Transplantation for Myelofibrosis

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I will include in our discussion:

- **Primary Myelofibrosis (PMF)**
- **MF after Polycythemia vera (PV)**
- **MF after Essential Thrombocythemia (ET)**

Outline

- **Why transplant patients with myelofibrosis?**
- **How safe is transplantation?**
- **How effective is transplantation?**
- **Who should be transplanted and when?**
- **Summary and conclusions**

Primary goal:
The best treatment for every patient !

Myeloproliferative neoplasms (MPN) are dieseases of blood forming stem cells:

Hence, replacing the abnormal stem cells with healthy stem cells should cure the disease.

Risk Factors (DIPSS)

-Developed for non-transplanted patients-

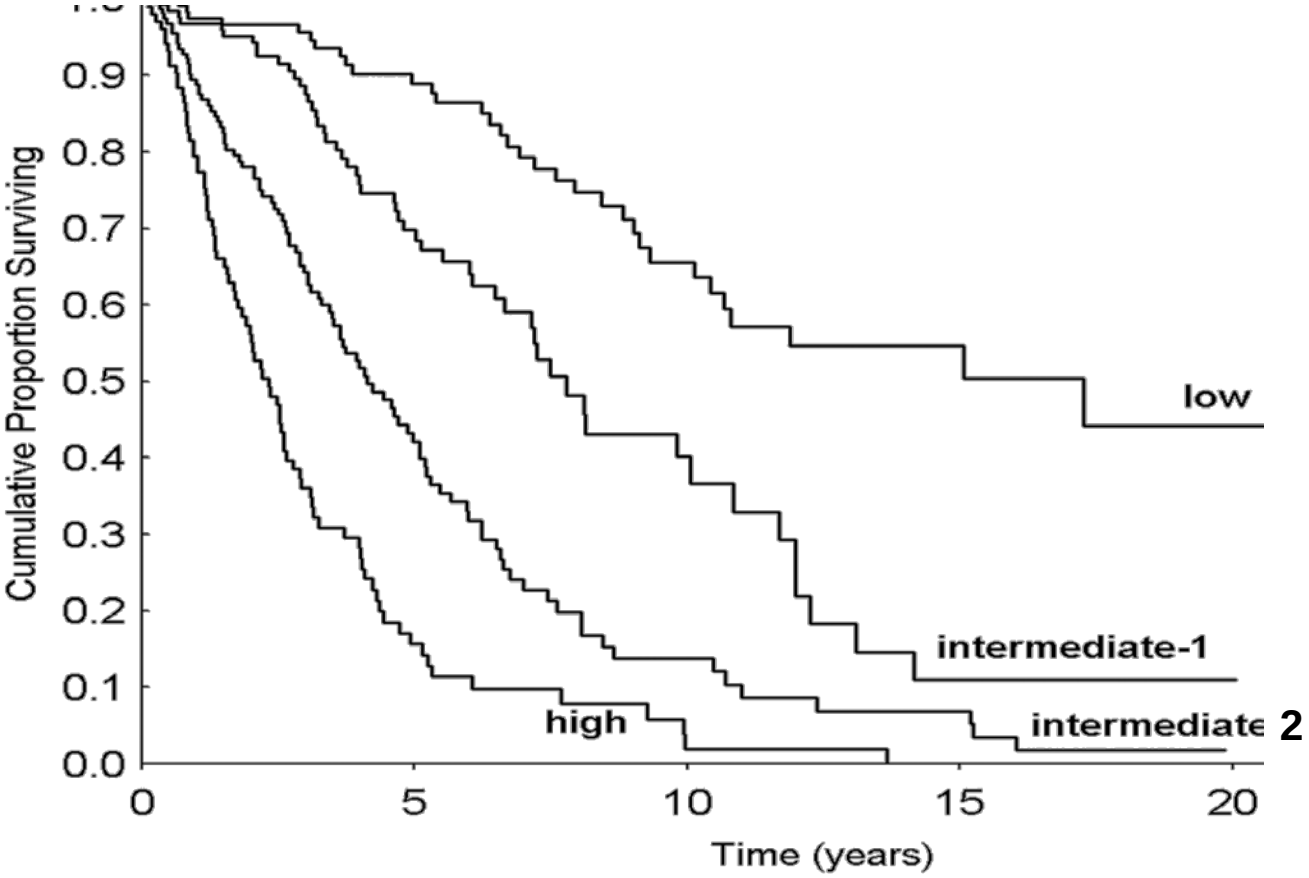
- Anemia
- WBC > 25,000
- Myeloblasts in blood
- Age (> 65 years)
- Symptoms

