Allogeneic Stem Cell Transplantation for Elderly Myelofibrosis Patients (> 60 years)

Pro: allo

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Primary or post ET/PV myelofibrosis is a malignant hematopoietic stem cell disease mainly of elderly patients (median age at diagnosis 65-70)
Myeloproliferative Neoplasms (MPN)

- **CML**: Chronic neutrophilic leukemia
- **PV**: Polycythemia vera
- **ET**: Essential Thrombocytopenia
- **PMF**: Primary Myelofibrosis
- **Mastocytosis**
- **MPN, unclassifiable**

**Bcr-Abl**
- **CML**: Present
- **PV**: Absent

**JAK2 617F**
- **PV**: Present (ca. 95%)
- **ET**: Present (ca. 50%)
- **PMF**: Present (ca. 50%)

**KIT**
- Present
- **Cutaneous**
- **Systemic**
- **Mast cell leukemia**
- **Mast cell sarcoma**
- **Extracutaneous mastocytosis**
Primary or post ET/PV myelofibrosis has a variable course of the disease.
# Primary myelofibrosis (n=1054): IPSS score

**Risk factors**

<table>
<thead>
<tr>
<th>Risk Category</th>
<th>Med. OS</th>
<th>Median Survival (months)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low rik (0)</td>
<td>med. OS</td>
<td>135</td>
</tr>
<tr>
<td>Intermediate 1 (1)</td>
<td>med. OS</td>
<td>95</td>
</tr>
<tr>
<td>Intermediate 2 (2)</td>
<td>med. OS</td>
<td>48</td>
</tr>
<tr>
<td>High (≥ 3)</td>
<td>med. Os</td>
<td>27</td>
</tr>
</tbody>
</table>

1. Age ≥ 65 years
2. Constitutional symptoms
3. Circulating blasts ≥ 1%
4. Hb ≤ 10 g/dl
5. WBC ≥ 25 x 10⁹/l

*Cervantes et al., Blood 2009, Passamonti et al Blood 2010*
Risk model according IPSS: non transplant

Non-transplant (n=1054) : Cervantes et al., Blood 2009
Myelofibrosis Conventional Therapy

### Anemia
- Thalidomide 50-400 mg
- Prednisone 0.5 mg/kg/day
- Danazol 400 mg po bid
- Erythropoietin 40,000 U SC weekly

### Symptomatic splenomegaly
- Hydroxyurea 500 mg tid
- Hydroxyurea + EPO
- Splenectomy
- Spleen-radiation

**New options:**
- Lenalidomide
- Pomalidomide
- JAK2 inhibitors

Anemia
Symptomatic splenomegaly
Conventional treatment (incl. JAK2 inhibitors and lenalidomide) can improve symptoms, but none has been shown to prolong survival in PMF patients.
Overall survival after RIC allogeneic stem cell transplantation in 103 myelofibrosis patients (EBMT trial)

67% (95% CI: 55-79%)
Fact 4

Allogeneic stem cell transplantation can cure PMF patients but there is a risk for transplant-related morbidity and mortality.
Fact 5: Age is an important risk factor

- Age ≤ 55 years
- Age > 55 years
A 63 year old otherwise healthy patients with no comorbidities but with intermediate II or high risk

Myelofibrosis has despite conventional treatment a median life expectancy of only 4 or 2 years, respectively
Life expectancy (according UNO)
A 61 year old otherwise healthy patients with no comorbidities but with intermediate II or high risk Myelofibrosis has despite conventional treatment a median life expectancy of only 4 or 2 years, respectively. If this patient would not have PMF the life expectancy (at least in the western world) would be 80 to 84 years for a female pts and 75 to 79 years for a male pts. This patient would loose about 15 to 20 years of life... Is this acceptable or satisfied for the patient and the treating physician? Certainly „no“.....
### Allograft in Myelofibrosis in EBMT

<table>
<thead>
<tr>
<th></th>
<th>2002</th>
<th>2010</th>
</tr>
</thead>
<tbody>
<tr>
<td>Allograft</td>
<td>153</td>
<td>467</td>
</tr>
<tr>
<td>RIC</td>
<td>76 (50%)</td>
<td>302 (~ 65%)</td>
</tr>
<tr>
<td>&gt; 50 yrs</td>
<td>86 (56%)</td>
<td>353 (~ 75%)</td>
</tr>
</tbody>
</table>

unpublished EBMT data
Allogeneic SCT in myelofibrosis patients > 60 years

n = 30
Median age: 65 years (r. 60 – 78 yrs)
MUD n = 15
MRD n = 15
Various conditioning regimen

Samuelson et al., BJH 2011
Allogeneic haematopoietic cell transplantation for myelofibrosis in 30 patients 60–78 years of age

Samuelson et al BJH 2011
Allogeneic SCT in elderly PMF patient
(German experience)

- $n = 57$

- Median age: 64 yrs (60-73)

- **Donor:**
  - MUD: $n = 32$
  - Mismatch MUD: $n = 15$
  - Related: $n = 10$

- **IPSS:**
  - Intermediate 1: $n = 7$
  - Intermediate 2: $n = 10$
  - High: $n = 36$

- **Conditioning regimen:** Busulfan 10 mg/kg/ fludarabine

*unpublished data*
Allogeneic SCT in elderly PMF pts (median age 64y)
(MRD n= 10  and MUD n= 32)

unpublished data
Allogeneic SCT in elderly PMF pts (median age 64y)
(intermed.-1: n= 6; intermed.-2: n= 11 high: n= 36)

unpublished data
Allogeneic SCT in elderly PMF pts (median age 64y) (IPSS high: n= 36: 3 vs >3 risk factors)
Treatment decision for elderly PMF

Allografting

treatment related mortality  potential cure
alternative options

Balance according: 1. performance status/ comorbidity
2. life expectancy (e.g. IPSS)