Welcome & Introductions

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MDS: Diagnosis and Treatment Update

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Myelodysplastic Syndrome: Let's build a definition

- Myelo – bone marrow
What is bone marrow?

What does bone marrow do?

Bone Marrow Produces

<table>
<thead>
<tr>
<th>White Blood Cells</th>
<th>Red Blood Cells</th>
<th>Platelets</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fight Infection</td>
<td>Carry Oxygen</td>
<td>Control Clotting</td>
</tr>
</tbody>
</table>
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%

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

<table>
<thead>
<tr>
<th>Factor</th>
<th>Evidence</th>
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<tbody>
<tr>
<td>Increasing Age</td>
<td>++++</td>
</tr>
<tr>
<td>Male Gender</td>
<td>++++</td>
</tr>
<tr>
<td>Chemotherapy Agents/XRT</td>
<td>++++</td>
</tr>
<tr>
<td>Benzene/Solvents</td>
<td>+++</td>
</tr>
<tr>
<td>Smoking</td>
<td>++</td>
</tr>
<tr>
<td>Pesticides/Herbicides/Fertilizers</td>
<td>++</td>
</tr>
<tr>
<td>Ionizing Radiation</td>
<td>+</td>
</tr>
<tr>
<td>Hair Dye</td>
<td>+</td>
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</table>

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 thrombocytthemia)
- 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 v2.2013

### IPSS-R Prognostic Score Values

<table>
<thead>
<tr>
<th>Prognostic variable</th>
<th>0</th>
<th>0.5</th>
<th>1</th>
<th>1.5</th>
<th>2</th>
<th>3</th>
<th>4</th>
</tr>
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<tbody>
<tr>
<td>Cytogenetics</td>
<td>Very Good</td>
<td>Good</td>
<td>Intermediate</td>
<td>Poor</td>
<td>Very poor</td>
<td></td>
<td></td>
</tr>
<tr>
<td>BM Blast %</td>
<td>≤2</td>
<td>&gt;2 - &lt;5%</td>
<td>5 – 10%</td>
<td>&gt;10%</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Hemoglobin</td>
<td>≥10</td>
<td>8 - &lt;10</td>
<td>&lt;8</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Platelets</td>
<td>≥100</td>
<td>50 - &lt;100</td>
<td>&lt;50</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ANC</td>
<td>≥0.8</td>
<td>&lt;0.8</td>
<td></td>
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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

Low-risk
(IPSS low, INT-1)
(BM blasts < 10%)

Any age
• Iron chelation
• Growth factors (Epo + G-CSF)
• MTI (5-AZA/decitabine)
• Lenalidomide (5q-)
• Immune modulation
• Clinical trial

High-risk
(IPSS INT-2, high)
(BM blasts ≥ 10%)

Age < 60
• Intensive chemotherapy
• MTI (5-AZA/decitabine)
• Clinical trial

Age ≥ 60
• MTI (5-AZA/decitabine)
• Clinical trial
• Intensive chemotherapy

1 Consider in younger patients with diploid cytogenetics
2 Consider earlier in younger patients

Failure/Progression
Failure
Failure

Allo SCT

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

Atallah. Cancer Inv. 2008;26:208-16
Question and Answer Session

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

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