Overview

• Introduction to MDS
• Diagnosis, Classification, and Risk stratification
• Treatment of Lower Risk MDS
• Treatment of Higher Risk MDS
• Novel and Emerging Therapies
• Questions and Answers
Myelodysplastic Syndromes

- Shared features:
  - Low blood counts
  - Clonal overgrowth of bone marrow cells
  - Risk of transformation to acute leukemia
- Afflicts 15,000 – 45,000 people annually
- Incidence rises with age (mean age 71)

MDS Incidence Rates 2000-2008

US SEER Cancer Registry Data

**Etiology of MDS**

- **<10%**
  - Familial or Congenital
  - Often early onset and part of a larger syndrome

- **10-15%**
  - Topoisomerase II inhibitors
  - Ionizing radiation
  - DNA alkylating agents
  - Peaks 1-3 or 5-7 years following exposure

- **80%**
  - "De novo" (idiopathic, primary)
  - Median age ~71 years; increased risk with aging

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**Differentiation**

- Normal
- Early MDS
- Advanced MDS
- Secondary AML
Making the Diagnosis

Diagnostic Overlap

- Aplastic Anemia
- Paroxysmal Nocturnal Hematuria
- Myelodysplastic Syndromes (MDS)
- Acute Myeloid Leukemia (AML)
- Myeloproliferative Neoplasms
- T-LGL
- Fanconi Anemia
**Minimal Diagnostic Criteria**

**Cytopenia(s):**
- Low hemoglobin, or
- Low neutrophil count, or
- Low platelet count

**MDS “decisive” criteria:**
- >10% dysplastic cells in 1 or more lineages, or
- 5-19% blasts, or
- Abnormal karyotype typical for MDS, or
- Specific mutation typical of MDS

**Other causes of cytopenias and morphological changes EXCLUDED:**
- Vitamin B12/folate deficiency
- HIV or other viral infection
- Copper deficiency
- Alcohol abuse
- Medications (esp. methotrexate, azathioprine, recent chemotherapy)
- Autoimmune conditions (ITP, Felty syndrome, SLE etc.)
- Congenital syndromes (Fanconi anemia etc.)
- Other hematological disorders (aplastic anemia, LGL disorders, MPN etc.)

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**Bone Marrow Biopsy**

From: NCCN Guidelines for Patients: MDS
The Bone Marrow

Chromosomes and Mutation Testing
Classification of MDS Subtypes

<table>
<thead>
<tr>
<th>Subtype</th>
<th>Blood</th>
<th>Bone marrow</th>
</tr>
</thead>
<tbody>
<tr>
<td>MDS with single lineage dysplasia (MDS-SLD)²</td>
<td>Single or bicytopenia</td>
<td>Dysplasia in ≥10% of one cell line, &lt;5% blasts</td>
</tr>
<tr>
<td>MDS with ring sideroblasts (MDS-RS)</td>
<td>Anemia, no blasts</td>
<td>≥15% of erythroid precursors with or without sideroblasts, or ≥5% ring sideroblasts if SF3B1 mutation present</td>
</tr>
<tr>
<td>MDS with multilineage dysplasia (MDS-MLD)</td>
<td>Cytopenia(s), ≤1 x 10⁹/L monocytes</td>
<td>Dysplasia in ≥10% of cells in ≥2 hematopoietic lineages, ≤15% ring sideroblasts, &lt;5% blasts</td>
</tr>
<tr>
<td>MDS with excess blasts-1 (MDS-EB-1)</td>
<td>Cytopenia(s), ≤2%–4% blasts, ≤1 x 10⁹/L monocytes</td>
<td>Unilineage or multilineage dysplasia, 5%–9% blasts, no Auer rods</td>
</tr>
<tr>
<td>MDS with excess blasts-2 (MDS-EB-2)</td>
<td>Cytopenia(s), 5%–19% blasts, ≤1 x 10⁹/L monocytes</td>
<td>Unilineage or multilineage dysplasia, 10%–19% blasts, ± Auer rods</td>
</tr>
<tr>
<td>MDS, unclassifiable (MDS-U)</td>
<td>Cytopenias, ±1% blasts on at least 2 occasions</td>
<td>Unilineage dysplasia or no dysplasia but characteristic MDS cytogenetics, &lt;5% blasts</td>
</tr>
<tr>
<td>MDS with isolated del(5q)</td>
<td>Anemia, platelets normal or increased</td>
<td>Unilineage erythroid dysplasia, isolated del(5q), &lt;5% blasts</td>
</tr>
<tr>
<td>Refractory cytopenia of childhood</td>
<td>Cytopenias, &lt;2% blasts</td>
<td>Dysplasia in 1–3 lineages, &lt;5% blasts</td>
</tr>
<tr>
<td>MDS with excess blasts in transformation (MDS-EB-T)²</td>
<td>Cytopenias, 5%–19% blasts</td>
<td>Multilineage dysplasia, 20%–29% blasts, ± Auer rods</td>
</tr>
</tbody>
</table>
Prognosis & Risk Assessment
MDS Treatment is Highly Risk Stratified

