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Poor Graft Function, Graft failure and Relapse in Myelofibrosis patients following allo-HCT

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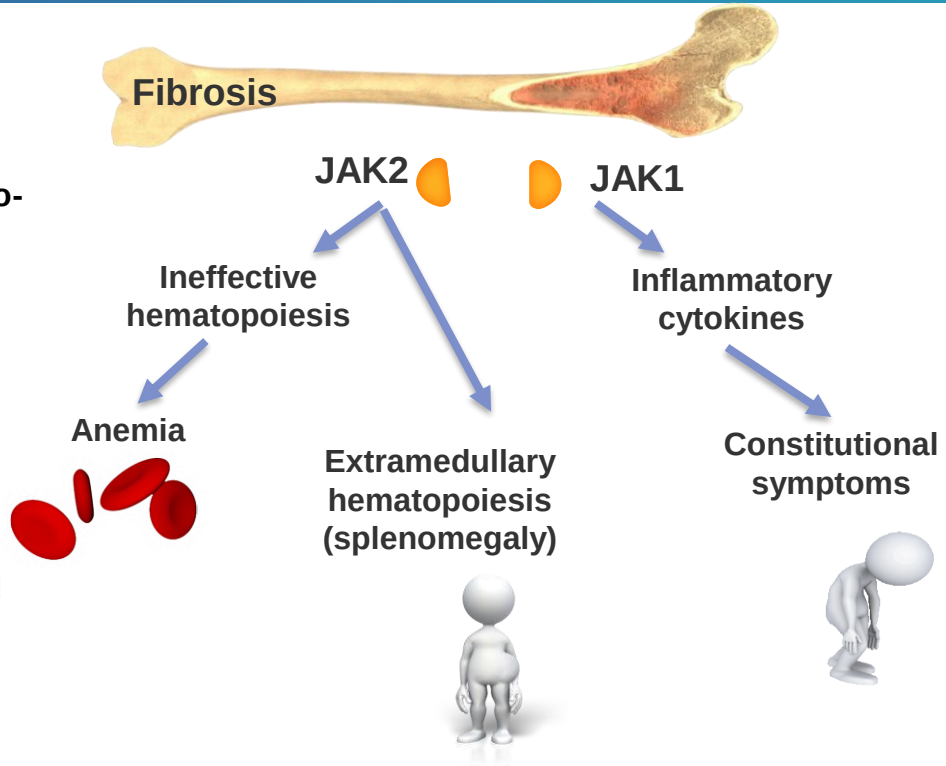
Co-Chair of the Scientific Council of the EBMT and Chair of the CMWP

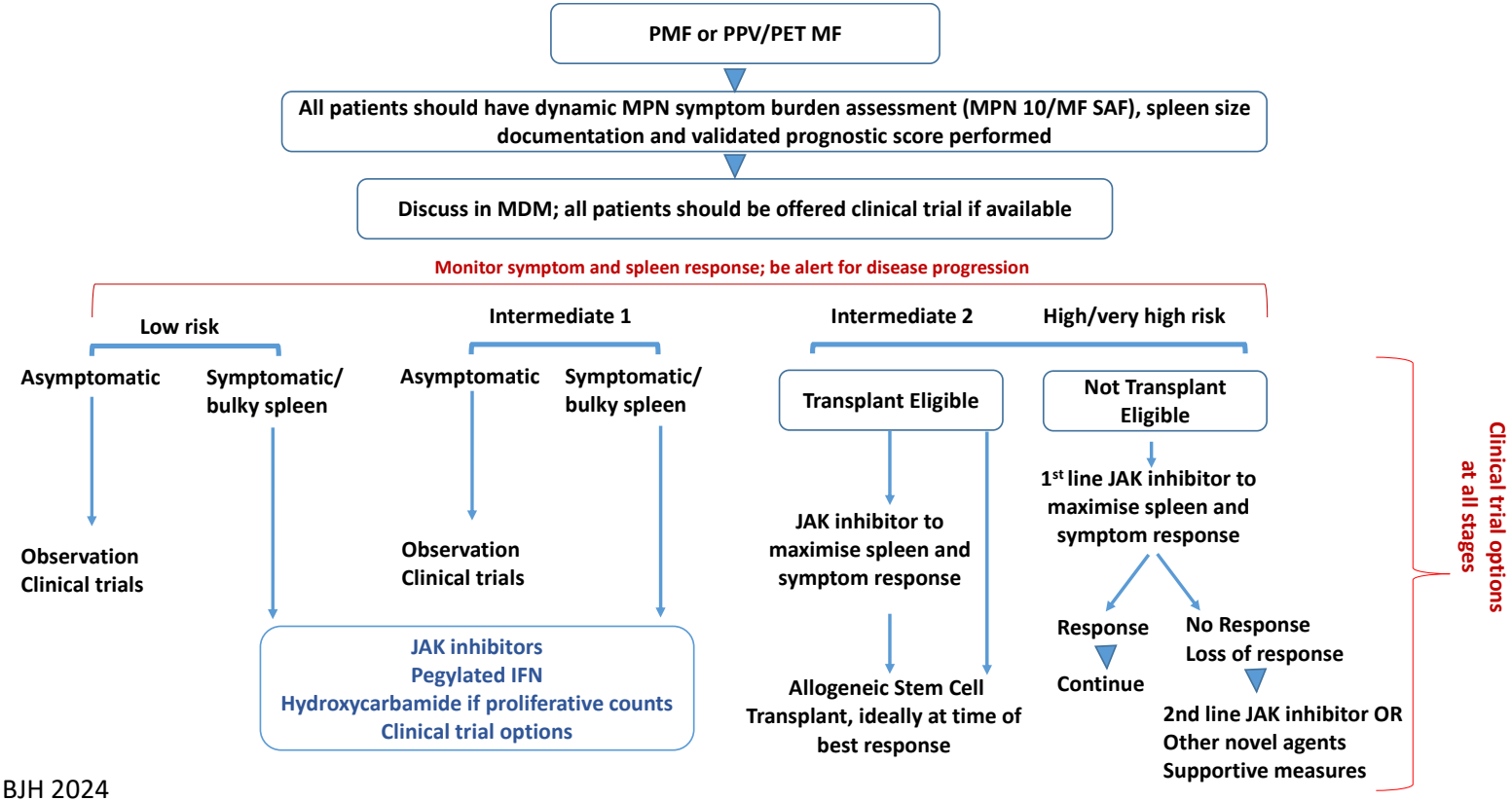
Allo-HCT for Myelofibrosis

- **Worst prognosis amongst all the chronic MPNs**
- **Individuals may have a high degree of associated co-morbidity**
  - **Transplant related morbidity and mortality tend to be higher**
- **Timing of SCT may often controversial**
  - **? Early versus Late in disease course**
- **Role of novel agents such as JAKi and others in transplant algorithm for Mf increasingly established**
- **Despite advances RELAPSE remains a significant challenge.**



