French & English SFGM-TC Day

February 07, 2024

10:00 to 16:00

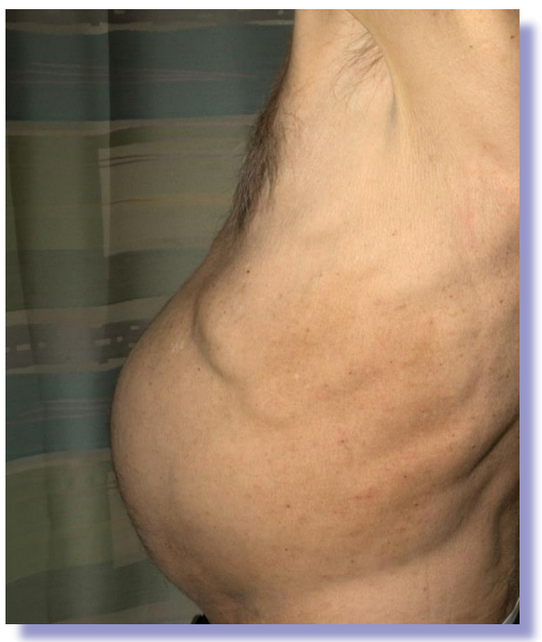
Musée des Moulages – Hôpital Saint Louis – PARIS

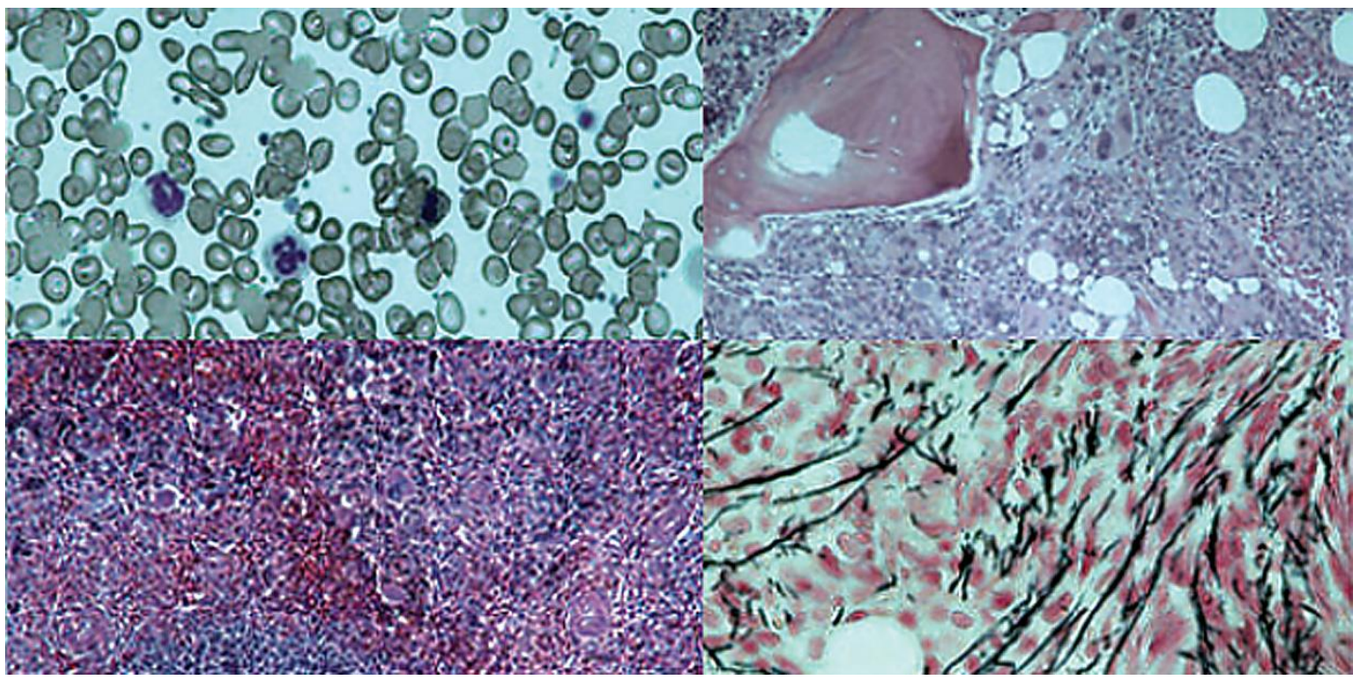
«Role of transplantation in myelofibrosis»

