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Il secondo trapianto è ancora utile? NO

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Pierre Fabre						x	
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Secondo trapianto!

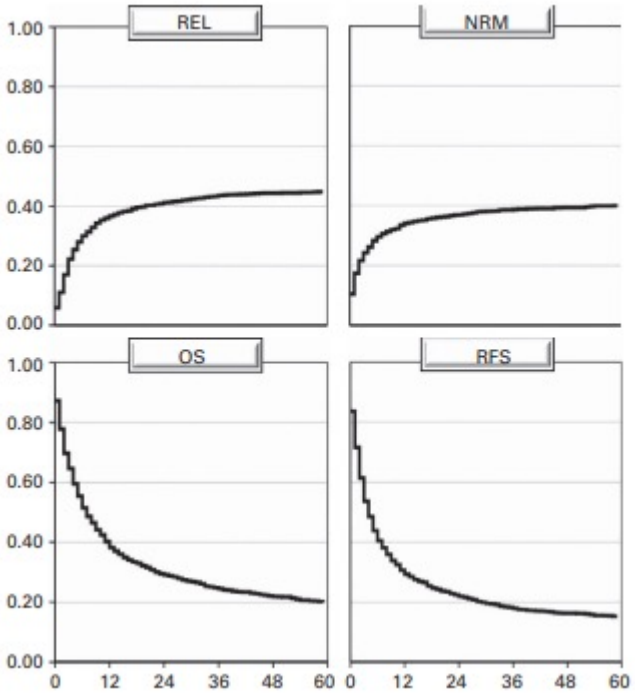
Razionale : rescue di un paziente con LAM recidivato : quando?
per chi?
perché?
dopo quale tipo di trapianto?
in quale stato di malattia?

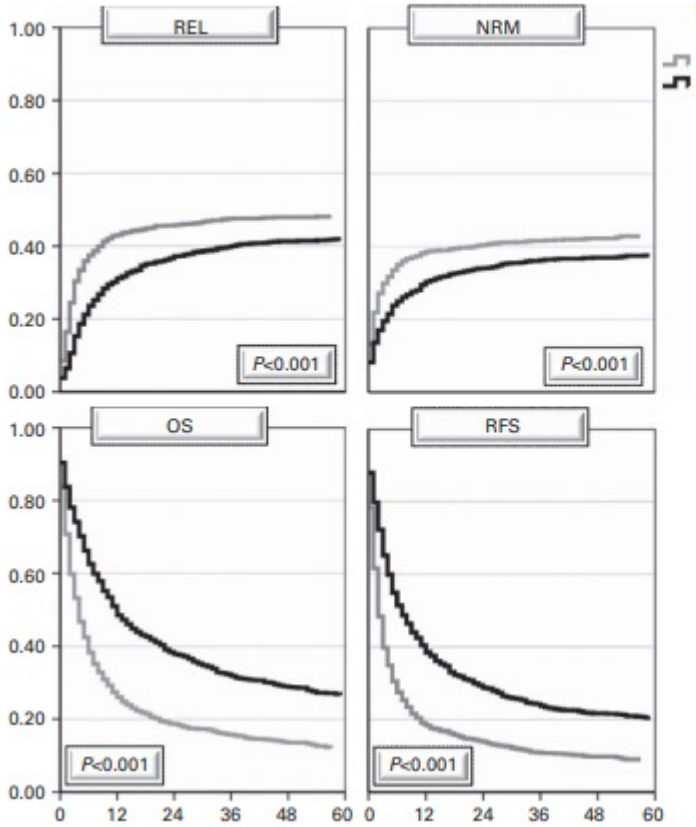
Una speranza per chi?: ematologo? Paziente? familiari? Donatore?

2632 second allogeneic transplantations (40% ntation .
Fifteen percent of the patients remained relap
Patients with **CML** had a better survival than p
In a multivariate analysis, factors associated v remission
duration after the first transplantation, longe , absence of
GvHD after cation

st transplant rvival.

nt-related m





Ruutu T et al : BMT 2015

FHCRC
81 pazienti
AML /MDS
2006-2022
1% dei trapianti
10% IBMTR
Specifically, the primary reason(s) precluding HCT2 were leukemia-related in 152 (50%) patients, toxicities/adverse events following salvage therapy in 24 (8%) patients, complications from HCT1 in 9 (3%) patients, and a combination of these factors in 21 (7%) patients. Additionally, 97 (32%) patients underwent alternative therapeutic approaches (eg, DLI) with HCT2 not being considered, and 2 (1%) patients were in the process of planning HCT2 at the time of the chart review

