

**I Buffy coat non sono tutti  
uguali : fonti di cellule staminali  
e risultati clinici**

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**Ospedale San Martino Genova**

**Genova novembre 2009**

# Trapianto allogenico (1976-2009)

- Indicazioni ( patologie )
- Fattori prognostici
- Eta' pazienti e donatori
- Tipo di donatore
- Sorgente delle cellule staminali
- Protocolli condizionamento

# **TRAPIANTO DI CELLULE STAMINALI EMOPOIETICHE (HSC)**

**- AUTOLOGO (midollo o periferiche paziente)**

**1) DX-->TRATTAMENTO-->**

**2) Raccolta di HSC --> criopreservazione**

**3) Condizionamento -->**

**4) Rinfusione cellule autologhe**

**5) Profilassi e terapia infezioni**

**- ALLOGENICO (midollo,PBSC cordone donatore)**

**1) DX--> TRATTAMENTO**

**2) Identificazione donatore idoneo**

**3) Condizionamento -->**

**4) Profilassi della GvHD**

**5) Reinfusione cellule eterologhe**

**6) Profilassi e terapia delle infezioni**

# **CELLULE STAMINALI EMATOPOIETICHE (HSC)**

- **CELLULE STAMINALI MIDOLLARI**
- **CELLULE STAMINALI DA SANGUE PERIFERICO,  
previa stimolazione con fattore di crescita (GCSF)**
- **CELLULE STAMINALI DA CORDONE OMBELICALE**

# TRAPIANTO DI CELLULE STAMINALI EMOPOIETICHE (HSC)

## RELAZIONE PAZIENTE /DONATORE

- **FAMIGLIARE**
- **NON CORRELATO**

## GRADO DI ISTOCOMPATIBILITA'

- **HLA IDENTICO**
- **MISMATCHED :**
  - 1 Ag MISMATCHED**
  - 2 Ag MISMATCHED**
  - APLOIDENTICO**

# Study Schema - Donor

Identical Sibling Donor  
Age 16-60



**R**

*PBPC*



*Bone-marrow*



*Leukapheresis D5 (6, 7)*



*Harvest*



# PRELIEVO DI MIDOLLO

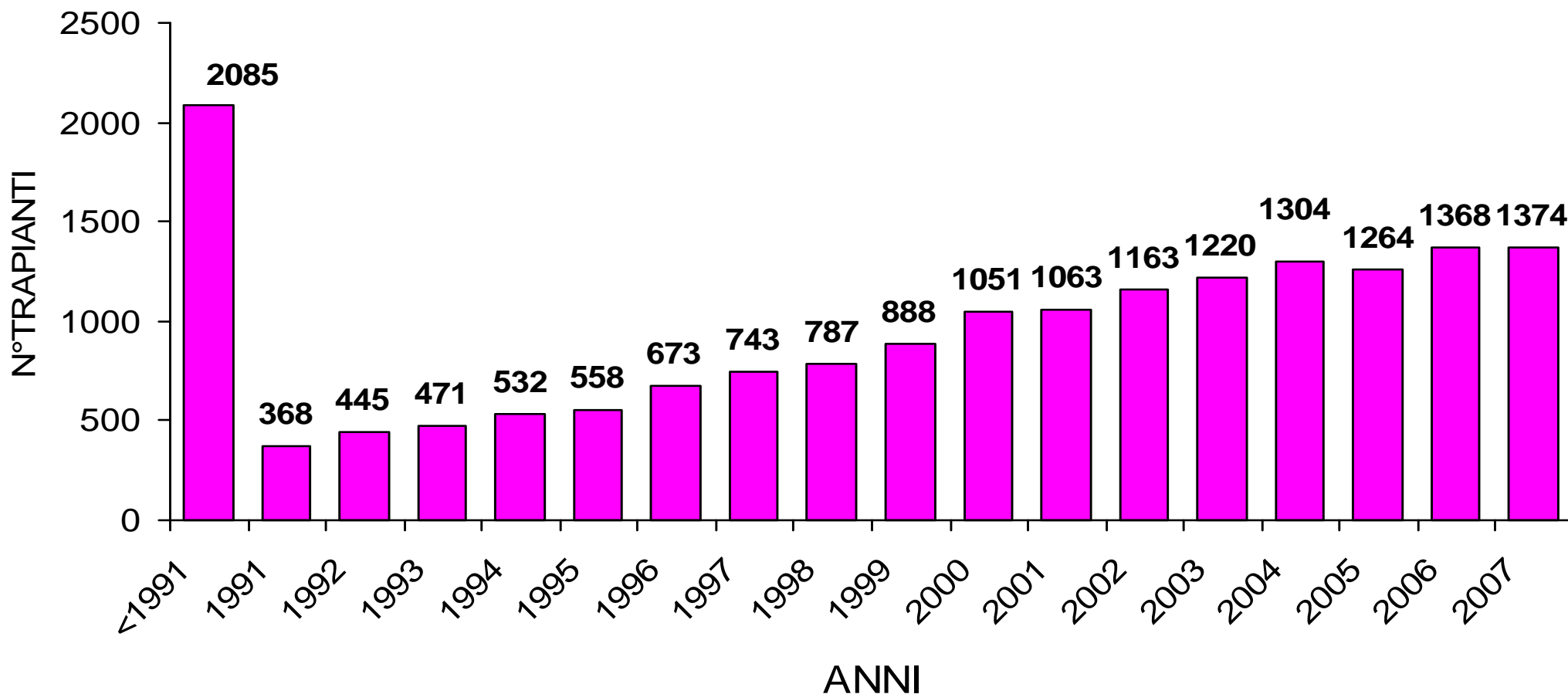
- **Idoneita' donatore**
- **in anestesia generale**
- **Creste iliache posteriori**
- **Plurime aspirazioni da 2-3 ml con un unico buco cutaneo**
- **Filtrazione midollare**
- **Infusione vena periferica**

# PRELIEVO DI PBSC

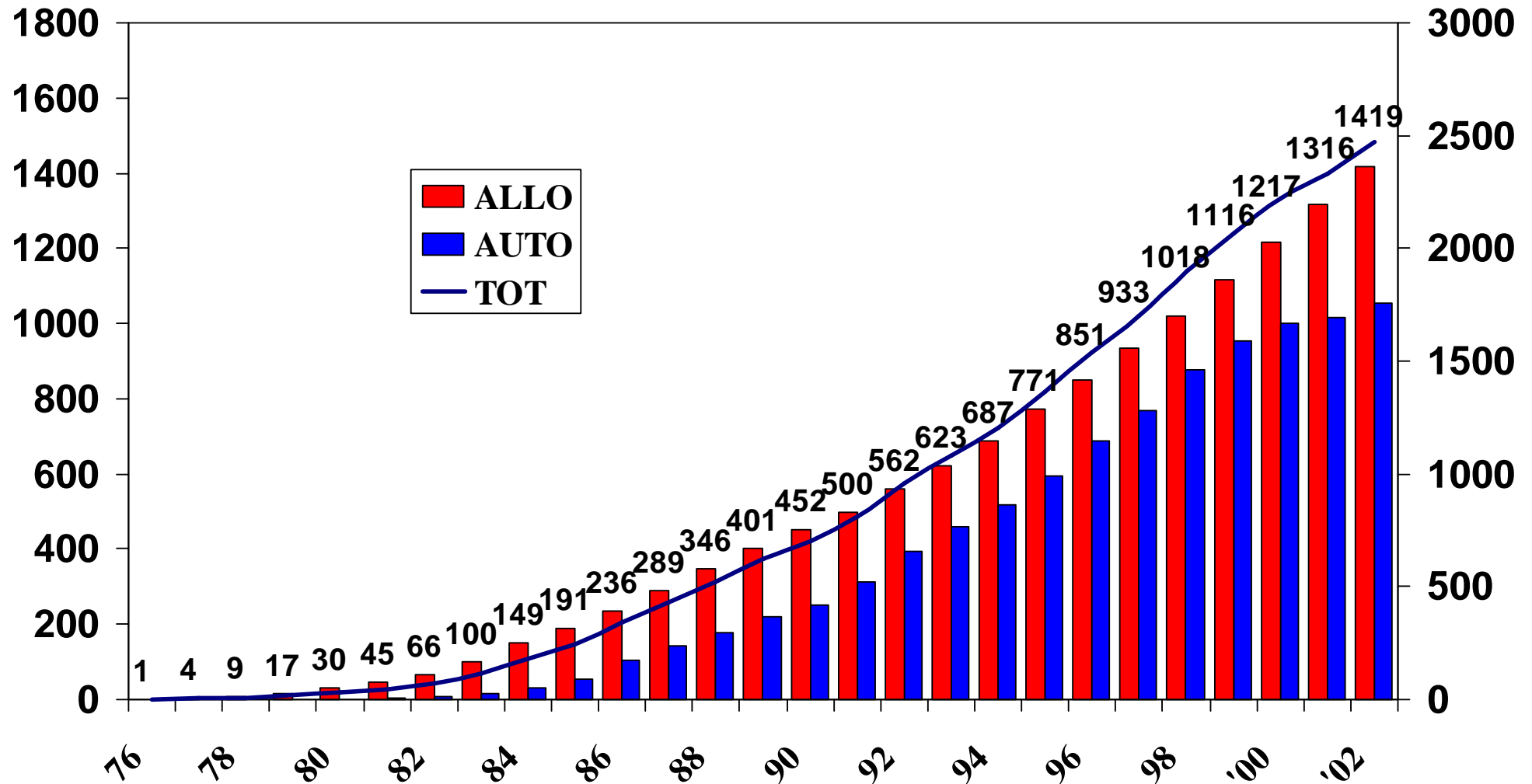
- **Idoneita' donatore**
- **non richiede anestesia generale**
- **somministrazione di fattore di crescita per mobilizzare**
- **Leucoaferesi da sangue periferico**
- **Infusione vena periferica**

