# Hot Topic: Outpatient Transplant Issues

Jennifer Frith, RN, BSN, OCN
Duke University Health System


## Historical Perspective

- Transplant Program opened in 1984
- Internationally recognized for its novel approaches to treating leukemia, lymphoma, and myeloma
- Performed over 3000 transplants
- Currently perform 240+ per year
- 1992 opened first outpatient facility off campus
  - Breast Cancer 98%
  - Single preparative regimen
  - High-dose chemotherapy as inpatient
  - Transplant administered as outpatient
    - Stay in a neighboring hotel minutes away from clinic appointments and emergency care

## Types of Transplants Performed

- Outpatient
  - Autologus
    - Carmustine (BCNU)
  - Allogeneic ablative
    - Post engraftment
  - Allogeneic reduced intensity
    - Haplo-identical
- Inpatient
  - Dual Umbilical Cord
    - Post engraftment

## Comprehensive Care

- Daily Clinic
  - Current phases of transplant
    - Stem Cell priming
    - Preparative regimen
    - Post transplant care
  - Supportive Care
  - Clinical Trials
  - Open 10 hours 7 days a week
- Return Clinic
  - Pre transplant workup
  - Follow up care
- Aphresis Suite
  - NMDP
  - Stem Cell collection
  - Photopheresis

## Isolation

- Screen for VRE weekly
- Accommodate in rooms
- Gown/Gloves placed on entryway into clinic
- Identify early
  - Able to adjust antibiotic regimen accordingly
  - Consistent practice
- Portable Hepa Filter System

## Multidisciplinary Team

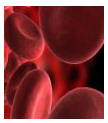
- Attending physicians
  - Inpatient/outpatient
- Coordinators
  - Physicians based
  - Physician assistants and nurse practitioners
  - Follow throughout process
  - Point person for patients, families and local physician
- Daily Care Providers
  - Physician assistants and nurse practitioners
  - Alternate rotation inpatient/outpatient
  - Responsible for daily care

- Nursing Staff
  - Registered nurses
    - OCN Certified
    - Chemotherapy/Biotherapy Certified
    - Stem Cell Administration
  - Nursing Care Assistants
    - Phlebotomy Certified
- Additional staffing on site
  - Clinical Nurse Specialist
  - Triage Nurse
  - Dietician
  - Clinical Pharmacist
  - Social Workers
  - Financial Counselors
  - PRMO
  - PT therapist (future)

# Support Services

- Pharmacy
  - On site
  - Pxysis
  - Curlin pump
  - Weekend Coverage
    - Communicate plan for weekend and holidays
    - Satellite backup support inpatient 9th floor pharmacy
- Home Infusion
  - TPN Support
  - IV Ganciclovir/Foscarnet
  - Cytoxan prime hydration fluids

# Support Services Continued



- Phlebotomy Suite
  - New and Return patients
- Laboratory
  - On site
  - ABC, Chemistry and urine analysis
  - Additional labs to hospital
- Transfusion Services
  - Off site
  - Active type and screen
  - Turn around times varies
- Courier
  - Full time
- Volunteers
  - Hospitality Cart
- Recreation therapy
- Meditation Room
- Family Lounge

# Patient Resources

- Allo/Auto binder
  - Given at each new patient visit
    - Reinforcement of verbal information given
    - Resources materials
  - Bring daily
    - Intake/output log
    - Vital sign sheets
    - Records of daily labs
    - Medications Sheets
      - Medication Reconciliation

# Patient Resources Continued

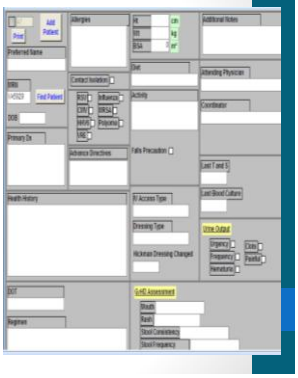
- New patient and Discharge Class
  - Taught by CNS and nursing staff
- Caregiver Support Group
  - Led by Social Workers
- Quality of Life Support Group
  - Led by Behavioral Medicine
  - Held twice a week
  - 10 different topics discussed on a rotating basis
    - Managing Fatigue, Pain Management, Enhancing Communication Skills, Decreasing Stress & Tension, Increasing Enjoyment in Life, Improving Concentration & Memory, Enhancing Social Support, Brief Relaxation Techniques, and Adapting to Chronic Illness