NO MOLECULAR DATA

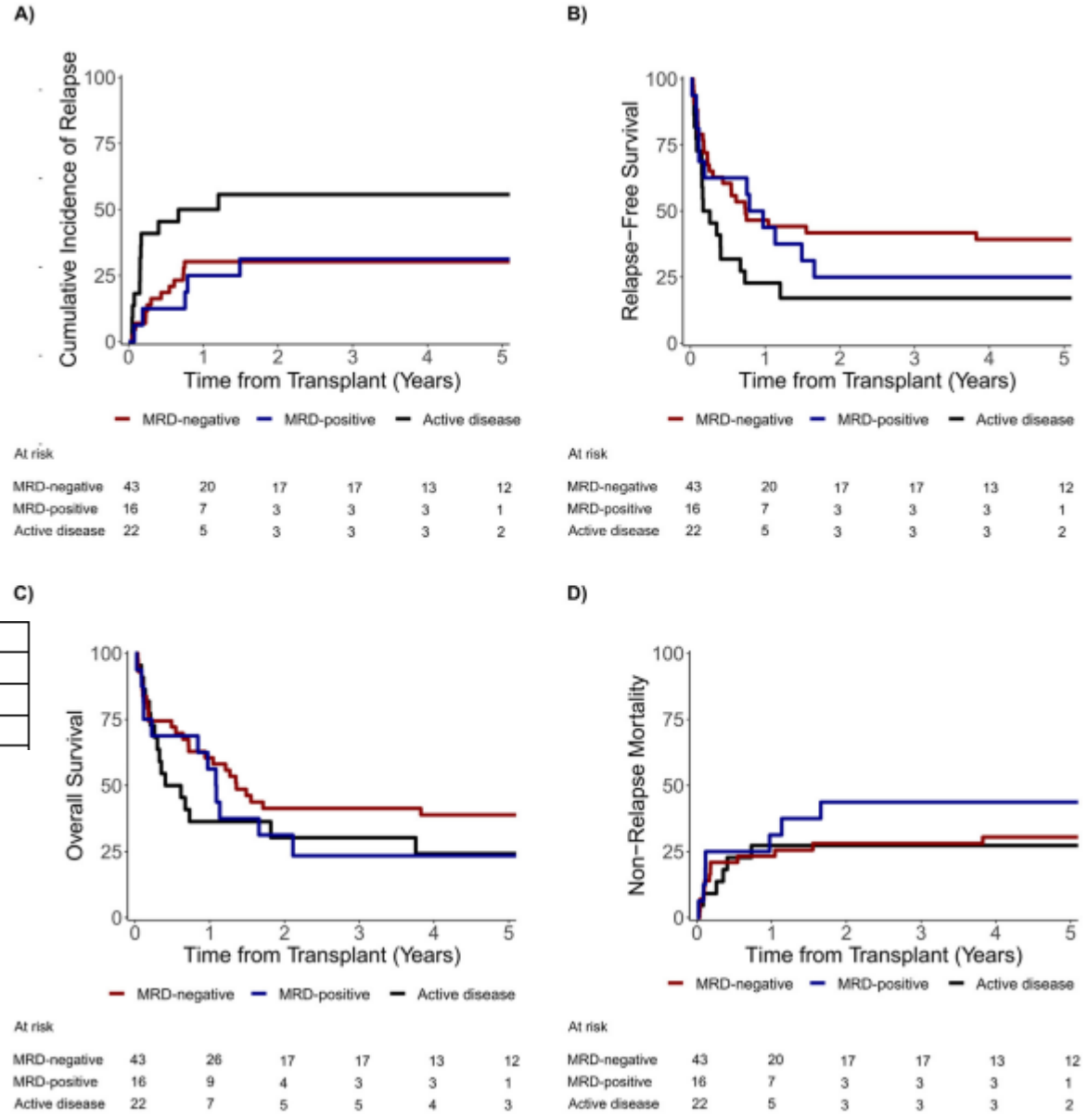
Rodríguez-Arbolí E et al TCT 2024

ELN 2022 cytogenetic risk, *n* (%)	
Favorable	4 (5)
Intermediate	48 (59)
Adverse	26 (32)
Missing/not reported	3 (4)
Secondary disease, *n* (%)	16 (20)

