

# Relapse after allogeneic stem cell transplantation

Xavier Poiré, MD, PhD

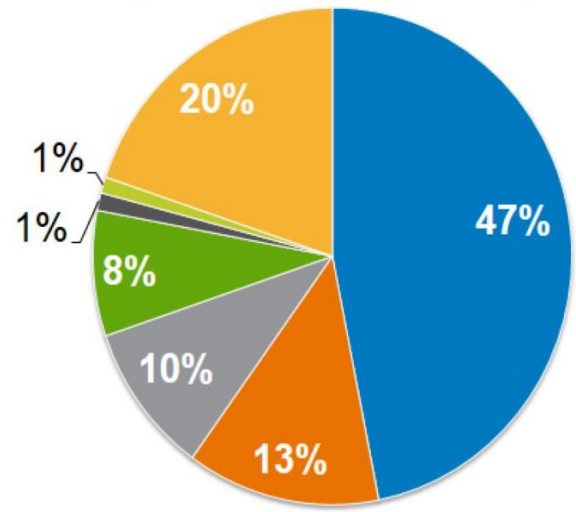
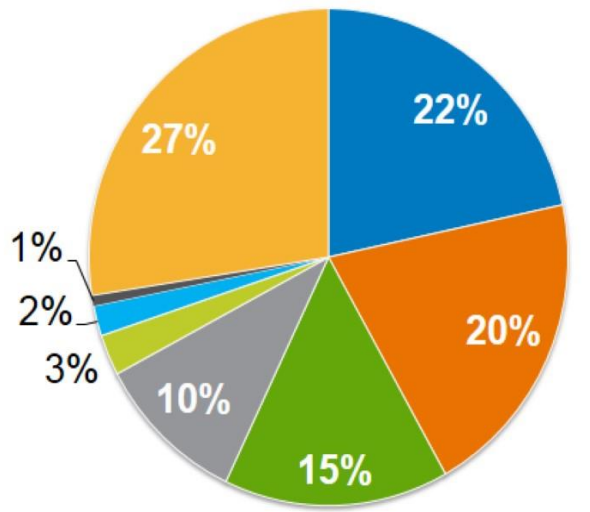
16/03/2024

# RELAPSE AFTER SCT = MAJOR CAUSE OF TREATMENT FAILURE

## Causes of Death after Unrelated Donor HCT done in 2014-2015

Died within 100 days post-transplant

Died at or beyond 100 days post-transplant\*



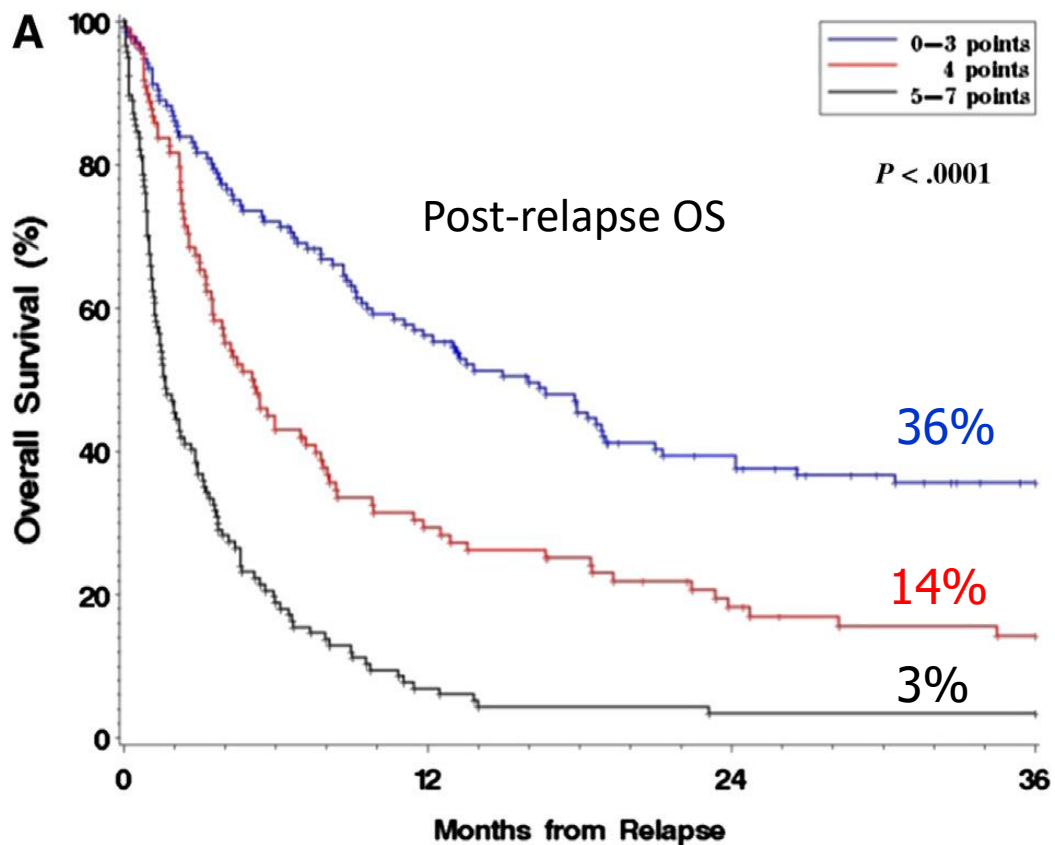
- Primary Disease
- Infection
- Organ Failure
- GVHD
- Hemorrhage
- Graft Rejection
- Second Malignancy
- Other

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- Infection
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\* Data reflects 3-year mortality

# PROGNOSIS OF RELAPSE

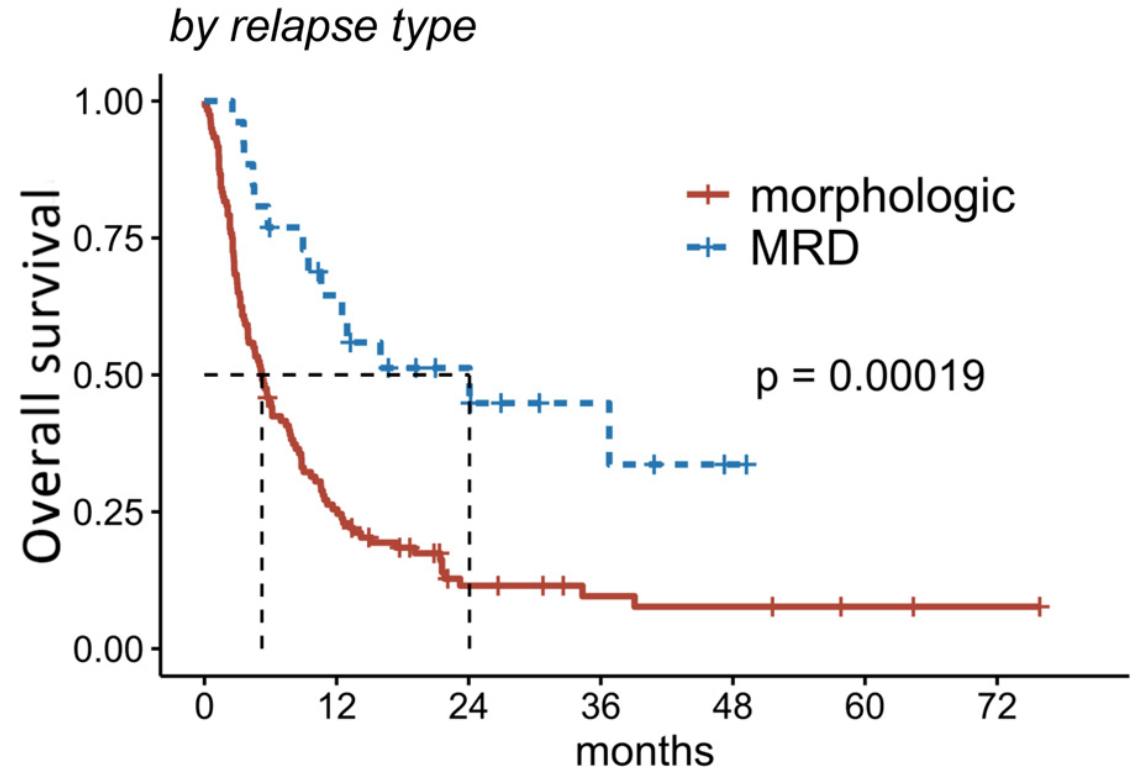


Thanarajasingam et al., BBMT 2013

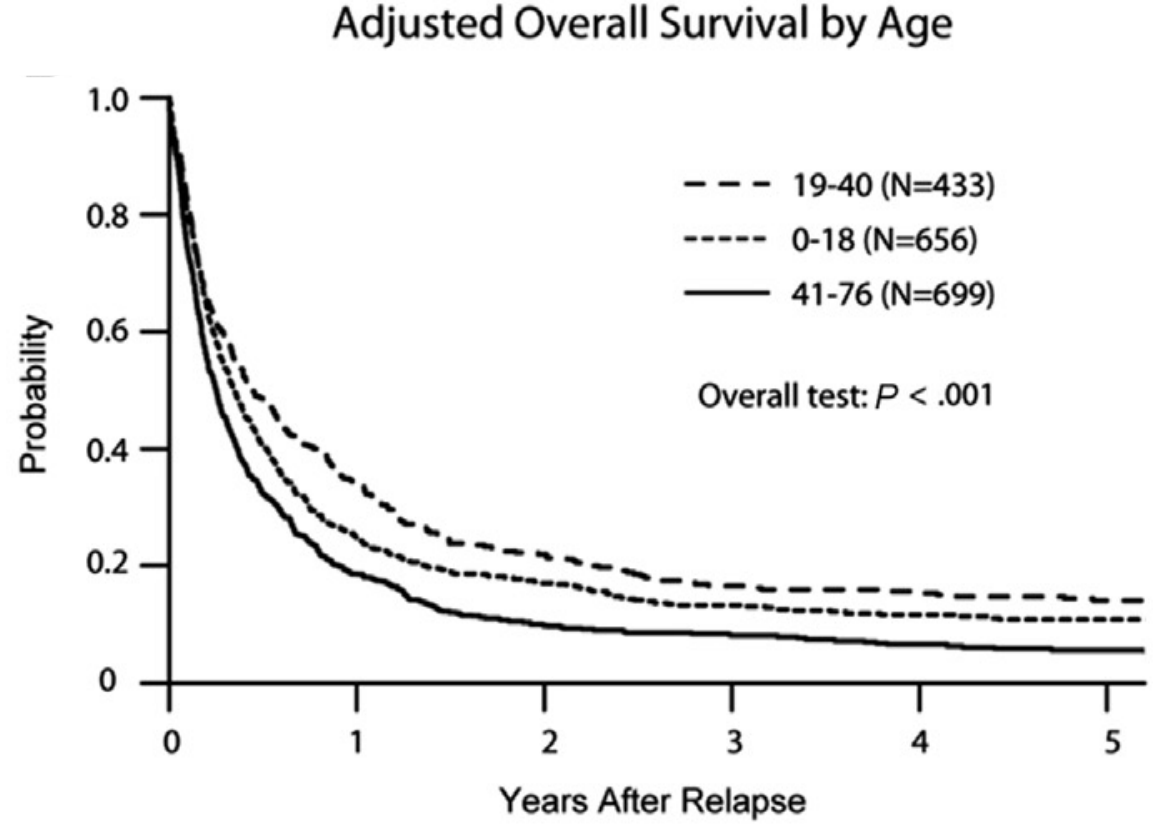
## Prognostic factors

- **Time to relapse**
  - > 24 mo (0), 6-24 mo (1), 3-6 mo (2), <3 mo (3)
- **Disease-risk index**
  - Low: indolent NHL, CLL, CP-CML (0)
  - Int: aggressive NHL, MDS (1)
  - High: high-risk AML (2)
- **Myeloablative conditioning** (1)
- **Prior GvHD** (1)