Allogeneic Stem Cell Transplantation for Primary Myelofibrosis

Eduardo Olavarría

BMT Director
Imperial College Healthcare NHS Trust



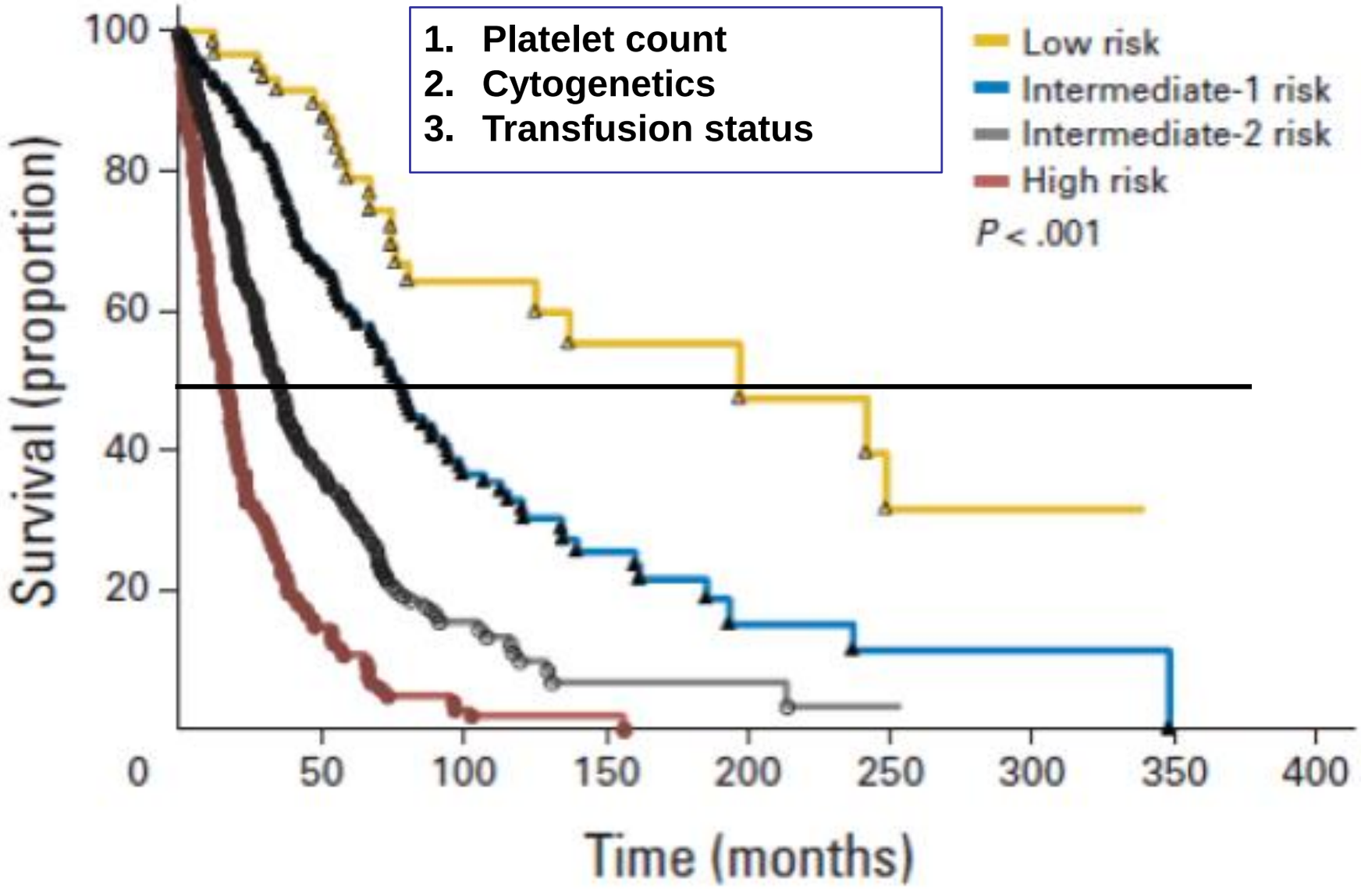


Overview

Myelofibrosis: who to transplant and when?

- Prognosis and prognostic factors: **the who?**
- Timing of a possible allogeneic SCT: **the when?**