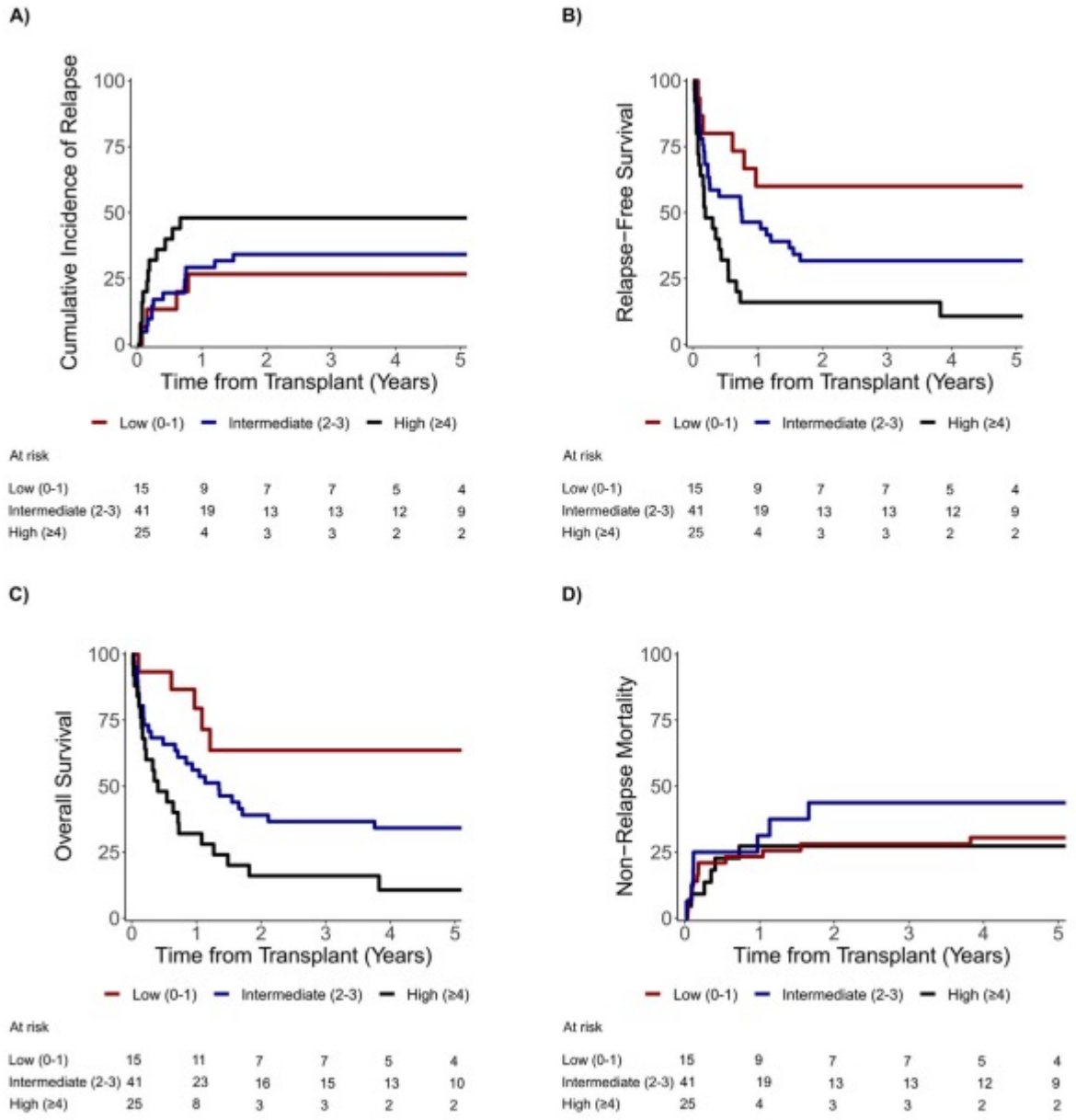
Disease status at second HCT, *n* (%)	
Morphologic remission (MRD^{neg})	43 (53)
Morphologic remission (MRD^{pos})	16 (20)
Active disease	22 (27)

DIFFERENT DONORS

Rodríguez-Arbolí E et al TCT 2024



<6 MESI
MALATTIA ATTIVA
HCT-CI ALTO



Rodríguez-Arbolí E et al TCT 2024

How risky is a second allogeneic stem cell transplantation?