# GITMO Trapianto Allogeneico

## ALLOTRAPIANTI REGISTRATI

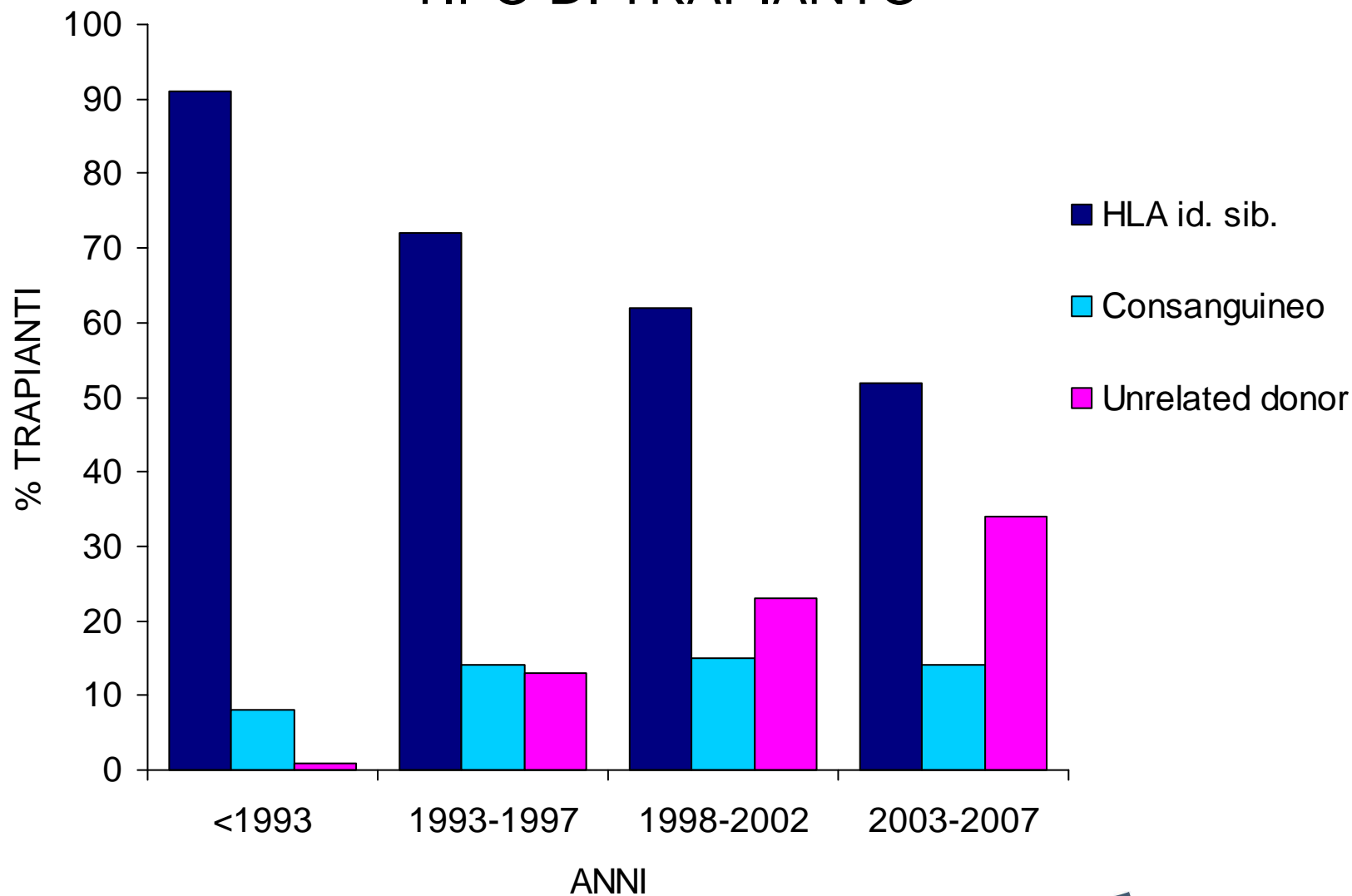


# Trapianti Genova San Martino 1976-2008



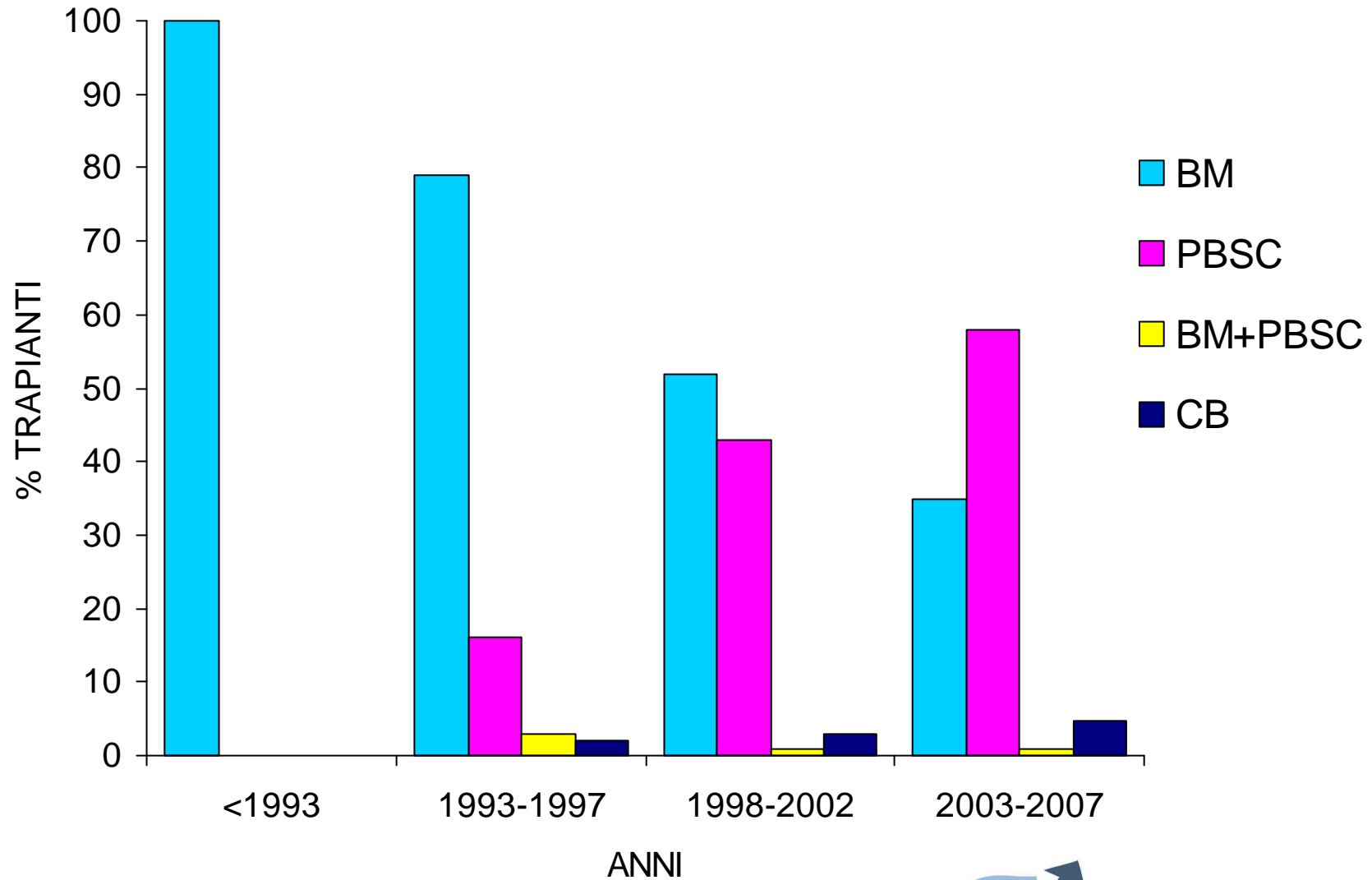
# GITMO Trapianto Allogeneico

## TIPO DI TRAPIANTO

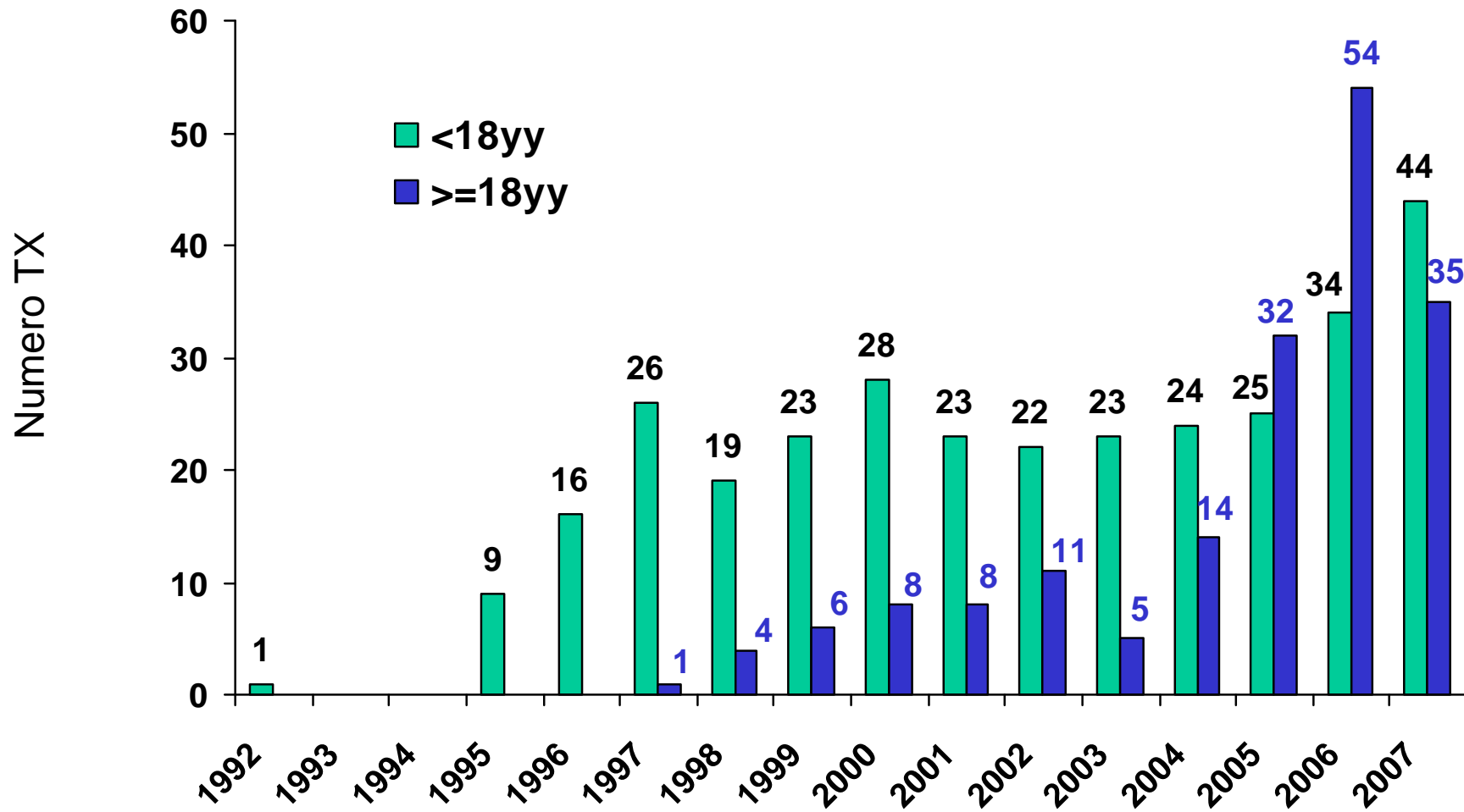


# GITMO Trapianto Allogeneico

## SORGENTE DELLE CELLULE STAMINALI



## Allo - trapianti da Cord Blood eseguiti in ITALIA



# Severe events in donors after allogeneic hematopoietic stem cell donation

J. Halter, Y. Kodaera, A. Uspizua et al.  
for the European Group for Blood and Marrow Transplantation  
(EBMT) activity survey office  
HAEMATOLOGICA 2009

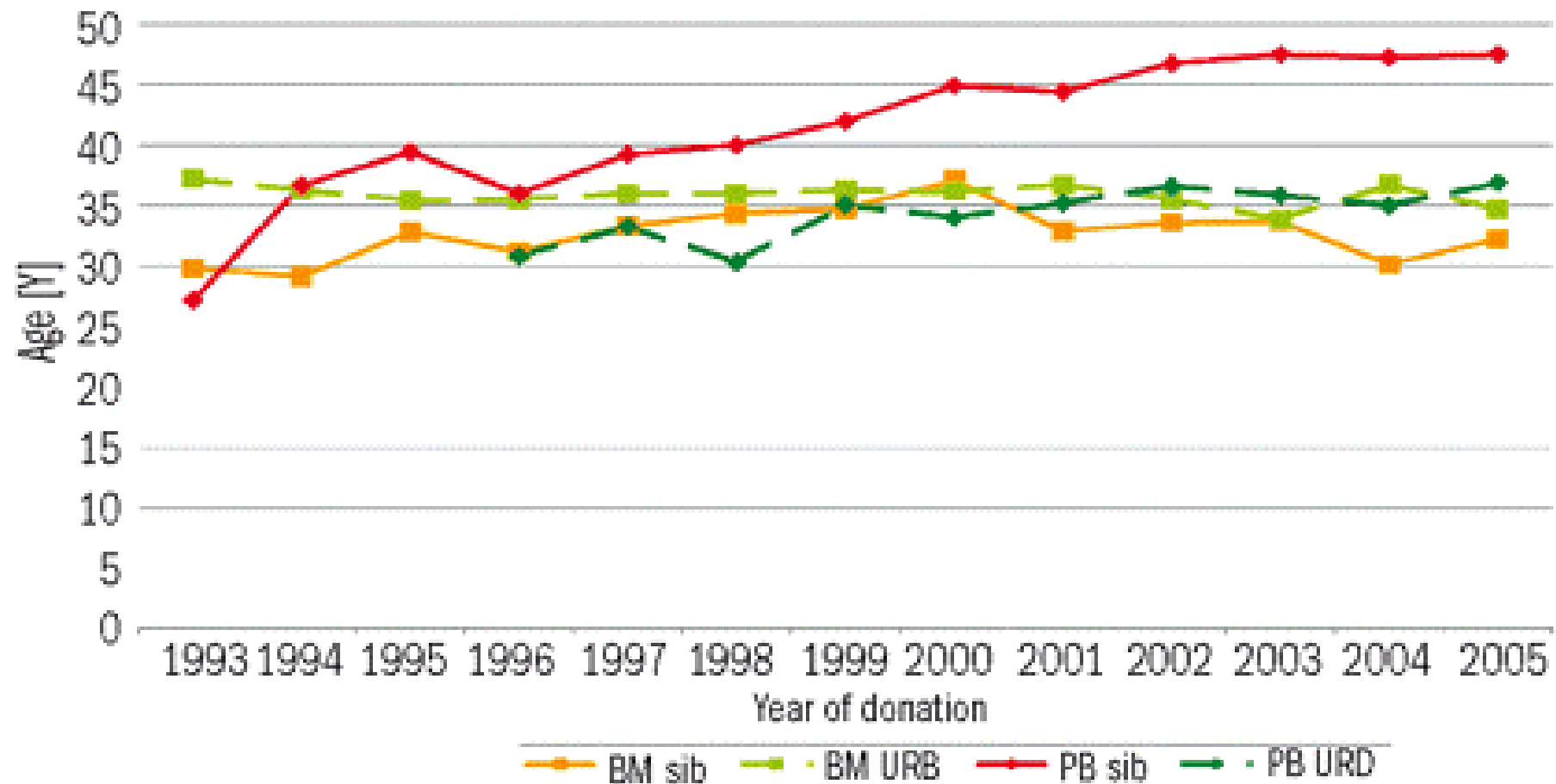
# Severe events in donors after allogeneic hematopoietic stem cell donation

- 262 center 51.024 allo HSCT (1993 - 2005)
- 27.770 BM 23.254 PBSC
- 5 fatal events 1 in BM 5 in PBSC
- 37 SAE 12 in BM 25 in PBSC
- 20 hematological malignancies 8 after BM donation and 12 after PBSC donation

# Donor Adverse Events

	<b>BMT</b>	<b>PBPCT</b>
<b>Any adverse events</b>	<b>57%</b>	<b>65%</b>
<b>Pain skeletal</b>	<b>2%</b>	<b>26%</b>
<b>Headache</b>	<b>5%</b>	<b>13%</b>
<b>Alk.Phosphatase</b>	<b>0%</b>	<b>5%</b>
<b>LDH increased</b>	<b>0%</b>	<b>9%</b>
<b>Myalgia</b>	<b>0%</b>	<b>8%</b>
<b>Nausea</b>	<b>7%</b>	<b>2%</b>
<b>Vomiting</b>	<b>5%</b>	<b>0%</b>
<b>Anaemia</b>	<b>10%</b>	<b>0%</b>
<b>Access pain</b>	<b>23%</b>	<b>1%</b>

### Median age of hematopoietic stem cell donors



Median age of donors donating from 1993 – 2005 registered in the EBMT ProMISe database (n=19,503) by donor type and stem cell source. Peripheral blood stem cell-transplants from matched unrelated donors started in 1996 only. BM sib = sibling bone marrow donor; BM URD = unrelated bone marrow donor; PB sib = sibling donor of peripheral blood stem cells; PB URD = unrelated donor of peripheral blood stem cells.

**Table 1.** Characteristics of donors who died within 30 days after stem cell donation.

Donor number	Age (years)	Sex	Mode of harvest	Mobilization	Number of harvest days	Died on day	Donor-recipient relationship	Cause of death
1	38	Male	BM	n.a.	1	15	Related	Massive pulmonary embolism after diagnosis of deep vein thrombosis and pulmonary embolism on day 7. Antithrombin III deficiency was later diagnosed in the family but was unknown at the time of donation
2	67	Male	PB	G-CSF	2	29	Related	Subarachnoid hematoma on day 1. Died on day 29.
3	43	Male	PB	G-CSF	2	15	Related	Cardiac arrest (no autopsy). Risk factors: arterial hypertension, heavy smoker
4	52	Male	PB	G-CSF	2	17	Related	Cardiac arrest Risk factor: smoker
5	27	Male	PB	G-CSF	1	0	Related	Cardiac arrest after human error (see text). Resuscitation unsuccessful

**Table 2.** Severe adverse events among 51,024 stem cell donations.

Stem cell source event	N.	Bone marrow Comment	N.	Peripheral blood Comment
<i>Cardiovascular</i>				
Myocardial infarction			2	
Cardiac arrest	4	All during or shortly after harvest		
Supraventricular arrhythmia			1	Probably related to catheter. Needed transesophageal stimulation
Severe hypertension	2	Former normotensive donors	1	Required treatment for 1 month post-donation in a former normotensive donor
<i>Thromboembolic</i>				
PE/DVT			7	Between day -2 and day 30 of harvest. Three events occurred before day 0
Stroke	1	Due to HIT antibodies		
<i>Pulmonary complications</i>				
TRALI			1	Due to priming the cell separator with erythrocyte concentrates (pediatric donor)
Lung edema	1	At the end of anesthesia after two donations within 1 month. Needed mechanical ventilation for 24h.		
<i>Hemorrhage</i>				
Subdural hematoma			1	Day 21 after donation
Unspecified	1	Recovered after transfusion of four units of red blood cells	1	Hemorrhage from femoral artery after insertion of central venous catheter
<i>Seizures</i>				
			1	Due to severe electrolyte disorder during apheresis
<i>Splenic rupture</i>				
			5	
<i>Unspecified</i>	3		5	
<b>Total</b>	<b>12</b>		<b>25</b>	

PE/DVT: pulmonary edema/deep vein thrombosis; HIT: heparin-induced thrombocytopenia; TRALI: transfusion-related acute lung injury.