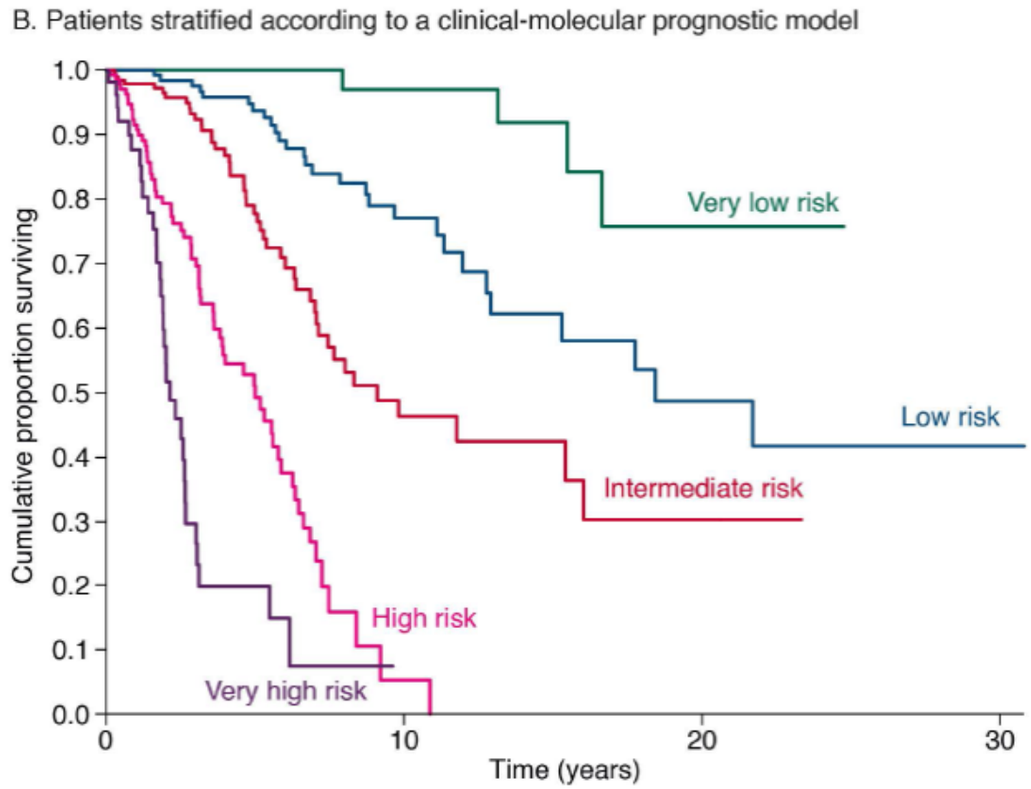
DIPSS Plus



Gangat N et al. J Clin Oncol. 2011. 29:392-7

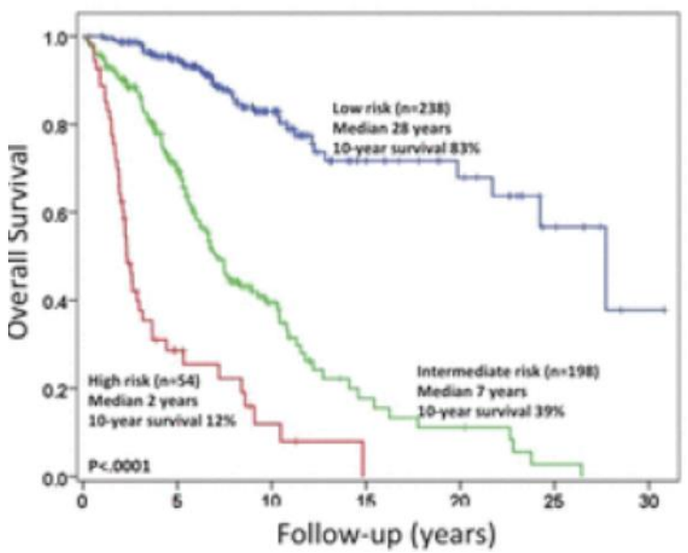
MIPSS and MIPSS70+

MULTIVARIATE ANALYSIS		
Variables	**HR (95% CI)**	**P**
Age >60yrs	3.8 (2.60-5.51)	<0.0001
Hb <100g/L	1.4 (1.01-1.99)	0.04
Constitutional Symptoms	1.5 .(1.13-2.16)	0.007
PLT <200x10^9/L	2.5 (1.77-3.42)	<0.0001
Triple Negativity	3.9 (2.20-6.80)	<0.0001
JAK2/MPL mutation	1.8 (1.11-2.90)	0.016
ASXL1 mutation	1.4 (1.06-1.99)	0.02
SRSF2 mutation	1.7 (1.08-2.58)	0.02



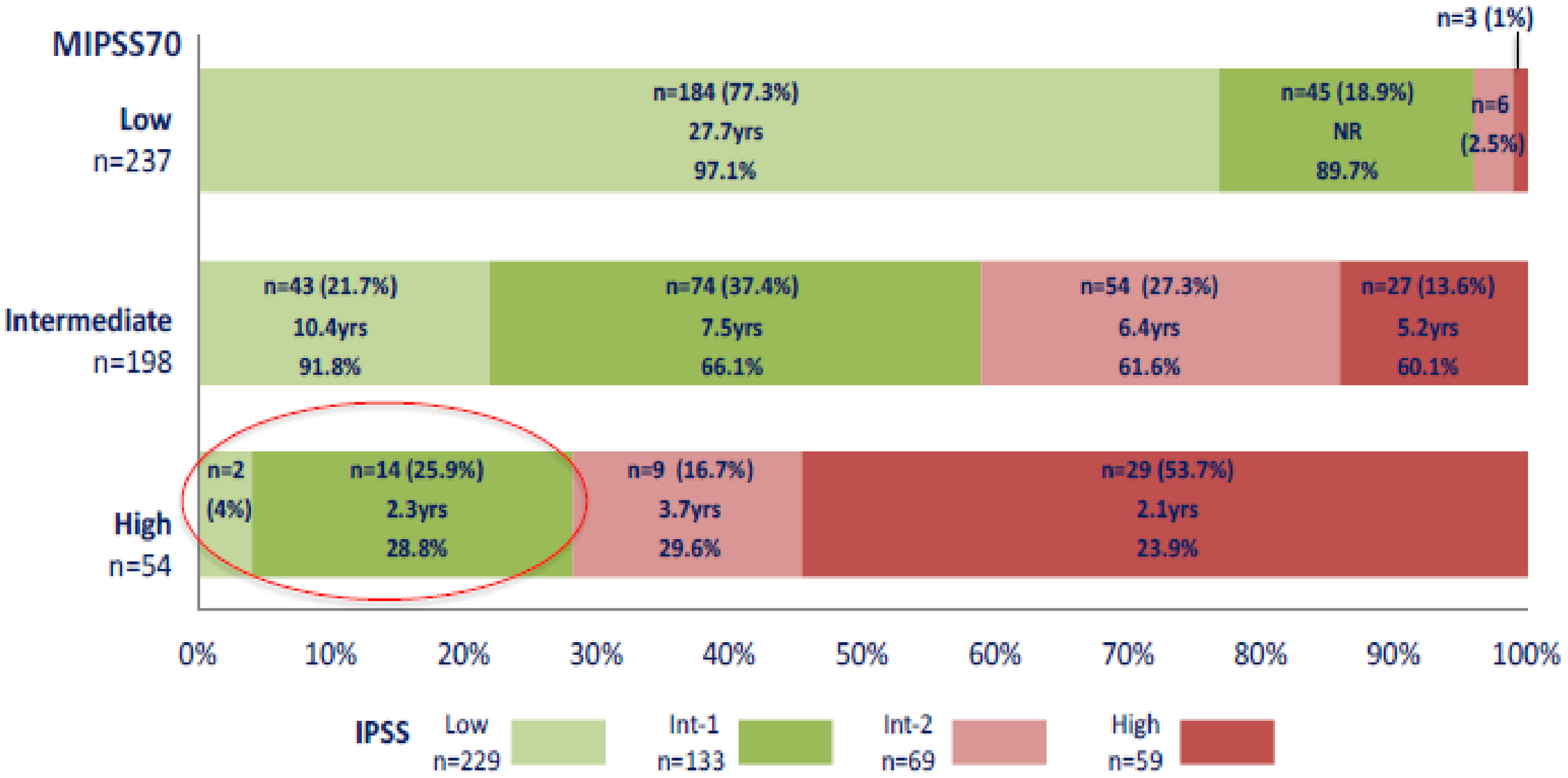
Variables	HR (95% CI)	P	Weighted value
Hb <100g/L	1.9 (1.32-2.71)	<0.001	1
WBC >25x10^9/L	3.8 (2.21-6.64)	<0.001	2
PLT <100x10^9/L	3.2 (2.09-4.77)	<0.001	2
PB blasts ≥2%	1.7 (1.17-2.54)	.006	1
Constitutional Symptoms	2.18 (1.57-3.03)	<0.001	1
Grade ≥2 BM fibrosis	1.9 (1.34-2.71)	<0.001	1
Absence *of CALR* Type1	1.9 (1.21-2.96)	.005	1
HMR category*	1.8 (1.26-2.49)	.004	1
≥2 HMR mutations	3.9 (2.43-6.40)	<0.001	2

