FONDAZIONE ITALIANA SINDROMI MIELODISPLASTICHE

Clinica e Terapia delle Sindromi Mielodisplastiche

28 maggio 2022

Il trapianto allogenico: quando e per chi?

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Sistema Sanitario Regione Liguria
Istituto di Ricovero e Cura a Carattere Scientifico

Confluenza di interessi

- DMC chair: Vertex Pharmaceuticals Incorporated (MA) and CRISPR Therapeutics AG (CH) / Celgene (BSM)
- DMC member: Vifor Pharma
- Advisory board: Novartis / Blue Bird Bio / Menarini Stemline /Glaxo / GILEAD /
- Consultant: Menarini Stemline
- Speaker: GILEAD-Kite

Agenda

- Questions to be addressed before referring to a transplant center.
  - Referring
  - Who
  - When
  - A few data

Other questions

- Transplant eligibility
- Donor availability / selection
- Conditioning regimen (intensity /age/ HCT-CI/ mutations)
- TRM
- GvHD prophylaxis
- Post transplant treatment

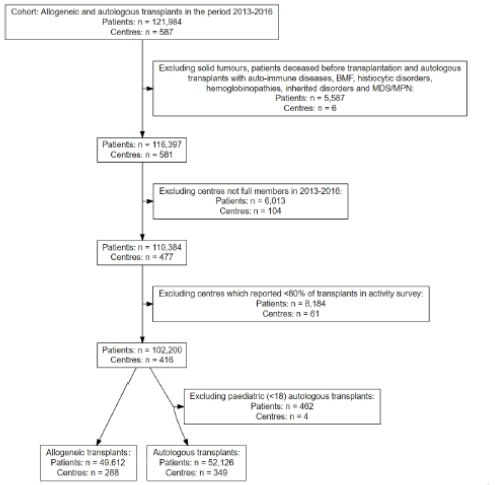
FONDAZIONE ITALIANA SINDROMI MIELODISPLASTICHE

ACCREDITED BY: JACIE Joint Accreditation Committee ISCT | EBMT

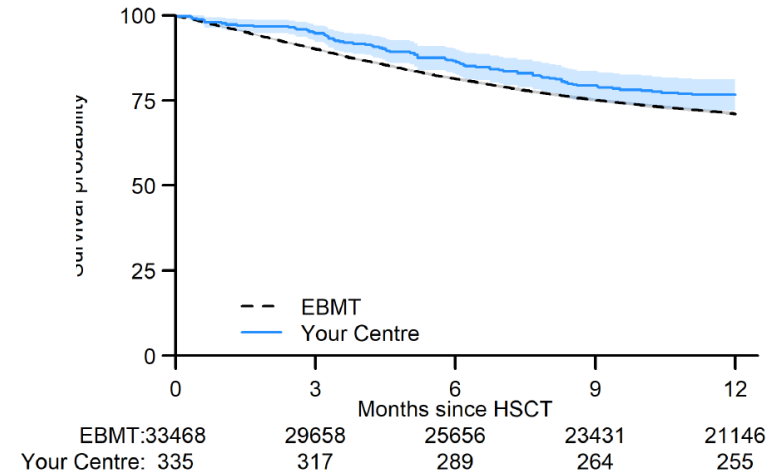
EBMT

Referring to a transplant center EBMT-JACIE Benchmarking project.

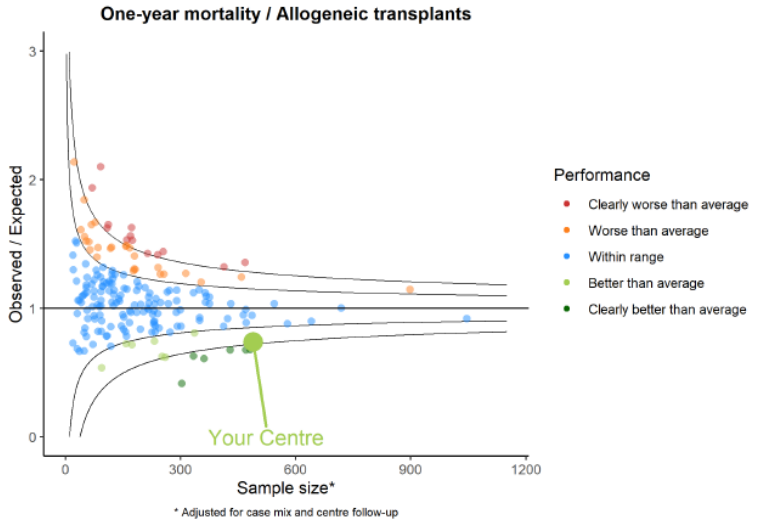
Allogeneic transplantation (288 centers, 49612 patients)



Only centres classified as GREEN or AMBER are included in benchmarking of clinical outcomes.



EBMT:	33468	29658	25656	23431	21146
Your Centre:	335	317	289	264	255



* Adjusted for case mix and centre follow-up

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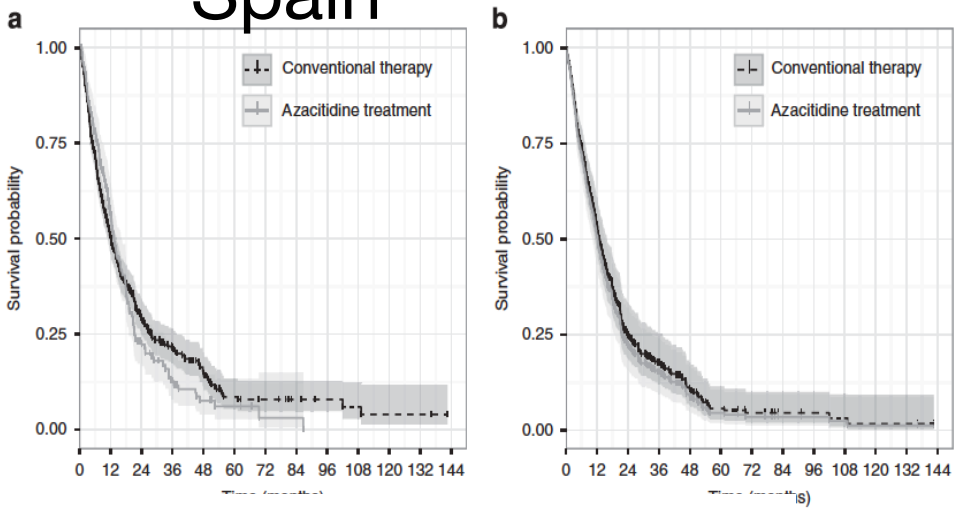
Statement

»

» Allogeneic HCT is the only available possibility to cure MDS
  – No curative alternatives
  – Survival vs disease free survival