1. Verma A, et al. *Cancer Metast Rev.* 2003;22:423-434. 2. Mughal TI, et al. *Int J Gen Med.* 2014;7:89-101.

Allo-HCT for Myelofibrosis

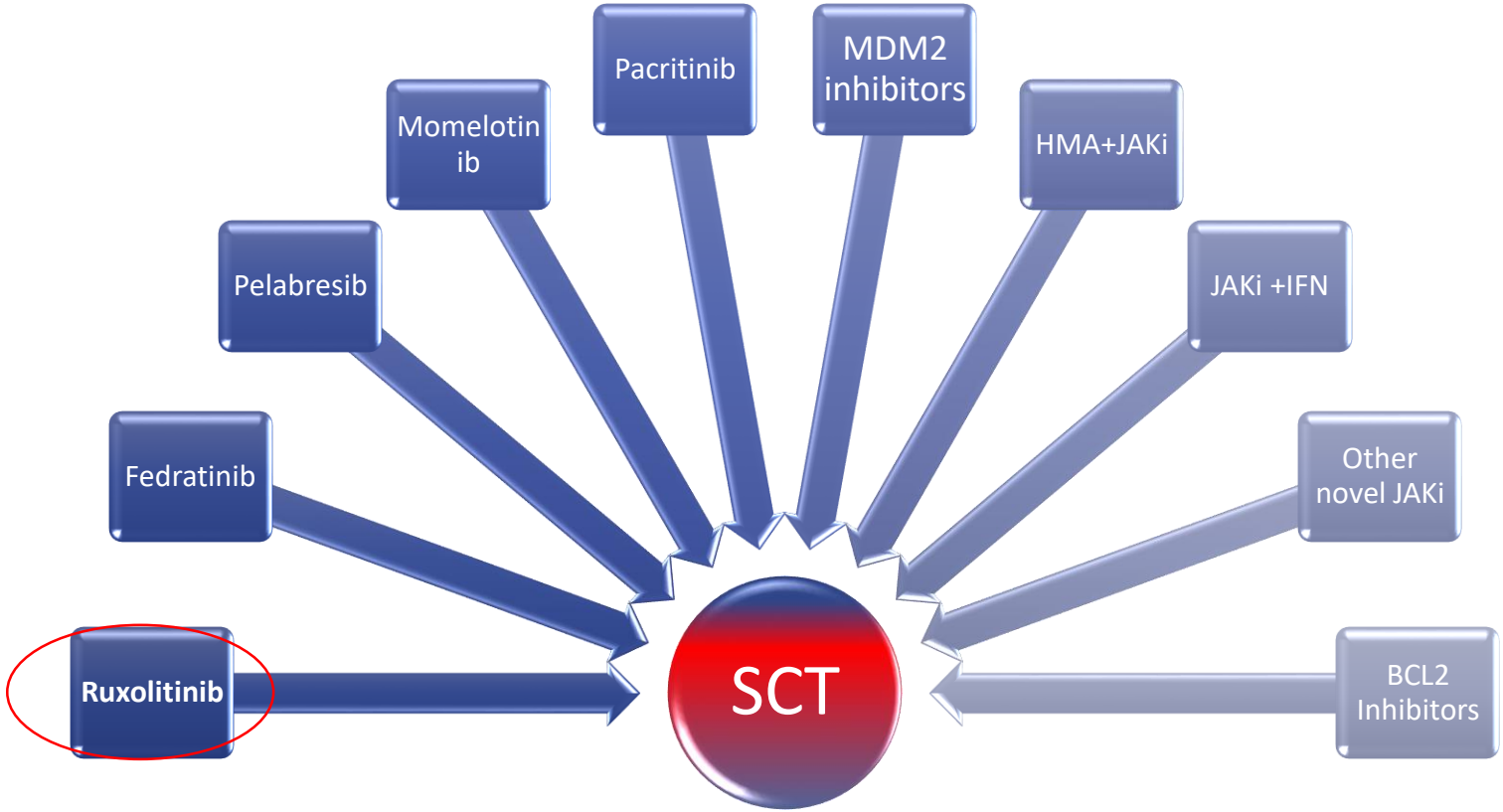


McLornan et al BJH 2024

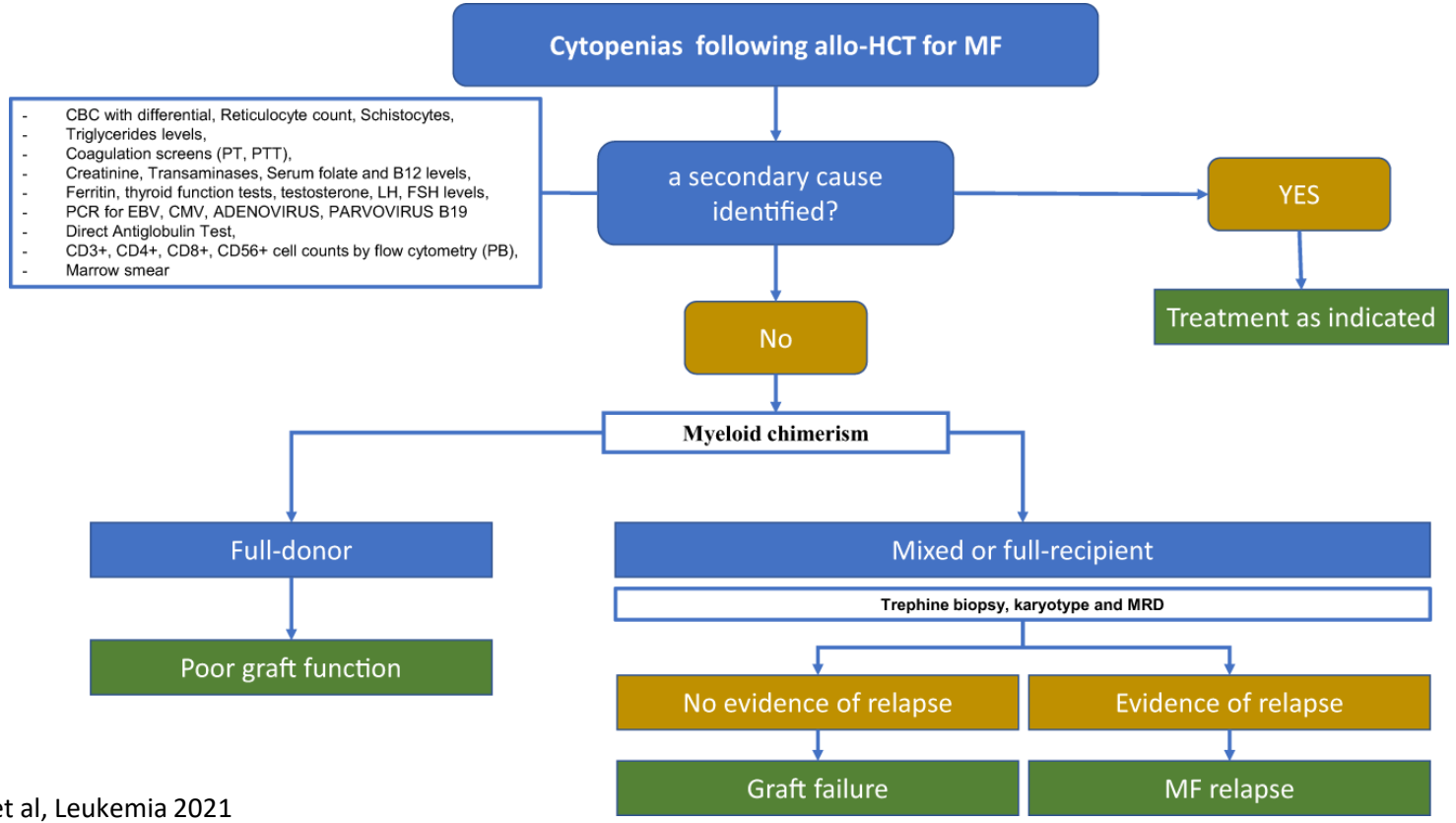
Challenges?...there are many

- Elderly patients >65 years referred for allo-SCT – how old is too old?
- Timing of allo-SCT on JAKi
- Splenectomy yes versus no?
- Conditioning choice
- Integration of JAKi and other into conditioning/ post-allo maintenance
- Management of poor graft function and graft failure
- Relapse

Expanding Array of Pre-Allo Therapies



CYTOPAENIA FOLLOWING ALLO-HCT FOR MYELOFIBROSIS



McLornan D et al, Leukemia 2021

Poor Graft Function in MF Allo-HCT

- Definition is variable but **in general** cytopenia in at least two hematopoietic lines (neutrophil count $\leqslant 1.5 \times 10^9$/L, platelet count $\leqslant 30 \times 10^9$/L, Hb $\leqslant 8.5$ g/dL) **for at least 2 weeks beyond day +14** after engraftment in the presence of **FDC**

- **Given incidence of Poor Graft Function in MF is this still a relevant set of diagnostic criteria?**

- Absence of **severe GvHD, CMV reactivation, relapse or drug-related myelosuppression. Easy to describe – harder to rule out in clinical practice**

- **Cytopaenias are frequently accompanied by a hypocellular bone marrow although this is not always the case.**

McLornan et al. Leukemia 2021

Poor Graft Function

Risk Factors: Patient/ Disease

Bulky splenomegaly

Older age? M>F

Prior HLA-sensitisation

DSA in haplo allo-HCT

Timing Post Transplant

Lasting for > 2 consecutive weeks following documented engraftment, beyond day+14