# PROGNOSIS OF RELAPSE

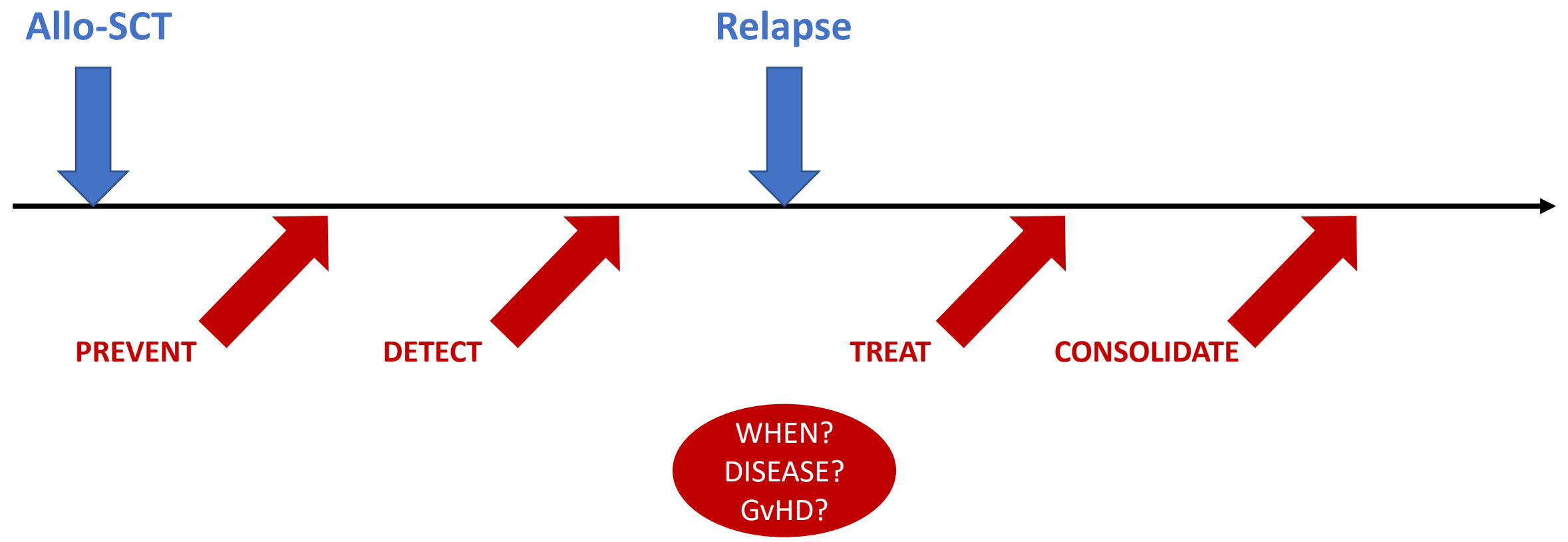


Zuanelli Brambilla et al., TCT 2021



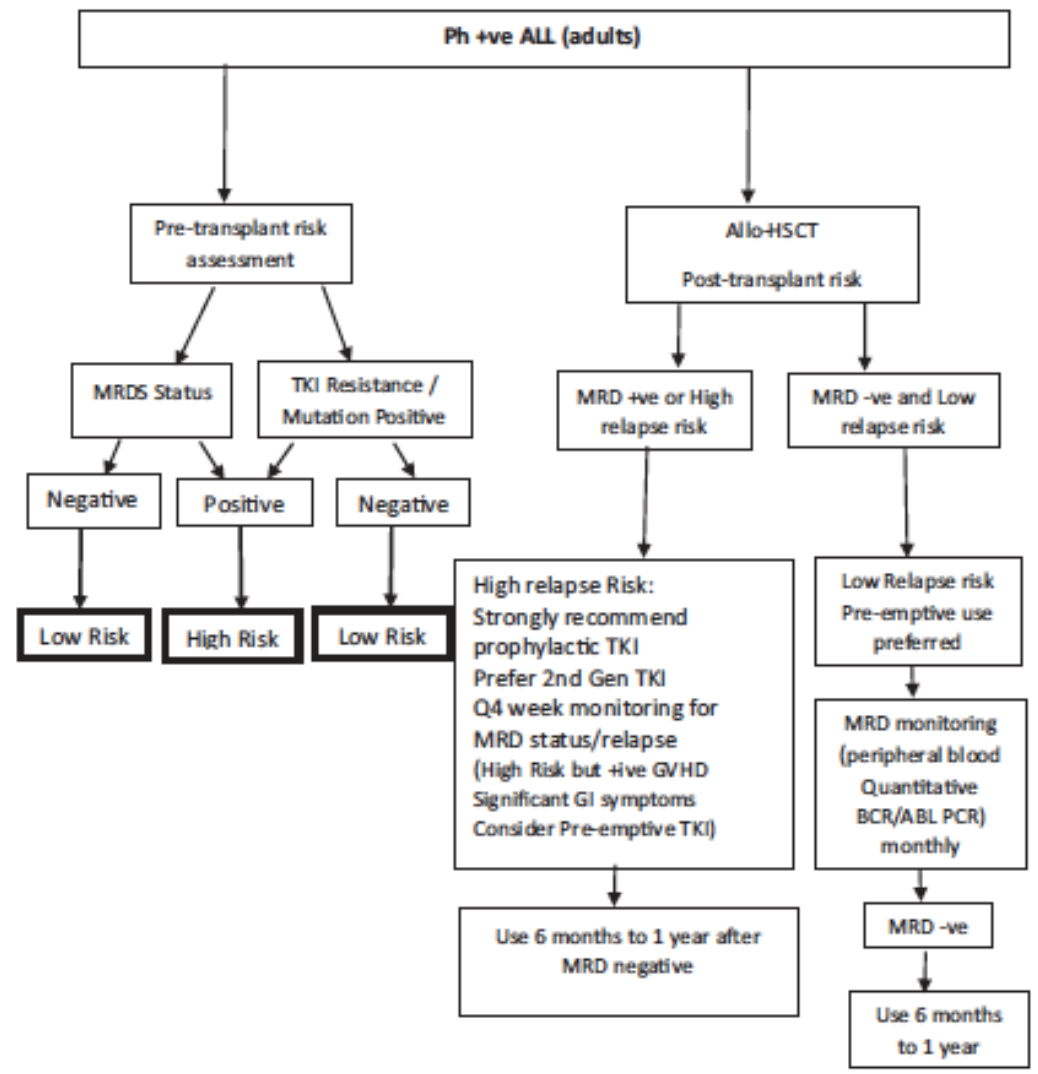
Bejanyan et al., BBMT 2015

# TIMELINE OF RELAPSE

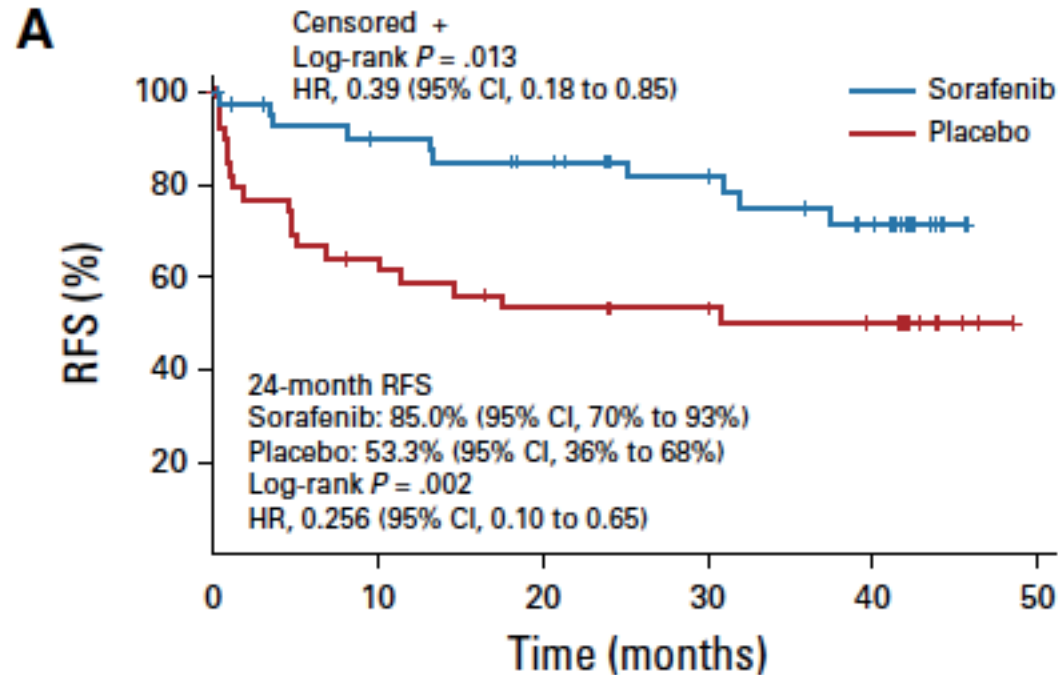


# TKI AFTER ALLO FOR PH+ ALL

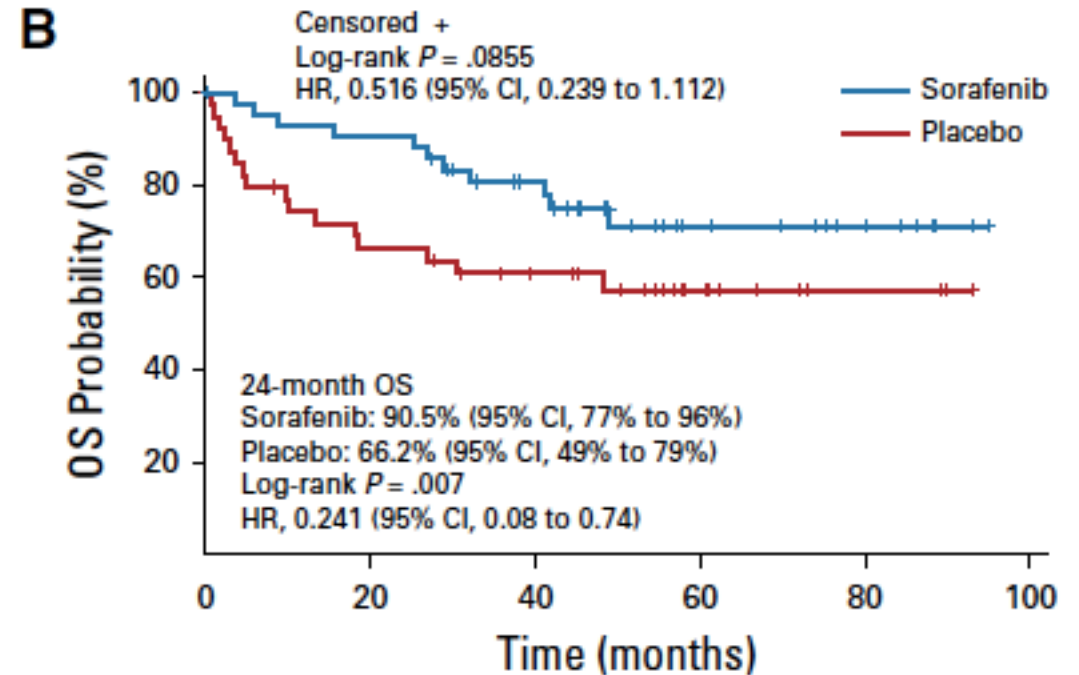
PREVENT



Warraich et al. BBMT 2020

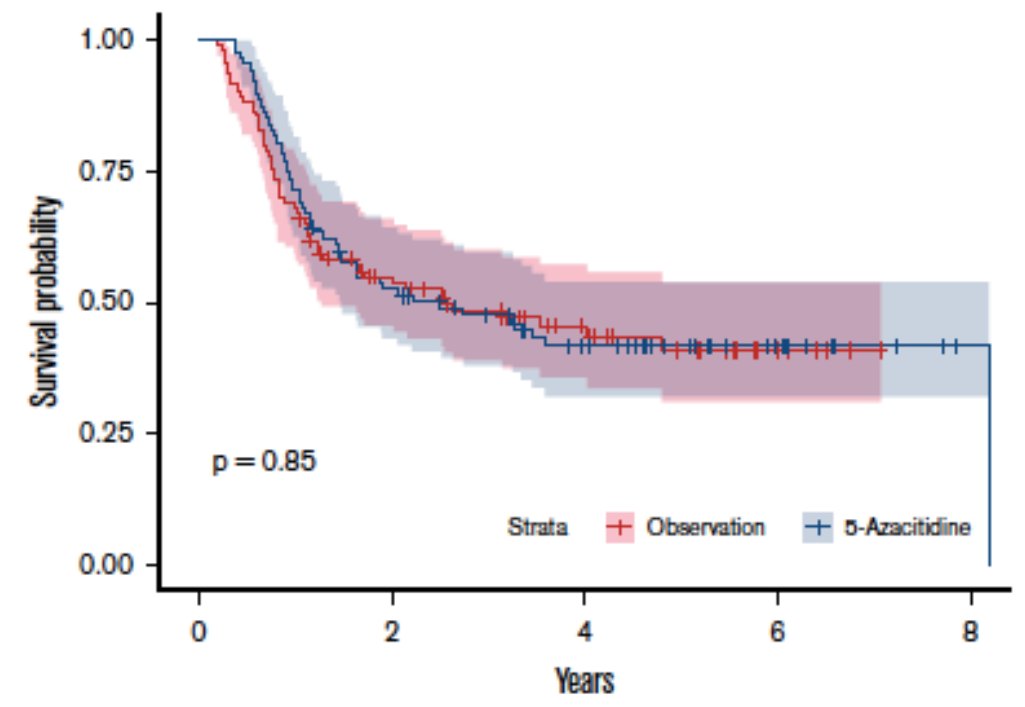
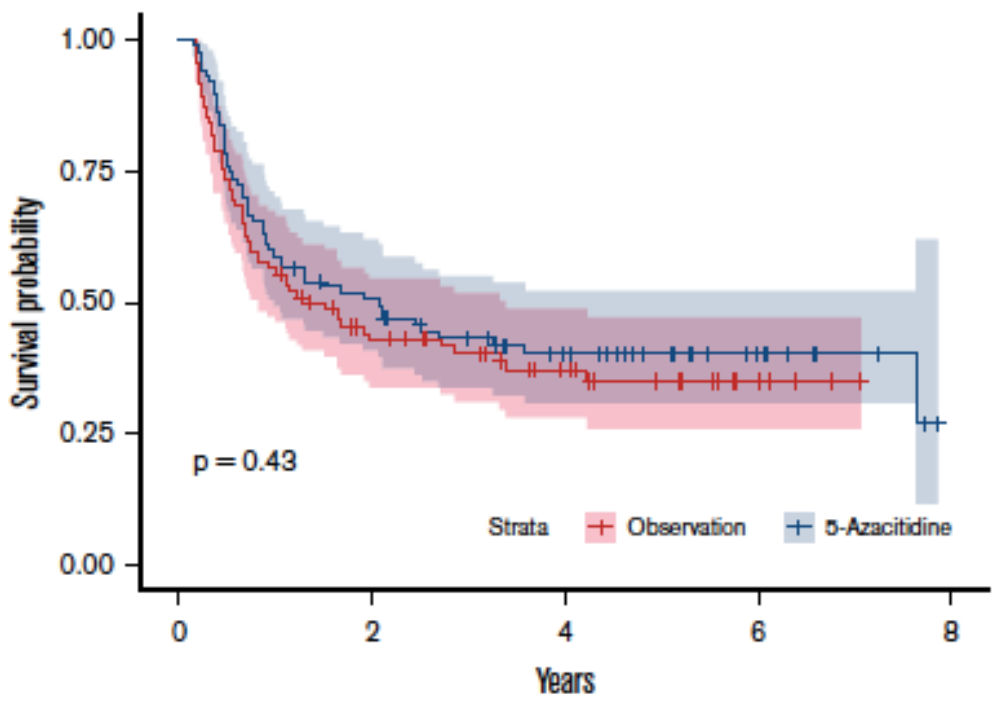


No. at risk:	0	10	20	30	40	50
Placebo	40	24	19	17	14	0
Sorafenib	43	35	31	25	18	0



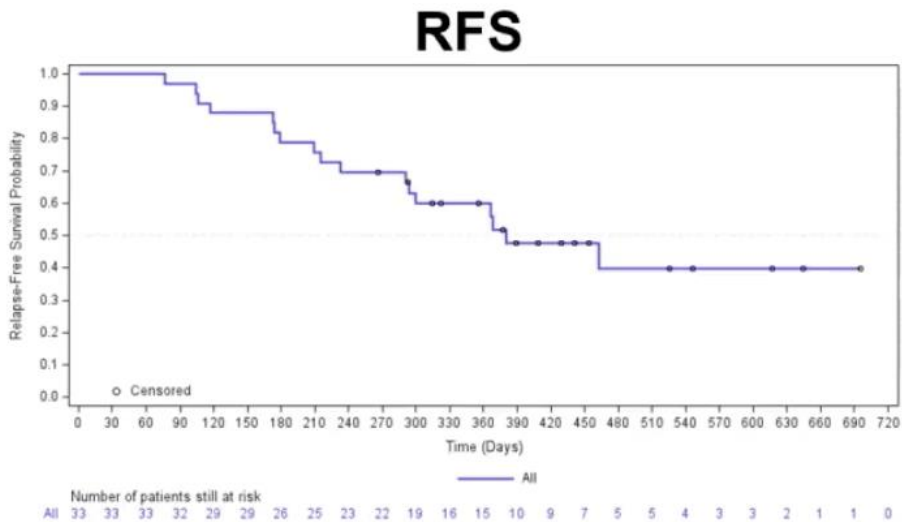
No. at risk:	0	20	40	60	80	100
Placebo	40	25	19	9	3	0
