Prognosis risk scores and transplant specifc (MTSS) score for myelofbrosis

Score	Adverse factors (puntos)	Risk group and median SRV
IPSS	Age > 65 years (1 p) Constitutional symptoms (1 p) Hb <100 g/L (1 p) Leucocytes >25 × 10^9/L (1 p) Blasts in PB ≥1% (1 p)	Low (0 p), 11.3 years Intermediate-1 (1 p), 7.9 years Intermediate-2 (2 p), 4 years High (3–5 p), 2.3 years
DIPSS	Age > 65 years (1 p) Constitutional symptoms (1 p) Hb <100 g/L (2 p) Leucocytes >25 × 10^9/L (1 p) Blasts in PB ≥1% (1 p)	Low (0 p), not reached Intermediate-1 (1–2 p):,14.2 years Intermediate-2 (3–4 p), 4 years High (5–6 p), 1.5 years
DIPSS plus	DIPSS Int-1 (1 p) DIPSS Int-2 (2 p) DIPSS high (3 p) Platelets <100 × 10^9/L (1 p) Transfusion requirement (1 p) Unfavorable karyotype[a] (1 p)	Low (0 p), 15.4 years Intermediate-1 (1 p), 6.5 years Intermediate-2 (2–3 p), 2.9 years High (4–6 p), 1.3 years
MIPSS70	Leucocytes >25 × 10^9/L (2 p) Hb <100 g/L (1 p) Constitutional symptoms (1 p) BM fibrosis grade ≥ 2 (1 p) Blasts in PB ≥ 2% (1 p) CALR typ1 (1 p) Platelets <100 × 10^9/L (2 p) HMR (1 p) HMR ≥2 (2p)	Low (0–1 p) 27.7 years Intermediate (2–4 p) 7.1 years High (≥5 p) 2.3 years
MTSS	Platelets <150 × 10^9/L (1 p) Leucocytes >25 × 10^9/L (1 p) Karnosfsky <90% (1 p) Age ≥ 57 years	Low (score 0–2) OS 90% (5 years) NRM 10% Intermediate (score 3–4) OS 77% (5 years), NRM 22%
	NonCALR/MPL mutation (2 p) ASXL-1 (1 p) Mismatch unrelated donor (2 p)	High (score 5) OS 50% (5 years) NRM 36% Very high (≥6) OS 34% (5 years) NRM 57

Risk Factors

- Advanced age and HLA-mismatched donor were independent predictive factors for reduced survival (Kroger et al. 2009)
- Transplantation outcomes in accelerated phase are similar to chronic phase while outcome in blastic phase is worse (Gagelmann et al. 2022a, b; Orti et al. 2023)

Disease-Specifc Risk Factors

- The EBMT/ELN consensus paper recommended allo-HCT for patients less than 70 years with an estimated median survival of less than 5 years.
- This would include patients with IPSS or DIPSS intermediate-2 and high risk and is based on a comparison between transplanted and non-transplanted patients in the pre-ruxolitinib era (Kroger et al. 2015a, b).
- Patients with intermediate-1 risk can be considered for allo-HCT if other high-risk features such as ASXL1 mutation, more than 2% peripheral blasts, refractory transfusion-dependent anemia, or adverse cytogenetics according to DIPSS plus are present (Kroger et al. 2015a).

Transplant-Specifc Risk Factors

- In most of the transplant studies, alternative donors were associated with a worse outcome independent of disease-specifc risk factors.
- CBT resulted in a high risk of graft failure (Robin et al. 2014).
- Haplo-identical donor with PT-CY as GVHD prophylaxis is currently under investigation, but more recent EBMT data reported a 5-year survival of only 38% (Raj et al. 2016).

Transplant-Specifc Risk Factors

- The intensity of the conditioning regimen has not been investigated within prospective studies, but retrospective comparisons of MAC and RIC preparative regimens resulted in similar outcome. (McLornan et al. 2019; Gagelmann et al. 2022a, b)
- Because of the reduced toxicity and a generally older age of patients with myelofbrosis, RIC regimens are currently used more frequently and account for about two-thirds of allotransplants for myelofbrosis reported to the EBMT registry.

MTSS

- Recently, the transplant-specifc risk score (MTSS) including molecular genetics, platelet, and WBC count as well as Karnofsky index, age, and stem cell donor can predict outcome after allo-HCT (Gagelmann et al. 2019a, b).

