EARLY TRANSPLANTATION FOR MYELOFIBROSIS

YES!

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DISCLOSURES

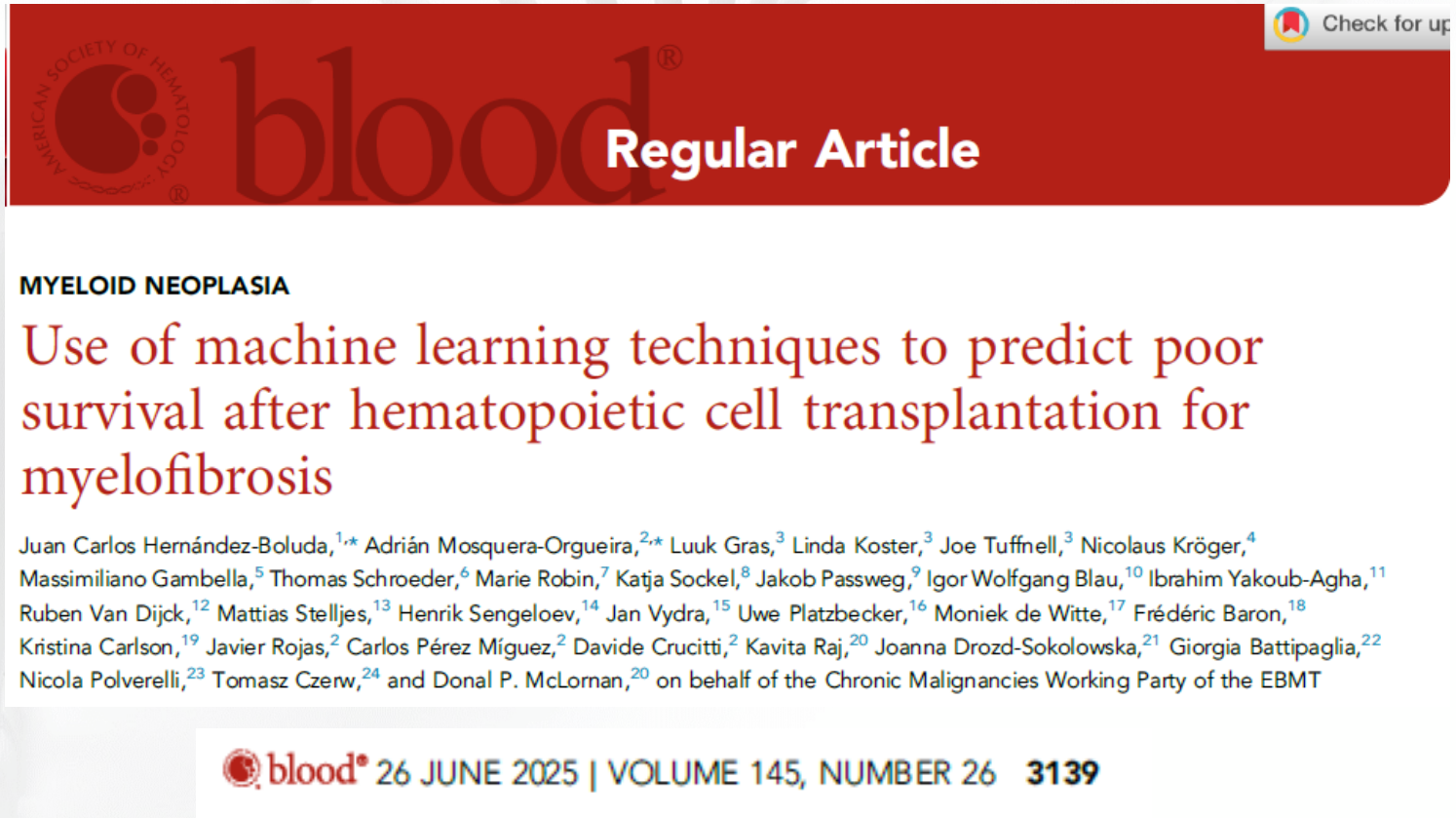
- I am a transplanter…
- My only other disclosure relevant to this presentation is prior research support from Incyte (Ruxolitinib, etc)

FACTS

- Allogeneic stem cell transplantation is the only potentially curative therapy for primary or secondary myelofibrosis
- Advances in molecular diagnostics allow us to better risk-stratify patients
- Advances in transplant medicine have made allogeneic transplantation less risky
  - Better GVHD prophylaxis and treatment, such as PTCy and/or inclusion of Ruxolitinib into GVHD prophylaxis
  - Use of reduced intensity conditioning regimens
  - Better supportive care—particularly important for MF given variable engraftment kinetics

WHO IS AN ALLOGENEIC TRANSPLANT CANDIDATE?