Sorafenib	43	38	28	12	7	0

Burchert et al. JCO 2020

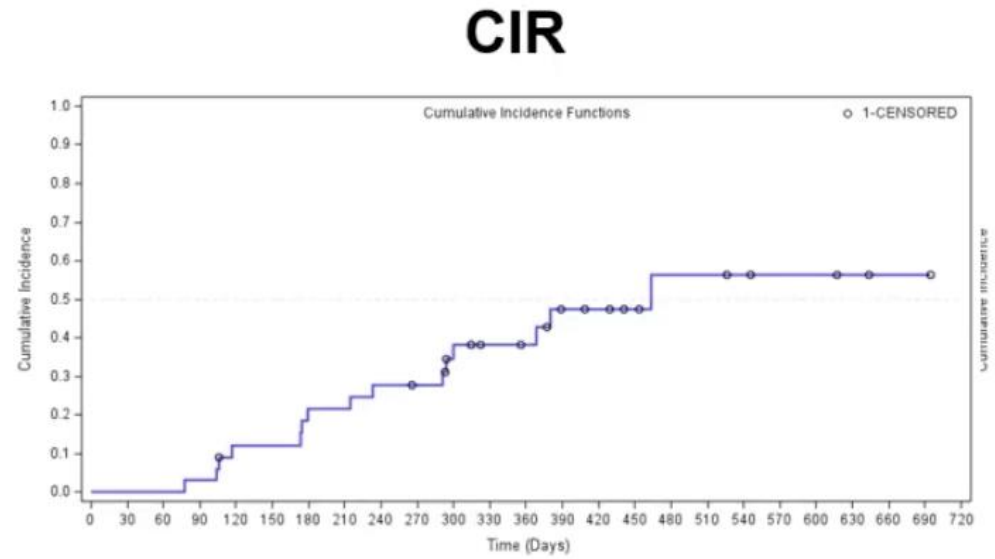


Oran et al. Blood Adv 2020





**Median RFS = 12.5 months (95% CI 9.6, NR)**  
**1-year RFS = 59.9% (95% CI 41.0, 74.4)**



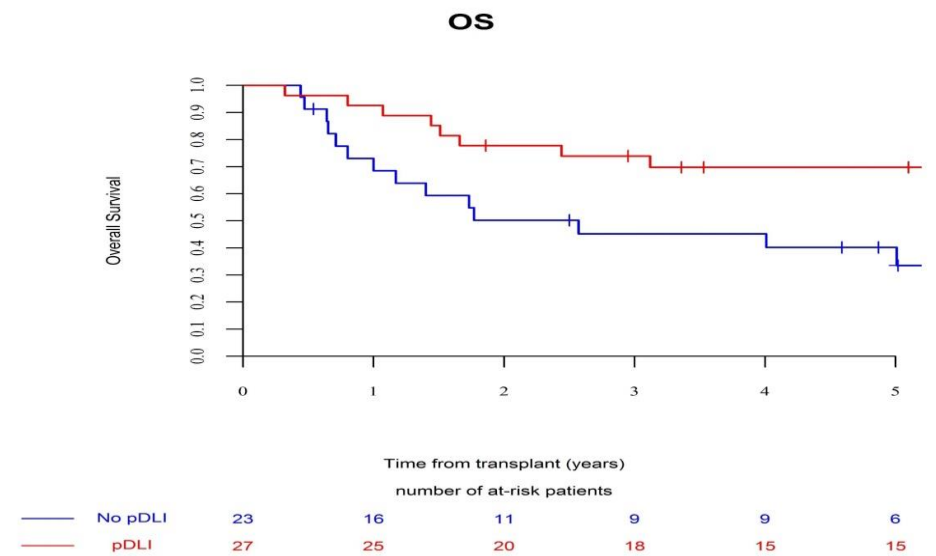
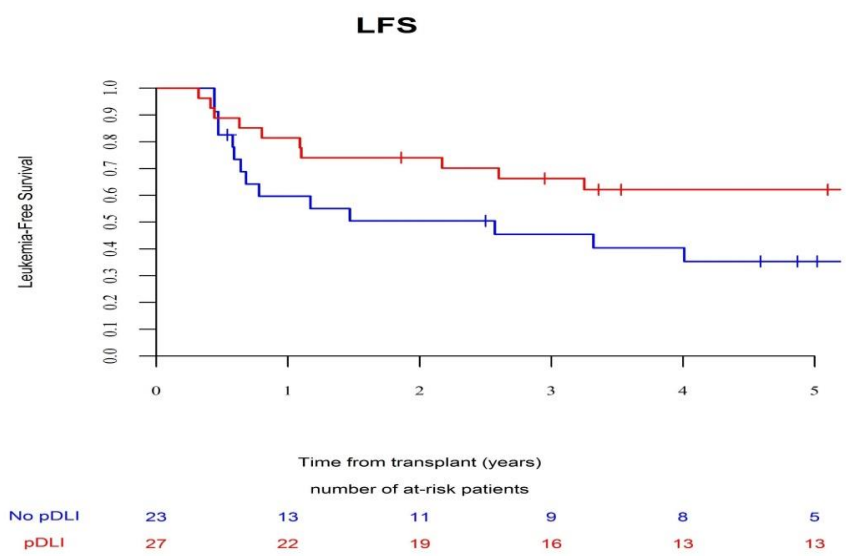
**Median CIR = 15.2 months (95% CI 9.6, NE)**  
**1 year CIR = 38.3% (95% CI 23.7, 57.6)**

Mishra et al, JCO 2022

# PROPHYLACTIC DLI FOR AML

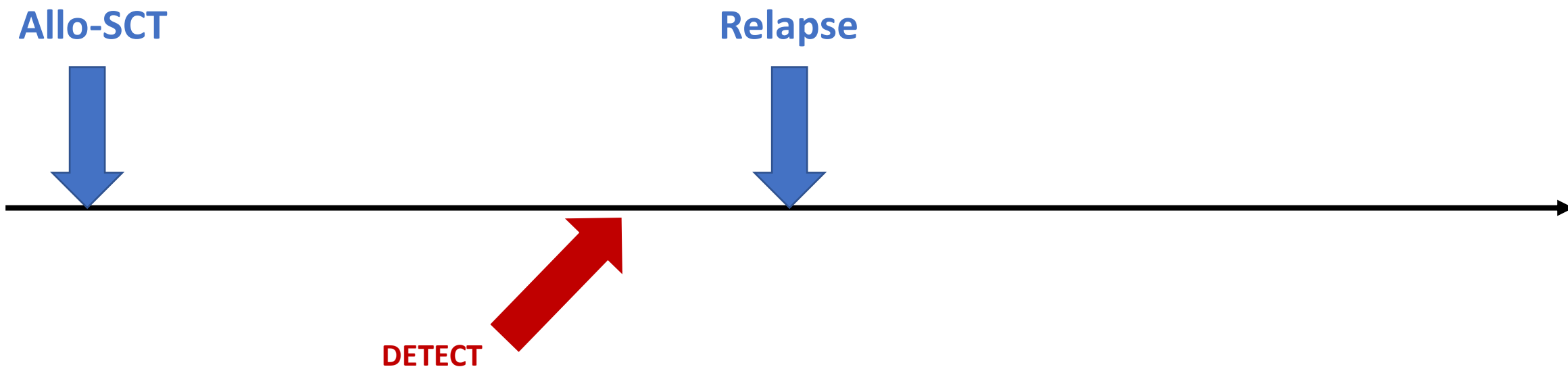
PREVENT

	CONTROLS	pDLI	P-value
LFS	35.3%[14.9-55.8]	62.1%[43.5-80.7]	<b>0.118</b>
OS	40.2%[19.3-61]	69.8%[52.2-87.3]	<b>0.036</b>

