Myelodysplastic Syndromes (MDS) “Enhancing the Nurses Role in Management”

Christa Roe, RN, BS, OCN
Malignant Hematology Department
H Lee Moffitt Cancer Center & Research
Tampa, Florida
• **MDS Disease background:**
  - What is MDS and how common?
  - How and why do we stage patients?

• **MDS treatment options:**
  - Goals of therapy.
  - Lower risk MDS Treatment.
  - Clinical trials.

• **Factors influencing treatment choice:**
  - Physical.
  - Psychosocial.

• **The Nurse’s responsibilities in shared decision making:**
  - Assessment.
  - Education.
What is MDS?

- A group of malignant hematopoietic disorders characterized by:
  - Bone marrow failure with resultant cytopenias and related complications
  - Macrocytic anemia is the most common presentation
  - The disease has a tendency to progress to Acute Myeloid Leukemia.
  - Of Greek origin “Myelo” prefix means marrow and “dysplasia” is a term to describe abnormal looking blood cells.

Diagnostic Criteria

- Dysplasia in ≥ 10% of all cells in 1 of the following lineages in the bone marrow smear: erythroid, neutrophilic, or megakaryocytic or > 15% ring sideroblasts (iron stain)
- 5% to 19% myeloblast cells.
- Specific chromosomal abnormality (by conventional karyotyping or FISH).
Is MDS a “malignant neoplasm”?

- MDS is a cancer diagnosis according WHO.
- Cancer is a term that describes disease(s) in which a mutation of a normal cell proliferates uncontrollably and invades surrounding tissues, or blood and lymphatic systems.
- MDS is spectrum of disorders.
- In a recent survey
  - 10% of patients agreed that MDS represented “cancer” compared with 46% of HCP and 59% of physicians.

How common is MDS?

• One of the most common hematological malignancies or “Blood Cancers”.
• Estimates of 40,000 new cases in the US are diagnosed every year.
• The majority of patients are above the age of 60.
• Presents slightly more in males.

**IPSS is the most common tool used for staging of MDS**

<table>
<thead>
<tr>
<th>Prognostic variable</th>
<th>Score Value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0</td>
</tr>
<tr>
<td>Bone marrow blasts</td>
<td>&lt; 5%</td>
</tr>
<tr>
<td>Karyotype*</td>
<td>Good</td>
</tr>
<tr>
<td>Cytopenias†</td>
<td>0/1</td>
</tr>
</tbody>
</table>

**Total Score**

<table>
<thead>
<tr>
<th>Risk</th>
<th>Low</th>
<th>Intermediate I</th>
<th>Intermediate II</th>
<th>High</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median survival, yr</td>
<td>5.7</td>
<td>3.5</td>
<td>1.2</td>
<td>0.4</td>
</tr>
</tbody>
</table>

*Good = normal, -Y, del(5q), del(20q); intermediate = other karyotypic abnormalities; poor = complex (≥ 3 abnormalities) or chromosome 7 abnormalities.

†Hb < 10 g/dL; ANC < 1800/μL; platelets < 100,000/μL.

# Revised IPSS

<table>
<thead>
<tr>
<th>Risk group</th>
<th>Points</th>
<th>% of Patients</th>
<th>Median survival, years</th>
<th>Time until 25% of patients develop AML, years</th>
</tr>
</thead>
<tbody>
<tr>
<td>Very low</td>
<td>≤ 1.5</td>
<td>19 %</td>
<td>8.8</td>
<td>Not reached</td>
</tr>
<tr>
<td>Low</td>
<td>&gt; 1.5 – 3</td>
<td>38 %</td>
<td>5.3</td>
<td>10.8</td>
</tr>
<tr>
<td>Intermediate</td>
<td>&gt; 3 – 4.5</td>
<td>20 %</td>
<td>3.0</td>
<td>3.2</td>
</tr>
<tr>
<td>High</td>
<td>&gt; 4.5 – 6</td>
<td>13 %</td>
<td>1.6</td>
<td>1.4</td>
</tr>
<tr>
<td>Very High</td>
<td>&gt; 6</td>
<td>10 %</td>
<td>0.8</td>
<td>0.73</td>
</tr>
</tbody>
</table>