Patient-Specifc Risk Factors

- Age
- comorbidities

Role of Splenectomy and JAK Inhibition

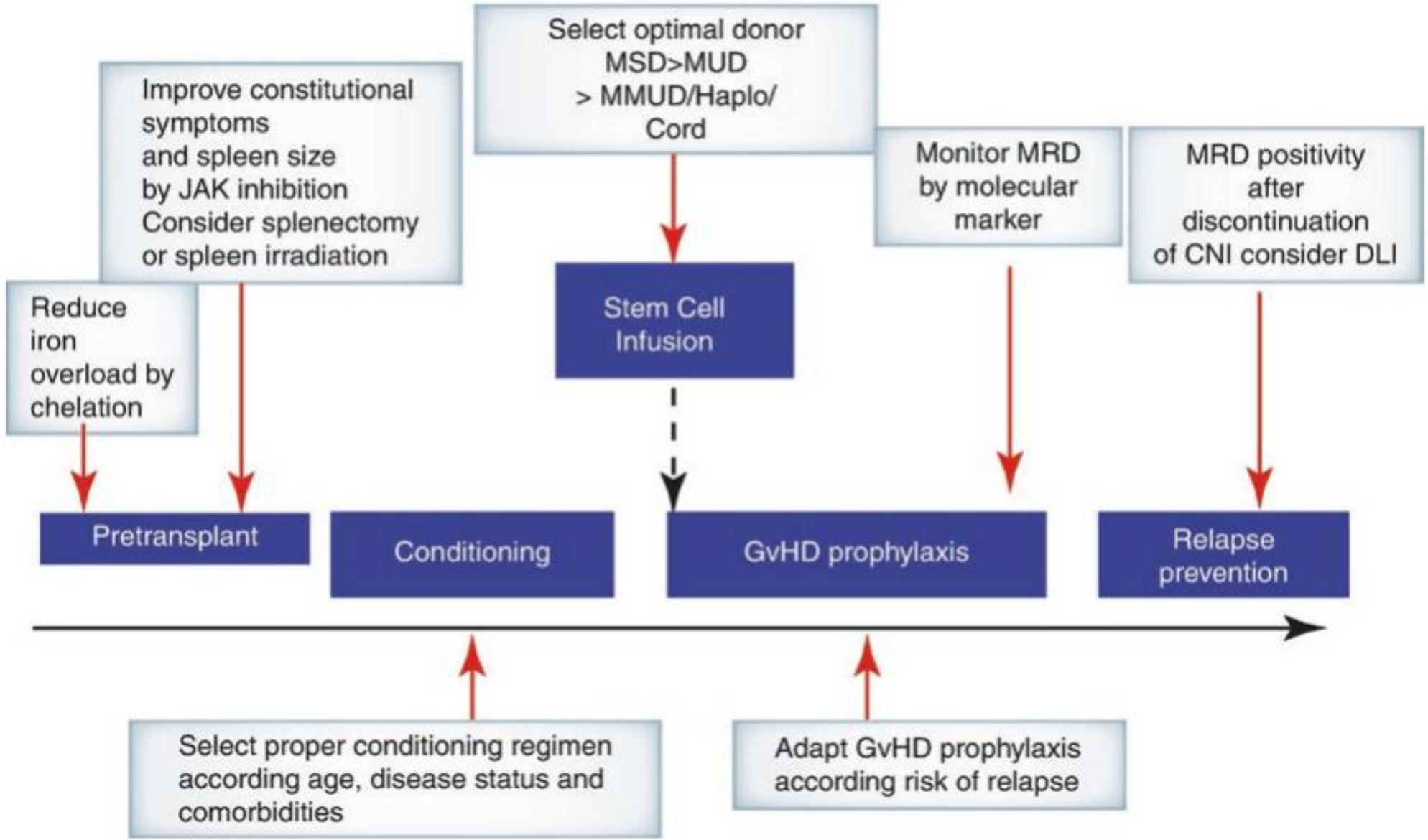
- Splenectomy is an option to reduce spleen size prior to transplantation, (Polverelli et al. 2021).
- Splenic irradiation to reduce spleen size has been reported successfully in single cases prior to conditioning.
- It is Recommended to use of ruxolitinib at least 2 months prior to HCT.
- More recent data suggests better outcomes after HCT if patients received transplant after responding to ruxolitinib rather than postponing the transplant until ruxolitinib failure (Kröger et al. 2021).

Impact of Molecular Remission and Posttransplant Adoptive Immunotherapy

- About 90% of myelofbrosis patients harbor one of the driver mutations JAK2V617F, calreticulin (CALR), or MPL which are used to monitor MRD in PB by highly sensitive qPCR or digital PCR to determine molecular remission (Wolschke et al. 2017). In a retrospective single center experience, no achievement of molecular remission on day 180 post-allograft was associated with a signifcantly higher incidence of a subsequent clinical relapse. Due to a graft-versus-myelofbrosis effect, donor lymphocyte infusion has been successfully applied in patients with molecular or hematological relapse to induce a molecular remission (Kröger et al. 2009; Gagelmann et al. 2023)

Impact of Molecular Remission and Posttransplant Adoptive Immunotherapy

- Furthermore, BM fibrosis is another hallmark of the disease, with rapid regression after alloHCT suggesting that fibrogenesis is a highly dynamic process. Systematic investigations have shown that about 60% of the patients have a complete or nearly CR of BM fibrosis on day+100, and the percentage of patients increased to 90% at day+180. Notably, those patients with a rapid resolution of BM fibrosis had the best long-term outcome (Kröger et al. 2007).


Select optimal donor
MSD>MUD
> MMUD/Haplo/
Cord
Improve constitutional
symptoms
and spleen size
by JAK inhibition
Consider splenectomy
or spleen irradiation
Monitor MRD
by molecular
marker
MRD positivity
after
discontinuation
of CNI consider DLI
Reduce
iron
overload by
chelation
Stem Cell
Infusion
Pretransplant
Conditioning
GvHD prophylaxis
Relapse
prevention
Select proper conditioning regimen
according age, disease status and
comorbidities
Adapt GvHD prophylaxis
according risk of relapse