- Age
  - Up to ~75 y
- Comorbidities
- Frailty
- Nutritional status
- Support system
- Health literacy
- ***Benefit of the doubt…***



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Check for up

MYELOID NEOPLASIA

Use of machine learning techniques to predict poor survival after hematopoietic cell transplantation for myelofibrosis

Juan Carlos Hernández-Boluda,[1,*] Adrián Mosquera-Orgueira,[2,*] Luuk Gras,[3] Linda Koster,[3] Joe Tuffnell,[3] Nicolaus Kröger,[4] Massimiliano Gambella,[5] Thomas Schroeder,[6] Marie Robin,[7] Katja Sockel,[8] Jakob Passweg,[9] Igor Wolfgang Blau,[10] Ibrahim Yakoub-Agha,[11] Ruben Van Dijck,[12] Mattias Stelljes,[13] Henrik Sengeloev,[14] Jan Vydra,[15] Uwe Platzbecker,[16] Moniek de Witte,[17] Frédéric Baron,[18] Kristina Carlson,[19] Javier Rojas,[2] Carlos Pérez Míguez,[2] Davide Crucitti,[2] Kavita Raj,[20] Joanna Drozd-Sokolowska,[21] Giorgia Battipaglia,[22] Nicola Polverelli,[23] Tomasz Czerw,[24] and Donal P. McLornan,[20] on behalf of the Chronic Malignancies Working Party of the EBMT

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PROGNOSTIC MODELS FOR MF – WHAT MATTERS?

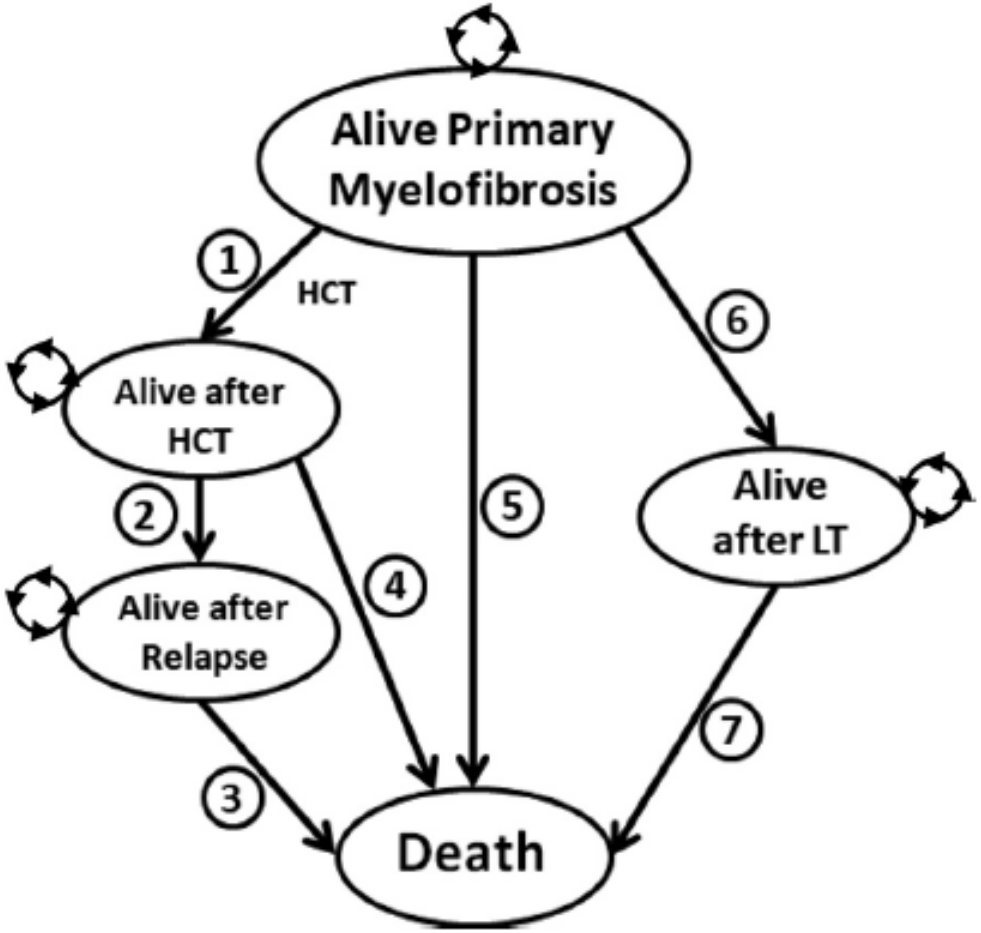
- Clinical
  - Age
  - WBC, Hgb, plts
  - Circulating blasts
  - Spleen size
  - Constitutional symptoms
- Cytogenetics
- Molecular
  - Driver mutations—Non-CALR1 mutations = bad
  - ASXL1, EZH2, SRSF2, IDH1/2 +/- U2AF1Q157 = bad (and the more of them the worse the outcome)
- ***Disease trajectory also must be considered***

