THE MDS FOUNDATION PRESENTS

The Myelodysplastic Syndromes: Challenges and Strategies for Effective Outpatient Management

May 3, 2012 • New Orleans, Louisiana

Meeting space has been assigned to provide a satellite symposium co-sponsored by The Myelodysplastic Syndromes Foundation and the Foundation for Care Management via an educational grant during the Oncology Nursing Society's (ONS) 37th Annual Congress, May 3–6, 2012 in New Orleans, Louisiana. The Oncology Nursing Society's assignment of meeting space does not imply product endorsement nor does the Oncology Nursing Society assume any responsibility for the educational content of the symposium.

This program is sponsored by The MDS Foundation, Inc. and the Foundation for Care Management.
Scientific Update: Recent Advances in Strategies for the Treatment of Myelodysplastic Syndromes: From Prognosis to Treatment Selection

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University of Chicago Medicine
Adult Hematologic Malignancy/Stem Cell Transplant
Nurse Practitioner
We’ve come along way

- Initially, MDS diagnosis focused solely on cell morphology and blast counts

Images courtesy of John Bennett, MD and Alan List, MD
Cytogenetics

- Cytogenetic advances began to influence the understanding of MDS in the 1990’s
- Advances in cytogenetic analysis have demonstrated that MDS is characterized by multiple cytogenetic defects
- Cytogenetics continue to affect the diagnosis, prognosis and treatment of MDS

46,XX[9]
46,XX,-5, del(9)(q21q34),del(11)(q21q23),del(20)(q11.2q13.3),+mar[11]
Diagnostic Advances
Cytogenetic Attributes

- Conventional metaphase cytogenetic (MC) analysis
  - Gold standard in karyotypic analysis
- Examines 20 actively dividing cells in metaphase
- Identifies chromosomal abnormalities
- MC cannot detect abnormalities in non-dividing cells
  - This has led to development of new technologies to enhance sensitivity of karyotype analysis

Single-Nucleotide Polymorphism (SNP) Array

- Overcomes limitations of MC
- Detects copy number alterations below the limit of standard cytogenetic analysis detection
- Identifies abnormalities in non dividing cells
- Allows for identification of abnormalities in specific genes that have prognostic significance
  - Some which have demonstrated differential responses to therapy
    - TET2 gene
    - TP53 gene

Gondek et al., 2008; Maciejewski & Mufti, 2008; Graubert, 2011, Tiu et al, 2011; Garcia-Manero, 2010
TET-2

- Produces an enzyme that affects DNA methylation state
- Its dysregulation may have a role in epigenetic alterations in MDS
- Mutated TET2 is an independent prognostic factor for increased response rate to azacitidine therapy
- Cytogenetic Location: 4q24

Itzykson et al. *Blood*. 2010; 116
TP53

- Mutation of TP53 is an independent predictor of poor prognosis MDS
- Mutation of TP53 predicts inferior response to hypomethylating agents and lenalidomide
- Cytogenetic Location: 17p13.1
- The official name of this gene is “tumor protein p53.”

Bejar et al 2011, Tiu et al, 2011
Diagnostic Advances: Molecular Attributes

- Flow Cytometry (FC)
- Based on quantitative and/or qualitative cell receptor or internal protein expression
- Studies point to need for additional refinement and standardization of quantification measures
- CD34-related parameters are good candidates
  - CD34+ stem cell compartment in MDS is altered

Classification Systems

- French-American-British (FAB) System
  - Based on morphology and blast percentage
- World Health Organization System
  - Added cytogenetics to FAB
  - Decreased % blasts to <20% for MDS
- MD Anderson Cancer Center discordance with review of outside slides
  - Diagnostic complexity of MDS
  - Need and value of expert hematopathologists
  - Diagnostic discrepancies between referral and tertiary care centers

# Myelodysplastic Syndromes: Classification Systems

<table>
<thead>
<tr>
<th>FAB</th>
<th>WHO</th>
<th>WHO 2008</th>
<th>DYSPLASIA</th>
<th>BLAST % (BM/PB)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Refractory anemia (RA)</td>
<td>RA</td>
<td>RC with unilineage dysplasia (RCUD)</td>
<td>Erythroid, Nonerythroid</td>
<td>All: &lt; 5/≤ 1</td>
</tr>
<tr>
<td></td>
<td>Myelodysplastic syndromes, unclassified</td>
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<tr>
<td></td>
<td>MDS-U</td>
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<tr>
<td></td>
<td>Refractory neutropenia</td>
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<tr>
<td></td>
<td>Refractory thrombocytopenia</td>
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<td></td>
<td>RCMD</td>
<td></td>
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<tr>
<td></td>
<td>Isolated del(5q)</td>
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</tr>
<tr>
<td>Refractory anemia with ringed sideroblasts (RARS)</td>
<td>RARS</td>
<td>RARS</td>
<td>Erythroid only, Erythroid + other (all &gt; 15% RS)</td>
<td>&lt; 5/≤ 1</td>
</tr>
<tr>
<td></td>
<td>RCMD-RS</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Refractory anemia with excess blasts (RAEB)</td>
<td>RAEB-1</td>
<td>RAEB-1</td>
<td>≥ 1 lineage</td>
<td>5–9/2–4</td>
</tr>
<tr>
<td></td>
<td>RAEB-2</td>
<td>RAEB-2</td>
<td>≥ 1 lineage</td>
<td>10–19/5–19</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>± Auer rods</td>
<td>≥ 20/—</td>
</tr>
<tr>
<td>RAEB in transformation</td>
<td>Acute myeloid leukemia</td>
<td>AML</td>
<td>Myeloid ± other</td>
<td></td>
</tr>
<tr>
<td></td>
<td>(AML)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chronic myelomonocytic leukemia (CMML)</td>
<td>MDS/myeloproliferative disorder (MPD)</td>
<td>MDS/myeloproliferative neoplasm (MPN)</td>
<td>Variable &gt; 1 × 10^9/L monocytosis</td>
<td>All: &lt; 20/—</td>
</tr>
<tr>
<td></td>
<td>CMML</td>
<td></td>
<td></td>
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<tr>
<td></td>
<td>Juvenile MML (JMML)</td>
<td></td>
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<tr>
<td></td>
<td>Atypical chronic myeloid leukemia (aCML)</td>
<td></td>
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</tr>
<tr>
<td></td>
<td>MDS/MPD-U</td>
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</tr>
</tbody>
</table>

From: Ridgeway et al, 2012
Classification and Prognostic Scorings Systems*

- 1997 IPSS(FAB): 816pts/3 databases
  - Marrow blasts, cytogenetics, cytopenias
- 2001 WHO classification
  - Dysplastic subgroups, RAEB-1,2, del(5q)
- 2007 WPSS: 1165pts/3 DBs
  - WHO subgroups, IPSS cytogenetics, RBC Transfusions
  - New cytogenetic classification: 2900 pts/4 databases
- 2011 IWG-PM Refined consensus system (IPSS-R)
  - 7012 pts/18 databases