HMR category includes mutations in U2AF1



Runni et al, Blood 2016
Vannuchi et al, 2017
Gugliemelli et al, 2018
Tefferi et al. Leukemia 2018

Patients' Redistribution Across IPSS and MIPSS70 Risk Scores



Courtesy of A M Vannucchi

So, who should we transplant?

We should transplant every patient that is unlikely to do well with non-transplant therapies and that is likely to do well after transplant.

Mary Horowitz, Hammersmith Advances in Haematology Course, June 2017

High Risk Group (IPSS, DIPSS, DIPSS Plus)
Under the age of 70 years

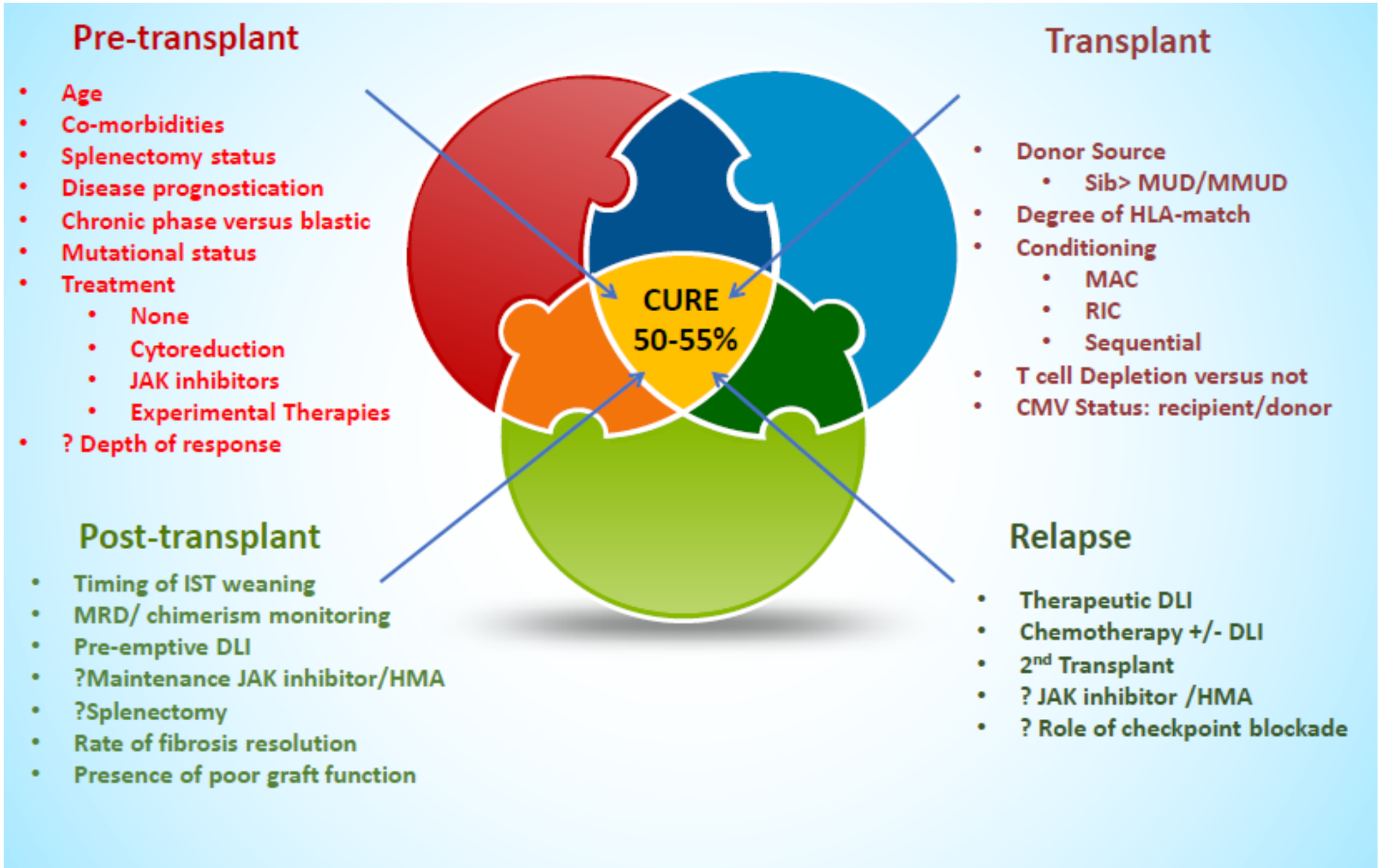
Molecular profile unfavourable (MIPSS70+)
Triple negative, ASXL1, SRSF2, U2AF1 mutations