**Table 3. Hematologic malignancies observed in 51,024 stem cell donors.**

Donor number	Age	Sex	Relationship	Mode of harvest	Mode of mobilization	Number of donations	Diagnosis	Interval between donation and diagnosis	Treatment	Outcome	Duration of follow-up
06	20	F	Unrelated	BM	—	1	AML M2	1y6m	Allogeneic HSCT	Alive in CR	2y
07	n.r.	F	Syngenic twin	BM	—	1	AML M1	12y	n.r.	n.r.	n.r.
08	n.r.	M	Sibling	BM	—	1	T-ALL	12y2m	n.r.	Died	n.a.
09	1	M	Sibling	BM	—	1	B-ALL	10m	Chemotherapy	Alive in CR	6y
10	n.r.	n.r.	Sibling	BM	—	1	NHL low grade (follicular)	6y	Radiotherapy	Alive in CR	n.r.
11	53	M	Sibling	BM	—	1	DLBCL	4m	Chemo-/ radiotherapy	Died from lymphoma	8y
12	n.r.	n.r.	n.r.	BM	—	n.r.	Lymphoma	n.r.	n.r.	n.r.	n.r.
13	57	F	Sibling	BM	—	1	Nasopharyngeal plasmacytoma	7m	Radiation, surgical resection	Alive in CR	10y
14	34	F	Sibling	PB	G-CSF	1x2	AML	2y8m	Chemotherapy/ allogeneic HSCT	Alive in CR	1y
15	38	F	Sibling	PB	G-CSF	1x2	ALL	1y5m	Chemotherapy	Died in induction	na.
16	47	F	Sibling	PB	G-CSF	1	MPN	4y3m	n.r.	n.r.	n.r.
17	n.r.	n.r.	Sibling	PB	n.r.	n.r.	CLL (familial?)	several years	n.r.	n.r.	n.r.
18	25	n.r.	Sibling	PB	n.r.	1	NHL low grade	9m	Chlorambucil	Alive in CR	3y3m
19	45	F	Sibling	PB	G-CSF	1(BM)*	NHL low grade	7y3m	Chemotherapy	Alive in CR	9m
20	41	M	Sibling	PB	G-CSF	1x2	DLBCL	4y3m	Chemotherapy	Alive in CR	4y
21	28	M	Sibling	PB	G-CSF	1	HD	1y	Chemotherapy	Alive	2y
22	68	M	Sibling	PB	G-CSF	1	Splenic maginal zone lymphoma	7y	none	Alive	1y
23	n.r.	n.r.	n.r.	PB	n.r.	n.r.	Malignancy not specified	n.r.	n.r.	n.r.	n.r.
24	n.r.	n.r.	n.r.	PB	n.r.	n.r.	Malignancy not specified	n.r.	n.r.	n.r.	n.r.
25	n.r.	n.r.	n.r.	PB	n.r.	n.r.	Malignancy not specified	n.r.	n.r.	n.r.	n.r.

\*No apheresis due to intolerance after completion of G-CSF mobilization, donor finally underwent BM harvest. AML: acute myeloid leukemia; ALL: acute lymphoblastic leukemia; NHL: non-Hodgkin's lymphoma; DLBCL: diffuse large B-cell lymphoma; MPN: myelo-proliferative neoplasm; CLL: chronic lymphocytic leukemia; HD: Hodgkin's disease; CR: complete remission.

**aim : compare PB with BM  
in HLA identical SIB Tx**

**donors**

**speed /quality of engraftment  
acute GvHD  
chronic GvHD**

**TRM, relapse, survival**

**Random**

**Neutrophils 0.5**

**Platelets 20**

**PB**

**BM**

**PB**

**BM**

**Can G5 - - - 16 22 .001**

**EBMT G10 post 12 15 .001 15 20 .001**

**Seattle G16 - 16 21 .001 13 19 .001**

# CONCLUSION 1

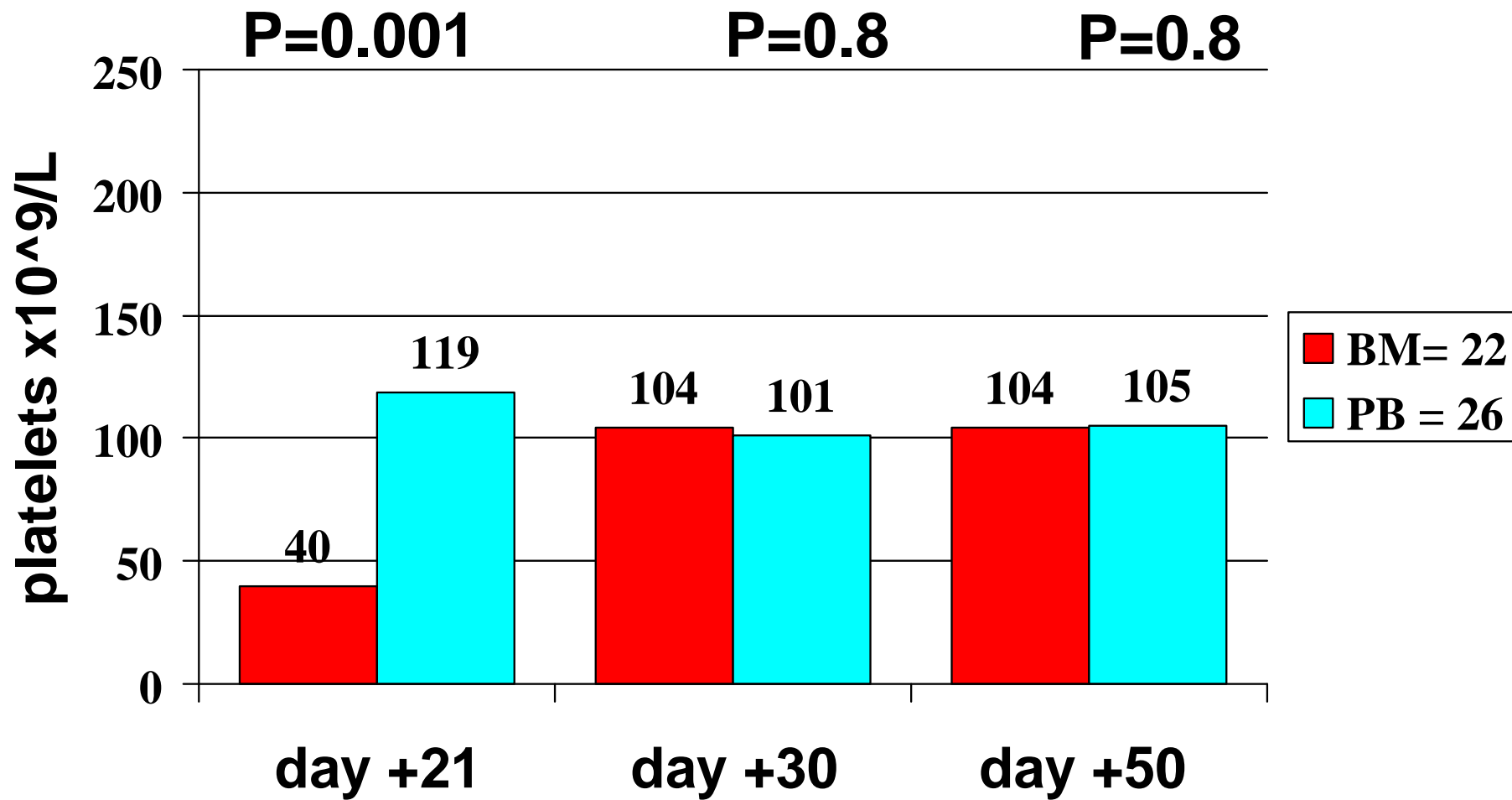
neutrophil and platelet engraftment

is faster

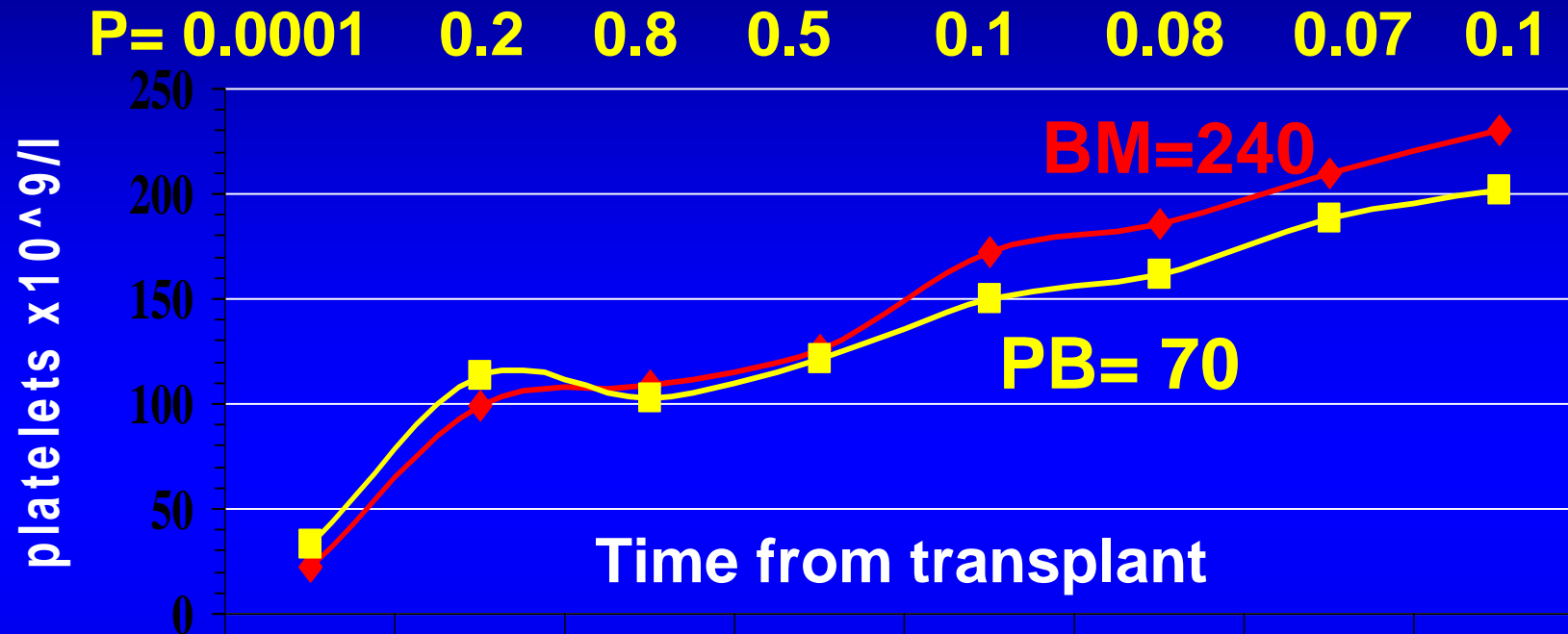
following allo-PB Tx

# Platelet counts after allo-HSCT

## HLA id sibs; THIO-CY; BM vs PB



# 310 concurrent HLA id HSCT (1994- 2000)



	day 21	day 50	day 100	6 months	1 year	2 yy	2-5 yy	>5 yy
◆ BM	22	99	109	126	172	186	210	230
■ PB	33	113	103	121	150	162	188	202

## CONCLUSION 2

graft function is

similar

following allo-PB or BM Tx

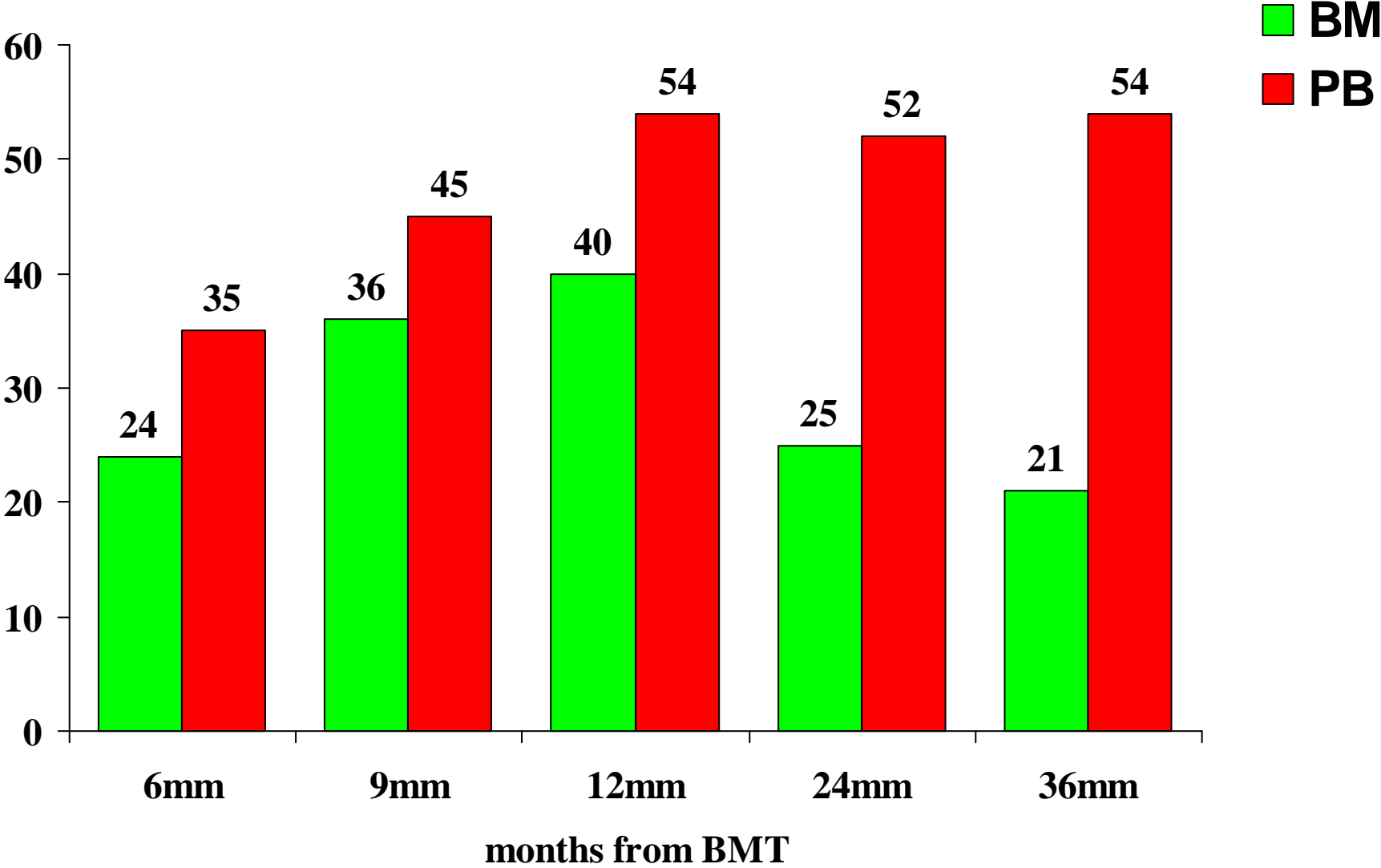
**aim : compare PB with BM  
in HLA identical SIB Tx**