Mutational Effect?
No evidence

Risk Factors: Transplant

Low Dose CD34+

Unrelated Donors/MMRD

Major ABO Incompatibility

Trephine Biopsy
Frequently hypocellular but may be normo- or even hypercellular

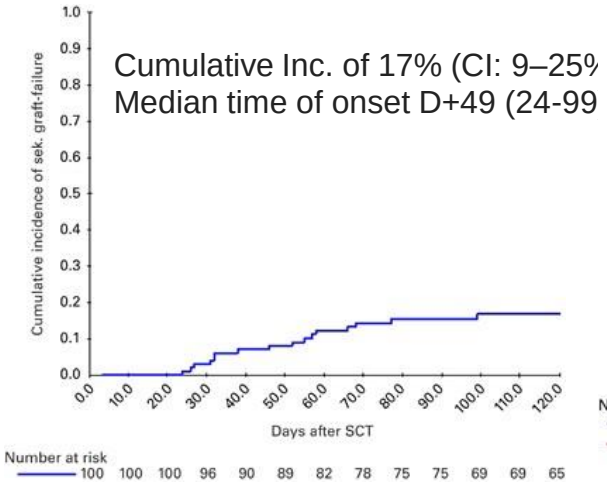
Chimerism
Full Donor Chimerism

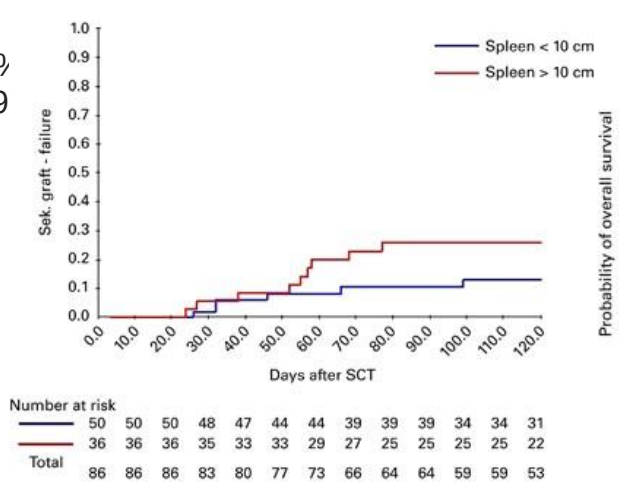
MRD
Not required for Definition

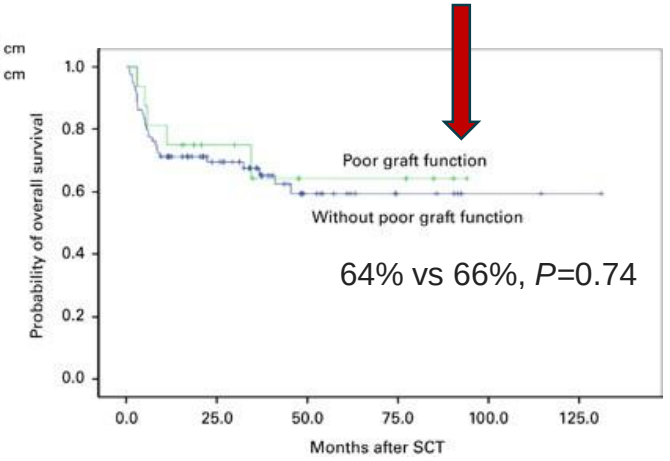
McLornan et al. Leukemia 2021

Poor Graft Function in MF Allo-HCT

- Cytopenia in at least two hematopoietic lines (neutrophil count ⩽1.5 × 10^9/L, platelet count ⩽30 × 10^9/L, Hb ⩽8.5 g/dL) for at least 2 weeks beyond day +14 after engraftment in the presence of FDC
- Absence of severe GvHD, CMV reactivation, relapse or drug-related myelosuppression.



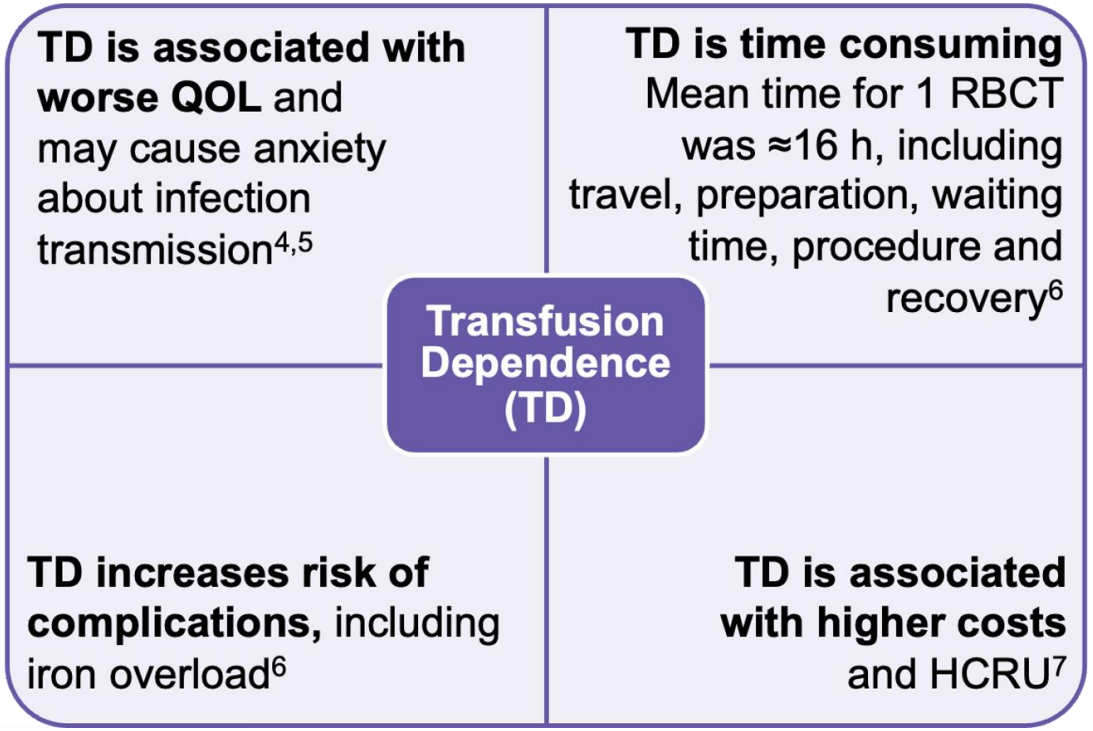




Alchalby et al Bone Marrow Transplantation (2016)

Transfusion Dependence

Poor Graft Function in MF Allo-HCT



Suggested Management of Poor Graft Function

1. Anti-infective prophylaxis based on time post allo-HCT, neutrophil count and lymphocyte subset recovery

2. Growth factor support with recombinant human EPO (RHuEPO) and GCSF can be considered but this is not a long-term solution. Insufficient evidence at present for routine use of TPO agonists although widely used -remains experimental

3. Consideration to **CD34+ selected SCB**, either fresh or cryopreserved, in the presence of full donor chimerism. Optimal timing of this approach however needs further evaluation as does the risk of GVHD.

4. For some patients with persistent, bulky splenomegaly, there are reports of resolution following post allo-HCT splenectomy.

5. For eligible patients, if significant, severe and unresponsive PGF persists, some may be considered suitable for **2nd allo-HCT**.

6. Insufficient evidence at present for routine use of Mesenchymal Stem Cell infusions. Use remains experimental and more robust evidence is required.

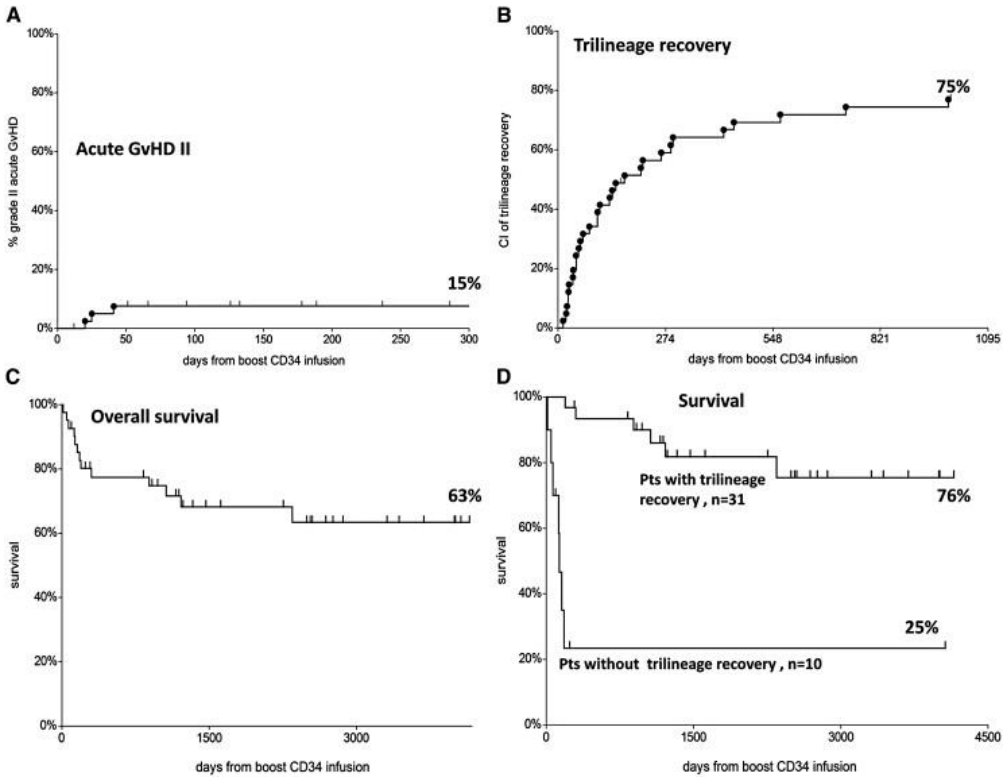
McLornan et al. Leukemia 2021

Selected CD34 Top Up Studies in Poor Graft Function

	Askaa et al 2014	Klyuchnikov et al 2014	Stasia et al 2014	Cuadrado et al 2020
Year of Publication	2014	2014	2014	2020
No. of Patients	18	32	41	62
Myelofibrosis	**6**	**14**	**4**	**2**
Interval to top up	113	140	150	440
CD34+ Cell dose	3.7	3.4	3.4	3.2
Hematological recovery	72%	81%	75%	76%
Stable HR	yes	yes	yes	yes
GVHD rates III-IV	2	4	0	4
De Novo Chronic	0	0	0	5
Median Follow up	1072	900	1245	2252
Acturial survival	3-yr 40%	3-yr 45%	3-yr 63%	**5yr-** 54%

