




Updates on Allogenic Stem Cell Transplantation for MDS

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Outline

- Nature of the disease
- Transplant related mortality based on age and HCT CI
- MDS prognostic models
- Evidence to support allogenic transplant in MDS elderly patients
- Role of bridging therapy pre-transplant
- Myeloablative vs RIC
- Disparity in MDS referrals for transplant



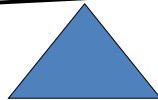
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Nature of disease

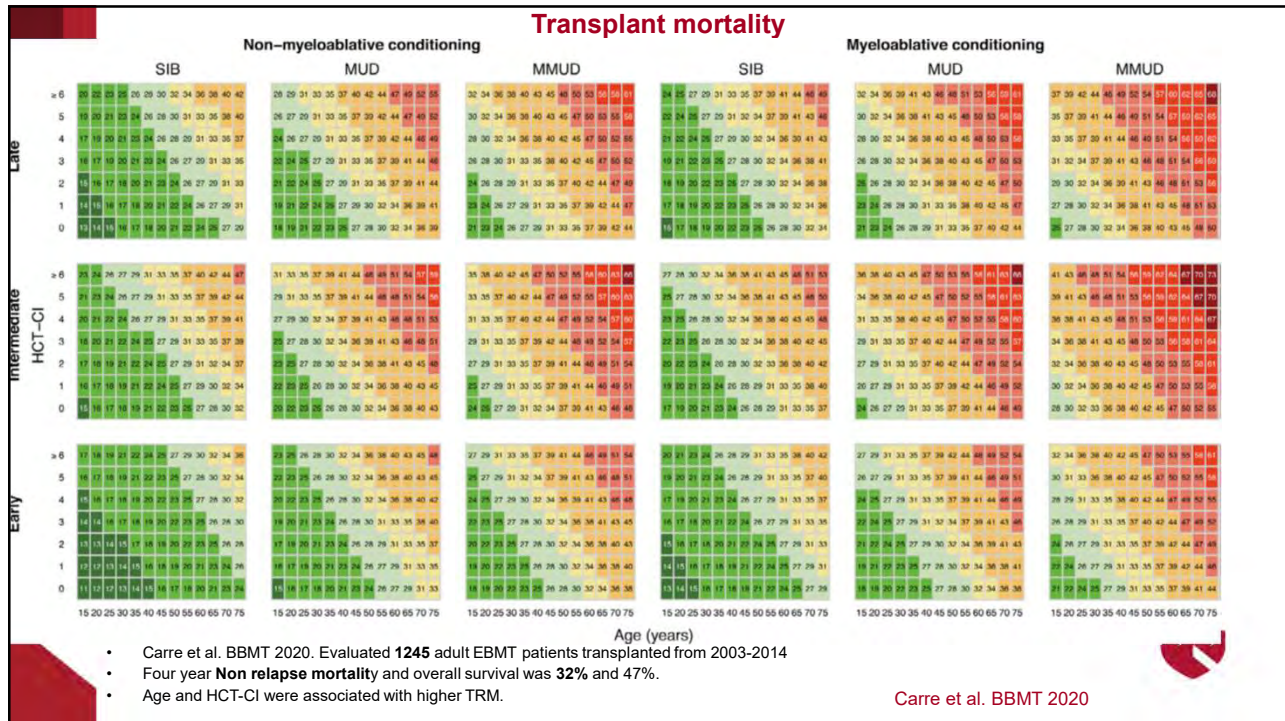
1. A group of clonal hematopoietic stem cell malignancies with heterogenous rate of transformation into acute myeloid leukemia.
2. The median age at diagnosis is 70-77. (86% of patients were aged ≥ 60)
3. Transplant associated mortality ranges from (11-73%) *Carre et al. BBMT 2020*

