Success with MDS

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Objectives

1. Identify common reporting issues for MDS/MPN data fields

2. Review correct reporting practices for MDS/MPN data fields

3. Identify additional training resources
Outline

• Diagnosis & Disease Classification
• Cytogenetic Abnormalities
• Lines of Therapy
• Transformations
• Disease Status
• Resources for Data Managers
What is MDS/MPN?

MYELODYSPLASTIC SYNDROME

MYELOPROLIFERATIVE NEOPLASM
What is MDS/MPN?

**MYELO** relating to the bone marrow

**DYSPLASTIC** ineffective cell production

**SYNDROME** cluster of symptoms, creating a distinct clinical picture

A disease characterized by ineffective production of blood cells.
What is MDS/MPN?

**MYELO** relating to the bone marrow

**PROLIFERATIVE** increasing in numbers

**NEOPLASM** cell multiplication is uncontrolled

A disease characterized by uncontrolled blood cell production.
Diagnosing and Classifying MDS/MPN

MDS Subtypes
- RARS
- RCUD
- RCMD
- RAEB 1 & 2
- Isolated del(5q)
- MDS, unclassifiable

MPN Subtypes
- CIMF
- CNL
- CEL, NOS
- PCV
- ET
- MPN, unclassifiable

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TRAINING & DEVELOPMENT
Diagnosing and Classifying MDS/MPN

Source of many reporting questions and errors

Diagnosis Standard: bone marrow biopsy (BMBx)

Subsequent BMBx for monitoring disease status and transformations.
Bone Marrow Biopsy & CBC

- Review diagnostic bone marrow biopsy
  - See interpretation, diagnosis and/or comments by pathologist
  - Review concurrent progress notes for heme/onc interpretation
- Review CBC with differential for peripheral blood anomalies
  - Critical data for International Prognostic Scoring System
- Review Appendix X for MDS/MPN diagnostic criteria
MDS-U, MPN-U, MDS/MPN-U

• Unclassifiable subtypes are rare
• Ask clinician to review pathology if unclear

• CIBMTR sees many “-unclassifiable” subtypes reported
  – Ensure all resources have been referenced prior to reporting a subtype as “-unclassifiable” subtype
History of MDS or MPN

- Patients may have long hx of MDS or MPN
  - Years of polycythemia vera or essential thrombocythemia
- Ensure you use the original diagnosis date
  - If MPN turns into MDS, ensure MPN diagnosis date and MDS transformation reported.
Concurrent MDS & AML Diagnosis

• If MDS and AML were diagnosed at the same time:
  – Report Pre-TED Q 359: “Did AML transform from MDS” : NO
  – Do not complete Pre-TED MDS questions
  – Do not complete F2014: MDS Pre-HCT

But do complete these forms if MDS was diagnosed and then **transformed** to AML
Cytogenetic Abnormalities

• Report Cytogenetic testing performed at diagnosis on Pre-TED (Q497)

• Report Cytogenetics immediately prior to preparative regimen on Pre-TED (Q540)

• Report Cytogenetics immediately prior to each pre-HCT line of therapy on the Pre-HCT MDS Form 2014 (Q58)
Cytogenetics Example

• A recipient was diagnosed with MDS
• Karyotype and FISH testing at diagnosis revealed the following abnormalities:
  – Deletion of 5q
  – Loss of chromosome 7
  – Translocation between chromosomes 6 and 9

Karyotype: 45,XX,del(5)(q13q32),t(6;9)(q25;q22),-7
Cytogenetics Example

Karyotype:
45,XX,del(5)(q13q32),t(6;9)(q25;q22), -7
Lines of Therapy

• CIBMTR audit finds frequent errors in lines of therapy questions on F2014: MDS Pre-HCT

• Several sections of lines of therapy:
  – Pre-therapy labs (including cytogenetics)
  – Systemic therapy (including some supportive therapies)
  – Other therapies
  – Best Response to line of therapy
  – Relapse/Progression

• Option for multiple lines of therapy
Lines of Therapy

• Lines of therapy can be distinguished by a combination of:
  – Change in therapy
  – Change in dose
  – Change in disease status
  – Transformation
  – Protocol
Lines of Therapy Issues

• **Don’t** report every systemic therapy in one instance
  – **Do** review the therapy history for distinct lines of therapy

• **Don’t** forget to report supportive therapies
  – **Do** remember that iron chelators and growth factors appear on the form.
Transformations

- MDS and MPNs can transform to higher grade disease
- MDS can transform to a higher grade MDS, such as RAEB-1 to RAEB-2
- MDS can transform to AML ($\geq$ 20% blasts)
- MPN can transform into MDS or AML
Transformations

