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RIUNIONE NAZIONALE GITMO

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La leucemia acuta: il ruolo del trapianto nei pazienti anziani e fragili

Contro - trapianto nella LAM/MDS

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Disclosures of Giovanni Marconi

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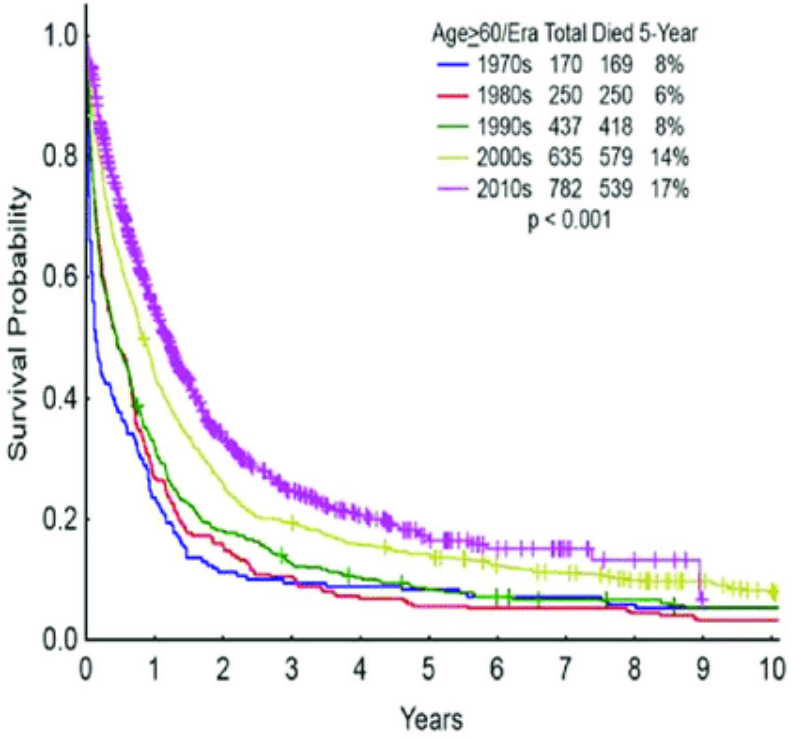
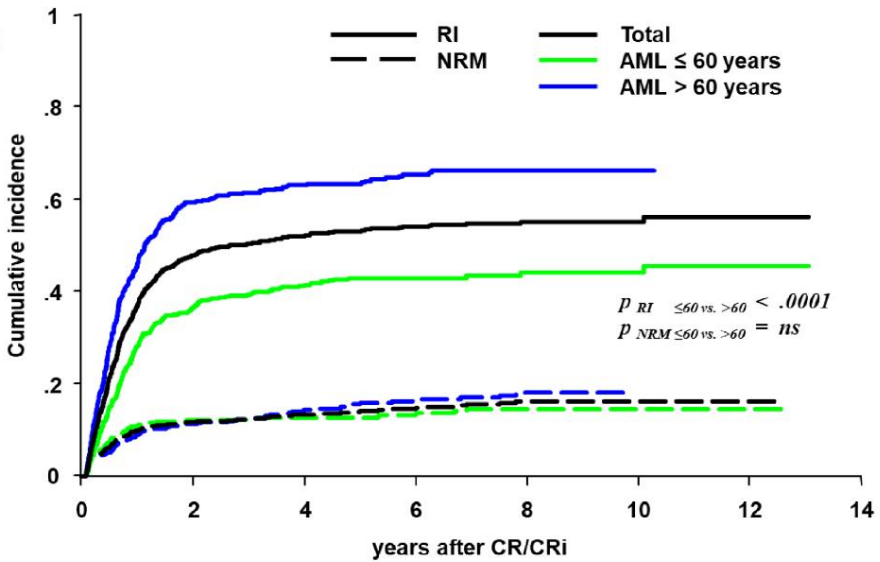
Astrazeneca	x				x		
Daiichi Sankyo	x						
Enable Lifescience			x			x	
Immunogen			x			x	
Jansenn					x		
Jazz			x		x	x	
Menarini			x		x	x	
Pfizer	x		x		x	x	
Ryvu			x			x	
Servier			x		x	x	
Syros	x		x		x	x	
Takeda					x		
UKNEQUAS					x		