# Major Concerns

- Emergency Service
  - 2 Code carts/ 1 AED
    - Developed a mobile emergency kit
  - No clear define process
    - Meet with our affiliates Duke Life Flight and Durham County EMS
    - Developed an algorithm which simplifies which mode of transport is needed ACLS vs. BLS
    - One phone call
    - Clear concise communication

**Electronic Kardex**

- No formal RN report handoff
  - No clear overview of patient's daily care
  - Increase risk for error and could comprise patient safety
- Initiated in January
- Centrally located
- Easily Maintained
- Generational Friendly



## Team Communication

- Round daily
- Collaborative inpatient/outpatient department meeting
- Clear set protocols operate smoothly
- Able to view all inpatient/outpatient information
- Charge Nurses collaborate
  - Important for patient flow

**Housing**

- Big Challenge
  - Corporate housing
- Furnished apartments
- Close to hospital
- Caring house

**Third Party Payers**

- Reimbursement
  - Pay out of pocket then reimbursed
- No housing benefits
  - All out of pocket
- Individualized
  - Fair amount of work that goes into ensuring proper housing

# Hot Topics in HSCT Nursing: Mobilization Strategy Controversies

Kim Schmit-Pokorny, RN, MSN, OCN®
University of Nebraska Medical Center
Omaha, Nebraska

## Disclosures:

- Genzyme - Consultant

## Objective:

- After this presentation, the participant will be able to describe and compare several peripheral blood stem cell mobilization strategies.

## Comparison of Stem Cells in Bone Marrow and Peripheral Blood

| Bone Marrow | Peripheral Blood |
|---|---|
| • High Concentration | • Low Concentration |
| • Process 750 cc | • Process 40,000 to 80,000 cc |

## Mobilization: Definition

Method of stimulating the stem cells that originate in the bone marrow to increase in number and move into the peripheral blood

## Mobilization: Goal

- Mobilize sufficient cells capable of regenerating a full array of hematopoietic cell lineages
- Achieve adequate engraftment defined as:
  - Absolute neutrophil count > 0.5 x $10^9$/L in 10-12 days
  - Platelet count > 20 x $10^9$/L in 15-30 days
- Minimum: 2 x $10^6$/CD34+ cells/kg (Koc, 2000, Pusic, 2008)
- Higher number correlates with more rapid engraftment (Bensinger 1995, Pusic, 2008, Vogel 1998)

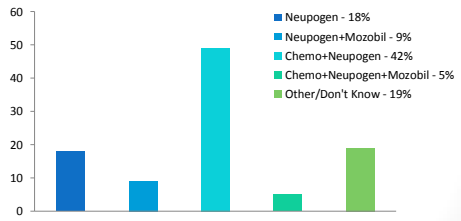
## Current Methods of Mobilization

- Hematopoietic growth factors
  - Most commonly used
    - Filgrastim, Pegfilgrastim, Sargramostim
- Chemotherapeutic agents + growth factors
  - Cyclophosphamide, etoposide, melphalan
  - Disease-specific regimens: ICE and IVE + Filgrastim or sargramostim
- Chemokine Antagonists
  - Plerixafor

