

MYELOFIBROSIS

Timing and outcome of allogeneic transplants

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Allogeneic transplantation and MF

indications for transplant

the donor

the conditioning

REVIEW

Indication and management of allogeneic stem cell transplantation in primary myelofibrosis: a consensus process by an EBMT/ELN international working group

NM Kröger¹, JH Deeg², E Olavarria³, D Niederwieser⁴, A Bacigalupo⁵, T Barbui⁶, A Rambaldi⁷, R Mesa⁸, A Tefferi⁹, M Griesshammer¹⁰, V Gupta¹¹, C Harrison¹², H Alchalby¹, AM Vannucchi¹³, F Cervantes¹⁴, M Robin¹⁵, M Ditschkowski¹⁶, V Fauble¹⁷, D McLornan^{12,18}, K Ballen¹⁹, UR Popat²⁰, F Passamonti²¹, D Rondelli²² and G Barosi²³

DIPSS PLUS

Int1

78

Int2 high

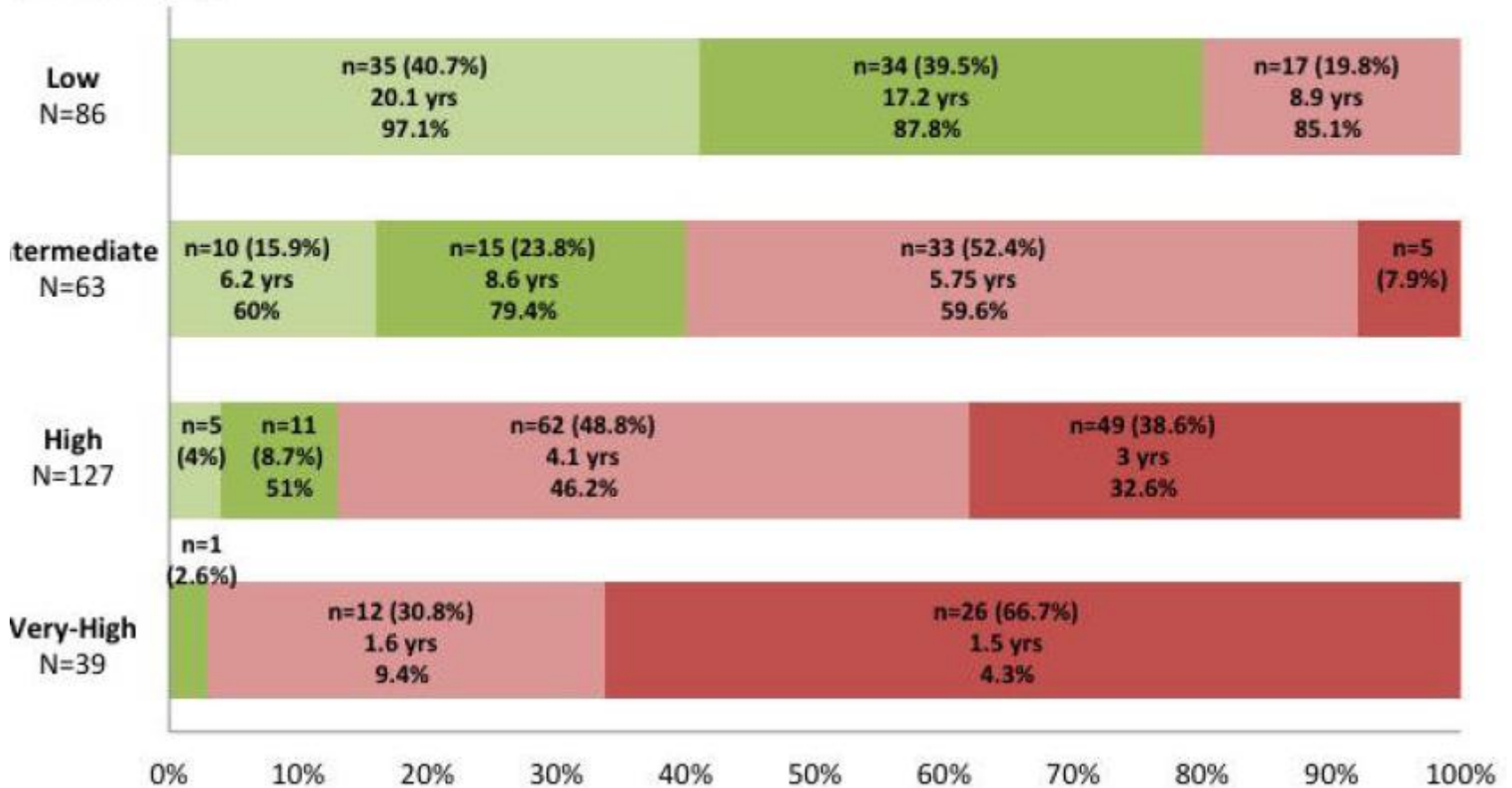
36 16

Median OS mm

MIPSS760: Guglielmelli et al, JCO 2018



MIPSS70-plus

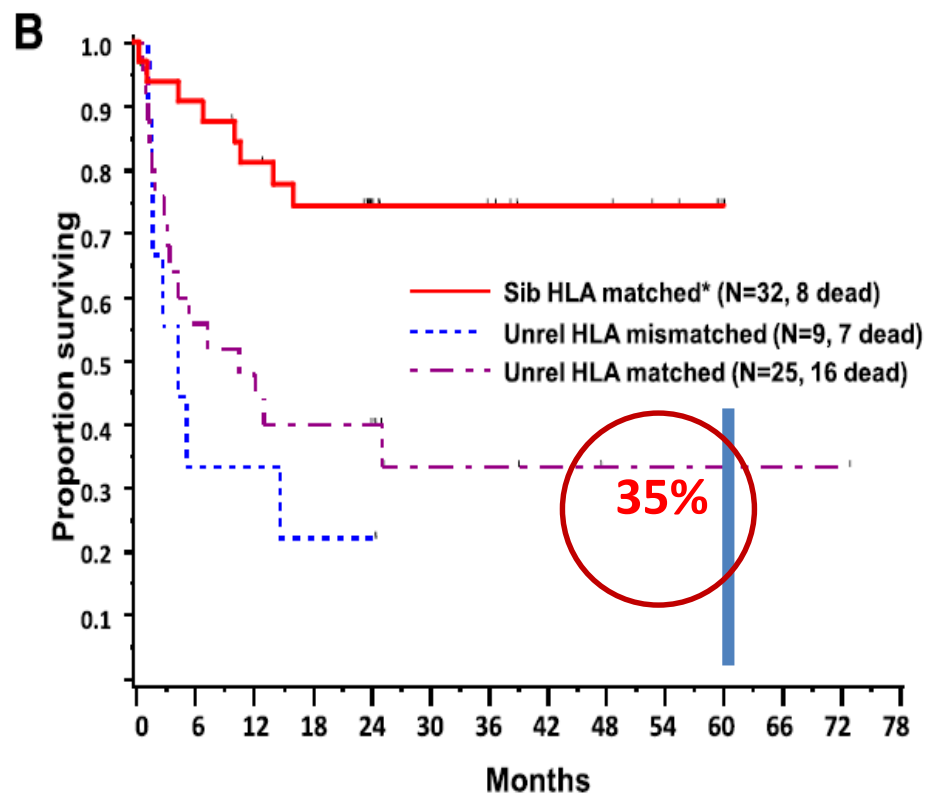




MPD-RC 101 prospective study of reduced-intensity allogeneic hematopoietic stem cell transplantation in patients with myelofibrosis

Damiano Rondelli, Judith D. Goldberg, Luis Isola, Leah S. Price, Tsiporah B. Shore, Michael Boyer, Andrea Bacigalupo, Alessandro Rambaldi, Marco Scarano, Rebecca B. Klisovic, Vikas Gupta, Bjorn Andreasson, John