FONDAZIONE ITALIANA SINDROMI MIELODISPLASTICHE

Spain



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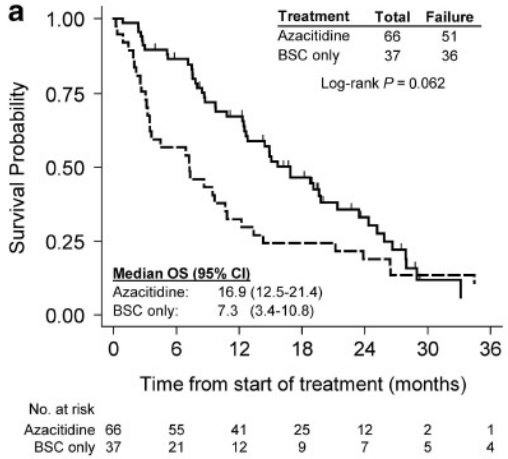
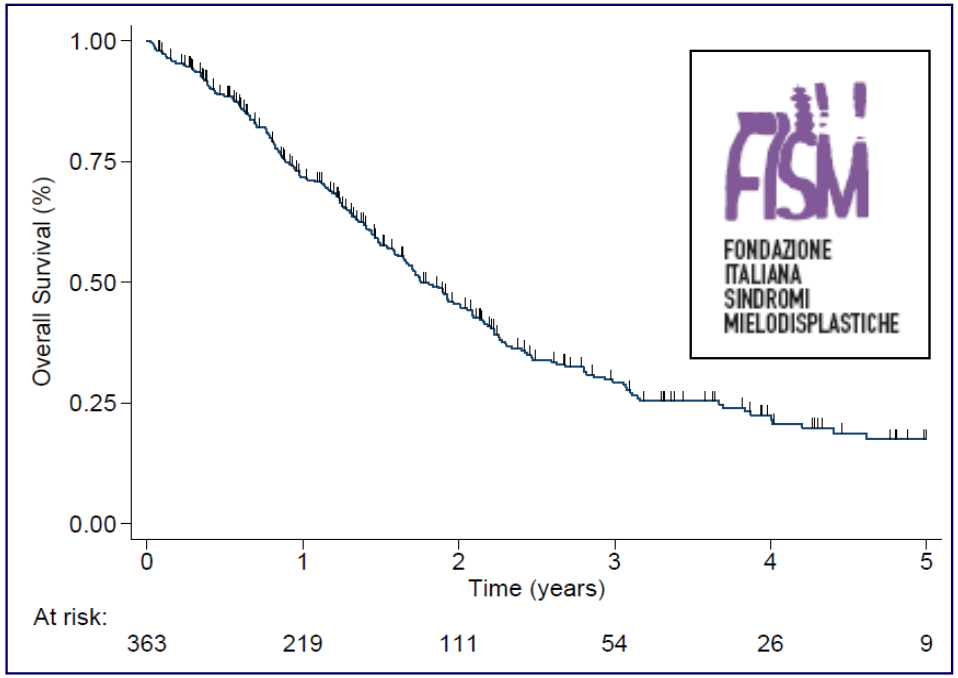
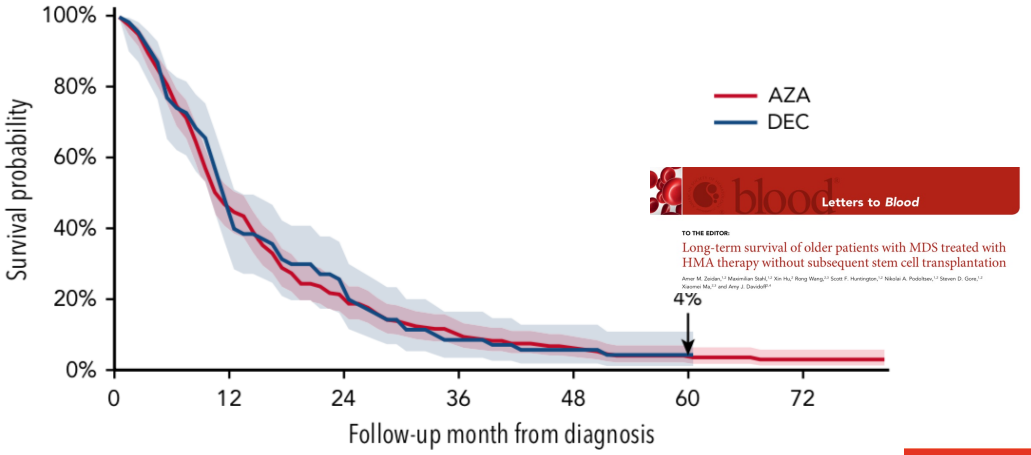






Questions

» Question 1 - Who ?

– Who are the patients for whom a curative intent is reasonable.

» Question 2 – When ?

– How to maximize curative possibility.