**Lower Risk**
- Observation
- EPO
- Lenalidomide
- Immune suppression
- Iron Chelation

**Higher Risk**
- Azacitidine
- Decitabine
- Allo-HSCT
- Clinical Trials

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**IPSS-Revised (IPSS-R)**

<table>
<thead>
<tr>
<th>Cytogenetic Risk Group</th>
<th>IPSS-R Karyotype Abnormalities (10 categories)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Good</td>
<td>del(13q), -Y</td>
</tr>
<tr>
<td>Intermediate</td>
<td>+6, +7q, +7q, +12, +21</td>
</tr>
<tr>
<td>Poor</td>
<td>del(5q), -7, del(7q), complex with 3 abnormalities</td>
</tr>
<tr>
<td>Very Poor</td>
<td>Complex with &gt; 3 abnormalities</td>
</tr>
</tbody>
</table>

**IPSS-R Parameter**
- Cytogenetic Risk Group
- Bone Marrow Blast %
- Hemoglobin (g/dL)
- Platelet Count (x 10^5/L)
- Absolute Neutrophil Count (x 10^3/L)

<table>
<thead>
<tr>
<th>IPSS-R Risk Group</th>
<th>Points</th>
<th>% of Patients</th>
<th>Median survival, years</th>
<th>Time to 25% with AML, years</th>
</tr>
</thead>
<tbody>
<tr>
<td>Very low</td>
<td>≤ 1.5</td>
<td>10%</td>
<td>8.8</td>
<td>Not reached</td>
</tr>
<tr>
<td>Low</td>
<td>&gt; 1.5</td>
<td>38%</td>
<td>5.3</td>
<td>10.8</td>
</tr>
<tr>
<td>Intermediate</td>
<td>&gt; 3.5</td>
<td>20%</td>
<td>3.3</td>
<td>3.2</td>
</tr>
<tr>
<td>High</td>
<td>&gt; 5.5</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>

Limitations of the IPSS-R

- Considers only UNTREATED patients
- IPSS-R does not consider somatic mutations
- Somatic mutations are common in MDS
- Several mutated genes have prognostic significance independent of the IPSS-R

### Most Frequently Mutated Genes

#### Tyrosine Kinase Pathway
- JAK2
- KRAS
- FLT3
- BRAF
- PTPN11

#### Transcription Factors
- RUNX1
- ETV6
- GATA2
- WT1
- PHF6

#### Others
- TP53
- STAG2
- SMC3
- RAD21
- DDX41
- NPM1

#### Epigenetic Dysregulation
- DNMT3A
- EZH2
- IDH 1 & 2
- TET2
- DNMT3A

#### Splicing Factors
- SF3B1
- U2AF1
- ZRSR2
- PRPF8
- SF3A1
17 genes sequenced in 1996 patients with OS data

- **ASXL1**
- **NPM1**
- **CBL**
- **NRAS**
- **DNMT3A**
- **RUNX1**
- **ETV6**
- **SRSF2**
- **EZH2**
- **TET2**
- **IDH1**
- **TP53**
- **IDH2**
- **U2AF1**
- **JAK2**
- **SF3B1**

