Transplantation for MPN 2021
(PMF, PV, ET)

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Outline

• Classifications
• Transplant Indications
• Transplant Strategies
• Outcome
Risk Classification

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

- Abnormal chromosomes
- Low platelet count
- Requiring transfusions

- Mutations
  - JAK2, MPL1, CALR
  - ASXL1, p53, etc

DIPSS

DIPSS plus

MIPSS and more
However

- Extramedullary disease, portal or pulmonary hypertension, are not included in current risk classification schemes, but increase the risk of non-relapse morbidity and mortality after transplantation.
Transplant Indications

- Marrow failure/cytopenias
- Disease “acceleration”
- Leukemic transformation
- Failure of non-transplant modalities
Progression-free survival by DIPSS plus
(all regimens)

Samuelson B et al BBMT 24:386, 2017

N= 233
P=0.0001
Non-Relapse Mortality (adjusted)

P=0.02

Samuelson B et al BBMT 24:386, 2017
Age and Survival

P=0.04

Samuelson B et al BBMT 24:386, 2017
Pre-Tx Ruxolitinib

R.B. Salit et al, BMT 55:70, 2020
RIC for PMF – OS, PFS and Relapse

V. Gupta et al, BBMT 2014
Salvage after Ruxolitinib

A. Kuykendall et al, Annals of Hematology, 97: 435, 2018
Impact of Mutations
Relapse-Free Survival by Mutation #

1/11 ≥ 3 (survived)

< 3 N = 22

≥ 3 N = 22

p < 0.001

E. Stevens et al, BBMT 26:1371, 2020
### “Additional” Mutations and Transplant Outcome

(48 patients)

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<tr>
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<th>≤2 mutations</th>
<th>≥3 mutations</th>
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<tr>
<td>Survived &gt;1 year after Transplantation</td>
<td>79%</td>
<td>41%</td>
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<tr>
<td>Death from Non-Relapse Causes</td>
<td>13%</td>
<td>35%</td>
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<tr>
<td>Relapse</td>
<td>8%</td>
<td>24%</td>
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E. Stevens et al, BBMT 26:1371, 2020
A. Haris et al, Blood Advances 3 : 83, 2019
Overall Survival and NRM

A. Haris et al, Blood Advances 3 :83, 2019
Simplified Transplant Risk Score
Transplant Risk Score and Outcome

• Mortality
  – ↑ with HCT-Cl ≥ 3 (+1), HLA ≠ unrelated donor, Cord blood (+1)
  – ↓ post-Tx CY (-1)

• 5-year survival (by score)
  – -1 = 79%
  – 0 = 55%
  – +1-2 = 32%

• MTSS did not discriminate

Hernandez-Boluda et al, BBMT (TCT) 26:2237, 2020
Transplant Risk Score and Outcome

Hernandez-Boluda, Pereira et al  TCT 26: 2237, 2020
Prognosis after Post Tx Relapse

- N=94 surviving in CR ≥ 5 years
  - Of these, 13 (14%) relapsed at a median of 7.1ys
  - Treated with DLI (N=7) or 2nd Tx (N=4)
  - N=8 (72%) achieved CR, 7 survived > 3 ys following relapse

Atagunduz et al, BBMT (TCT) 26:2279, 2020
Risk of Disease Progression

• Signals of “impending” transformation
  • Short term: IDH1/2, Runx 1, U2AF1
  • Long term: TP53, NRAS, BCORL1

• Risk of transformation (in PV and ET)
  • SRSF2, ASXL1, RUNX1, EZH2, IDH1/2, TP53
  • SF3B1 predominantly in ET

D.L Paz et al Blood Advances 4(19)4887, 2020
A. Tefferi et al, Br.J. Haematology 2020
Transplantation for Myelofibrosis with Leukemic Transformation

OS and PFS by Chemotherapy response

H. Alchalby et al., ..... 2014
Thoughts on Genetics and treatment options

• Relevance of early acquisition of JAK2 mutation
  – Jak 46/1, germ line variant
  – Target genes: ATM, SH2B3, CHEK2; non-coding regions

• CHIP
  – Aging
  – Inflammation, infection

• Pre-emptive/adjuvant therapy
  – Targets pre-transplant
  – Post-transplant adjuvant treatment
Summary and Conclusions

• Tx does cure many patients with MF
  – With high or reduced intensity regimens
• Outcome is superior
  – In early/lower grade disease
  – In the absence of (multiple) high risk mutations
  – In the absence of co-morbidities
  – With the use of post-Tx Cytoxan
• Salvage is possible after post-Tx relapse
Thank you

- Bart Scott, Rachel Salit
- Janghee Woo
- Jerry Radich, Emily Stevens
- Barry Storer, Ted Gooley
It takes a (big) team
Relapse-Free Survival by ASXL1

E. Stevens et al, BBMT 26:1371, 2020
Germline genetic variants and CHIP

- 97691 paired samples from TOPmed
- 4229 developed CHIP
  - Three loci associated with CHIP
    - Near TET2 (chromosome 4)
    - TERT (chromosome 5)
    - Intergenic region KPNA4 – TRIM59 (chro. 3)

Bick et al, Nature 586:763, 2020