Adapted from Stasia et al, 2014

CD34 Selected Cells for the Treatment of Poor Graft Function

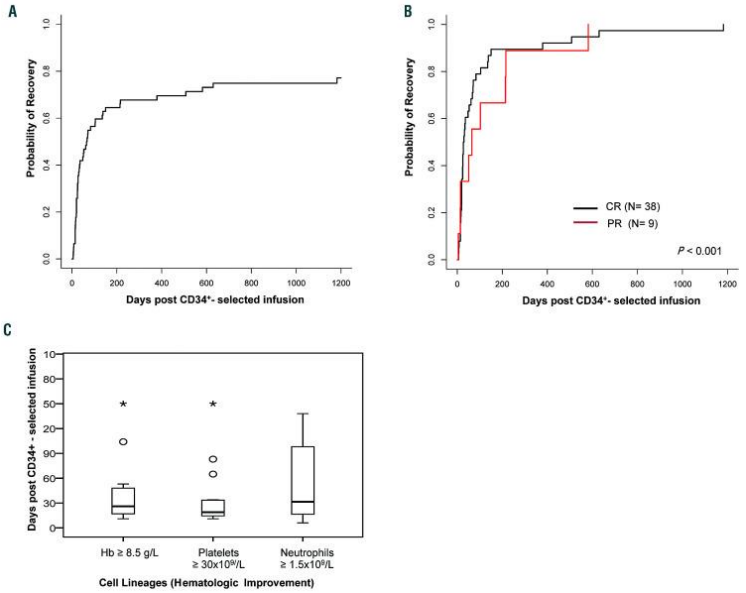


Stasia et al, 2014

CD34 Top Up 'Boost'

	N	OR (95% CI)	*P*-value
Active infection at the time of CD34⁺-selected infusion			
Yes	24	1.0	
No	36	38.9 (3.9-388.3)	0.002
Missing values	2		
R/D CMV status			
Other	37	1.0	
Negative/negative	23	16.8 (1.4-195.8)	0.02
Missing values	2		
R/D sex			
Unmatched	31	1.0	
Matched	29	24.4 (2.3-254.5)	0.008
Missing values	2		

R/D: recipient/donor; CMV: cytomegalovirus.



Cuadrado et al, 2020

Post Transplant Splenectomy for Poor Graft Function

- Evidence base is limited to selected centres and small case series/ case reports
- Advocates feel attractive if persistent bulky splenomegaly, >9 months with persistent cytopaenias and transfusion dependency
- However, significant morbidity and mortality in non-transplant setting of up to 6-9%
- Effects on immune reconstitution ?
- Risk/ Benefit ratio
- **Not something I do in my practice but would like to discuss!**

Primary and Secondary Graft Failure in MF Allo-HCT

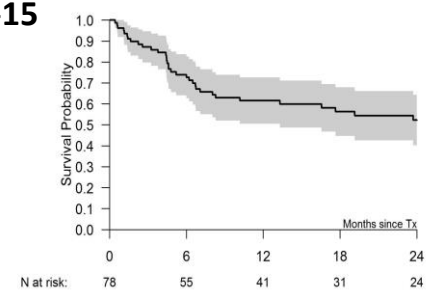
- **Graft failure rates have improved overtime but MF patients remain at higher risk of both primary and secondary GF, particularly with MMRD**
- **MF allo-HCT- bulky splenomegaly, hostile microenvironment and iron overload etc**
- **Primary GF is defined by an ANC <0.5X10^9/L by day+28 following stem cell return, haemoglobin <80 g/L and platelets <20 × 10^9/L (EBMT criteria)**
- **Secondary GF frequently represents a heterogeneous group in 'real world' practice -presence of an ANC <0.5 × 10^9/L occurring after initial engraftment not related to relapse, infection, or drug toxicity.**
- **Clearly donor, recipient, conditioning influence rates. ? Effect of JAKi unknown**

McLornan et al. Leukemia 2021

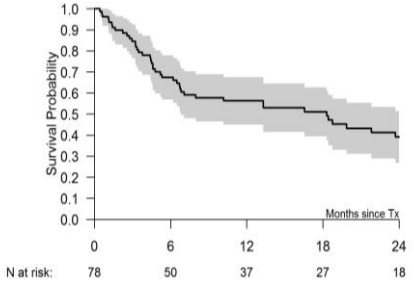
MMRD Allo-HCT and Risk of GF/ Relapse

- 56 patients; median age 57 underwent MMRD allo **2009-15**
- 70% MAC and 30% RIC
- 66% BM and 34% PB CD34+
- **Most common TBF with PTCy**
- **Neutrophil engraftment 82%; median 20 days**
- CI of cGVHD at 1 year was 45% (32-58)
- At 2years CI of **primary graft failure** was **9%** (1% to 16%)
  - **secondary GF** was **13%** (95% CI 4% to 22%).

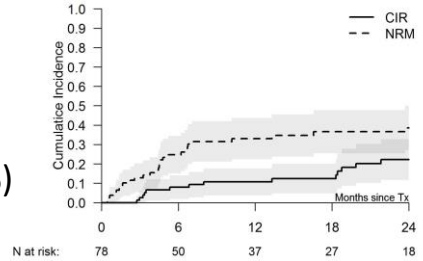
(a) Overall Survival



(b) Progression Free Survival



(c) CIR and NRM



Median FU 32 Months, 1-2- yr OS 61% and 56%

2yr CIR: 19% (7-31%)

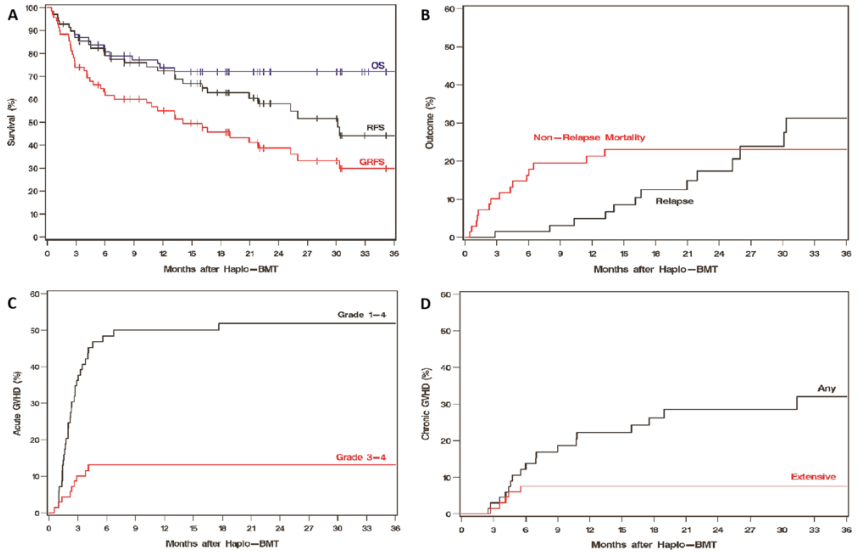
2yr NRM was 38% (24-51%)

Raj et al, BMT 2019

Role of MMRD

- Median age at BMT was 63 years (range, 41–74).
- Conditioning regimens were RIC in 54% and nonmyeloablative in 39%.
- PTCy
- PB grafts were used in 86%
- Spleen size ≥22 cm or prior splenectomy (HR 6.37, 95% CI 2.02–20.1, *P* = 0.002), and BM grafts (HR 4.92, 95% CI 1.68–14.4, *P* = 0.004) were associated with increased incidence of relapse

N=69



OS, RFS, and graft-versus-host-disease (GVHD)-free-RFS were 72% (95% CI 59–81), 44% (95% CI 29–59), and 30% (95% CI 17–43).

Kunte et al, 2021

Role of Haploidentical?