Rate of Leukemic Transformation

Transplant mortality

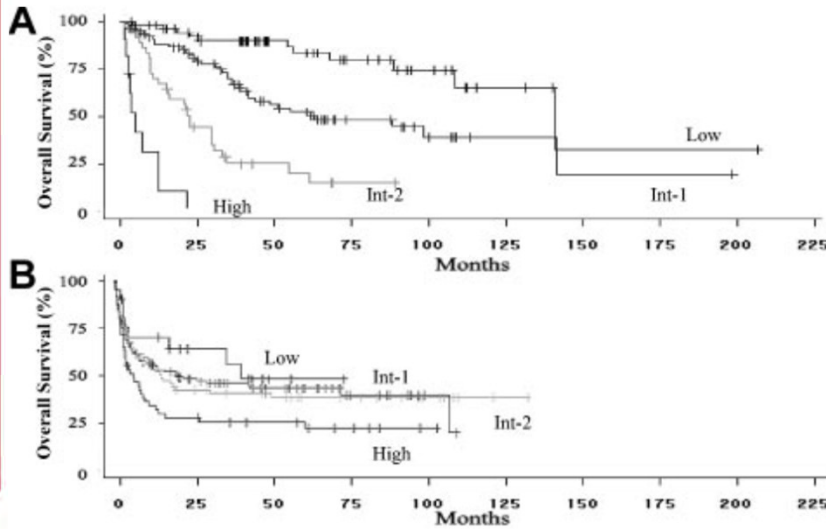


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Transplant based on MDS Prognostic Model IPSS



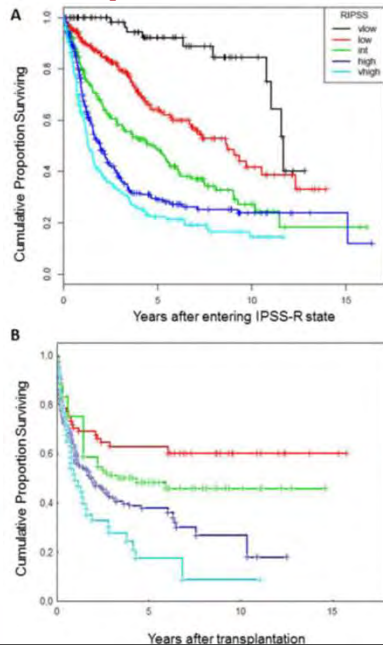
- Markov model to examine transplant timing
- 184 non transplant vs 490 transplant Pts
- Pts with Int 2 & high risk benefited from early transplant.
- Int 2 median survival was 2.5 years with no transplant



Cutler et al. Blood 2004

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Transplant based on MDS Prognostic Model IPSSR



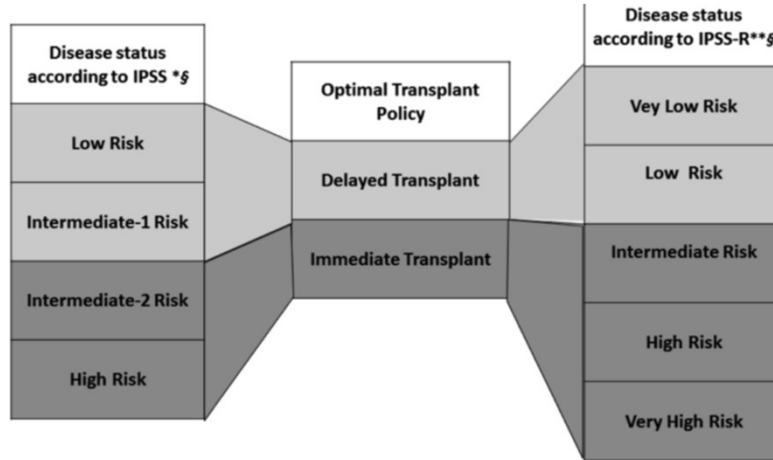
- Markov model to examine transplant timing
- 961 Pts with no transplant, 499 Pts with transplant, & 278 Pts with HMA
- The estimated life expectancy was maximized when transplantation was delayed until progression from the very low or low risk to the intermediate risk.
- Intermediate risk median survival was 5 years with no transplant
- Compared to IPSS, IPSSR upstaged 29% of the pts to higher risk stage which benefited from transplant