Mascarenhas, Meir Wetzler, Alessandro M. Vannucchi, Josef T. Prchal, Vesna Najfeld, Attilio Orazi, Rona S. Weinberg, Crystal Miller, Giovanni Barosi, Lewis R. Silverman, Giuseppe Prosperini, Roberto Marchioli and Ronald Hoffman

	SIBS	US
Year	2007-11	2007-11
Pts	32	34
Condit	FLU MEL	FLU MEL
Engr	97%	76%
Sec GF	6%	12%
TRM	22%	59%



MF 1

alternative donors (UD) much worse than SIBS (? GvHD , infect, toxicity)

5 year OS of alt Don TX=

30-35% (1989- 2017)

MF 2

conditioning regimens:

1 alkylating agent + FLU

TBI 200 + FLU

? *Can 2 alkylating improve the outcome*



Biology of Blood and Marrow Transplantation

journal homepage: www.bbmt.org



Improved Outcome of Alternative Donor Transplantations in Patients with Myelofibrosis: From Unrelated to Haploidentical Family Donors



Stefania Bregante¹, Alida Dominietto¹, Anna Ghiso¹, Anna Maria Raiola¹, Francesca Gualandi¹, Riccardo Varaldo¹, Carmen Di Grazia¹, Teresa Lamparelli¹, Silvia Luchetti¹, Simona Geroldi¹, Lucia Casarino¹, Sarah Pozzi¹, Elisabetta Tedone¹, Maria Teresa Van Lint¹, Federica Galaverna¹, Giovanni Barosi², Andrea Bacigalupo^{3,*}

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Alternative donors
Conditioning regimen
GvHD prophylaxis