Intermediate-2 Risk Group (IPSS, DIPSS, DIPSS Plus)
Under the age of 70 years (65 years if CALR+)

Intermediate-1 Risk Group (IPSS, DIPSS, DIPSS Plus)
Under the age of 65 years and refractory anaemia

Eduardo Olavarria – Personal Opinion, February 2024

Factors affecting transplant outcomes



McLornan et al, Haematologica. 2019 Apr;104(4):659-668.

Comprehensive clinical-molecular transplant scoring system for myelofibrosis undergoing stem cell transplantation

MTSS Prognostic score to determine prognosis after allo-SCT using clinical, molecular and transplant-specific information of a total of 361 myelofibrosis patients.

1. **Age ≥ 57 years**
2. **Karnofsky performance status < 90%**
3. **Platelet count < 150 x 109/L**
4. **Leukocyte count > 25 x 10^9/L prior to transplantation**
5. **HLA-mismatched unrelated donor**
6. **ASXL1 mutation and non-CALR/MPL driver mutation genotype**

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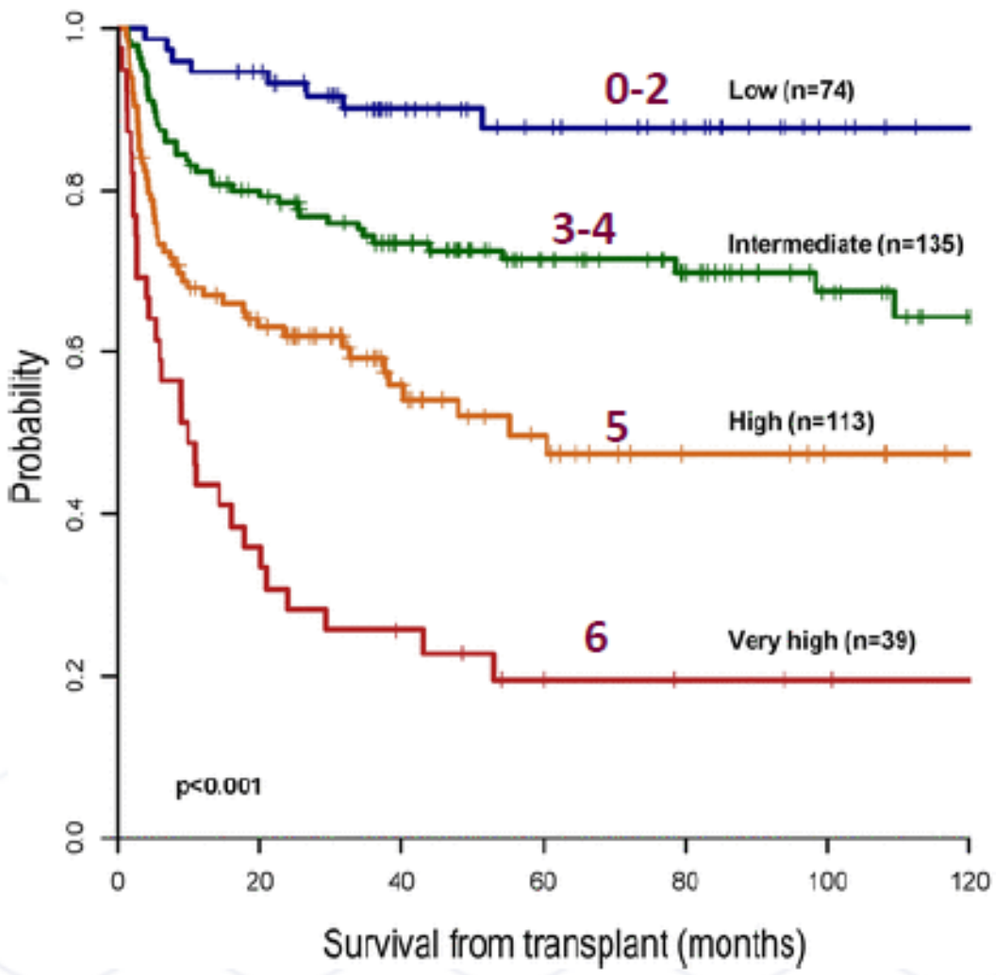
Increasing score was predictive of OS, NRM ($p < 0.001$) and applicable to PMF and sMF



Gagelmann et al, 2019 Blood

Is the co-morbidity index applicable to patients with Myelofibrosis?