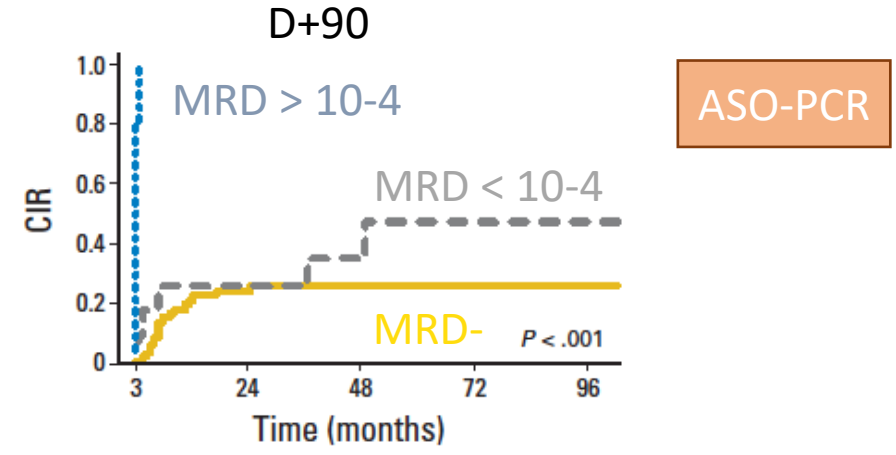
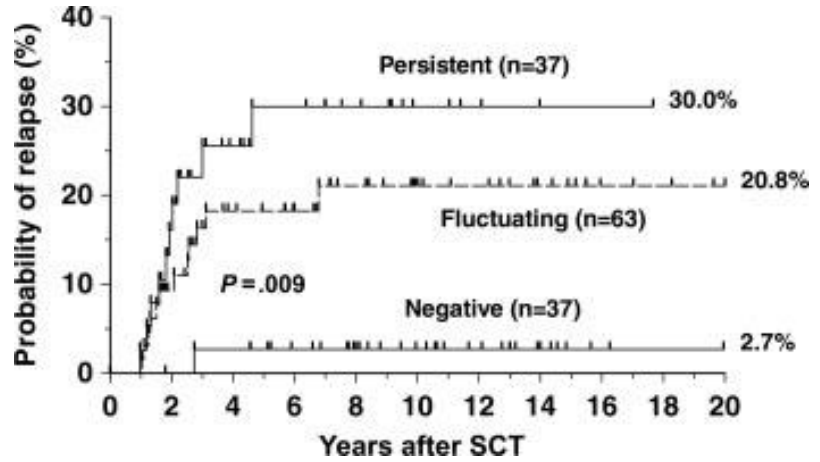


Schmid et al, BMT 2022

# TIMELINE OF RELAPSE



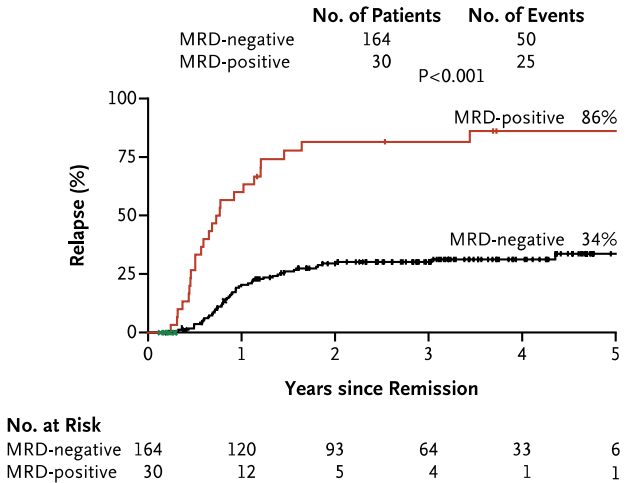
ALL



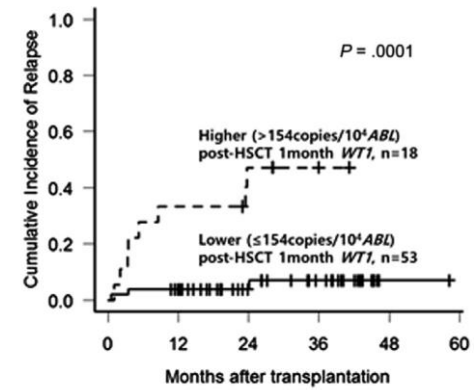
Kaeda et al. Blood 2006

	78	40	22	11	3
Neg	12	6	5	2	1
< 10 <sup>-4</sup>	5	0	0	0	0
≥ 10 <sup>-4</sup>					

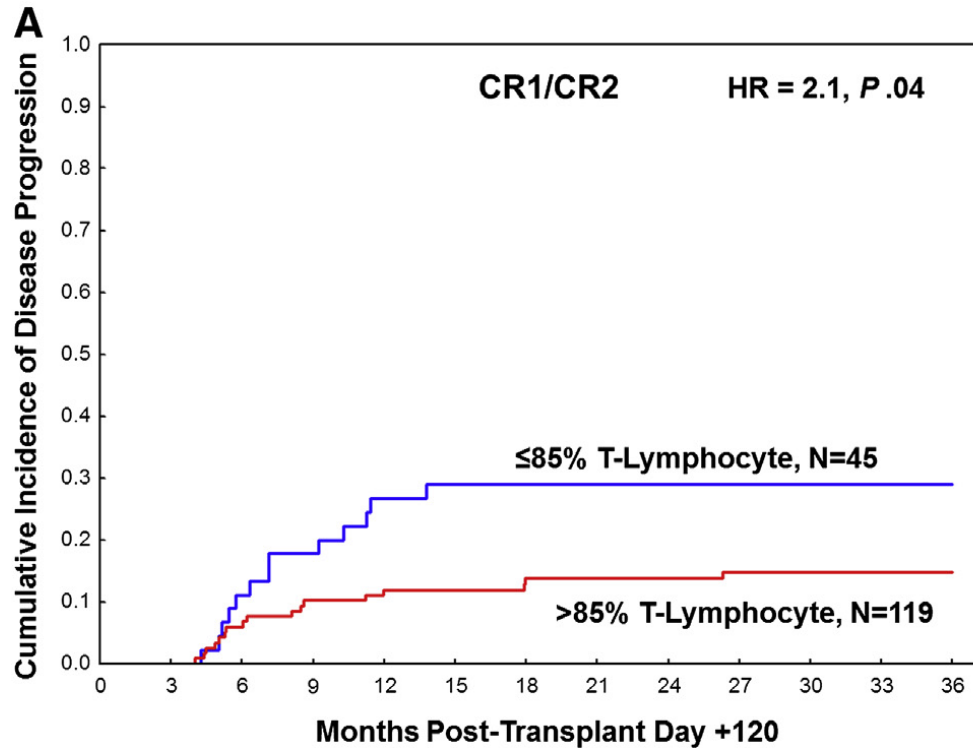
AML



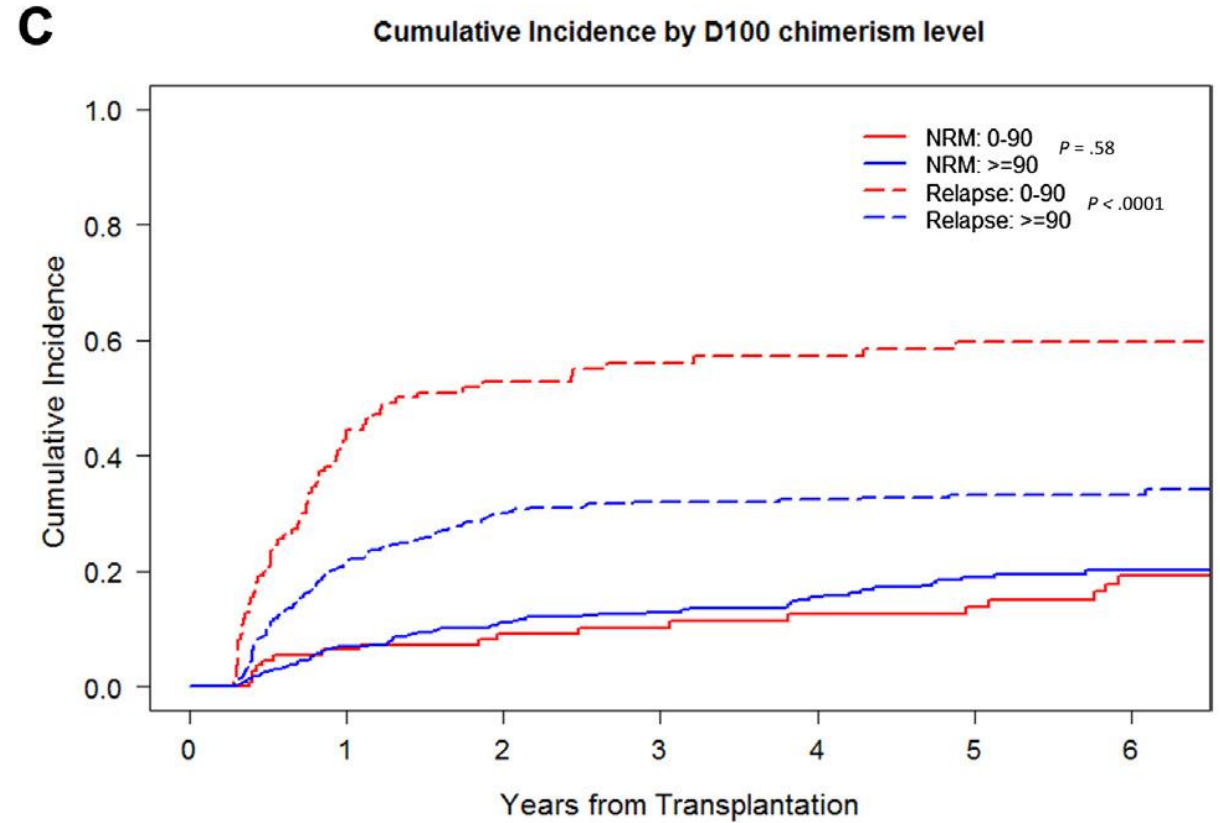
Bader et al. JCO 2015



Yoon et al. BBMT 2015



Lee et al BBMT 2015



Koreth et al BBMT 2014

**Table 5**  
Predicted 1-Year OS and DFS Probabilities for 9 Combinations Obtained from 3 Specific Combinations of Patient Prognostic Covariates and 3 Pairs of Percent Chimerism Values at Days 30 and 90