First Allo between 2013-2019 for MF
N=1057 patients

- **MMRD-PTCy, MSD, MUD, MMUD**

Characteristic		HD (121)	MSD (n=312)	MUD (n=574)	MMUD (n=68)
Age at BMT in years - median (range)		63 (34-75)	61 (21-73)	63 (32-78)	60 (38-72)
Male sex - no. (%)		73 (60)	185 (59)	329 (57)	40 (59)
Race/Ethnicity - no. (%):	White, not Hispanic	72 (60)	250 (80)	515 (90)	52 (76)
	African-American, not Hispanic	19 (16)	17 (5)	12 (2)	9 (13)
	Asian, not Hispanic	8 (7)	18 (6)	11 (2)	1 (1)
	Hispanic	17 (14)	20 (6)	21 (4)	5 (7)
	Other	1 (1)	4 (1)	8 (1)	0 (0)
Sub-diagnosis - no. (%):	Primary Myelofibrosis	85 (70)	210 (67)	395 (69)	49 (72)
	Post-ET/Post PV	35 (29)	99 (32)	168 (29)	19 (28)
Time from diagnosis to BMT - median (min-max)		34 (2-401)	28 (2-417)	29 (2-522)	31 (4-363)
Donor age, median (range), year - median (min-max)		33 (16-63)	58 (18-76)	28 (18-60)	29 (18-57)
Conditioning regimen intensity - no. (%):	MAC	32 (26)	147 (47)	253 (44)	31 (46)
	RIC/NMA	87 (72)	157 (50)	314 (55)	36 (53)
GVHD prophylaxis - no. (%):	PTCy-based	121 (100)	29 (9)	59 (10)	11 (16)
	CNI + MMF	0 (0)	37 (12)	75 (13)	8 (12)
	CNI + MTX	0 (0)	215 (69)	374 (65)	43 (63)
	CNI +/- Others	0 (0)	30 (10)	59 (10)	6 (9)
Follow-up in months - median (range)		36 (9-77)	46 (13-100)	48 (4-98)	49 (23-98)

Jain T et al, TCT 2023

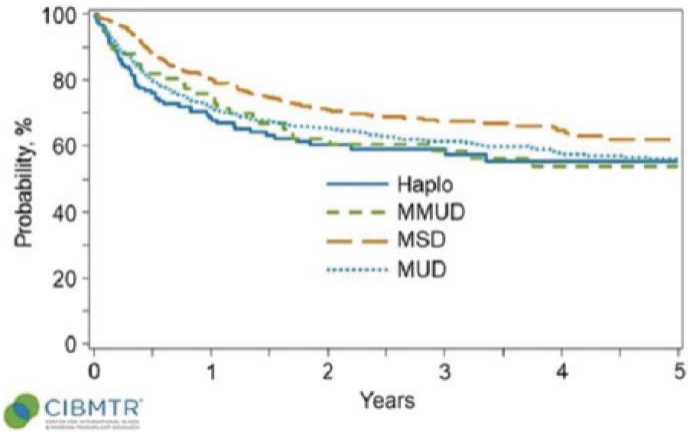
Role of Haploidentical

OS at <3 month superior for MSD; mostly due to less NRM

No difference between MUD; HD-PTCy or MMUD

OS						
Variable		N	HR	95% CI Lower limit	95% CI Upper limit	P value
Main effect (donor type) ≤3 months	HD-PTCy	121	1.000			
	MSD	309	0.221	0.106	0.463	<.0001
	MUD	563	0.740	0.425	1.289	0.2878
	MMUD	67	0.787	0.283	2.188	0.6460
Contrast:	MSD vs MUD		0.299	0.168	0.531	<.0001
	MSD vs MMUD		0.281	0.085	0.927	0.0371
	MUD vs MMUD		0.941	0.382	2.314	0.8942
Main effect (donor type) >3 months	HD-PTCy	102	1.000			
	MSD	298	0.913	0.603	1.383	0.6684
	MUD	497	0.920	0.619	1.366	0.6790
	MMUD	59	1.009	0.629	1.619	0.9713

	NRM				Relapse				DFS			
		95% CI				95% CI				95% CI		
	HR	Lower limit	Upper limit	P value	HR	Lower limit	Upper limit	P value	HR	Lower limit	Upper limit	P value
HD-PTCy	1.000				1.000				1.000			
MSD	0.809	0.625	1.048	0.1092	0.918	0.667	1.262	0.5969	0.809	0.625	1.048	0.1092
MUD	0.947	0.708	1.268	0.7166	0.976	0.680	1.402	0.8962	0.947	0.708	1.268	0.7166
MMUD	0.860	0.588	1.257	0.4356	0.845	0.548	1.303	0.4461	0.860	0.588	1.257	0.4356



Jain T et al, TCT 2023

Suggested Management of Graft Failure

- Prevention by minimising risk factors where possible and early detection is paramount.
- Urgent Aspirate and trephine/ Cyto and chimerism
- Address myelosuppressive drugs, viral infections (particularly CMV), treatment of GVHD.
- If suspected GF, optimisation/weaning of immunosuppressive therapy is dependent on timing
- Growth factors are often instituted but there is little supporting evidence*.
- Donor Lymphocyte Infusions: role in increasingly mixed donor-host chimerism?
- **2nd allo-HCT for Primary GF and refractory secondary GF** (after addressing contributing factors)

McLornan et al. Leukemia 2021

Introduction to the Relapse Problem

- **Risk of Relapse is a composite of many factors: host, disease and graft**
- **Relapse rates vary according to study and range between: 18-40% depending on study and era**
- **Not easy to predict and outcome of patients is highly variable**
- **Clearly defining relapse is made difficult by the dynamics of donor: recipient chimerism, variable rates of MRD clearance and widely varying rates of resolution of marrow fibrosis and splenomegaly.**
- **Management strategies are often heterogeneous making robust recommendations difficult**
- **Treatment of established relapse following SCT presents huge challenges**

McLornan et al. Leukemia 2021

IMPACT OF RUXOLITINIB ON ALLO-SCT OUTCOME: CMWP OF EBMT STUDY

Evaluated the impact of RUX on outcome in **551** MF patients Allo-SCT between 2012 and 2016 either without (n = 274) or with (n = 277) ruxolitinib pretreatment.

RUX pre-treatment group was divided into:

1. ongoing spleen response (n=91) with spleen response ≥ 50% (n=25) and spleen response < 50% (n=66).

2. No ongoing spleen response (n=104): either loss of spleen response (n=23) or no spleen response at all (n=81).

Kroger et al , Leukemia 2021

IMPACT OF RUXOLITINIB ON ALLO-SCT OUTCOME: CMWP OF EBMT STUDY

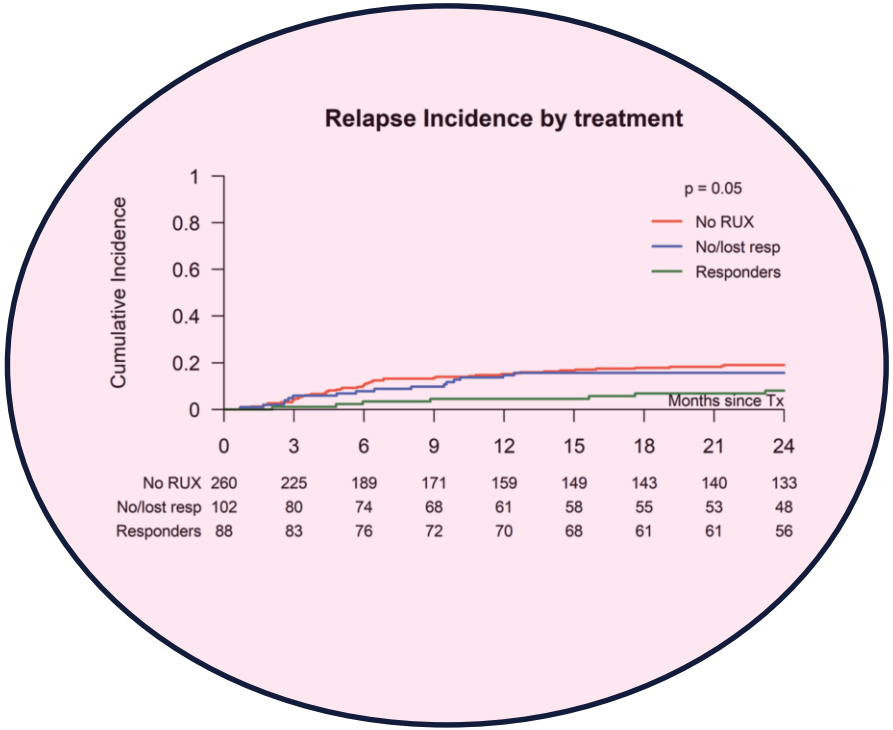
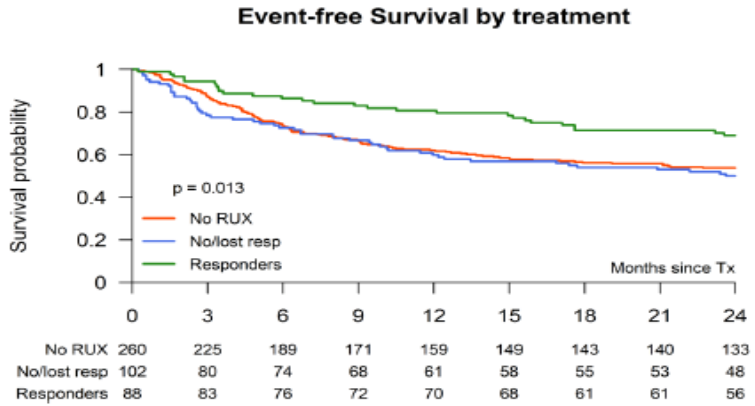


Figure 4 Event-free survival after allogeneic stem cell transplantation of RUX responder vs. no/lost responders vs. non-RUX pretreatment



Kroger et al , Leukemia 2021

Real World Transplant Practice in MF

- Survey was sent to a total of 65 centres experienced in allo-HCT for MF across Europe in February 2020.
    - By time of survey closure, a total of 36 centres (55%) completed the survey.