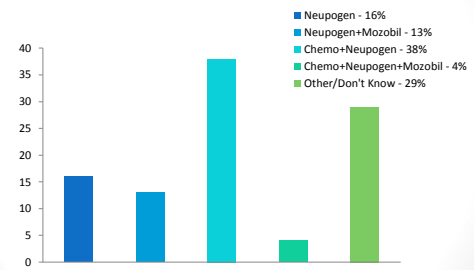
## Other Methods to Mobilize Stem Cells

- Epinephrine
- Exercise
- Apheresis
- Hydrocortisone

## What is the most commonly used initial mobilization strategy at your facility for patients with lymphoma?



## What is the most commonly used initial mobilization strategy at your facility for patients with multiple myeloma?




## Variables to Successful Stem Cell Mobilization

**Donor-related**

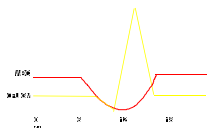
- Age older than 60 years
- Multiple courses of chemotherapy
- Chemo agents: Melphalan, Nitrosoureas, procarbazine, nitrogen mustard, alkylating agents, platinum compounds
- Type of malignancy: NHL, HD
- Radiation to marrow producing sites

**Procedure-related**

- Central access devices
- Cell separation devices

- Best predictor of an adequate collection is the number of CD34+ cell/μL in the blood on the morning of collection, both for good mobilizers and for poor mobilizers.[1-5]
- Commence collection when a particular number of CD34+ cells/μL is present (usually a number between 8 and 20) in order to increase the likelihood of collecting at least 2–4 x $10^6$ CD34+ cells/kg in a single apheresis, i.e., an acceptable number of HPCs for either one or two autologous transplants or a single allogeneic transplant.[6,7]

## Chemotherapy for Mobilization



Chemotherapy causes a transient increase or overshoot in circulating stem cells (Richman, Weiner, & Yankee, 1976)

## History of Chemotherapy Mobilization

- 1986 - 6 independent centers published reports of peripheral blood stem cell transplant
  - Collection following chemotherapy to treat disease: Bell, Castaigne, Korbling, Reiffers, & Tilly

## Chemotherapy Mobilization

Chemotherapeutic agents + growth factors

- Cyclophosphamide, etoposide, melphalan
- Disease-specific regimens: ICE, IVE, DHAP, etc.

+ G-CSF or GM-CSF

## Limitations of Chemotherapy Induced Mobilization

- Not all patients mobilize stem cells
  - heavily pretreated
  - tumor in marrow
  - solid tumors
- Difficult to determine optimal time to begin
- Morbidity & mortality from chemotherapy for mobilization (infection, hospitalization, transfusion support, death)

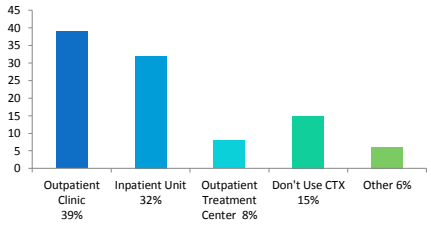
To, 1990

## Chemotherapy Mobilization

- Studies have demonstrated greater hematopoietic stem cell yields with the use of chemotherapeutic agents plus G-CSF than with the use of G-CSF alone[1-3]

| Study | Disease State | Mobilization Regimen | n | Median Total CD34+ Cells (x $10^6$/kg) |
|---|---|---|---|---|
| Bensinger, 1995 | MM, Leukemia | Chemo + G-CSF or GM-CSF | 124 | 10.75 |
| | Other | G-CSF | 119 | 5.21 |
| Desikan, 1998 | MM | CY + G-CSF | 22 | 33.4 |
| | | G-CSF | 22 | 5.8 |
| Narayanasami, 2001 | NHL, HD | CY + G-CSF | 24 | 7.2 |
| | | G-CSF | 22 | 2.5 |

## If utilizing Cytoxan as a mobilizing agent, where is this administered?




## History of Hematopoietic Growth Factor Mobilization

Hematopoietic Growth Factors:

- Socinski , 1988, Sargramostim
  - GM-CSF alone - Incr number of circulating progenitor cells 18-fold
  - GM-CSF + chemo incr number of circulating progenitor cells 60-fold
- Duhrsen, 1988, Filgrastim
  - Pronounced increase in number of circulating progenitor cells

## Growth Factors used for Mobilization

- Filgrastim (G-CSF, Neupogen)
- Sargramostim (GM-CSF, Leukine)
- PIXY321
- Flt 3
- Erythropoietin
- Interleukin - 3
- Stem Cell Factor
- IL-11
- ???