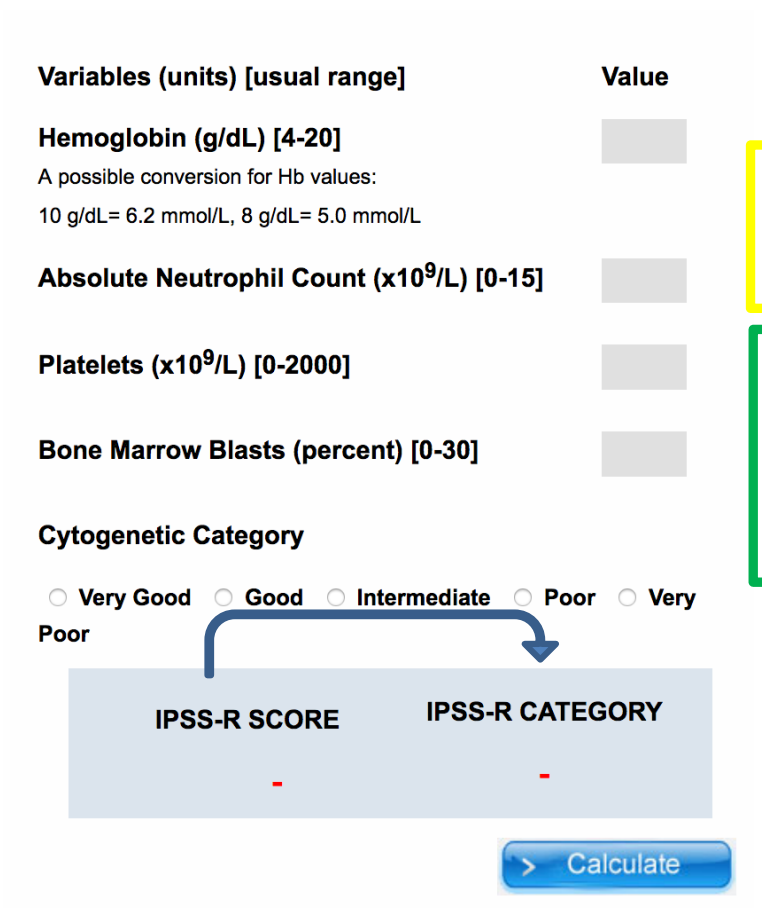
Question 1

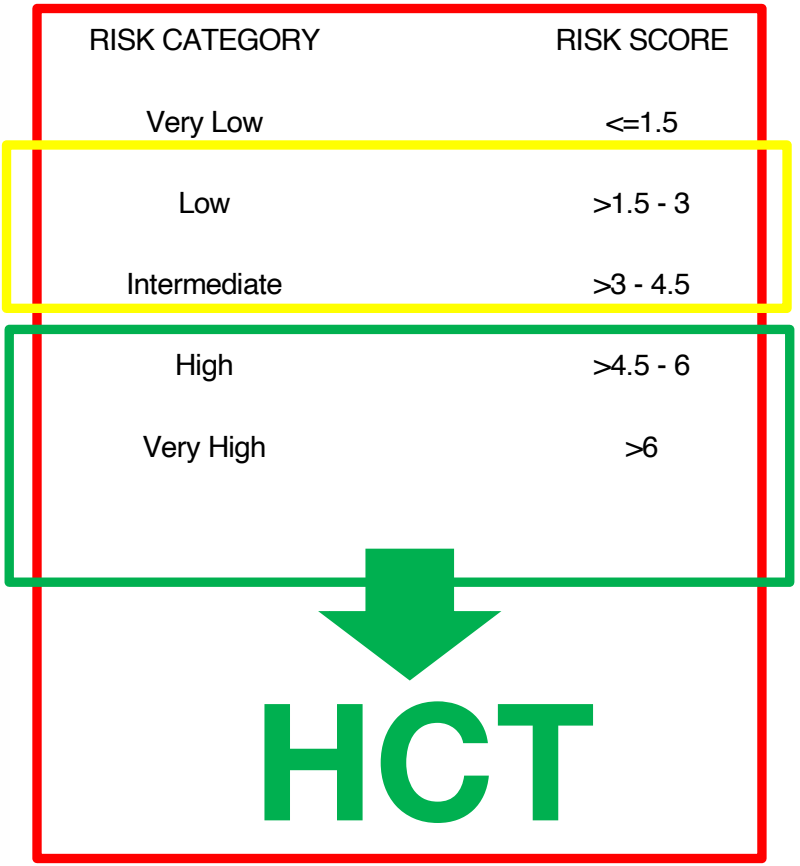
»

» Who are the patients for whom a curative intent is reasonable.

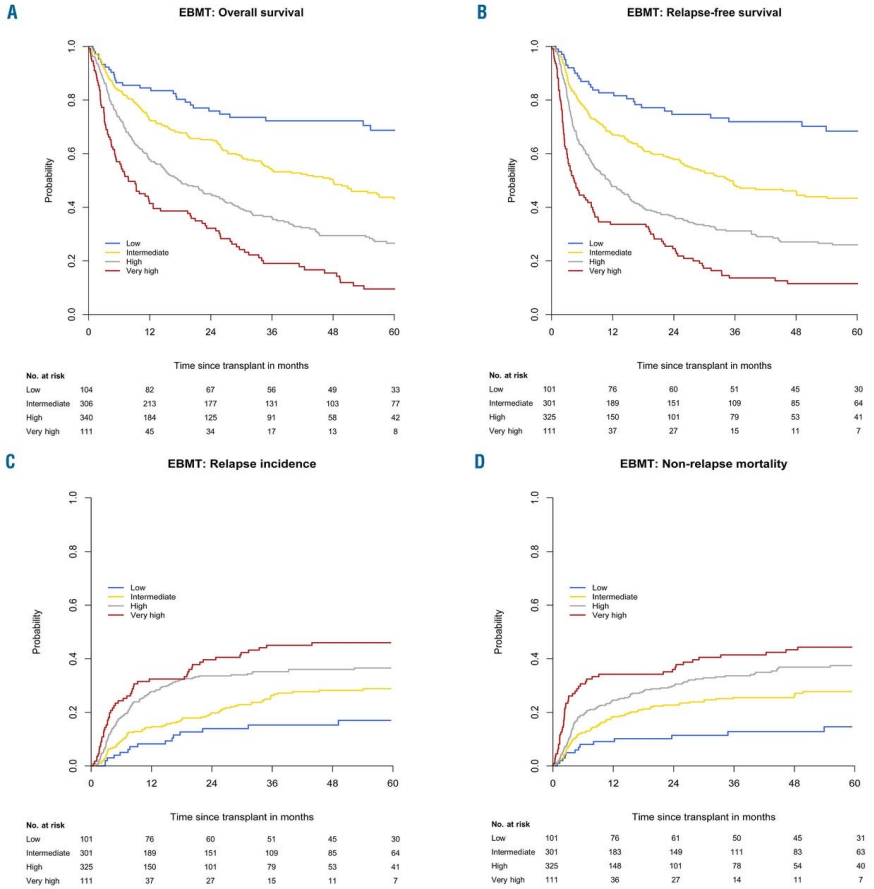
- Disease
- Age
- wiliness
- Clinical condition, organ damage (HCT-CI)

Revised International Prognostic Scoring System (IPSS-R)



