Sindromi Mielodisplastiche ad alto rischio: terapia e indicazioni al trapianto

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Terapia MDS: Obiettivi

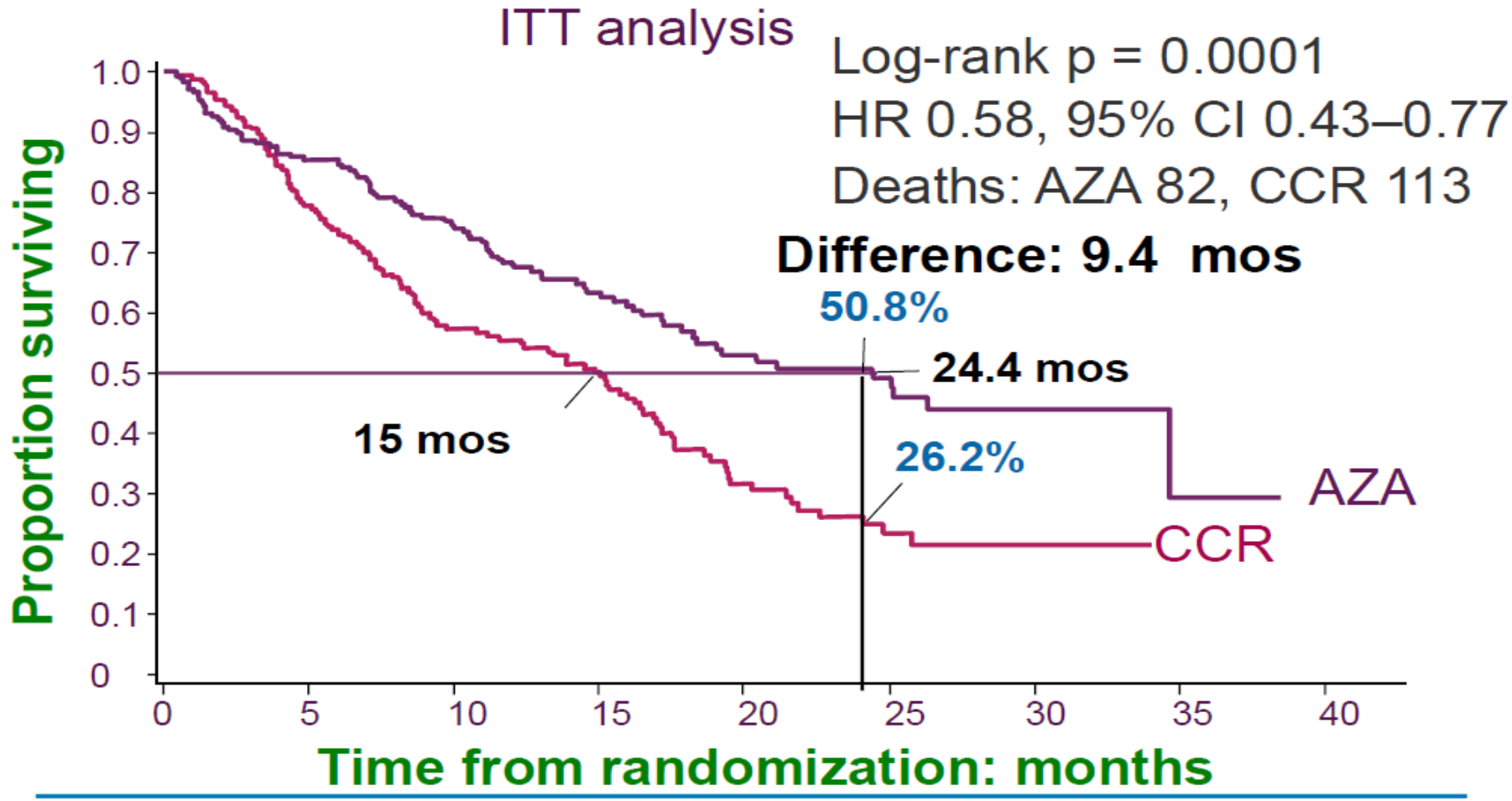
- Migliorare i sintomi (agire sulle citopenie) e prevenire le complicanze
- Prolungare la sopravvivenza
- Mantenere / migliorare la qualità di vita

Sindromi Mielodisplastiche ad alto rischio

Obiettivi: Prolungare la sopravvivenza ed impedire la progressione in LAM

- AZACITIDINA
- TRAPIANTO ALLOGENICO DI CSE
  Unica terapia curativa
- TRIALS CLINICI

AZACITIDINA NELLE MDS AD ALTO RISCHIO



CI, confidence interval; ITT, intention-to-treat.

Fenaux P, et al. Lancet Oncol. 2009;10:223-32.