![Overall Survival](image1.png)

![Time to AML Evolution](image2.png)
Age Dependence of the IPSS-R

Variables (units) [usual range]

- Hemoglobin (g/dL) [4-20]
  - Value: 10.2
- Absolute Neutrophil Count ($\times 10^9$/L) [0-15]
  - Value: 1.1
- Platelets ($\times 10^9$/L) [0-2000]
  - Value: 76
- Bone Marrow Blasts (percent) [0-30]
  - Value: 7

Cytogenetic Category

- Very Good
- Good
- Intermediate
- Poor
- Very Poor

IPSS-R SCORE

- Value: 4.5

IPSS-R CATEGORY

- intermediate

Age-adjusted calculation of risk (IPSS-RA):
(only for survival estimation)

- Age: 72 Years
- IPSS-R SCORE
  - Value: 4.56
- IPSS-R CATEGORY (including age)
  - high

www.ipss-r.com
## Therapeutic Objectives for Patients with MDS

<table>
<thead>
<tr>
<th>MDS Type (IPSS)</th>
<th>Treatment Goals</th>
</tr>
</thead>
</table>
| lower-risk      | • Achieving RBC-TI  
                  • Hematologic improvement  
                  • Improving QoL |
| higher-risk     | • Overall survival and AML transformation  
                  • Altering disease’s natural history  
                  • Improving QoL |

QoL, quality of life; RBC, red blood cell; TI, transfusion independence.

Treatment of Lower Risk MDS
When do we need to treat lower risk MDS?

• The goal of treatment in lower risk MDS is to improve the patient’s blood counts and alleviate related symptoms.

• In asymptomatic patients with adequate counts treatment may not be needed or indicated.
  • Providing confidence to patients in observation as an acceptable option is a major educational role for nurses.
  • There is no evidence that early treatment benefit the patients.
  • A majority of patients will need treatment for anemia to reduce or eliminate red blood cell transfusions.
  • Occasionally, treatment is directed to improve platelets or neutrophils.
Supportive Care

- RBC transfusions are used for anemic patients who experience fatigue and/or shortness of breath. The frequency varies from patient to patient.
- MDS patients who require periodic red cell transfusions typically receive two units. Most of doctors will transfuse RBC if hemoglobin is less than 8 g/dl.
  - The role of the nurse is to assess the patient’s need for transfusion
    - Anemia related symptoms.
    - Comorbidities.
- There are several concerns related to RBC transfusions
  - Iron overload
  - Risk of retaining excess fluid
  - Transmission of infection
    The role of the nurse is to assess and educate patients about transfusion complications, reactions.
- Despite the concerns, red cell transfusions improve the quality of life for patients with symptomatic anemia.
- Some patients may need platelets transfusion.
Erythroid Stimulating Agents (ESA)

- Used in lower risk MDS patients.
- First step for managing anemia.
- No difference between epoietin and darbepoietin. (dose equivalence).
- Start with a 8-12 weeks trial, if no response is elicited consider adding G-CSF weekly.
- Epoietin starting dose is 40,000 units weekly and may be escalated to 60,000 weekly.
- Average duration of response is 12-18 months among patients.
- No indication to continue with subsequent line of therapy.
ESA Nursing implications

• Identifying those patients who will benefit from ESA.
  • Symptomatic anemia: typically Hgb < 10 g/dl.
  • Assessing factors that predict higher response:
    • serum erythropoietin level.
    • Transfusion burden.

• Educating the patient about ESAs and its side effects.