DIPPS

- Abnormal chromosomes
- Low platelet count
- Needing transfusions

DIPPS plus

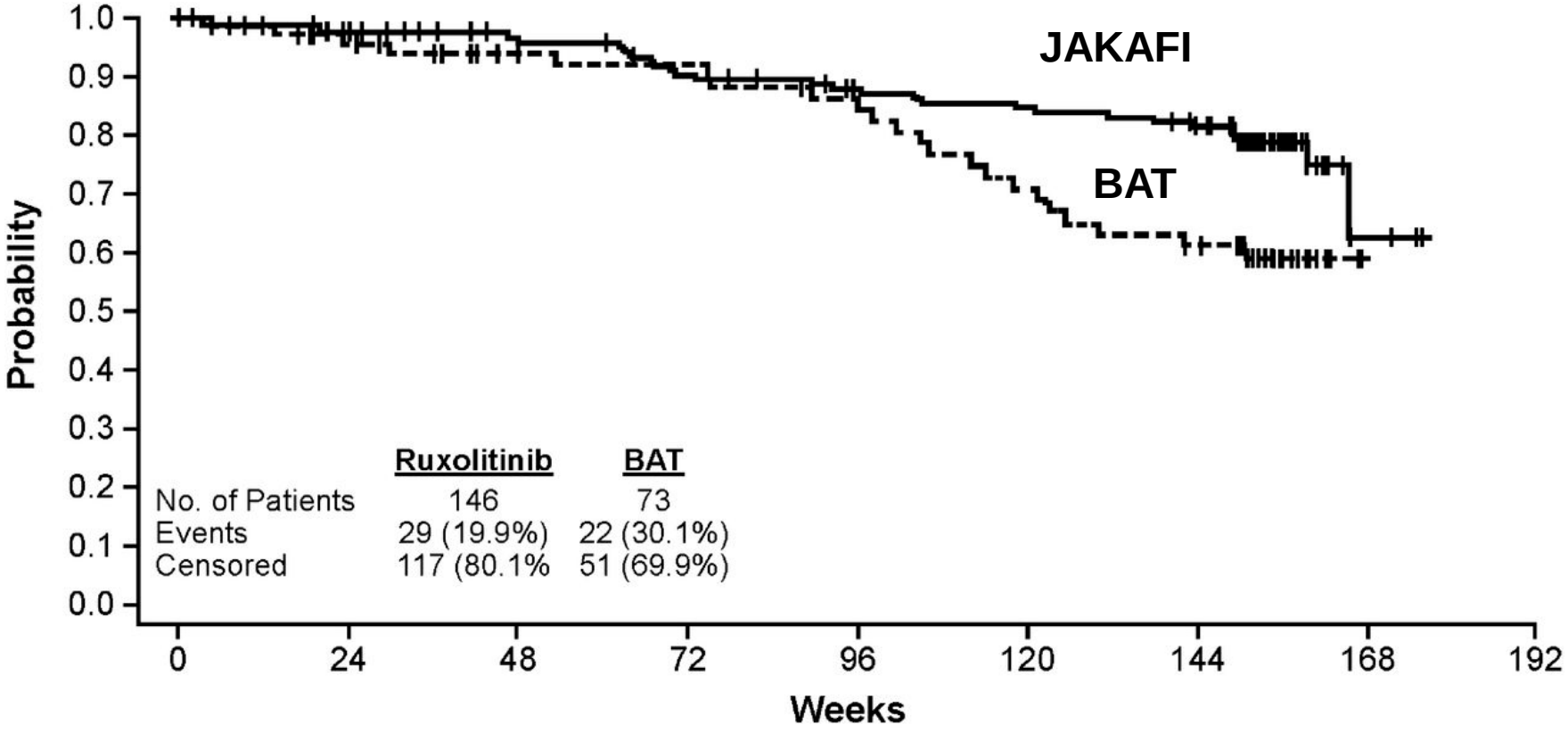
Survival by DIPSS Category
(no transplant)



Passamonti F, et al. *Blood*. 2010;115:1703

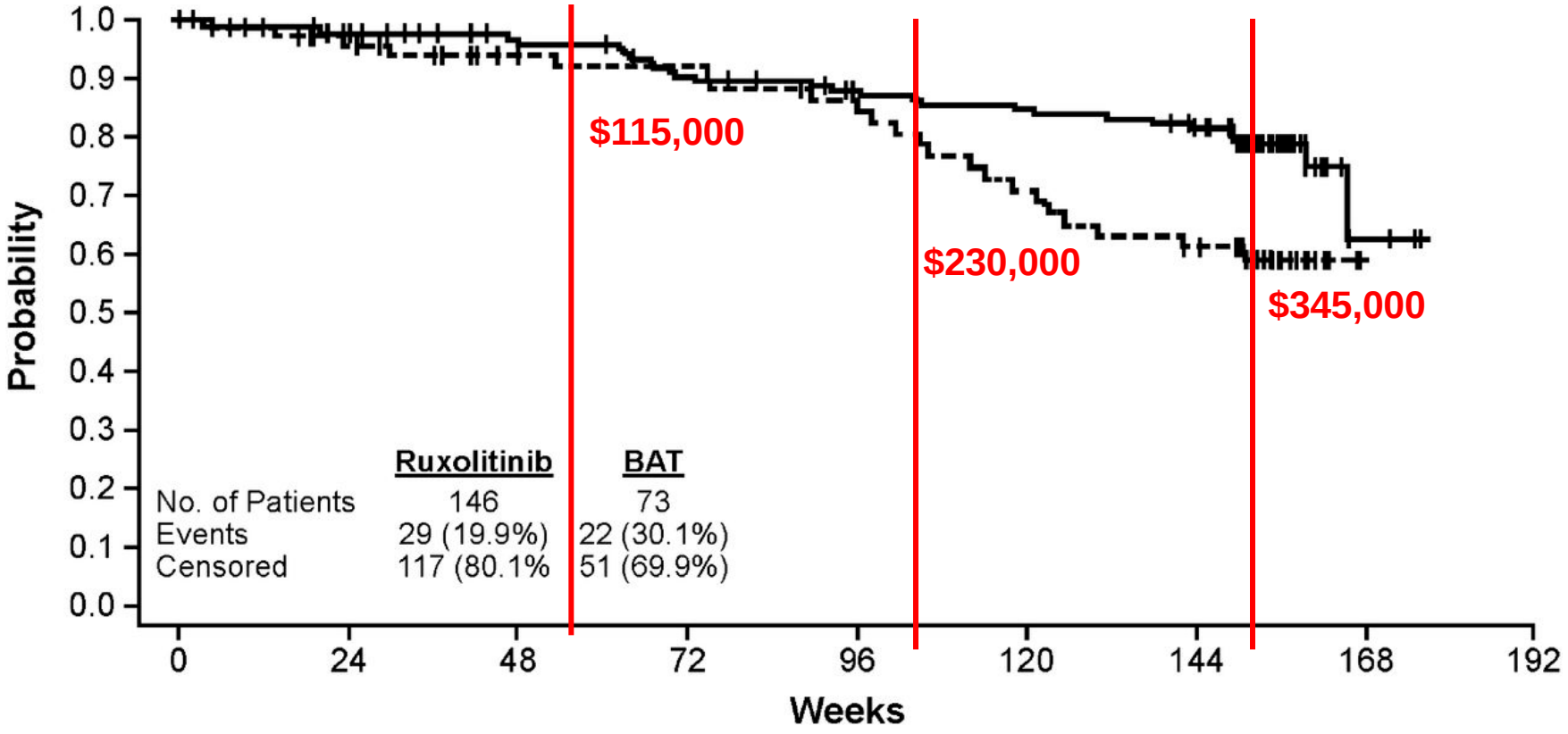
The availability of JAK2 inhibitor(s) is changing the landscape

Survival with JAK2 inhibitor therapy



Based on Cervantes F et al. Blood 2013;122:4047-4053

…….With some Financial Toxicity…….



