Transplantation for MPN 2021 (PMF, PV, ET)

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12th J. Niblack virtual Conference on MPN, Scottsdale, AZ, February 202

Outline

- Classifications
- Transplant Indications
- Transplant Strategies
- Outcome

Risk Classification

DIPSS

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



- Low platelet count
- Requiring transfusions
- Mutations



- ASXL1, p53, etc



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)



Non-Relapse Mortality (adjusted)



Samuelson B et al BBMT 24:386, 2017

Age and Survival



Samuelson B et al BBMT 24:386, 2017

Pre-Tx Ruxolitinib



RIC for PMF – OS, PFS and Relapse



Salvage after Ruxolitinib



A. Kuykendall et al , Annals of Hematology, 97: 435, 2018

Impact of Mutations

Relapse-Free Survival by Mutation #



"Additional" Mutations and Transplant Outcome (48 patients)

	≤2 mutations	≥3 mutations
Survived >1 year after Transplantation	79%	41%
Death from Non-Relapse Causes	13%	35%
Relapse	8%	24%

E.Stevens et al, BBMT 26:1371, 2020



Donor Type, Cytogenetics, Mutations, MIPSS70 and Transplant Outcome

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-CI ≥ 3 (+1), HLA ≠ unrelated donor, Cord blood (+1)

 $-\downarrow$ 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=227, Transplanted in 1994 2015
- N=94 surviving in CR \ge 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
- SF3B1predominantly 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

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; noncoding 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