Della Porta et al. Leukemia 2018

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MDS Prognostic Model IPSSR



* Cutler CS, Blood 2004; 104:579-85

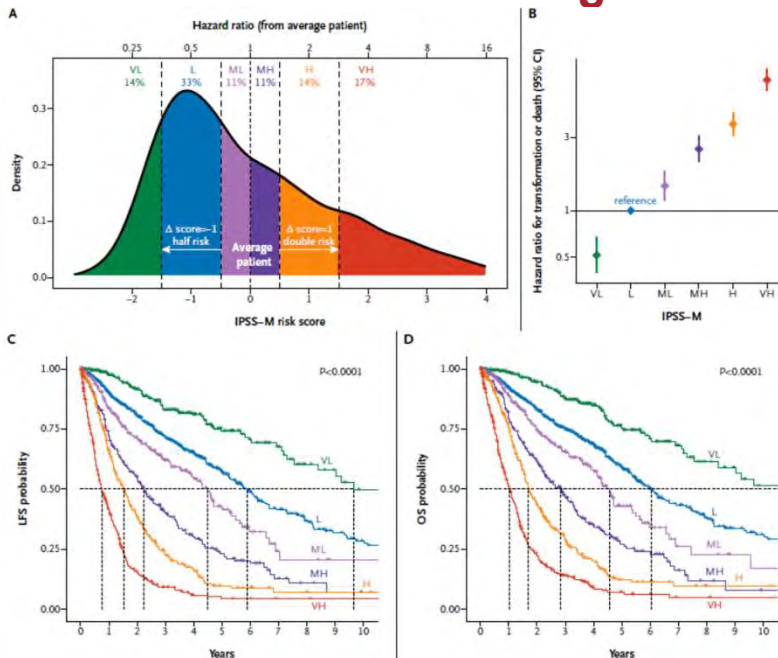
** Della Porta MG, Leukemia 2017, in press



Della Porta et al. Leukemia 2018

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Mutation based MDS Prognostic Model IPSS-M



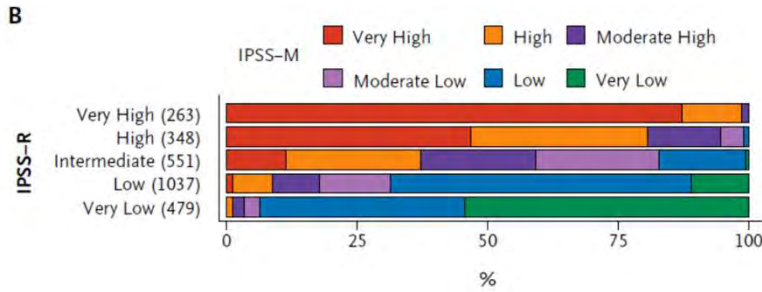
- Pre-therapy samples from 2957 patients with MDS were profiled for mutations in 152 genes
- TP53, MLL, FLT3 (ITD& TKD) had the highest negative prognostic impact
- Mutations in ASXL1, BCOR, EZH2, NRAS, RUNX1, STAG2, and U2AF1 were associated with adverse risk
- SF3B1α had a good prognostic impact



Bernard et al. NEJM 2022

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MDS Prognostic Model IPSS-M



- The IPSS-M model changed the staging for 46% of the patients. Upstaged in 74% and down staged in 26%

SF3B1 α is the SF3B1 mutation without co-mutations in BCOR, BCORL1, RUNX1, NRAS, STAG2, SRSF2, and del(5q).