Marked variations in assessment prior to allo-HCT, JAK inhibitors peri-transplant, molecular, histopathological and cytogenetic monitoring and approaches to the definition and management of relapse were apparent

McLornan et al, 2020 on behalf of EBMT

Real World Transplant Practice in MF: Relapse

- Broad agreement that clinicians utilised a combination of chimerism, MRD, cytogenetic analysis, marrow fibrosis grade, clinical and haematological findings to define relapse.
    - **comprehensive definition of relapse is required.**
- No evidence exists for prophylactic measures to reduce relapse risk, yet 8/33 (24%) responding centres were using either DLI alone, JAKi alone or in combination to attempt relapse risk modulation, clearly requiring evaluation in a clinical trial setting.
- **Approaches to either early or late relapse varied markedly, ranging from palliation, immunotherapy and further allo-HCT.**

McLornan et al, 2020 on behalf of EBMT

Defining Relapse for MF post allo-HCT is not as clear cut as other diseases

Response and Relapse Criteria in Myelofibrosis

NON-TRANSLANT SETTING IWG-MRT criteria

CR	Bone marrow:* Age-adjusted normocellularity; <5% blasts; ≤grade 1 MF‡ and
	Peripheral blood: Hemoglobin ≥100 g/L and <UNL; neutrophil count ≥ 1 × 10^9/L and <UNL;
	Platelet count ≥100 × 10^9/L and <UNL; <2% immature myeloid cells‡ and
	Clinical: Resolution of disease symptoms; spleen and liver not palpable; no evidence of EMH

NON-TRANSLANT SETTING IWG-MRT criteria

Relapse	No longer meeting criteria for at least CI after achieving CR, PR, or CI, or
	Loss of anemia response persisting for at least 1 month or
	Loss of spleen response persisting for at least 1 month

Tefferi et al, 2013

Defining Relapse for MF post allo-HCT is not as clear cut as other diseases

Survey of Real World Practice revealed marked heterogeneity

TRANSLANT SETTING

- No universally approved definition of relapse after allo-SCT for MF patients.
- Often heterogeneous post-allo course
  - only 50%-60% of patients show regression of the BM fibrosis in the early posttransplant period – often up to 12-24 months
- Expanding understanding of MRD predicting clinical relapse

Kroger et al, 2010

Haematological Remission and Relapse: requires normalization of blood counts and marrow cellularity / fibrosis but influenced by GVHD, PGF, Drug toxicity etc

Cytogenetic Remission and Relapse: Karyotype, SNP, FISH

MRD: dynamics variable ? At least 2 positive readings > 4 weeks apart by sensitive detection methods to define a molecular relapse when previous CMR.

Chimerism ? MMC level

In clinical practice often a combination of above

MRD Monitoring to predict/ prevent relapse

	n
Age, yr (range)	**58 (32-75)**
Gender	
Male	**79**
Female	**57**
IPSS	
Low/ intermediate-1	**17**
Intermediate-2/High	**111**
Missing	**8**
Donor Type	
Related	**26**
Unrelated	**110**
Conditioning	
Reduced Intensity (Busulphan/ Fludarabine-based)	**136**
Stem Cell Source	
Bone Marrow Derived	**2**
Peripheral Blood Derived	**134**
Acute	
Grade 2-4	**52 (38%)**
Grade 3-4	**25 (18%)**
Mutations	
JAK2 V617F	**n=101**
MPL	**n=4**
CALR	**n=31**

ORIGINAL ARTICLE

Impact of molecular residual disease post allografting in myelofibrosis patients

C Wolschke, A Badbaran, T Zabelina, M Christopeit, F Ayuk, I Triviai, A Zander, H Alchalby, U Bacher, B Fehse and N Kröger

Median Follow Up: 78 months (range: 49-101)

Estimated OS: 60% (95% CI: 50–70)

CIR: 26% at 5-years

On Day +100 and +180

- 27% and 11% had a detectable molecular marker in PB

Molecular clearance higher for *CALR*-mutated patients (92%) than for MPL- (75%) or JAK2V617F-positive patients (67%).

Wolschke et al, 2017

MRD Monitoring to predict/ prevent relapse

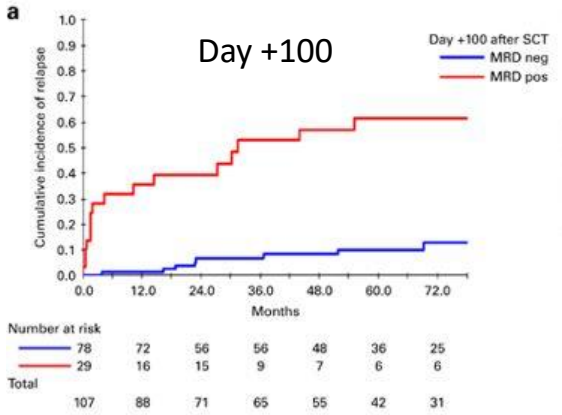
MRD Positivity

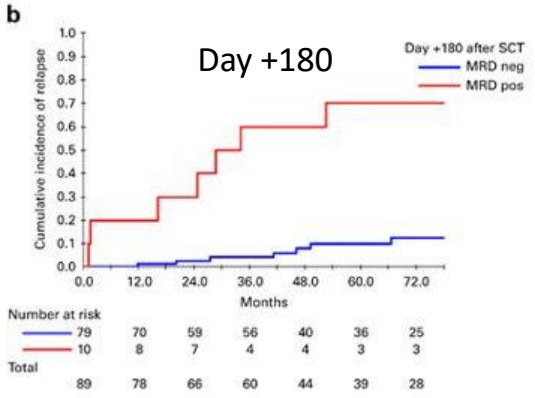
Day +100 risk of clinical relapse at 5 years (62% vs 10%, P=0.001)

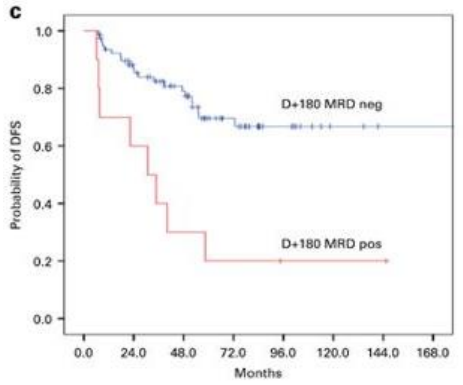
Day+180 risk of clinical relapse at 5 years of 70% as compared with 10% in MRD-negative patients (P=0.001).

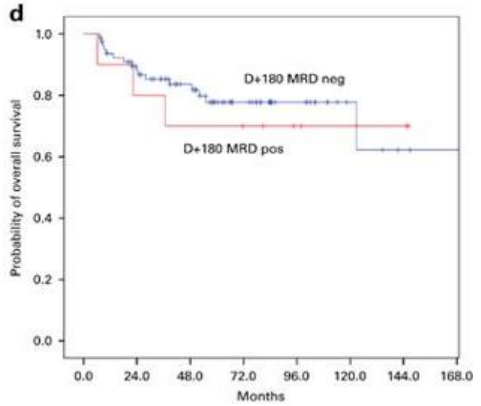
MVA for relapse beside high-risk disease status detectable MRD at day +180 has the highest risk of clinical relapse (HR: 8.37; 95% CI: 2.77–25.30, P=0.001).

Wolschke et al, 2017









Recommendations for MRD monitoring post allo-HCT

-Where a detectable MRD marker is present, testing should be performed at: day+100, day+ 180, day+ 270 and day+360 as a minimum or as guided by clinical scenario.

- **There is some evidence to suggest that longer term MRD monitoring is important.**

-Sensitive laboratory techniques are required, ideally with a sensitivity of 0.01-1%.

For JAK2 V617F monitoring, laboratories should ideally use an optimal quantitative PCR test kit, digital PCR or other sensitive methodology.

Both CALR and MPL MRD monitoring have been used for assessment of MRD.

- **There is still a lack of standardisation of quantitative results for CALR and MPL**

Utilisation of extended panels with NGS to provide MRD monitoring is currently unstandardised.

- **Evaluation is required in the context of a clinical trial.**

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Definition of Molecular and Cytogenetic Relapse

MRD: Definition of molecular persistence and relapse in MF allo-HCT is complicated by the variable kinetics of clearance of detectable MRD.

Molecular relapse can be defined as the reappearance of the established MRD marker *after documented clearance* confirmed by **two consecutive PB samples collected at least 28 days apart with persistence or rising levels over time.**

Cytogenetics: Cytogenetic relapse can be defined as detection of an informative previously detected chromosomal abnormality on G-banded, FISH or SNP-A analysis not meeting the criteria for morphological relapse.