Age as a negative prognostic factor, intensivelly treated AML

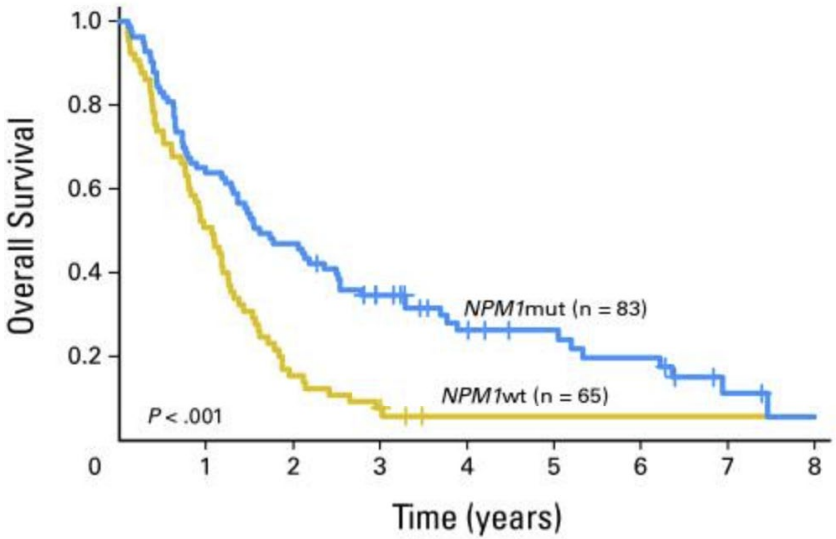


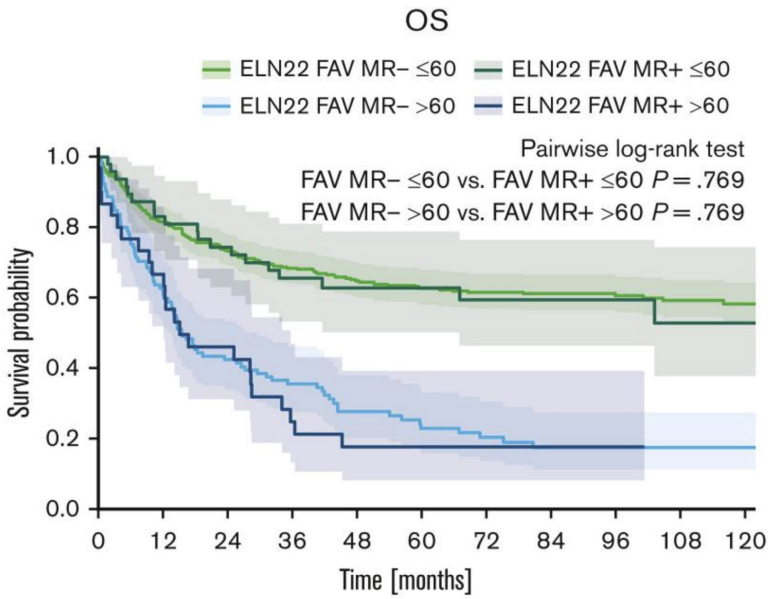


	n	RI % at 5 years	RI median (months)	NRM % at 5 years
total	1144	53.1 ± 1.5	-	14.3 ± 1.1
≤60 years	586	43.0 ± 2.2	-	12.7± 1.4
>60 years	588	63.5 ± 2.1	15.6	16.0 ± 1.7

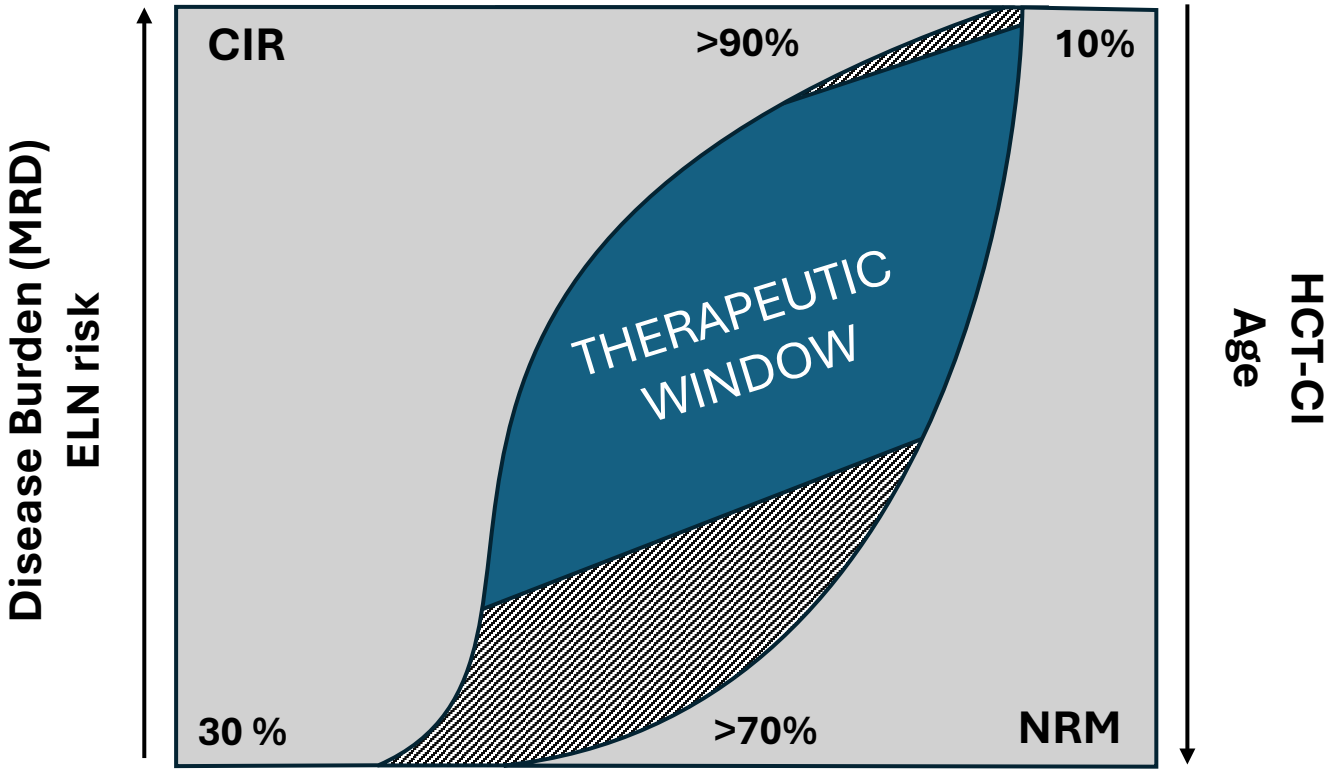
Hagop Kantarjian, BCJ 2021; Thomas Heinicke, Ann hemat 2023