## Hematopoietic Growth Factors for Mobilization

- Injected daily at least 4 days before apheresis and continued until end of apheresis (Pkg insert)
- Filgrastim 5 -10 mcg/kg/day
- Sargramostim 125-250 mcg/$m^2$/day
- GF most commonly given SQ, IV reported
- Usually given q day, may be BID, IV was reported as continuous infusions
- Administered: Outpt, self-injected, clinic
- Filgrastim - most commonly used GF for mobilization (Bensinger, DiPersio, and McCarty, 2009)

## Limitations of Growth Factors

- Insufficient stem cell mobilization and collection
  - 35% of patients with NHL had unsuccessful PBSC mobilization with G-CSF alone (N=52) (Micallef, 2000)
  - Collections of PBSCs from 23% of MM patients who received G-CSF alone were insufficient to support tandem transplantations (N=44)(Desikan, 1998)
  - GM-CSF is less effective than G-CSF( Weaver, 2000, Arora, 2004)
- Adverse events
  - bone pain reported in 33% of patients treated with G-CSF(Package insert)
  - Rare, but serious adverse events have occurred (Package insert)

## Plerixafor (Mozobil)

- Chemokine antagonist
- Reversible inhibitor of SDF-1a/CXCR4 binding
- Initially developed as inhibitor of HIV entry into CD4+ cells
- Caused rapid, transient leukocytosis in patients with HIV infection and healthy volunteers, stimulating interest in capacity to mobilize CD34+ cells

## Mechanism of Action

Plerixafor blocks the SDF-1/CXCR4 interaction releasing stem cells from the bone marrow into the circulating blood

## Mozobil™ (plerixafor injection) Indications and Usage

- Mozobil™ is indicated in combination with granulocyte-colony stimulating factor (G-CSF) to mobilize hematopoietic stem cells to the peripheral blood for collection and subsequent autologous transplantation in patients with non-Hodgkin's lymphoma and multiple myeloma



## Mozobil™ Administration

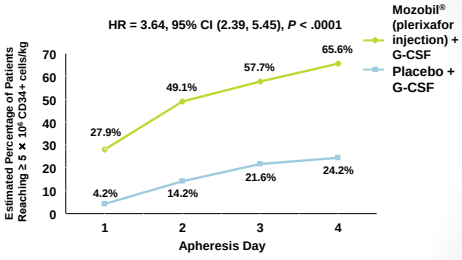
- Administer Mozobil™ subcutaneously approximately 11 hours prior to initiation of apheresis
  - G-CSF is to be administered each morning for 4 days prior to first evening dose of plerixafor and on each morning of apheresis
- Mozobil™ can be administered for up to 4 consecutive days
- Dose: 0.24 mg/kg SQ injection

Mozobil™ [prescribing information]. Cambridge, MA: Genzyme Corp; 2008.

## Phase III (NHL) Results: CD34+ Cell Mobilization

| | Plerixafor + G-CSF | Placebo + G-CSF | p value |
|---|---|---|---|
| Primary Endpoint<br>Patients achieved<br>≥ 5 x $10^6$ CD34+ cells/kg<br>in 4 or less days of apheresis | 59% | 20% | < 0.0001 |
| Secondary Endpoint<br>Patients achieved<br>≥ 2 x $10^6$ CD34+ cells/kg<br>in 4 or less days of apheresis | 87% | 47% | < 0.0001 |
| Secondary Endpoint<br>Patients proceeding to transplant | 90% | 55% | |

NHL Patients (%)[a] Achieving the Primary Endpoint – ITT Population




CI, confidence interval; G-CSF, granulocyte colony-stimulating factor; HR, hazard ratio; ITT, intention-to-treat; NHL, non-Hodgkin's lymphoma.

[a] Percentage of patients achieving collection goal expressed as Kaplan-Meier estimate.