Tossicità del trattamento con AZACITIDINA

Table 2 Most common[1] adverse events (AEs) with azacitidine

Adverse event[2]	Percent of patients			
	AZA-001 (*N* = 175)		CALGB 9221 (*N* = 150)	
	Any grade	Grade 3/4	Any grade	Grade 3/4
Patients with at least 1 individual AE occurring in ≥ 20% of patients in the azacitidine group in AZA-001	97.7	80.0	100.0	92.7
Anemia	51.4	13.7	74.0	60.7
Neutropenia	65.7	61.1	34.0	24.0
Thrombocytopenia	69.7	58.3	68.7	56.0
Constipation	50.3	1.1	39.3	3.3
Diarrhea	21.7	0.6	40.0	3.3
Nausea	48.0	1.7	67.3	5.3
Vomiting	26.9	0	48.0	2.7
Fatigue	24.0	3.4	47.3	5.3
Injection-site erythema	42.9	0	33.3	0.7
Injection-site reaction	29.1	0.6	3.3	0
Pyrexia	30.3	4.6	51.3	2.0

[1]Greater than or equal to 20% of azacitidine-treated patients in AZA-001.
[2]Multiple reports of the same preferred term for a patient are counted only once.

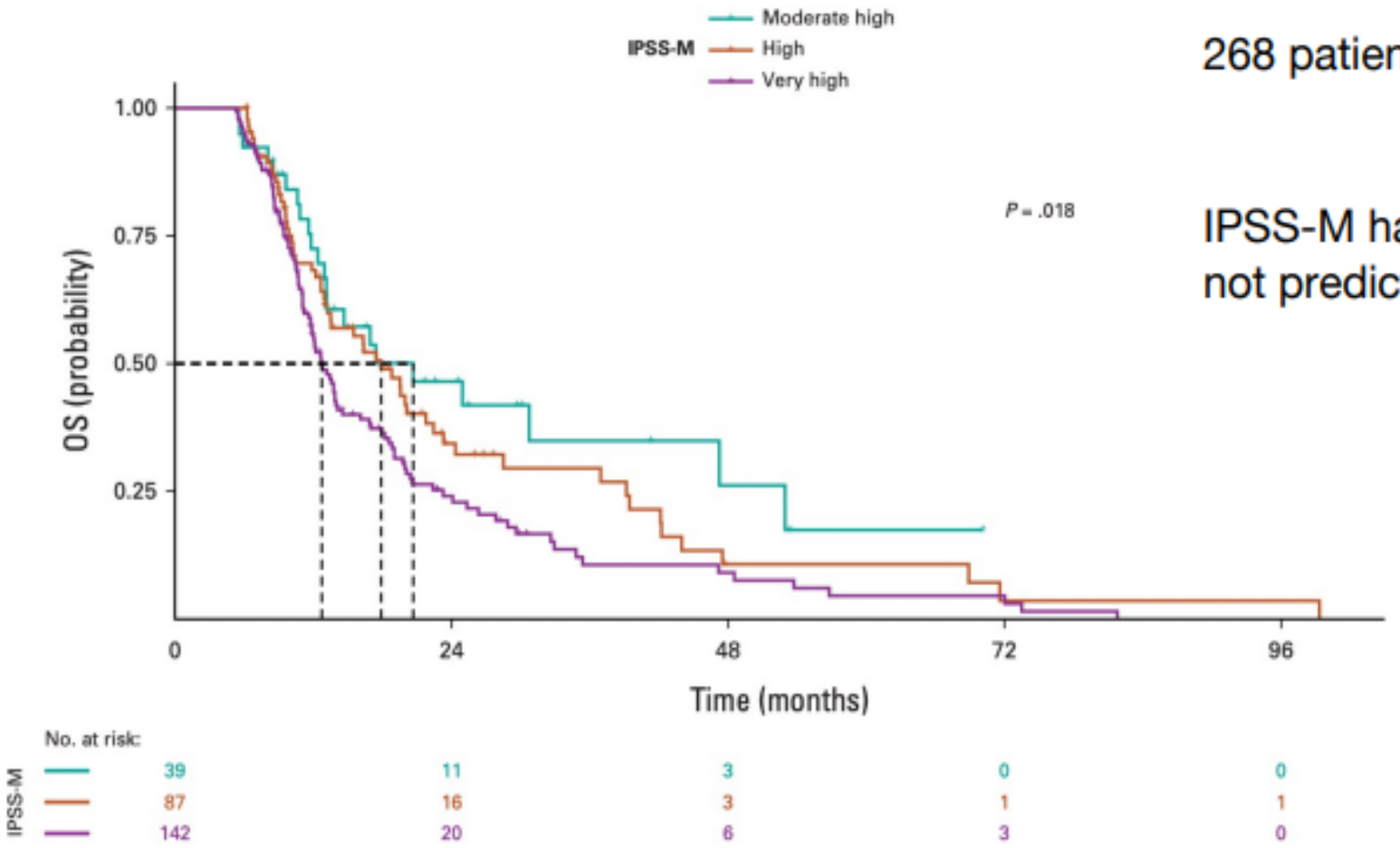
Santini V, Eur J Haemat 2010

Cosa abbiamo imparato dalla nostra esperienza con i farmaci ipometilanti

- Le risposte si notano dopo i primi 2-4 cicli di terapia
- Il raggiungimento anche del solo miglioramento delle citopenie migliora la sopravvivenza
- L'interruzione del trattamento provoca la perdita della risposta
- I pazienti con cariotipo complesso con TP53 pos possono rispondere sebbene per poco tempo
- I pazienti che non rispondono al trattamento o che ricadono hanno una sopravvivenza molto breve