*Preliminary data – final attributes and scores to be finalized by the IWG-PM
Greenberg, P. on behalf of the IWG-PM – MDS Symposium, ASH December 2011 – with permission
International Prognostic Scoring System (IPSS)

- Developed to understand independent variable for predicting clinical outcomes
- 3 areas of risk scores are identified
  - Cytopenias, bone marrow blasts, cytogenetics
- 4 risk groups are identified
  - Low
  - Intermediate 1
  - Intermediate 2
  - High
- 4 median survival estimates
  - Low—5.7 years
  - Intermediate 1—3.5 years
  - Intermediate 2—1.2 years
  - High—0.4 year

### IPSS Risk Categories and Survival†

<table>
<thead>
<tr>
<th>Variable/Score</th>
<th>0</th>
<th>0.5</th>
<th>1.0</th>
<th>1.5</th>
<th>2.0</th>
</tr>
</thead>
<tbody>
<tr>
<td>Marrow blasts (%)</td>
<td>&lt;5</td>
<td>5-10</td>
<td>---</td>
<td>11-20</td>
<td>21-30</td>
</tr>
<tr>
<td>Karyotype</td>
<td>Good</td>
<td>Intermediate</td>
<td>Poor</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cytopenias</td>
<td>0/1</td>
<td>2/3</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Risk Category</th>
<th>Numeric Score</th>
<th>Patient Distribution</th>
<th>Median Survival†</th>
<th>Evolution to AML</th>
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<td>5.7 years</td>
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<td>0.5-1.0</td>
<td>39%</td>
<td>3.5 years</td>
<td>3.3</td>
</tr>
<tr>
<td>Int-2</td>
<td>1.5-2.0</td>
<td>22%</td>
<td>1.2 years</td>
<td>1.1</td>
</tr>
<tr>
<td>High</td>
<td>≥ 2.5</td>
<td>8%</td>
<td>0.4 years</td>
<td>0.2</td>
</tr>
</tbody>
</table>

† Data generated prior to active therapies

Aims for Refining IPSS

- Determine impact of newer features for prognostic power
- Incorporate larger cytogenetic subgroups & re-assess their prognostic impact
- Analyze depth of cytopenias
- Provide better prognostic ability
- Maintain continuity, feasibility, flexibility

Greeberg, P. on behalf of the IWG-PM – MDS Symposium, ASH December 2011 – with permission
IPSS-R
18 Databases -11 Countries
7012 patients

- Austria
- Brazil
- Czech Rep
- France
- Germany
- Italy
- Japan
- Netherlands
- Scotland
- Spain
- USA

Greeberg, P. on behalf of the IWG-PM – MDS Symposium, ASH December 2011 – with permission
International Working Group for Prognosis in MDS (IWG-PM)

- Data vetted from data bases from 18 institutions
  - Primary untreated, accuracy, completeness, cytogenetics, outcomes
- Further assessed cytogenetics: standard ISCN
  - Cytogenetic committee review
- Data review, statistical weighting for predictive power
- Data analysis
- Final IPSS-R model generated

Greeberg, P. on behalf of the IWG-PM – MDS Symposium, ASH December 2011 – with permission
Inclusion criteria

- Primary MDS (FAB or WHO)
  - Marrow blasts ≤30%
  - PB blasts ≤19%
  - WBC ≤ 12,000/mm³ (ANC ≤ 8,000)
  - >2 months stable disease
- Marrow blasts, cytogenetics, hgb, ANC, platelet levels documented
- No disease-altering therapy during chronic phase
- Valid survival data
- Age > 16yo

Greeberg, P. on behalf of the IWG-PM – MDS Symposium, ASH December 2011 – with permission
Poor Prognostic Indices Considered in the IPSS-R

- PRBC transfusion dependency
  - Depth of anemia, iron overload

- Laboratory parameters
  - LDS>ULN, elevated $\beta_2$ microglobulin

- Comorbidity index/score
  - Cardiac most common

- Bone marrow features
  - Fibrosis, clustered CD34+ cells, megakaryocytic dysplasia,
    ↑cellularity, ↑angiogenesis

- Flow cytometry
  - CD34 coexpression: CD7, 117, 56, 44

- Modified cytogenetic subgroups

Combined Data Base Variables*

- 7012 patients
- Age: 71 yo (median)
- M:F 1.5:1
- Median follow up: 3.9yr
- Classification Systems
  - FAB 7000 pts
  - WHO 5504 pts (79%)
  - WPSS 2325 pts (33%)
- Additional Diagnostic Attributes:
  - RAEBt 6%
  - CMMol 9%
  - 5q- 4%
  - Ferritin 43%
  - TD - RBC 13% (32% w/data)
  - BM fibrosis 19%
  - LDH 61%
  - B2M 13%
  - PS-ECOG 36%

*Preliminary data – final attributes and scores to be finalized by the IWG-PM
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**Combined Data Base Variables (cont.)*

- **Cytogenetics (n=7001)**
  - IPSS – current and 1997:
    - Good – 75% (74%)
    - Intermediate: 13% (15%)
    - Poor: 12% (11%)
    - IPSS-R; V good/good/int/poor/v poor: 4/72/13/4/7%

- **IPSS categories, n=7008**
  - Low/int1/int2/high 37/40/16/7% (‘97:33/38/22/7)

- **WPSS categories, n=2325**
  - 22/32/20/20/4/5 (‘07;23/28/19/23/7)

*Preliminary data – final attributes and scores to be finalized by the IWG-PM

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IPSS-R: Modified Cytogenetic Prognostic Subgroups

- **Very Good**: 60.8 months
  - del(11q), -Y

- **Good**: 48.5 months
  - Normal, del(20q), del(5q) alone and double, del(12p)

- **Intermediate**: 24 months
  - +8, 7q-, i(17q), +19, +21, any other single or double, independent clones

- **Poor**: 14 months
  - der(3)q21/q26, -7, double including 7q-, complex (3 abnormalities)

- **Very Poor**: 5.7 months
  - Complex (>3 abnormalities)

# IPSS-R for MDS:
Prognostic Score Values/Risk Groups*

<table>
<thead>
<tr>
<th></th>
<th>0</th>
<th>1</th>
<th>1.5</th>
<th>1.5</th>
<th>2.5</th>
<th>3.5</th>
<th>5</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cyto</td>
<td>Very Good</td>
<td>Good</td>
<td>Int</td>
<td>Poor</td>
<td>Very Poor</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Blasts</td>
<td>&lt;5%</td>
<td></td>
<td>5-10%</td>
<td>11-30%</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hgb</td>
<td>&gt;10</td>
<td></td>
<td></td>
<td>&lt;10</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Plt</td>
<td>&gt;100</td>
<td></td>
<td>&lt;100</td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>ANC</td>
<td>&gt;0.8</td>
<td>&lt;0.8</td>
<td></td>
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<td></td>
</tr>
</tbody>
</table>