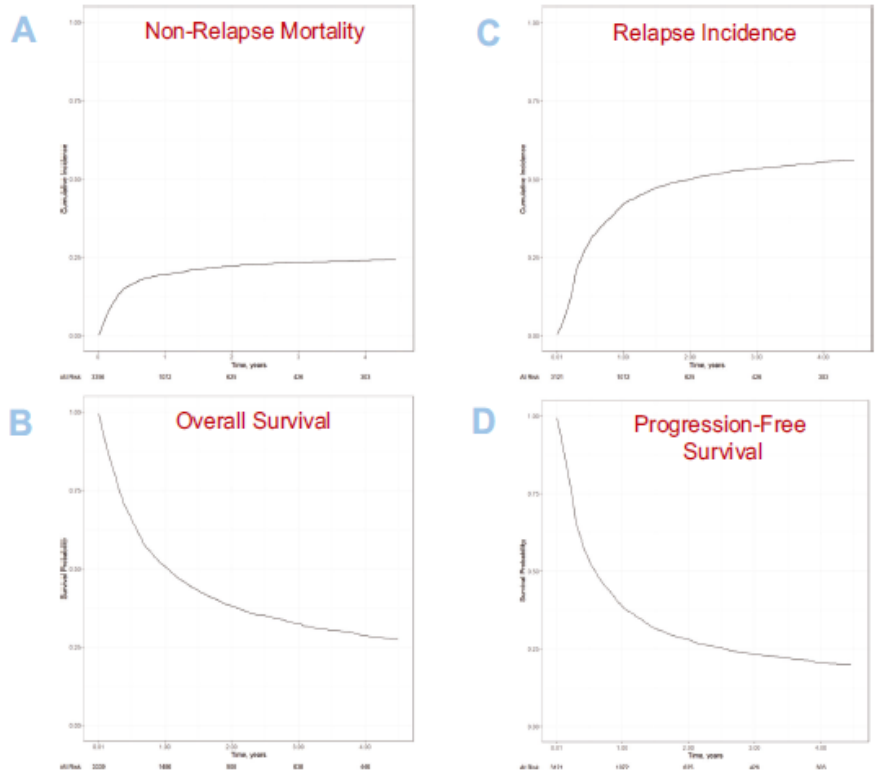
retrospective EBMT data set analysis.
3356 second alloSCTs performed 2011–21
AML 60%, ALL 15%, and MDS 8%.
Outcomes at two years after second alloSCT were: NRM 22%,
relapse incidence 50%, overall survival 38%, and progression-free survival 28%
risk factors for increased NRM were: older age, low performance score, high disease-risk-index, early relapse after the first alloSCT, unrelated/haploidentical donor, and GVHD before second alloSCT.
preferential use of a different donor (80%) at second alloSCT from first alloSCT.
different donor was not associated with any of the survival or GVHD endpoints