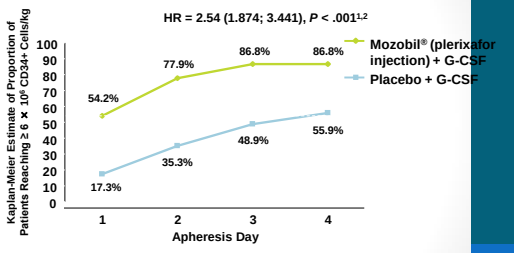
 DiPersio JF, et al. *J Clin Oncol*. 2009;27:4767-4773.

## Phase III (MM) Results: CD34+ Cell Mobilization

| | Plerixafor + G-CSF | Placebo + G-CSF | p value |
|---|---|---|---|
| Primary Endpoint<br>Patients achieved<br>≥ 6 x $10^6$ CD34+ cells/kg in 2 or less days of apheresis | 72% | 34% | < 0.0001 |
| Secondary Endpoint<br>Patients achieved<br>≥ 6 x $10^6$ CD34+ cells/kg in 4 or less days of apheresis | 76% | 51% | < 0.0001 |
| Secondary Endpoint<br>Patients proceeding to transplant | 96% | 88% | |

Median time to engraftment was Day 11 for PMN and Day 18 for platelets in both groups

MM Patients (%)[a] Achieving the Primary endpoint – ITT Population



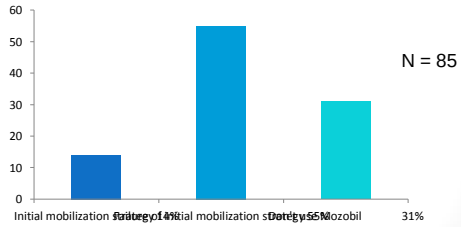

G-CSF, granulocyte colony-stimulating factor; HR, hazard ratio; ITT, intention-to-treat; MM, multiple myeloma.
[a] Percentage of patients achieving collection goal expressed as Kaplan-Meier estimate.
1. Mozobil® [prescribing information]. Cambridge, MA: Genzyme Corp; 2008. 2. DiPersio JF, et al. *Blood*. 2009;113:5720-5726.


## Plerixafor Side Effects

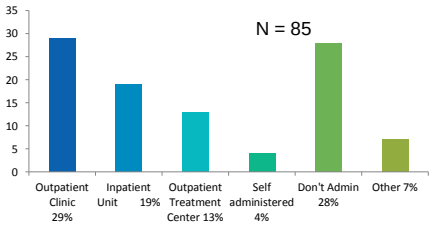
- Systemic reaction: urticaria, periorbital swelling, dyspnea, or hypoxia
- Vasovagal reaction (< 1%)
- Injection site reactions
- Gastrointestinal side effects: diarrhea, nausea, vomiting, flatulence, and abdominal pain



## How do you use Mozobil?




## Where is Mozobil administered?




## Comparison of Mobilization Pathways

## Are you conducting any mobilization studies with study drugs?

Yes, Please list:

- Mobilization of Auto PBSC in CD20+ Lymphoma Patients Using RICE, G-CSF, & Plerixafor
- Recently started Mozobil as 1st line for MM, Plan to dev algorithm for 1st line in NHL
- G-CSF

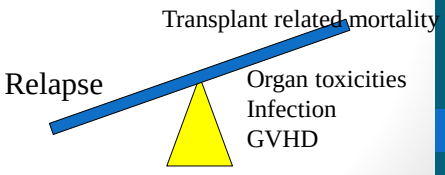
## Thank You!