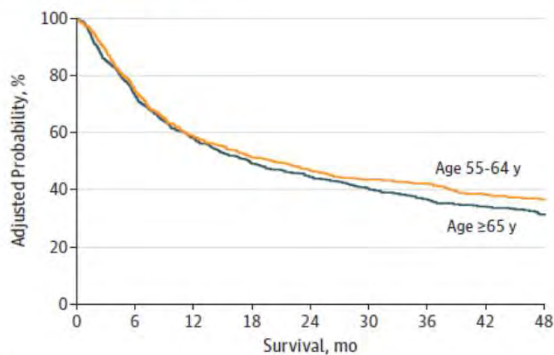


Bernard et al. NEJM 2022

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CIBMTR MDS Allogeneic Transplant Outcomes Based on Age

Figure 2. Overall Survival by Age



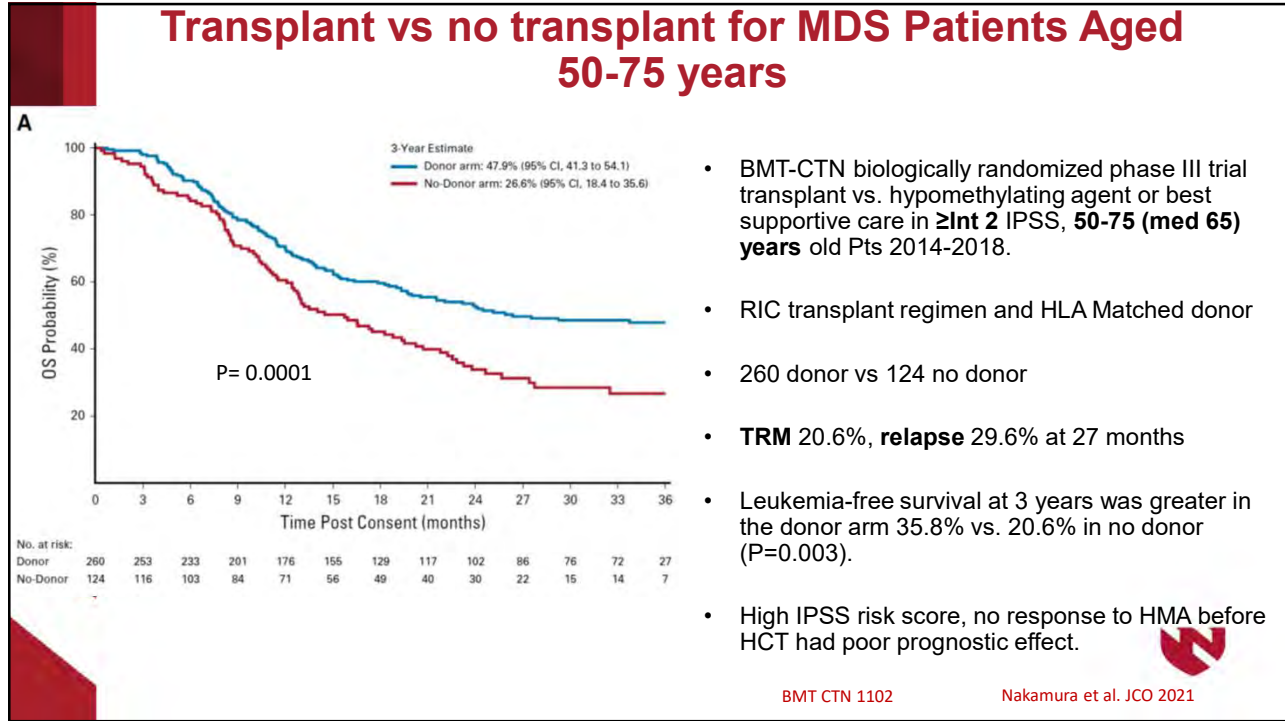
No. at risk		0	6	12	18	24	30	36	42	48
Aged ≥ 65 y	688	508	406	341	301	258	198	137	99	
Aged 55-64 y	592	445	350	306	278	245	209	141	103	

- CIBMTR **prospectively** evaluated outcomes of **688** pts ≥ 65 with **592** pts aged 55-64 between 2010-2014.
- For older Pts, med age was 68(65-79)
- No difference in patient or disease characteristics
- NRM at 3 years 28 vs 25%
- Overall survival rate were not significantly different
- Overall survival factors: HCT-CI ≥ 4 , IPSS-R scores, bone marrow blast $\geq 11\%$, and GVHD prophylaxis calcineurin inhibitor and methotrexate.

