Setting the stage for
Transplant in MPN

Jeanne Palmer, MD
Mayo Clinic, Arizona
What will be covered

What is a bone marrow transplant?
When to start thinking about bone marrow transplant
Timing of transplant
Understanding disease risk
Bone marrow transplantation

• Involves high dose/intermediate dose chemotherapy followed by hematopoietic stem cell infusion.
  • Chemotherapy helps reduce disease + suppress immune system
  • New blood system works better
  • New stem cells fight off underlying disease ‘graft versus myelofibrosis’

• Autologous: uses patients own stem cells, allows use of high dose chemotherapy
• Allogeneic: uses donor stem cells, either related or unrelated
Alternative names

- Alternative names:
  - Peripheral blood stem cell transplant
  - Hematopoietic stem cell transplant
  - Bone marrow transplant

- Bone marrow vs peripheral blood
  - Refers to how the hematopoietic stem cells are collected:
    - Bone marrow: through bone marrow harvest, a procedure performed in the OR
    - Peripheral blood collection: collected after giving neupogen via leukopheresis
Leukopheresis
How does transplant work

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.

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Conditioning

WHY WOULD I WANT TO DO THIS TO MYSELF?

SHOULD I PURSUE A CLINICAL TRIAL INSTEAD?
What are common concerns about transplant?

• Survey done on patients with MPN
• Less than half the patients were referred for transplant
• Of those who saw a transplant specialist, less than half planned on proceeding with transplant due to the following concerns
  • Quality of life
  • Financial implications
  • Caregiver
  • Graft versus host disease
• WHY??
  • Further studies ongoing to understand the thought process around transplant
Other considerations

• Physicians are human and have biases as well
  • Transplant physicians
  • Hematologists

• Blogs
  • Everyone experiences transplant differently
  • People like to share their experiences
Clinical trials and medical treatment

• There are good clinical trials and treatments in MF
  • No curative options yet
• This is a very individualized decision
When do I see a transplant specialist?

• Important to see a transplant specialist early in the disease course—even if you aren’t sure whether you will proceed with transplant or not
  • Understand and plan for the different resources needed for transplant
    • Caregiver
    • Financial
    • Lodging
  • Understand the process of transplant
• Have time to process all the information related to transplant
Who should I see?

- Helpful to see a transplant specialist who has knowledge regarding transplants for MF

  - The timing of transplant is a **SHARED** decision making process

  - There is no one answer that is correct for anyone

- Even if you don’t get a transplant at the center, good to have the discussion/opinion
What to expect during a bone marrow transplant consultation

• Bring a family member/friend
• Be prepared to be scared
• If you can, record the consultation
• If you have any doubts get a second opinion
So, when should I get a transplant?

- Generally transplant is reserved for higher risk patients
- It is important to KNOW YOUR RISK
- Can be dependent on life events
HOW DO WE DEFINE RISK?
Dynamic International Prognostic Scoring System

DIPSS scores/risk:

- 0 pts: low risk
- 1-2 pts: Intermediate – 1
- 3-4 pts: Intermediate – 2
- 5-6 pts: High risk

<table>
<thead>
<tr>
<th>DIPSS</th>
<th>DIPSS plus</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anemia (hgb &lt;10) (2 pts)</td>
<td>DIPSS score</td>
</tr>
<tr>
<td>WBC &gt;25</td>
<td>Platelets &lt;100</td>
</tr>
<tr>
<td>Blasts &gt;1%</td>
<td>Transfusion dependant</td>
</tr>
<tr>
<td>Constitutional symptoms</td>
<td>poor risk cytogenetics: complex karyotype or</td>
</tr>
</tbody>
</table>
|                            | any sole or two abnormalities including +8, -7/7q-,
|                            | -5/5q-, inv(3), i(17q), 12p-, 11q23 rearrangement |
| Age >60                    |                                                |

DIPSS plus scores/risk:

- 0 pts: low risk
- 1 pt: intermediate-1
- 2-3 pts: intermediate-2
- 4-6 pts: high risk
Clarification of risks

- Anemia–low red blood cell count. Hemoglobin (hgb) is consistently less than 10
- Thrombocytopenia - low platelet (plt) count, less than 100.
- Leukocytosis – high white blood cell count (WBC), consistently greater than 25
- Blasts – immature white blood cells
  - Note this does not mean you have leukemia unless blast % greater than 20%
- Abnormal karyotype
- Constitutional symptoms- fatigue, weight loss, decreased appetite, night sweats
Stem cell transplant spectrum timing tool

- This tool uses DIPSS score to give a sense of when a transplant should be considered

- Even in the case of low risk disease- good to start the conversation

- http://www.mpntransplant.com/
When to **think about a transplant**

- **DIPSS low risk or Int-1 risk**
- **DIPSS Int-2 risk**
- **DIPSS High risk, advanced disease with organ dysfunction**

Diagnosis of disease
When to do transplant

Too early! DIPSS low risk or Int-1 risk

Just right

DIPSS Int-2 risk

Too late! DIPSS High risk, advanced disease with organ dysfunction

Diagnosis of disease
Other factors that contribute to risk

• Driver mutation
• Cytogenetics
• Molecular mutations
Driver mutation

- Mutations that CAUSE the disease
  - JAK-2
  - MPL
  - CAL-R
- CAL-R is GOOD
- No mutations is unfavorable
Cytogenetics

- Cytogenetics (abnormal chromosomes found in your bone marrow)
  - complex karyotype (3 or more abnormalities) or sole or 2 abnormalities that include +8, −7/7q−, i(17q), inv(3), −5/5q−, 12p−, or 11q23 rearrangement

*These are not inherited... they are changes that occur only in disease cells*
Molecular mutations
“next generation sequencing”
Good news

- The disadvantages of high risk disease are usually overcome with transplant!!
When to **do** transplant

- **Too early!**
  - DIPSS low risk or int-1 risk

- **Just right**
  - Bad risk chromosomes/mutations

- **Too late!**
  - High risk, advanced disease with organ dysfunction

- **Good risk mutations**
Other considerations

- Symptom burden
- Ruxolitinib (Jakafi©)
- Transfusion dependence
- What gives you points??
Example #1

- 64 year old patient with primary myelofibrosis
- CAL-R positive
  - On 1/5/19 WBC 23K, 2% blasts, hgb 9.7, platelets 115 (DIPSS: 3)
  - On 2/5/19 WBC 26K, 0 blasts, hgb 10.2, platelets 150 (DIPSS: 1)
- Would this change if JAK2 positive?
- ASXL1 positive?
Example #2

• Patient is 58 year old female with post-essential thrombocythemia myelofibrosis

• MPL positive

• Hgb 7, requires transfusion every month, WBC 6.7, Blasts 0  DIPSS: 2
Example #3

- 65 year old male with primary myelofibrosis
- JAK2 positive
- Hgb 9.5, WBC 7.2, blasts 0, platelets 165  DIPSS: 3
Summary

• Bone marrow transplant is a curative option for myelofibrosis

• When the best time to undergo transplant is still under investigation

• Know your risk! The risk of disease as characterized by cytogenetics, molecular mutations etc
Survivors