# Conditioning Regimens in Allogeneic Transplant: To Reduce or Ablate- That is the Question

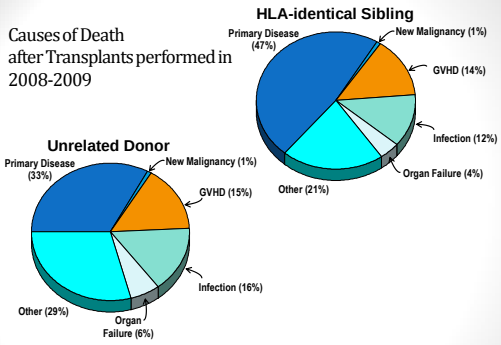
David Frame, Pharm.D.
Clinical Hematology, Oncology, BMT Specialist
Assistant Professor
University of Michigan
Ann Arbor, MI

## Balancing Outcomes in Allogeneic Transplant

Overall Survival




Causes of Death after Transplants performed in 2008-2009




Pasquini MC, Wang Z. CIBMTR Summary Slides, 2011. Available at: http://www.cibmtr.org

## How Do You Balance the Conditioning Regimen?

- What is Reduced Intensity?
- What are the rationales of Conditioning Regimens?
- What are the outcomes?
- What evidence do we have?

## Nursing Poll

- Do you have a clear understanding of the differences in ablative vs reduced intensity conditioning regimens?

YES 82%

## What are the definitions?

- Myeloablative:
  - Total body irradiation
    - single doses of ≥500 cGy
    - fractionated doses totaling ≥800 cGy
  - Busulfan doses of >9mg/kg
  - Melphalan doses of >150 mg/m2
  - Thiotepa > 10mg/kg

Giralt S, et al BBMT 2009;15:367

## What are the definitions?

- Characersitics of "Reduced Intensity"
  - Reversible Myelosuppression without stem cell support
  - Mixed chimerism at first assessment
  - Low rates of non-hematologic toxicity

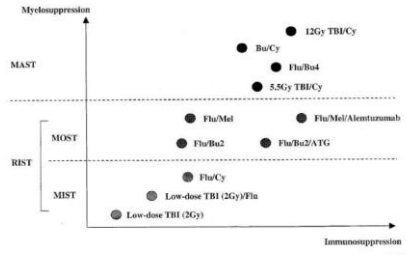
Giralt S, et al BBMT 2009;15:367

## What are the defintions?

- Non-myeloablative
  - Minimal myelosuppression with more immunosuppression
    - Fludarabine/Low dose TBI +/-ATG/Alemtuzumab)
- Reduced-intensity:
  - regimens with lower doses of irradiation, busulfan, or melphalan than those of myeloablative regimen
    - FluBu2, Flu Mel, FluCy +/- low dose TBI, +/- ATG

Giralt S, et al BBMT 2009;15:367

## Relative "Intensity" of Regimens




MAST= Myeloablative Stem Cell Transplant
RIST= Reduced Intensity Stem Cell Transplant
MOST= Moderate Intensity Stem Cell Transplant
MIST= Minimal Intensity Stem Cell Transplant

Kato, Curr Stem Cell Res and Therapy 2007

## Nursing Poll

- Do you have a clear understanding of the rationale of choosing one conditioning regimen over another?

YES 68%

## Rationale of Myeloablative Regimens

- Initial data indicated lower relapse rates with increasing doses of radiotherapy for AML/CML
  - Initial purpose of transplant = myeloablation with marrow rescue
- Greater Intensity = higher non-relapse mortality
  - No survival benefit in initial studies
  - Higher mortality from toxicities and GVHD

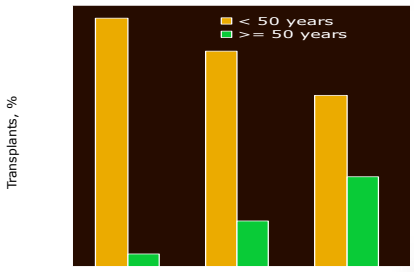
Clift RA, et al. Blood 1998;92:1455

## Rationale of Non-Myeloablative Regimens

- REDUCE TOXICITIES
- Low dose TBI provides enough immunosuppression to allow engraftment[1]
  - Effect enhanced with fludarabine
- Graft vs Tumor Effect[2]

1. Storb R et al. Blood 1997;89:3048
2. Levine JE et al, J Clin Onccol 2002;20:405

## Trends in Allogeneic Transplants Recipient Age 1989-2009




*** Transplants for AML, ALL, NHL, Hodgkin Disease, Multiple Myeloma**

Pasquini MC, Wang Z. CIBMTR Summary Slides, 2011. Available at: http://www.cibmtr.org