HOW DO WE THINK ABOUT WHAT TO DO AND WHEN?

- No prospective trials to address this question…
  - We do have randomized data for intermediate and higher risk MDS, and early transplant won (BMT CTN 1102; Nakamura et al. JCO, 2021)
- Retrospective studies generally suggest a long-term survival advantage in favor of allogeneic HSCT for higher risk patients (Kroger, N et al. Blood, 2015; K Gowin et al. Blood Advances, 2020)
- Once the disease progresses toward AML or becomes resistant to JAK inhibition, transplant is more difficult and outcomes are less favorable
- *There is no substitute for clinical judgment and close followup…*

MARKOV MODEL TO SIMULATE DISEASE TRAJECTORY AND SURVIVAL BASED ON TIMING OF HSCT

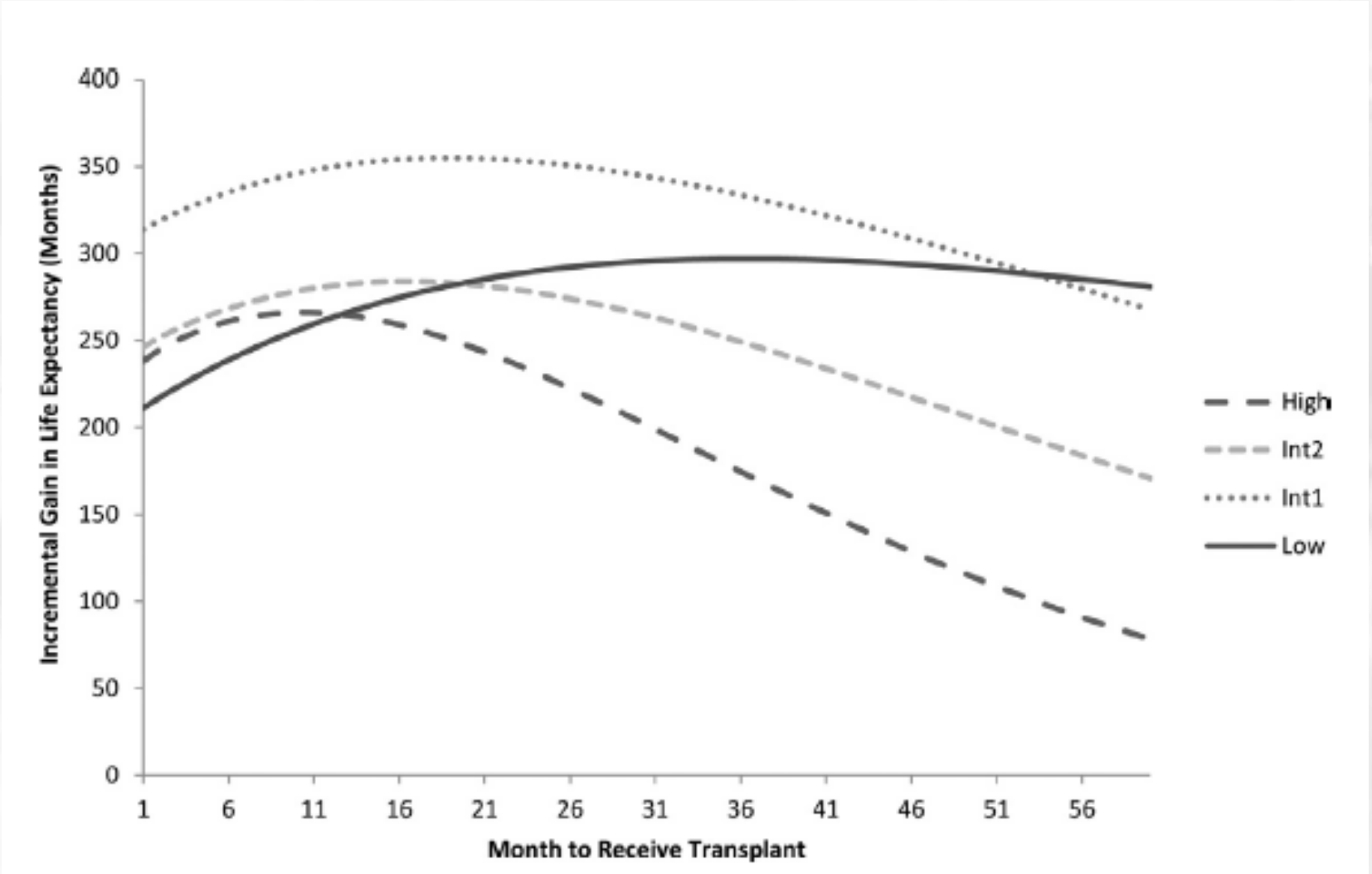
- Utilized the 4 DIPSS risk categories
- Risks and survival assumptions based on data from the literature for transplant and medical therapy for each risk cohort