IPSS-M prediction of OS in MDS treated with HMA

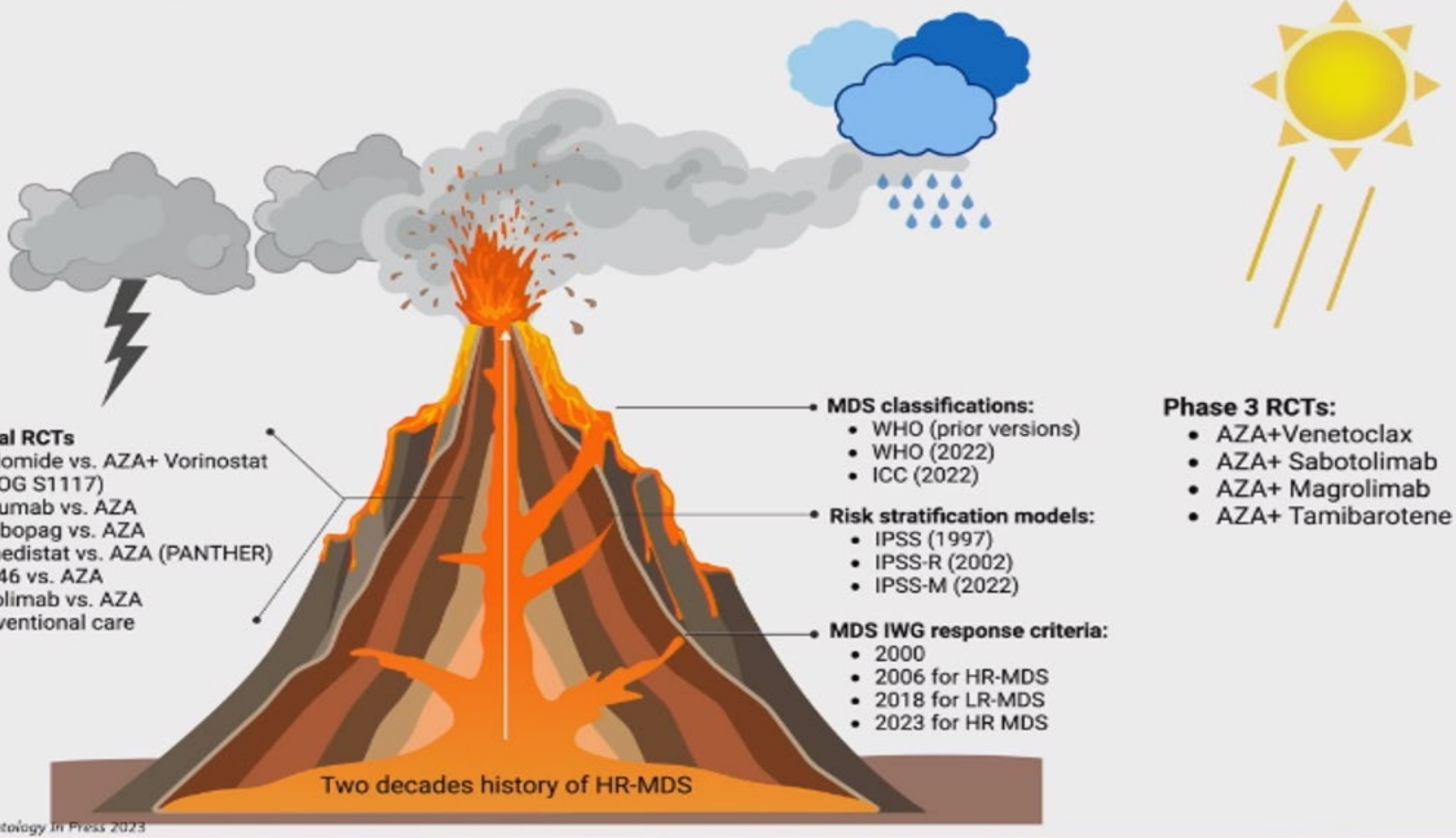
A



268 patients included

IPSS-M has prognostic value but not predictive

Sauta et al. JCO 2023



Sallman D and Xie Z, Hematology In Press 2023

Farmaci Ipometilanti Orali

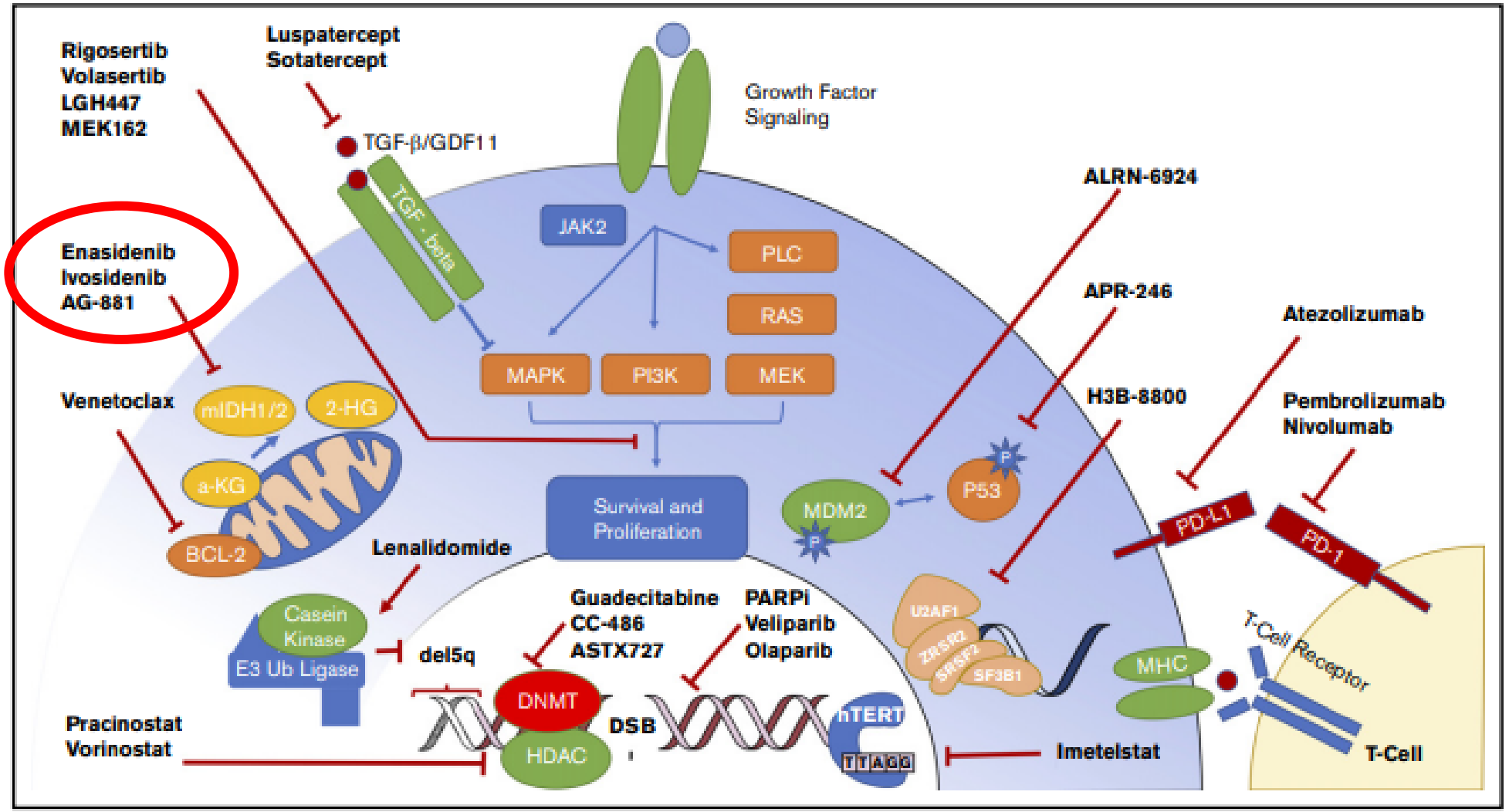
Cedazuridine/decitabine p.o. (100/35 mg) and decitabine (20 mg/m^2 for 5d q4w) crossover study followed by cedazuridine/decitabine p.o. (100/35 mg) maintenance	NCT02103478	Intermediate- or higher-risk MDS and CMML

Garcia-Manero, Blood Advance 2020

Cedazuridine/decitabine p.o. (100/35 mg) and decitabine (20 mg/m^2 for 5d q4w) crossover study followed by cedazuridine/decitabine p.o. (100/35 mg) maintenance	ASCERTAIN NCT03306264	MDS, AML and CMML