Patients >60yo intensively treated

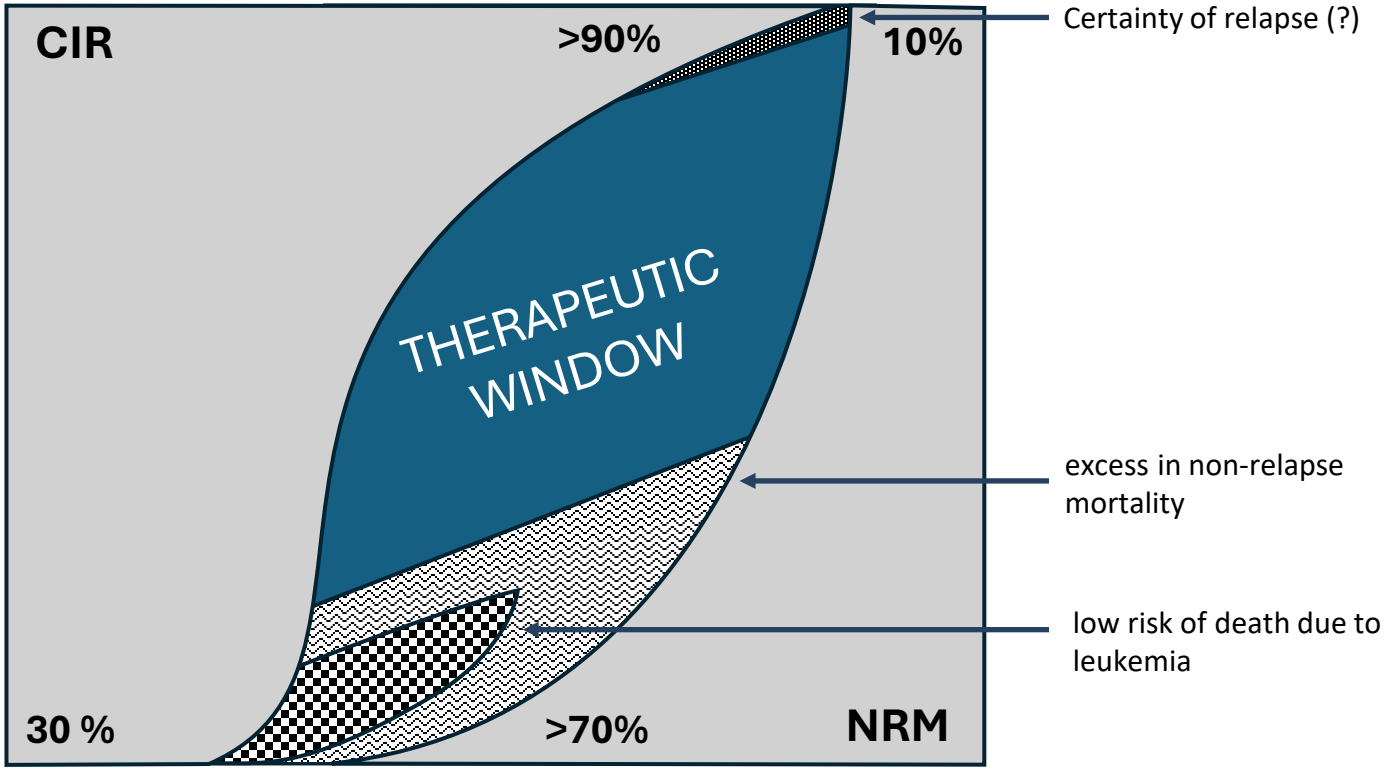




Therapeutic window of HSCT in CR1 after intensive treatment >60yo



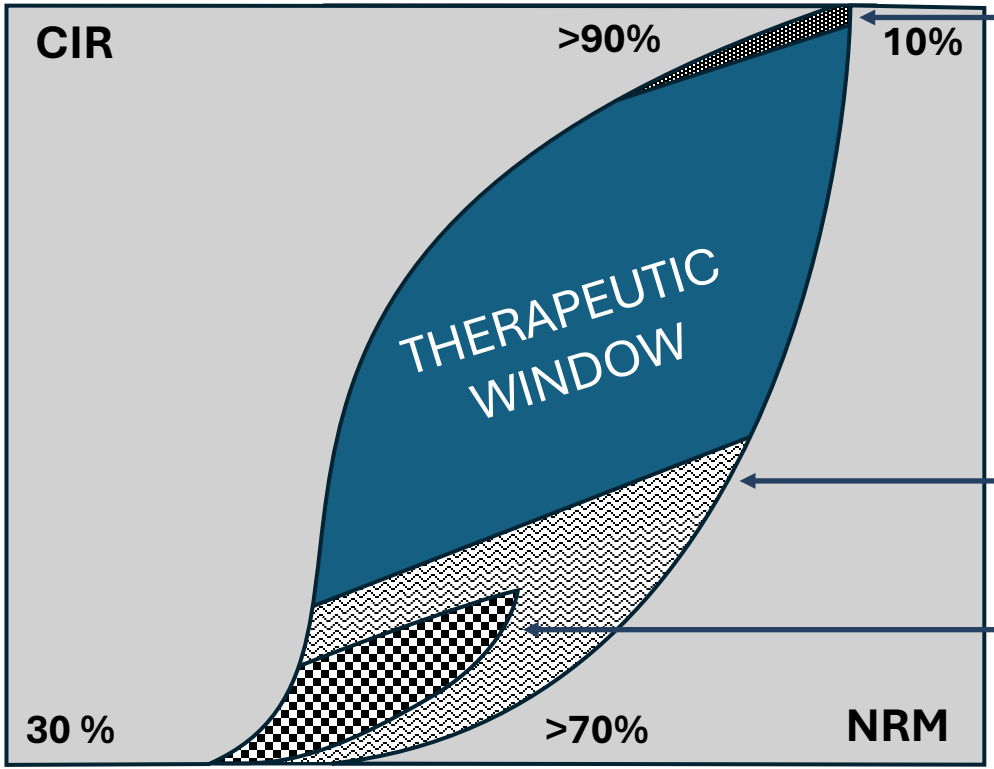
Who's out of therapeutic window?



Who's out of therapeutic window?