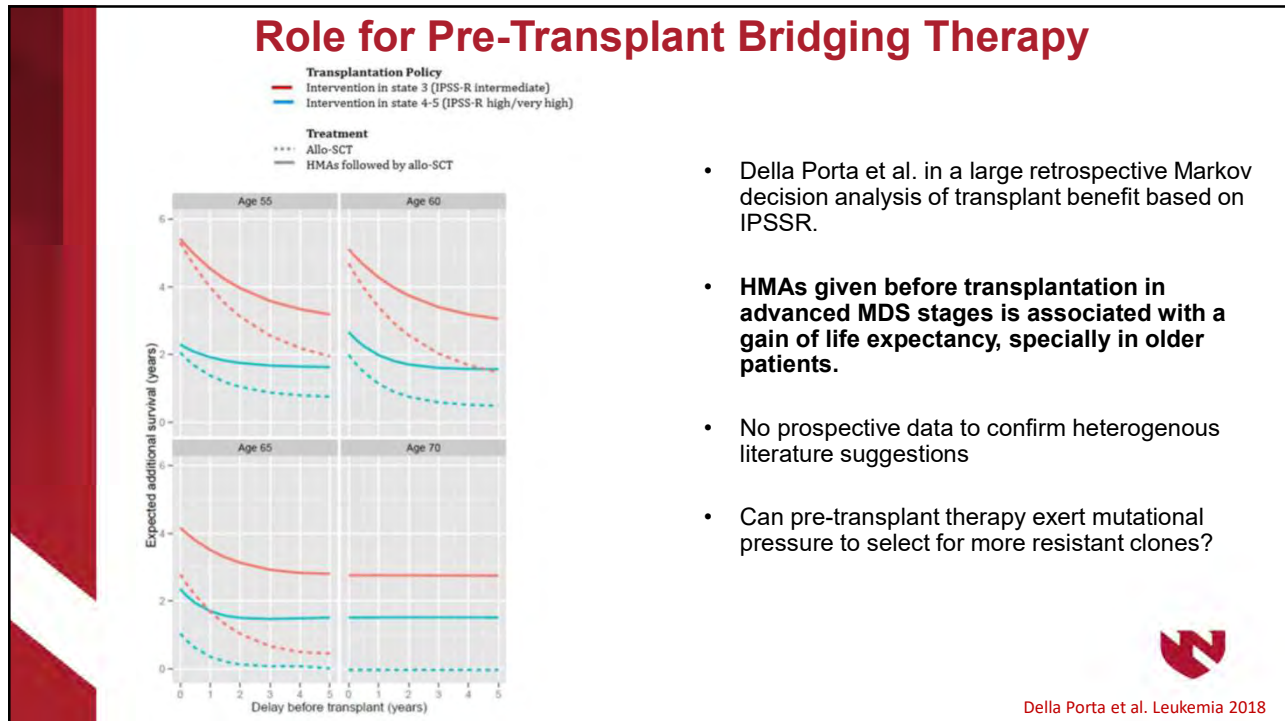


Attalah et al. JAMA 2020

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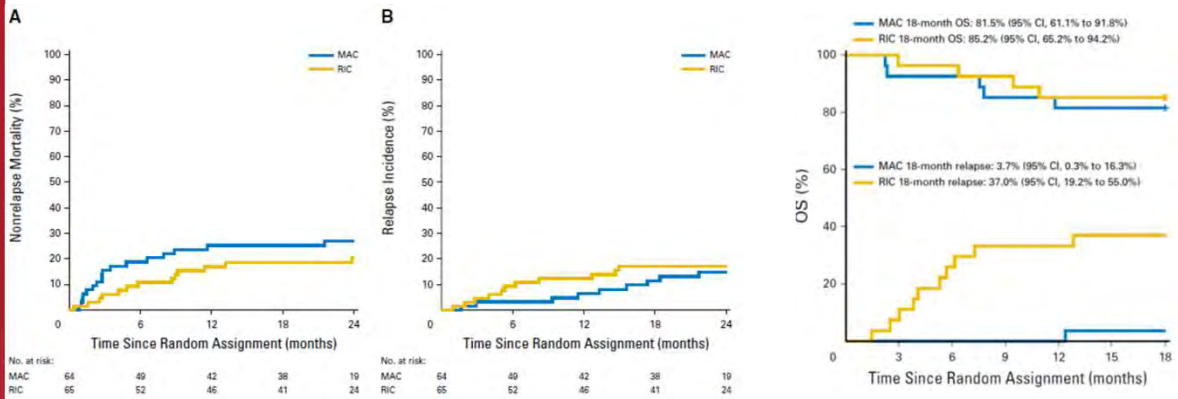


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Myeloablative vs Reduced Intensity Regimen



- Phase III randomized EBMT trial
- 60 pts per arm
- Busulfan/Cyclophosphamide for MA
- 50% of Pts received ATG

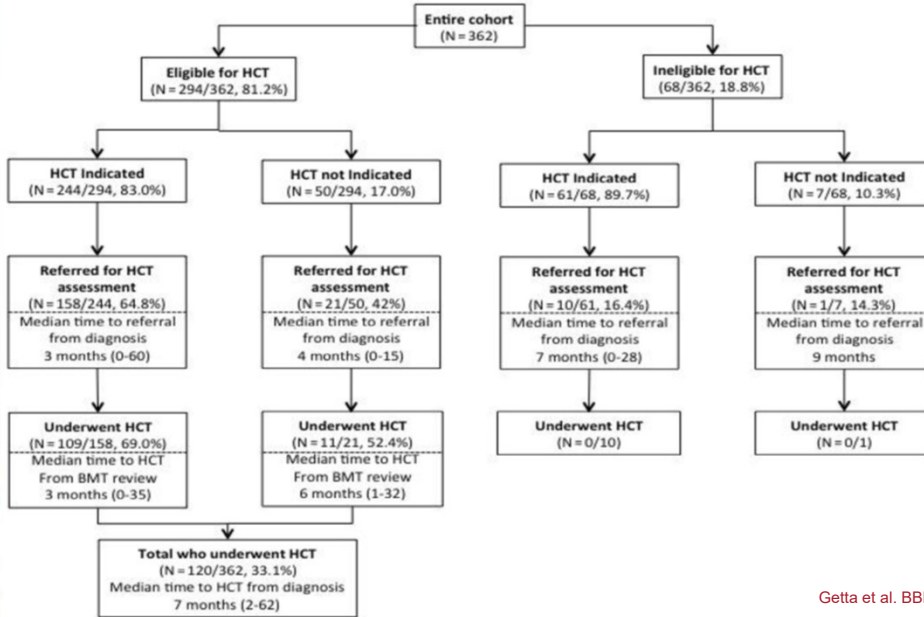
Kroger et al. JCO 2017

- Phase III randomized BMT-CTN trial
- 27 MDS pts per arm
- RFS approached significance

Scott et al. JCO 2017

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Utilization of transplant For MDS



Getta et al. BBMT 2017

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Utilization of transplant For MDS

Memorial Sloan Kettering
N=326
newly dx MDS 2008-2015

65% (158) referred to HCT

33% underwent HCT

Reasons for non referral:

- Dx 2008-2015
- Age \geq 65
- Low blast %

Getta et al. BBMT 2017



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Summary

- New IPSS-M calculator incorporated gene mutation data into the prognostic forecast
- Age by itself is not a barrier to transplant
- Non relapse mortality in MDS have improved over the last decade
- Early transplant evaluation is important for all newly diagnosed MDS patients



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