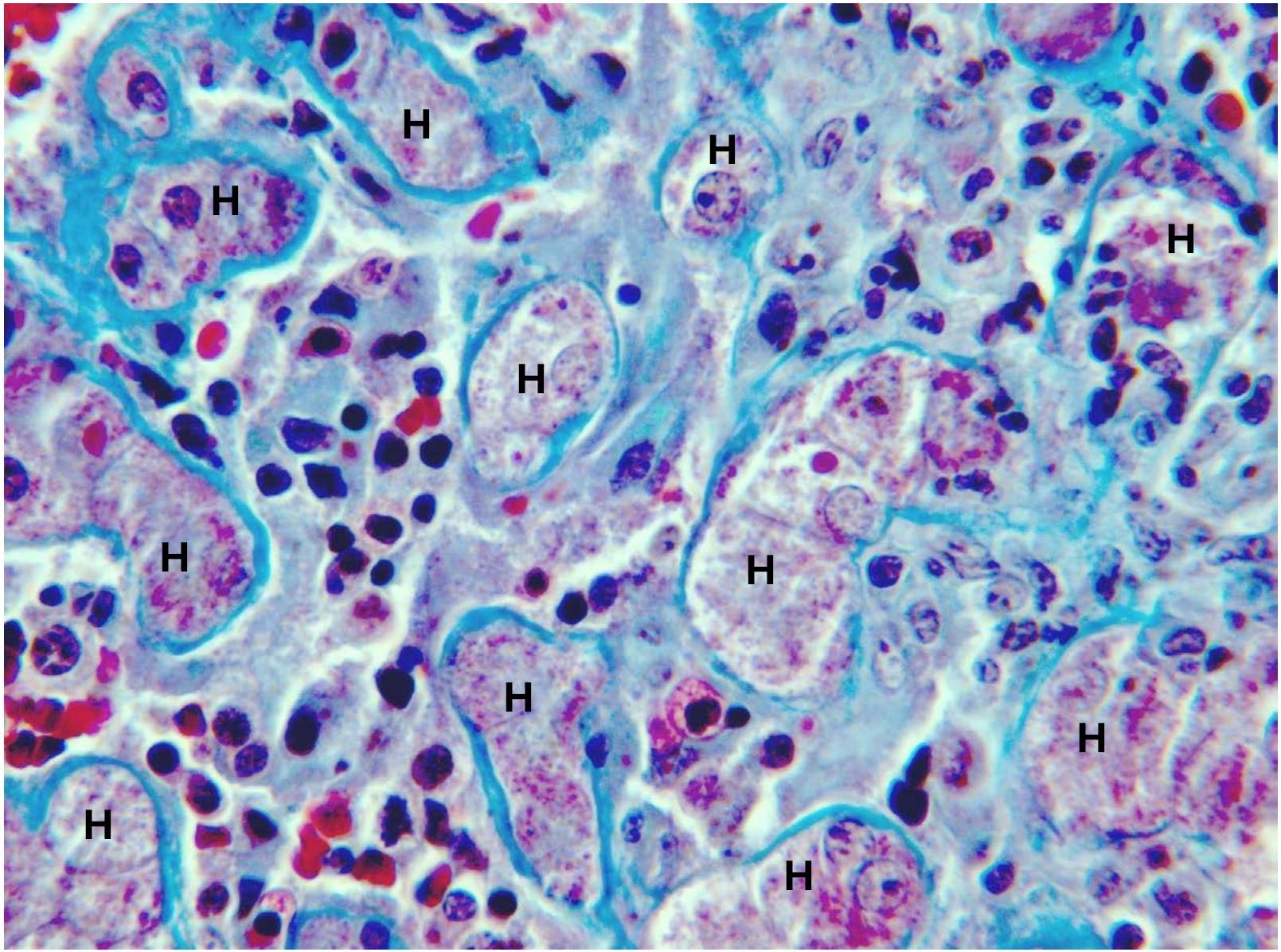
Based on Cervantes F et al. Blood 2013;122:4047-4053

These findings are impacting transplant decisions and modifying transplant strategies

Not included in current classifications:

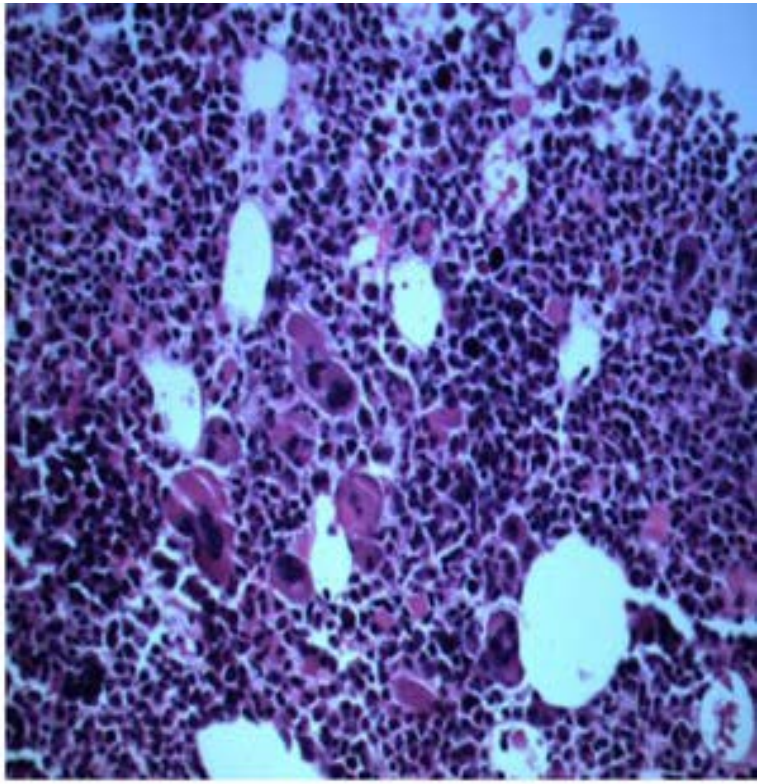
- *Severity* of marrow fibrosis (and fibrosis in *other organs*)
- Spleen size (portal hypertension)
- Duration of the disease
- DNA mutations