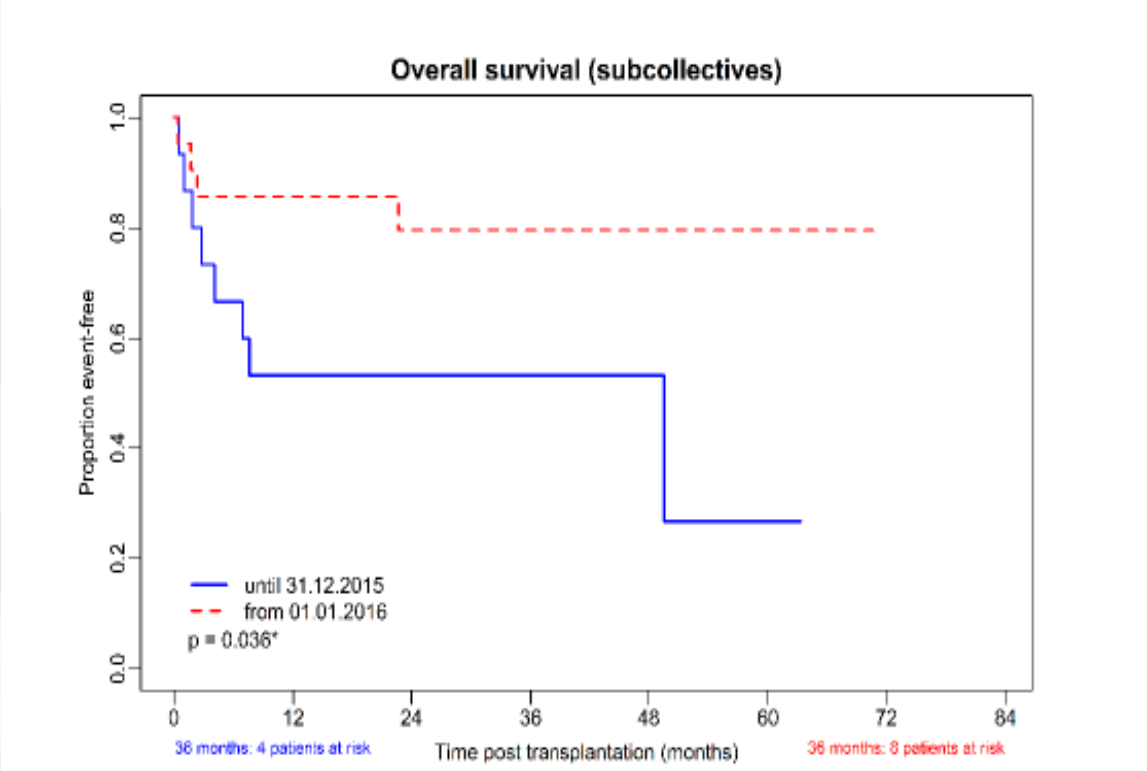
Cipkar C, et al. Transplantation and Cellular Therapy, 2022; 28:189-194.