## Risk Groups

1. Very Low: 0-2
2. Good: >2-3.5
3. Intermediate: >3.5-5
4. High: >5-6
5. Very High: >6

*Preliminary data – final attributes and scores to be finalized by the IWG-PM

Greenberg, P. on behalf of the IWG-PM – MDS Symposium, ASH December 2011 – with permission
### IPSS-R:
Prognostic Subgroup Clinical Outcomes*

<table>
<thead>
<tr>
<th></th>
<th>1 Very Low</th>
<th>2 Good</th>
<th>3 Intermediate</th>
<th>4 Poor</th>
<th>5 Very High</th>
</tr>
</thead>
<tbody>
<tr>
<td>OS</td>
<td>8.7</td>
<td>5.3</td>
<td>3.0</td>
<td>1.6</td>
<td>0.8</td>
</tr>
<tr>
<td>AML, 25%</td>
<td>NR</td>
<td>10.7</td>
<td>4.0</td>
<td>1.4</td>
<td>0.8</td>
</tr>
</tbody>
</table>

* Medians, years

*Preliminary data – final attributes and scores to be finalized by the IWG-PM

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Therapeutic Strategies for MDS

- **Low-Risk**
  - Management of symptomatic cytopenias and symptoms
    - PRBC, ESAs
    - Immunomodulatory Agents
    - Immunosuppressive Agents
    - Thrombopoietin receptor agonists
      - Romiplostim, eltrombopag

- **High Risk**
  - Prolonged survival
    - Hypomethylating agents, HCT

From: Ridgeway et al, 2012, CJON
<table>
<thead>
<tr>
<th>AGENT</th>
<th>TARGET</th>
<th>MOA</th>
<th>TRIAL/POPULATION</th>
<th>RESPONSE</th>
<th>GRADE 3/4 AES</th>
</tr>
</thead>
<tbody>
<tr>
<td>ARRY-614&lt;sup&gt;a&lt;/sup&gt;</td>
<td>P38/Tie-2</td>
<td>Antineoplastic, anti-inflammatory, and antiangiogenic activity</td>
<td>Phase I/low or Int-1 risk (N = 100)</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Entinostat (SNDX-275/MS-275)&lt;sup&gt;b&lt;/sup&gt;</td>
<td>Histone DAC</td>
<td>Class 1 HDAC1 and HDAC3 inhibitor</td>
<td>Combination with azacitidine; phase III/high risk (N = 150)&lt;sup&gt;c&lt;/sup&gt;</td>
<td>HR and CyR did not differ between AZA/Pbo versus AZA/entinostat</td>
<td>• Thrombo: 63% • Fatigue 23%</td>
</tr>
<tr>
<td>Erlotinib&lt;sup&gt;d&lt;/sup&gt;</td>
<td>EGFR signaling leads to DNA synthesis and proliferation</td>
<td>Tyrosine kinase inhibitor that blocks EGFR signaling</td>
<td>Phase II/Int-2 and high risk (N = 24)&lt;sup&gt;e&lt;/sup&gt;</td>
<td>ORR: 17%</td>
<td>• Diarrhea: 21% • Thrombo: 17% • Rash: 17%</td>
</tr>
<tr>
<td>Everolimus (RAD-001)&lt;sup&gt;f&lt;/sup&gt;</td>
<td>mTOR</td>
<td>Inhibitor of mTOR that induces G&lt;sub&gt;1&lt;/sub&gt; arrest</td>
<td>Phase II/low and Int-1 risk (not yet recruiting)&lt;sup&gt;g&lt;/sup&gt;</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Ezatiostath&lt;sup&gt;h&lt;/sup&gt;</td>
<td>GST P1-1</td>
<td>Stimulates proliferation of myeloid precursors</td>
<td>Phase I/Int-2 (N = 45)</td>
<td>HI: 38%</td>
<td>• Neutropenia: 7%</td>
</tr>
<tr>
<td>ON-0110.Na&lt;sup&gt;i&lt;/sup&gt;</td>
<td>Polo-1 kinase, PI3K, AKT</td>
<td>Inhibits mitotic progression and induces apoptosis</td>
<td>Phase II/Int-1, Int-2, high risk (N = 10)&lt;sup&gt;j&lt;/sup&gt;</td>
<td>ORR: 50%</td>
<td>• GI: 10% • Dysuria: 10% • Fatigue: 10% • Epistaxis: 10% • No heme toxicities</td>
</tr>
<tr>
<td>Panobinostat (LBH589)&lt;sup&gt;k&lt;/sup&gt;</td>
<td>Histone DAC</td>
<td>Pan DAC inhibitor, inhibits differentiation and induces apoptosis</td>
<td>Phase II/relapsed or refractory MDS (N = 10)&lt;sup&gt;l&lt;/sup&gt;</td>
<td>70% had stable disease</td>
<td>• Thrombo: 80% • Neutropenia: 70% • Leukopenia: 60% • Anemia: 50% • Febrile neutropenia: 20%</td>
</tr>
</tbody>
</table>

From: Ridgeway et al, 2012, CJON
Scientific Developments in Management of MDS

- Risk-adapted treatment selection—IPSS
- Low-Int-1: improve hematopoiesis
  - Int-2: survival
  - Additional prognostic factors have been identified and the IPSS-R is being introduced
- Outcomes shift to include survival
- Identification of novel therapeutic targets
  - Molecular/tissue studies continue to clarify and identify existing and new targets
    - FC
    - TET-2
    - TP53 mutations

Practical Tools for Optimal Management of Myelodysplastic Syndromes

Sandra Kurtin, RN, MS, AOCN, ANP-C
Nurse Practitioner
Clinical Assistant Professor of Medicine
Adjunct Clinical Assistant Professor of Nursing
The University of Arizona Cancer Center
The Facts About MDS

- The average age at diagnosis is 73 years
- MDS remains an incurable *malignancy* for the majority of patients
- Allogeneic-HCT is the only potential “cure”
- The leading cause of death is the disease itself (~80%)
- Risk-stratified treatment strategies are key to optimal therapeutic outcomes

Dayyani et al., 2010; Kurtin et al, 2012
# IPSS Risk Categories and Survival

<table>
<thead>
<tr>
<th>Variable/Score</th>
<th>0</th>
<th>0.5</th>
<th>1.0</th>
<th>1.5</th>
<th>2.0</th>
</tr>
</thead>
<tbody>
<tr>
<td>Marrow blasts (%)</td>
<td>&lt;5</td>
<td>5-10</td>
<td>---</td>
<td>11-20</td>
<td>21-30*</td>
</tr>
<tr>
<td>Karyotype</td>
<td>Good</td>
<td>Intermediate</td>
<td>Poor</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cytopenias</td>
<td>0/1</td>
<td>2/3</td>
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<td>≥ 2.5</td>
<td>8%</td>
<td>0.4 years</td>
<td>0.2</td>
</tr>
</tbody>
</table>

Life expectancy at 75 years US: 12.5 years
Life expectancy at 65 years US: 19.8 years