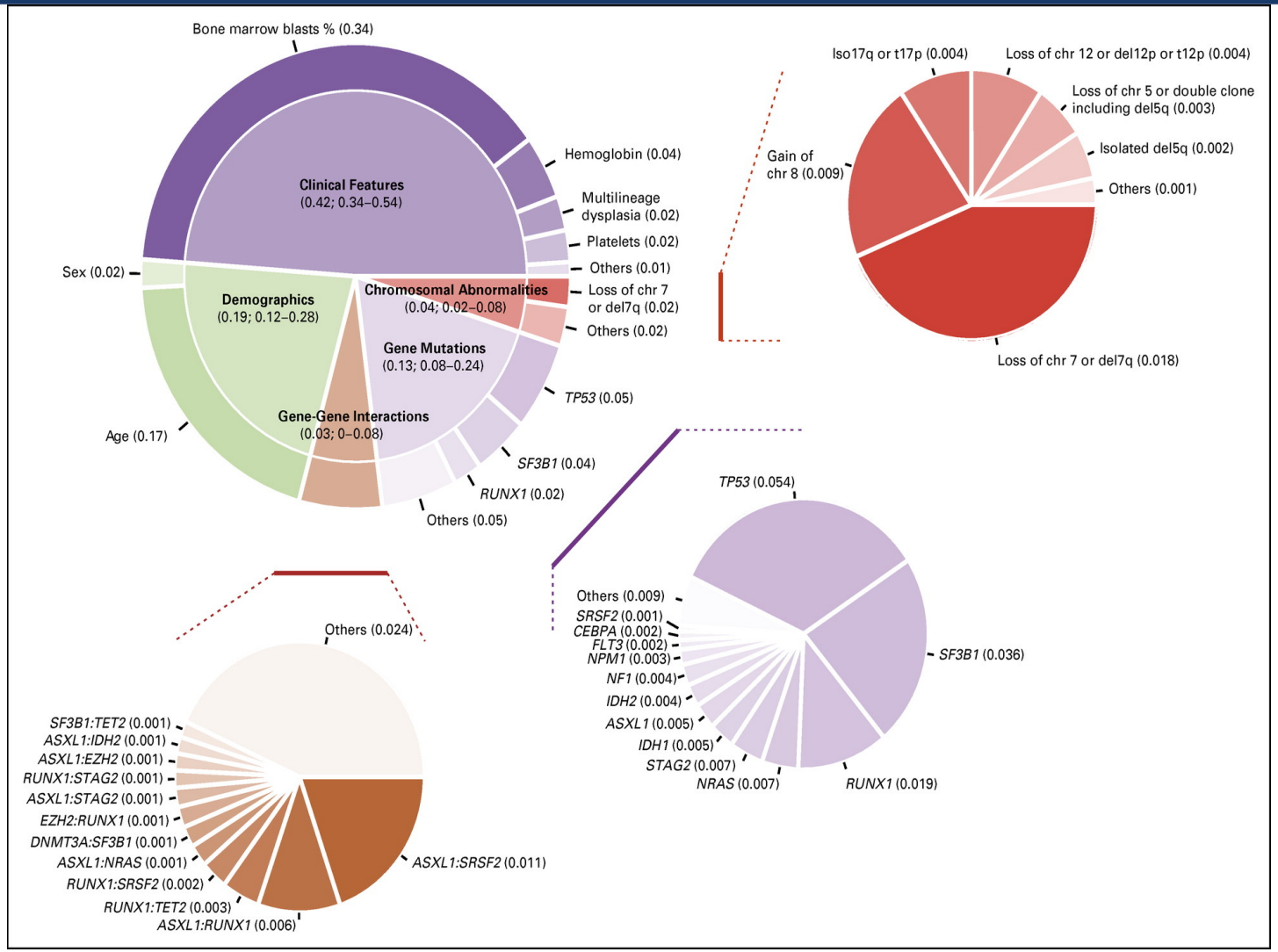


Kaplan-Meier analysis of survival following allogeneic stem cell transplantation in patients with myelodysplastic syndrome stratified according to each risk group of the EBMT transplant-specific risk score.



Nico Gagelmann et al. Haematologica 2019;104:929-936

haematologica
Journal of the European Hematology Association
Published by the Ferrata Storti Foundation



Bersanelli M et al. JCO 2021

Classification and Personalized Prognostic Assessment on the Basis of Clinical and Genomic Features in Myelodysplastic Syndromes

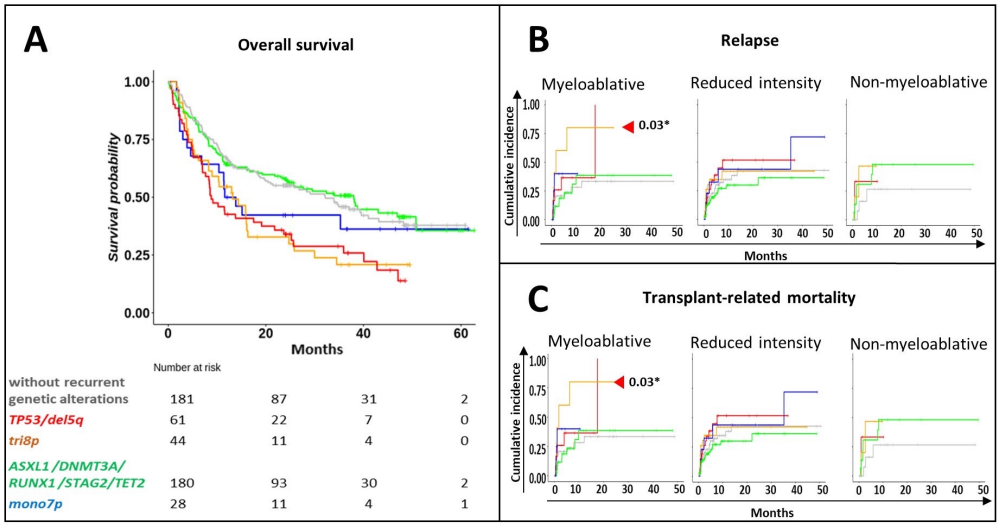
Fraction of explained variation that was attributable to different prognostic factors for overall survival

ASH 2021. #3678 Genomic Subgroups Impact Post-Transplant Survival in Patients with Myelodysplastic Syndrome: A CIBMTR Analysis

Tao Zhang, PhD[1],*

494 patients

Figure.1 The characteristics of molecular signatures and survival outcomes in MDS patient genomic subgroups. A. Survival curve of post-transplant overall survival outcome in different MDS patient subgroups. B. Cumulative risk curve of relapse in different MDS patient subgroups. C. Cumulative risk curve of transplant-related mortality in different MDS patient subgroups.



Conclusion

- Molecular signatures from MDS patient genomes at HCT may provide an independent prognosis of post-transplant survival.
- The choice of regimen intensity could be informed by knowledge of the individual genomic signature of a given MDS patient.

Answer- 1

»

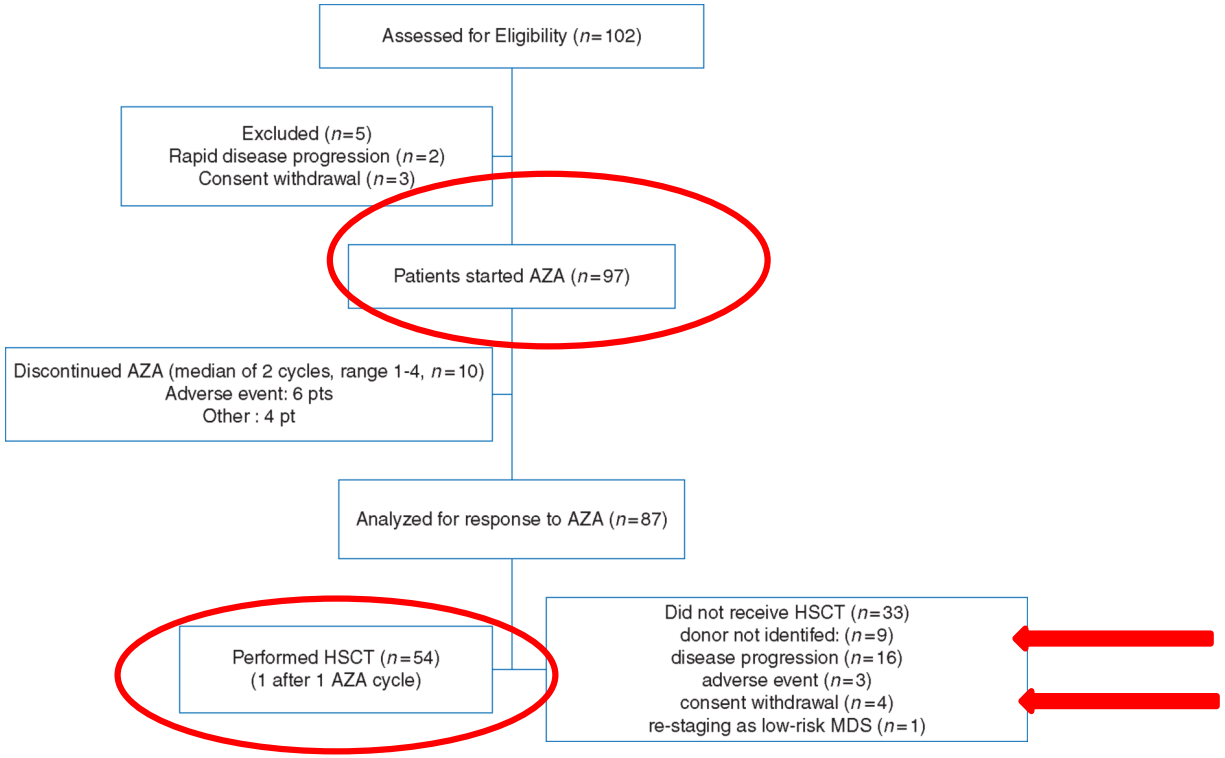
» Who are the patients for whom a curative intent is reasonable ?
  - Disease: Intermediate/ high/ very high R-IPSS and lower risk with well defined clinical and/or molecular risk
  - Age <70-75 years
  - Clinical condition, organ damage (HCT-CI)
  - wiliness

Question 2 – When ?