more HAPLO mm family
more TBF
PT-CY

Year 2000-2010

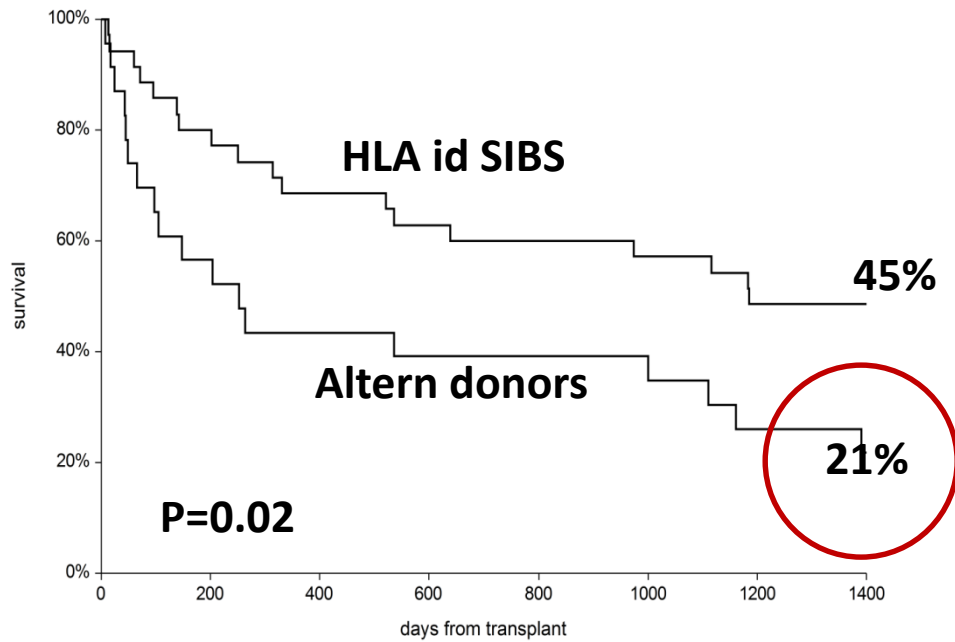


Fig. 3a

Year 2011-2014

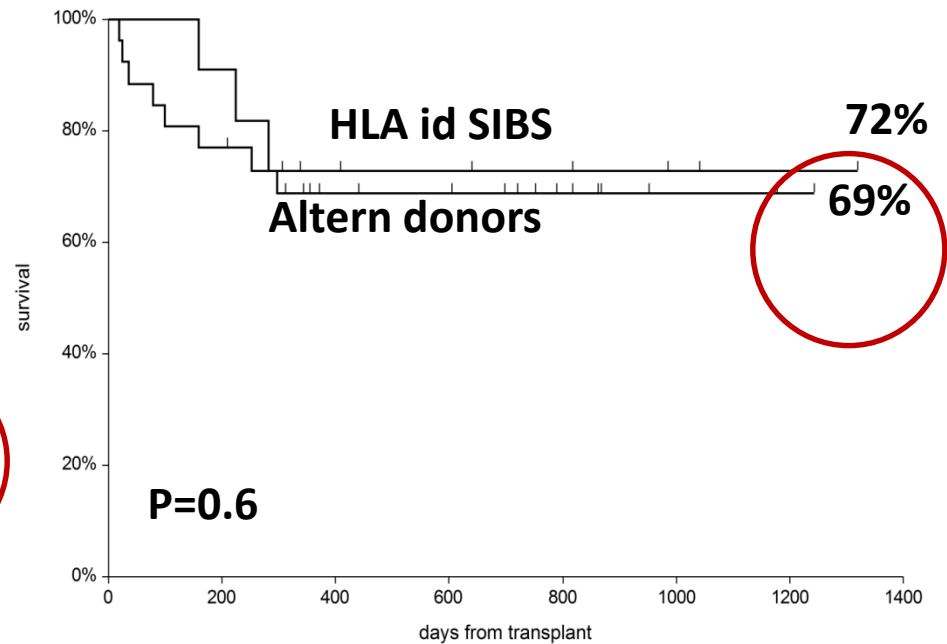


Fig. 3b

MF 3

**# perhaps the combination of 2
alkylating agent + FLU**

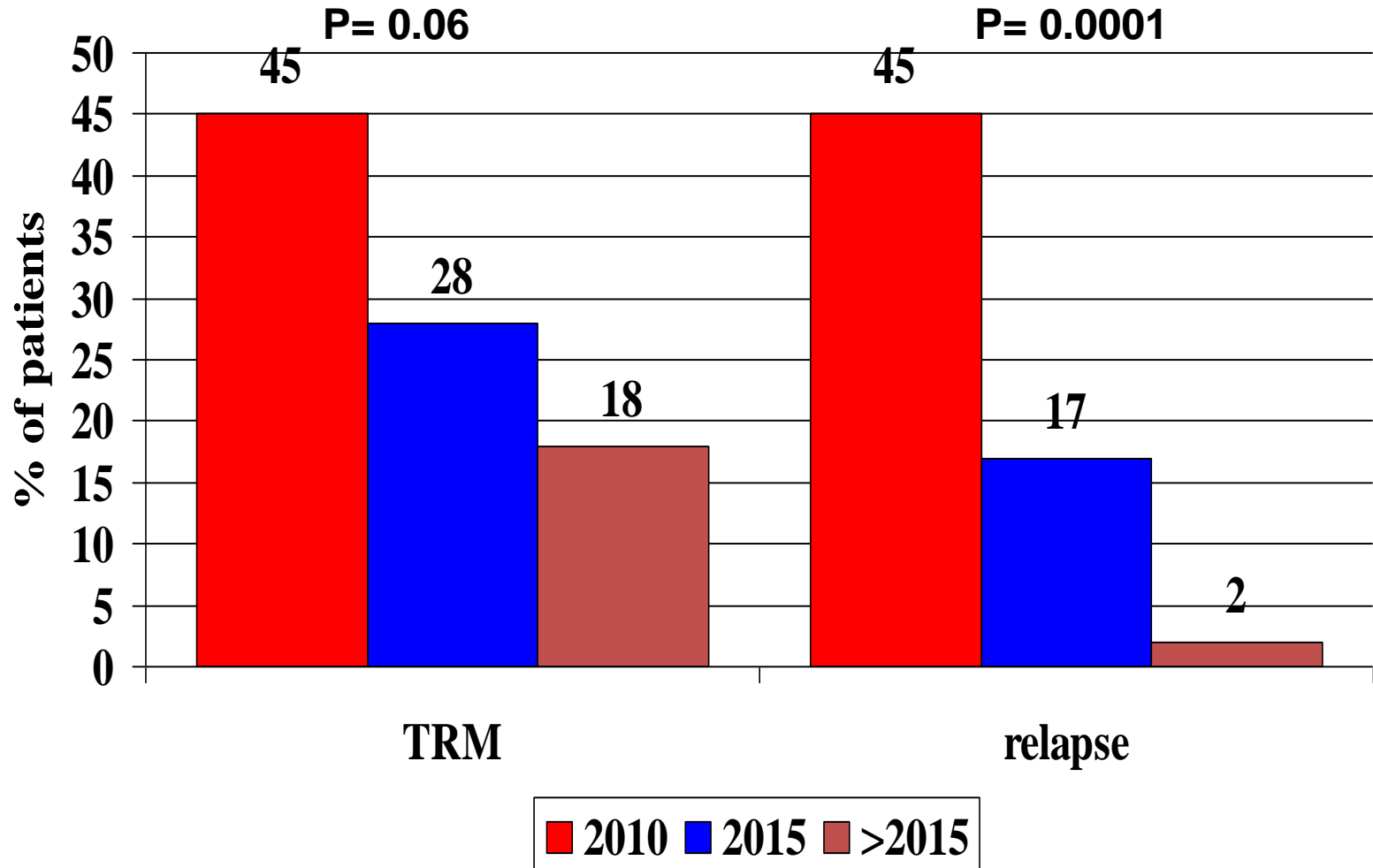
Is better than 1 alkylating agent?