• Monitoring patients during therapy:
  • Assess response by checking blood counts every 1-3 weeks based on baseline and treatment schedule.
  • Continuously assess for side effects and manage accordingly.
Lenalidomide in MDS

- Lenalidomide is the standard of care for lower risk MDS with del 5q[^1,2]
  - Transfusion independence by IWG (67%).
  - 90% of patients respond within 3-4 months and duration of response is almost 3 years.
- MDS-004 supports 10 mg as appropriate starting dose:
  - Higher TI for 10 mg.
  - Greater proportion of cytogenetic responses vs 5 mg (41% vs 17%).
  - No significant differences in hematological toxicity.
- MDS-001, MDS-002 and MDS-005 provided evidence that lenalidomide could be a choice for anemia treatment in lower-risk non-del(5q) pts with adequate platelets and neutrophil count[^3,4]

Lenalidomide: Nursing Implications

- Identifying those patients who will benefit from lenalidomide.
  - Lower risk MDS with del 5 q chromosomal abnormality.

- Educating patients about Lenalidomide:
  - Revassist program.
  - Setting patients expectations:
    - There is a high chance of response
    - Expected 3-4 months of treatment before response.
    - Anticipating cytopenia with treatment and need for holding treatment but reassuring patient that this is a sign of response.
Lenalidomide: Nursing Implications

- Expected side effects:
  - Cytopenia
  - Rash
  - GI: upset and diarrhea
  - Hypothyroidism.
  - Leg cramps

- Monitoring patients during therapy:
  - Weekly CBC/diff first 8 weeks and then monthly after.
  - 80% of patients will need dose interruption within 3 weeks and on average treatment is held for 3 weeks then restarted with 5 mg po daily.
  - Continuously assess and manage other adverse events.
Immunosuppressive Therapy (IST)

- One course Anti-thymocyte globulin (ATG) +/- Cyclosporine-A (CSA)
- Positive variable for IST response\[^{1,2}\]
  - Age is the strongest variable for response ( < 60 year)
  - HLA-DR 15 status
  - Short Duration of disease.
  - Trisomy 8
  - Hypoplastic MDS
  - PNH clone

- Responses are durable and trilineage responses are observed\[^{2}\]

IST: Nursing Implications

- Identifying those patients who will benefit from ATG/CS:
  - Young < 60 year, lower risk MDS and HLA-DR15 positive.

- Educating patient about ATG/CSA:
  - Setting patients expectations:
    - Hospitalization- 5 days for ATG
    - Expected 4-6 month after starting treatment achieve a response.
  - Expected side effects:
    - ATG
      - Infusion reactions
      - Cytopenia
      - Serum sickness
      - Infections
    - Cyclosporine
      - Renal toxicity.
      - Hypertension.
      - Electrolytes imbalance.
      - Neurological toxicity.
      - GI toxicity.
      - Hisutism.
      - Infection.

- Monitoring patients during therapy
  - ATG is administered in the hospital, monitor for infusion and anaphylactic reactions.
  - Weekly CBC, CMP, cyclosporine trough levels at the beginning and then as needed clinically.
  - Continuously assess and manage other adverse events.
# Iron Chelation Therapy in MDS

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Transfusion status</td>
<td>▪ Received &gt; 20 RBC transfusions</td>
<td>▪ Transfusion dependent, requiring 2 units/mo for &gt; 1 yr</td>
</tr>
<tr>
<td></td>
<td>▪ Continuing transfusions</td>
<td></td>
</tr>
<tr>
<td>Serum ferritin level</td>
<td>▪ &gt; 2500 μg/L</td>
<td>▪ 1000 μg/L</td>
</tr>
<tr>
<td>MDS risk</td>
<td>▪ IPSS: low or intermediate-1 risk</td>
<td>▪ IPSS: Low- or Int-1</td>
</tr>
<tr>
<td></td>
<td>▪ WHO: RA, RARS and 5q-</td>
<td>▪ WHO: RA, RARS and 5q-</td>
</tr>
<tr>
<td>Patient profile</td>
<td>▪ Candidates for allografts</td>
<td>▪ Life expectancy &gt; 1 yr and no comorbidities that limit progress</td>
</tr>
<tr>
<td></td>
<td></td>
<td>▪ A need to preserve organ function</td>
</tr>
<tr>
<td></td>
<td></td>
<td>▪ Candidates for allografts</td>
</tr>
</tbody>
</table>