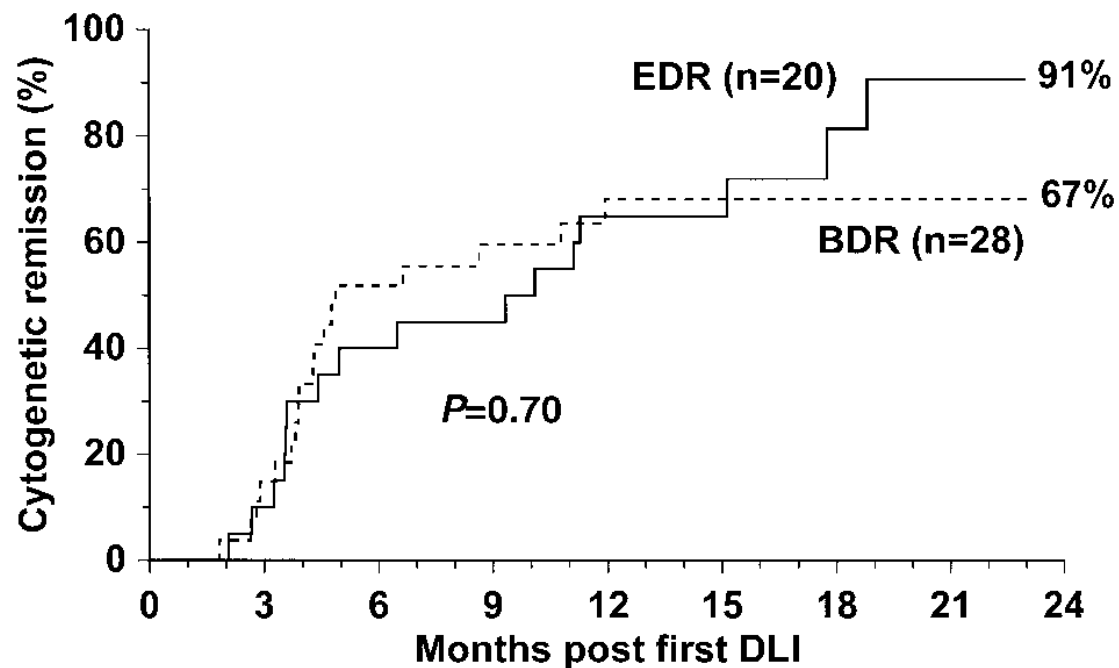
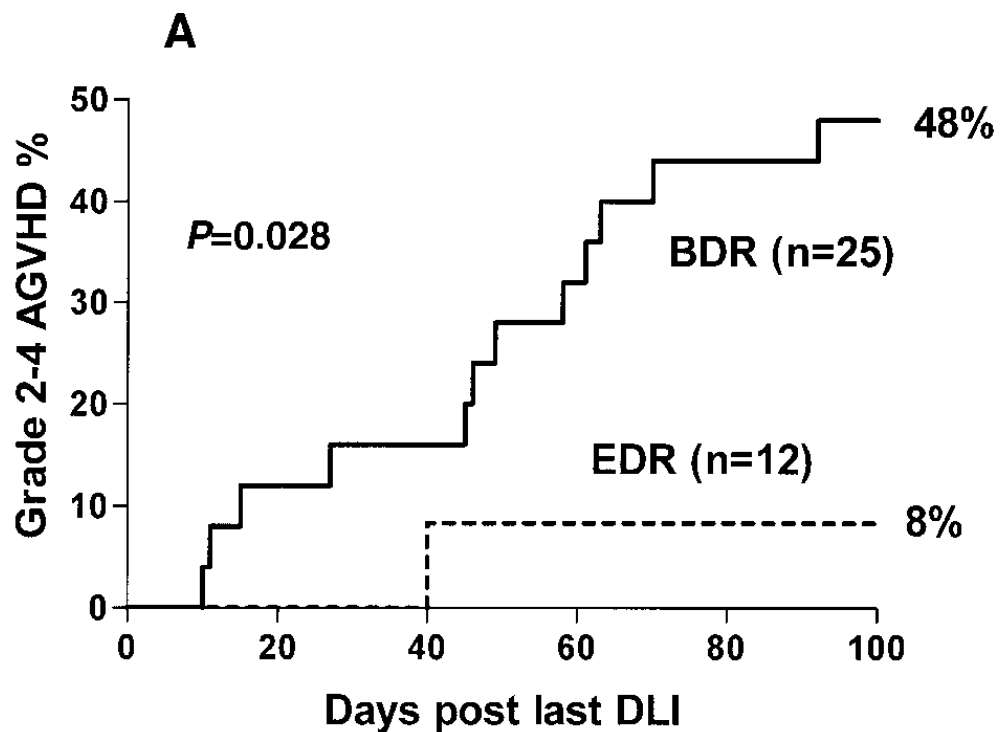
Patient Characteristics	% Chimerism at Days (30, 90)	Predicted Probabilities at 1 Year Post-SCT			
		OS		DFS	
		<i>P</i>	95% CI	<i>P</i>	95% CI
Complete remission	95, 95	.780	.689, .884	.737	.643, .845
Allotype = MRD	95, 100	.949	.918, 1.000	.638	.459, .887
Cytogenetics = good	95, 90	.718	.616, .836	.615	.478, .792
Active disease	95, 95	.402	.269, .601	.412	.287, .593
Allotype = MUD	95, 100	.826	.648, 1.000	.272	.083, .895
Cytogenetics = poor	95, 90	.296	.176, .498	.244	.113, .529
Active disease	95, 95	.842	.724, .978	.687	.505, .935
Allotype = MRD	95, 100	.918	.816, 1.000	.576	.326, 1.000
Cytogenetics = intermediate	95, 90	.581	.367, .918	.550	.322, .940

CI indicates confidence interval; MUD, matched unrelated donor; MRD, matched related donor.

Predicted values are based on the fitted joint models for percentage of T cell or myeloid cell chimerism and OS or DFS summarized in [Table 3](#).

Tang et al BBMT 2014

Low ( $\sim 10^6$ CD3+/kg)	High ( $\sim 10^7$ CD3+/kg)
<ul style="list-style-type: none"> <li>– MRD</li> <li>– Mixed Chimerism</li> <li>– Indolent disease</li> <li>– Unrelated</li> <li>– Early after SCT</li> <li>– History of GvHD</li> </ul>	<ul style="list-style-type: none"> <li>– Frank Relapse</li> <li>– Aggressive disease</li> <li>– Sibling</li> <li>– Late after SCT</li> <li>– No history of GvHD</li> </ul>

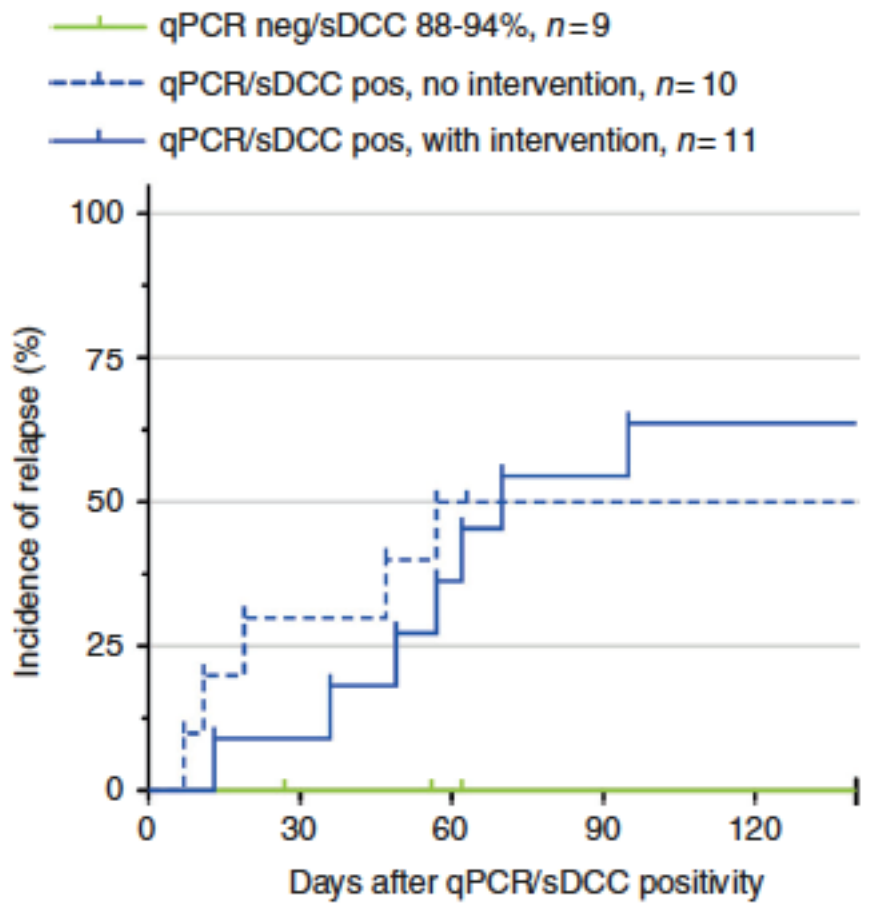


Dazzi et al. Blood 2000



# MRD MONITORING VERSUS CHIMERISM?

PREVENT



21 relapses within 2 years (N=94)

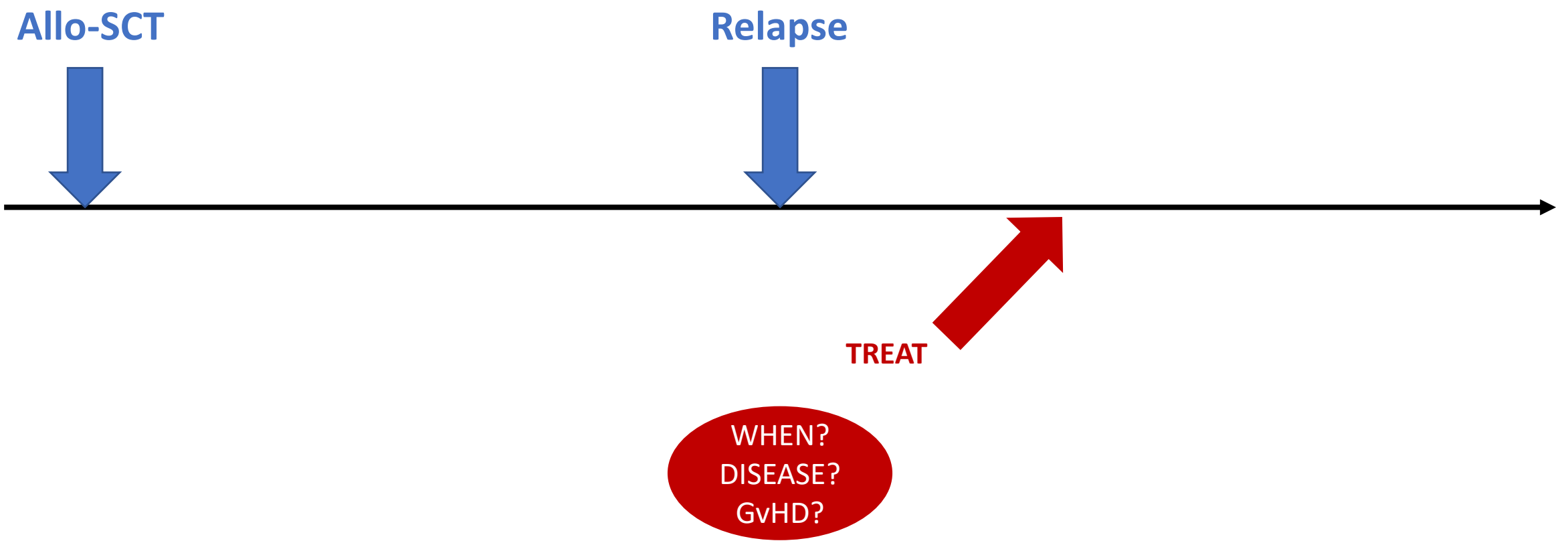
12 relapse detected by qPCR and/or sDCC

Median time to relapse 47 days

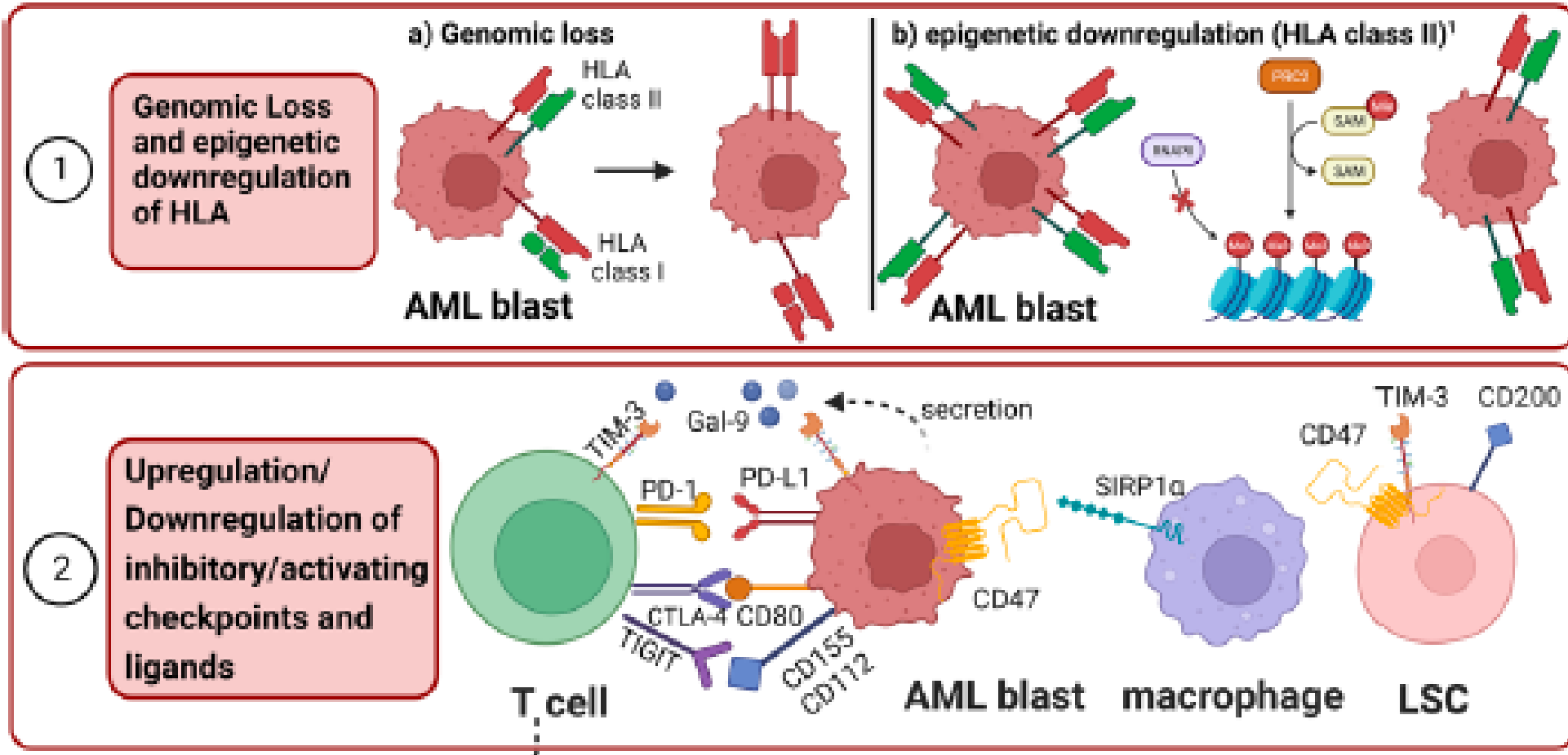
Sensitivity  
 75% for combined qPCR/sDCC  
 69% for qPCR  
 56% for sDCC