Tools to avoid transplant

- Good prediction models
- Reliable monitoring
- Effective rescue

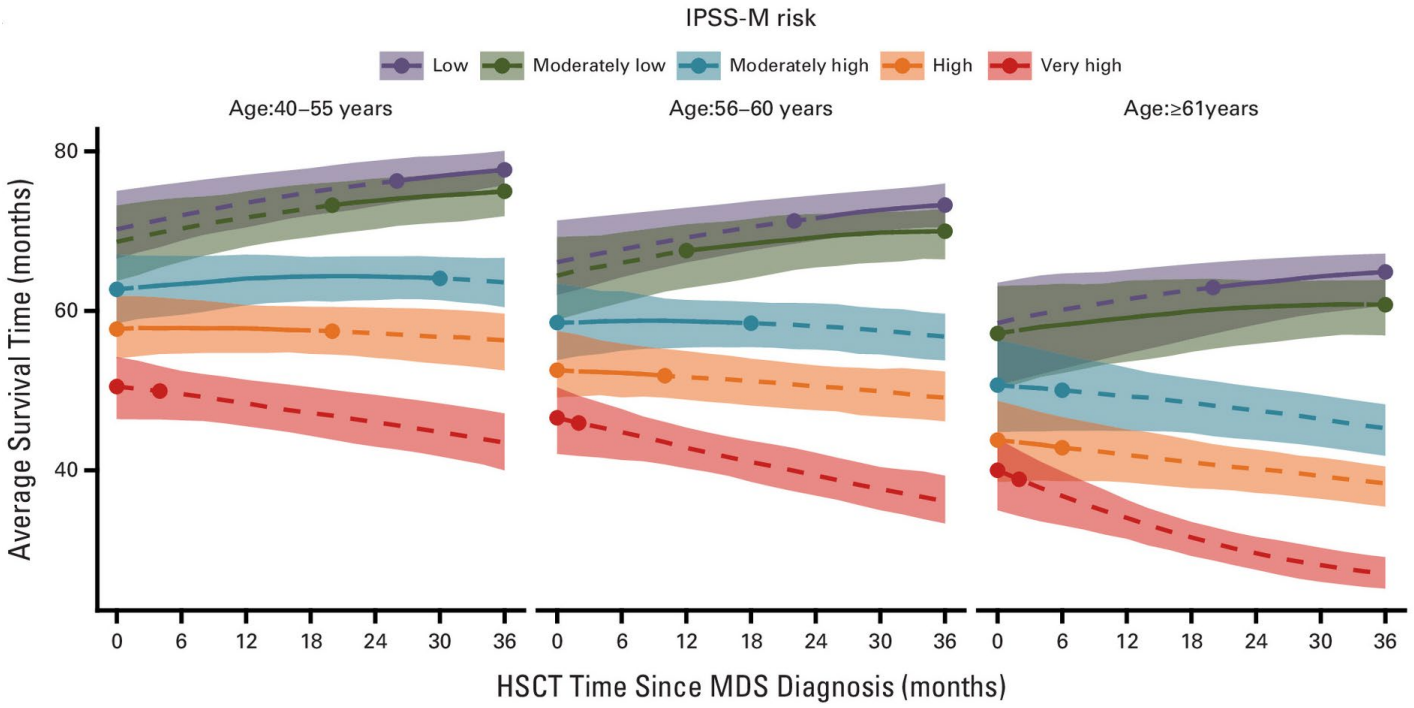


Certainty of relapse (?)

excess in non-relapse mortality

low risk of death due to leukemia

MDS: a model in which delaying HSCT may be beneficial for a subset



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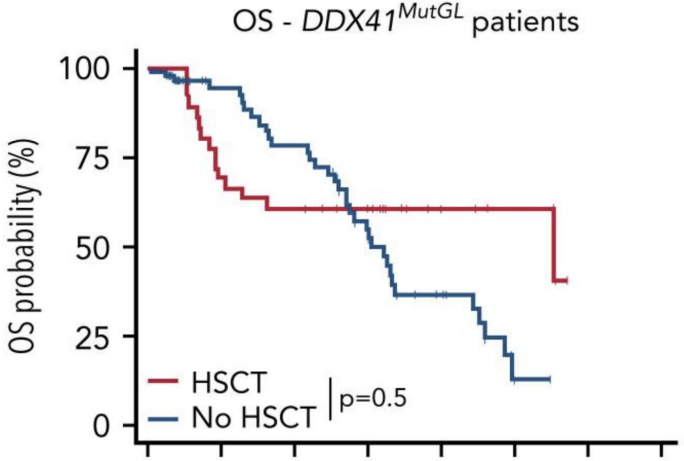
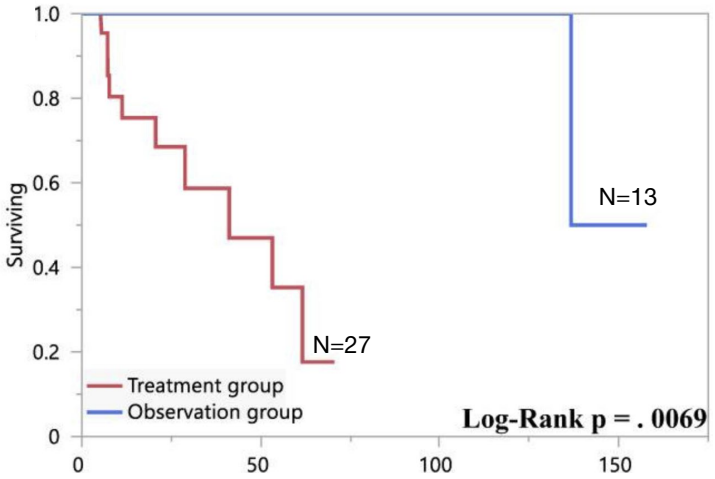
Low risk of death with conservative approaches