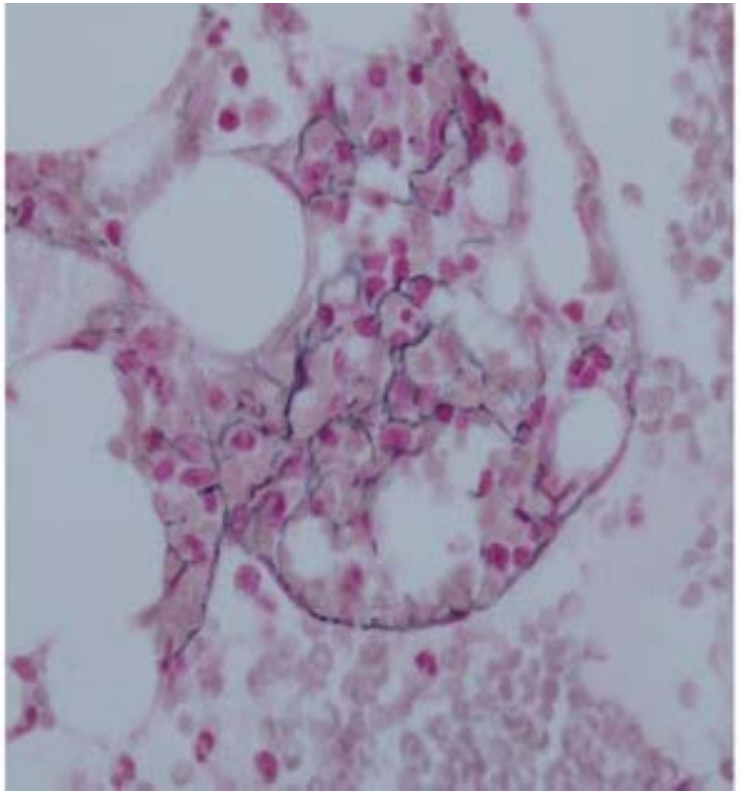
The liver in myelofibrosis: Hepatic sinusoidal fibrosis caused by EMH



H = hepatocytes. Note extensive EMH and collagen deposition (blue stain) in sinusoids.

Fibrosis and Hematopoiesis in the Lung





Could those factors be important for *transplantation*?

- Severity of marrow fibrosis (and fibrosis in other organs) ►Non-relapse mortality
- Spleen size ►Delayed engraftment; difficult transfusion support
- Duration of the disease ►More comorbidities (medical problems developing over time)
- Mutations ► ?

Results with Transplantation

Patient and Disease Characteristics

No. of patients	**170**
Age (ys) range (median)	**12.1–78.9 (51.5)**
Months from diagnosis to HCT (ms), range (median)	**2-314 (15)**
Type of myelofibrosis,#	
Primary /post-ET/-post-PV	**102 / 46/22**
***JAK2* mutation, #**	
yes/no	**43/51**
Unknown	**76**

Scott *et al.,Blood* 119:2657-2664, 2012

Disease Characteristics (#/%)

- **Splenectomy[1]**
  - **No** **136 (80)**
  - **Yes** **31 (18)**
- **DIPSS Score**
- **Low** **21 (12)**
- **Intermediate-1** **48 (28)**
- **Intermediate-2** **50 (30)**
- **High** **51 (30)**

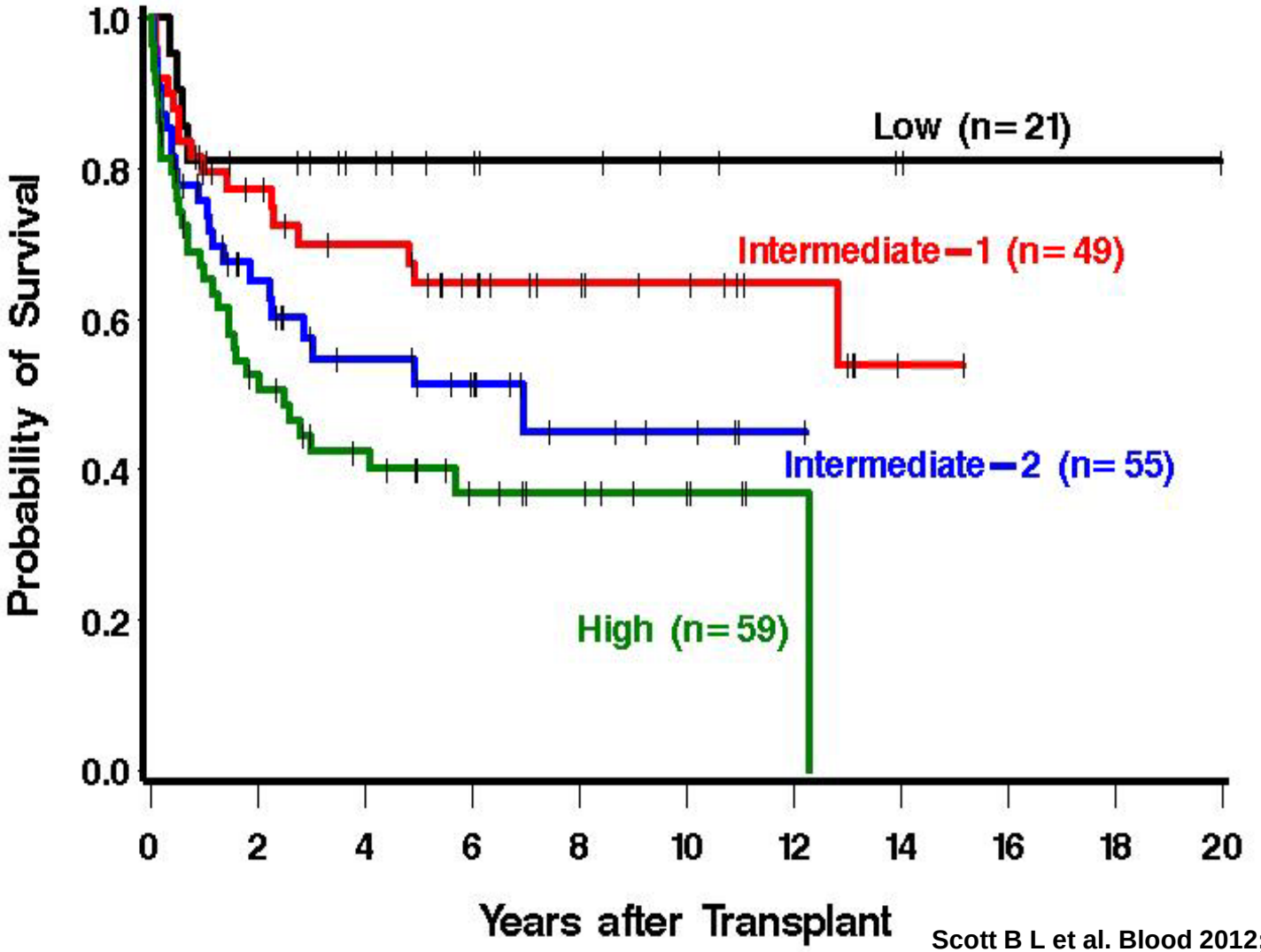
1 = Data missing in 3

Transplant Characteristics

- **Related Donor** **N= 83 (50%)**
- **Unrelated Donor** N= **84 (50%)**
- **Source of Stem Cells**
- Bone Marrow N= 45 (26%)
- Peripheral Blood N=125 (74%)