reduced difference SIB /ALT

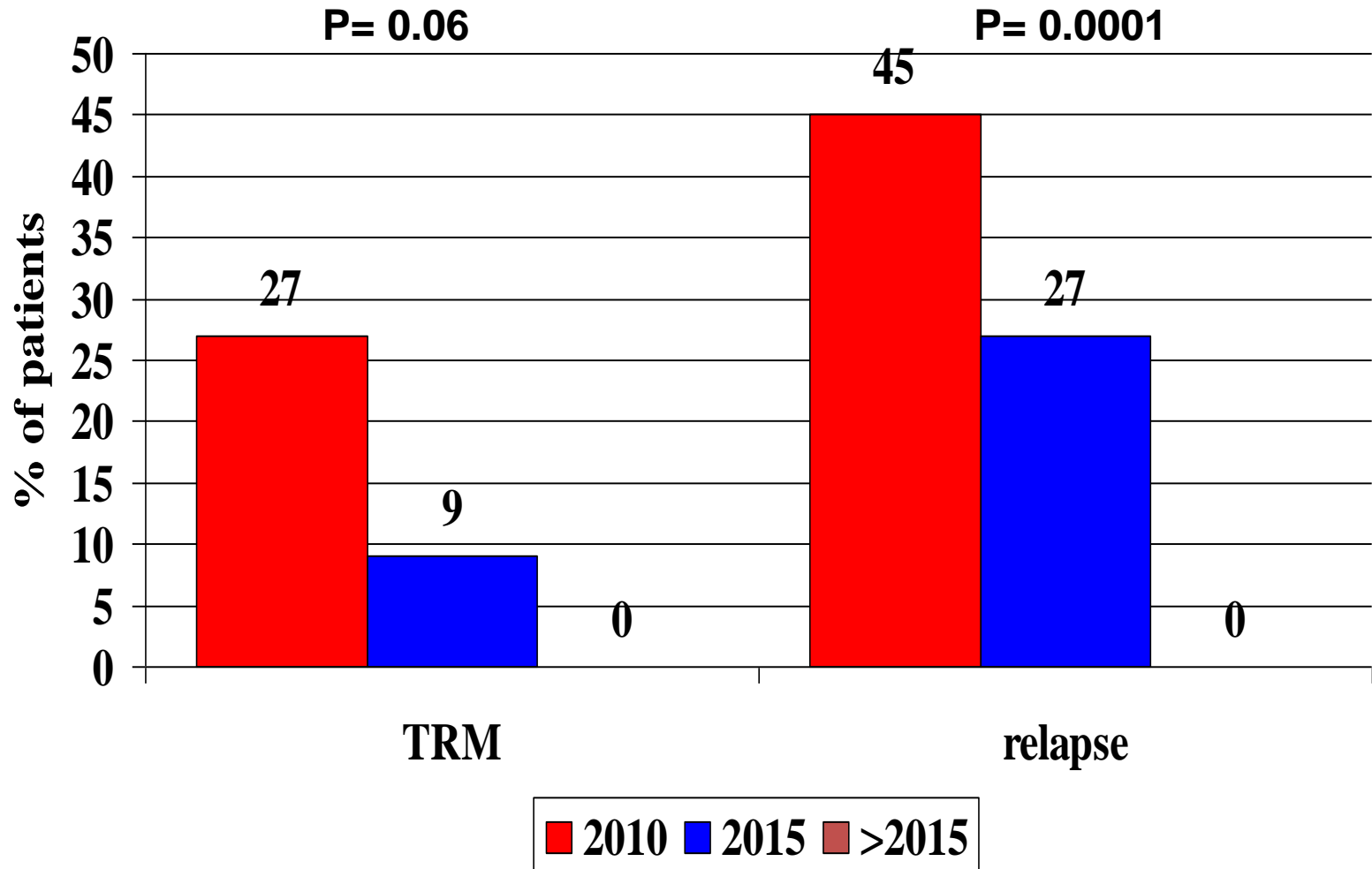
Clinical data of 158 allo Tx for Myelofibrosis

	<2010	2011-2015	>2015
N=	61	46	44
Median age	52	57	58
Age >60	16%	34%	41%
DIPSS int2-high	40%	85%	93%
Int Dx Tx (days)	909	770	550
Conditioning TBF	2%	73%	100%
Donor SIBS=	62%	24%	14%
HAPLO	78	61%	64%
UD	30%	15%	22%
Median FU	1140	987	370

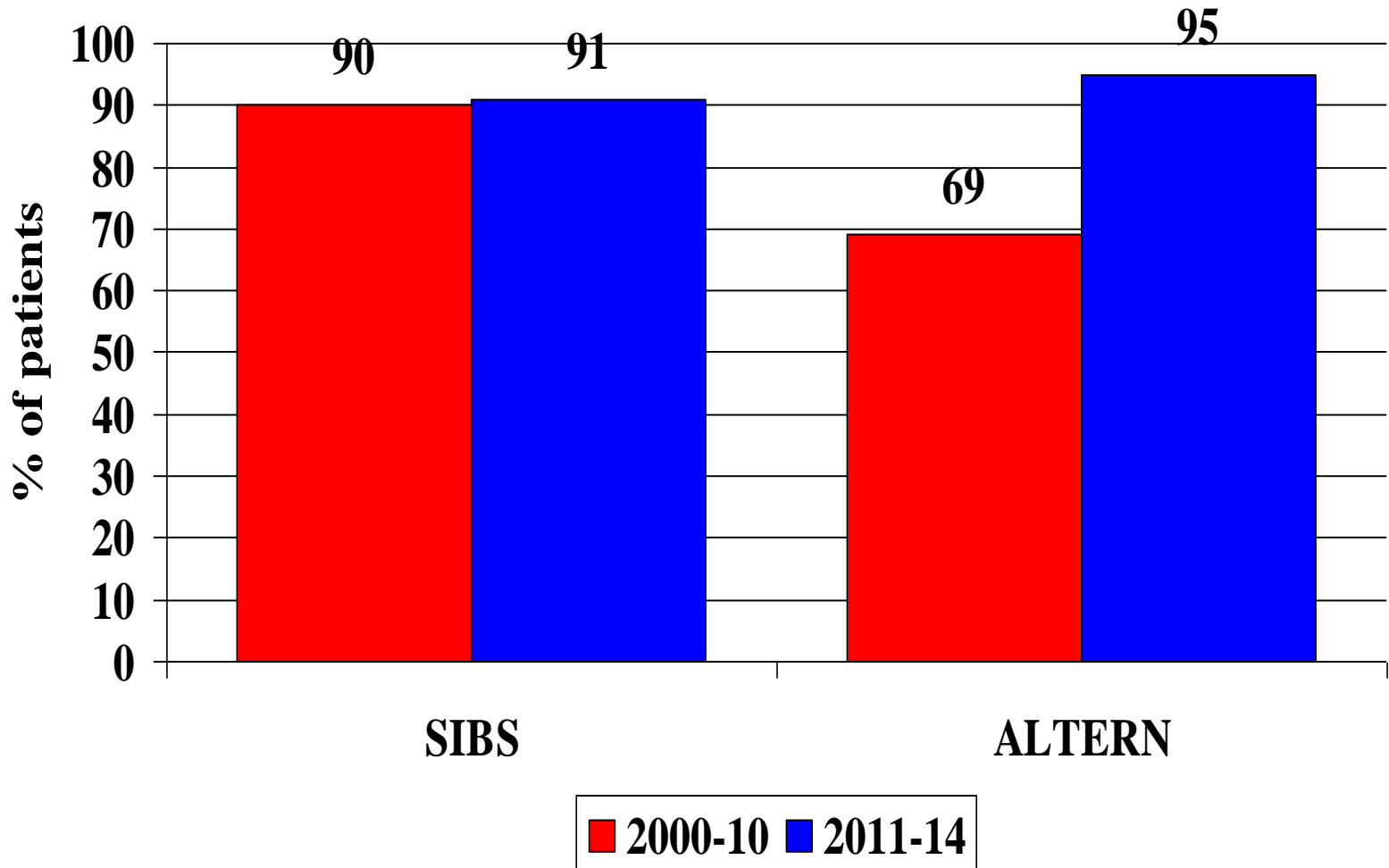
Alt don Tx for MYELOFIBROSIS (genova-gemelli)
n=97