- Transformations do not occur to lower grade

Increasingly Aggressive Histology of Common Transformations

<table>
<thead>
<tr>
<th>Condition</th>
<th>RCUD/RARS/Childhood MDS</th>
<th>RCMD</th>
<th>RAEB-1</th>
<th>RAEB-2</th>
<th>AML</th>
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</thead>
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<tr>
<td>Chronic Neutrophilic Leukemia</td>
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<td></td>
<td></td>
<td>AML</td>
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<td>Polycythemia Vera</td>
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<td>MDS (any)</td>
<td></td>
<td>AML</td>
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<td>AML</td>
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<td>AML</td>
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<tr>
<td>JMML/CMML</td>
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<td></td>
<td></td>
<td>AML</td>
</tr>
</tbody>
</table>
Transformation Example

Diagnosis: RAEB -1 (7% blasts)
Date: 4/13/15

Transformation: RAEB-2 (14% blasts)
Date: 6/4/15

Bone Marrow: 6% blasts
Date: 9/29/15

Reporting
Diagnosis: RAEB-1 (on 4/13/15)
Transformation: RAEB-2 (on 6/4/15)

Do not report an additional transformation to RAEB-1— it’s a lower histology than RAEB-2 and the lower blast percentage likely reflects therapy for RAEB-2.
MDS/MPN to AML Reporting

Pre-TED (Rev 4.0)
- Primary disease: AML
- Complete AML section
- Q359: Did AML transform from MDS? YES
- Report AML cytogenetic/molecular markers between AML dx and HCT
- Complete MDS questions 480-527

F2010 (Rev 3.0)
- Report MDS as antecedent disorder (Q11)
- Remaining data related to AML diagnosis and later
- Do not report previously reported MDS labs on F2010

F2014 (Rev 3.0)
- Report All MDS data from Diagnosis through transformation (Question 126)
- Last evaluation and disease status prior to transplant is not collected on F2014
Transformations & 10-CMS MDS Study

• Do not enroll recipients whose disease has transformed from MDS to AML prior to transplant
  – The indication for HCT would be AML (not MDS)
  – AML is already a covered indication for HCT under CMS

• Recipients who receive a transplant for MDS which then transforms to AML after transplant will remain in the study
Subsequent HCT & Disease Inserts

• 2400
  – Report all diagnosis information for each subsequent transplant

• 2014
  – Only report diagnosis information once

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<table>
<thead>
<tr>
<th>Subsequent Transplant</th>
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<tbody>
<tr>
<td>If this is a report of a second or subsequent transplant for the same disease subtype and this baseline disease insert has not been completed for the previous transplant (e.g., patient was on TED track for the prior HCT, prior HCT was autologous with no consent), begin the form at question one. If this is a report of a second or subsequent transplant for a different disease, begin the form at question one.</td>
</tr>
</tbody>
</table>

Is this the report of a second or subsequent transplant for the same disease?
- [ ] yes - Go to question 123
- [ ] no - Go to question 1
Disease Status

- Compile all relevant data
- Establish a baseline
- Identify treatment intervals
- Utilize the disease status criteria
- Review discrepancies
## Disease Status

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<tr>
<th>Date</th>
<th>% Blasts in BM</th>
<th>% Blasts in blood</th>
<th>HGB</th>
<th>Platelets</th>
<th>ANC</th>
<th>RBC TFSN</th>
<th>PLT TFSN</th>
<th>BM Interp</th>
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<th>CC/FISH</th>
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<th>Molecular</th>
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<td>Stop Vidaza, Prednisone &amp; GCSF</td>
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**TRAINING & DEVELOPMENT**
**Disease Status**

**Comprehensive Disease Specific Manuals**

- 2010/2110: Acute Myelogenous Leukemia (AML)
- 2011/2111: Acute Lymphoblastic Leukemia (ALL)
- 2013/2113: Chronic Lymphocytic Leukemia (CLL)
- 2014/2114: Myelodysplastic Syndrome/Myeloproliferative Neoplasms (MDS/MPN)

**MDS/MPN Response Criteria**

- 2014: MDS/MPN Pre-HCT
- 2014: MDS/MPN Post-HCT

**Complete Remission (CR)**

*Requires all of the following maintained for a minimum of four weeks:*

- **Bone marrow evaluation:**
  - < 5% myeloblasts with normal maturation of all cell lines

- **Peripheral blood evaluation:**
  - Hemoglobin ≥ 11 g/dL untransfused without erythropoietic support
  - ANC ≥ 1000/mm³ without myeloid growth factor support
  - Platelets ≥ 100,000/mm³ without thrombopoietic support
  - 0% blasts in blood
Disease Status & Transformations

• If an MDS/MPN transforms to AML, report only AML disease status
• AML does not transform into MDS

• If MDS features are present in bone marrow, even if blasts < 5%, AML cannot be in CR
Data Manager Resources

• Forms Instructions Manual Sections:
  – 2400
  – 2010/2110
  – 2014/2114
  – Appendices X & Z

• Past Presentations
  – Cytogenetics by Dr. Weisdorf - Tandem 2015 & 2016

• eLearning Module in development
Questions?

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