**acute GvHD  
chronic GvHD**

<b>Random</b>	<b>aGvHD III-IV</b>			<b>cGvHD ext</b>		
	<b>PB</b>	<b>BM</b>		<b>PB</b>	<b>BM</b>	
<b>Can 228 pts</b>	<b>23%</b>	<b>15%</b>	<b>ns</b>	<b>80%</b>	<b>60%</b>	<b>0.1</b>
<b>EBMT 350 pts</b>	<b>28%</b>	<b>16%</b>	<b>.001</b>	<b>52%</b>	<b>25%</b>	<b>.001</b>
<b>Seattle 172 pts</b>	<b>15%</b>	<b>12%</b>	<b>ns</b>	<b>46%</b>	<b>35%</b>	<b>0.5</b>

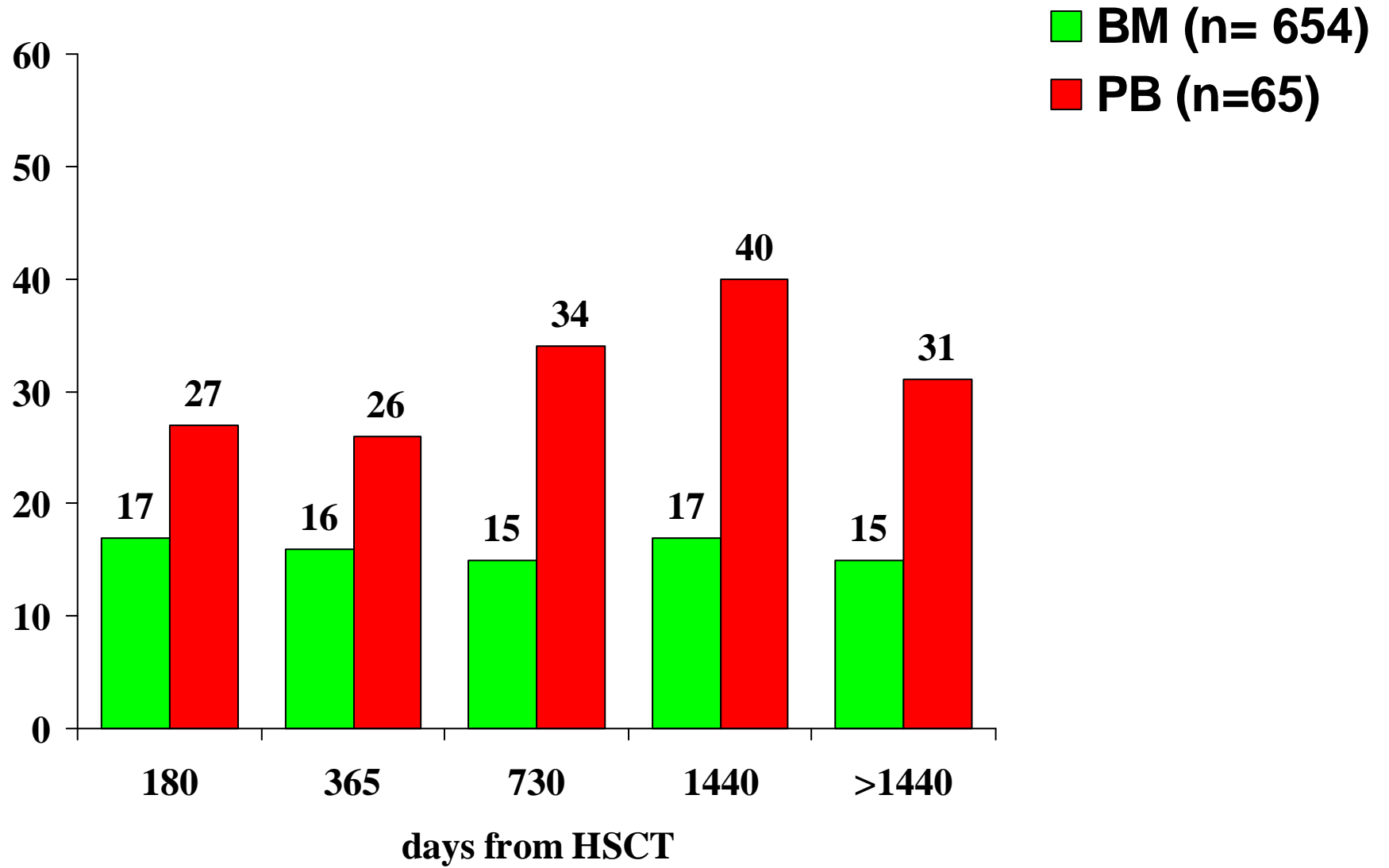
# EBMT trial (Schmitz et al 2001)

% with chronic GvHD

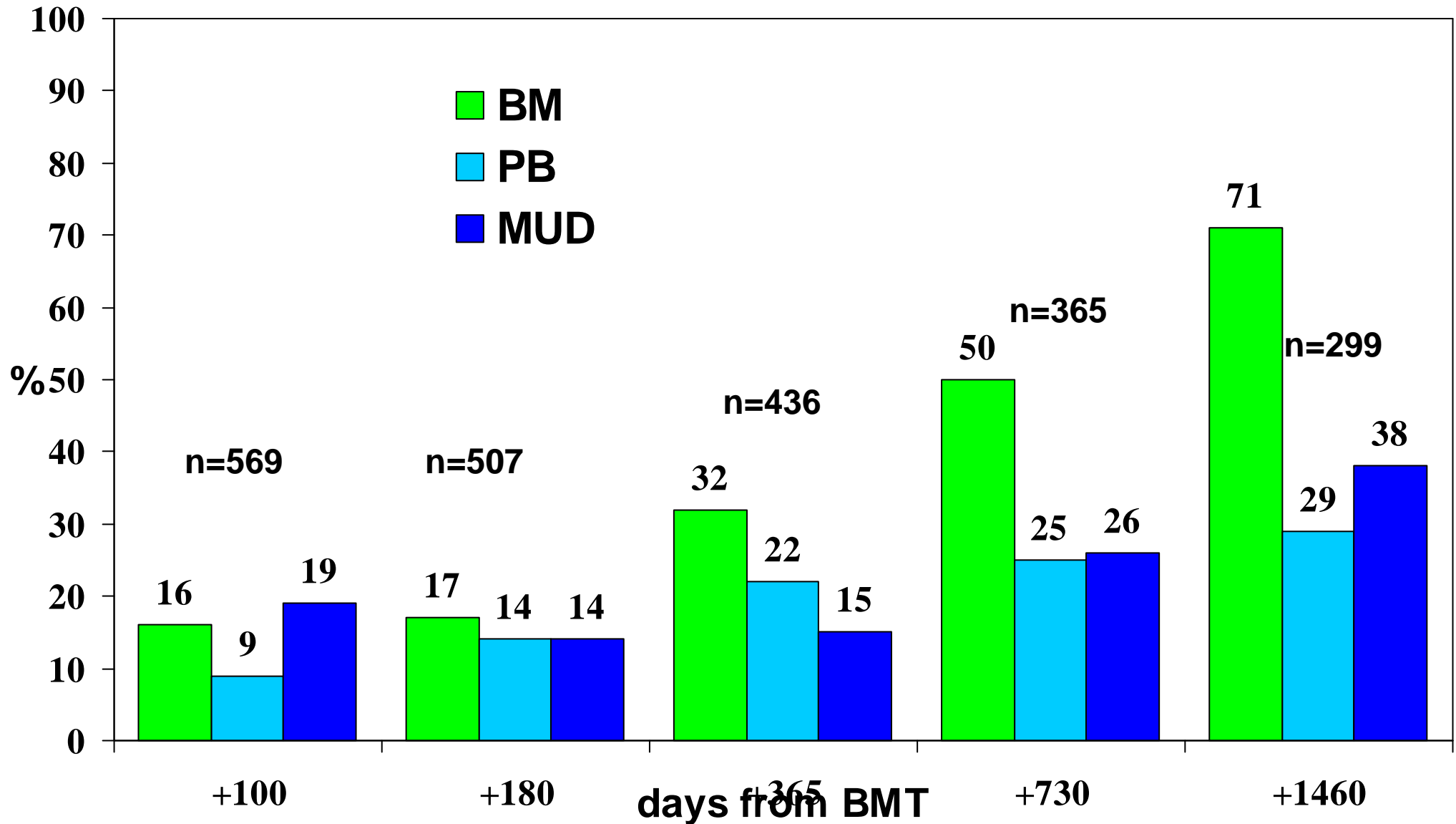


# GE SM : BM vs PB

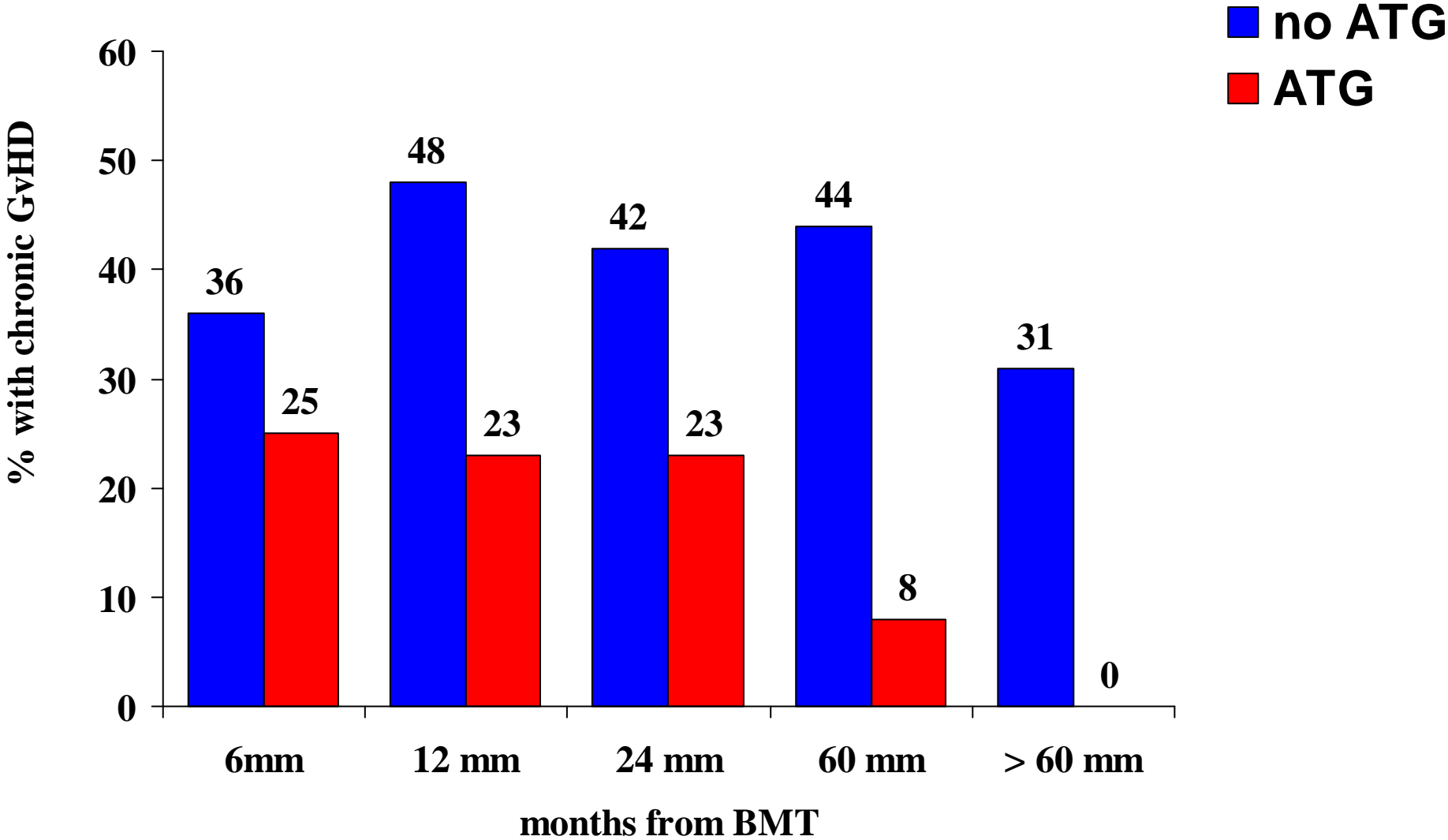
% with chronic  
GvHD



# Percentage of patients stopping CyA po



**210 Alt. Don. HSCT (GE SM):  
effect of ATG in the conditioning regimen and cGvH**



## **CONCLUSION 3**

**acute GvHD III-IV**  
**is similar**

**extensive cGvHD**  
**is increased**

**following allo-PB or BM Tx**  
**p value depends on numbers**

**aim : compare PB with BM  
in HLA identical SIB Tx**

**TRM, relapse, survival**

<b>Retrospective</b>			<b>TRM</b>	<b>REL</b>	<b>Surv</b>	<b>comments</b>
<b>Bensing</b>	<b>1996</b>	<b>74</b>	<b>=</b>	<b>=</b>	<b>=</b>	<b>faster engr, fewer Tx</b>
<b>Majolino</b>	<b>1996</b>	<b>9</b>				<b>more cGvHD</b>
<b>Przepiorka</b>	<b>1997</b>	<b>55</b>	<b>=</b>	<b>=</b>	<b>=</b>	<b>subst advantage</b>
<b>Bacigalupo</b>	<b>1998</b>	<b>97</b>	<b>=</b>	<b>=</b>	<b>=</b>	<b>comp outcome</b>
<b>Ustun</b>	<b>1999</b>	<b>80</b>	<b>=</b>	<b>=</b>	<b>=</b>	<b>fewer Tx; more cGvHD</b>
<b>Russell</b>	<b>1999</b>	<b>87</b>	<b>=</b>	<b>lower</b>	<b>=</b>	<b>low rel; QOL low</b>
<b>Champlin</b>	<b>2000</b>	<b>824</b>	<b>=</b>	<b>lower</b>	<b>=</b>	<b>better for adv dis</b>

<b>RANDOM</b>			<b>TRM</b>	<b>REL</b>	<b>Surv</b>	<b>comments</b>
<b>Schmitz*</b>	<b>1998</b>	<b>66</b>	<b>=</b>		<b>=</b>	<b>no difference</b>
<b>Vigorito</b>	<b>1998</b>	<b>37</b>	<b>=</b>	<b>=</b>	<b>=</b>	<b>increased cGvHD</b>
<b>Powles</b>	<b>1999</b>	<b>39</b>	<b>=</b>	<b>lower</b>	<b>better</b>	<b>Less relapse</b>
<b>Bensinger</b>	<b>2001</b>	<b>168</b>	<b>less</b>	<b>less</b>	<b>better</b>	<b>better for advanced dis</b>
<b>Heidal</b>	<b>2000</b>	<b>61</b>	<b>=</b>	<b>lower</b>	<b>=</b>	<b>preferable; long term?</b>
<b>Schmitz</b>	<b>2000</b>	<b>360</b>	<b>=</b>	<b>=</b>	<b>=</b>	<b>increased a+cGvHD</b>
<b>Couban</b>	<b>2000</b>	<b>228</b>	<b>less</b>	<b>=</b>	<b>bett</b>	<b>less TRM</b>