ICT

• Box warnings
  • Noted more often when administered in excess of iron burden
• Deferoxamine: ocular and auditory disturbances, acute renal failure, hepatic dysfunction, adult respiratory distress syndrome, growth retardation in children
• Deferasirox: renal failure, hepatic failure, gastrointestinal hemorrhage
• Deferiprone: agranulocytosis, infection (leading to death)

ICT: Nursing Implications

• Identifying those patients who will benefit from ICT:
  • Patients with evidence of iron overload due to RBC transfusions typically present after 15-20 units.
  • Elevated serum ferritin levels in laboratory studies.
  • Lower risk MDS.

• Educating patients about ICT:
  • Monitoring Iron overload.
  • Options of ICT: Desferral pump versus oral iron chelation.
  • Expected side effects.

• Monitoring patients during therapy:
  • Weekly CBC, CMP for first 1-2 month and monthly thereafter.
  • Observe renal function and GI toxicity with Deferasirox.
  • Continuously assess and manage adverse events.
Treatment of Higher Risk MDS
Hypomethylating Agents

- Two medications approved by FDA:
  - Azacitidine: First FDA approved drug for MDS.
  - Decitabine.
- Administered subcutaneously or intravenously.
- Low dose chemotherapy with unique mechanism of action.
- In general well tolerated by patients.
- Response rates of 40-50%.
Hypomethylating Agents (HMA)

• Azacitidine is the preferred HMA given OS data in higher risk MDS.
• HMA are standard of care for higher risk MDS
  • 7 day regimen is preferred
• HMA are treatment option for lower risk MDS patients
  • Thrombocytopenia
  • 5 day regimen is accepted for administration.
HMA: Nursing Implications

- Identifying those patients who will benefit from HMA:
  - Higher risk MDS patients.
  - Lower risk MDS patients with thrombocytopenia or a subsequent line of therapy for anemia.

- Educating patients about HMA:
  - Setting patients expectations:
    - Responses seen at 4-6 month.
    - Worsening of blood counts during the first two cycles.
    - Need to continue therapy among responders.
  - Expected side effects:
    - Myelosuppression.
    - Nausea and vomiting.
    - Constipation.
    - Injection site reactions.

- Monitoring patients during therapy:
  - Weekly CBC at the beginning of therapy.
  - Assessing responses after 4-6 cycles.
Allogeneic Hematopoietic Stem Cell transplant

Allogeneic Stem Cell Transplant (HSCT): Nursing Implications

• Identifying those patients who will benefit from HSCT:
  • Fit and no major comorbidities.
  • Higher risk MDS.
  • Decision about pursuing allo SCT is complex and is a multi-disciplinary approach including active participation of the patient/family need to be involved.

• Educating the patients about HSCT:
  • Setting patients expectations:
    • Transplant procedure.
    • Transplant logistics.
    • Quality of life issues and need for caregiver.
  • Expected side effects:
    • Chemotherapy related.
    • Infections.
    • GVHD.

• Monitoring patients after HSCT:
  • After transplant intense monitoring up to 1 year with frequent visits, and bone marrow aspirate/biopsy repeats.
Salvage Therapy After Azacitidine Failure: Clinical Trials offers best non transplant outcome

*Log-rank comparison of BSC vs intensive CT ($P = .04$), investigational therapy ($P < .001$), or alloSCT ($P < .001$).
†Comparison of intensive CT vs investigational therapy ($P = .05$), intensive CT vs ASCT ($P = .008$), or IT vs ASCT ($P = .09$).