»

» How to maximize curative possibility.

Feasibility of allogeneic stem-cell transplantation after azacitidine bridge in higher-risk myelodysplastic syndromes and low blast count acute myeloid leukemia: results of the BMT-AZA prospective study



Voso MT et al. Ann of Onc 2017

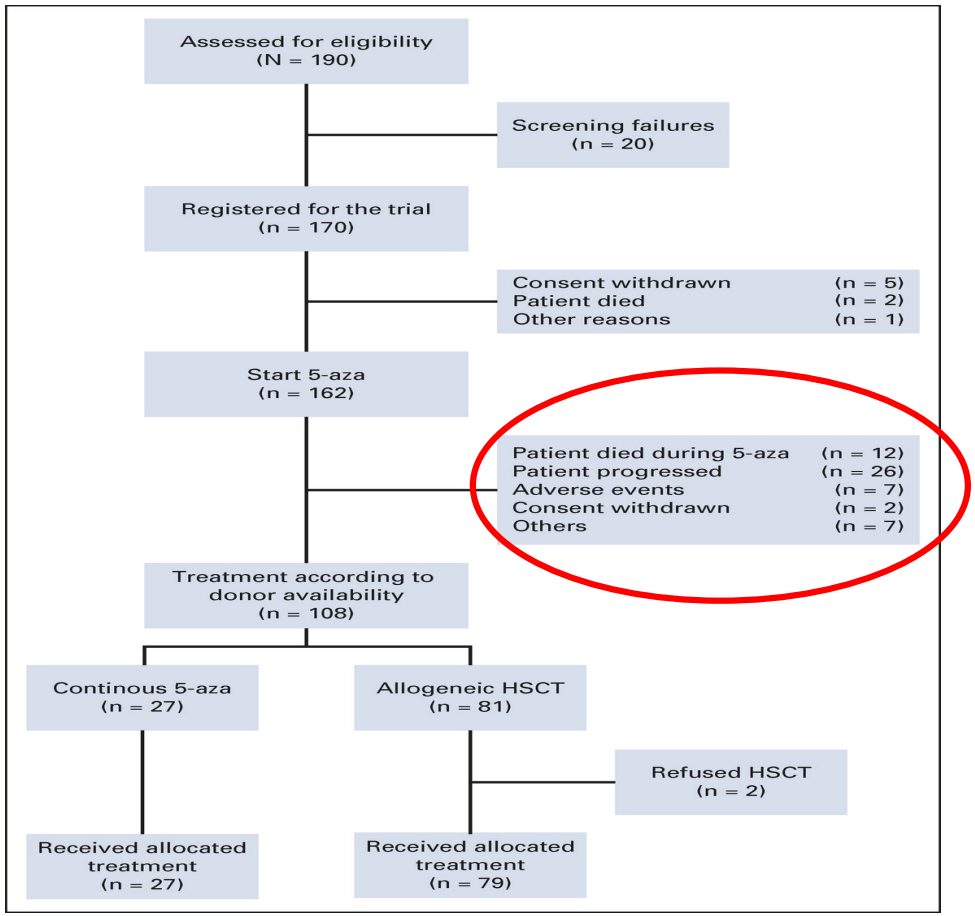


FIG 1. Flow diagram. 5-aza, 5-azacytidine; HSCT, allogeneic stem-cell transplantation.

German MDS Study Group and the German Cooperative Transplant Study Group

Prospective multicenter phase 3 study comparing 5-azacytidine (5-Aza) induction followed by SCT vs continuous 5-Aza according to donor availability in elderly MDS pts (55-70 years) (VidazaAllo Study)

D·MDS
Deutsche MDS-Studiengruppe

Published in: Nicolaus Kröger; Katja Sockel; Christine Wolschke; Wolfgang Bethge; Richard F. Schlenk; Dominik Wolf; Michael Stadler; Guido Kobbe; Gerald Wulf; Gesine Bug; Kerstin Schäfer-Eckart; Christof Scheid; Florian Nolte; Jan Krönke; Matthias Stelljes; Dietrich Beelen; Marion Heinzelmann; Detlef Haase; Hannes Buchner; Gabriele Bleckert; Aristoteles Giagounidis; Uwe Platzbecker; *Journal of Clinical Oncology* 2021 393318-3327.

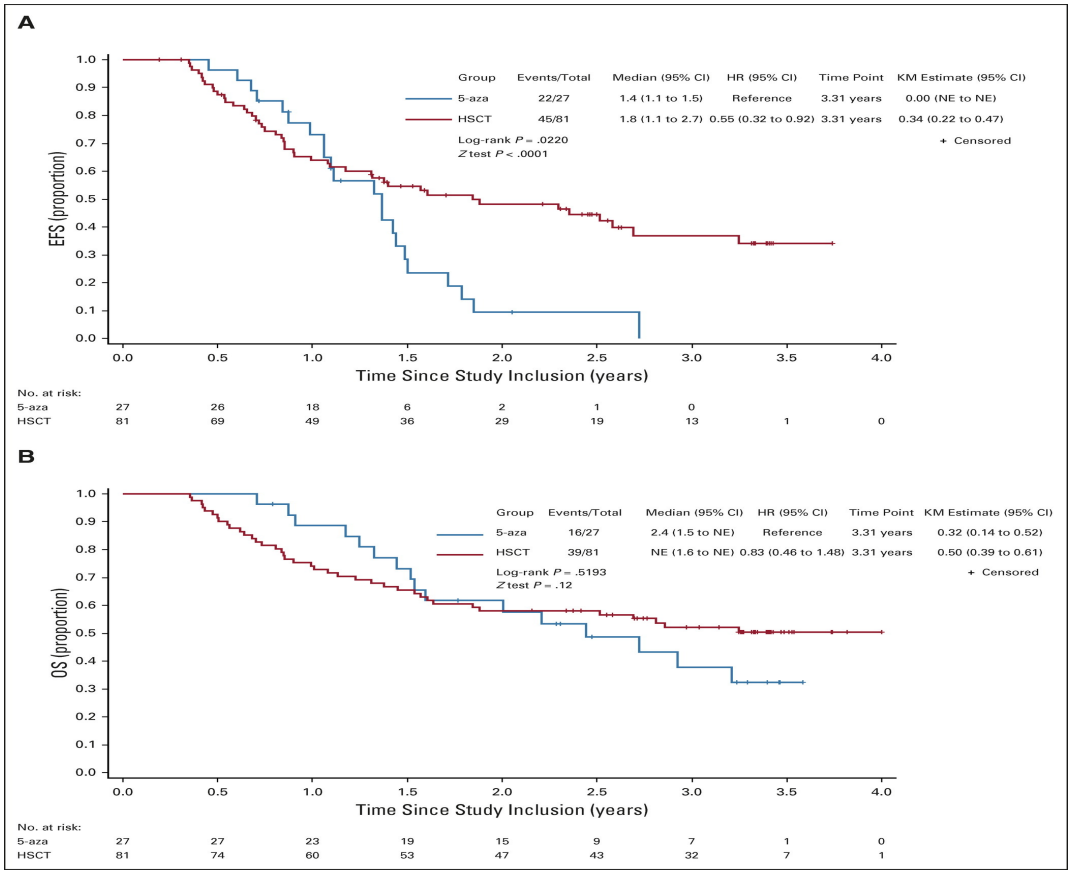


FIG 2. Kaplan-Meier estimates of (A) EFS and (B) OS after allocation to 5-aza or HSCT. 5-aza, 5-azacytidine; EFS, event-free survival; FAS, full analysis data set; HR, hazard ratio; HSCT, allogeneic stem-cell transplantation; KM, Kaplan-Meier; NE, not evaluable; OS, not evaluable, overall survival.