† Data generated prior to active therapies

* > 20% blasts denotes AML

Survival and AML Evolution by IPSS Classification

From diagnosis in untreated patients

Current and Revised IPSS with Survival and Risk of Leukemic Transformation

<table>
<thead>
<tr>
<th>Category</th>
<th>Score</th>
<th>Median Survival (yrs)</th>
<th>Evolution to AML yrs (25%)</th>
<th>Revised Risk Category</th>
<th>Revised Median Survival (yrs)</th>
<th>Evolution to AML yrs (25%)</th>
<th>R-IPSS Median Survival (yrs)</th>
<th>Evolution to AML yrs (25%)</th>
</tr>
</thead>
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<td>Low</td>
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<td>10.1</td>
<td>6.8</td>
<td>NR</td>
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<td>Intermediate-1</td>
<td>0.5-1.0</td>
<td>3.5</td>
<td>3.3</td>
<td>Intermediate</td>
<td>2.3</td>
<td>2.8</td>
<td></td>
<td></td>
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<tr>
<td>Intermediate-2</td>
<td>1.5-2.0</td>
<td>1.2</td>
<td>1.1</td>
<td>High</td>
<td>1.5</td>
<td>1.2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>High:</td>
<td>&gt;2.5</td>
<td>0.4</td>
<td>0.2</td>
<td>Very High</td>
<td>0.9</td>
<td>0.7</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Greenberg et al. *JNCCN.* 2011;9:30-56
Co-morbidities and MDS

- 600 consecutive patients evaluated at MD Anderson using Adult Co-morbidity Evaluation-27 (ACE-27)

- Median overall survival
  - Overall - 18.6 months ($P<.001$ for all)
  - No co-morbidities - 31.8 months
  - Mild – 16.8 months (HR 1.3)
  - Moderate – 15.2 months (HR 1.6)
  - Severe – 9.7 months (HR 2.3)

- Patients with severe co-morbidities have a 50% decrease in median survival independent of age or IPSS risk group.
  - Low-risk – 43 months
  - Intermediate risk – 23 months
  - High-risk – 9 months

Functional Status, Frailty and Co-morbidities

- **Functional Status**: Measures by ECOG and KPS
  - ADLs:
    - ability to bath, dress, toilet and maintain continence, transfer, and eat independently
  - IADLs:
    - finances, shopping, housekeeping, transportation, and self-medication

- **Co-Morbidities**

- **Frailty**:
  - weight loss, weakness, poor nutritional intake, cognitive impairment and poor endurance
  - Cardiovascular Health Study (n=5317): frailty associated with hospitalization, falls, declining ADLs including diminished mobility, and death (p<.001)

# NCCN Senior Adult Oncology

## General Approach to Therapy

<table>
<thead>
<tr>
<th>Patient Characteristics</th>
<th>Approach to Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Functionally independent without comorbidities</td>
<td>Candidates for most forms of therapy with consideration of goals of treatment/expected outcomes</td>
</tr>
<tr>
<td>Intermediate functional impairment unable to tolerate intensive life-prolonging curative therapy</td>
<td>Application of individualized pharmacologic approach</td>
</tr>
<tr>
<td>Major functional impairments or complex comorbidities</td>
<td>Candidates for palliative therapies only</td>
</tr>
<tr>
<td>Poor prognosis and limited functional status</td>
<td>Symptom management and supportive care</td>
</tr>
</tbody>
</table>

MDS, Transfusions, and Survival

- 2,253 newly diagnosed MDS patients
  - median age of 77
- Transfusion dependent patients with MDS
  - higher incidence of dyspnea, hepatic disease, and infections (all p<0.001)
  - 82% experienced a cardiac event within 3 years of follow-up (p<0.001).
  - increased risk of death (age-adjusted) when compared to other MDS patients (HR 2.41, 95% CI, P<.001)

# Pivotal Trials for FDA Approved Agents

## REGISTRATION TRIALS

<table>
<thead>
<tr>
<th>Agent</th>
<th>Study ID</th>
<th>Phase</th>
<th>Efficacy &amp; Safety</th>
</tr>
</thead>
<tbody>
<tr>
<td>Azacitidine</td>
<td>CALBG 9221</td>
<td>I/II</td>
<td>(2000) Efficacy &amp; Safety</td>
</tr>
<tr>
<td></td>
<td>CALGB 8421</td>
<td>II</td>
<td></td>
</tr>
<tr>
<td>Lenalidomide</td>
<td>MDS 001</td>
<td>I/II</td>
<td>(2002) Efficacy &amp; Safety</td>
</tr>
<tr>
<td>Decitabine</td>
<td>D 0007</td>
<td>I/II</td>
<td>(2003) Efficacy &amp; Safety</td>
</tr>
</tbody>
</table>

## CONFIRMATORY AND EXPANSION TRIALS

<table>
<thead>
<tr>
<th>Study</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>AZA—001</td>
<td>Phase III international multicenter Expansion trial Int-2—high-risk MDS</td>
</tr>
<tr>
<td>MDS—002</td>
<td>Phase II multicenter trial lenalidomide in non-del(5q) low–Int-1 MDS confirmed activity in non-(del)5q MDS safety and efficacy</td>
</tr>
<tr>
<td>ADOPT Trial</td>
<td>Phase III randomized multicenter trial Established new dosing guidelines</td>
</tr>
<tr>
<td>MDS—003</td>
<td>Phase II multicenter trial Lenalidomide in del(5q) led to FDA approval based on efficacy and safety</td>
</tr>
<tr>
<td></td>
<td>Outpatient treatment feasible</td>
</tr>
</tbody>
</table>

Individualized Treatment

- **Treatment Triggers:** Initiation of disease modifying therapy
  - Transfusion dependence
  - Progressive or symptomatic cytopenias
  - Increasing blasts
  - High-risk disease

- **Individualized treatment selection**
  - Performance status (good vs poor)
  - Comorbidities
  - IPSS risk category (low/Int-1 vs Int-2/high)
    - Low/Int-1: improve hematopoiesis
    - Int-2/high: survival
  - Primary vs secondary MDS
  - Cytogenetic status (del[5q], complex karyotype)
  - Lifestyle

Key Principles of Therapy in MDS
Treatment Goals and Duration

- MDS is not curable without allogeneic HCT
  - Not an option for the majority of patients
- Not every patient will have a complete response
  - Hematologic improvement, stable disease, and transfusion independence are good things
- Treatment should continue until disease progression or unacceptable toxicity
  - Methylation is a continuous process and is associated with leukemogenesis
  - Limited FDA approved agents currently available

Kurtin, S. *JAdPrO*, 2011, submitted for publication
The Challenge: Getting Through the First Few Cycles of Treatment

- Time is required for the best response: a minimum of 4-6 months
- Cytopenias often get worse before they get better
- This may be concerning to the patient (and providers)
- There are strategies for management
  - Dose modifications/delays
  - Supportive care
  - Set expectations and provide support

ANC (Neutrophil Granulocytes)

ANC ref. value

ANC Mean ± 97.5 CI


Working together for the best response
Continued Treatment
Opportunity for Response

