An Introduction to Bone Marrow Transplant
Rushang Patel, MD, PhD, FACP
Florida Hospital Medical Group

Introduction to Blood Cancers

How is SCT/BMT different from other transplants

Difference between ..... solid organ and stem cell transplant

Where does SCT fit in the treatment of blood cancers?
• Almost never done as a first step
• Is not offered instead of chemotherapy
• First, control the cancer with few cycles of chemotherapy
• Then, perform SCT
Types of Stem Cell Transplants

**Autologous**
- Stem cells obtained from the patient
- Stem cells frozen in lab before conditioning chemotherapy
- Rejection is never a problem
- Fast recovery
- For Myeloma and Lymphoma

**Allogeneic**
- Stem cells from a donor
- Donor must ‘match’ (what do we mean by a match?)
- Rejection can occur in both directions ()
- Takes longer for immune system to recover
- For other blood cancers like AML, ALL, MDS, etc.

**Autologous Stem Cell Transplant**
*From ‘auto’ – one’s own*
Allogeneic Stem Cell Transplant

From a DONOR

- ‘Complicated one’
- Trying to treat with a ‘double attack’
  - Chemotherapy
  - Immunotherapy (donor immune system fighting patient cancer)
- Cannot be done successfully without a great team

Compliant Patient + Supportive Caregiver(s) + BMT providers = Great Team

Donor and Source

- Donor
  - Related
  - Unrelated (volunteer, cord blood)
- Source
  - Bone marrow (requires going to the OR)
  - Peripheral blood (collected by apheresis after giving G-CSF e.g. Neupogen®)

SOURCE MATCH DONOR

- Marrow
- Peripheral Blood
- Haplo (5/10)
- Matched (10/10)
- UnMatched (8 or 9/10)

Related
UnRelated
What do we mean when we say that someone is a ‘match’

- Not blood type match
- Match means at HLA loci
- 6 main HLA loci – A, B, C, DP, DQ, DR on each set of chromosome – total 12
- 5 of 6 (total 10) are important
- So:
  - 10/10 = full match
  - 8 or 9/10 = mismatch
  - 5/10 = half match (haplo)

Matched Sibling Donor

The Transplant Journey

- General principles:
  - Do it if benefits >> risk
- Autologous SCT
  - Myeloma – upfront
  - Lymphoma – at relapse OR refractory (exception – MCL)
- Allogeneic SCT
  - Acute leukemia - risk stratify
    - Low risk AML, ALL... at relapse
    - Other AML, ALL... Upfront (after induction)
  - Chronic leukemia – ONLY if refractory OR high risk gene abnormality predictive of aggressive behavior OR blast phase
    - CML – T315I mutation
    - CML – p53 involvement
  - AA/MDS/MF/MPN – high risk categories

Benign hematologic conditions = Solids
Non-hematologic conditions = Brain/CNS SCT, hematologic disorders
The Transplant Journey

Evaluation – Need for transplant? (Disease Risk Stratification)
Evaluation – Transplant candidacy? (pre-transplant testing and donor identification)

1st visit
2w – 2m

Be the match!!

Conditioning Chemotherapy

- Different from the chemotherapy given at time of diagnosis
- Given right before the stem cell transplant
- Purpose is to:
  - Remove any leftover disease
  - ‘Make room’ for the donor cells
  - Suppress host (patient) immune system
- Confusing classification
  - Myeloablative
  - Non-myeloablative
  - Reduced Intensity

Intensity
- Best
- Useful but risky
- Not so useful
- Worst

Toxicity
The Transplant Journey

Evaluation – Need for transplant? (Disease Risk Stratification)
Evaluation – Transplant candidacy? (pre-transplant testing and donor identification)

The Actual Transplant Process
(Conditioning Chemotherapy, Stem Cell Infusion and Engraftment)

Immediate Post-Engraftment Period
(Infusion support, full-dose immunosuppression, Infection control, more frequent visits)

1st visit: 2w–2m
2nd visit: 3–4 wk
3rd/4th visit: First 3 months

Beyond 3 months …

Late Post-Engraftment Period
(Better immune system, Wean off antibiotics, Taper off immunosuppression, Chronic GVHD monitoring, Vaccinations, long-term survivor care, less frequent visits!!)

The Dream Transplant

Good Stuff (Desire it)
- Engraft
- Immune Reconstitution
- Immune Tolerance
- GvT (Tumor Free Survival)

Bad Stuff (Avoid it)
- Graft Failure (TRM)
- Infection (TRM)
- GVHD (TRM)
- Relapse

GVHD vs GVT (the holy grail of transplant)

DONOR body
- GVT (Tumor Free Survival)
- Donor immune system

PATIENT body
- GVHD (TRM)
- Patient immune system

DONOR immune system
- GVT

PATIENT immune system
- GVHD
Variables of the ‘Transplant Equation’

- Indication (hematologic malignancy)
- State of the disease
  - CR
  - MRD / active disease
- Donor
  - Auto
  - Allo
  - related (full, haplo), unrelated (10/10, 9/10, cord blood)
- Source
  - BM – less T-cells
  - PB – more T-cells
- Conditioning regimen
  - MA
  - NMA / RIC
- GVHD prophylaxis
  - what, when, how much
- ID prophylaxis
  - anti-microbials – what, when, how much

How do I answer “What are my chances?”

Complications of Allogeneic SCT

- Rejection
  - Donor stem cells never really ‘take’ in the patient’s body

- Infections
  - Bacterila
  - Fungal
  - Viral

- Graft vs Host Disease (GVHD)
  - Donor cells thrive in patient’s body but reject (‘don’t like being in there’) and fight with patient’s normal cells.
  - Skin
  - Liver
  - GI
  - Lungs
  - Eyes

Hmm ... sounds really complicated! Can it be done safely? YES
What’s new?

- New and widely available:
  - Haplo-identical transplant

- New and experimental:
  - Graft engineering
  - Off the shelf donor cells
  - Stem Cell Expansion
  - Better anti-biotics
  - Antigen-specific T-cells for infection control
  - Better GVHD medications

Donor Availability for Transplantation

- Only 20-25% of patients will have a matched related donor (10/10 allele match) for transplantation

- Probability of finding a matched unrelated donor (MUD) in the world wide registries varies with race/ethnicity of the recipient:
  - 50% Caucasians
  - 30% Hispanics
  - 10% or less for African-Americans or Asians

- The likelihood of finding an unrelated donor - highest within their own race/ethnic group

- Time to transplantation with a MUD donor is up to 2-4 months

Haploidentical Transplantation

- Advantages of using a half matched related donor:
  - Almost universal donor availability: >95% of patients will have a half matched donor in the immediate family (children, parents, siblings)
  - Fast procurement of stem cells – transplant possible within 2 weeks (when patient is in remission or at the time of maximum reduction of tumor burden)
  - Donor remains available to collect other cells for cellular therapy, if needed

Haplo-identical Donor