Published in: Nicolaus Kröger; Katja Sockel; Christine Wolschke; Wolfgang Bethge; Richard F. Schlenk; Dominik Wolf; Michael Stadler; Guido Kobbe; Gerald Wulf; Gesine Bug; Kerstin Schäfer-Eckart; Christof Scheid; Florian Nolte; Jan Krönke; Matthias Stelljes; Dietrich Beelen; Marion Heinzelmann; Detlef Haase; Hannes Buchner; Gabriele Bleckert; Aristoteles Giagounidis; Uwe Platzbecker; *Journal of Clinical Oncology* 2021 393318-3327.
DOI: 10.1200/JCO.20.02724.

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HSCT in MDS

San Martino experience 2018-2022.

	MDS	Secondary AML
Patients	25	24
R-IPSS Low/Intermediate /high very high	7/8/10	------
Pre HSCT therapy no /yes	21/4 (AZA 4)	3/21 (chemo 8; CPX 9; AZA 2; AZA/VEN 2)
Source (BM/PB)	16/9	13/11
Donor MSD/MUD/HAPLO /MMUD	5/6/14/0	0/5/17/2
AGE	63 (43-75)	67 (18-73)
Median duration follow up	25 mo (interquartile range 15-35)	

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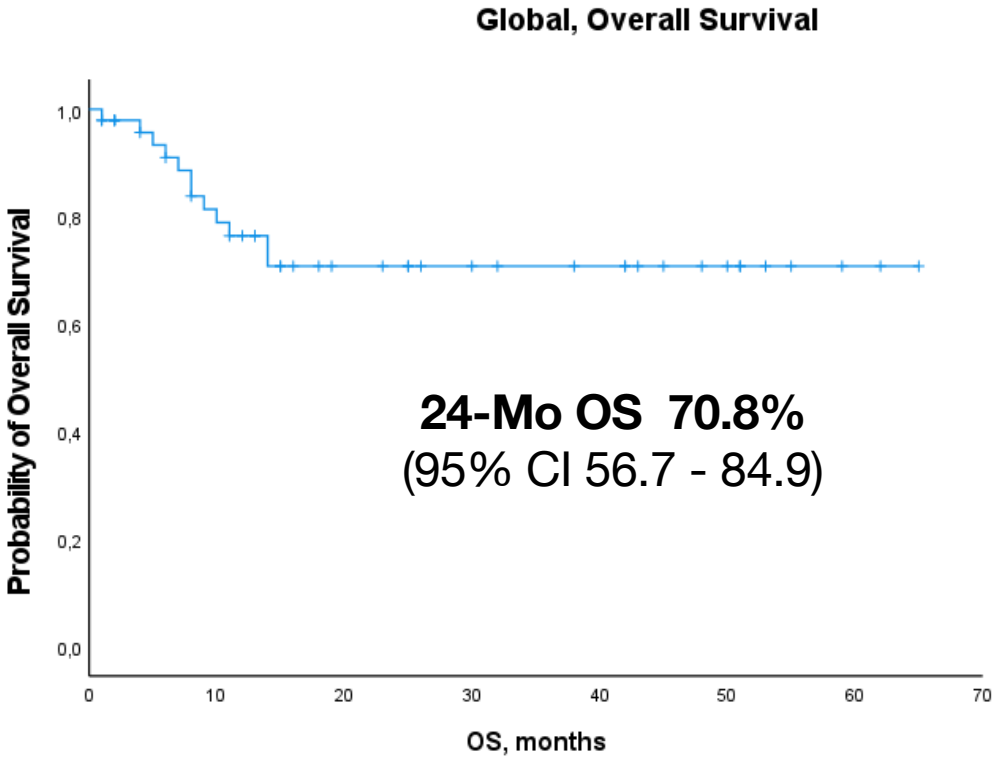
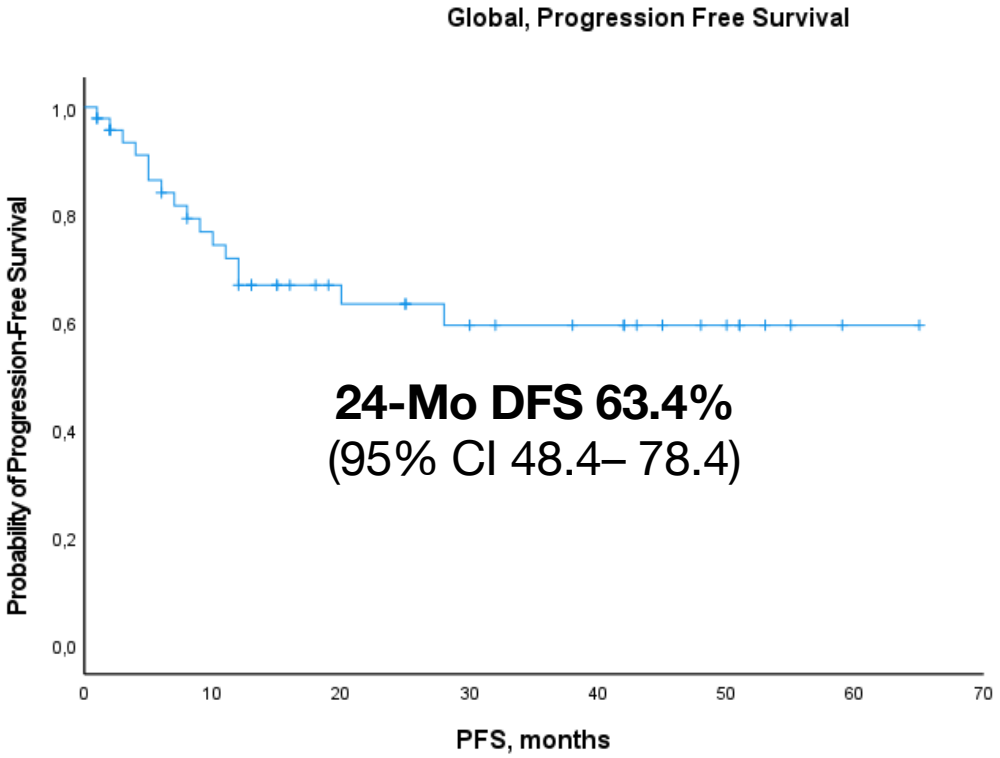
FONDAZIONE ITALIANA SINDROMI MIELODISPLASTICHE

HSCT in MDS
San Martino experience 2018-2022.
49 consecutive patients (MDS + Secondary AML)