Short duration of treatment
Inferior Benefit

Treatment perceived as too complex or too toxic; Age

doi:10.1016/j.leukres.2010.10.017
Continued Treatment Opportunity for Response

Short duration of treatment Inferior Benefit

Perceived Lack of Benefit

Treatment perceived as too complex or too toxic; Age

doi:10.1016/j.leukres.2010.10.017
Continued Treatment Opportunity for Response

Short duration of treatment Inferior Benefit

Patient does not recall instructions

Perceived Lack of Benefit

Treatment perceived as too complex or too toxic; Age

Continued Treatment Opportunity for Response

Short duration of treatment Inferior Benefit

- Patient experiences side effects
- Patient does not recall instructions
- Perceived Lack of Benefit
- Treatment perceived as too complex or too toxic; Age

doi:10.1016/j.leukres.2010.10.017

- Continued Treatment Opportunity for Response
- Short duration of treatment Inferior Benefit
  - Patient experiences side effects
  - Patient does not recall instructions
  - Perceived Lack of Benefit
  - Treatment perceived as too complex or too toxic; Age
Continued Treatment Opportunity for Response

Short duration of treatment Inferior Benefit

Patient experiences side effects
Patient does not recall instructions
Perceived Lack of Benefit
Treatment perceived as too complex or too toxic; Age

Setting Expectations
Blueprints for Treatment

doi:10.1016/j.leukres.2010.10.017
Continued Treatment Opportunity for Response

Short duration of treatment Inferior Benefit

Rapid identification and treatment of adverse events
Setting Expectations
Blueprints for Treatment

Patient experiences side effects
Patient does not recall instructions
Perceived Lack of Benefit
Treatment perceived as too complex or too toxic; Age

doi:10.1016/j.leukres.2010.10.017
Sub-Group Analysis of the AZA-001: Elderly patients >75 years with high risk disease

- 87 elderly > 75 years
- High risk disease: IPSS: Int-2 or High
- AZA significantly improved OS compared to BSC
  - 2 year OS rates 55% vs 15% (p<0.001)
- AZA generally well-tolerated
  - Adverse events most common in the first 2 cycles

<table>
<thead>
<tr>
<th>AE (grade 3/4)</th>
<th>Cycle 1-2</th>
<th>Cycle 3-4</th>
<th>Cycle 5-6</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>AZA</td>
<td>BSC</td>
<td>AZA</td>
</tr>
<tr>
<td>Anemia (%)</td>
<td>2</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Neutropenia (%)</td>
<td>15</td>
<td>6</td>
<td>8</td>
</tr>
<tr>
<td>Thrombocytopenia (%)</td>
<td>14</td>
<td>10</td>
<td>8</td>
</tr>
<tr>
<td>Fatigue (%)</td>
<td>0</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Pyrexia (%)</td>
<td>0</td>
<td>0</td>
<td>1</td>
</tr>
</tbody>
</table>

Seymour et al. 2010, Crit Rev Onc/Heme 76;218-227.
Setting Expectations and Empowering the Patient and Family

- **Setting Expectations: Blueprints for Treatment**
  - Cytopenias are **expected**
  - Require close monitoring during the first 8-12 weeks of therapy.
    - Create a plan for follow-up
  - Likely to improve with treatment response but may not return to normal - “new normal”

- **Empower the patient and family to track, report and manage**
  - Treatment tracker, Transfusion records
  - Early identification of AEs, how and when to report or manage

Kurtin. *JAdPrO* , 2011
**Patient Identification:**
- **Name:**
- **DOB:**
- **MR#**
- **Visit#**

**DIAGNOSIS:**
- MDS

<table>
<thead>
<tr>
<th>ICD 9: 238.7</th>
<th>REGIMEN: Lenalidomide</th>
<th>HT: CM</th>
<th>WT: KG</th>
<th>BSA: M²</th>
</tr>
</thead>
</table>

**Approved Indications:**

**References:**

**Allergies (Drug, Food, Environmental)**
- **□** No Known Drug Allergies  □ No Known Food Allergies  □ No Known Environmental Allergies

<table>
<thead>
<tr>
<th>COURSE #: _______ of _________</th>
<th>Start date for cycle #1 of therapy: _____________________</th>
</tr>
</thead>
</table>

**MEDICATION AND DOSE**

<table>
<thead>
<tr>
<th>1</th>
<th><strong>PATIENT’S DOSE</strong></th>
<th><strong>ROUTE</strong></th>
<th><strong>ADMINISTRATION TIME, AND FREQUENCY</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>1 Lenalidomide (Revlimid®)</td>
<td>□ 10 mg  □ 5 mg</td>
<td>By mouth</td>
<td>Once tablet daily with or without food at the same time each day  □ Days 1-21 every 28 days  □ Daily  □ Other: ______________________________</td>
</tr>
</tbody>
</table>

**Begin Therapy:** (day 1) ____________________

<table>
<thead>
<tr>
<th>Treatment Parameters: Do Not Initiate Treatment If: (will use clinic standards if not indicated)</th>
</tr>
</thead>
<tbody>
<tr>
<td>WBC &lt;  PLT &lt;  Bilirubin &gt;  ANC &lt;  CR &gt;</td>
</tr>
</tbody>
</table>

**Protocol modification (reason):**
- Effective date:

**Other Provider Signature:** ID # Date/Time:

**Attending Provider Signature:** ID # Date/Time:

### PRE-TREATMENT EVALUATION:

<table>
<thead>
<tr>
<th></th>
<th>Description</th>
<th>Consent Form Signed: Date: __________________________ (included in HER)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Informed Consent</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>Registration with Revassist ®: <a href="http://www.revassist.com">www.revassist.com</a></td>
<td>Must be prescribed through Revassist program for safety</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Celgene Customer Care Center toll-free at 1-888-423-5436</td>
</tr>
<tr>
<td>3</td>
<td>Pre-treatment laboratory</td>
<td>CBC, differential, platelet count, Complete Metabolic Panel Serum</td>
</tr>
<tr>
<td></td>
<td></td>
<td>erythropoietin level TSH, serum testosterone (men only)</td>
</tr>
<tr>
<td>4</td>
<td>Pre-treatment patient education</td>
<td>Consultation with Clinical Coordinator/Patient Navigator</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Chemotherapy education course: Date:</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Treatment and Transfusion tracking tool</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Lenalidomide (Revlimid ®) patient information packet</td>
</tr>
<tr>
<td>5</td>
<td>Referral to financial coordinator</td>
<td></td>
</tr>
</tbody>
</table>

### 6 Common Adverse Events

- Myelosuppression – most common
- Rash – generally transient, pruritus is common in early phase of treatment
- Diarrhea
- Use with caution in renal impairment – refer to Micromedex
- Analog of Thalidomide- Lenalidomide is nonteratogenic in animal studies

### FOLLOW-UP PROTOCOL:

<table>
<thead>
<tr>
<th></th>
<th>Description</th>
<th>Weekly Laboratory Analysis for first 8 weeks</th>
<th>Provider/Nursing Visit for toxicity check, reinforcement of teaching (first 8 weeks)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td></td>
<td>CBC, differential, platelet count, Complete Metabolic Panel</td>
<td>Provider visit (99214) weekly every other week Other</td>
</tr>
<tr>
<td>2</td>
<td></td>
<td>Nursing visit (99211) weekly every other week Other</td>
<td></td>
</tr>
</tbody>
</table>