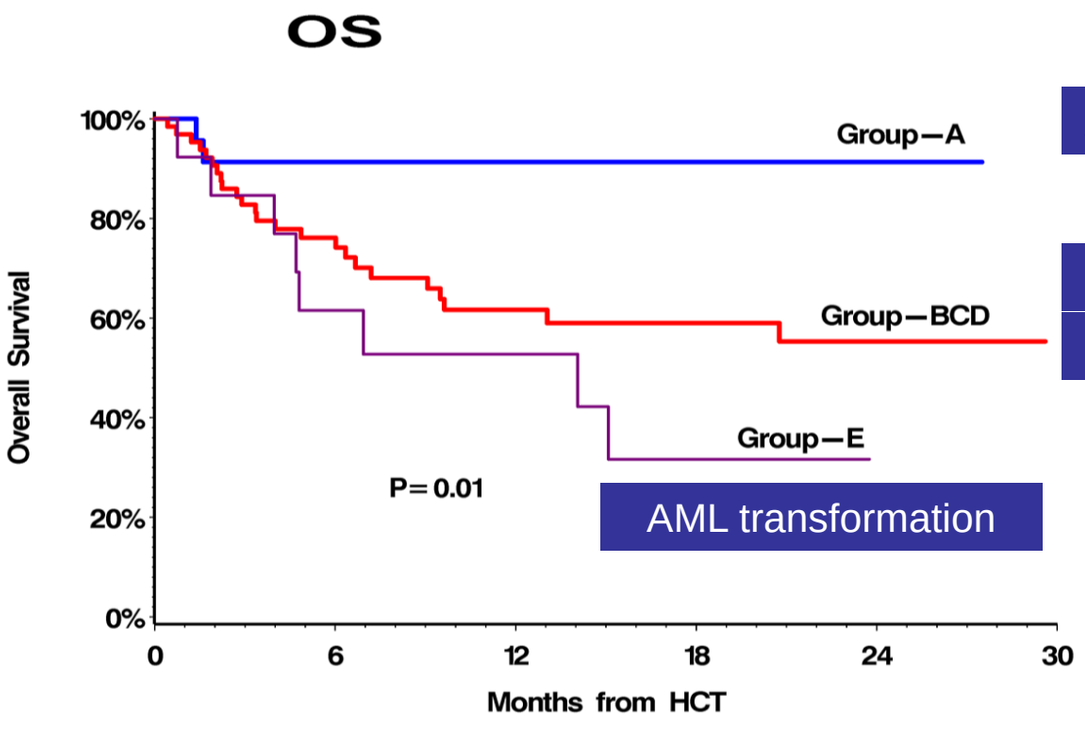
Comorbidity	HCT-CI weighted scores
Arrhythmia	1
Cardiac	1
Inflammatory bowel disease	1
Diabetes	1
Cerebrovascular disease	1
Psychiatric disturbance	1
Hepatic, mild	1
Obesity	1
Infection	1
Rheumatologic	2
Peptic ulcer	2
Moderate/severe renal	2
Moderate pulmonary	2
Prior solid tumor	3
Heart valve disease	3
Severe pulmonary	3
Moderate/severe hepatic	3

Sorror M, et al. Blood 2005 106;2912-2919

In Theory Ruxolitinib Could…

Ruxolitinib on PMF	Ruxolitinib on SCT
Improve symptoms (co-morbidities)	↓ TRM (NRM)
Reduce Splenomegaly	↓ TRM Graft Failure
Reduce Allelic Burden	↓ Relapses??
Improve Cytokine Profile	↓ TRM GVHD??
Improve Marrow Fibrosis	↓ Graft Failure