Garcia-Manero, Lancet Hematology 2024

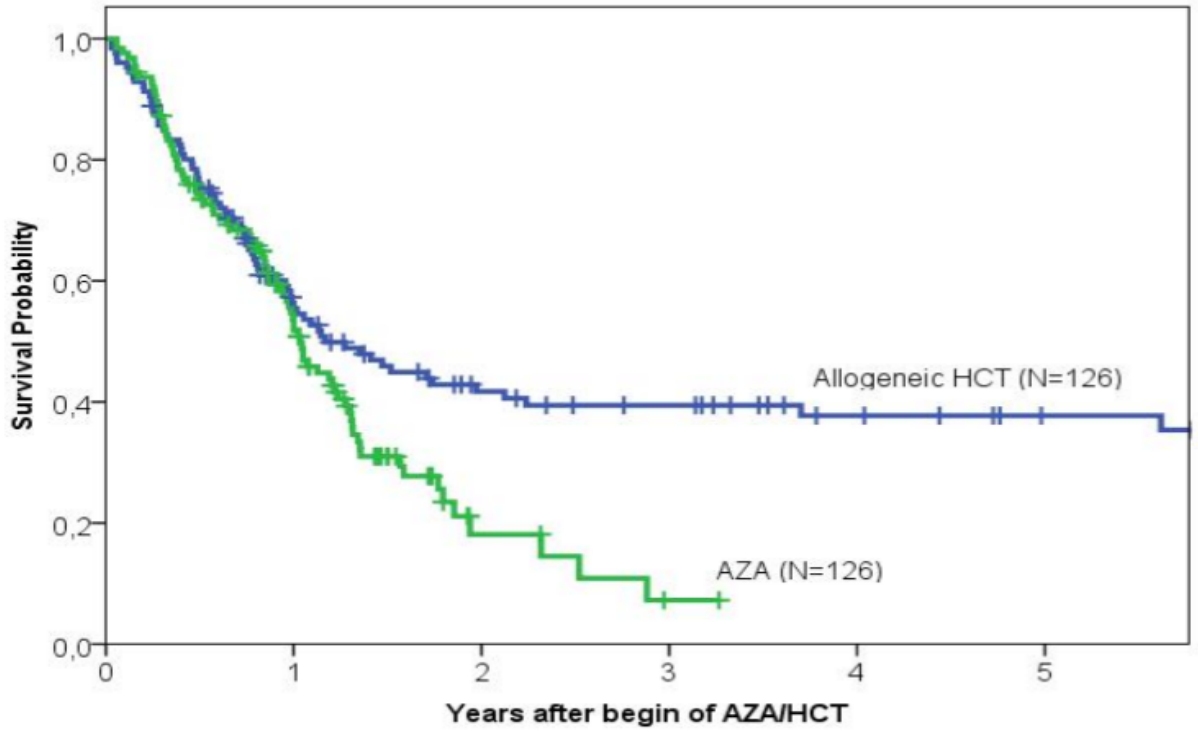
Targhet Therapy



Aleshin et al, Blood Advance 2018

Il trapianto allogenico rimane l'unica terapia curativa nelle MDS

(Platzbecker, BBMT, 2012)



Median follow-up of 20 months 3-year OS was 39% for HCT and 7% for 5-aza

Prospective comparison of allogeneic stem cell transplantation and conventional therapy in high-risk MDS

Authors	Conditioning	Compared to	Age in years	Donor (matched) *vs.* no donor, N	LFS, %	OS, %
Robin *et al.*[47]	RIC and MAC	HMA (76%) and others	50-70	112 *vs.* 50	ND	at 4 years: 37 *vs.* 15 *P*=0.02
Nakamura *et al.* (BMT-CTN 1102)[46]	RIC (different regimens)	HMA or best supportive care	50-75	260 *vs.* 124	at 3 years: 35.8 *vs.* 20.6 *P*=0.03	at 3 years: 47.9 *vs.* 26.6 *P*=0.001
Kröger *et al.* (VidazaAllo-Study)[45]	RIC (busulfan-based)	Azacitidine	50-70	81 *vs.* 27 [no donor: treated with azacitidine]	at 3 years: 34 *vs.* 0 *P*<0.0001	at 3 years: 50 *vs.* 32 *P*=0.12

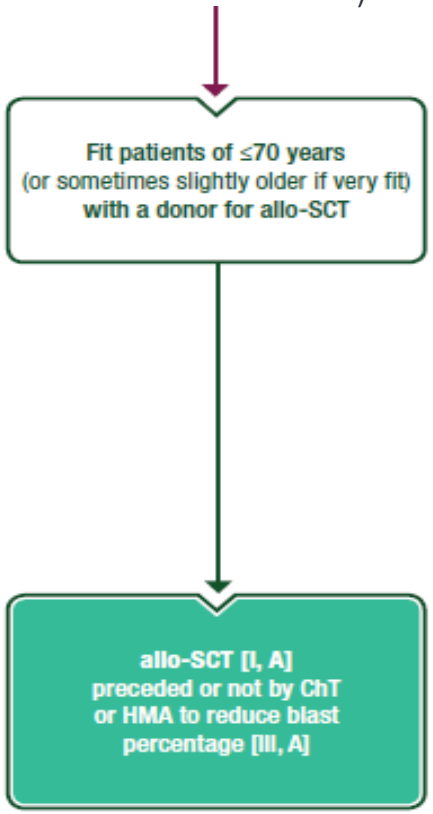
Trapianto allogenico di CSE nelle MDS

Il rapporto rischio/beneficio del
Trapianto Allogenico di CSE è determinato da:

- Selezione del paziente
- Il momento ottimale del trapianto

Chi candidiamo al Trapianto Allogenico?

MDS ad alto rischio (IPSS-R)
HIGH, VERY HIGH,
INTERMEDIATE RISK)



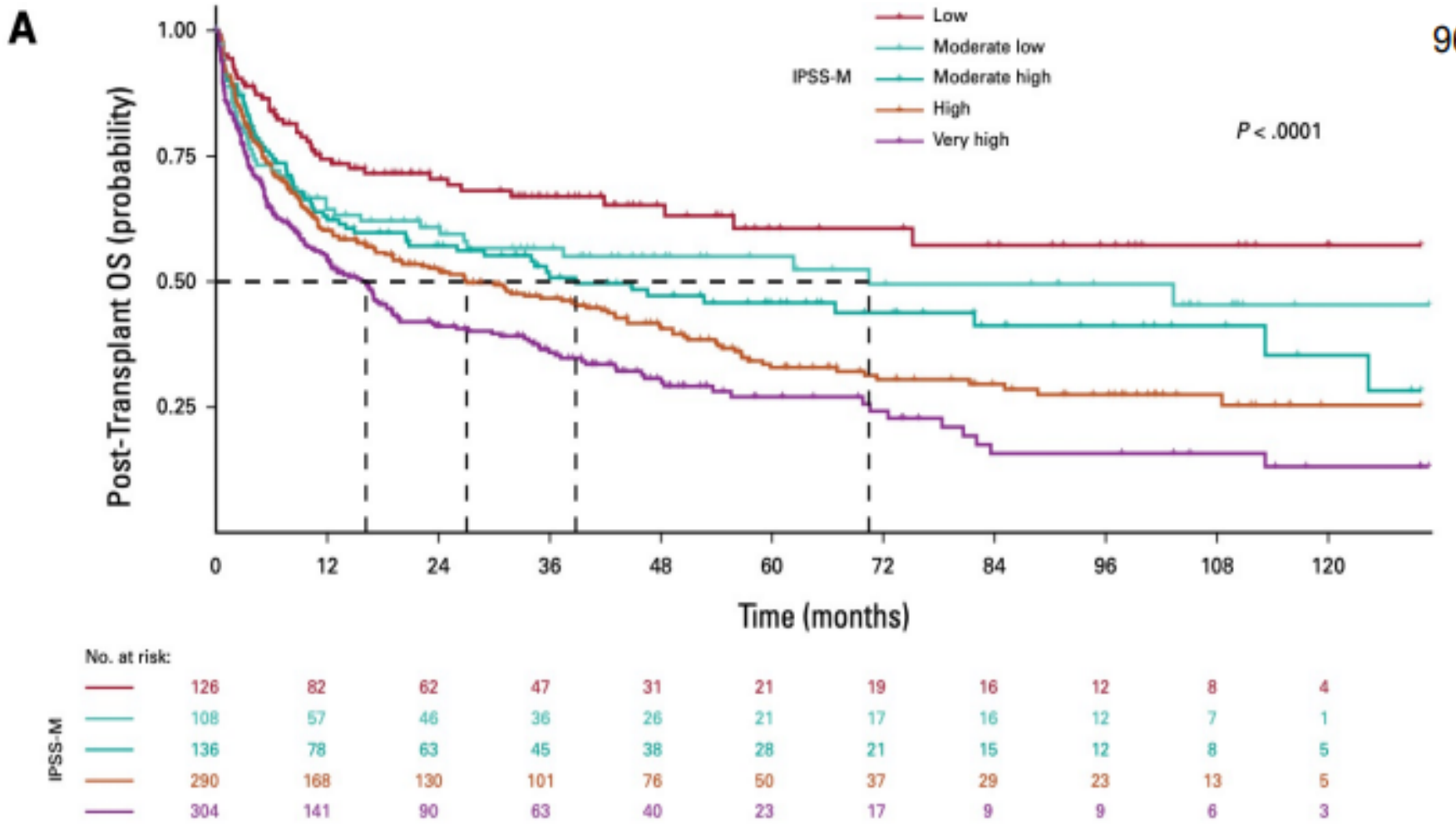
PAZIENTE
- Età
- Comorbidità
- Performance Status