McLornan et al. Leukemia 2021

Recommendations for Chimerism Analysis

Predominantly, chimerism assessment is performed on PB but marrow -if performed -should also be assessed. **PB lineage specific chimerism is recommended.**
PB chimerism testing should be performed at the following time points: day+30, day+100, day+ 180, day+ 270 and day+360, as a minimum or as guided by clinical scenario. There is some evidence to suggest that longer term chimerism testing is important.
Frequently chimerism assessment is paired with MRD assessment when there is a suitable marker; recommended to increase predictive value.
Complete chimerism–frequently defined as >95% of cells being DONOR
Increasing mixed myeloid chimerism (>5% in the tested lineage compared to previous sample of same type) associated with higher RR
Utilising chimerism to predict and define relapse requires careful individualised interpretation of chimerism kinetics.
Role of CD34 specific chimerism in MF requires further evaluation

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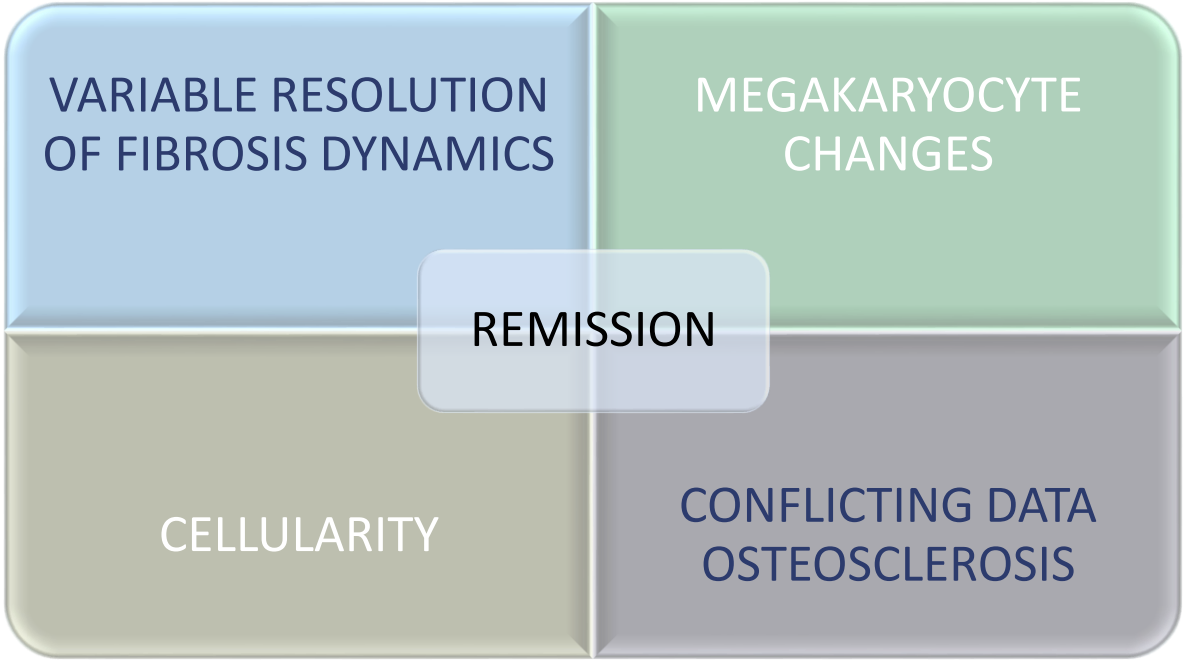
Considerations to morphological relapse



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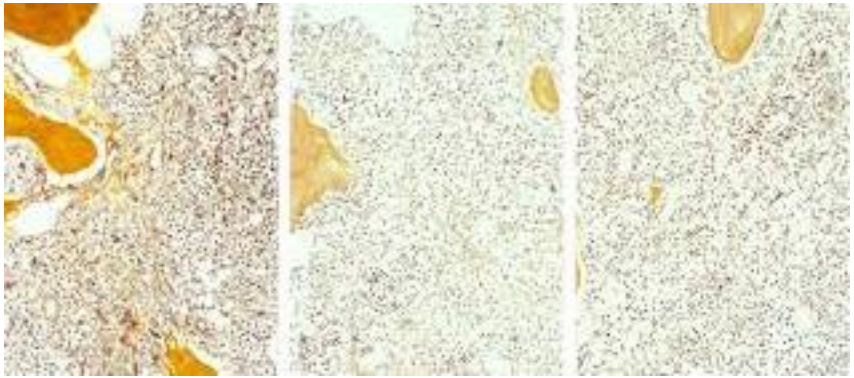
DYNAMICS OF FIBROSIS RESOLUTION

RESOLUTION OF MYELOFIBROSIS



BEFORE MF-3. DAY+30 MF-1. DAY+100 MF 0

- Kroger *et al* correlated regression of BMF on day 30 and 100 after dose- reduced allo-HCT in 57 pati

Table 3
Reduction of BMF at Day +30 and Day +100 after allo-SCT

Time	Level of Reduction, n (%)			
	None	One Grade	Two Grades	Three Grades
Day +30 (n = 48)	28 (59)	14 (29)	4 (8)	2 (4)
Day +100 (n = 44)	9 (21)	16 (36)	12 (27)	7 (16)

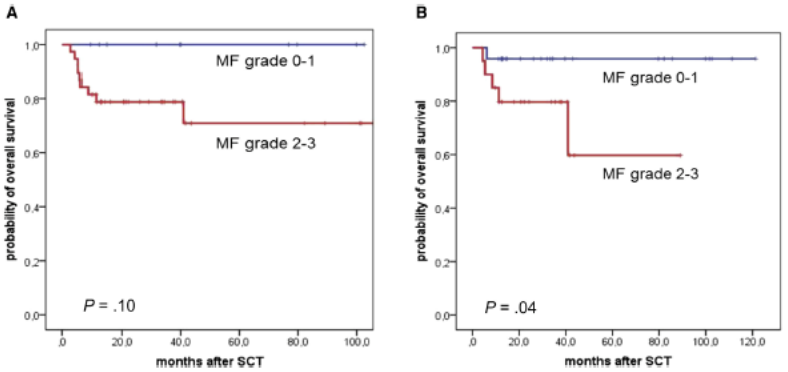


Figure 2. Overall survival according to fibrosis regression on day 30 (A) (based on 48 patient) and day 100 (B) (based on 44 patients) post allografting.

Kroger et al, 2007, 2014

MORPHOLOGICAL FEATURES OF RELAPSE

In the presence of post-transplant normalization of morphology and a documented reduction in fibrosis, criteria for relapse include:

1. **Increase in age adjusted cellularity** and **abnormal ME** ratio.

2. **Megakaryocytic abnormalities** typical of MF (pleomorphism, hyperchromasia, cloud like nuclei,clusters).

3. **Increase in grade of reticulin / collagen fibrosis** (previously formed new bone usually takes a long time to be resorbed / resolve and therefore this should not be used in grading post-transplant unless its density is significantly greater than the pre-transplant biopsy or there is active evidence of continuing new bone deposition)

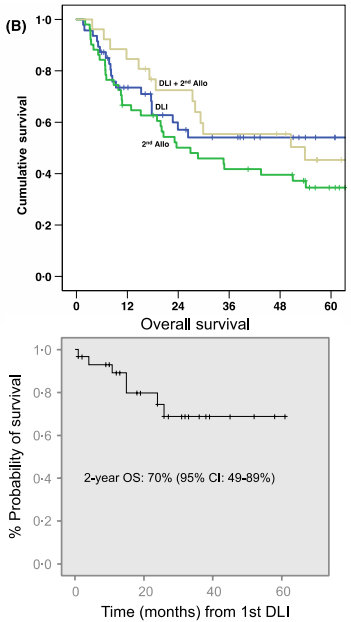
Relapse: Management Approaches

Treatments after relapse following allo-HSCT

- Few data on optimal strategy after 1st transplant failure/relapse.

1. EBMT retrospective analysis of 202 patients with MF.
   - Median OS from the time of relapse of 22.9 months
     - 23% pts DLI → 76.2 months
     - 11% chemotherapy alone → 22.9 months
     - 20% DLI & chemotherapy → 22.9 months
     - 25% 2nd allo-HSCT alone → 26.9 months
     - 13% DLI & 2nd allo-HSCT → 53.9 months
   - *Beneficial role for adoptive immunotherapeutic approaches with DLI and/or 2nd allo-HSCT.*

2. *Two-step strategy (DLI & 2nd RIC-allo-HSCT) effective and well-tolerated according to a multicentric study with 30 pts.*



1. D McLornan et al., British Journal of Haematology, 2018, 182, 418–422
2. Klyuchnikov E, British Journal of Haematology, 2012, 159, 172–181

Slide courtesy of M Nabergoj

DLI for MF?

Transplantation and Cellular Therapy
Available online 24 August 2023
In Press, Journal Pre-proof What's this?

Adoptive immunotherapy via Donor lymphocyte infusions following allogeneic haematopoietic stem cell transplantation for Myelofibrosis: A real world, retrospective multi-centre study.