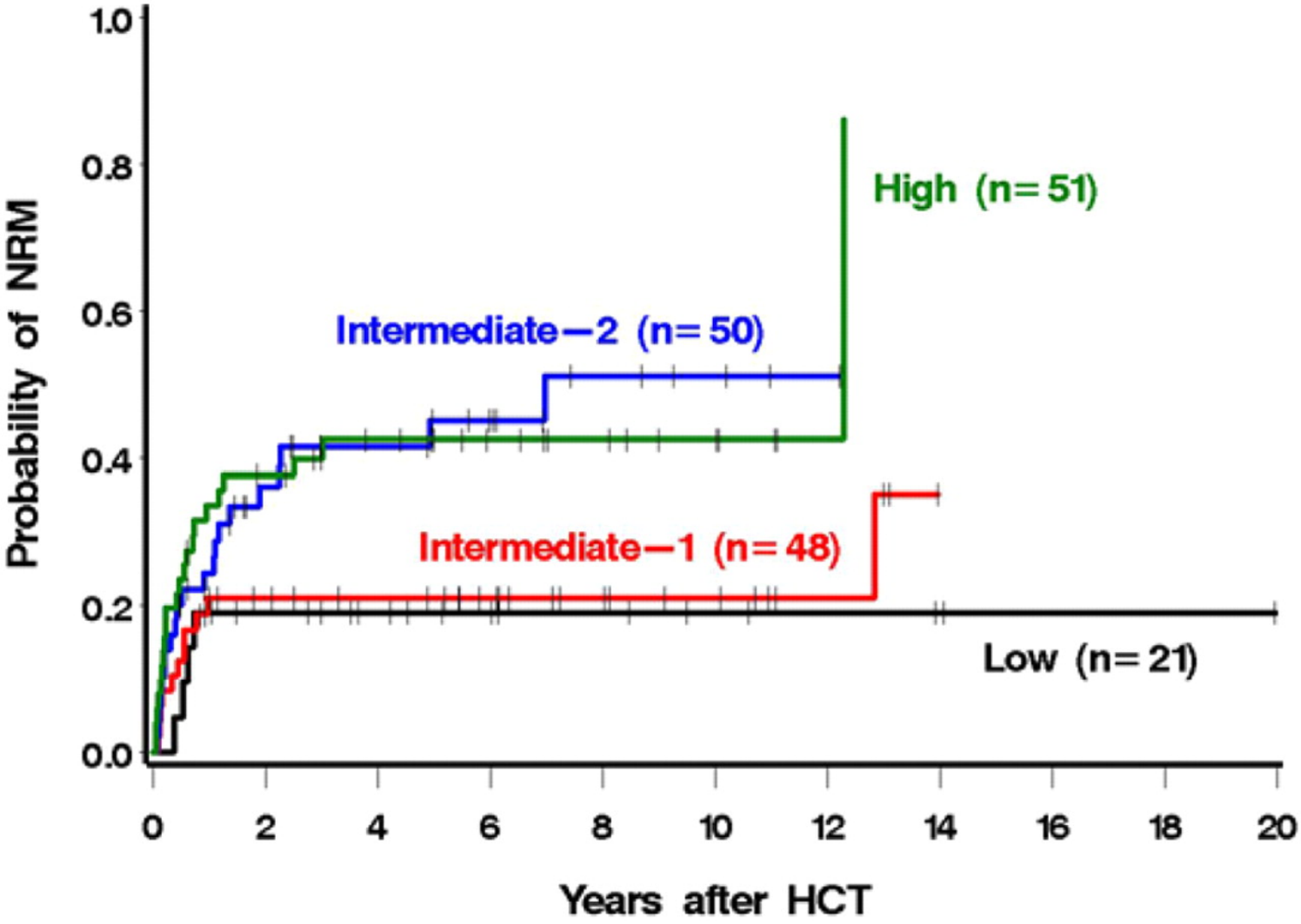
Scott *et al.,Blood* 119:2657-2664, 2012