Wethmar et al, BMT 2020

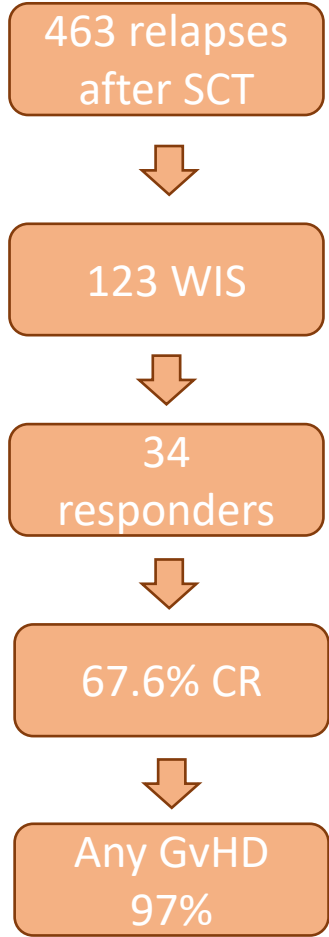
# TIMELINE OF RELAPSE



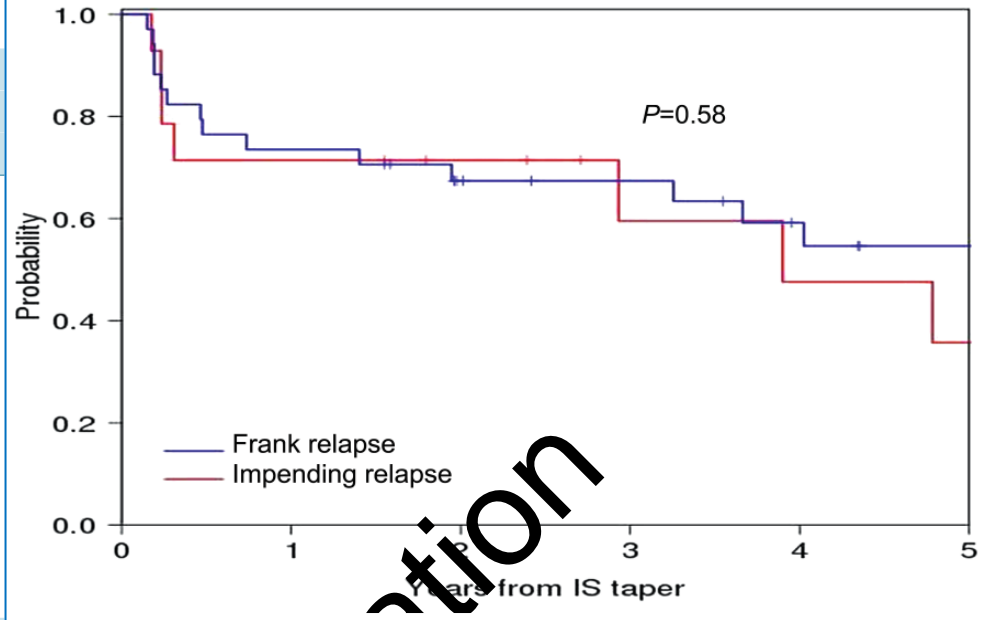
# MECHANISMS OF RELAPSE



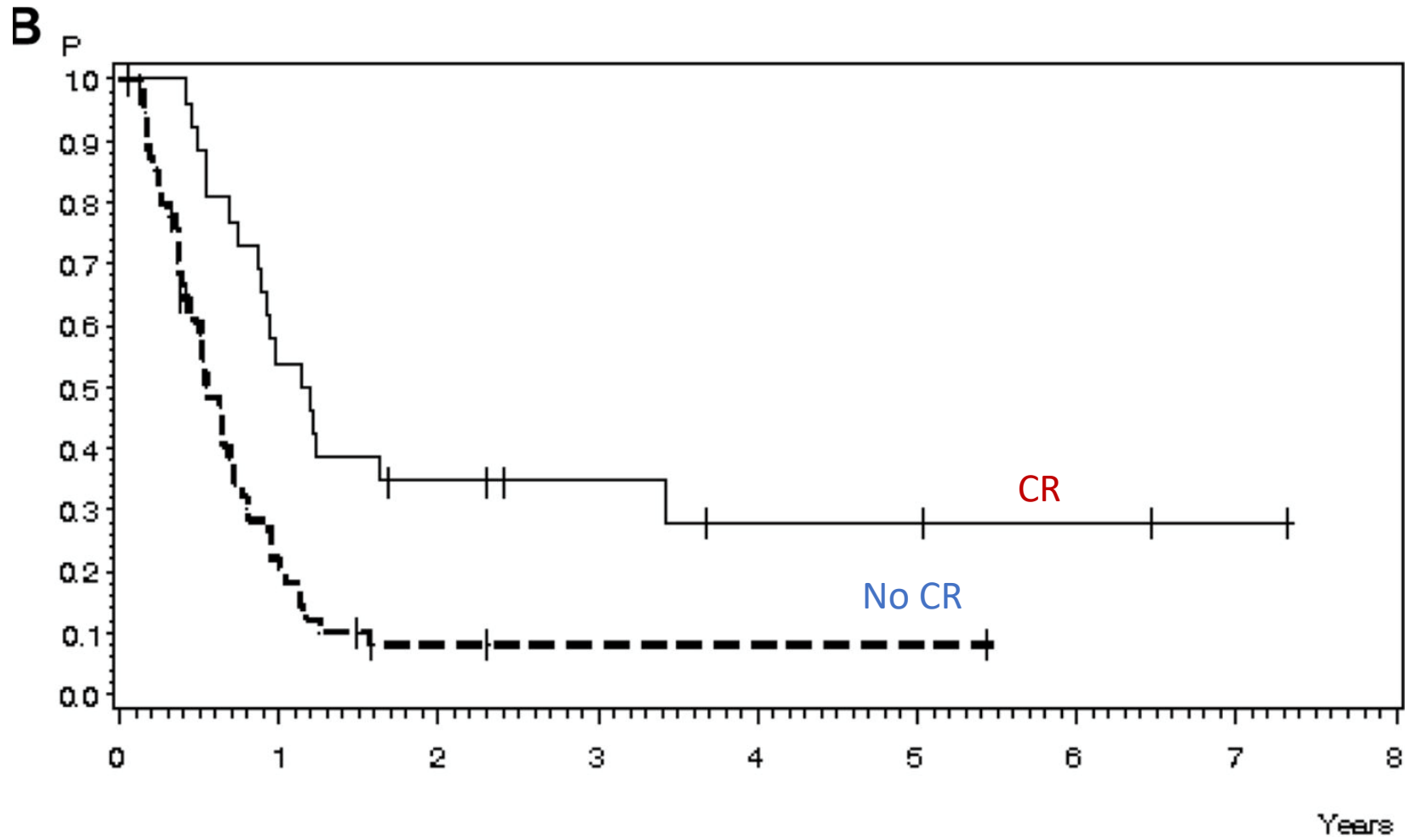
Sauerer et al. Mol Cancer 2023



Characteristic (n %)	Non-responders (n=89)	Responders (n=34)	P
Age at HCT, median (range)	58 (21-71)	58 (27-70)	0.28
Patients' gender			0.83
Male	59 (66.3)	24 (70.6)	
Female	30 (33.7)	10 (29.4)	
Diagnosis			<0.0001
Acute myeloid leukemia	61 (68.5)	9 (26.5)	
CLL/PLL/PLL	1 (1.1)	4 (11.8)	
Hodgkin disease	3 (3.4)	4 (11.8)	
MMPD	1 (1.1)	2 (5.9)	
Acute lymphocytic leukemia	2 (2.2)	0	
MDS	10 (11.2)	8 (23.5)	
MPD	6 (6.7)	0	
Mixed MDS/MPD	1 (1.1)	0	
Non-Hodgkin disease	4 (4.5)	7 (20.6)	
Myeloid diagnosis	78 (87.6)	17 (50.0)	<0.0001