From the IWG-PM Collaborative Meta-analysis

Impact of Mutations by IPSS-R Group

- **TP53**
- **ETV6**
- **ASXL1**
- **EZH2**
- **RUNX1**
Prognostic Mutations by Blast % (<5%)

Prognostically Adverse Mutations in MDS

From the IWG-PM Collaborative Meta-analysis
Prognostic Mutations by Blast % (5-30%)

Karyotype Features and TP53 and Survival

Median Overall Survival:
- 7.2 months
- 14.4 months
- 31.2 months

TP53 mutated MDS
Poor prognosis due to early relapse

MDS

TP53 mutation
Median OS = 8 months

No TP53 mutation

Survival

No TP53 mutation

TP53 mutation

p < 0.0001

Relapse

No TP53 mutation

TP53 mutation

p < 0.0001

Risk Adapted
Patient Specific Therapy
Treatment Options for MDS

Observation
Erythropoiesis stimulating agents
Granulocyte colony stimulating factor
Iron chelation
Red blood cell transfusion
Platelet transfusion
Lenalidomide
Immune Suppression
Hypomethylating agent
Stem cell transplantation

Clinical Trials – often the best option

MDS Treatment is Highly Risk Stratified

Lower Risk
- Observation
- ESAs
- Lenalidomide
- Immune suppression
- Iron Chelation

Higher Risk
- Azacitidine
- Decitabine
- Allo-HSCT
- Clinical Trials
Treating Lower Risk MDS

Primary Goal: to improve QUALITY OF LIFE

1. Do I need to treat at all?
   - No advantage to early aggressive treatment
   - Observation is often the best approach

2. Are transfusions treatment?
   - No! They are a sign that treatment is needed.

Treating Lower Risk MDS

Primary Goal: to improve QUALITY OF LIFE

What if treatment is needed?

1. Is my most effective therapy likely to work?
   - Lenalidomide (Revlimid)

In del(5q) – response rates are high

50%-70% respond to treatment

Median 2-years transfusion free!
Treating Lower Risk MDS

Primary Goal: to improve QUALITY OF LIFE

Is my second most effective therapy likely to work?
- Red blood cell growth factors
- Erythropoiesis Stimulating Agents (ESAs)
- Darbepoetin alfa (Aranesp)
- Epoetin alfa (Procrit, Epogen)
- Lance Armstrong Juice → EPO

Erythropoiesis Stimulating Agents

Primary Goal: to improve QUALITY OF LIFE

ESAs – act like our own erythropoietin

<table>
<thead>
<tr>
<th>Serum EPO level (U/L)</th>
<th>RBC transfusion requirement</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;100</td>
<td>&lt;2 Units / month = +2 pts</td>
</tr>
<tr>
<td>100-500</td>
<td>≥2 Units / month = -2 pts</td>
</tr>
<tr>
<td>&gt;500</td>
<td>-3 pts</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Response Rate</th>
<th>Total Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>High likelihood</td>
<td>&gt; +1</td>
</tr>
<tr>
<td>Intermediate likelihood</td>
<td>-1 to +1</td>
</tr>
<tr>
<td>Low likelihood</td>
<td>&lt; -1</td>
</tr>
<tr>
<td></td>
<td>Response Rate</td>
</tr>
<tr>
<td>High likelihood</td>
<td>74% (n=34)</td>
</tr>
<tr>
<td>Intermediate likelihood</td>
<td>23% (n=31)</td>
</tr>
<tr>
<td>Low likelihood</td>
<td>7% (n=39)</td>
</tr>
</tbody>
</table>