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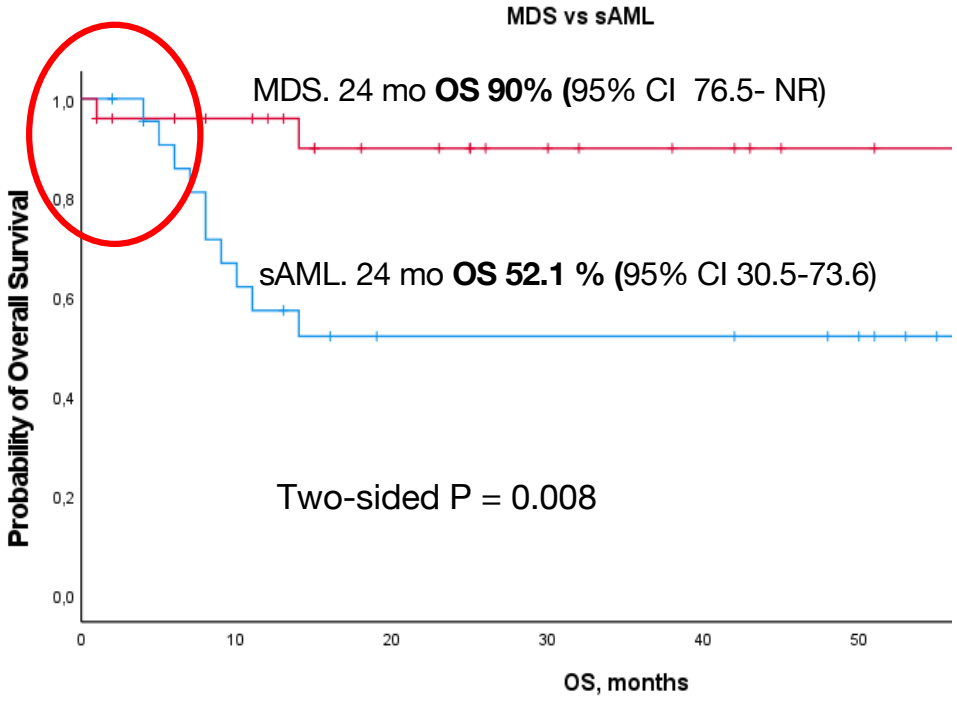
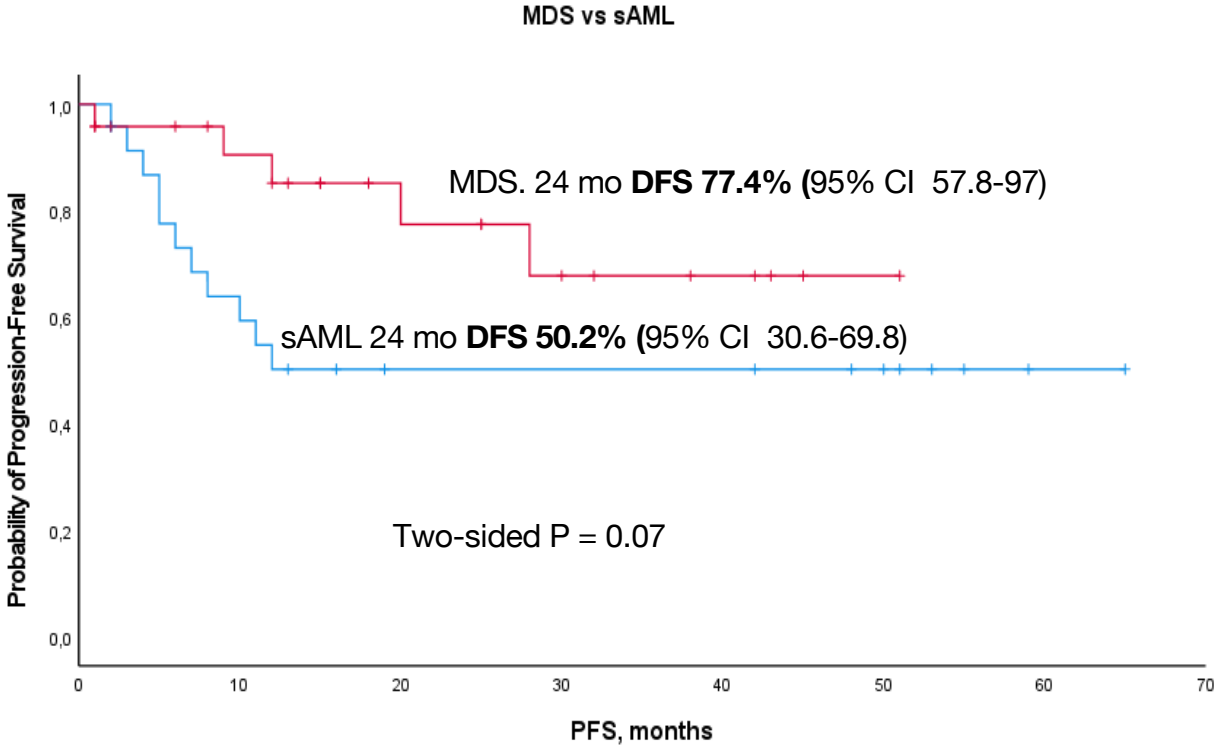
FONDAZIONE ITALIANA SINDROMI MIELODISPLASTICHE

HSCT in MDS and secondary AML
San Martino experience 2018-2022. 49 consecutive patients