## Why is this is Hot Topic?

- NO PROSPECTIVE, RANDOMIZED TRIALS
- Many Retrospective Evaluations
  - Selection Bias
  - Not controlled for "Intensity" of Regimen
  - Not controlled for GVHD prophylaxis
  - Not controlled for type of transplant (MUDvsMRD, BMvsPB)
  - Not controlled for chemosensitivity or disease severity
  - Not controlled for types of disease

## Similarities between Groups

- N= 315 Reduced Intensity vs 407 Myeloablative
- All Matched Sibling Donor Transplants for AML
- All over age 50
- Transplanted 1997-2003
- 60% CR1, 30% advanced disease
- Cytogenetics and FAB classification
- FluBu (<8 mg/kg) 53%, Flu +low dose TBI 24%
- TBI, CY/TBI, BuCy

## Differences between Groups

- PBSC 90% RIC vs 69% MA
- GVHD prophylaxis
  - 88% CSA/MTX ( MA) vs 44 % RIC
  - 2% CSA/MMF (MA) vs 19% RIC
  - 40% CSA alone for RIC

## Transplanted Related Mortality Higher with Myeloablative

## GVHD Higher with Myeloablative

p= 0.003

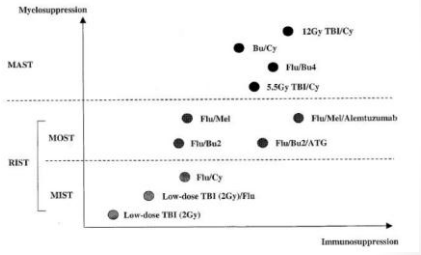
## Disease Relapse Higher with RIC

## SAME Overall Survival

## Reduced Intensity = Older Age ?

- Advantage of Reduced Intensity
  - Decreased Regimen Related Acute toxicities
  - Allows for Transplanting Patients that May NOT have been previously eligible
    - Older Age
    - Lower Performance Score
    - More morbidities

## Are all Regimens Equal?




MAST= Myeloablative Stem Cell Transplant
RIST= Reduced Intensity Stem Cell Transplant
MOST= Moderate Intensity Stem Cell Transplant
MIST= Minimal Intensity Stem Cell Transplant

Kato, Curr Stem Cell Res and Therapy 2007

## Nursing Poll

- Does your center routinely use Total Body Irradiation as a standard conditioning regimen?

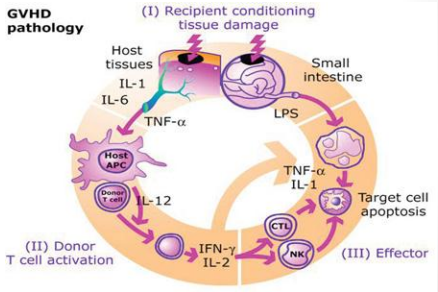
YES 72%

## BuCY vs CY/TBI Meta-Analysis

- TBI/CY regimen
  - Lower relapse for ALL and AML but higher CML
  - Lower transplant-related mortality (TRM)
  - Higher DFS in ALL/AML but same in CML
  - higher rates of cataract (OR 12.69)
  - Higher interstitial pneumonitis (OR 1.7)
- BU/CY regimen had higher VOD and hemorrhagic cystitis

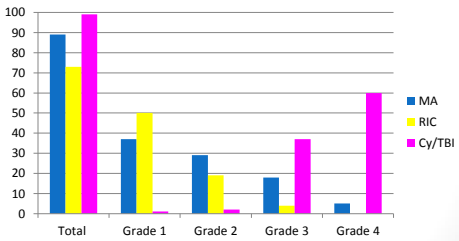
Shi Xia X, et al Leukemia & Lymphoma, January 2010; 51(1): 50–60

## Greater Intensity, Greater Risk of GVHD




Courtesy of Ferrara, Reddy Hill GR et al, Blood 1997;90:3204

## Regimen Related Toxicities Mucositis




Scott BL, *et al*. Leukemia 2006; 20: 128-35.
Spielberger R, et al NEJM 2004;351:2590

## Is there a "Kindler/Gentler" Myeloablative Regimen?

- Will Dose Intensity be more important if advanced disease or active disease?
- Would it be feasible to still give myeloablative regimen to older patient?

