MDS Diagnosis and Treatment Update

LEUKEMIA & LYMPHOMA SOCIETY®
fighting blood cancers

Welcome & Introductions

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Gail J. Roboz, MD

Weill Medical College of Cornell University
NewYork-Presbyterian Hospital

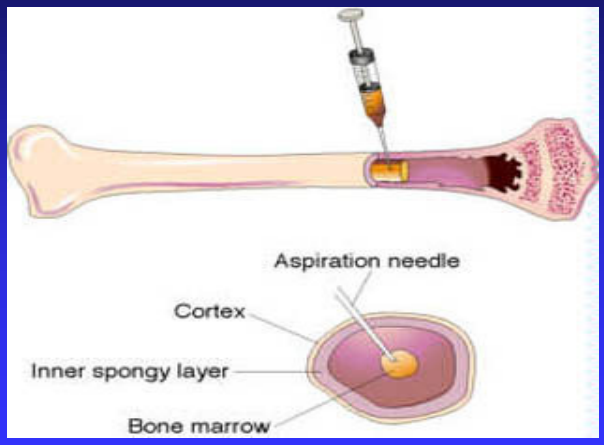
MDS: Diagnosis and Treatment Update

Gail J. Roboz, M.D.
Director, Leukemia Program
Associate Professor of Medicine
Weill Medical College of Cornell University
The New York Presbyterian Hospital

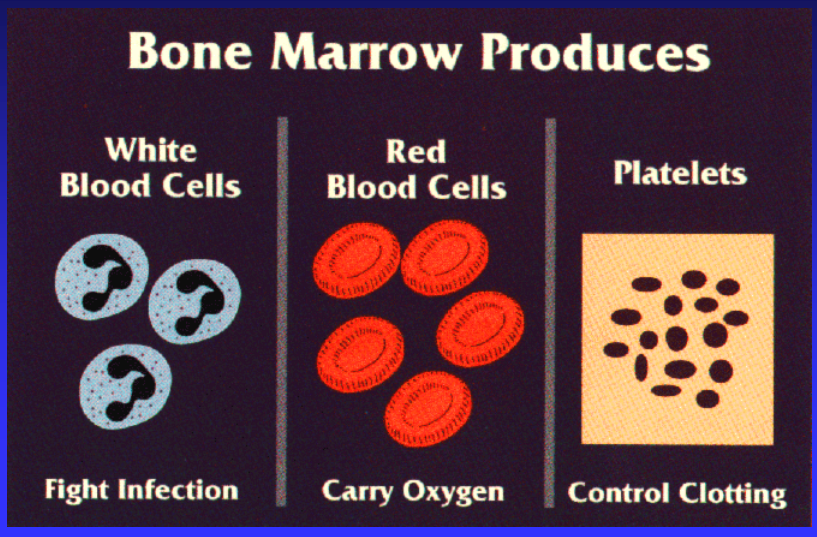
Myelodysplastic Syndrome: Let's build a definition

- Myelo – bone marrow

What is bone marrow?



What does bone marrow do?



Dysplastic

- Dysplasia –abnormal appearance of cells when viewed under the microscope
- Difference shapes, sizes, granules (particles within cells)
- Can be caused by many medical conditions, not only MDS

Syndrome

- Collection of signs and symptoms associated together

Myelodysplastic Syndrome

- Heterogeneous group of clonal hematopoietic stem cell disorders characterized by ineffective hematopoiesis, progressive pancytopenia, morphologic abnormalities and propensity to transform to AML
- Dysplastic hematopoiesis
  - Impaired differentiation
  - Accumulation of blasts
  - Hypercellular bone marrow in ~90%
- Peripheral cytopenias
- Risk of progression to AML in 25-35%
- Abnormal bone marrow cytogenetics in ~50%

1. Cazzola M, Malcovati L. *N Engl J Med.* 2005;352:536-538
2. Heaney ML, Golde DW. *N Engl J Med.* 1999;340:1649-1660
3. Hofmann W-K, et al. *Hematol J.* 2004;5:1-8
4. MDS Foundation Resource Center. Available at: http://www.mdsresourcecenter.org/

Risk Factors

- Cause is unknown in >80% of patients
- Prior exposure to chemotherapy and/or radiation
- Advancing age
- Congenital diseases (Fanconi anemia, congenital neutropenia, rare familial MDS)
- ? Environmental toxins

MDS Risk Factors

Factor	Evidence
Increasing Age	++++
Male Gender	++++
Chemotherapy Agents/XRT	++++
Benzene/Solvents	+++
Smoking	++
Pesticides/Herbicides/Fertilizers	++
Ionizing Radiation	+
Hair Dye	+

Slide Courtesy of S. Strom

Bone Marrow Failure: Signs and Symptoms

Anemia

- Fatigue, pallor
- Shortness of breath, decreased exercise tolerance
- Exacerbation of heart failure, angina