## Update IBMTR 824 patients (Tx 95-96)

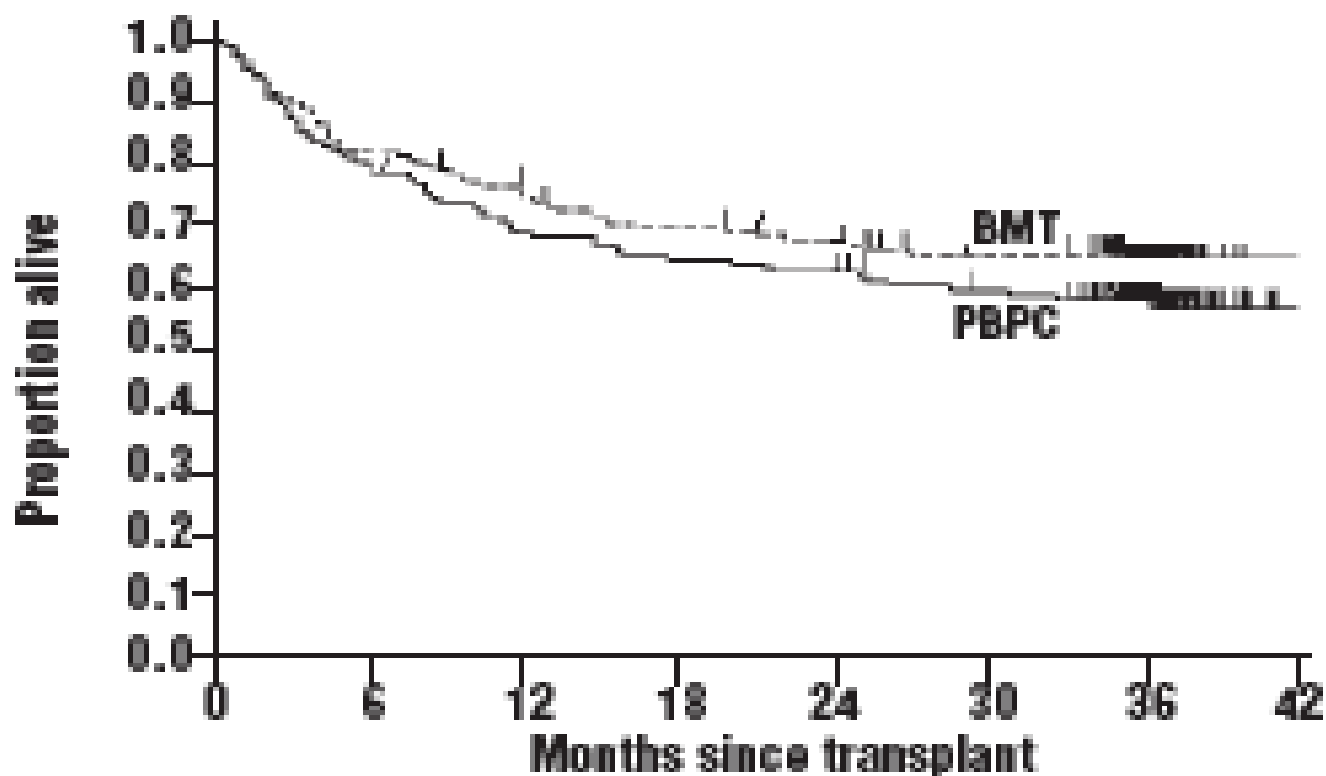
	<b>BM</b>	<b>PB</b>	
<b>number</b>	<b>536</b>	<b>288</b>	
<b>alive 1stFU</b>	<b>360 (67%)</b>	<b>195 (67%)</b>	
<b>alive 2ndFU</b>	<b>267 (50%)</b>	<b>125 (43%)</b>	
<b>cGvHD</b>	<b>42%</b>	<b>65%</b>	<b>0.0001</b>

**relapse** no significant difference early/ advanc

**TRM** higher in PB (CMLCP)

**Survival** ac.leuk 1st BM > PB adv no diff

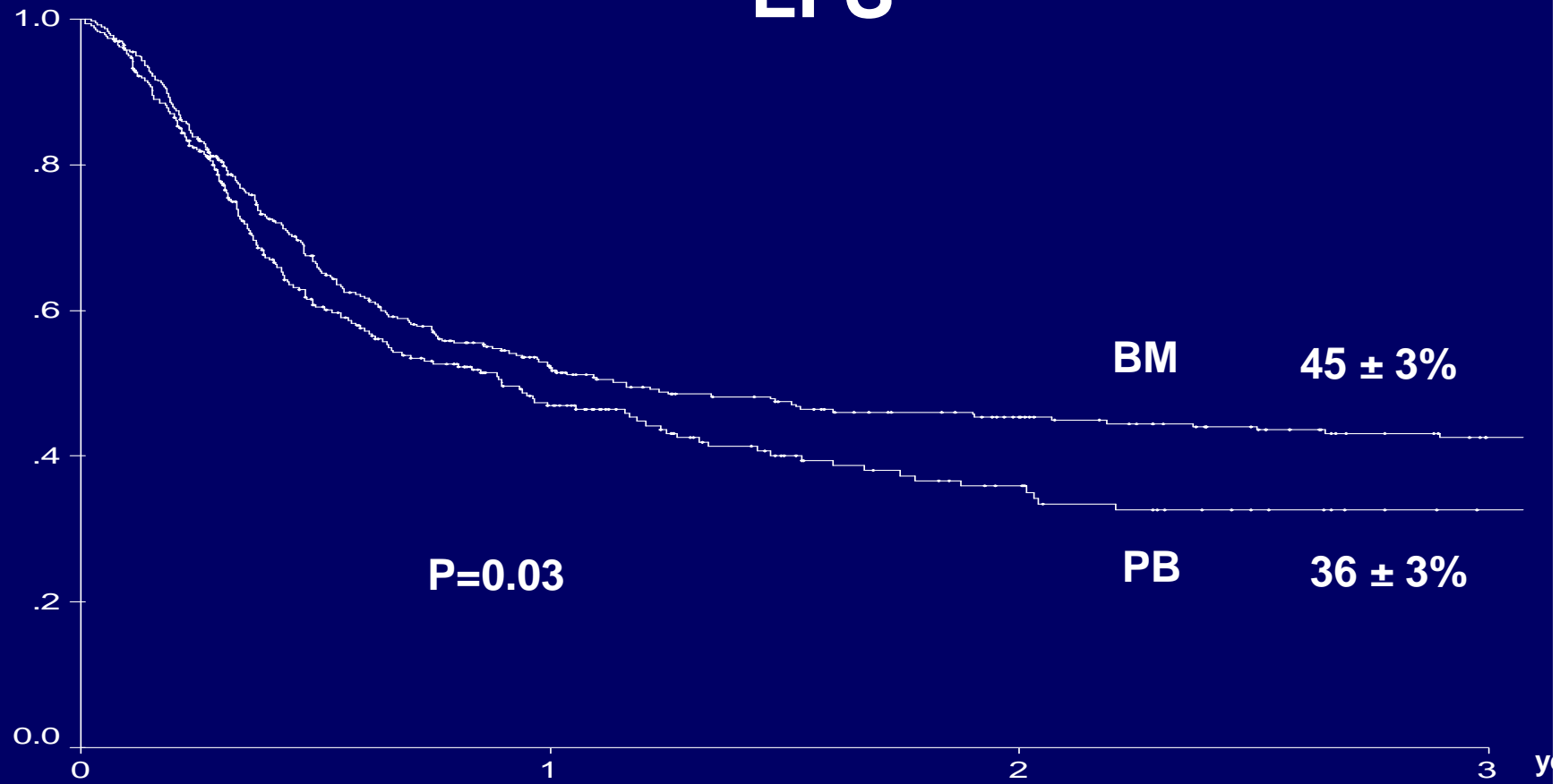
**CML CP** BM >>>PB Adv PB>BM

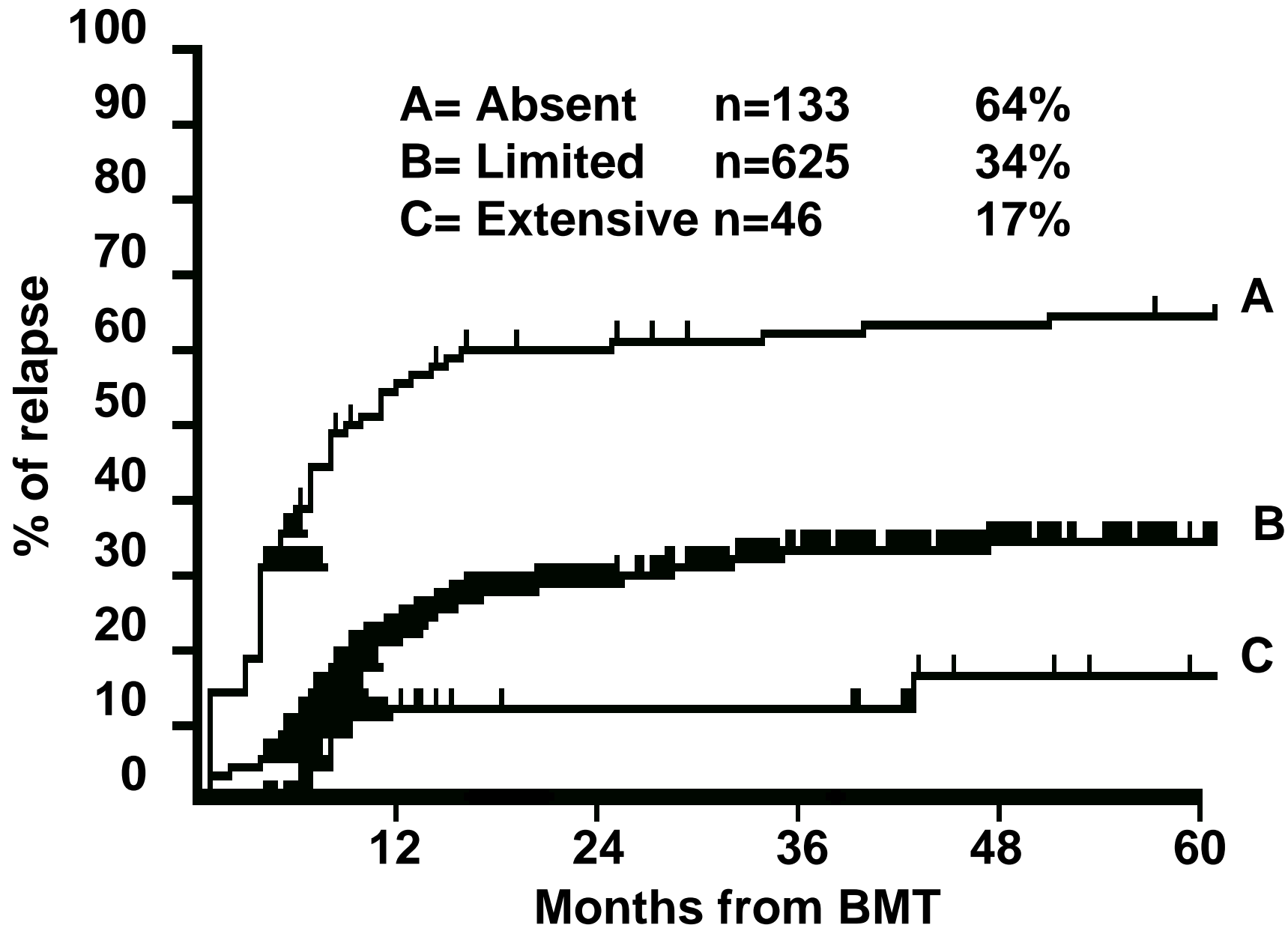


BMT	N=166	136	123	113	107	98	68	4
PBPC	N=163	131	111	104	100	92	53	1

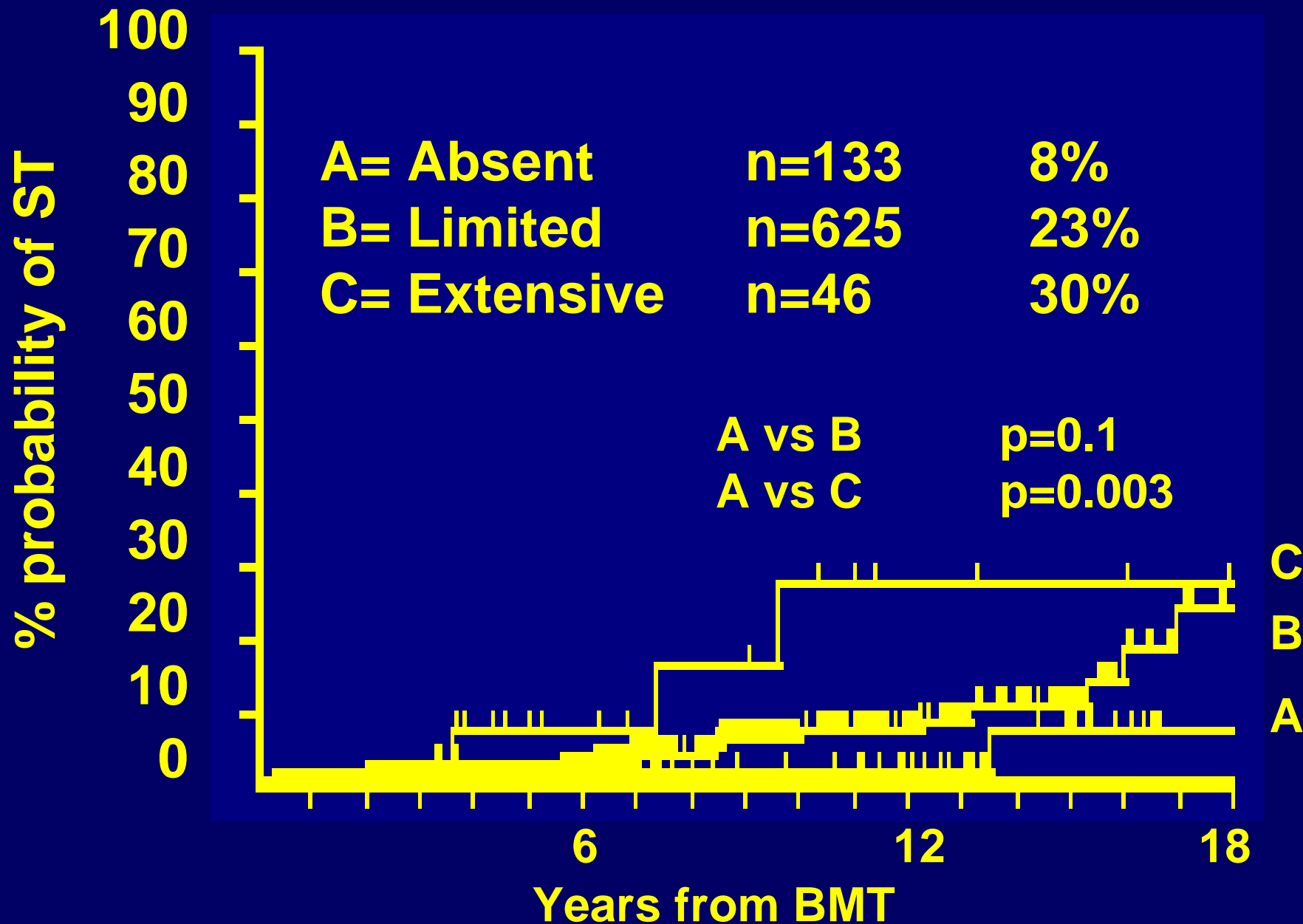
**Figure 4.** Three-year overall survival among patients treated with filgrastim-mobilized peripheral blood progenitor cells (n = 163) or bone marrow (n = 166; intent-to-treat population).