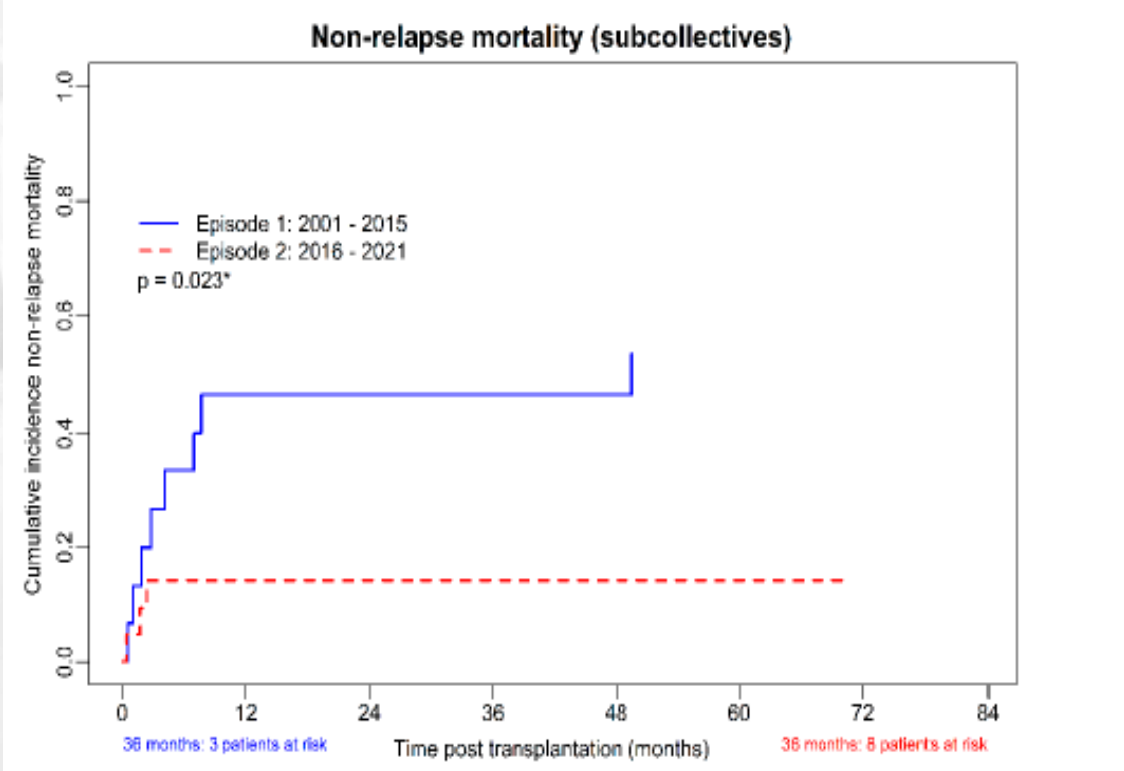
SIMULATION OF LIFE EXPECTANCY GAINED FAVORS EARLIER TRANSPLANTATION FOR HIGHER RISK PTS (INT2/HIGH +/-INT1 RISK)

- All patients eventually derived benefit from transplantation
- Greatest incremental benefit seen in the lower risk groups, but most benefit was realized when HSCT done sooner for the intermediate and higher risk pts



PRE-TRANSPLANT RUXOLITINIB HAS IMPROVED TRANSPLANT OUTCOMES





Macherndl-Spindle S, et al. Cancers, 2024; 16(19):3257.