Clinical Trials: Nursing Implication

- Clinical trials are considered the standard of care for treating MDS patients.
- Nurses play a crucial role in educating patients about the process of clinical trials, expectations and clearing any misconceptions.
- Moffitt Cancer Center Malignant Hematology SLIC project.
Factors Influencing Treatment Choice Physical and Psychosocial
Physical Factors Influencing Treatment: Nursing Implications

- Age:
  - Goal and selection of therapy.
- Functional status.
- Comorbidities:
  - Selection of therapy.
  - Adjustment of treatment doses.
  - Addressing impact of MDS on comorbidities.
Psychosocial Factors Influencing Treatment: Nursing Implications

- Patient disease perception.
- Coping with Disease.
- Quality of life.
- Patient support: Family and caregivers.
- Logistics of treatment.
- Financial implications for patients.
Disparity in Perceptions of Disease Characteristics, Treatment Effectiveness, and Factors Influencing Treatment Adherence

- Only 29% of patients reported that MDS was ever “curable” compared with 52% of physicians (P < .001).
- Physician, nurses, and patient perceptions of specific MDS therapies were significantly different, especially regarding health-related quality of life during treatment, adverse events, and the impact of treatment on patient activities.
- HCP viewed the potential benefits of active treatment as being significantly greater than did patients.
- Patients perceived the actual treatment experience more positively than physicians or nurses.
- Nurses were less sanguine about the benefit of specific therapies and were more aware of the burdens on patients than physicians, possibly because of more frequent contact with patients undergoing therapy.

Several non disease specific tools used for QOL assessment in MDS.

QUALMS-1 is MDS disease specific Quality of Life Scale developed at Dana Farber and being validated externally.

Moffitt Cancer Center PI: Sara Tinsley
Sara.tinsley@moffitt.org
Nurse Responsibility in Shared Decision Making
To Summarize

- Maintain a major influence in the patients education.
  - Disease.
  - Treatment.
  - Coping.
- Identifying most appropriate therapy options for patients based on:
  - Disease risk.
  - Efficacy and adverse events of therapies.
  - Physical factors such as comorbidities.
  - Psychosocial factors.
- Educating patients and caregivers about disease expectations.
- Monitoring and addressing adverse events.
- Assessing patient benefit from therapy.
1. Which of the following is true about patients and health care providers perception for Myelodysplastic syndromes (MDS):

a. All doctors and health care providers recognize MDS as cancer but only 50% of patients do.

b. Physician, nurses, and patient perceptions of specific MDS therapies were similar regarding health-related quality of life during treatment, adverse events, and the impact of treatment on patient activities.

c. Nurses are more aware of the disease burden on patients than physicians, possibly because of more frequent contact with patients undergoing therapy.
1. Which of the following is false regarding use of Lenalidomide in del 5 q lower risk MDS:

   a. Lenalidomide yields 67% transfusion independence rate with median duration of response 2-3 years.

   b. Almost 80% of patients will need dose interruption in first 8 weeks but cytopenias on therapy predict the response.

   c. Major side effects with Lenalidomide in MDS include myelosuppression, rash, GI upset and diarrhea.

   d. Lenalidomide response is observed at 4 weeks in 90% of the patients.
Acknowledgement

Patients and Caregivers

Moffitt MDS Program
Rami S Komrokji
Alan List
Eric Padron
Jeffrey Lancet
Javier Pinilla-Ibarz
Lubomir Sokol
PK Burnette
Sheng Wei
Dana Rollison
Sara Tinsley
Najla Al Ali
Lisa Nardelli
Hanadi Ramadan
Amanda Cameron
Cindy Benoit
Beth Finley Oliver

MDS Clinical Consortium

Edward P Evans Foundation

Aplastic Anemia and MDS Foundation

Christa.roe@moffitt.org