## FluBu4 vs BuCy for AML

Non-Relapse Mortality

| | Bu Flu | BuCy2 |
|---|---|---|
| 100-day | 2% | 9% |
| 1year | 7% | 18% |

BBMT 2004;14:672

## FluBu4 in Elderly AML
### Outcomes not changed with older age

- ONE Year TRM = 19%

Alatrash G, Biol Blood Marrow Transplant 2011;17: 1490-1496

## FluBu2/ATG Lowers Non-Relapse Mortality but Same Relapse Rate as FluBu4/ATG

Hamadani M, Hematol Oncol 2011; 29: 202–210

## FluBu2 similar survival to FluBu4

Hamadani M, Hematol Oncol 2011; 29: 202–210

## FluBu2 Superior to BuCY or CVB in CLL

Peres E, Bone Marrow Transplantation (2009) 44, 579–583

## Kinetic Maximization of Busulfan

- Phase I trial
- 90 hour Continuous Infusion
- Dose escalated to specific AUC

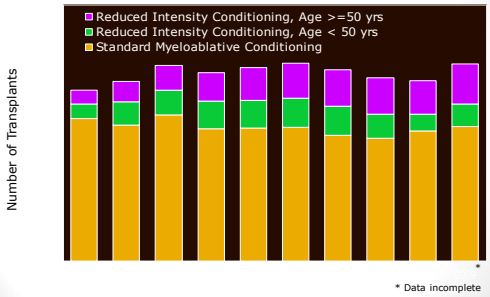
- Relapse higher and OS lower in group with lowest AUC

Walko C, ASBMT 2012 a42

## Do You Still Have A Clear Understanding of Choosing One Regimen Over Another?

Randomized CTN Trial Open for AML

Allogeneic Transplants, Registered with the CIBMTR, 2000-2009
- by Conditioning Regimen Intensity & Age -




# Perhaps We Need More Active Regimens?

- Phase I/II Clofarabine (20mg-40mg/m2/day x 5 days) plus Busulfan 3.2 mg/kg/day x 4days with targeted AUC 4800
- Nonremission hematologic malignancies
- AML 100% CR, 1 year OS 48%, 2 yr OS 35%

Magenau J, Blood 2011;118:4258

# Is it a Package Deal?
## Combined Effect of Conditioning intensity, TBI and graft source

- Sibling Donors (3191), Unrelated donors (2370)
- Compared 6 Treatment Categories
  - **MA + TBI + PBSCs**
  - **MA + nonTBI + PBSCs,**
  - **MA + TBI + BM**
  - **MA + nonTBI +BM**
  - **RIC + PBSC**
  - **RIC + BM**

Jagasia M, et al. Blood 2012;119:296

Acute GVHD Grade B-D | TRM | Overall Mortality

| | SD | URD | SD | URD | SD | URD |
|---|---|---|---|---|---|---|
| MA /TBI/ PB | Ref | Ref | Ref | Ref | Ref | Ref |
| MA /TBI/ BM | | ↓ | | | ↓ | |
| MA /noTBI/PB | | | | | ↓ | |
| MA/ noTBI/BM | ↓ | ↓ | | | | |
| RIC + PBSC | ↓ | ↓ | | ↓ | | |
| RIC + BM | | ↓ | | | | |

Jagasia M, et al. Blood 2012;119:296

# Summary
## To Reduce or Ablate?

- No Randomized, Prospective Trials
- Nonmyeloablative Transplants Demonstrate
  - Comparable Engraftment
  - Reduced Toxicities
  - Reduced to Equal GVHD
  - Higher Relapse
  - May be better for Unrelated Donors
- All Reduced Intensity Not equivalent
  - May depend more on disease