### Transfusion Tracker

**Name:** John Smith  
**DOB:** 10/01/1930  
**Blood Type:** E  
**Initial Diagnosis:** Refractory Cytopenias with Multilineage Dysplasia  
**RCMD** – September 1, 2000  
**Cytogenetics:** 46, XY, del(5)(q13q33)[13]/46,XY[7]  
**IPSS Score:** inter-1 / inter-2 / high

| Date of First Transfusion/Number of Lifetime Transfusions: September 30, 2000 / 6 units |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Date of transfusion | Date of transfusion | Number transfused | Total # transfused | Transfusion complications | Leukocytes (x10^9/L) | Hemoglobin (g/dL) | WBC/platelets transfused | Platelets/µL |
| 10/5/2001 | 60 | 2 PRBC | 8 | None | 221 | 8.4 | 2300 / 759 | 193,000 |
| 12/7/2001 | 60 | 2 PRBC | 10 | None | 2700 / 1404 | 185,000 |
| 2/11/2002 | 66 | 2 PRBC | 12 | None | 2000 / 1219 | 200,000 |
| 3/22/2002 | 38 | 2 PRBC | 14 | None | 223 | 8.1 | 2600 / 899 | 103,000 |
| 4/2/2002 | 0 | 14 | n/a | 223 | 9.1 | 2700 / 1728 | 103,000 |
| 4/16/2002 | 0 | 14 | n/a | 223 | 7.6 | 2600 / 1170 | 140,000 |
| 4/22/2002 | 31 | 2 PRBC | 16 | None | 7.6 | 1800 / 510 | 119,000 |
| 4/24/2002 | 0 | 16 | n/a | 8.9 | 1500 / 300 | 112,000 |
| 4/28/2002 | 0 | 16 | n/a | 8.6 | 1100 / 549 | 105,000 |
| 5/10/2002 | 0 | 16 | n/a | 8.6 | 1000 / 140 | 78,000 |
| 5/14/2002 | 0 | 16 | n/a | 8.6 | 1100 / 660 | 66,000 |
| 5/21/2002 | 0 | 16 | n/a | 9.0 | 1900 / 1102 | 61,000 |
| 5/29/2002 | 0 | 16 | n/a | 10.2 | 2600 / 1300 | 58,000 |
| 6/1/2002 | 0 | 16 | n/a | 11.3 | 3000 / 1350 | 53,000 |
| 6/4/2002 | 0 | 16 | n/a | 11.3 | 3100 / 1178 | 61,000 |
| 6/11/2002 | 0 | 16 | n/a | 315 | 11.7 | 2200 / 853 | 57,000 |
| 9/9/2011 | 3427 days | 16 | n/a | 288 | 12.3 | 3700 / 1820 | 105,000 |

**DATE** | **OTHER THERAPIES** | **NOTES**
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>4/2/2002</td>
<td>MDS-001 Trial started Lenalidomide 25 mg/day</td>
<td>NOTES</td>
</tr>
<tr>
<td>4/22/2001</td>
<td>Two units of PRBCs transfused</td>
<td>NOTES</td>
</tr>
<tr>
<td>4/24/2002</td>
<td>Lenalidomide held due to neutropenia and thrombocytopenia</td>
<td>NOTES</td>
</tr>
<tr>
<td>5/21/2002</td>
<td>Resumed treatment with Lenalidomide at 10 mg/day</td>
<td>NOTES</td>
</tr>
<tr>
<td>10/8/2003</td>
<td>Lenalidomide held due to neutropenia and thrombocytopenia, no transfusions since 4/22/2002</td>
<td>NOTES</td>
</tr>
<tr>
<td>11/4/2003</td>
<td>Resumed Lenalidomide 5mg daily</td>
<td>NOTES</td>
</tr>
<tr>
<td>3/1/2004</td>
<td>Lenalidomide changed to 21 days on 7 days off – syncopated schedule due to protocol modification</td>
<td>NOTES</td>
</tr>
<tr>
<td>9/9/2011</td>
<td>Continue on Lenalidomide 5 mg daily 2/12/11 days</td>
<td>NOTES</td>
</tr>
</tbody>
</table>

Strategies to Minimize Adverse Events

- Supportive care is essential for all patients with MDS to improve quality of life
  - Transfusion support, Growth factors, management of infections, management of co-morbidities, chelation therapy, referrals to supportive services

- Minimize AEs in patients on active therapies
  - Dose adjustment, drug holidays, or administration of growth factors to allow safe continuation of therapy.
  - Clear guidelines to the patient and family for early reporting of AEs or strategies for independent management

Kurtin. *JAdPrO*, 2011
Trilineage Response Following 4 Cycles of Azacitidine

Patient Response Over 9 Years of Lenalidomide Treatment
Sustained Moderate But Asymptomatic Cytopenias–A New “Normal”

Passion for the Patients  *LIVING* with MDS
Patient and Family Support Throughout the Continuum of Care

Jayshree Shah
APN-C, AOCN, MSN, BSN, BS, RN, CCRP
John Theurer Cancer Center
Hackensack University Medical Center
Leukemia Division
Key Principles for Educating the Patient and Caregiver

- Understand Disease State
- Available treatment options
- Expected duration of therapy
- Potential adverse events
- Strategies for taking an active role in their care
- Effective patient, caregiver and HCP communication results in better outcome

Kurtin et al, CJON, 2012
Factors noted to limit treatment options

- Fear of toxicity
- Limited expectation of benefit
- Ageism
- Cost of treatment
- Strain on caregivers

Several surveys of patients & providers have underscored the ambiguity in describing MDS as a myeloid malignancy resulting in reluctance to offer disease modifying treatments based on risk analysis.

1. Carreca & Balducci, 2009; Kurtin 2010
2. Kurtin & Demakos, 2010; Sekeres, 2011; Sekeres et al., 2011
Common Adverse Events

- **All agents**
  - Myelosuppression (may also be disease related)
    - Anemia, neutropenia, thrombocytopenia
  - Nausea and vomiting
  - Constipation
  - Renal and hepatic toxicities

- **Drug-specific adverse events**
  - Azacitidine: injection-site reactions
  - Lenalidomide: rash, pruritus, diarrhea, safety program for lenalidomide

- **Iron overload**
  - Chelation therapy may be associated with cytopenias, renal and hepatic toxicities

Transfusion Risks: Iron Overload

- Each unit of PRBC adds 250 mg of unexcretable iron into the patient’s blood
  - At 20-40 RBC transfusions (5-10 g iron)
  - Elevated serum ferritin (1,000-2,000 mg/L), liver, and/or cardiac iron