Survival after Transplantation



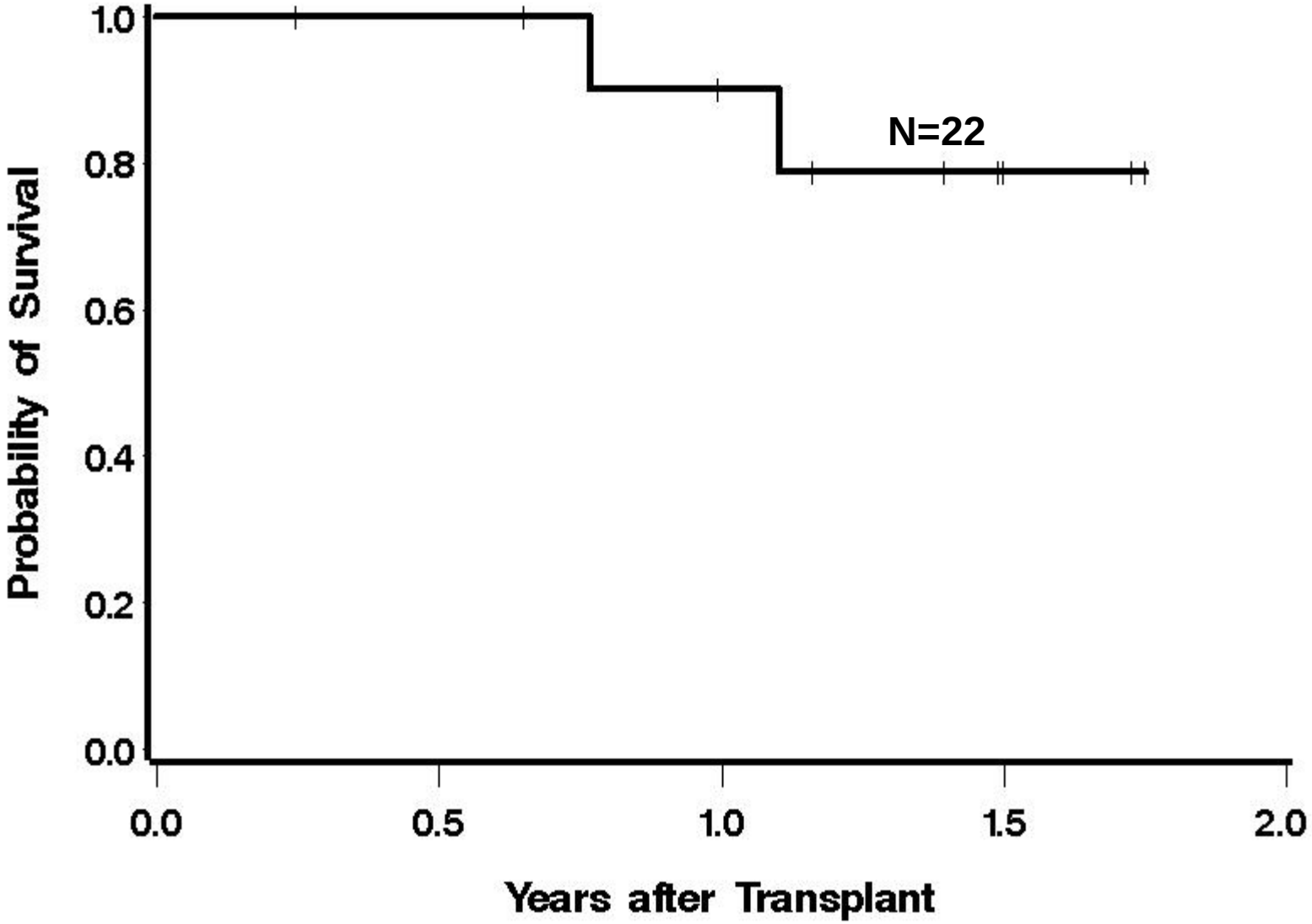
Scott B L et al. Blood 2012;119:2657-2664

Non-Relapse Mortality by DIPSS



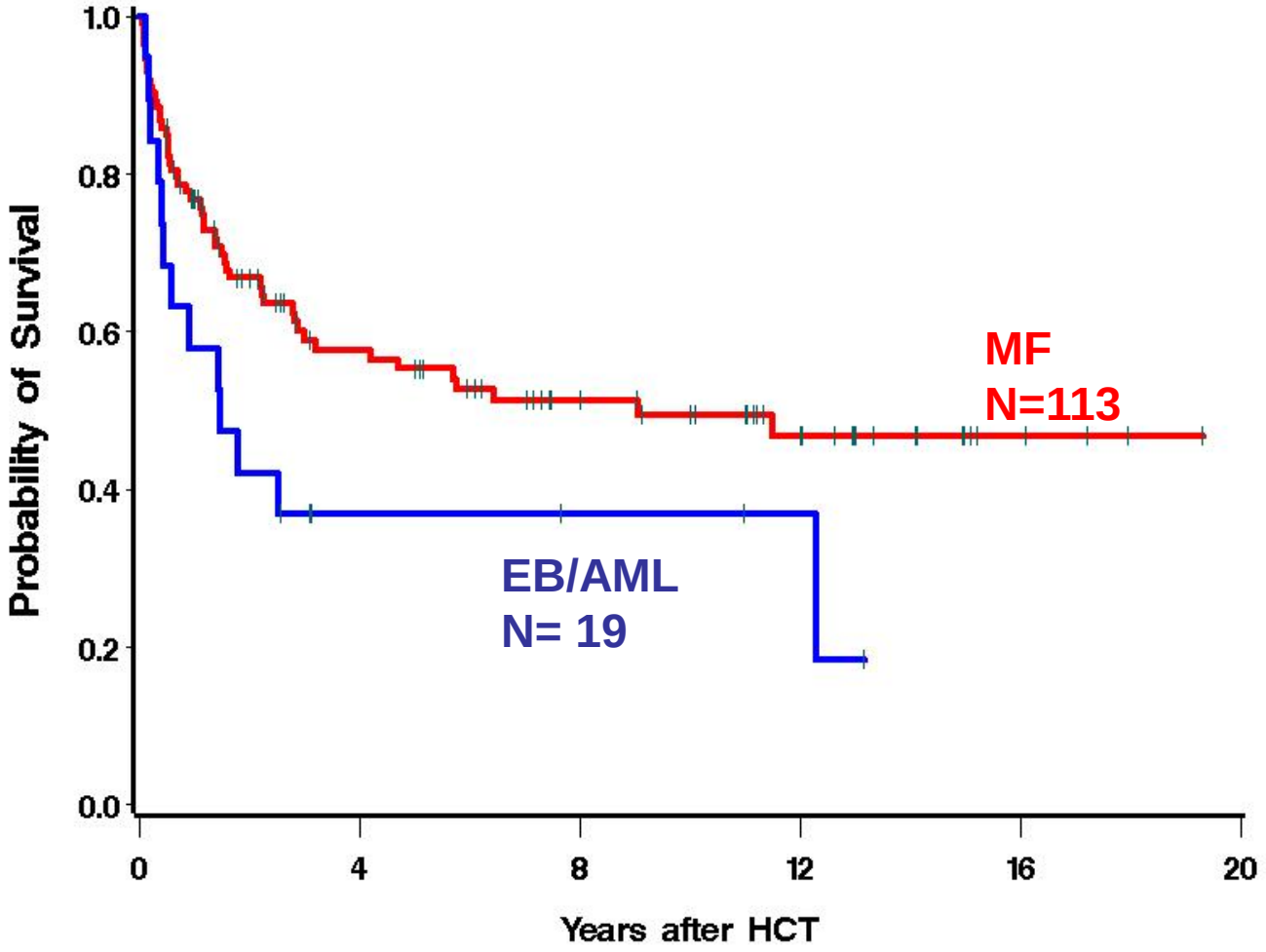
Scott B L et al. Blood 2012;119:2657-2664