Hellstrom-Lindberg E et al Br J Haem 2003; 120:1037
Treating Lower Risk MDS

Primary Goal: to improve QUALITY OF LIFE

Is a LEN +/- ESA likely to work?
In non-del(5q) MDS patients:

![Graph showing RBC-Ti ≥ 8 Weeks and RBC-Ti ≥ 24 Weeks for LEN (n=160) and Placebo (n=79)]

Toma et al, Leukemia. 2016 Apr;30(4):897-905

Treating Lower Risk MDS

Primary Goal: to improve QUALITY OF LIFE

What my next most effective therapy?

- Immunosuppression

Some MDS patients have features of aplastic anemia

- Hypoplastic bone marrow (too few cells)
- PNH clones
- Certain immune receptor types (HLA-DR15)
**Immune Suppression for MDS**

**Primary Goal:** to improve **QUALITY OF LIFE**

Swiss/German Phase III RCT of ATG + Cyclosporin (88 patients)

- Mostly men with Lower Risk MDS
- CR+PR: 29% vs. 9%
- No effect on survival
- Predictors of Response:
  - hypocellular aspirate
  - lower aspirate blast %
  - younger age
  - more recent diagnosis


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**Guidelines for Lower Risk MDS**

**Primary Goal:** to improve **QUALITY OF LIFE**

1. Do I need to treat? - symptomatic cytopenias
2. Is LEN likely to work? - del(5q) or after ESA
3. Are ESA likely to work? - Serum EPO < 500
4. Is IST likely to work? - hypocellular, DR15, PNH
5. Think about iron! - 20 or more transfusions
6. Consider AZA/DEC
7. Consider HSCT or clinical trial!
Novel Treatments for Lower Risk MDS

Luspatercept

EPO/ESAs

Hemoglobin synthesis

ESAs
TPO mimetics
G-CSF (neupogen)

BFU-E  CFU-E  Pro E  Baso E  Poly E  Ortho E  Retic  RBC

TGF-β
Luspatercept

ESAs
TPO mimetics
G-CSF (neupogen)

Promoting Red Cell Production

Luspatercept (ACE-536) and Sotatercept (ACE-011)
Promoting Red Cell Production

Luspatercept (ACE-536) and Sotatercept (ACE-011)

**MEDALIST Trial - Change in Hemoglobin Concentration**

- Median peak hemoglobin increase in luspatercept responders: 2.55 g/dL (1–4.1 g/dL)

<table>
<thead>
<tr>
<th>Analysis Week Visit</th>
<th>Hb Mean Change ± SE from Baseline (g/dL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td>-1</td>
</tr>
<tr>
<td>1</td>
<td>0.5 ± 0.3</td>
</tr>
<tr>
<td>2</td>
<td>1.0 ± 0.4</td>
</tr>
<tr>
<td>3</td>
<td>1.5 ± 0.5</td>
</tr>
<tr>
<td>6</td>
<td>2.0 ± 0.6</td>
</tr>
<tr>
<td>9</td>
<td>2.5 ± 0.7</td>
</tr>
<tr>
<td>12</td>
<td>3.0 ± 0.8</td>
</tr>
<tr>
<td>13</td>
<td>3.5 ± 0.9</td>
</tr>
<tr>
<td>15</td>
<td>4.0 ± 1.0</td>
</tr>
<tr>
<td>18</td>
<td>4.5 ± 1.1</td>
</tr>
<tr>
<td>21</td>
<td>5.0 ± 1.2</td>
</tr>
<tr>
<td>24</td>
<td>5.5 ± 1.3</td>
</tr>
</tbody>
</table>

- Analysis Week Visit: 24

- **P < 0.0001**

<table>
<thead>
<tr>
<th>Number of patients</th>
<th>Responder†</th>
<th>Non-responder</th>
<th>Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Responder</td>
<td>153</td>
<td>33</td>
<td>33</td>
</tr>
<tr>
<td>Non-responder</td>
<td>153</td>
<td>51</td>
<td>61</td>
</tr>
<tr>
<td>Placebo</td>
<td>76</td>
<td>60</td>
<td>60</td>
</tr>
</tbody>
</table>

† LS mean difference (95% CI) for luspatercept responders versus placebo: 1.08 (0.84, 1.31), P < 0.0001.