- Iron accumulation results in end-organ damage

<table>
<thead>
<tr>
<th>ORGANS</th>
<th>COMORBIDITIES &amp; END EFFECTS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heart</td>
<td>Increase risk of cardiac –related event, myocardial infarction, congestive heart failure, arrhythmias</td>
</tr>
<tr>
<td>Liver</td>
<td>Increase risk of cirrhosis, hepatic dysfunction w/elevated levels,</td>
</tr>
<tr>
<td>Endocrine</td>
<td>Leads to hypogonadism, hypothyroidism, and diabetes</td>
</tr>
</tbody>
</table>
### Which Patients With MDS Are Likely to Benefit Most From Management of Iron Overload?

| Transfusion status | • Transfusion dependence  
• Requiring 2 units/month for > 1 year  
• Received 20-30 packed RBC units |
|-------------------|--------------------------------------------------------------------------------|
| Serum ferritin     | • 1,000 ug/L (MDS Foundation)  
• > 2,500 ug/L (NCCN)  
• Or evidence of significant tissue iron overload with continued transfusion dependence |
| MDS risk           | • IPSS: Low- or int-1  
• WHO: RA, RARS, and 5q |
| Patient profile    | • Candidates for allografts  
• Life expectancy > 1 year  
• Free of comorbidities that limit prognosis  
• A need to preserve organ function |

NCCN Clinical Practice Guidelines in Oncology: Myelodysplastic Syndromes—v.2.2010.
## FDA Approved Iron Chelation Therapies

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Deferoxamine (Desferal)</th>
<th>Deferasirox (Exjade)</th>
<th>Deferiprone (Ferriprox)</th>
<th>Phlebotomy</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Dosage</strong></td>
<td>i.m. 0.5 – 1 mg/day</td>
<td>p.o. 20-40 mg/kg/day</td>
<td>p.o. 75 mg/kg/day</td>
<td>Venipuncture</td>
</tr>
<tr>
<td></td>
<td>s.c. 20-40 mg/kg/day</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Half-life (hours)</strong></td>
<td>6</td>
<td>8-16</td>
<td>2-3</td>
<td>n/a</td>
</tr>
<tr>
<td><strong>Schedule</strong></td>
<td>Administered over 8-24 hours, 5-7 days/week</td>
<td>Once a daily</td>
<td>Three times daily</td>
<td>1-2 weekly</td>
</tr>
<tr>
<td><strong>Routes of iron excretion</strong></td>
<td>Urine, stool</td>
<td>Urine, stool</td>
<td>Urine</td>
<td>n/a</td>
</tr>
<tr>
<td><strong>Toxicities &amp; adverse effects</strong></td>
<td>Ocular, auditory, localized site injection reaction, allergic</td>
<td>Renal, hepatic, rash, myelosuppression, GI disturbances</td>
<td>GI, hepatic disturbances myelosuppression</td>
<td>Non-invasive</td>
</tr>
<tr>
<td></td>
<td>reaction, growth and skeletal abnormalities</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Website</strong></td>
<td><a href="http://www.desferal.net">www.desferal.net</a></td>
<td><a href="http://www.us.exjade.com">www.us.exjade.com</a></td>
<td><a href="http://www.ferriprox.com">www.ferriprox.com</a></td>
<td>n/a</td>
</tr>
</tbody>
</table>

Shah et al, CJON, 2012
Iron Chelation Therapy: Safety and Patient Monitoring

- Pancytopenia
  - Neutropenia, agranulocytosis, thrombocytopenia have been reported in MDS patients
    - Baseline and regular monitoring

- Auditory
  - High-frequency hearing loss, decreased hearing
    - Baseline and yearly audiology evaluation

- Ocular
  - Cataracts, lens opacities, increased pressure, retinal disorders
    - Baseline and yearly slit-eye and fundoscopic exam

Iron Chelation Therapy: Safety and Patient Monitoring (cont)

- **Renal toxicity**
  - Increase in serum creatinine
    - Rare cases of acute renal failure have been reported
  - Intermittent proteinuria
    - Baseline and regular monitoring
    - Dose delay or reduction may be necessary

- **Hepatotoxicity**
  - Elevated transaminase levels
    - Baseline and regular monitoring
    - Dose delay or reduction may be necessary

- **Gastrointestinal toxicity**
  - Diarrhea
    - May use antidiarrheal medications
    - Dose reduction may be necessary
  - Nausea
    - Take at bedtime
    - Avoid taking with dairy products

## Guidelines for Monitoring Chelation Therapy

<table>
<thead>
<tr>
<th>Test</th>
<th>Baseline</th>
<th>During therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serum ferritin</td>
<td>X</td>
<td>Every three months</td>
</tr>
<tr>
<td>Serum transaminase levels</td>
<td>X</td>
<td>Monthly</td>
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<tr>
<td>Serum creatinine</td>
<td>X</td>
<td>Monthly</td>
</tr>
<tr>
<td>Liver iron stores (T2 MRI)</td>
<td>X</td>
<td>Annually</td>
</tr>
<tr>
<td>Granulocyte levels</td>
<td>X</td>
<td>Monthly for MDS pts</td>
</tr>
<tr>
<td>Myocardial iron stores (T2 MRI)</td>
<td>X</td>
<td>Annually</td>
</tr>
<tr>
<td>Auditory testing</td>
<td>X</td>
<td>Annually</td>
</tr>
<tr>
<td>Ophthalmic testing</td>
<td>X</td>
<td>Annually</td>
</tr>
</tbody>
</table>

Sources:
Building Blocks of Hope:
A Patient and Care Giver Guide for
LIVING with MDS

International Nursing Leadership Board
The MDS Foundation
The Building Blocks of Hope
Answering Common Questions About MDS

- Understanding the Diagnosis of MDS
- How is MDS diagnosed?
- What are my treatment options?
- What are the common side effects of treatment, and what can be done to control them?
- What new treatments are on the horizon to treat patients with MDS?
- What are the consequences of blood transfusion?
- Should I receive iron chelation therapy?
- How do I select a bone marrow transplant center?
- What can I do to keep myself healthy?

Kurtin, et al. (2012) CJON
What Can I do To Stay Healthy?

- Balanced Diet
- Daily Activity/Exercise
- Avoid Infection
- Avoid Bleeding
- Continue to Enjoy Things You Love - LIVE
- Get Enough Rest
- Take Advantage of Available Resources
- Ask for Help When Needed
- Be an Active Participant in Building Hope

Kurtin, et al. (2012) CJON
Key Points for Patients & Family Living with MDS

- **S**upportive care
- **A**dvocate and ask questions
- **F**ormulate a plan
- **E**ngage in activities
- **T**rack & **T**alk
- **Y**ou
Navigating the Web for MDS: Web-based Resources for Patients and Health Care Providers

Sara M. Tinsley, ARNP, AOCN
Nurse Practitioner
Moffitt
Supporting the MDS Patient, their Caregivers and Health Care Providers

- Myelodysplastic syndromes are a class of incurable diseases requiring compassionate, clear, and consistent communication among healthcare providers (HCPs), patients, and caregivers.