NO MOLECULAR DATA

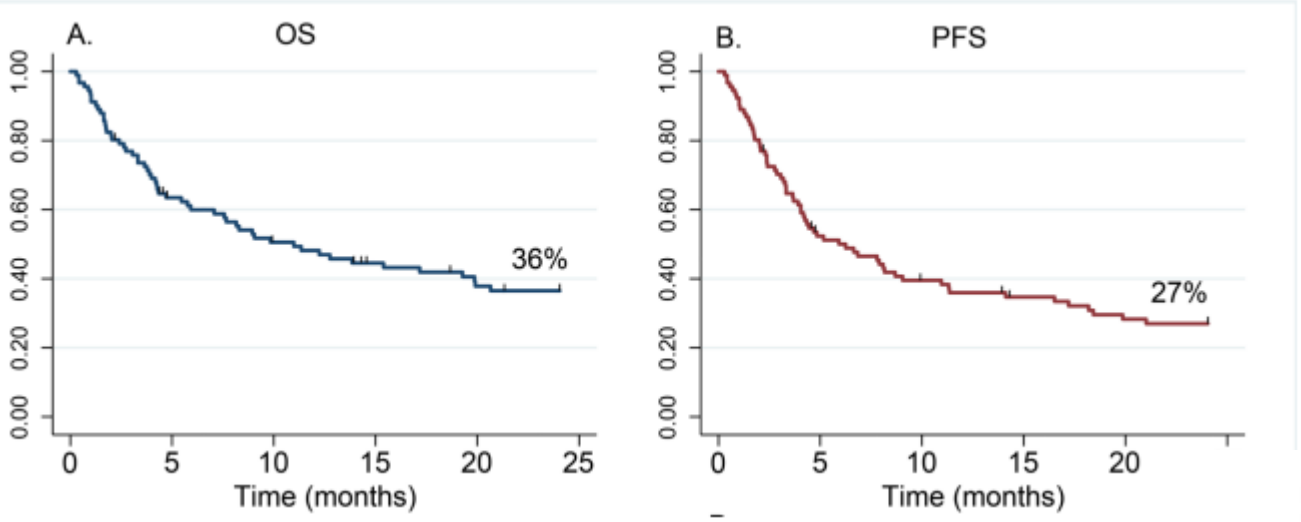
Penack O et al : Leukemia 2024

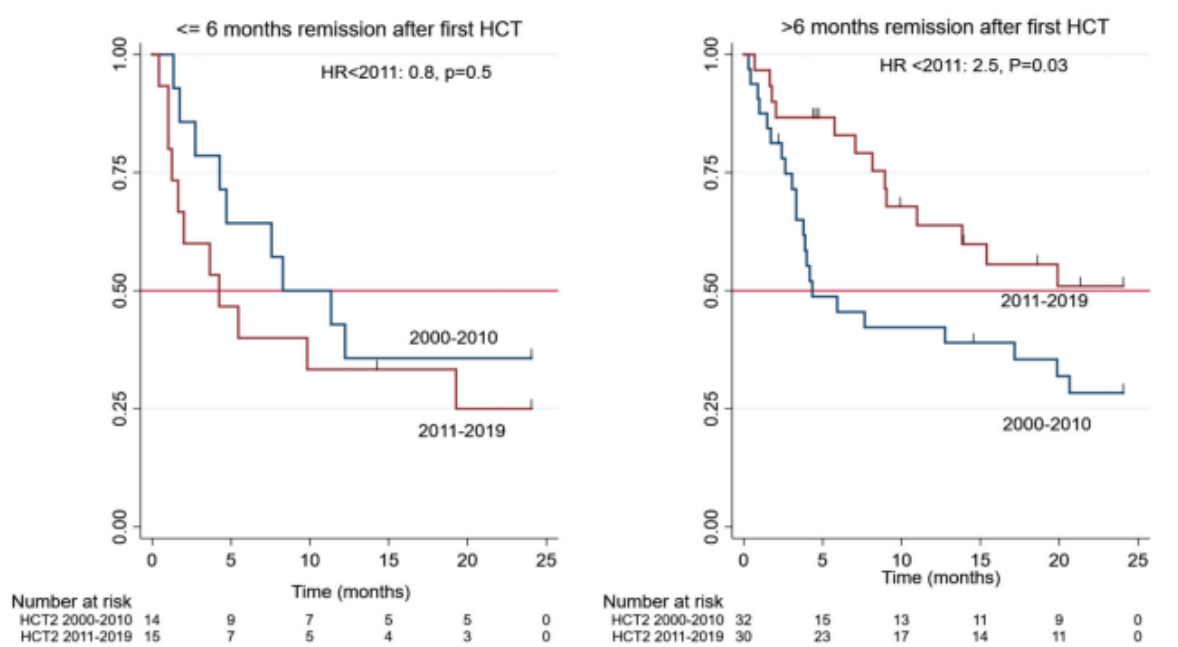
Myeloablative conditioning		
No	1207 (36.4%)	1828 (56.1%)
Yes	2110 (63.6%)	1432 (43.9%)
Missing count	39	96
Total body irradiation		
No	2446 (73.0%)	2543 (76.6%)
Yes	905 (27.0%)	778 (23.4%)
Missing count	5	35
GVHD prevention regimen		
Cyclosporine A + MMF based	1457 (45.0%)	1223 (38.7%)
Cyclosporine A + MTX based	936 (28.9%)	705 (22.3%)
Cyclosporine A based	393 (12.1%)	383 (12.1%)
Tacrolimus/Sirolimus + MMF based	242 (7.5%)	538 (17.0%)
Tacrolimus/Sirolimus + MTX based	48 (1.5%)	44 (1.4%)
Tacrolimus/Sirolimus based	58 (1.8%)	99 (3.1%)
Other	103 (3.2%)	168 (5.3%)
Missing count	119	196
In vivo T cell depletion for second alloSCT		
No		1560 (48.6%)
Campath		142 (4.4%)
ATG		1506 (46.9%)