Only patients with RBC-TI ≥ 8 weeks during weeks 1–24 are included. Hb measurement was excluded within 14 days after a RBC transfusion unless within 3 days prior to another RBC transfusion. Mean and SE were not calculated if the number of patients was < 8 in the luspatercept non-responder group or < 4 in the placebo group. SE, standard error.
Platelet Growth Factors

**Eltrombopag or Romiplostim** - TPO mimetics

ESAs
TPO mimetics
G-CSF (neupogen)

Eltrombopag and Romiplostim - approved, but not yet in MDS

Initial concern about increasing blasts and risk of AML

Follow-up suggests both drugs are safe in lower risk patients


Hypomethylating Agents in LR-MDS

Randomized study of **Azacitidine 75 mg/m² x 3 days vs. Decitabine 20 mg/m² x 3 days** on a 28-day cycle in lower-risk MDS.

*Conclusion – 3-day Decitabine is a viable regimen for LR MDS*

<table>
<thead>
<tr>
<th>Table 2. Response</th>
</tr>
</thead>
<tbody>
<tr>
<td>Parameter</td>
</tr>
<tr>
<td>Morphologic response, N</td>
</tr>
<tr>
<td>CR</td>
</tr>
<tr>
<td>mCR</td>
</tr>
<tr>
<td>HI</td>
</tr>
<tr>
<td>Overall</td>
</tr>
<tr>
<td>Transfusion response, N</td>
</tr>
<tr>
<td>RBC</td>
</tr>
<tr>
<td>Platelets</td>
</tr>
<tr>
<td>RBC + Platelets</td>
</tr>
<tr>
<td>Overall</td>
</tr>
</tbody>
</table>

Treatment of Higher Risk MDS

Hypomethylating Agents

Inhibitors of DNA methyl transferases:

Azacitidine
VIDAZA

Decitabine
DACOGEN

![Chemical structures of Azacitidine and Decitabine]

[Graph showing survival rates]

Analysed Population = All Patients
---

Decitabine (N=89)
Supportive Care (N=81)
Azacitidine vs Decitabine

AZA-001 Phase III: AZA vs. Id-ARA-C vs. supportive care

OS benefit: + 9.5 mos

Time to AML: 17.8 vs. 11.5 mos

TI: 45% vs. 11%

Azacitidine Response:

ORR: ~50%

CR: ~17%

Median time to response: 3 cycles (81% by cycle 6)


Novel Treatments for Higher Risk MDS
Guidelines for Higher Risk MDS

**Goal:** to improve **DURATION OF LIFE**

**Special Considerations:**

- **Refer for Transplant Early**
  - Even patients in their 70’s can benefit from RIC transplant

- **AZA > DEC (for now)**
  - AZA has been shown to have a survival advantage, DEC has not (yet)

- **Don’t forget Quality of Life**
  - Consider treatment palliative and weigh against patient needs

- **Look for Clinical Trials**
  - Few option after AZA are available and none are approved

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**Outcomes After Azacitidine**

- Data available on 435 pts
  - from AZA001, J9950, J0443, French compassionate program
- **Overall median survival after azacitidine failure: 5.6 months**