Response to Ruxolitinib and SCT

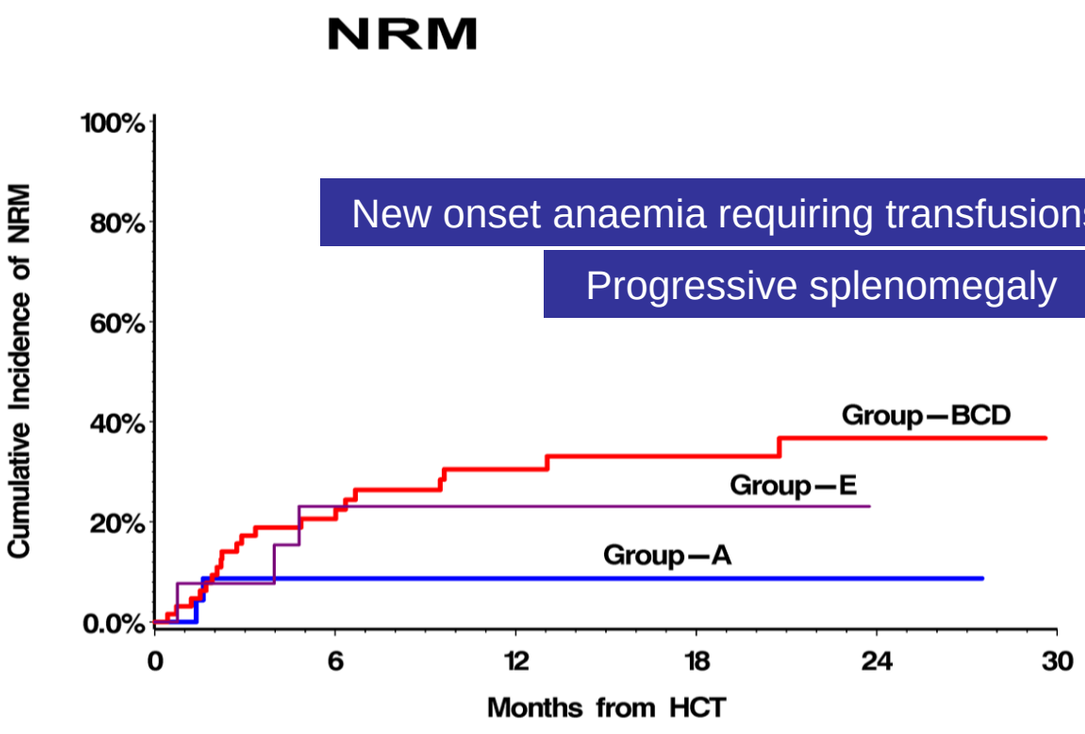


At least ≥50% reduction in splenomegaly

Progressive splenomegaly

New onset anaemia requiring transfusions

AML transformation



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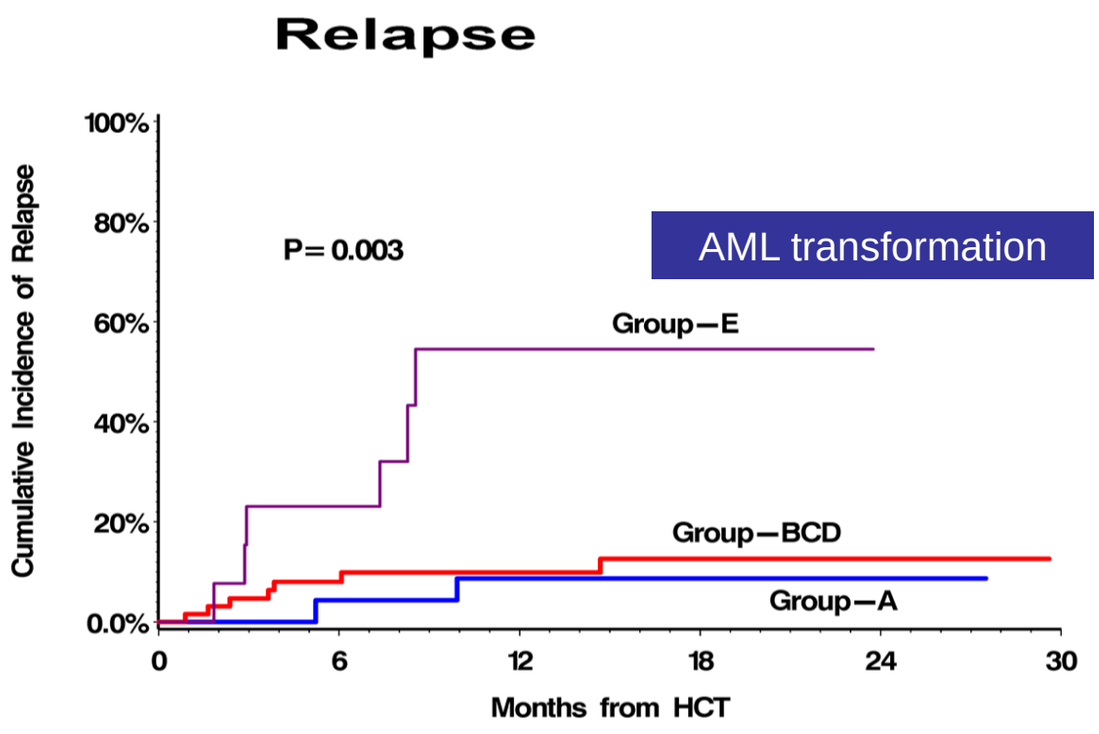
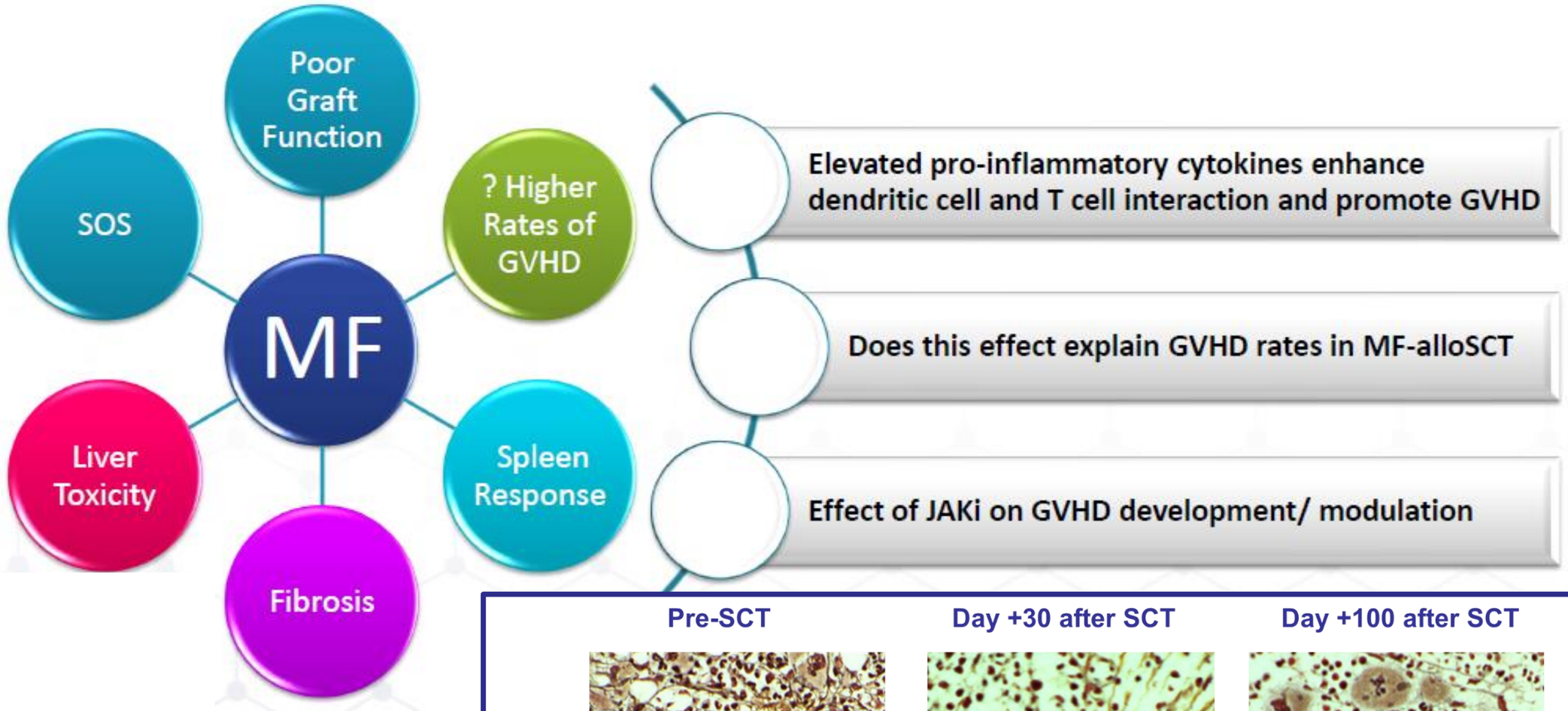