DDX41

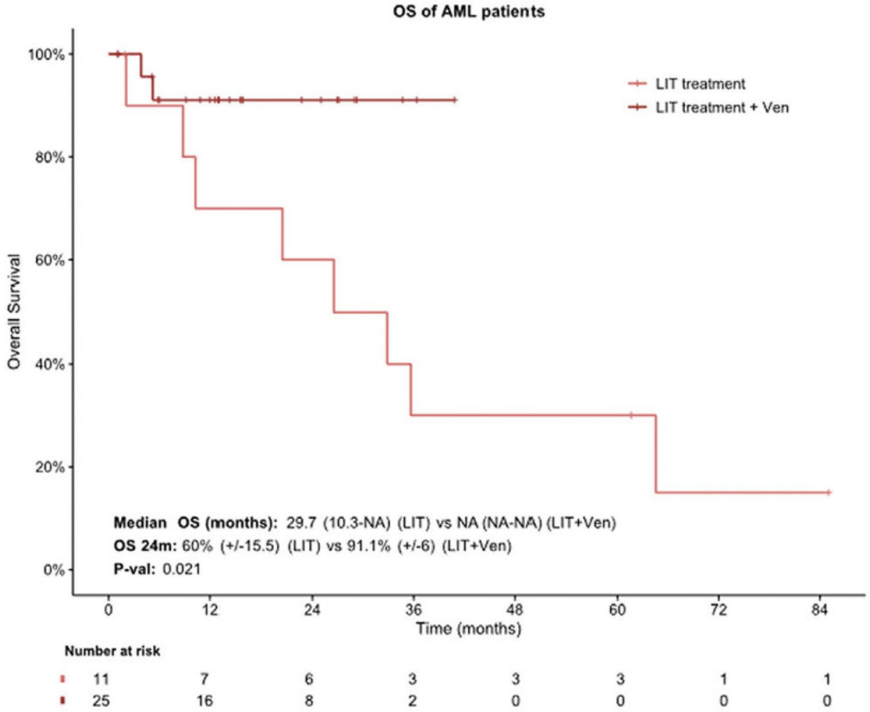


DDX41mut pts treated with CHT do not benefit form HSCT



… and may not benefit from intensive treatment at all

DDX41 has exquisite sensitivity to venetoclax

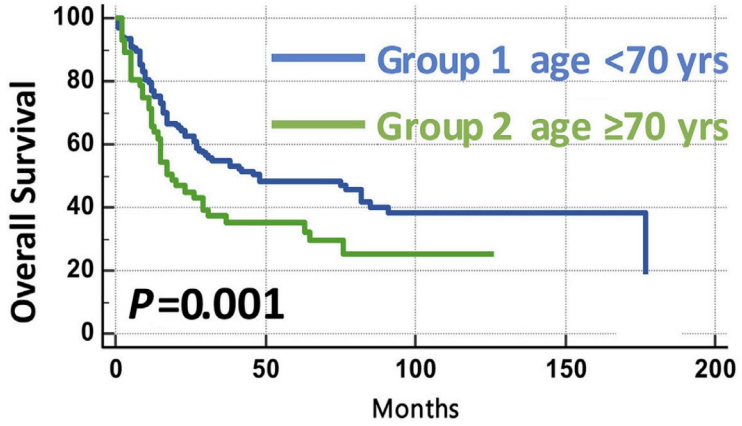


Center/author	CR+CRi	Alive at 3yr
MDACC/ Bataller	22/25 (88%)	22/25* (88%)
Mayo/Naana	10/10 (100%)	6/10** (60%)

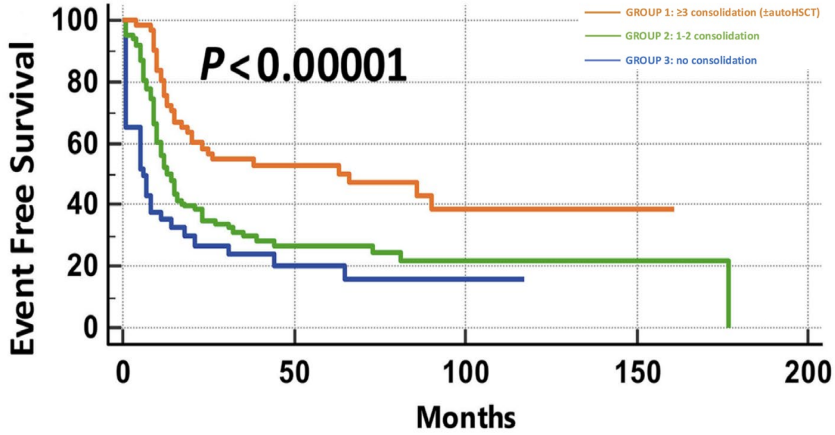
** 1 early death and 2 deaths after relapse*

