Transplantation for Myelofibrosis

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Scottsdale, February 21, 2015
I will include in our discussion:

- Primary Myelofibrosis (PMF)
- MF after Polycythemia vera (PV)
- MF after Essential Thrombocythemia (ET)
Outline

• Why transplant patients with myelofibrosis?
• How safe is transplantation?
• How effective is transplantation?
• Who should be transplanted and when?
• Summary and conclusions
Primary goal:
The best treatment for every patient!
Myeloproliferative neoplasms (MPN) are diseases of blood forming stem cells:

Hence, replacing the abnormal stem cells with healthy stem cells should cure the disease.
Risk Factors (DIPSSS)
-Developed for non-transplanted patients-

• Anemia
• WBC > 25,000
• Myeloblasts in blood
• Age (> 65 years)
• Symptoms

• Abnormal chromosomes
• Low platelet count
• Needing transfusions
Survival by DIPSS Category
(no transplant)

The availability of JAK2 inhibitor(s) is changing the landscape
Survival with JAK2 inhibitor therapy

Based on Cervantes F et al. Blood 2013;122:4047-4053

<table>
<thead>
<tr>
<th></th>
<th>Ruxolitinib</th>
<th>BAT</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of Patients</td>
<td>146</td>
<td>73</td>
</tr>
<tr>
<td>Events</td>
<td>29 (19.9%)</td>
<td>22 (30.1%)</td>
</tr>
<tr>
<td>Censored</td>
<td>117 (80.1%)</td>
<td>51 (69.9%)</td>
</tr>
</tbody>
</table>
……With some Financial Toxicity………

Based on Cervantes F et al. Blood 2013;122:4047-4053
These findings are impacting transplant decisions and modifying transplant strategies.
Not included in current classifications:

• **Severity** of marrow fibrosis (and fibrosis in *other organs*)
• Spleen size (portal hypertension)
• Duration of the disease
• DNA mutations
H = hepatocytes. Note extensive EMH and collagen deposition (blue stain) in sinusoids.
Fibrosis and Hematopoiesis in the Lung
Could those factors be important for *transplantation*?

- Severity of marrow fibrosis (and fibrosis in other organs) ➤ Non-relapse mortality
- Spleen size ➤ Delayed engraftment; difficult transfusion support
- Duration of the disease ➤ More comorbidities (medical problems developing over time)
- Mutations ➤ ?
Results with Transplantation
### Patient and Disease Characteristics

<p>| | |</p>
<table>
<thead>
<tr>
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</thead>
<tbody>
<tr>
<td><strong>No. of patients</strong></td>
<td>170</td>
</tr>
<tr>
<td><strong>Age (ys) range (median)</strong></td>
<td>12.1–78.9 (51.5)</td>
</tr>
<tr>
<td><strong>Months from diagnosis to HCT (ms), range (median)</strong></td>
<td>2-314 (15)</td>
</tr>
<tr>
<td><strong>Type of myelofibrosis,#</strong></td>
<td></td>
</tr>
<tr>
<td>Primary /post-ET/-post-PV</td>
<td>102 / 46 / 22</td>
</tr>
<tr>
<td><strong>JAK2 mutation, #</strong></td>
<td></td>
</tr>
<tr>
<td>yes/no</td>
<td>43 / 51</td>
</tr>
<tr>
<td>Unknown</td>
<td>76</td>
</tr>
</tbody>
</table>

Scott et al., *Blood* 119:2657-2664, 2012
### Disease Characteristics (#/%)

- **Splenectomy\(^1\)**
  - No: 136 (80)
  - Yes: 31 (18)

- **DIPSS Score**
  - Low: 21 (12)
  - Intermediate-1: 48 (28)
  - Intermediate-2: 50 (30)
  - High: 51 (30)

\(^1\) Data missing in 3
Transplant Characteristics

- Related Donor \( N = 83 \ (50\%) \)
- Unrelated Donor \( N = 84 \ (50\%) \)
- Source of Stem Cells
  - Bone Marrow \( N = 45 \ (26\%) \)
  - Peripheral Blood \( N = 125 \ (74\%) \)

Scott et al., Blood 119:2657-2664, 2012
Survival after Transplantation

- Low (n=21)
- Intermediate-1 (n=49)
- Intermediate-2 (n=55)
- High (n=59)

Years after Transplant

Scott B L et al. Blood 2012;119:2657-2664
CY → BU Conditioning

Rezvani, et al, BBMT 2013
Survival by disease stage

MF
N=113

EB/AML
N=19

H.J.Deeg et al
Overall Survival by Age

BU 10 mg/kg
Flu 180 mg/m²

age ≤ 55 years

age > 55 years

Kröger et al, Blood, 114:5264, 2009
### Survival without and with Transplantation (by DIPSS)

<table>
<thead>
<tr>
<th>DIPPS Risk</th>
<th>Survival (median; years)</th>
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<tbody>
<tr>
<td></td>
<td>No Transplant (at reporting)</td>
<td>Transplant (med F/U 5.9)</td>
<td></td>
</tr>
<tr>
<td>Low</td>
<td>Not reached</td>
<td>Not reached</td>
<td></td>
</tr>
<tr>
<td>Intermediate 1</td>
<td>14.2</td>
<td>Not reached</td>
<td></td>
</tr>
<tr>
<td>Intermediate 2</td>
<td>4</td>
<td>7</td>
<td></td>
</tr>
<tr>
<td>High</td>
<td>1.5</td>
<td>2.5</td>
<td></td>
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</tbody>
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B.Scott, HJ Deeg et al, Blood, 2012
Osteosclerosis: Regression after \textit{high dose conditioning} and HCT (H&E; x250)
Problems

- GVHD
- Organ toxicity
- (Relapse)
Decision Tree

DIPSS Score*

Low (0 points) →
Periodic reassessment →
Observation or conventional therapies

Int-1 (1-2 points) →
Cytogenetic studies (or other clinical features) →
Favorable →
Conventional-conditioning HCT

Unfavorable† →
Younger age, low comorbidity

Int-2/High (≥ 3 points) →

Yes

No

Reduced-intensity HCT

A.Gerds
Summary

• HCT offers effective, curative therapy for patients with MF
  – Follow-up extending beyond 20 years
  – Few relapses

• Safety has improved
  – Decreasing NRM

• Donors are available for most patients

• HCT for MF is appropriate for many patients with advanced MF and for select patients with early stage disease
Thank you

- Ted Gooley
- Barry Storer
- Bart Scott
- Keith Loeb
- And, of course, all our patients