PHASE 2 STUDY OF RUXOLITINIB ADDED TO TAC/MTX FOR GVHD PROPHYLAXIS

Figure 1

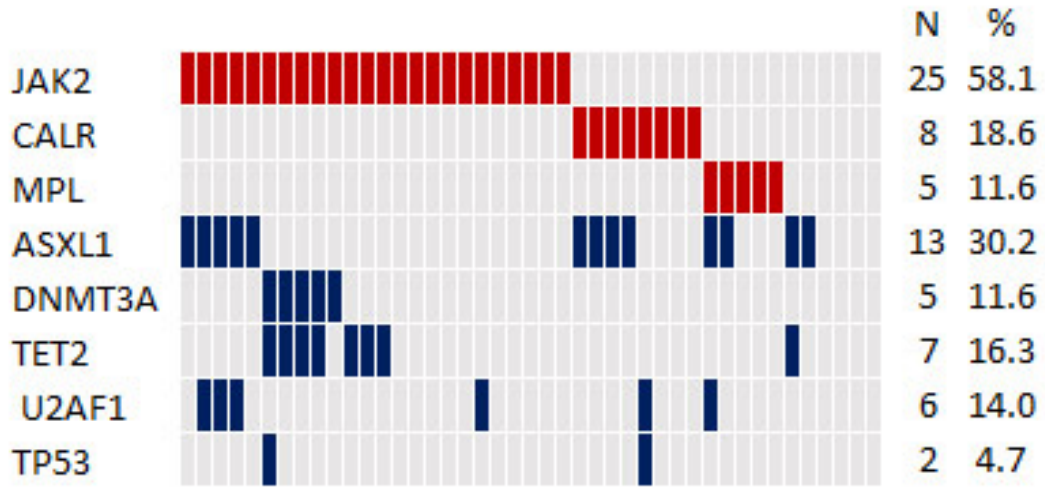
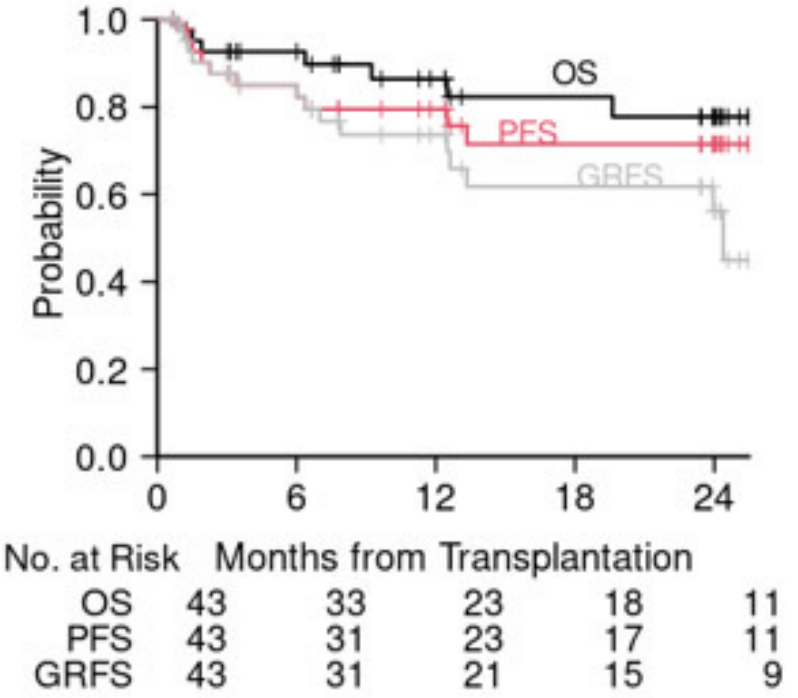


Figure 2



Hobbs GS, et al. Blood, 2023; 142(supp.1):2103.

CONCLUSIONS

- MF patients who are potentially transplant eligible should be evaluated early
  - Donor identification
  - Timing—requires close followup and collaboration with the transplant team
- Molecular analysis of MF patients is essential for decision making
- JAK inhibitor therapy for at least 2-3 months prior to transplant seems to help with reduction of transplant toxicities and risk
  - Ruxolitinib can be continued post-transplant and may improve NRM and outcomes without compromising engraftment
- Early transplantation should be considered for:
  - Higher risk disease by clinical and molecular parameters
  - Aggressive disease trajectory
  - Young patients

QUESTION: WHO WILL YOU TRUST?

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