<table>
<thead>
<tr>
<th>Subsequent therapy</th>
<th>Number of patients (%)</th>
<th>Median survival</th>
</tr>
</thead>
<tbody>
<tr>
<td>Allogeneic transplant</td>
<td>37 (9%)</td>
<td>19.5 months</td>
</tr>
<tr>
<td>Investigational therapy (e.g. IMiD, HDACi, other)</td>
<td>44 (10%)</td>
<td>13.2 months</td>
</tr>
<tr>
<td>Intensive cytotoxic therapy (e.g., 3&amp;7)</td>
<td>35 (8%)</td>
<td>8.9 months</td>
</tr>
<tr>
<td>Low-dose chemotherapy (e.g., LDAC, 6-MP)</td>
<td>32 (7%)</td>
<td>7.3 months</td>
</tr>
<tr>
<td>Palliative / supportive care</td>
<td>122 (28%)</td>
<td>4.1 months</td>
</tr>
<tr>
<td>Subsequent therapy unknown</td>
<td>165 (38%)</td>
<td>3.6 months</td>
</tr>
</tbody>
</table>

*Slide borrowed from Dr. David Steensma*

Jabbour E et al *Cancer* 2010;116(16):3830-4
Treatment of Higher Risk MDS

We need **BETTER** therapies!

We need **MORE** therapies!

Targeting Mutant *TP53* with APR-246

*Sallman D et al ASH 2019*
Targeting Cell Death with Venetoclax

Venetoclax - a BCL2 specific inhibitor

Approved for CLL and for AML in combination with an HMA
In trials for MDS in combination with HMA

Pevonedistat

In Phase III study in combination with Azacitididine
for higher risk MDS/CMML/AML
Harnessing the Immune System

Anti-TIM-3 Antibody MBG453

Higher Risk MDS and AML
Treated in combination with decitabine
Early phase studies appear safe
Has evidence of activity
Represents a new paradigm in MDS treatment

Magrolimab (5F9) – Anti-CD47

Anti-Leukemic Activity is Observed with Magrolimab + AZA in MDS and AML

Sallman D et al ASCO 2019
Acknowledgements

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Bejar Lab

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Armon Azizi
Raluka Ciochina
Laura Williams

UC San Diego
Moores Cancer Center

All of our PATIENTS and INFUSION CENTER nurses and staff!

Questions?
Q&A SESSION
Treatment Advances for Myelodysplastic Syndromes (MDS)

• Ask a question by **phone**:  
  – Press star (*) then the number 1 on your keypad.

• Ask a question by **web**:  
  – Click “Ask a question”  
  – Type your question  
  – Click “Submit”

Due to time constraints, we can only take one question per person. Once you’ve asked your question, the operator will transfer you back into the audience line.

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LLS EDUCATION & SUPPORT RESOURCES

• Information Specialists  
  Master’s level oncology professionals, available to help cancer survivors navigate the best route from diagnosis through treatment, clinical trials and survivorship.  
  – EMAIL: infocenter@LLS.org  
  – TOLL-FREE PHONE: 1-800-955-4572

• Caregiver support: www.LLS.org/caregiver

• Free education booklets: www.LLS.org/booklets

• Free telephone/web programs: www.LLS.org/programs

• Live, weekly online chats: www.LLS.org/chat

• LLS Community: www.LLS.org/community

• Information about leukemia: www.LLS.org/leukemia
• LLS Patient Podcast, *The Bloodline with LLS*

Listen in as experts and patients guide listeners in understanding diagnosis, treatment, and resources available to blood cancer patients: [www.thebloodline.org](http://www.thebloodline.org)

• Education Videos

Free education videos about survivorship, treatment, disease updates, and other topics: [www.LLS.org/educationvideos](http://www.LLS.org/educationvideos)

• Patti Robinson Kaufmann First Connection Program

Peer-to-peer program that matches newly diagnosed patients and their families: [www.LLS.org/firstconnection](http://www.LLS.org/firstconnection)

• Free Nutrition Consults

Telephone and e-mail consultations with a registered dietitian: [www.LLS.org/nutrition](http://www.LLS.org/nutrition)

• What to Ask

Questions to ask your treatment team: [www.LLS.org/whattoask](http://www.LLS.org/whattoask)

• Other Support Resources

LLS community, blogs, support groups, financial assistance, and more: [www.LLS.org/support](http://www.LLS.org/support)
THANK YOU!