- The majority of patients and caregivers want to understand their disease, prognosis, available treatment options, expected duration of therapy, potential adverse events, and strategies for taking an active role in their care.
Supporting the MDS Patient, their Caregivers and Health Care Providers

- Effective patient, caregiver, and HCP communication will promote patient and caregiver participation in the decision making process and self-care

- A number of Web-based resources provide resources for patients, caregivers and health care providers

http://cjon.sup.mds-foundation.org
MDS-Specific Organizations (alphabetical order)

- **Life Beyond Limits**
  - [http://mdslifebeyondlimits.org](http://mdslifebeyondlimits.org)
  - Brings together an independent group of MDS experts to raise awareness of ageism in access to care for patients with MDS

- **MDS Beacon**
  - [http://mdsbeacon.com](http://mdsbeacon.com)
  - Objective and unbiased news and other information related to MDS
MDS-Specific Organizations
(alphabetical order)

- **MDS Foundation**
  - [http://mds-foundation.org](http://mds-foundation.org)
  - Multidisciplinary, international, nonprofit organization dedicated to the education of professionals, patients, and caregivers; facilitation and support of clinical trials; and development and support of patient advocacy groups

- **United Kingdom MDS Patient Support Group**
  - [http://mdspatientsupport.org.uk](http://mdspatientsupport.org.uk)
  - Offers support, information, referral advice, and patient information in the United Kingdom
Global Patient Support Groups

NEW! NOW FORMING: MYELODYSLASTIC SYNDROMES
PHILADELPHIA PATIENT & FAMILY SUPPORT GROUP. WOULD
YOU LIKE TO JOIN A LOCAL SUPPORT GROUP IN THE
PHILADELPHIA, PENNSYLVANIA AREA?

IF YOU LIVE IN THE PHILADELPHIA METROPOLITAN AREA AND
ARE INTERESTED IN JOINING A SUPPORT GROUP FOR
PATIENTS WHO HAVE MDS, CALL 1-800-MDS-0839 OR
EMAIL AHASSAN@MDS-Foundation.org. Click here to learn
more!

The MDS Foundation has developed a strategy for setting up patient
groups and assistance is now available to organize support groups for
MDS patients. Any member of the Foundation, patients, friends, family
members, and caregivers are invited to join with us to move this project
forward. Would you be interested in joining a few other people to help
start a needed support group for MDS in your area?

http://www.mds-foundation.org/global-patient-support-groups/
Clinical Trials

Clinical trials study new interventions (drugs or procedures) to evaluate their safety and effectiveness in humans. Trials follow a careful set of steps, allowing for the systematic gathering of information to answer questions and confirm hypotheses that were formed earlier, in either laboratory experiments or preliminary trials.

If you are an MDS patient, you may wish to discuss a trial with your primary treating physician to see if you qualify as a candidate.

Announcing New MDS Trial

- CLINICAL RESEARCH TRIAL WITH RIGOSERTIB (ON01910.Na)
- www.onconova.com
- www.mdtrial.com

Click here for a list of international trials.

To submit information on your clinical trials for publication, you

http://www.mds-foundation.org/clinical-trials/
Organizations That Include MDS Within the Scope of Hematologic Malignancies

- **Aplastic Anemia and MDS Foundation**
  - [http://www.aamds.org](http://www.aamds.org)
  - Nonprofit health organization dedicated to supporting patients and families living with aplastic anemia, MDS, paroxysmal nocturnal hemoglobinuria, and related bone marrow failure disease

- **Leukaemia and Lymphoma Research Foundation**
  - [http://leukaemialymphomaresearch.org](http://leukaemialymphomaresearch.org)
  - Programs for support of all of the different blood cancers for patients and their families
Health professionals are the primary source of information for patients. The purpose of this toolkit is to provide resources for healthcare providers to communicate with and support patients with MDS. These materials will help you share the necessary information efficiently and effectively.

The toolkit contents are based on the needs identified by MDS patients in the survey conducted by AA&MDSIF and summarized in The Oncologist in 2011 (Perceptions of Disease State, Treatment Outcomes, and Prognosis Among

http://www.aamds.org/treating-mds-toolkit
Organizations That Include MDS Within the Scope of Hematologic Malignancies

- **Leukaemia Care**
  - [http://www.leukaemiacare.org.uk](http://www.leukaemiacare.org.uk)
  - Resources for people affected by Hodgkin, non-Hodgkin, and other lymphomas; myeloma; MDS; aplastic anemia; and myeloproliferative disorders

- **Leukemia and Lymphoma Society**
  - [http://www.lls.org](http://www.lls.org)
  - Mission is to cure leukemia, lymphoma, Hodgkin disease, and myeloma and improve the quality of life of patients and their families
Myelodysplastic Syndromes

The information in this section about myelodysplastic syndromes (MDS) can help you talk with members of your healthcare team and take an active role in your treatment. Knowing what to expect and being able to make informed decisions about your cancer treatment are important aspects of coping with your disease. You can skim sections to find what you want to read now - and continue reading whenever you’re ready for more information.

What You Should Know

» MDS is a diagnosis of cancer.
» Hematologists and oncologists are specialists who treat people who have MDS or other types of blood cancer.
» Treatment outcomes vary widely among patients; results depend on many individual factors.

What You Should Do

» Seek treatment in a cancer center where doctors are experienced treating patients with MDS.
» Talk with your doctor about your diagnostic tests and what the results mean.
» Ask your doctor whether a clinical trial is a good treatment option for you.

http://www.lls.org/#/diseaseinformation/myelodysplasticsyndromes/
Myelodysplastic Syndrome

Myelodysplastic syndrome (MDS) is the name of a group of conditions that occur when the blood-forming cells in the bone marrow are damaged. This damage leads to low numbers of one or more type of blood cells. If you (or a loved one) are worried about developing a myelodysplastic syndrome, have just been diagnosed, are going through treatment, or are trying to stay well after treatment, the Detailed Guide or Overview can help you find the answers you need.
Financial Assistance Programs

- American Cancer Society: [http://cancer.org](http://cancer.org)
- Anthony Nolan Trust: [http://anthonynolan.org](http://anthonynolan.org)
- CancerCare Co-Payment Assistance Foundation: [http://cancercarecopay.org](http://cancercarecopay.org)
- Cancer Financial Assistance Coalition: [http://cancerfac.org](http://cancerfac.org)
- Chronic Disease Fund: [http://cdfund.org](http://cdfund.org)
- HealthWell Foundation: [http://healthwellfoundation.org](http://healthwellfoundation.org)
- Lance Armstrong Foundation: [http://livestrong.org](http://livestrong.org)
Financial Assistance Programs

- Leukemia and Lymphoma Society:  [http://lls.org/copay](http://lls.org/copay)
- Patient Advocate Foundation Program/Co-Pay Relief Program:  [http://copay.org](http://copay.org)
The MDS Foundation
International Nurse Leadership Board
http://mds-foundation.org/nursing-leadership-board-nlb/

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- Sara M. Tinsley, ARNP, AOCN
  Tampa, Florida, United States
MDS Patient Outreach and Advocacy Program

Patients or caregivers may contact the patient liaison directly by calling (toll-free) 800-637-0839 or via e-mail to ahassan@mds-foundation.org