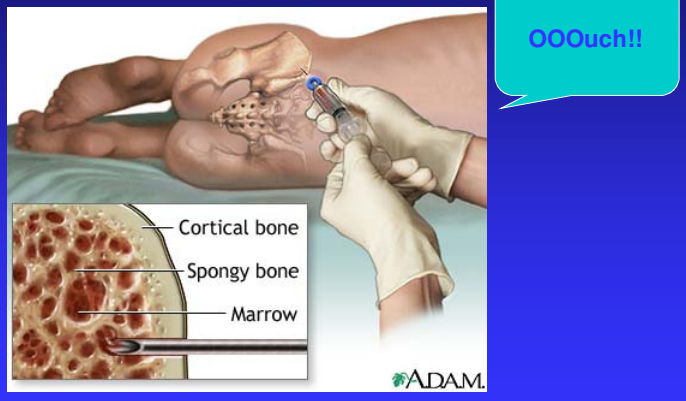
Neutropenia

- Active infection (bronchitis, sinusitis, pneumonia, etc.)
- Risk of infections

Thrombocytopenia

- Petechiae, bruising, bleeding
- Risk of bleeding

Performing a bone marrow aspiration



Other diseases of bone marrow failure

- Hematologic conditions: congenital (hereditary sideroblastic anemia, congenital dyserythropoietic anemia, Fanconi anemia, etc.)
- Nutritional: deficiencies of vitamin B12, folate, iron
- Aplastic anemia (AA)
- Pure red cell aplasia
- Paroxysmal nocturnal hemoglobinuria (PNH)
- Systemic mastocytosis
- Hairy cell leukemia (HCL)
- Large granular lymphocyte disease (LGL)
- Myeloproliferative syndromes (idiopathic myelofibrosis, advanced polycythemia vera or essential thrombocythemia)
- Toxins (alcohol, medications, etc)
- Chronic diseases, viral infections, malignancies

Required Initial Evaluation
NCCN (2013) Guidelines

- H&P
- CBC with diff, platelet count, & retic
- Examination of peripheral blood smear
- BM aspirate with iron stain and cytogenetics
- BM biopsy
- Baseline serum EPO level prior to RBC transfusion
- RBC folate and serum B12
- Serum iron/TIBC/ferritin
- Check thyroid function
- Documentation of transfusion history

NCCN Practice Guidelines in Oncology: Myelodysplastic Syndrome v.2.2013

IPSS-R Prognostic Score Values

Prognostic variable	0	0.5	1	1.5	2	3	4
Cytogenetics	Very Good		Good		Intermediate	Poor	Very poor
BM Blast %	≤2		>2 - <5%		5 – 10%	>10%	
Hemoglobin	≥10		8 - <10	<8			
Platelets	≥100	50 - <100	<50				
ANC	≥0.8	<0.8					

Greenberg et al, Blood, 2012, epub ahead of print.

Newer prognostic models

- Better age stratification (60=90??)
- Duration of diagnosis
- Prior treatments
- Prior transfusions
- Secondary disease
- Performance status
- ?? Molecular diagnostics

How is MDS treated?

- Supportive Care (transfusions, antibiotics, growth factors, ? iron chelation)
- Hypomethylating agents (azacitidine, decitabine)
- Immunomodulators (e.g. lenalidomide)
- Hematopoietic stem cell transplantation
- Novel Agents/Clinical trials

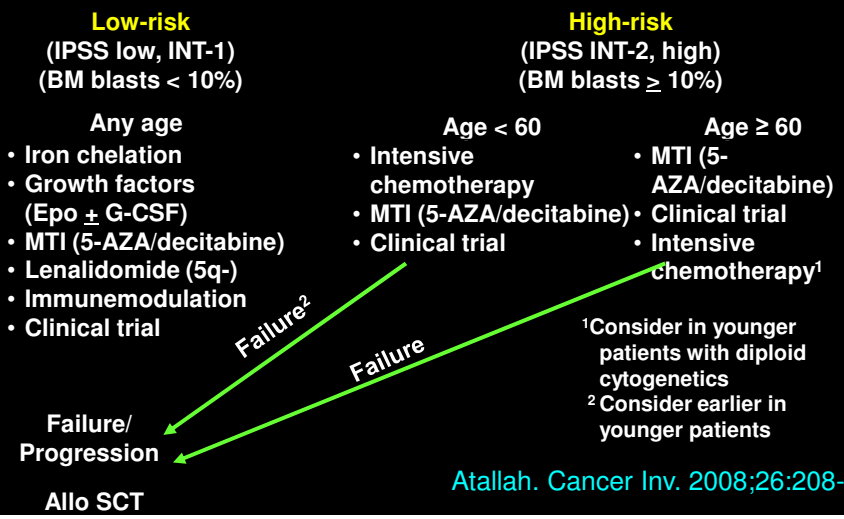
But, before we decide “how” to treat, we need to know…

- Why are we treating???

Goals of Treatment

- If possible, cure me
- If you can’t cure me, at least make me live longer and feel better
- If you can’t make me live longer, at least make me feel better
- If you can’t even make me feel better, then get me another doctor and go back to school…

Proposed treatment algorithm for patients with MDS



Atallah. Cancer Inv. 2008;26:208-16

Essentials for an MDS patient:

- Know your risk group
- Know your treatment options, including whether you should be considering stem cell transplant and/or clinical trials
- Know what results are reasonable to expect from your treatment
- Know the potential side effects
- Know about resources (e.g. the LLS)
- Include your caregiver in treatment planning

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Question and Answer Session

Dr. Roboz's slides are available for download at www.LLS.org/programs

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The Leukemia & Lymphoma Society's (LLS) Co-Pay Assistance Program offers financial assistance to qualified MDS patients to help with treatment-related expenses and insurance premiums. Patients may apply online or over the phone with a Co-Pay Specialist.

- **WEBSITE: www.LLS.org/copay**
- **TOLL-FREE PHONE: (877) LLS-COPAY**

View our webcast on *Advances in Blood Cancers: Update on Treatment for MDS* at **www.LLS.org/webcasts**.

For more information about MDS and other LLS programs, please contact an LLS Information Specialist.

- **TOLL-FREE PHONE: (800) 955-4572**
- **EMAIL: infocenter@LLS.org**