Delay first to second alloSCT, years	
Median [Q1, Q3]	1.7 (0.9, 3.4)
[Min, Max]	0.1–27.8
Delay relapse to second alloSCT, years	
Median [Q1, Q3]	0.4 (0.2, 0.8)
[Min, Max]	0.0–19.6



Penack O et al : Leukemia 2024





No molecular data

Yalniz FF et al TCT 2021

Il caso di TP53

Author	Study type	Disease	Pts with *TP53* LOF receiving allo-HCT	Subset with high-risk cytogenetics	DFS from time of HCT	OS from time of HCT
MDS						
Lindsley et al[25]	Registry	MDS	*TP53* mut: 289 pts	Not listed	Not listed	3-y OS: ~15% (complex)
Yoshizato et al[26]	Registry	MDS including subset with sAML	*TP53* mut: 98 pts	Complex: 86 pts	Not listed	Median OS: 4.3 mo 3-y OS: ~10% (complex)
AML						
Middeke et al[23]	Registry	AML	17p abnl: 201 pts	Monosomal: 77 pts Complex: 180 pts	3-y EFS: 9% (monosomal) 3-y EFS: 9% (complex)	3-y OS: 11% (monosomal) 3-y OS: 11% (complex)
Middeke et al[22]	3 multicenter clinical trials	AML	*TP53* mut: 40 pts	Adverse†: 40 pts	3-y PFS: 7.5% (adverse)	3-y OS: 10% (adverse)
Luskin et al[27]	Single center	AML	*TP53* mut: 9 pts	Adverse‡: 6 pts	All relapsed (adverse; range, 1.6-18.6 mo after HCT)	Not listed
Poire et al[24]	Registry	AML	17p abnl: 125 pts	Monosomal: 86 pts −5/5q-: 58 pts	2-y: 17% (monosomal) 2-y: 11% (−5/5q-)	2-y OS: 19% (monosomal) 2-y OS: 16% (−5/5q-)
Najima et al[28]	Single center	AML (nonremission)	*TP53* mut: 23 pts	Monosomal: 11 pts	Not listed	All died within 12 mo post allo-HCT (monosomal)
Grob et al[18]	4 multicenter clinical trials	MDS-EB AML	*TP53* mut: 59 pts	Complex: 48 pts	Not listed	3-y OS: ~10% (complex)
Loke et al[21]	Registry	AML	*TP53* mut: 179 pts	17p loss and/or complex: 126 pts	2-y PFS: 15.2% (17p loss and/or complex)	2-y OS: 24.6% (17p loss and/or complex)
AML						
Murdock et al[37]	Single center	33 pts	VAF < 0.1%	Pts with *TP53* mut clearance before allo-HCT did not experience DFS benefit		
Badar et al[38]	Registry	68 pts	"Clearance by NGS testing," not otherwise defined	Pts with *TP53* mut clearance before allo-HCT did not experience DFS benefit		

VAF> o< 40%

the survival benefit of allo-HCT in *TP53*-mutated MDS/AML with biallelic loss and/or adverse-risk cytogenetics has not been established.

Disease characteristics	Patient characteristics	Offer allo-HCT?	Comments
Monoallelic *TP53* mutation without complex karyotype	Fit for allo-HCT	Yes, if both criteria were met	Standard fitness criteria applied.
Biallelic *TP53* loss ± complex karyotype	KPS ≥ 90 and HCT-CI < 4•	Consider	•Score intended as provisional guidance rather than absolute threshold. Consider the use of alternative nonrelapse mortality scoring systems.[70,71] Donor options may modify risk assessment (eg, we are less likely to pursue allo-HCT in an older patient with these characteristics if only alternative donor is available). Must clearly discuss risks, benefits, and expectations regarding posttransplant prognosis.
Biallelic *TP53* loss ± complex karyotype	KPS < 90 HCT-CI ≥ 4•	No	Consider referral for second opinion regarding allo-HCT.

Nawas TM et al Blood 2024

In conclusione

No alla maggior parte dei pazienti
Si a pazienti giovani, oltre 6 mesi da 1° TX, MRD- o senza malattia attiva e basso HCT-CI, testing e retesting NGS, ma quanti sono?
Cambio donatore HLA loss ?

Alternative

Targeted therapy

Trials clinici

DLI («no apparent difference in OS whether an allo-HCT2 or DLI was prescribed" **JAMA 2018**), stessi caveats <6m

Terapia di palliazione

L'altra faccia è il donatore