Kekre et al. Haematologica 2015



Gokbuget et al., Blood 2012



# TIMELINE OF RELAPSE

**Allo-SCT**



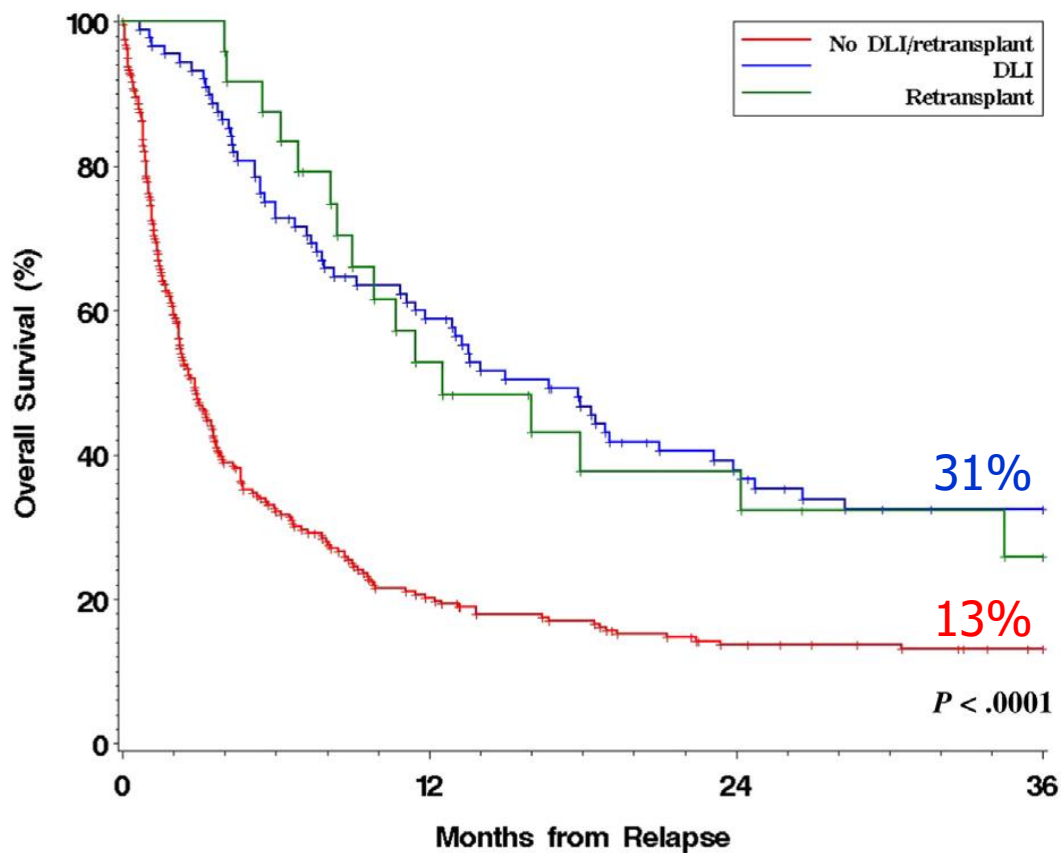
**Relapse**



**CONSOLIDATE**

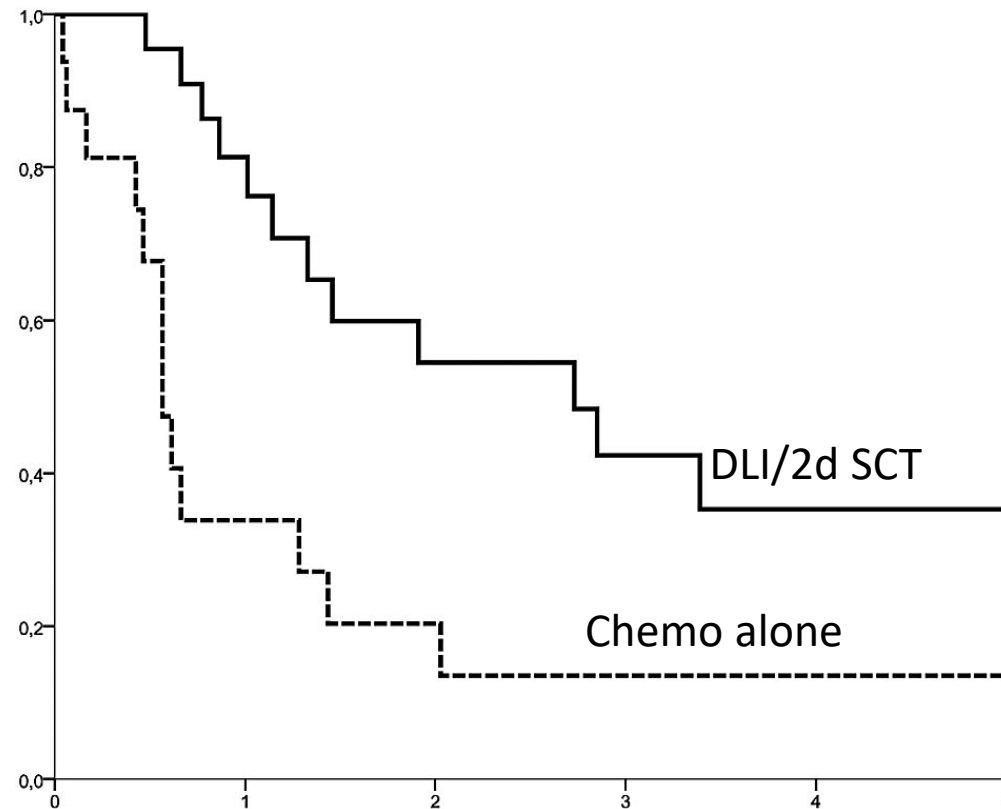


All diseases

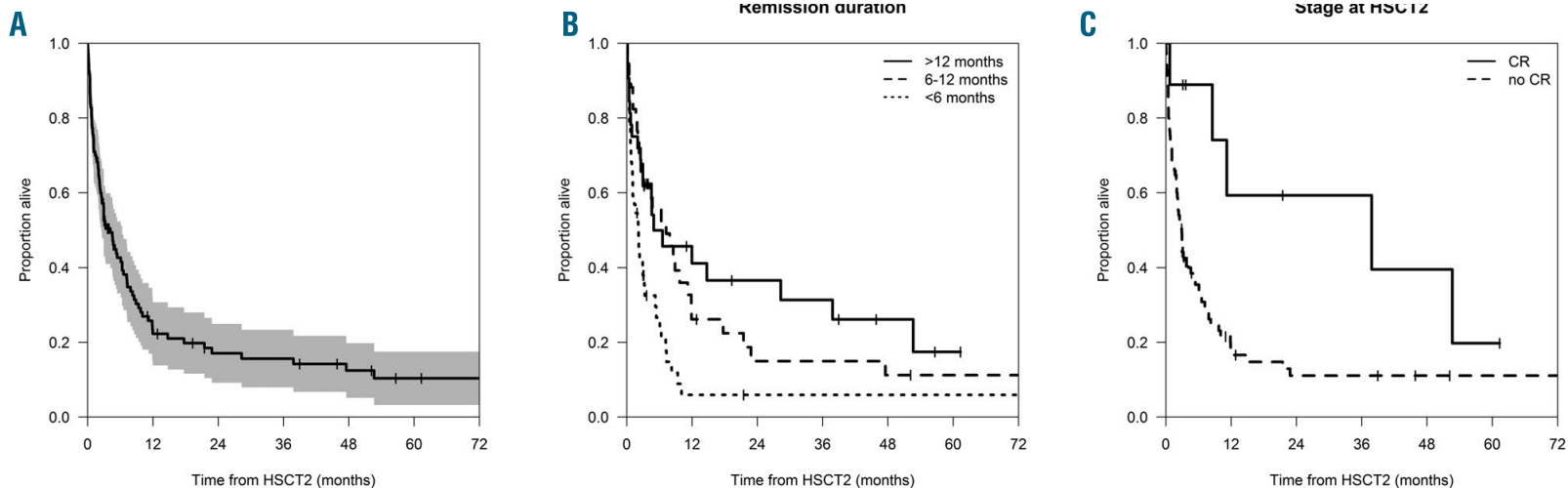


Thanarajasingam et al., BBMT 2013

AML

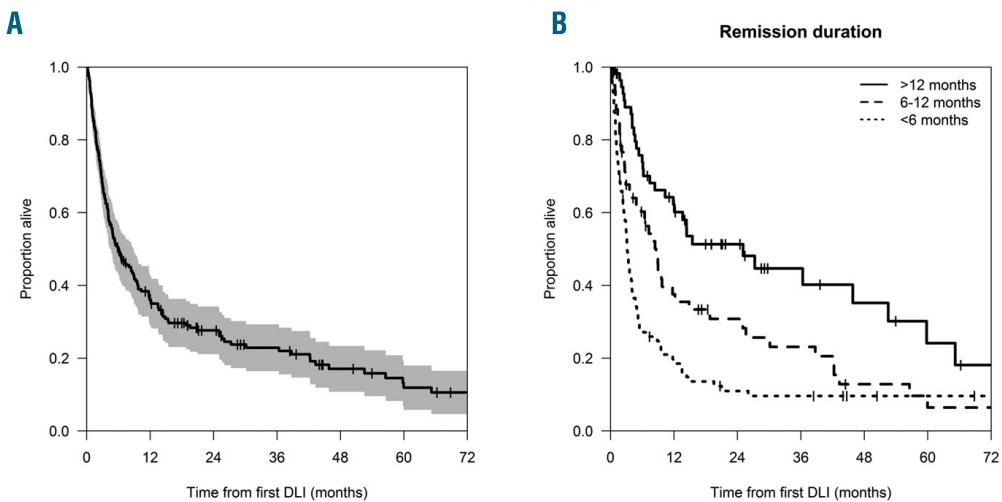


Schmid et al., Blood 2012



2d ALLO

LONGER REMISSION AFTER 1ST ALLO



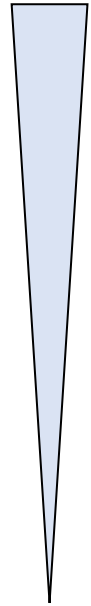
DLI

Schmid et al., Haematologica 2018



Single leukapheresis of the donor with peripheral leukocytes product containing lymphocytes, granulocytes, monocytes...

- Mixed chimerism/MRD+	80%
- CML	
- Chronic Phase	60-80%
- Accelerated/blastic	35%
- Low grade lymphoma	70-80%
- CLL	75%
- MM	45%
- Hodgkin lymphoma	40-45%
- AML/MDS	15-30%
- ALL	0-20%
- Aggressive lymphoma	10-20%

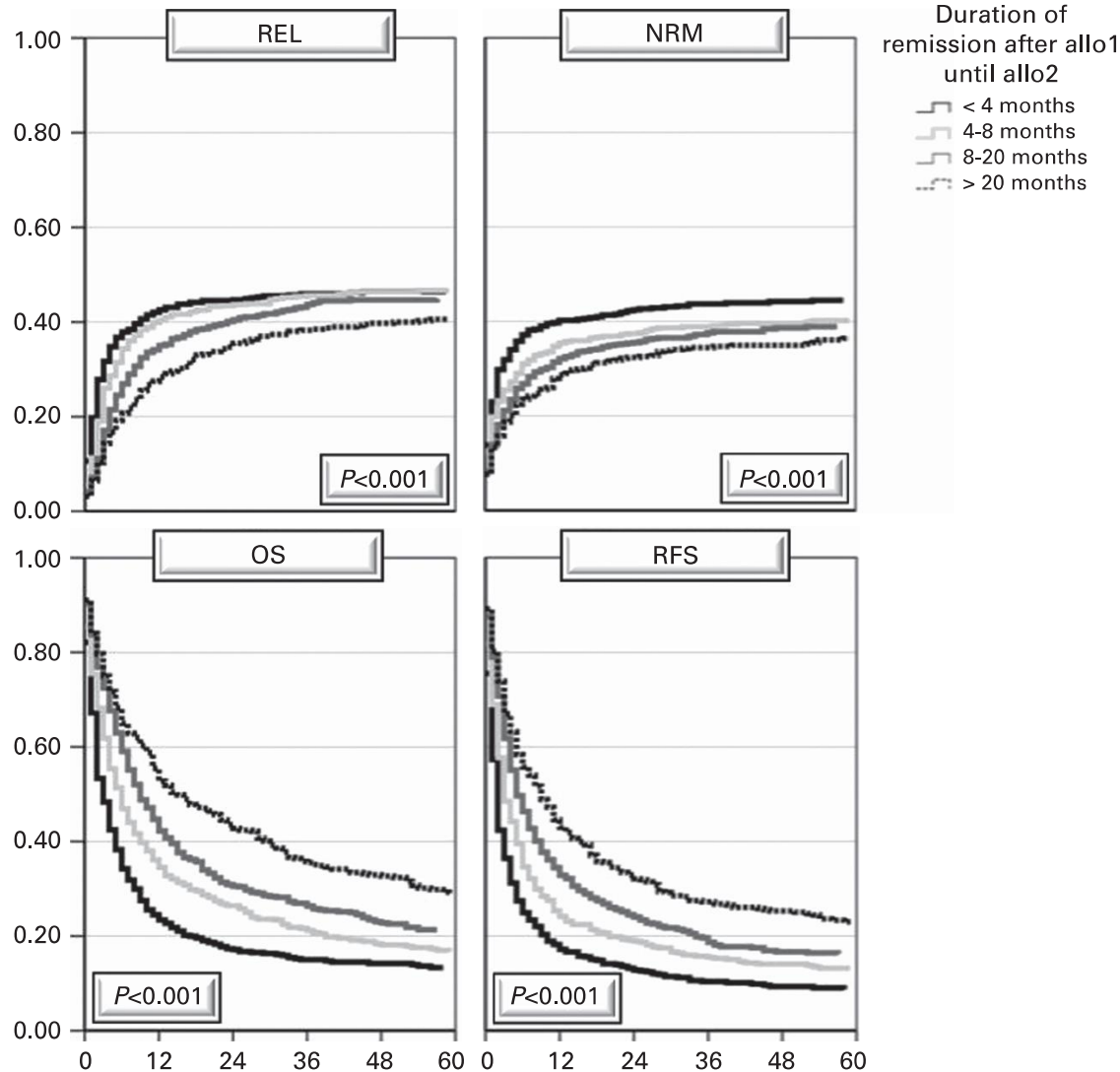


Decreased Efficacy

Complications :