HLA = SIB Tx for MYELOFIBROSIS (genova-gemelli)
n=61

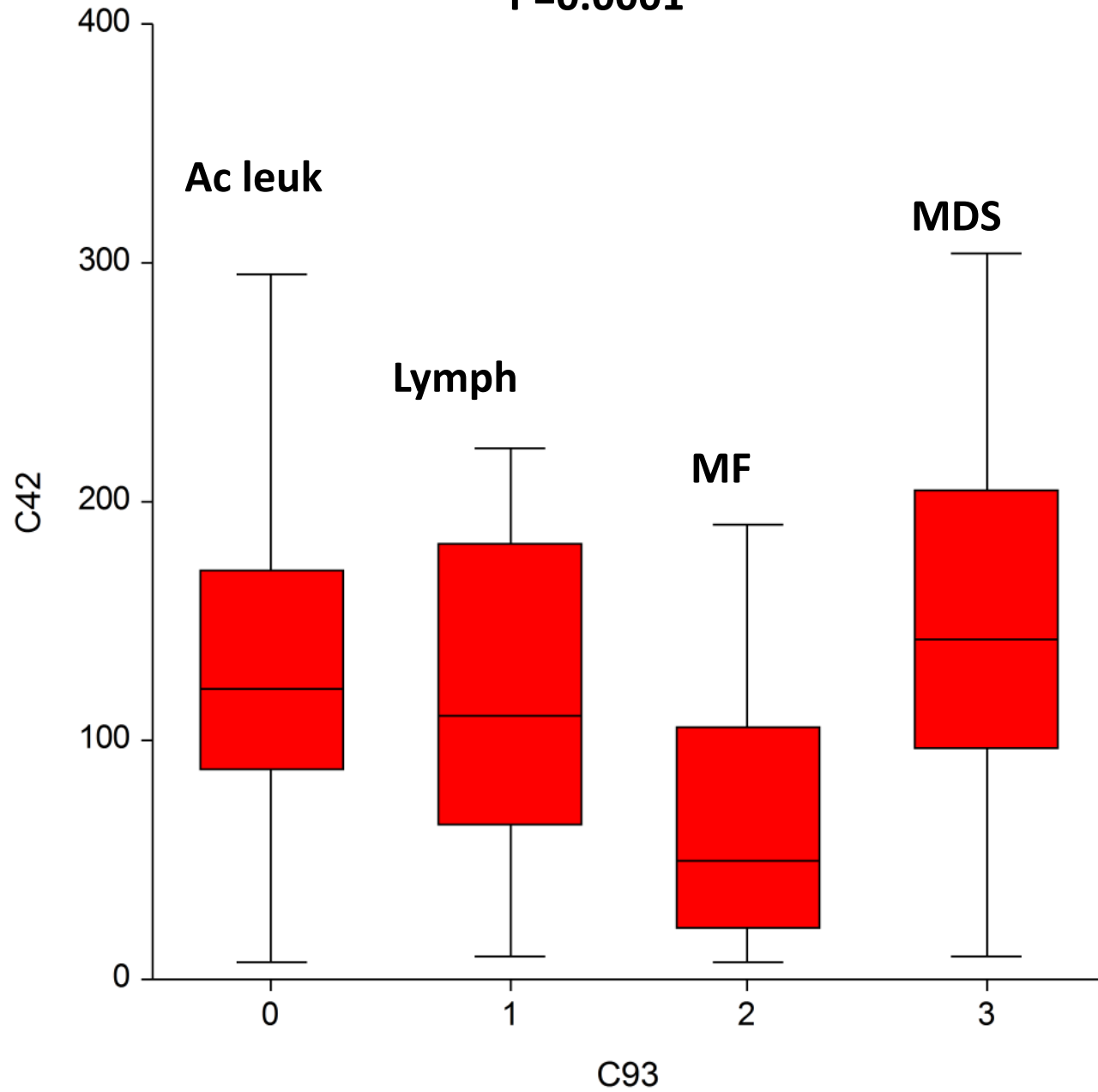


FULL DONOR CHIMERISM IN MYELOFIBROSIS POST ALLO TX

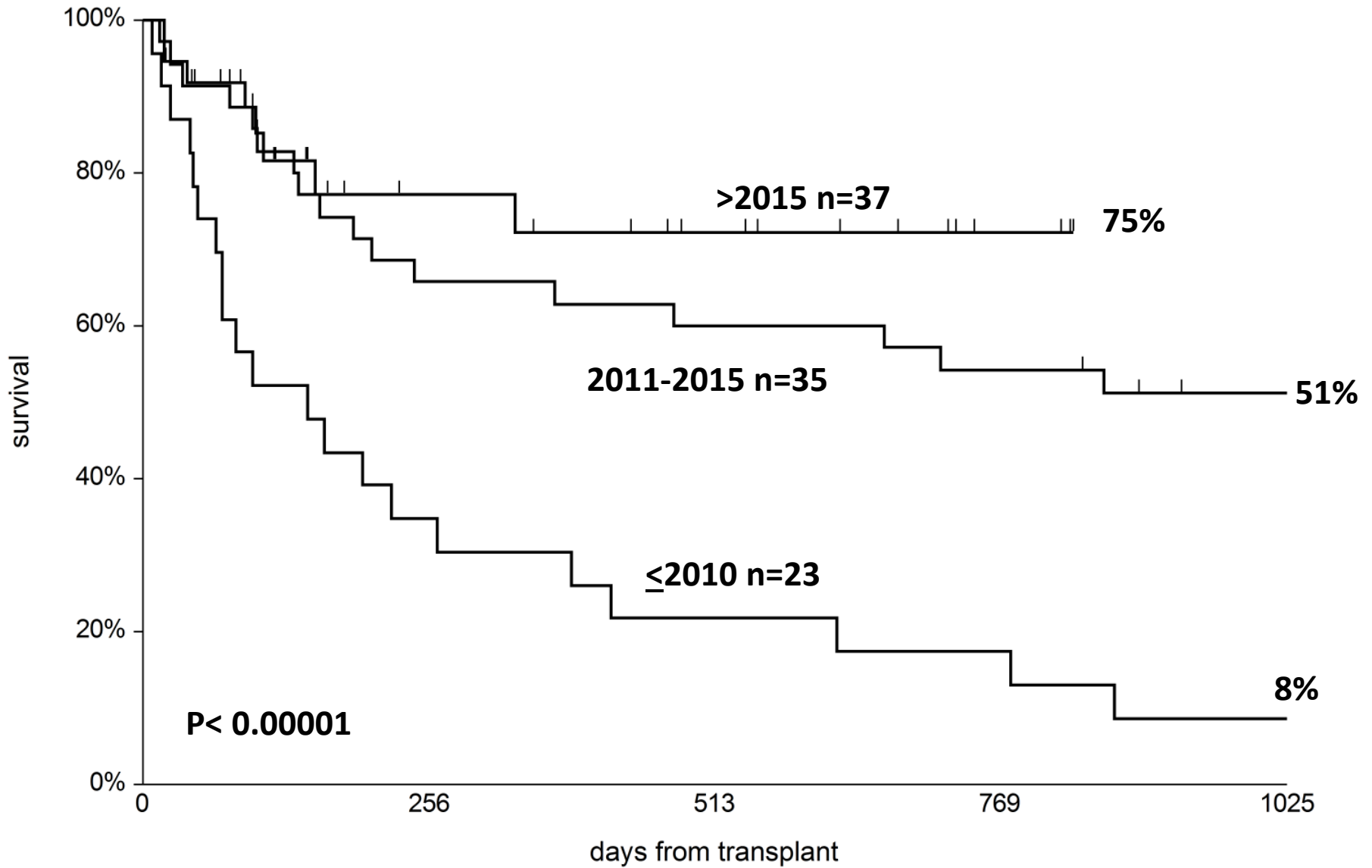


Platelets: day 50

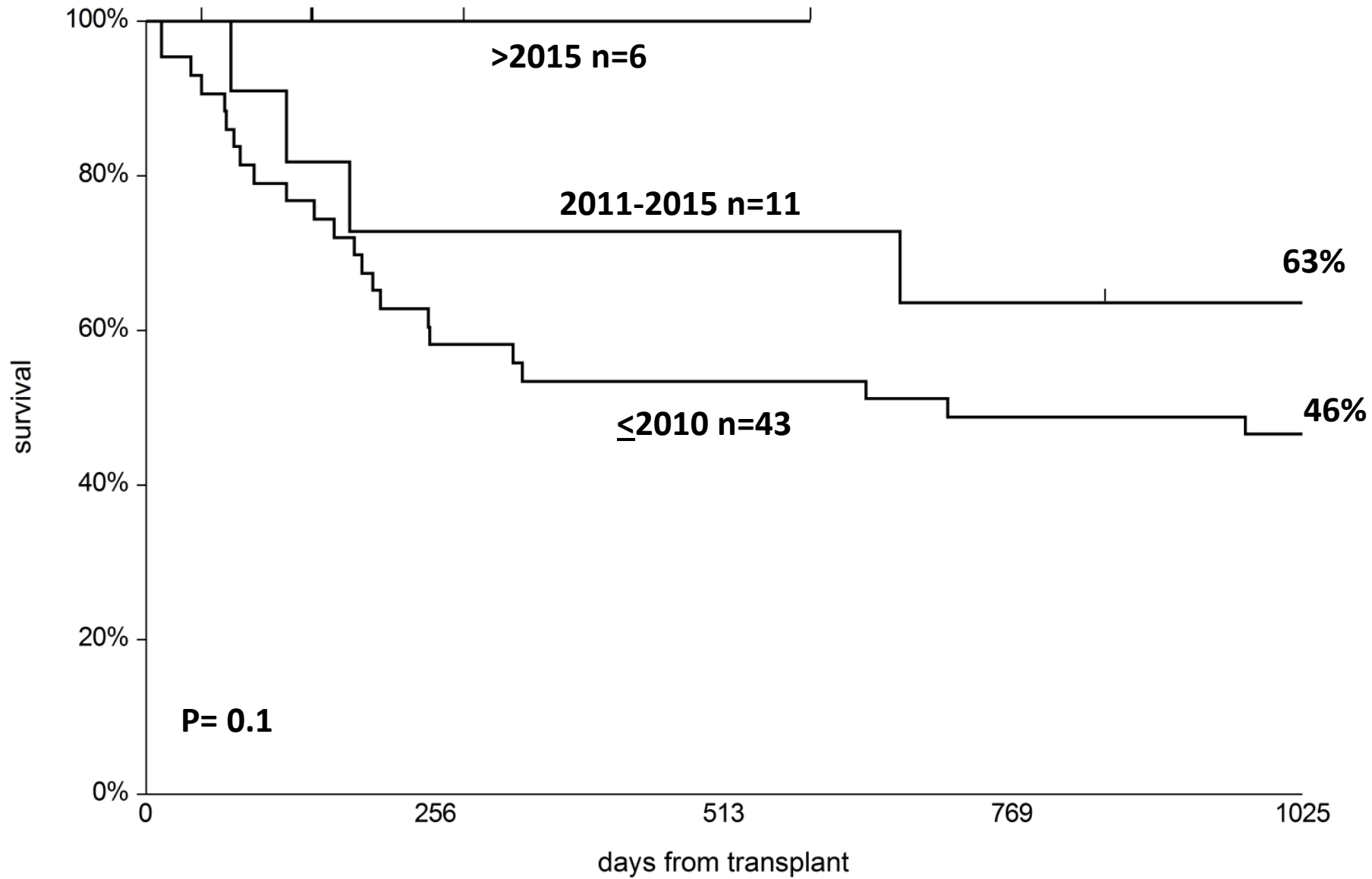
P=0.0001



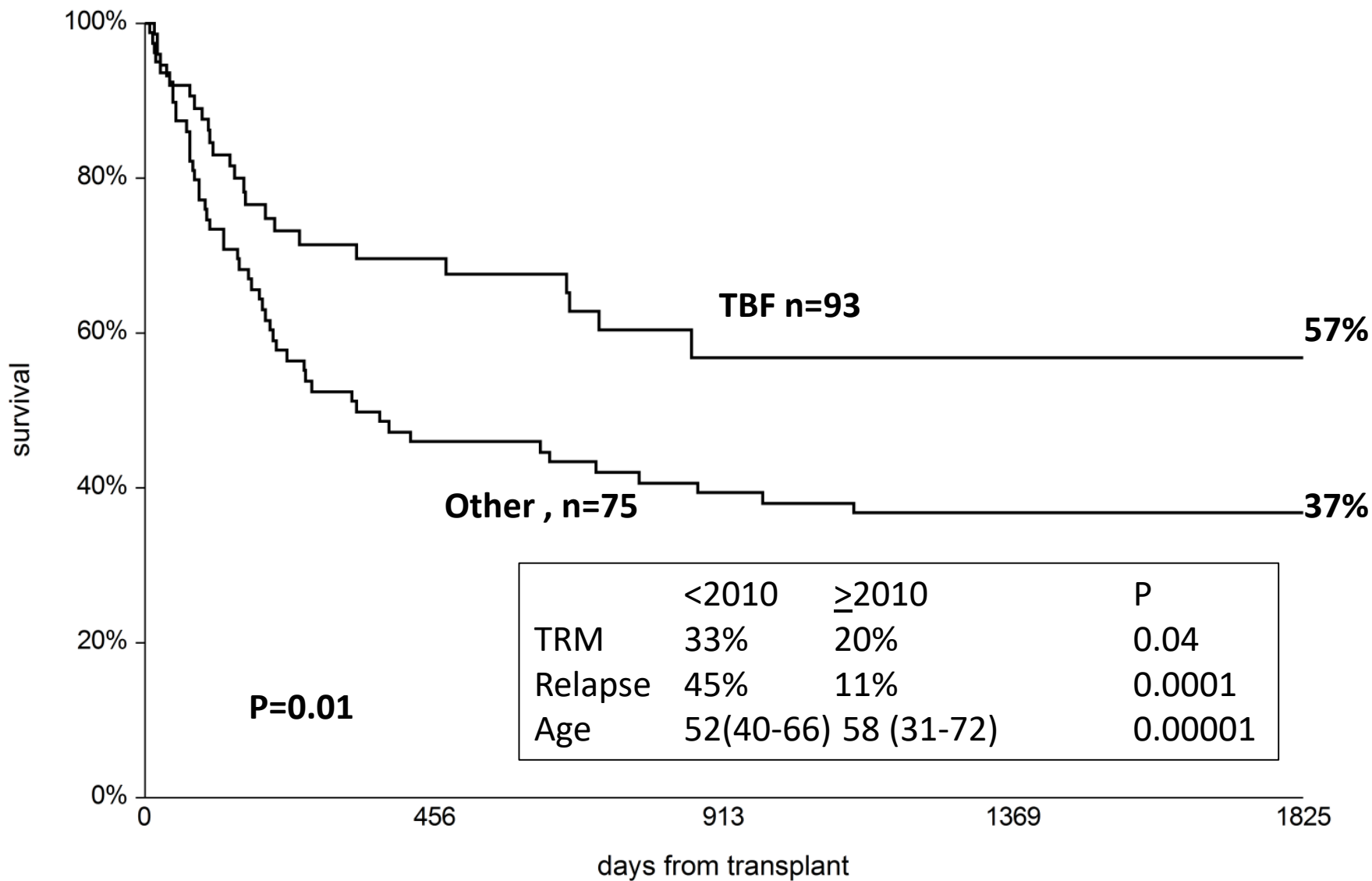
ALTERNATIVE DONORS : DFS



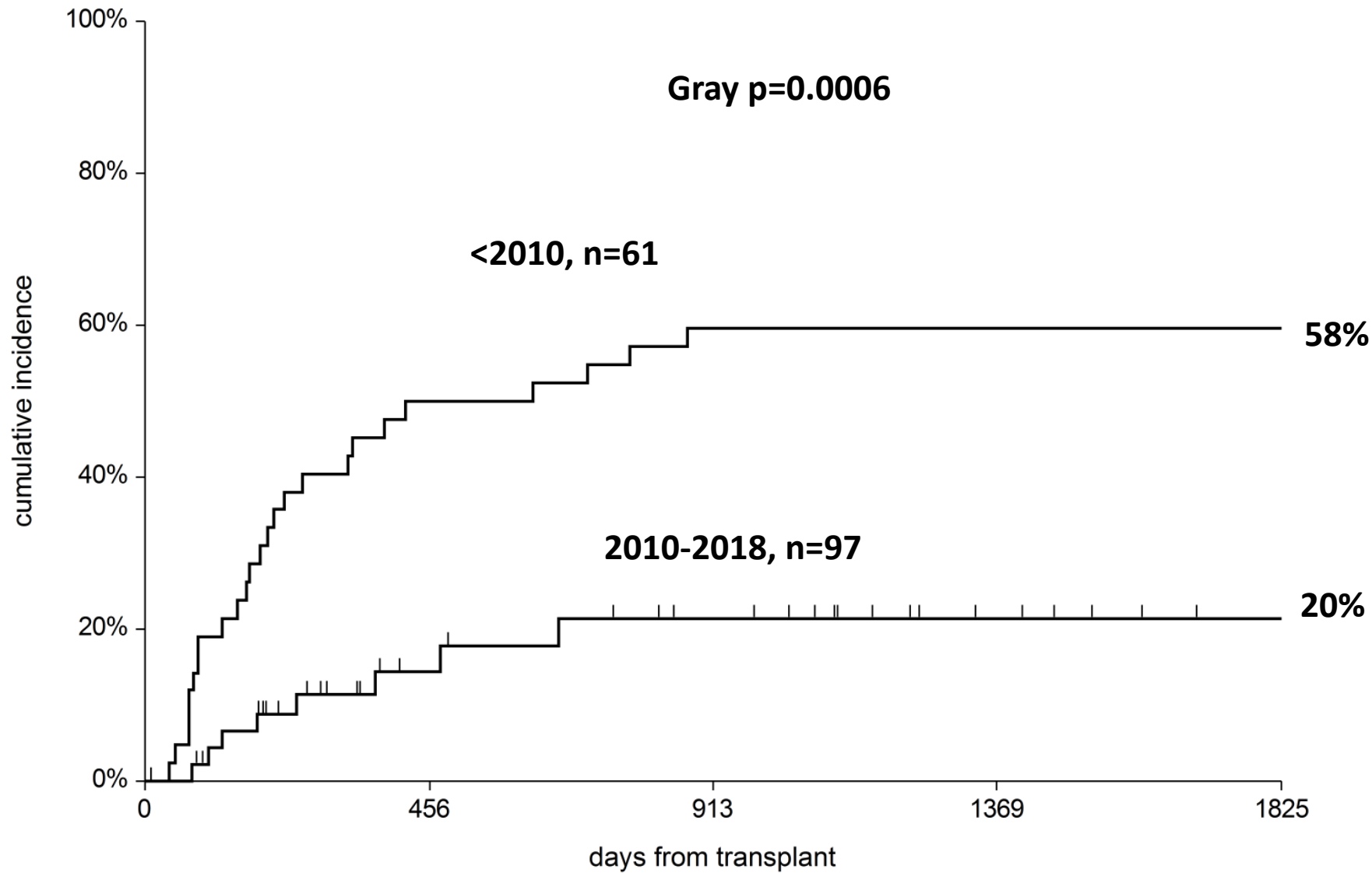
HLA ID SIBS : DFS



DISEASE FREE SURVIVAL in MF:
the effect of conditioning regimen



RELAPSE



Cox multivariate analysis on DFS

		RR	P
Year <2010	≤2015	0,29	0.01
	>2015	0.19	0.01
Donor SIB	fam mm	4.7	0.01
	UD	2.3	0.01
Condit :other	TBF	0.6	0.4
Age <40	>40	1.2	0.2
	>60	1.6	0.6

Why have results improved in the last years for alternative donor transplants in myelofibrosis?

Reduced TRM:

improved supportive care

improved TRM for alternative donor grafts

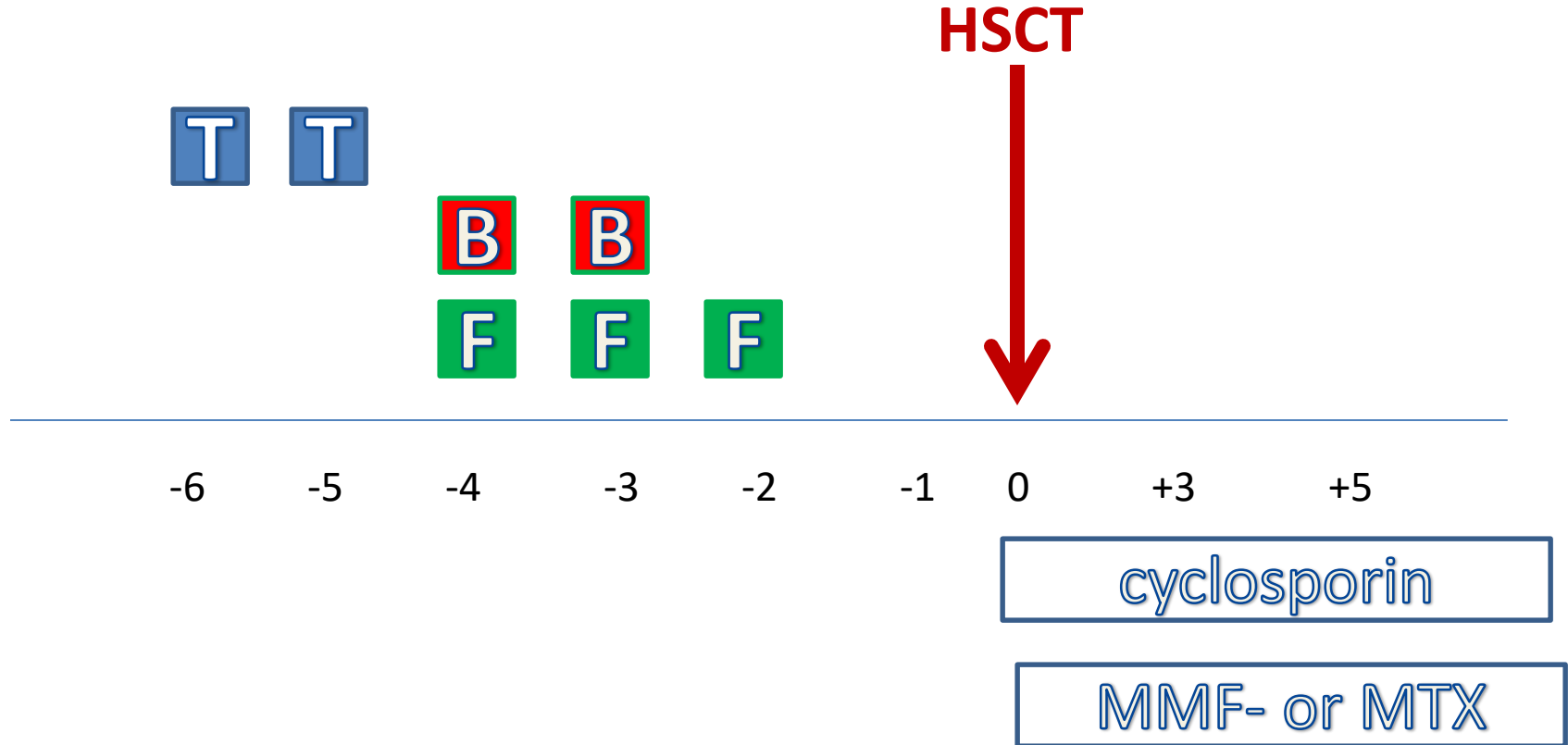
Reduced Relapse (+++):

Combined THIO+BU (TBF) instead of

Thio-FLU or BU-FLU or FLU-MEL

TBF program for MF

Sanz , *BMT* 2012, 47; 12897
Raiola, *BBMT* 2013; ; 19:117



Thiotepa 5 mg /kg

day -6-5

tot 10 mg/kg

Fludarabine 50 mg/m²

day 4-3-2

tot 150 mg/m²

Busulfan 3.2 mg/kg q24h

day -4-3

tot 6,4 mg/kg

MF 4: allogeneic HSCT

Safer + more effective Tx

Suggest earlier indication

Further improved outcome

BMT Unit Genova

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AM Raiola, M T Van Lint
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Data Center

*Rosi Oneto
M Daneri
C Frau*

Long standing collaboration

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AM Vannucchi*

BMT Unit Gemelli

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F Sora', I Innocenti, F
Autore, E Metafuni
G Zini, L Teofili, M
Bianchi, N Piccirillo

NURSES !

