Bone Marrow Transplant for MDS Patients

Lori Muffly MD MS
Assistant Professor of Medicine
Division of Blood and Marrow Transplantation
Stanford University
• BMT: The basics

• BMT for MDS: The evidence

• Innovative approaches to BMT for MDS
What is Bone Marrow?

- **Marrow** is the soft tissue inside bones that produces blood forming cells that mature into red blood cells, white cells and platelets (factory)
  - **Red Blood cells** – carry oxygen through our body
  - **White Blood cells** – help fight infection
  - **Platelets** – help control bleeding
What is an Allogeneic BMT?

• BMT = bone marrow (or stem cell) transplant

• Allogeneic = from a Donor
  – Someone “immunologically” compatible

• Transplant = Replace recipient (patient’s) bone marrow with the donor’s bone marrow
  – Replace RBC, platelets, WBC
How Do We Perform Allogeneic BMT?

• Medical transplant= NO SURGERY

STEP 1: Conditioning/Prep: Prepares Body to Accept Donor Stem Cells
  7-14 days

STEP 2: Infusion of Donor Stem Cells
  An hour

STEP 3: Stem Cells “Engraft”
  14-21 days

STEP 4: Prevent side effects & re-evaluate marrow to ensure NO MDS
  Many months

• How do we collect donor stem cells?
  – Bone marrow harvest in OR
  – Use stem cell booster and collect via peripheral veins
Why Do We Perform Allogeneic BMT?

- Transplant = Replace recipient (patient’s) bone marrow with the donor’s bone marrow
  - Replace RBC, platelets, WBC

New (donor) immune system can be very powerful at controlling blood cancer cells → CURE MDS
Annual Number of HCT Recipients in the US by Transplant Type

- Autologous
- Allogeneic

Number of Transplants

- 0
- 2000
- 4000
- 6000
- 8000
- 10000
- 12000
- 14000
- 16000

Years:
- 1980
- 1985
- 1990
- 1995
- 2000
- 2005
- 2010
- 2015

CIBMTR
CENTER FOR INTERNATIONAL BLOOD & MARROW TRANSPLANT RESEARCH
Selected Disease Trends for Allogeneic HCT in the US

Number of allogeneic BMTs/yr in US has doubled in recent years
Trends in Allogeneic HCT by Recipient Age

Transplants for AML, ALL, NHL, Hodgkin Disease, Multiple Myeloma
Trends in Allogeneic BMT Utilization for Adults ≥70 Years, by Disease

- AML
- MDS/MPS
- Non-Hodgkin lymphoma
- Others

Absolute No. HCTs ≥70 Years

Muffly et al Blood 2017
Why is Allogeneic BMT for MDS on the Rise?

• Historically, patients 65 and older with Medicare did not have coverage for BMT for MDS.

• On August 4th 2010, the Centers for Medicare and Medicaid services (CMS) established coverage for BMT for MDS through coverage with evidence development (CED).

• A Center for International Bone Marrow Transplant Research (CIBMTR) study comparing outcomes of patients 55-64 vs. 65 and older was approved in December 2010.

Atallah et al Blood 2017
Medicare Coverage with Evidence Development
MDS BMT Study

• The study compared the outcomes of:
  – 688 patients aged 65 and older and
  – 592 patients aged 55-64
  – who underwent allogeneic BMT for MDS from 2010-2014

• Survival at 100 days and at two years following BMT for MDS patients aged 65 and older is comparable to patients aged 55 to 64.

• Age alone should not be a determinant when considering BMT for patients with MDS.

Atallah et al Blood 2017
How Do We Determine Which MDS Patient to Transplant?

(Very) Low Risk Intermediate Risk IPSS-R

Poor performance Nonfit®
- Nontransplant strategies*
- Failure&
  - Transplant strategies#

Good performance Fit®
- No poor risk features**
  - Nontransplant strategies*
- Poor risk features**
  - Available donor
  - Transplant strategies#
How Do We Determine Which MDS Patient to Transplant?

(Very) Poor Risk IPSS-R

- Poor performance
  - Nonfit
    - Nontransplant strategies*
- Fit
  - Good performance
    - No suitable donor
    - Available donor
      - < 10% marrow blasts
        - Transplant strategies#
      - ≥ 10% marrow blasts
        - Cytoreductive therapy
          - Transplant strategies#

De Witte et al Blood 2017
What Are Outcomes after BMT for MDS?

• In general....

– 30-40% of intermediate/high risk MDS patients will be cured following allogeneic BMT

BUT

– Some patients will have serious morbidity/mortality from the transplant process and some patients will have recurrence of progression of MDS after BMT
How Can We Improve Allogeneic BMT for MDS?

**STEP 1:** Conditioning/Prep: Prepares Body to Accept Donor Stem Cells

- Alter the prep to target MDS cells

**STEP 2:** Infusion of Donor Stem Cells

- Engineer or optimize donor stem cells

**STEP 3:** Stem Cells “Engraft”

**STEP 4:** Prevent side effects & re-evaluate marrow to ensure NO MDS

- 1) Reduce toxicity of allogeneic BMT
- 2) Additional MDS targeting post-BMT
Phase I/II Clinical Trial of an MDS Stem Cell Targeting Antibody Plus Low Intensity Conditioning for Patients with MDS undergoing Allogeneic BMT
Reducing BMT Complications

- Phase III clinical trial conducted across the US aiming to improve post-BMT outcomes for patients with MDS and acute leukemia by reducing transplant toxicity.
Conclusions

• Allogeneic BMT is an immunotherapy that offers a potential for cure for intermediate/high risk MDS patients

• The use of allogeneic BMT for MDS (and for older adults) is rising

• New and innovative approaches to BMT are needed to further improve outcomes