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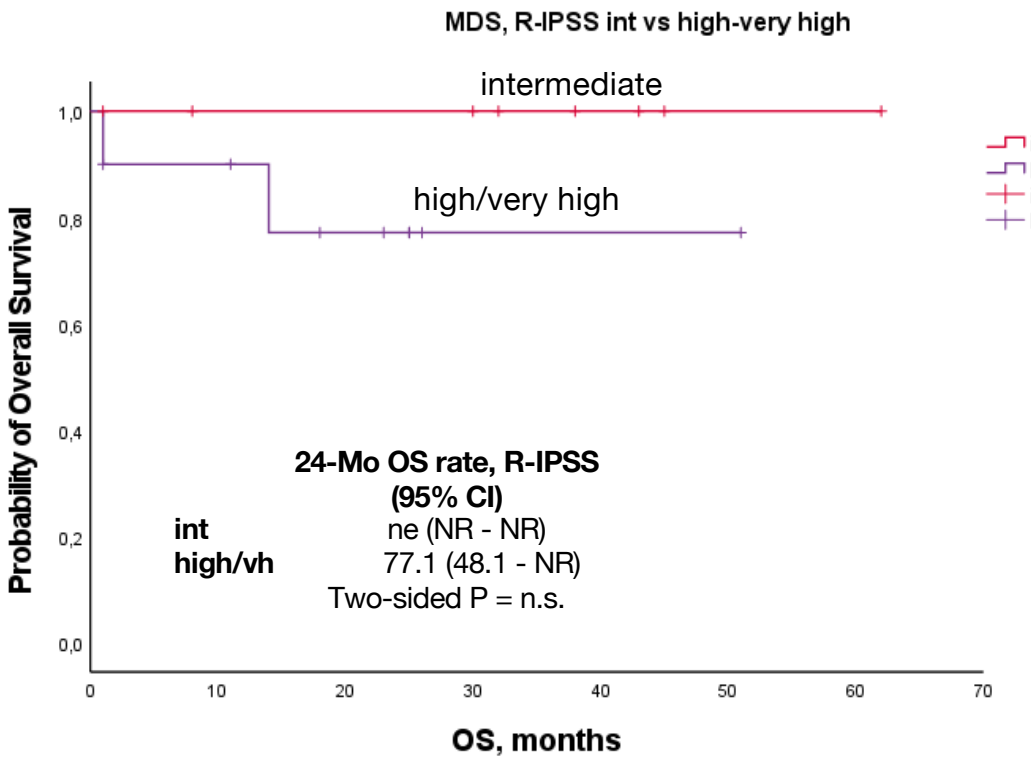
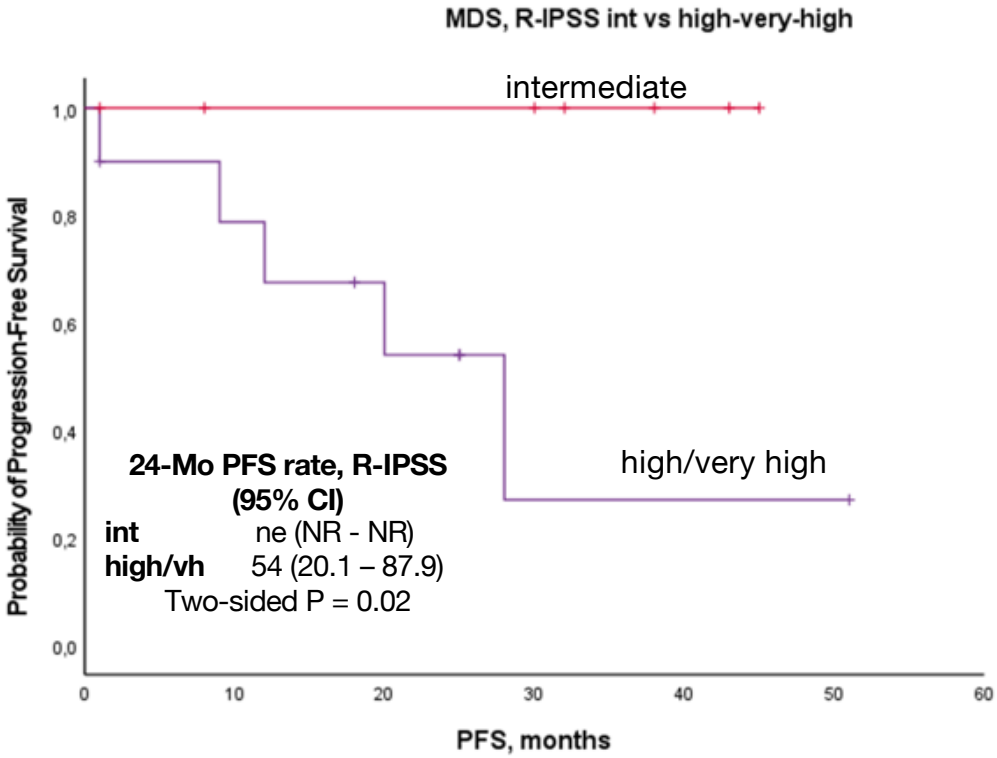
FONDAZIONE ITALIANA SINDROMI MIELODISPLASTICHE

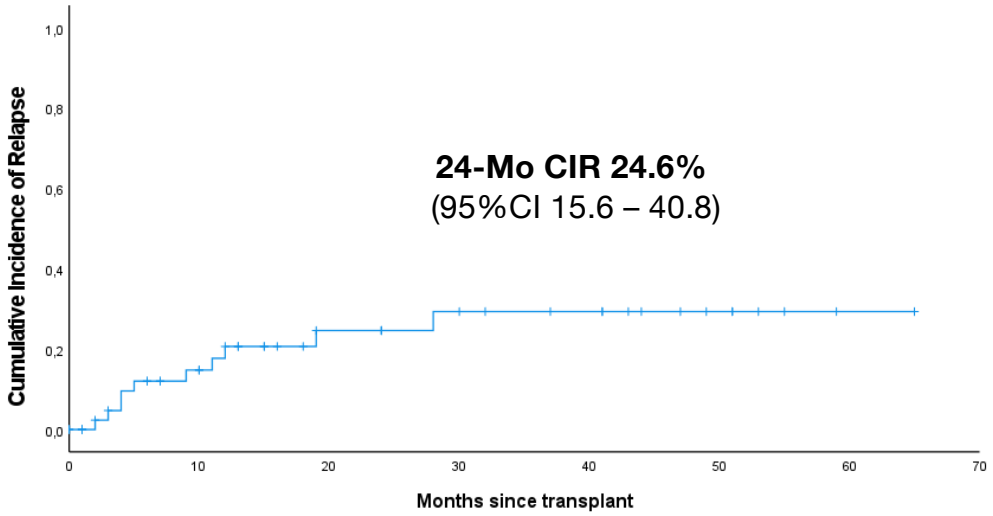
HSCT in MDS
San Martino experience 2018-2022. 25 consecutive patients



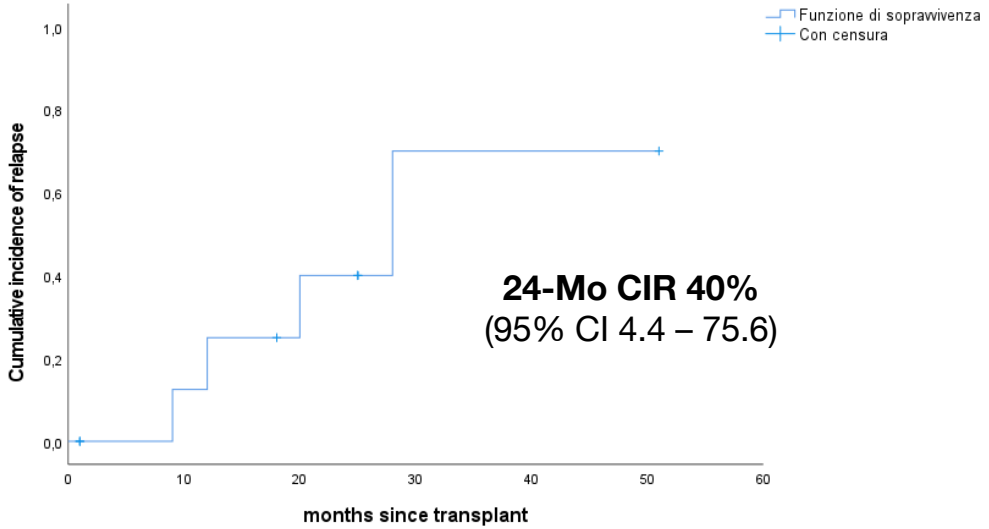


HSCT in MDS
San Martino experience 2018-2022. 25 consecutive patients

MDS R-IPSS **All patients,**
cumulative incidence of relapse



MDS R-IPSS high / very high,
cumulative incidence of relapse



Answer 2 – When ?

»

» How to maximize curative possibility.
  – Transplant consultation ASAP
  – Work together with transplanters
  – Post transplant treatment for higher risk

FONDAZIONE ITALIANA SINDROMI MIELODISPLASTICHE

Clinica e Terapia delle Sindromi Mielodisplastiche

28 maggio 2022

Thank you for your kind attention