Matched > Mismatched

• The Health of the Patient
  – Healthy Patient > Unhealthy Patient

• The presence of MDS or Leukemia
  – Without MDS/Leukemia > With MDS/Leukemia

• Improved HSCT procedures
Transplant SCN Survival by Era of Transplant

Fioredda et al. Blood 2015
What Determines a Successful SCN Transplant?

• The Availability of a Good Match
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• The Health of the Patient
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• The presence of MDS or Leukemia
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• Improved HSCT procedures
  – Future > Present > Past
What Determines a Successful SCN Transplant?

• The Availability of a Good Match
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• The Health of the Patient
  – Healthy Patient > Unhealthy Patient

• The presence of MDS or Leukemia
  – Without MDS/Leukemia > With MDS/Leukemia

• Improved HSCT procedures
  – Future > Present > Past

• Intensity of Conditioning
  – Myeloablative vs Reduced Intensity

Not Known Yet
Indications for Transplant in SCN

• Absolute Indications
  – No response to GCSF
  – Malignant transformation to AML/MDS

• Indications to consider transplant if a good match is available
  – Poor response to GCSF (high doses with ANC < 2000)
  – Mutation causing SCN associated with poor outcomes
Summary

• Hematopoietic stem cell transplant can cure SCN
• Outcomes are improved with a well matched donor, healthy patient, and absence of MDS or leukemia
• Hematopoietic stem cell transplant is improving, but still a risky procedure
  – Transplant is currently reserved for patients with poor response to G-CSF and/or development of MDS or leukemia