CY → BU Conditioning



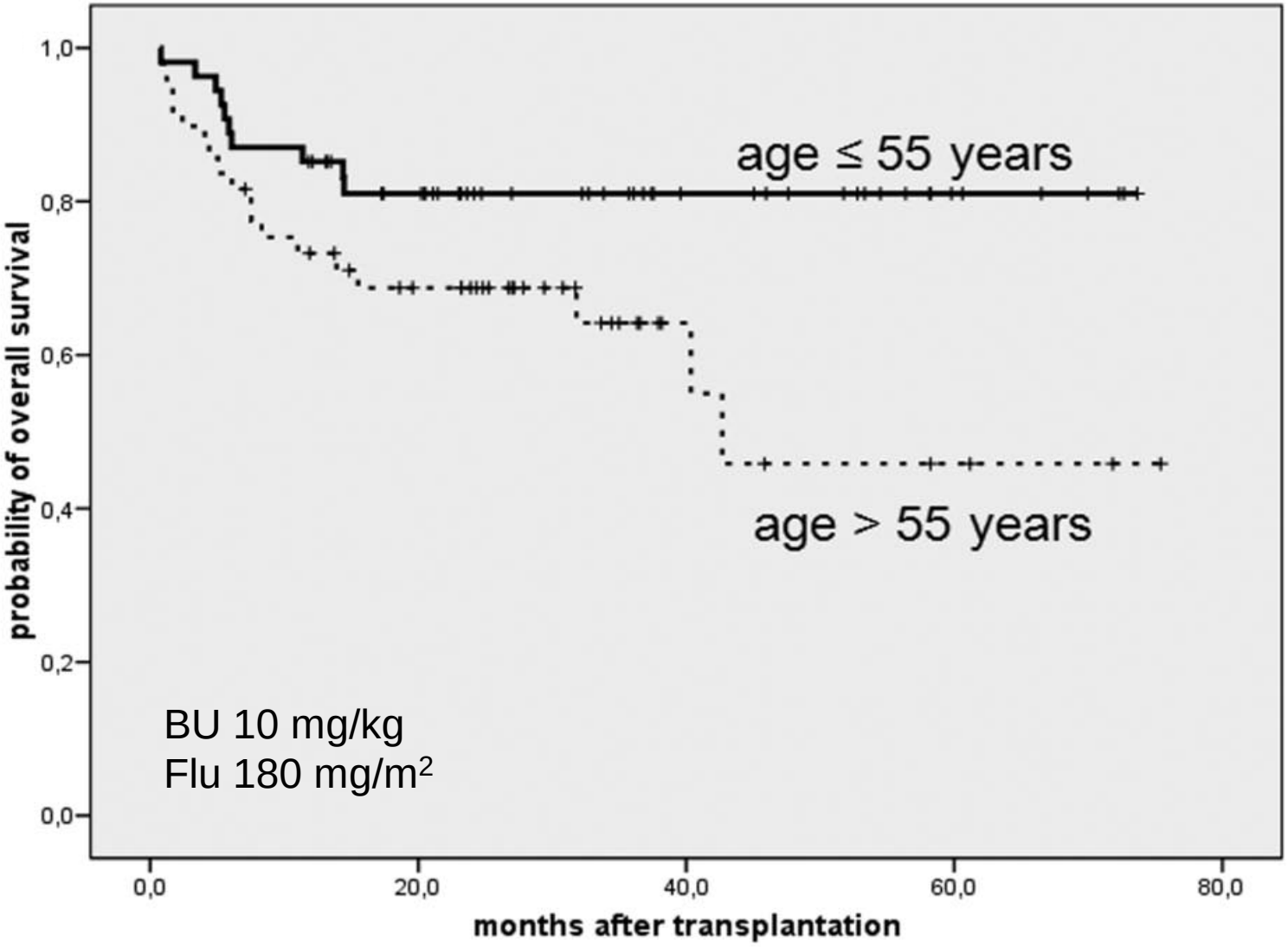
Rezvani, et al, BBMT 2013

Survival by disease stage



H.J.Deeg et al

Overall Survival by Age

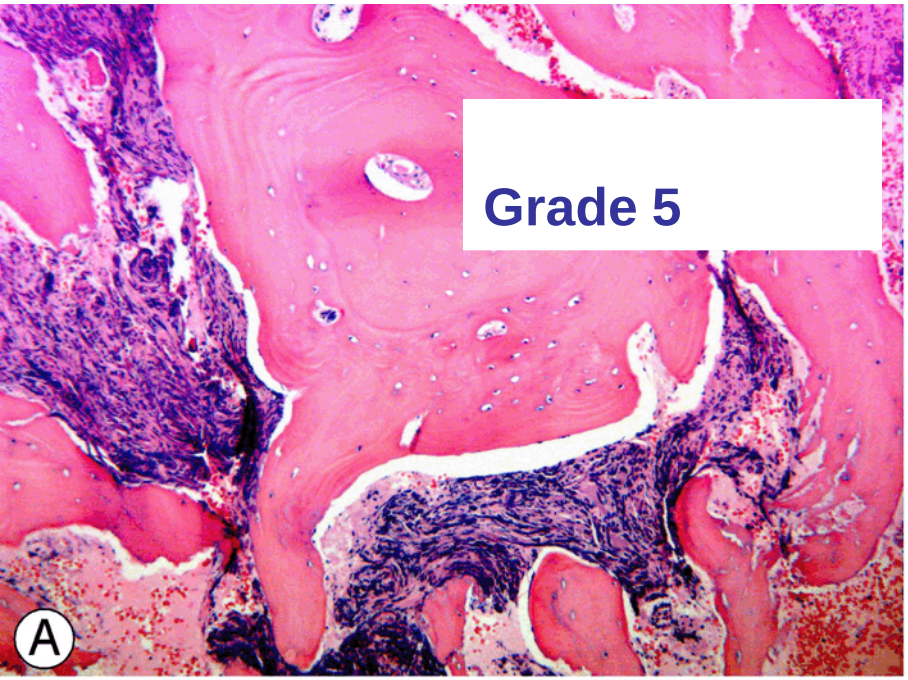


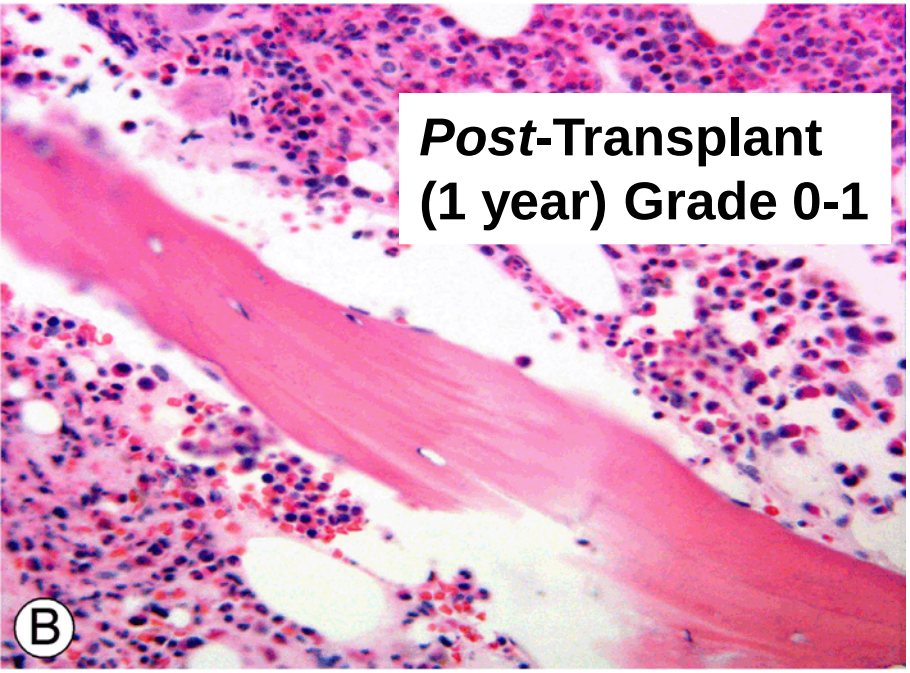
Kröger et al, Blood, 114:5264, 2009

Survival without and with Transplantation (by DIPSS)

DIPPS Risk	Survival (median; years)	
	No Transplant (at reporting)	Transplant (med F/U 5.9)
Low	Not reached	Not reached
Intermediate 1	14.2	Not reached
Intermediate 2	4	7
High	1.5	2.5

B.Scott, HJ Deeg et al, Blood, 2012





Osteosclerosis: Regression after *high dose conditioning* and HCT