*** 3 deaths in CR after HSCT, 1 death due to relapse*

A significant proportion of elderly CBF-AML achieve long term survival

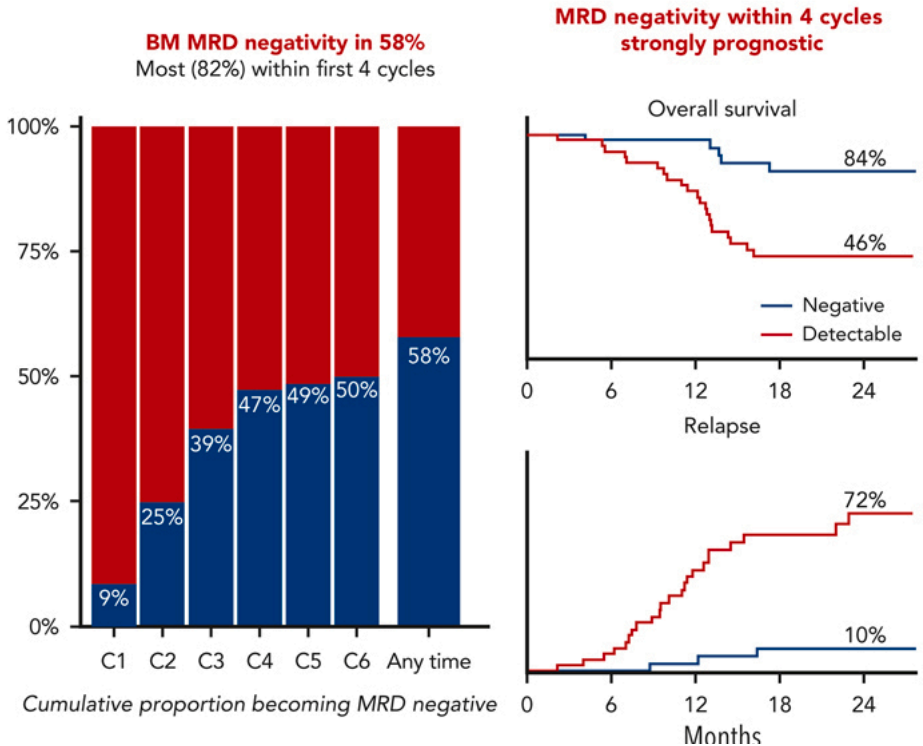


Number at risk				
Group: 1				
166	48	16	3	0
Group: 2				
56	15	4	0	0



Number at risk				
Group: 1				
46	5	2	0	0
Group: 2				
99	15	5	1	0
Group: 3				
64	25	9	2	0