- GvHD
- Aplasia
- TRM 5-44%

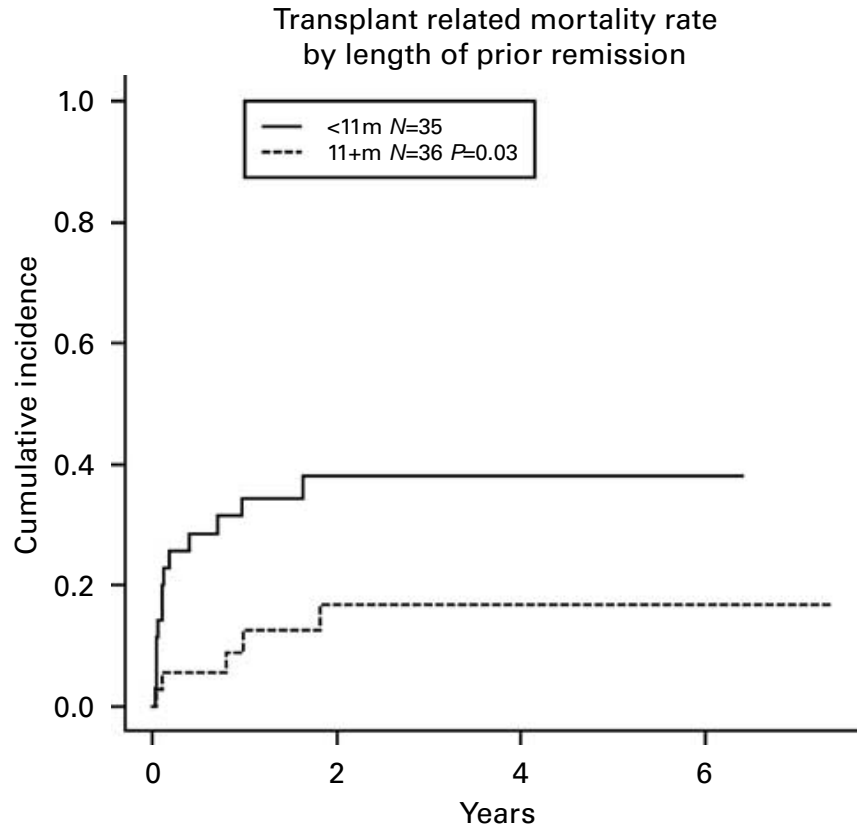
N=2632



- Risk factors for OS:**
- Age > 35 yo
  - Shorter duration of first remission
  - Interval between SCT < 1 y
  - Grade II-IV aGVHD
  - Chronic GvHD
  - Higher disease burden
  - EBMT score
  - Type of donor

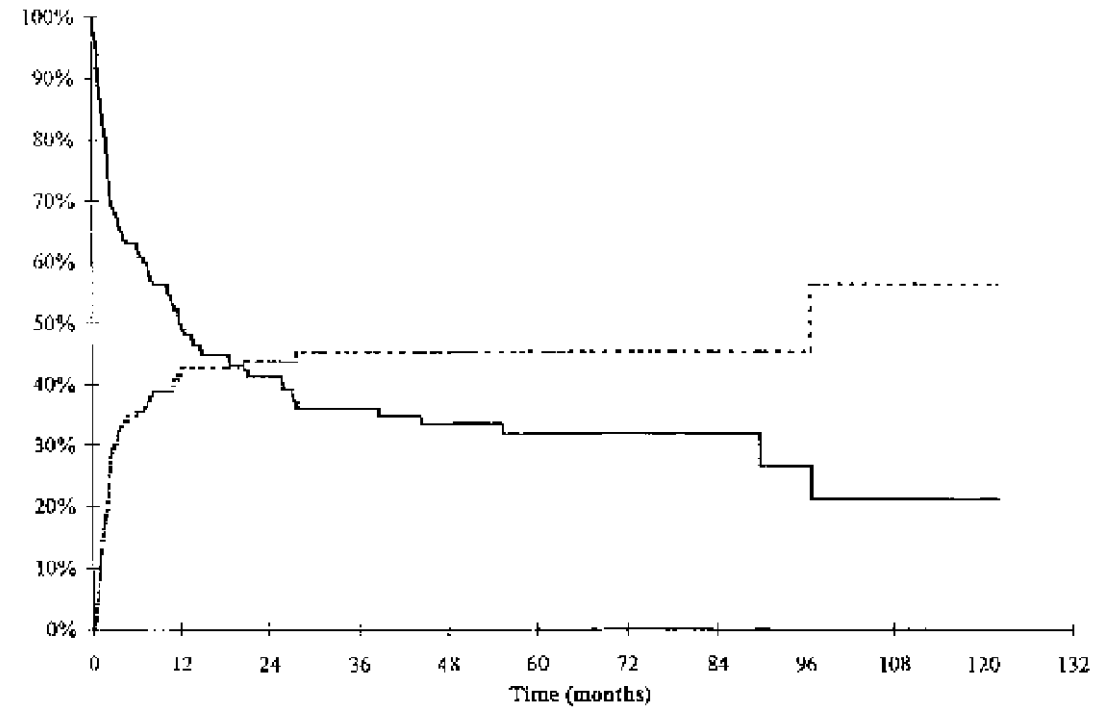
Ruutu et al, BMT 2015

## RIC



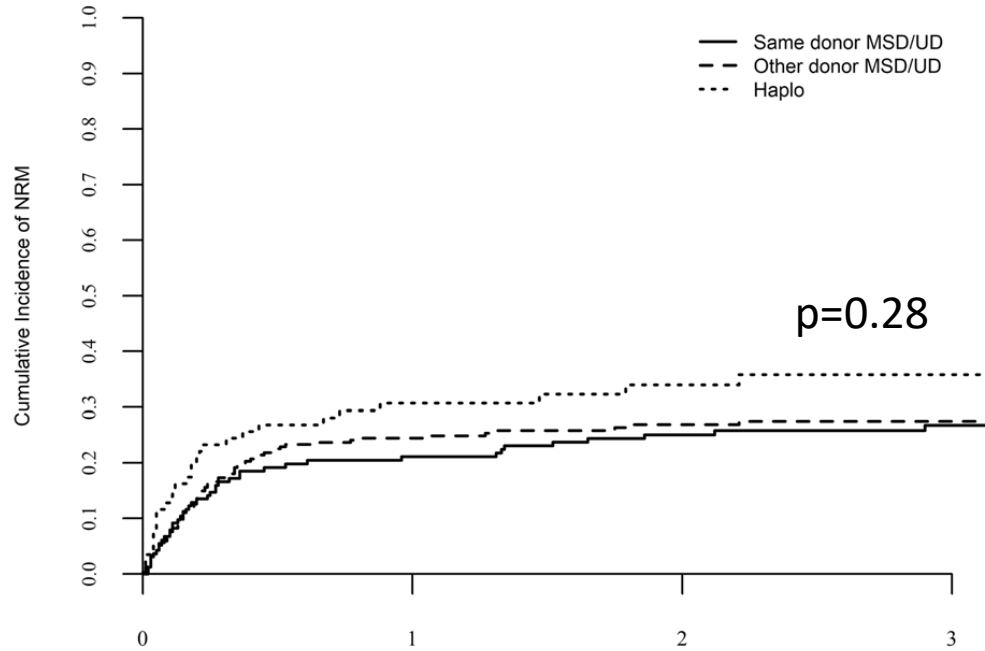
Shaw, BMT 2008

## MAC



Michallet, BJH 2000

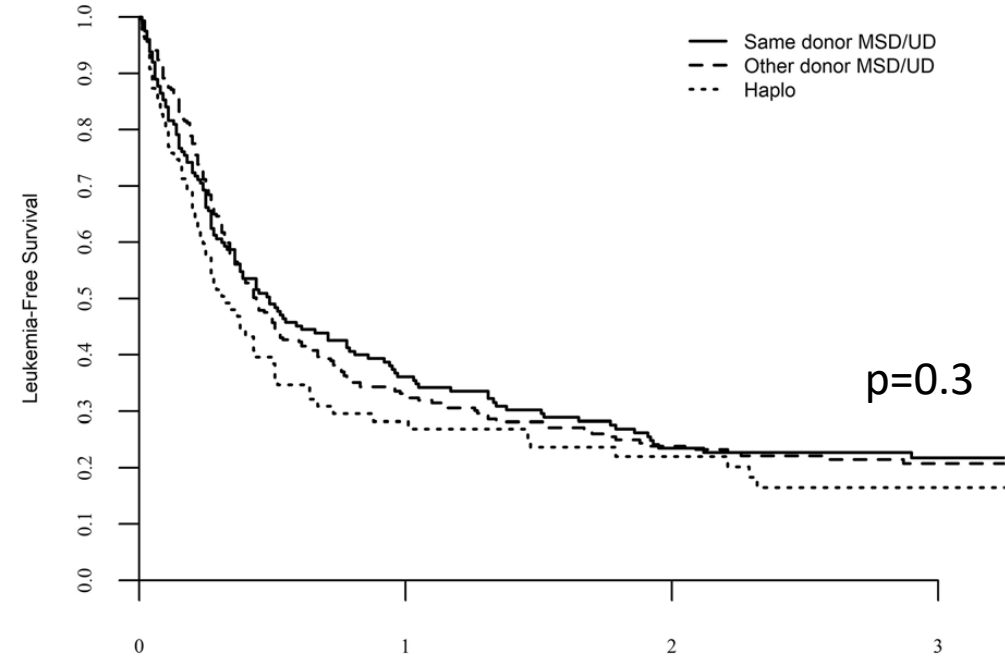
**NRM**



Time from transplant (years)  
number of at-risk patients

—	156	53	32	26
- -	312	85	44	27
...	88	21	13	7

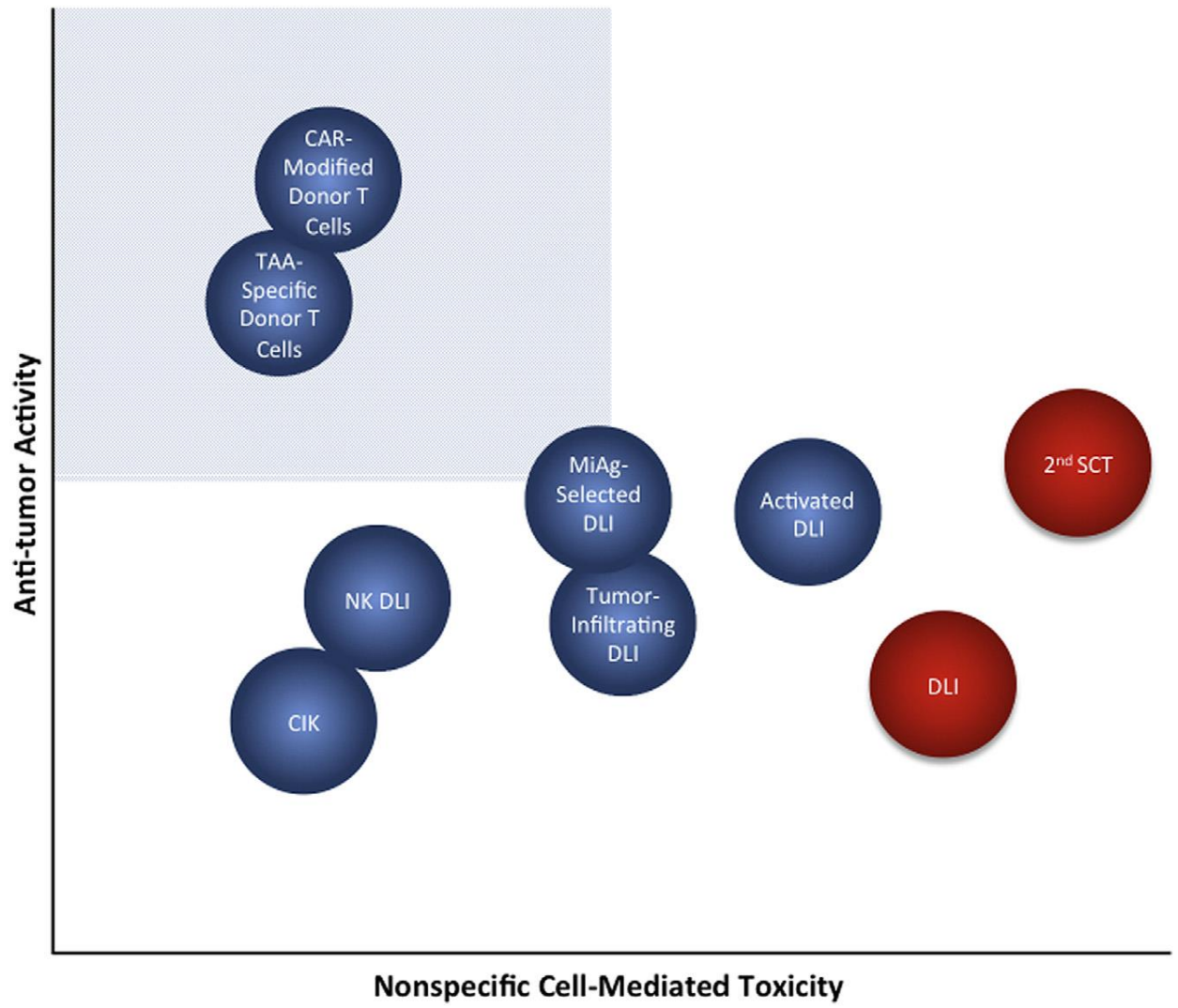
**LFS**



Time from transplant (years)  
number of at-risk patients

—	156	53	32	26
- -	312	85	44	27
...	88	21	13	7

Shimoni et al. BCJ 2019



# CONCLUSIONS

WHEN?  
DISEASE?  
GvHD?

Allo-SCT

Relapse