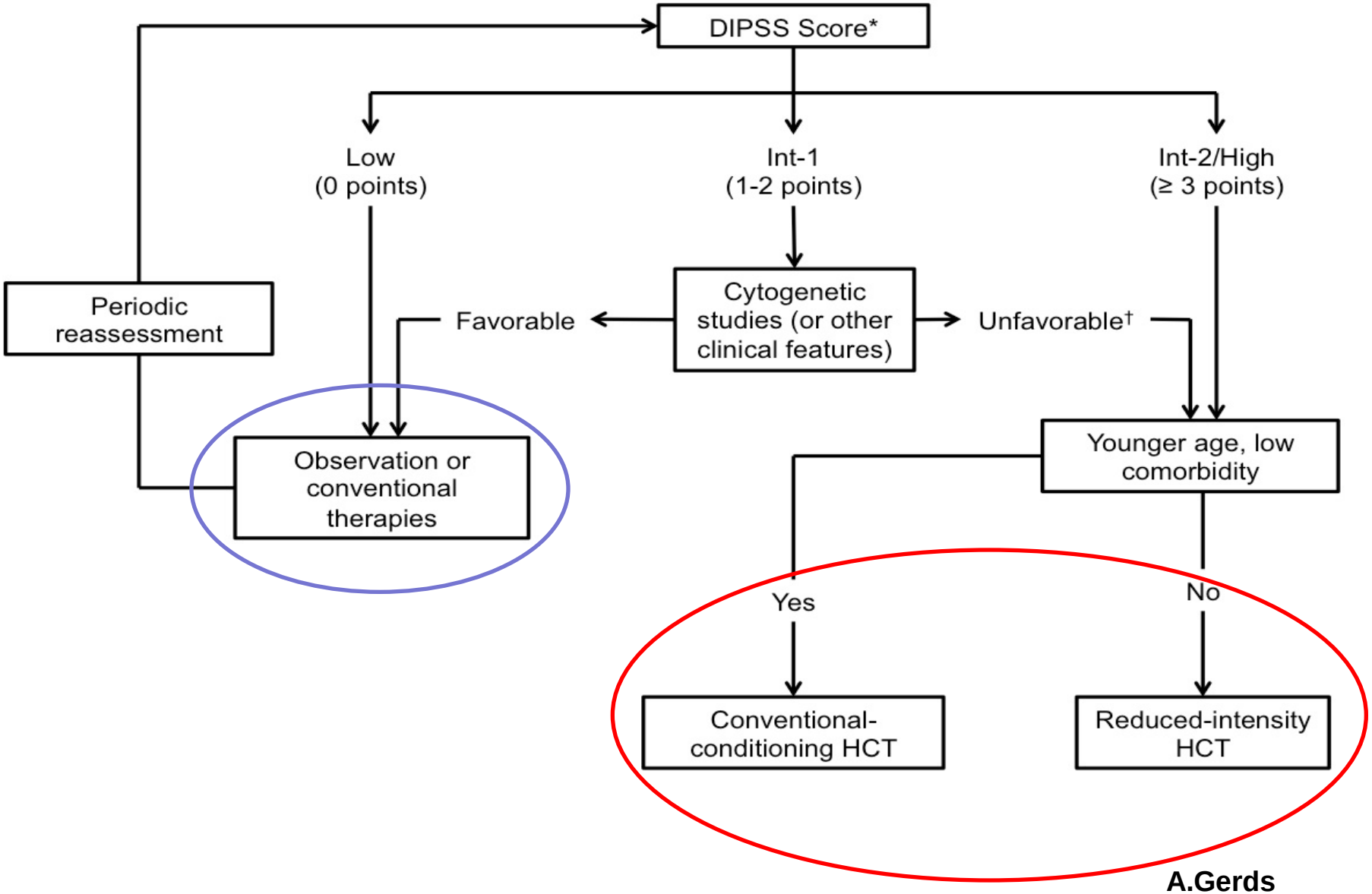
(H&E; x250)

G. Sale

Problems

- **GVHD**
- **Organ toxicity**
- **(Relapse)**

Decision Tree



A.Gerds

Summary

- **HCT offers effective, curative therapy for patients with MF**
  - Follow-up extending beyond 20 years
  - Few relapses
- **Safety has improved**
  - Decreasing NRM
- **Donors are available for most patients**
- **HCT for MF is appropriate for many patients with advanced MF and for select patients with early stage disease**

Thank you

- **Ted Gooley**
- **Barry Storer**
- **Bart Scott**
- **Keith Loeb**
- **And, of course, all our patients**