MALATTIA
- IPSS-R score
- Anomalie citogenetiche
- Mutazioni

TRAPIANTO
- Tipo di donatore
- Regime di condizionamento

Fenaux, ESMO guidelines (2020)

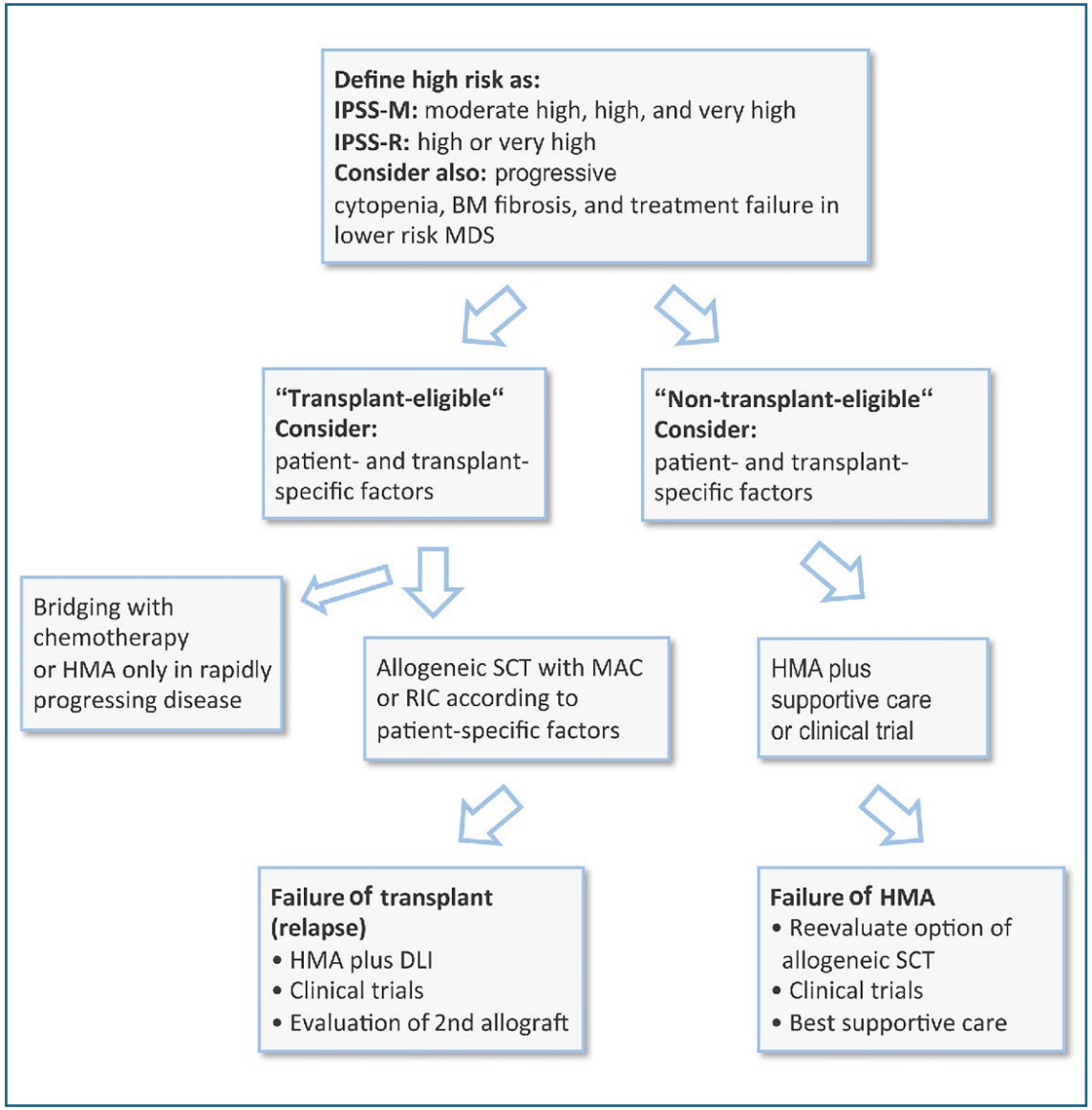
IPSS-M improves the prediction of OS in MDS treated with HSCT