# LFS





# cGvHD and Secondary Tumours



## **Conclusion studies PB**

- 1.faster engraftment**
- 2.no effect on graft function**
- 3.similar TRM (higher in early disease ?)**
- 4.similar acute GvHD (+?)**
- 5.similar survival (better in adv.pts/ worse CMLCP)**
- 6.more cGvHD (extensive) ---> less relapse ?**
- 7.more patients on IS therapy long term**

**puzzling data on the absence of cGvHD effect on relapse (B Torok Storb)**

***in the long term***

**more cGvHD**

**= more GvL (??)**

**=less relapse (??)**

**= more IS therapy**

**= more immune deficiency**

**= more sec Tum**

**=poorer QOL**

**=more late TRM**

***in the long term***

***advanced disease***

**PB**

**more cGvHD**

**= more GvL**

**=less relapse**

***early disease***

**BM**

**less cGvHD**

**better QOL**

**can live with relapse**

## **Genova BMT Andrea Bacigalupo**

**Maria T Van Lint**

**Francesco Frassoni**

**Teresa Lamparelli**

**Francesca Gualandi**

**Domenico Occhini**

**Stefania Bregante**

**Anna Maria Raiola**

**Carmen Di Grazia**

**Alida Dominietto**

**R Varaldo**

***Data Center***

***Rosi Oneto***

***Barbara Bruno***

***Nurses***

**II Divisione ematologia**

***Biologi Laboratorio 5/ II Piano***  
**5 Terra**

**Consulente scientifico Prof. A.M. Marmont**

**It. Bone Marrow Donor Registry (IBMDR)**

**IST Radioterapia CTO**



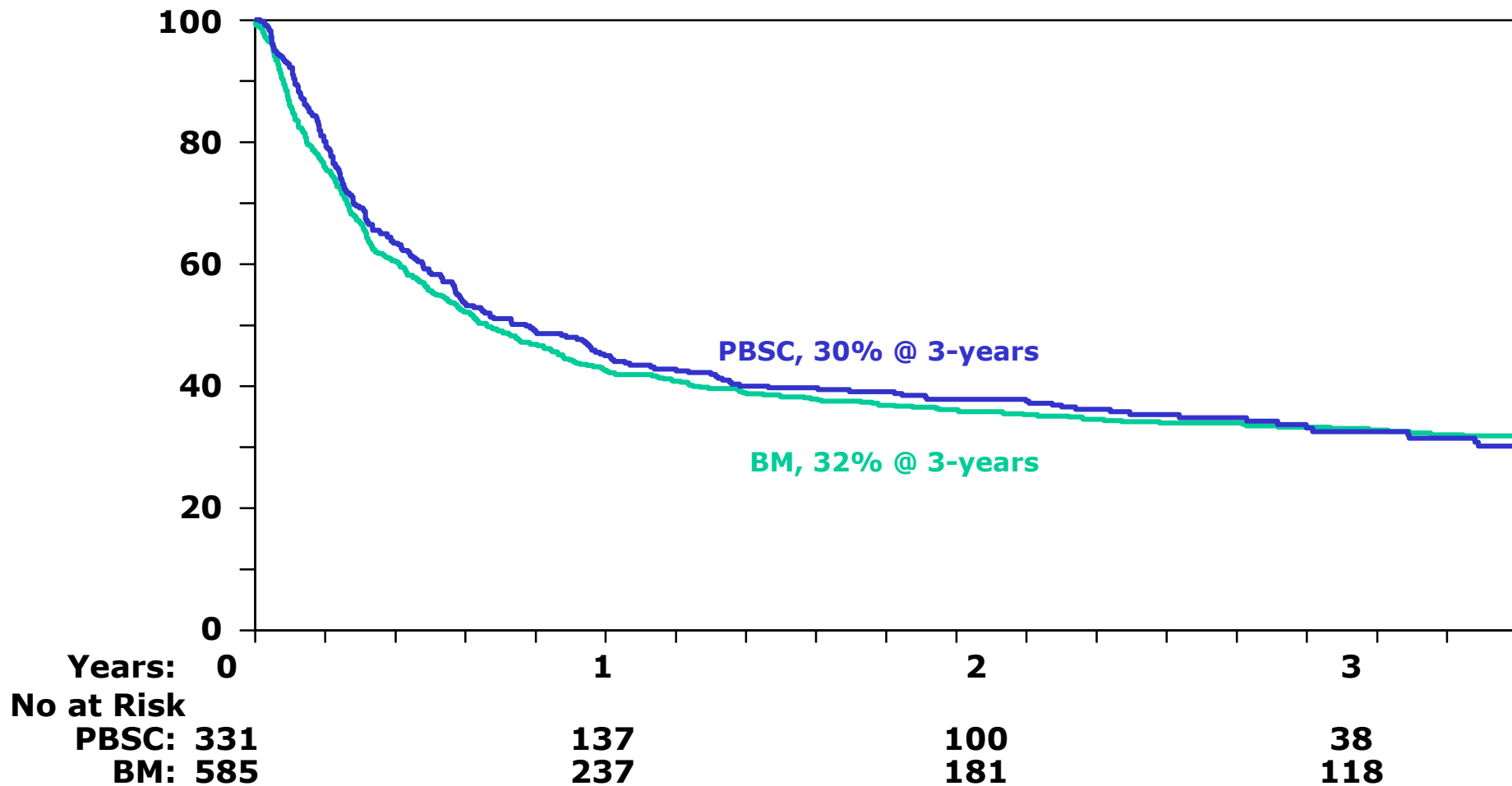
**Have PB grafts made  
UD TX more  
successful**

**??**

# Patient Selection

- PB=331 and BM=586
- U.S.
- 2000-2003
- 18-60 years of age
- ALL, AML, MDS and CML
- Median follow-up:
  - 34 and 38 months after PB and BM transplants

# Leukemia-free Survival



## **Future directions**

**# expansion of MSC / other accessory**

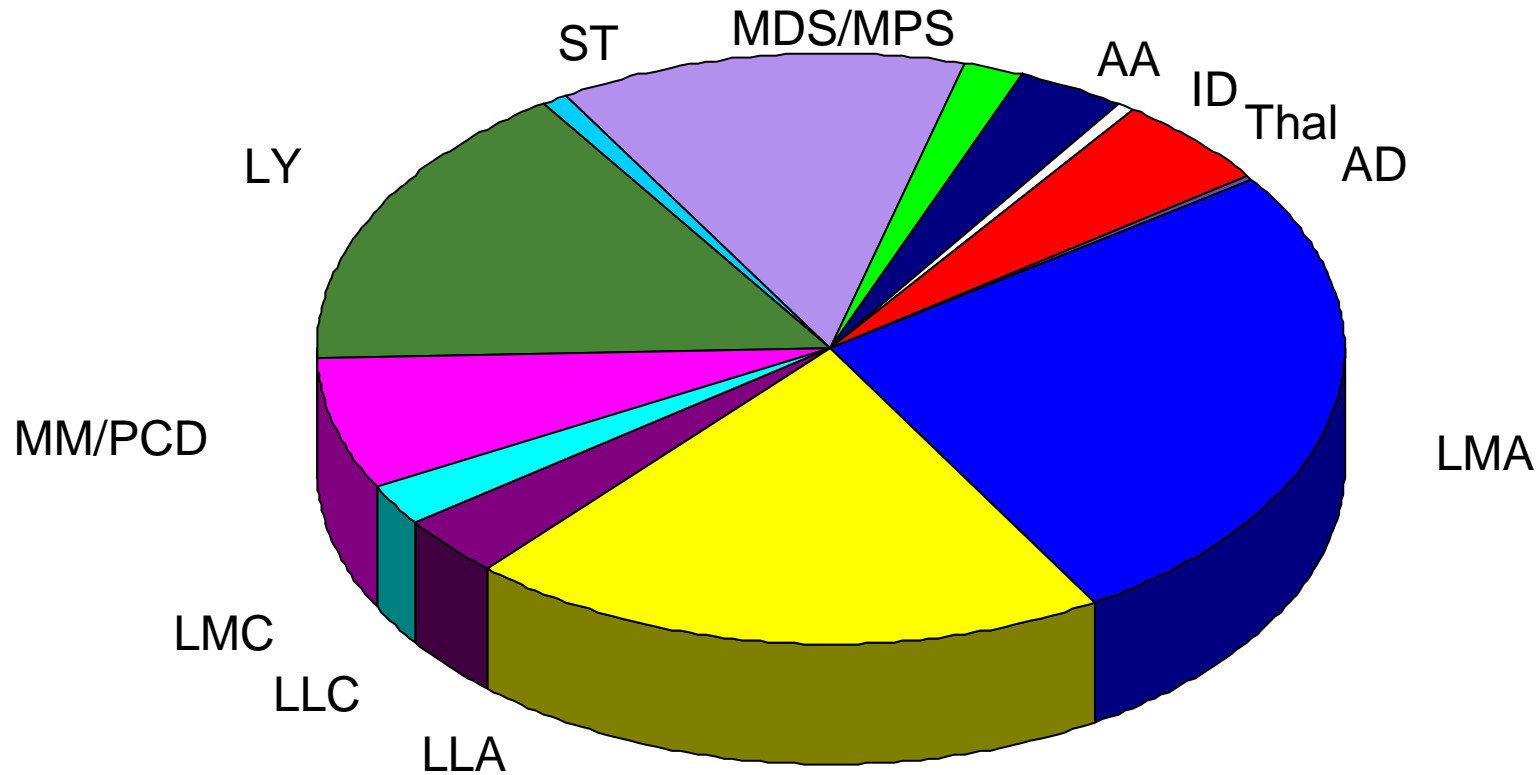
**# stem cell selection**

**# delayed /repeated stem cell infusions**

**# defined T cell dose**

**# expanded non allo-reactive T cells**

# GITMO Trapianto Allogeneico TRAPIANTI PER TIPO DI PATOLOGIA Attività 2007



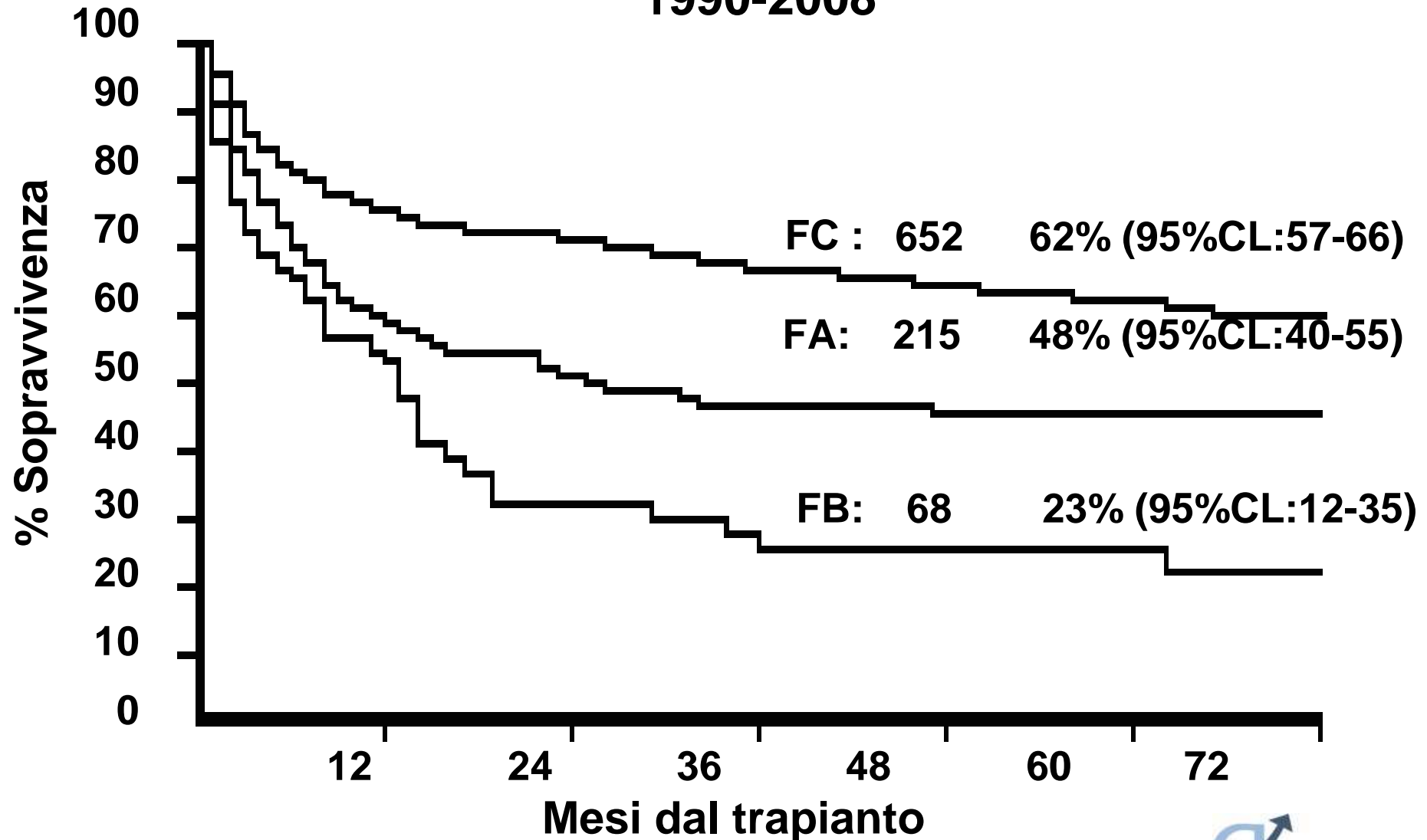
→ n=350  
 n=44  
 n=97  
 n=10  
 n=27  
 n=7  
 n=4