A. Rampotas [1], K. Sockel [2], F. Panitsas [3], C. Theuser [2], M. Bornhauser [2], R. Hernani [4], J.C. Hernandez- Boluda [4], A. Esquirol [5], D. Avenoso [6], P. Tsirigotis [7], M. Robin [8], T. Czerw [9], G. Helbig [10], C. Roddie [1], J. Lambert [1], D.P McLornan [1]

HemaSphere

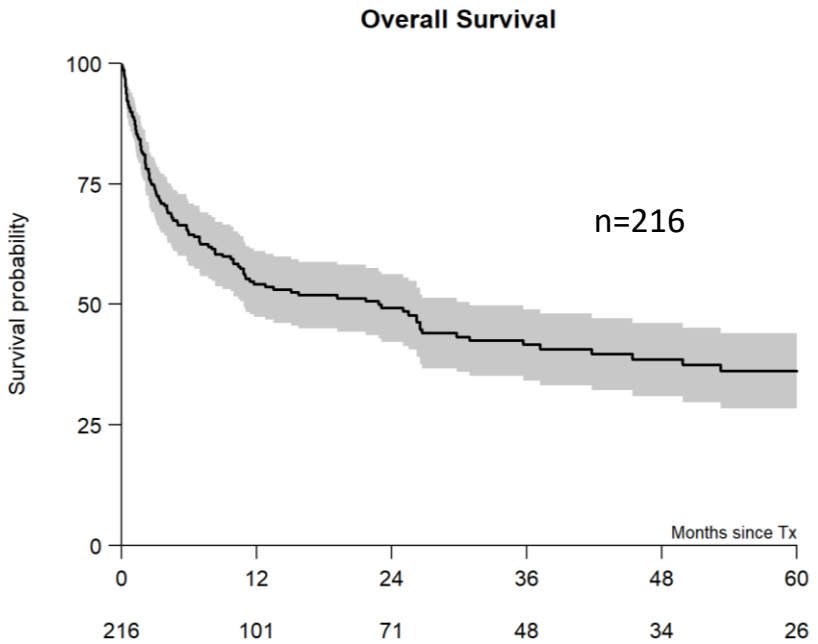
Hemasphere. 2023 Jul; 7(7): e921.
Published online 2023 Jun 30. doi: 10.1097/HS9.0000000000000921

PMCID: PMC10317484
PMID: 37404772

Donor Lymphocyte Infusion and Molecular Monitoring for Relapsed Myelofibrosis After Hematopoietic Cell Transplantation

Nico Gagelmann,[1] Christine Wolschke,[1] Anita Badbaran,[1] Dietlinde Janson,[1] Carolina Berger,[1] Evgeny Klyuchnikov,[1] Francis Ayuk,[1] Boris Fehse,[1] and Nicolaus Kröger[1]

Role of 2nd Allo-HCT for Relapse or Graft Failure



Median OS, months= 22.8 (95% CI: 10.9 – 35.7)
Median follow-up, months (IQR)= 40 (16.5, 72)

Overall survival (OS), % (95% CI)	
2-year OS	49 (42-56)

Univariate analysis for OS (significant)

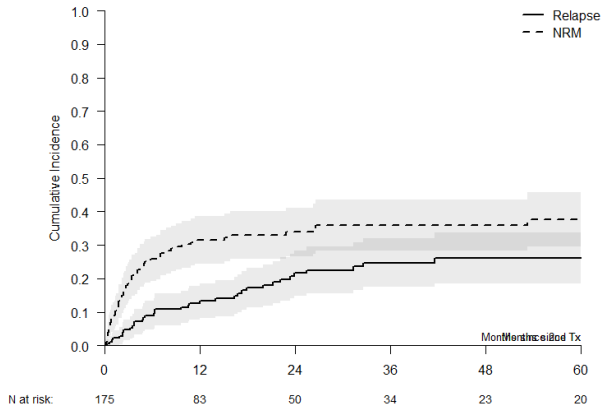
Variable		2-year OS (%)	P-value
Reason for 2nd allo-HCT	Relapse	52	0.02
	Failure	34	
Karnofsky	< 90	29	0.002
	≥90	54	
Time from 1st to 2nd allo-HCT (months)	≤12	43	0.025
	>12	58	

- **Use of either the original or a different donor appears to be associated with similar outcomes**
- **The stem cell source doesn't impact prognosis.**

Nabergoj et al on behalf of EBMT, BMT 2021

2nd Allo-HCT for Relapse or Graft Failure: NRM and Relapse Rates

Non relapse mortality & Relapse



Relapse, % (SE)	
2-year relapse	21.6 (3.4)
5-year relapse	26.0 (3.9)
Non relapse mortality (NRM), % (SE)	
2-year NRM	33.9 (3.7)
5-year NRM	37.7 (4.2)

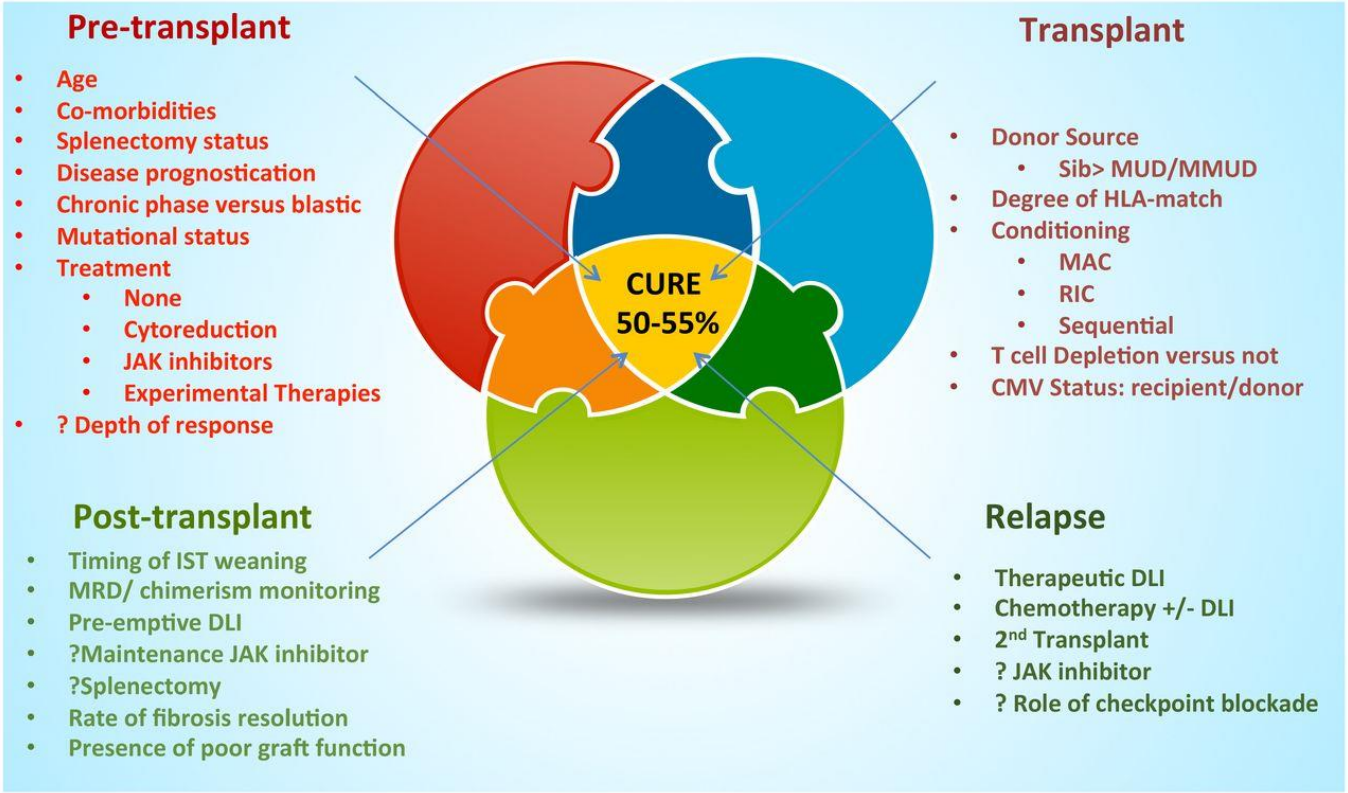
Univariate analysis for NRM

	Variables	2-year NRM (%)	P-value
Reason for 2nd allo-HCT	Relapse	31	0.06
	Failure	45	
Time from 1st to 2nd allo-HCT (months)	<=12	40	0.08
	>12	23	

Univariate analysis for Relapse: no significant factors

Nabergoj et al on behalf of EBMT, BMT 2021

FACTORS AFFECTING OUTCOMES IN MF ALLO-SCT



Summary

1) **Pivotal to distinguish between graft failure, poor graft function and relapse**

2) **Dynamic and variable resolution of morphological characteristics, MRD kinetics and chimerism can make practical definitions difficult**

3) **Pragmatic approach taken to molecular, cytogenetic and morphological relapse**

4) **Will guide IST wean and adoptive DLI use**

5) **Increased uptake of definitions to guide practice**

6) **Harmonise end points and intervention in real world settings**

7) **International consensus guidance on defining REMISSION post allo-HCT have been suggested**

Thanks!

EBMT