We have one goal: A world without blood cancers

Additional Information
Iron Balance and Transfusions

Daily intake
1.5 mg (0.04%)
Tightly regulated

Daily losses only
1.5 mg (0.04%)
Not regulated!

3-4 grams of Iron
in the body

Every three
units of blood

What About Iron Chelation?

More transfusions and elevated ferritin levels are associated with poor outcomes in MDS patients.

Are these drivers of prognosis or just reflective of disease?

Retrospective studies suggest survival advantage!

small prospective and large population based Medicare studies show survival benefit, INCLUDING hematologic responses (11-19%).

I consider treatment in lower risk, transfusion dependent patients with long life expectancy after 20+ transfusions.


Three ways are FDA approved:

- Deferoxamine (Desferal) – subcutaneous pump 8-12 hrs/day
- Deferasirox (Exjade/Jadenu) – powder/pill – once per day
- Deferiprone (Ferriprox) – oral pill form – 3x per day

But side effects and adverse events can be significant!

Deferasirox – renal, hepatic failure and GI bleeding
Deferiprone – agranulocytosis (no neutrophils!)
Stem Cell Transplantation

The Allogeneic Transplant Process

1. **Collection**
   - Stem cells are collected from the patient's bone marrow or blood.

2. **Processing**
   - Bone marrow or peripheral blood is taken to the processing laboratory where the stem cells are concentrated and prepared for the freezing process.

3. **Cryopreservation**
   - Bone marrow or blood is preserved by freezing (cryopreservation) to keep stem cells alive until they are infused into the patient's bloodstream.

4. **Chemotherapy**
   - High dose chemotherapy and/or radiation therapy is given to the patient.

5. **Infusion**
   - Thawed stem cells are infused into the patient.
**Trends in Transplantation**

**Goal of Hematopoietic Stem Cell Transplantation:**

#1) Replace a dysfunction host hematopoietic system with normal, healthy donor marrow.

#2) Allow the donor immune system to destroy the abnormal, diseased host cells (MDS).

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**Allogeneic Stem Cell Transplantation for MDS**

- **<5% of patients** with MDS currently undergo allogeneic SCT
- “Only curative therapy”
- Patients who go in to RIC allo SCT with <10% blasts appear to have lower relapse
- Optimal timing, pre-transplant therapy, conditioning unclear; usually reserved for IPSS Int-2/High (IBMTR Markov analysis)

- Survives transplant; MDS cured! (35-40%)
- Survives transplant; MDS recurs/persists (30-40%)
- Dies from complication of transplant (20-25%)

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Slide borrowed from Dr. David Steensma

Obstacles to Transplantation

Graft Rejection
- need to suppress the host immune system

Toxicity
- infection
- organ damage
- graft versus host disease

Finding a Donor
- siblings match only 25% of the time
- and are often too old or ill to donate

Overcoming Obstacles

Avoiding Graft Rejection
- better approaches to immune suppression

Less Toxicity
- better supportive care
- better antigen matching
- *reduced intensity conditioning*

Alternative Sources for Stem Cells
- haploidentical – “half” match
- umbilical cord blood stem cells
Reduce intensity conditioning transplantation in Older Patients with *De Novo* MDS

Trends in Allogeneic Transplants by Transplant Type and Recipient Age* 1990-2010
Allogeneic Transplants for Age > 20yrs, Registered with the CIBMTR, 1993-2010 - by Donor Type and Graft Source -

Related BM/PB
Unrelated BM
Unrelated PB
Unrelated CB