- Leucemia Mieloide Acuta
- Leucemia Linfatica Cronica
- MielMult/Plasmacell
- Tumori Solidi
- Errori genetici
- Immunodeficienze
- AD

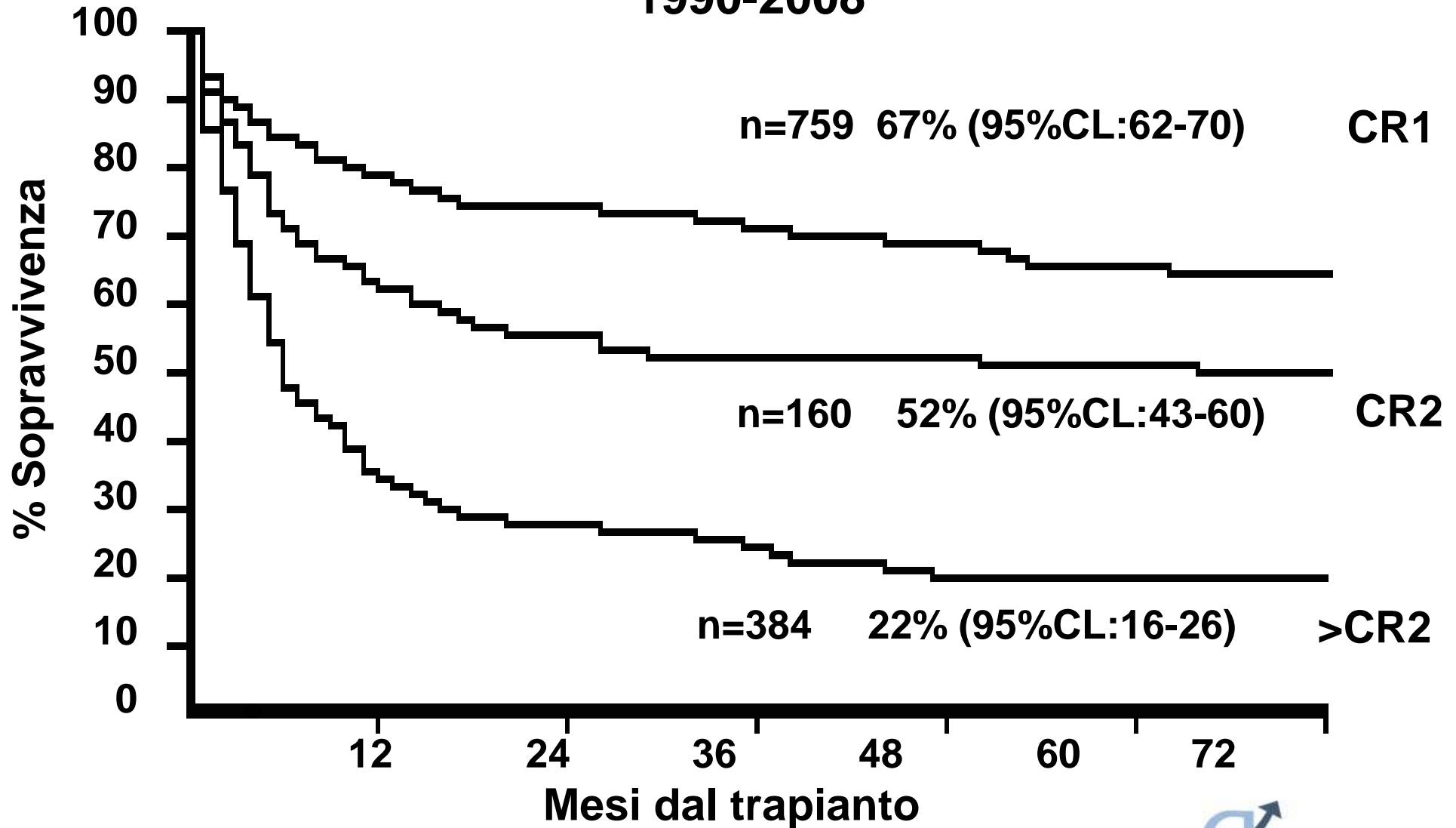


n=274 ■ Leucemia Linfatica Acuta  
 n=31 ■ Leucemia Mieloide Cronica  
 n=219 ■ Linfomi  
 n=171 ■ MDS/MPS  
 n=45 ■ Anemia Aplastica  
 n=68 ■ Talassemia

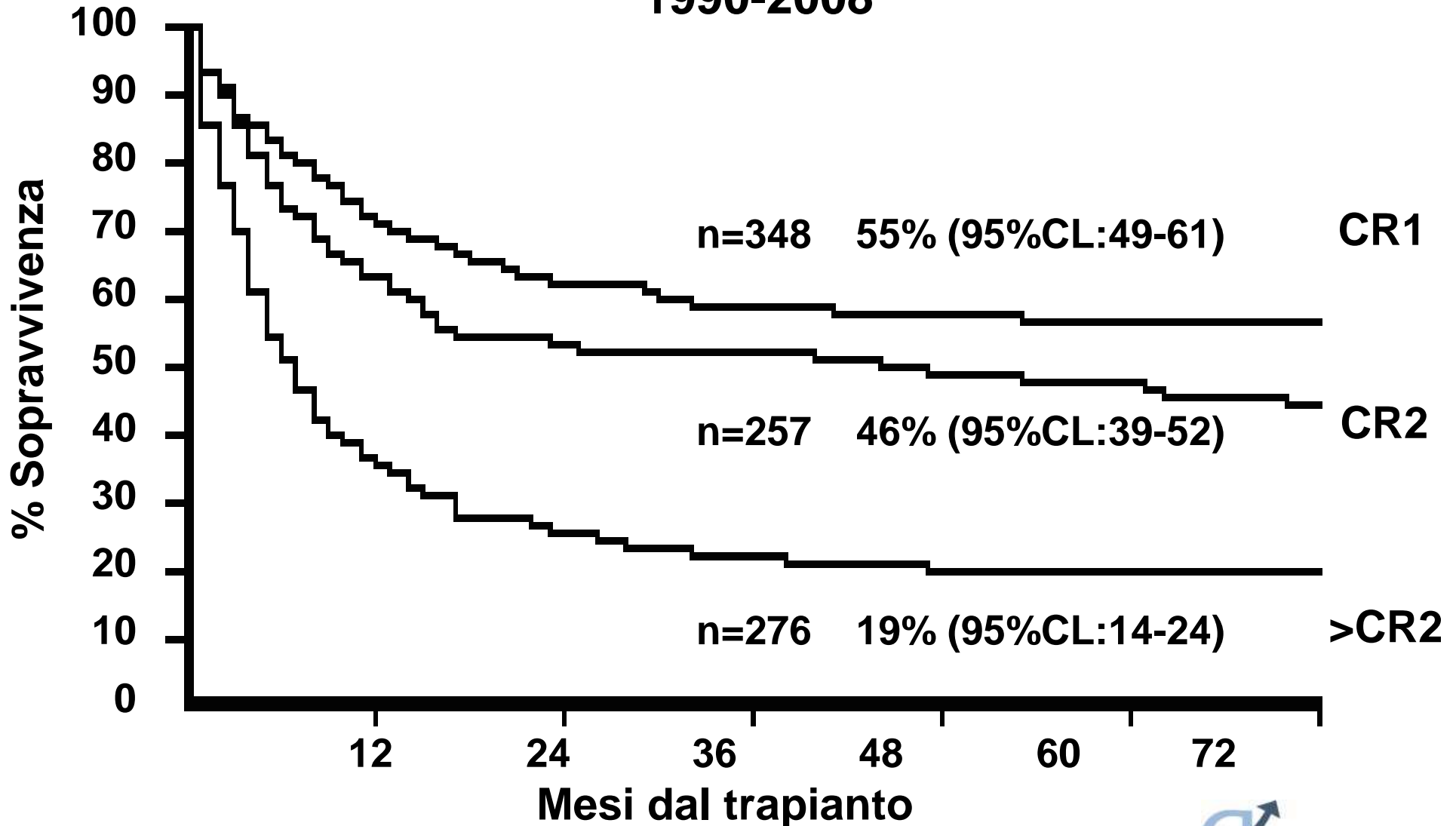
## Sopravvivenza nella LMC HLA id. sib. 1990-2008



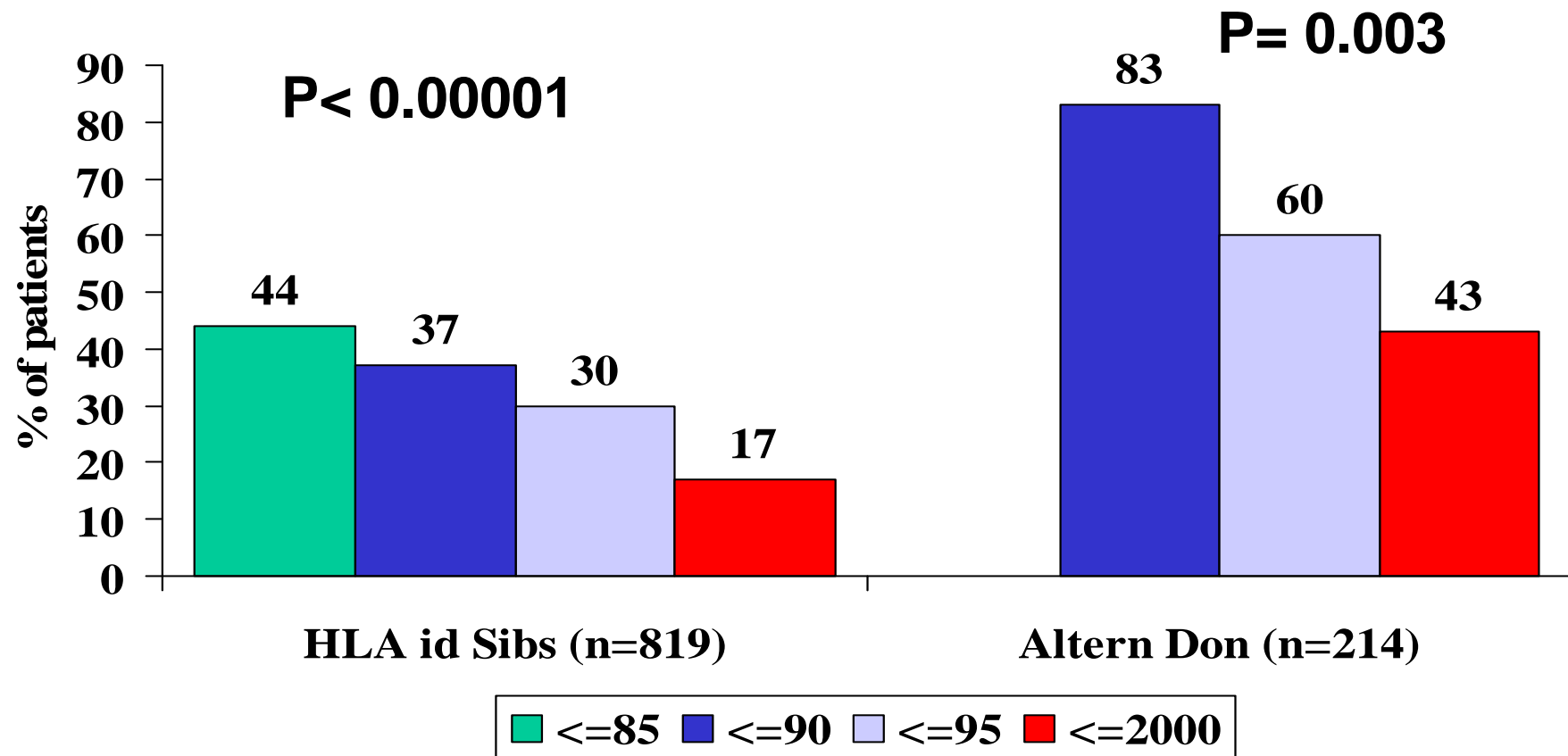
## Sopravvivenza nella LMA HLA id. sib. 1990-2008



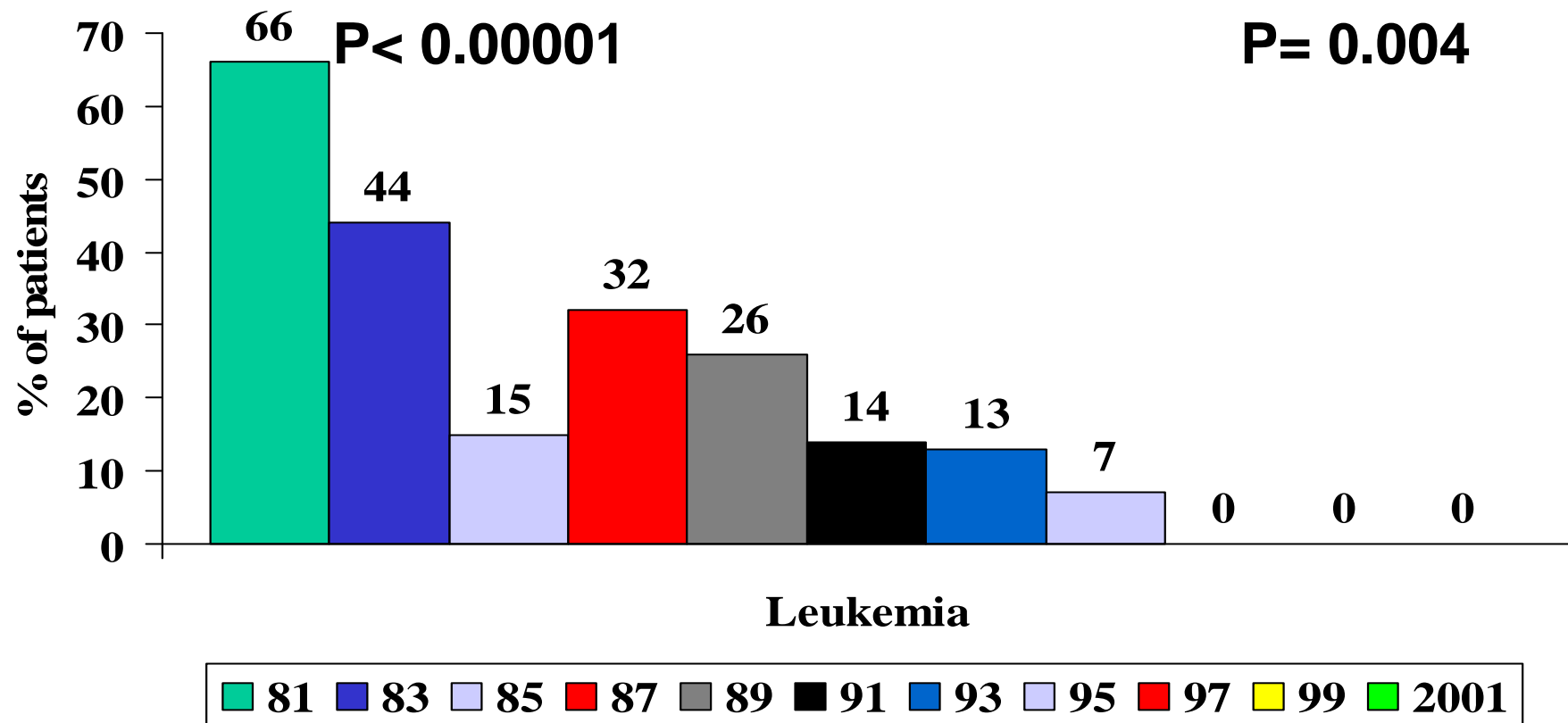
## Sopravvivenza nella LLA HLA id. sib. 1990-2008