NPM1



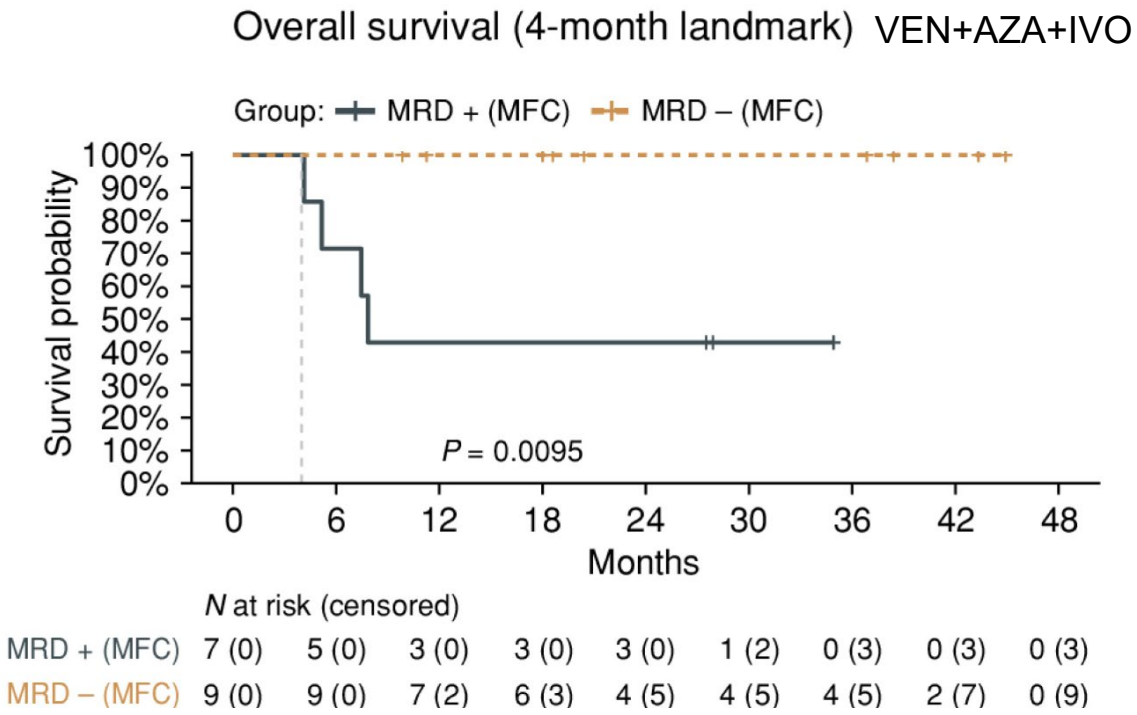
NPM1 mut
FLT3 neg

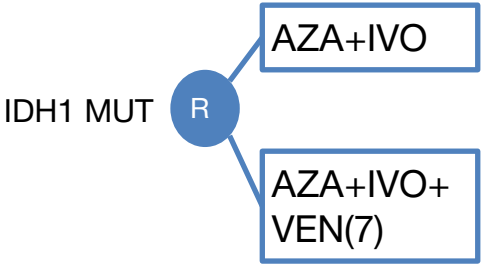
R

- 3+7 GO
- VEN+AZA 12 mesi

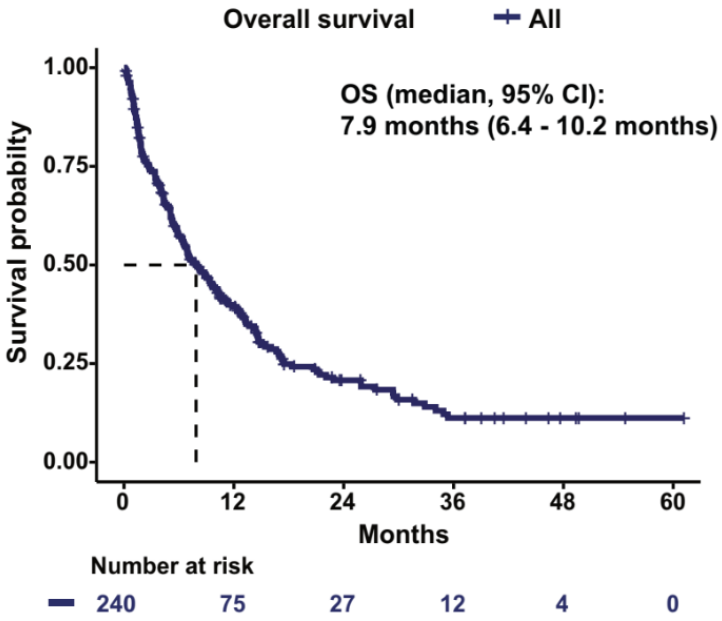
Jad Othman, blood, 2024

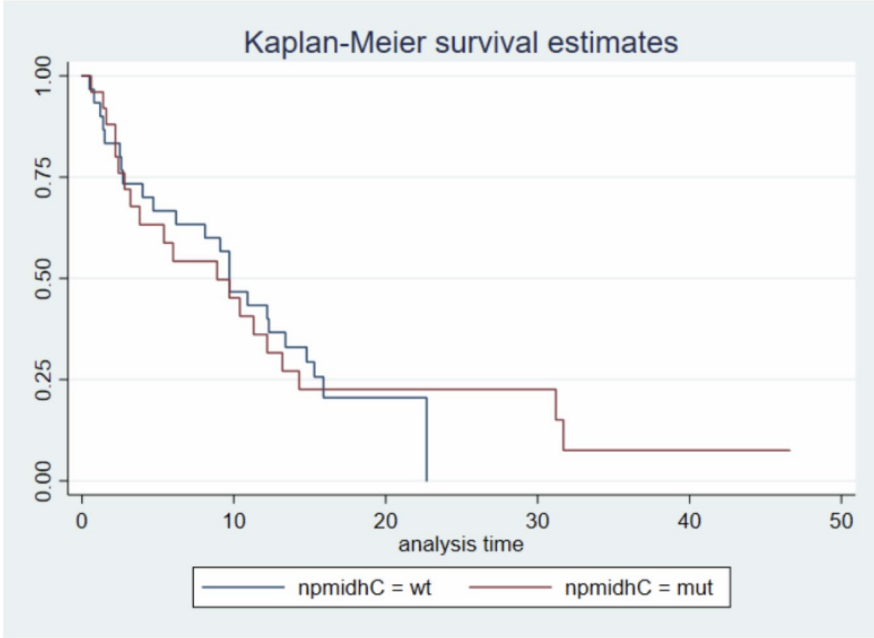
IDH1


Overall survival (4-month landmark) VEN+AZA+IVO
Group: MRD + (MFC) MRD – (MFC)
Survival probability
100%
90%
80%
70%
60%
50%
40%
30%
20%
10%
0%
P = 0.0095
0
6
12
18
24
30
36
42
48
Months
N at risk (censored)
MRD + (MFC) 7 (0) 5 (0) 3 (0) 3 (0) 3 (0) 1 (2) 0 (3) 0 (3) 0 (3)
MRD – (MFC) 9 (0) 9 (0) 7 (2) 6 (3) 4 (5) 4 (5) 4 (5) 2 (7) 0 (9)


IDH1 MUT
R
AZA+IVO
AZA+IVO+
VEN(7)

OS VEN+AZA relapse





Rabia Shahswar, Leukemia, 2024; G. Vetro (in preparation)

Remarks

- Standard chemotherapy has pitfalls in elderly, and remains largelly unsatisfactory
- VEN+AZA (and VEN+AZA+IVO) has subsets with exquisite sensitivity, and candidate as a transplant-sparing approach in selected patients
- Reliable MRD monitoring allow accurate decisions
- Effective rescue strategies are still missing

CBF AML MRD-LL or MRD neg

DDX41m MRD neg

NPM1m MRD neg

IDH1m MRD neg treated with triplets

I'd not consider transplant in CR1 in 15-20% of patients

(personal opinion)

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IMPACT - AML
European project on Relapsed/Refractory Acute Myeloid Leukemia

Resolve
MRD guided treatment

Ministero della Salute
MULTIDIMENSION-ALL
(PNRR-MR1-2023-12377495)

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