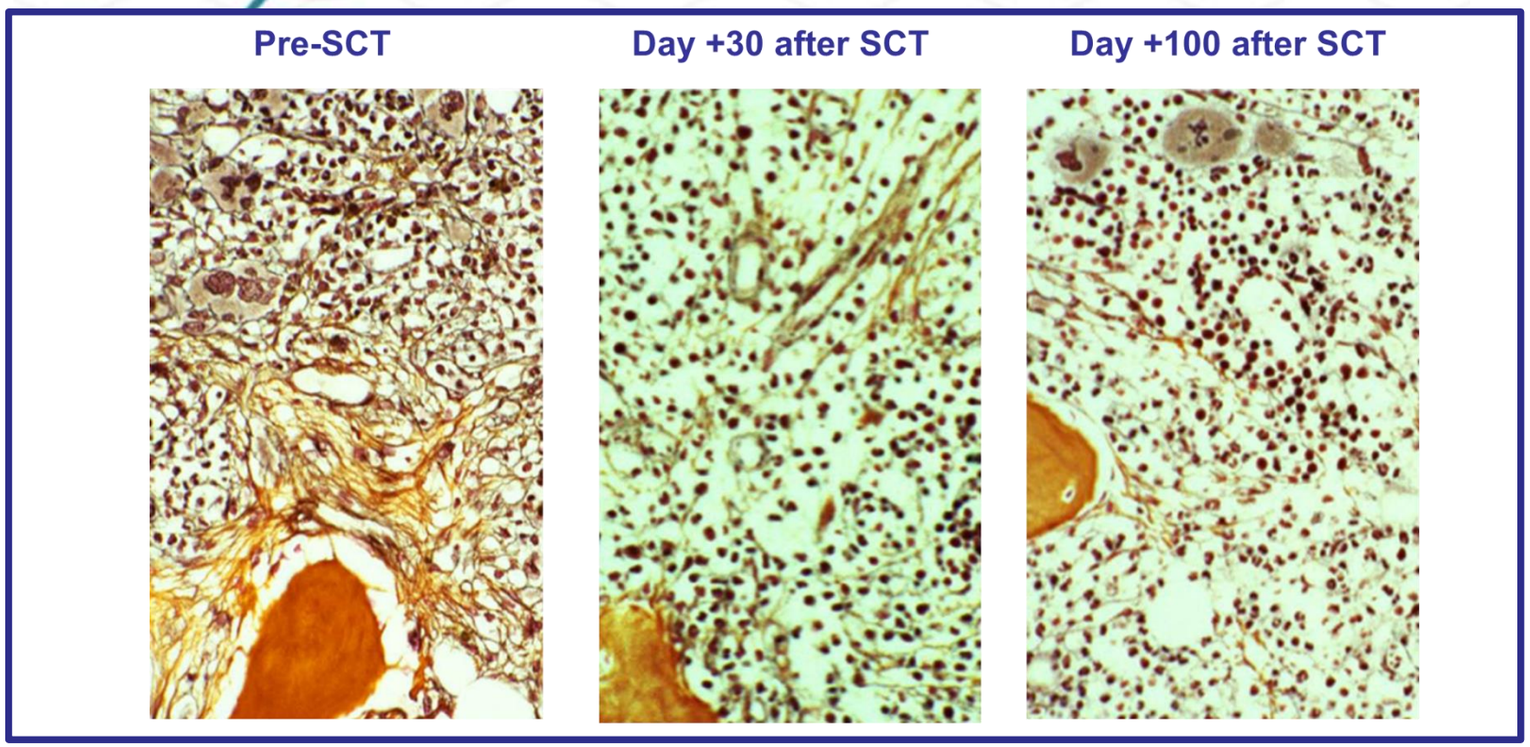
AML transformation

Shavanas et al., BBMT 2015

All SCT in Primary Myelofibrosis

These transplants are “special”





Kröger et al, Blood 2009, 114:5264,

Thank you for your attention