964 pts undergo HSCT

Sauta et al. JCO 2023

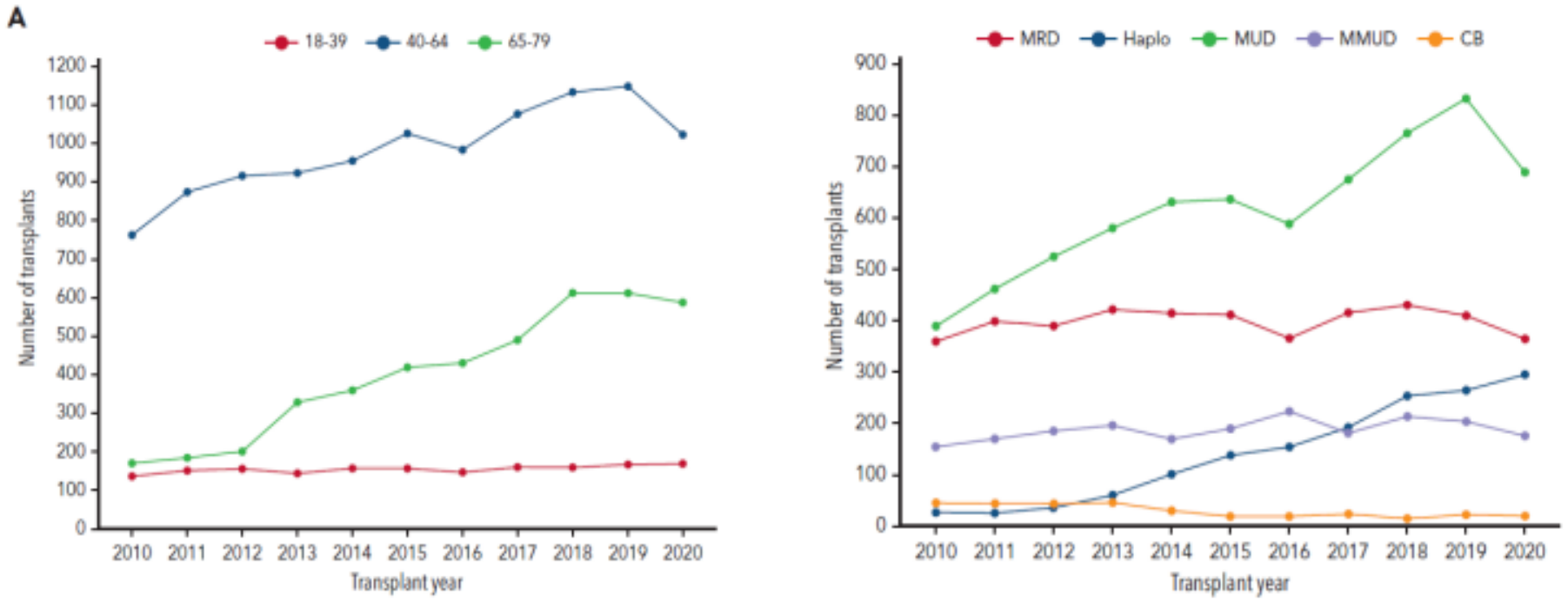
Chi candidiamo al Trapianto Allogenico?



Kroger, Haematologica 2025

Clinical-genomic profiling of MDS to inform allo-HCT: recommendations from an international panel on behalf of the EBMT

Carmelo Gurnari,[1,2] Marie Robin,[3] Lionel Adès,[3] Mahmoud Aljurf,[4] Antonio Almeida,[5] Fernando Barroso Duarte,[6] Elsa Bernard,[7] Corey Cutler,[8] Matteo Giovanni Della Porta,[9] Theo De Witte,[10] Amy DeZern,[11] Joanna Drozd-Sokolowska,[12] Eric Duncavage,[13] Pierre Fenaux,[3] Nico Gagelmann,[14] Guillermo Garcia-Manero,[15] Claudia Haferlach,[16] Torsten Haferlach,[16] Robert Hasserjian,[17] Eva Hellström-Lindberg,[18] Meagan Jacoby,[19] Austin Kulasekararaj,[20] R. Coleman Lindsley,[8] Jaroslaw P. Maciejewski,[2] Hideki Makishima,[21] Luca Malcovati,[22] Moshe Mittelman,[23] Anders E. Myhre,[24] Seishi Ogawa,[25] Francesco Onida,[26] Elli Papaemmanuil,[27] Jakob Passweg,[28] Uwe Platzbecker,[29,30] Lisa Pleyer,[31] Kavita Raj,[32] Valeria Santini,[33] Anna Sureda,[34] Magnus Tobiasson,[18] Maria Teresa Voso,[1] Ibrahim Yakoub-Agha,[35] Amer Zeidan,[36] Matthew Walter,[19] Nicolaus Kröger,[14] Donal P. McLornan,[32,*] and Mario Cazzola[22,*]



Gurnari et al, Blood 2025

Quando effettuare il Trapianto Allogenico di CSE ?

- Alto rischio IPSS-M : se paziente elegibile, trapianto subito
- Basso rischio IPSS-M : considerare subito il trapianto se:
  - Trasfusione-dipendente
  - Presenti mutazioni germline
  - MDS therapy related
  - Vexas con problematiche infiammatorie severe

Gurnari et al, Blood 2025

Grazie a tutti!!!

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