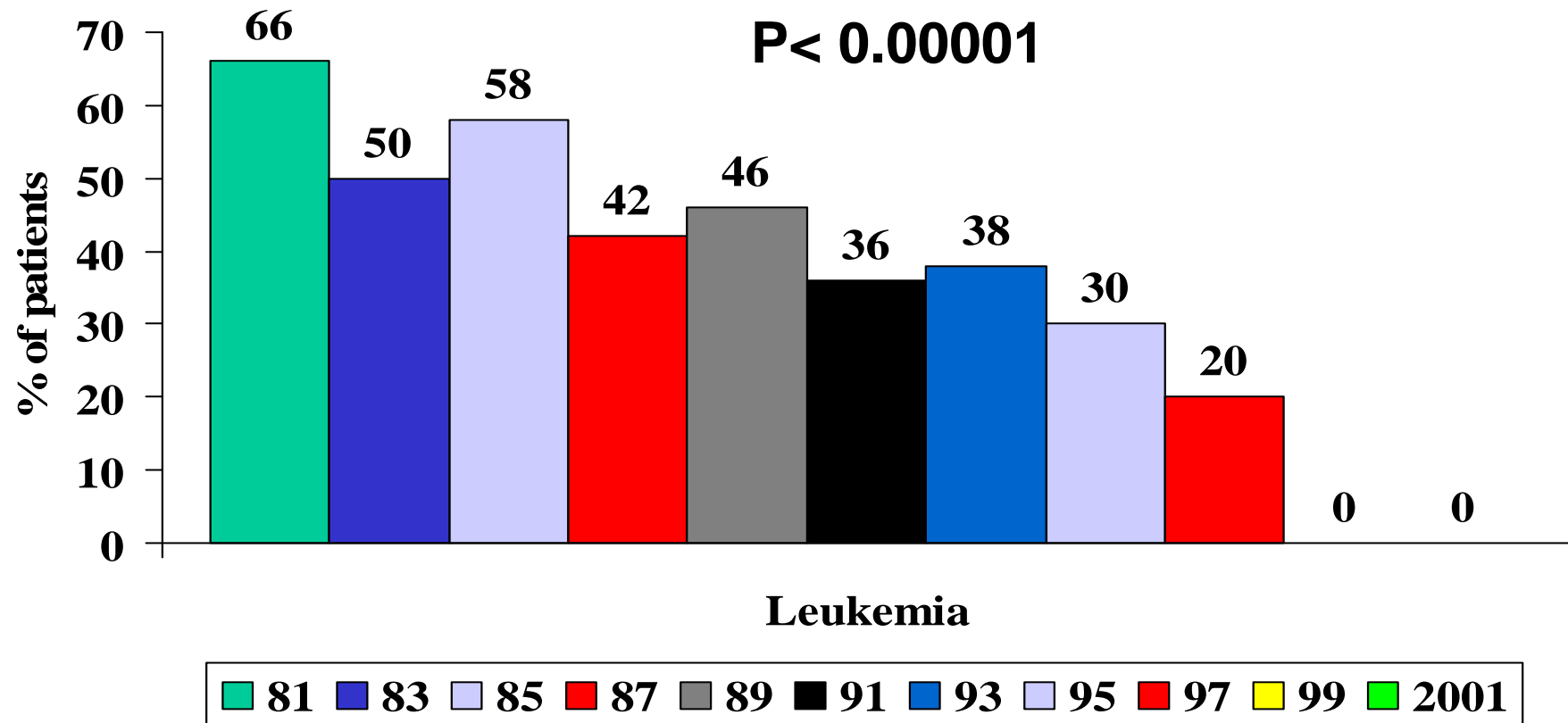
# Reduction of TRM : N= 1033 allo Tx , SM Genova



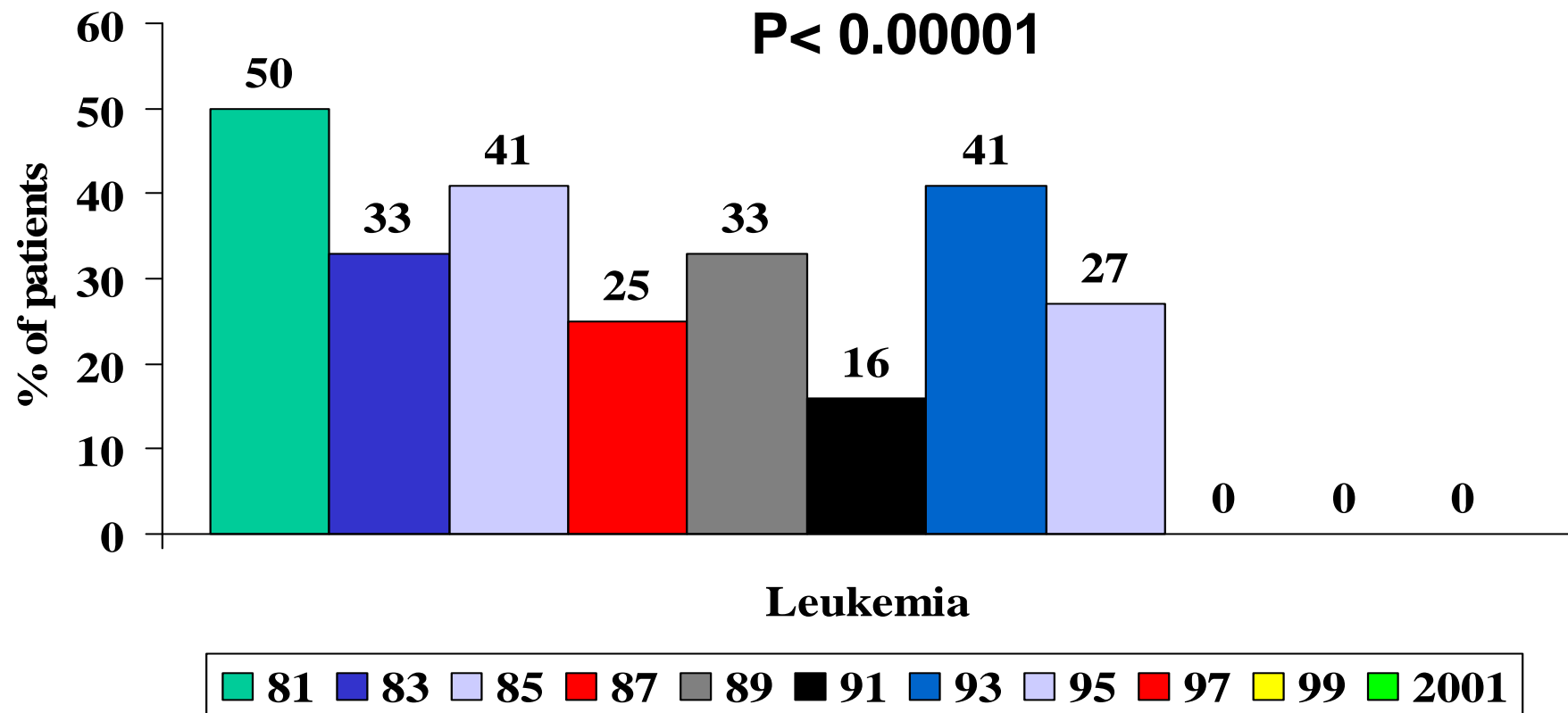
# Reduction of TRM in AML 1st CR HLA=sib N= 177 SM Genova



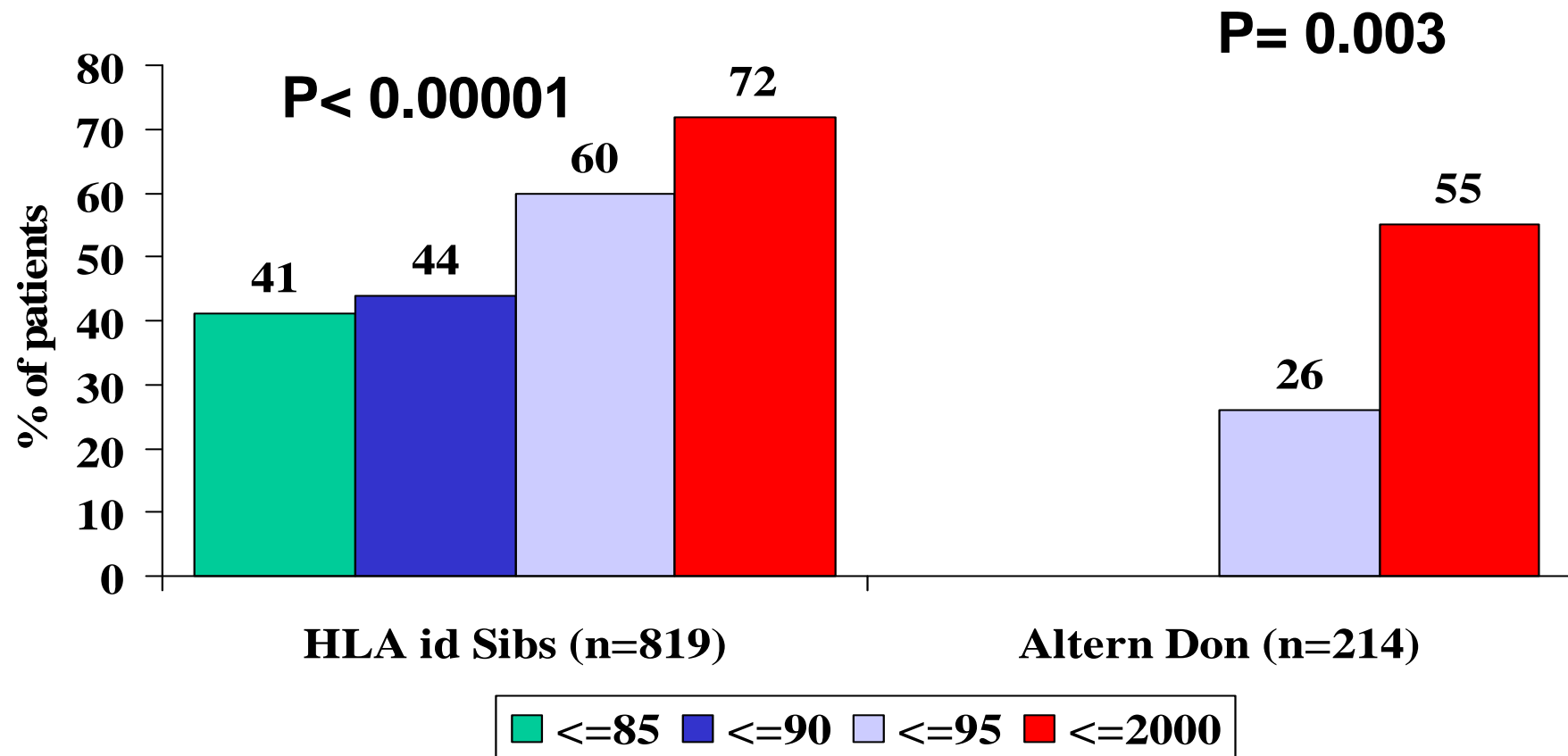
# Reduction of TRM in CML 1CP HLA=sib N= 172 SM Genova



# Reduction of TRM in ALL 1-2 CR HLA=sib N= 133 SM Genova



Improved survival with time :  
N= 1033 allo Tx , SM Genova



# Trapianto allogenico di midollo 2009

## Conclusioni

- Terapia curativa nel 70% dei paz. in fase precoce
- > numero donatori non familiari
- Atteachment sovrapponibile a PBSC
- Meno GVHD cronica estesa
- Ridotta mortalita' trapiantologica
- Follow up > 25 anni
- Terapie alternative non sempre ablative  
Follow up breve (3-4 anni)

# Study Schema - Donor

Identical Sibling Donor  
Age 16-60



**R**

*PBPC*



*Bone-marrow*



*Leukapheresis D5 (6, 7)*



*Harvest*



# Donor Hospitalisation

	<b>BMT</b>	<b>PBPCT</b>
<b>N</b>	<b>153</b>	<b>149</b>
<b>Mean</b>	<b>2.0</b>	<b>0.7</b>
<b>Median</b>	<b>2.0</b>	<b>0.0</b>
<b>Range</b>	<b>0.0 – 7.0</b>	<b>0.0 – 8.0</b>
	<b>p &lt; 0.0001</b>	
<b>0 nights</b>	<b>5 (3%)</b>	<b>111 (74%)</b>
<b>1 night</b>	<b>21 (14%)</b>	<b>9 (6%)</b>
<b>≥ 2 nights</b>	<b>127 (83%)</b>	<b>29 (20%)</b>

# Donor Restricted Activity

	<b>BMT</b>	<b>PBPCT</b>
<b>N</b>	<b>149</b>	<b>142</b>
<b>Mean (Days)</b>	<b>10.3</b>	<b>3.6</b>
<b>Median (Days)</b>	<b>6.0</b>	<b>2.0</b>
<b>Range</b>	<b>0.0 – 192.0</b>	<b>0.0 – 23.0</b>
	<b>p &lt; 0.0001</b>	
<b>0 days</b>	<b>3 (2%)</b>	<b>22 (15%)</b>
<b>1 day</b>	<b>10 (7%)</b>	<b>33 (23%)</b>
<b>2 – 7 days</b>	<b>76 (51%)</b>	<b>66 (46%)</b>
<b>≥ 8 days</b>	<b>60 (40%)</b>	<b>21 (15%)</b>

# Donor Adverse Events

**BMT**

**PBPCT**

<b>Any adverse events</b>	<b>57%</b>	<b>65%</b>
<b>Pain skeletal</b>	<b>2%</b>	<b>26%</b>
<b>Headache</b>	<b>5%</b>	<b>13%</b>
<b>Alk.Phosphatase</b>	<b>0%</b>	<b>5%</b>
<b>LDH increased</b>	<b>0%</b>	<b>9%</b>
<b>Myalgia</b>	<b>0%</b>	<b>8%</b>
<b>Nausea</b>	<b>7%</b>	<b>2%</b>
<b>Vomiting</b>	<b>5%</b>	<b>0%</b>
<b>Anaemia</b>	<b>10%</b>	<b>0%</b>
<b>Access pain</b>	<b>23%</b>	<b>1%</b>

## Retrospective

PMN Plt Tx aGvHD

Bensingher 1996 74 faster faster fewer =

Przepiorka 1997 55 faster faster fewer =

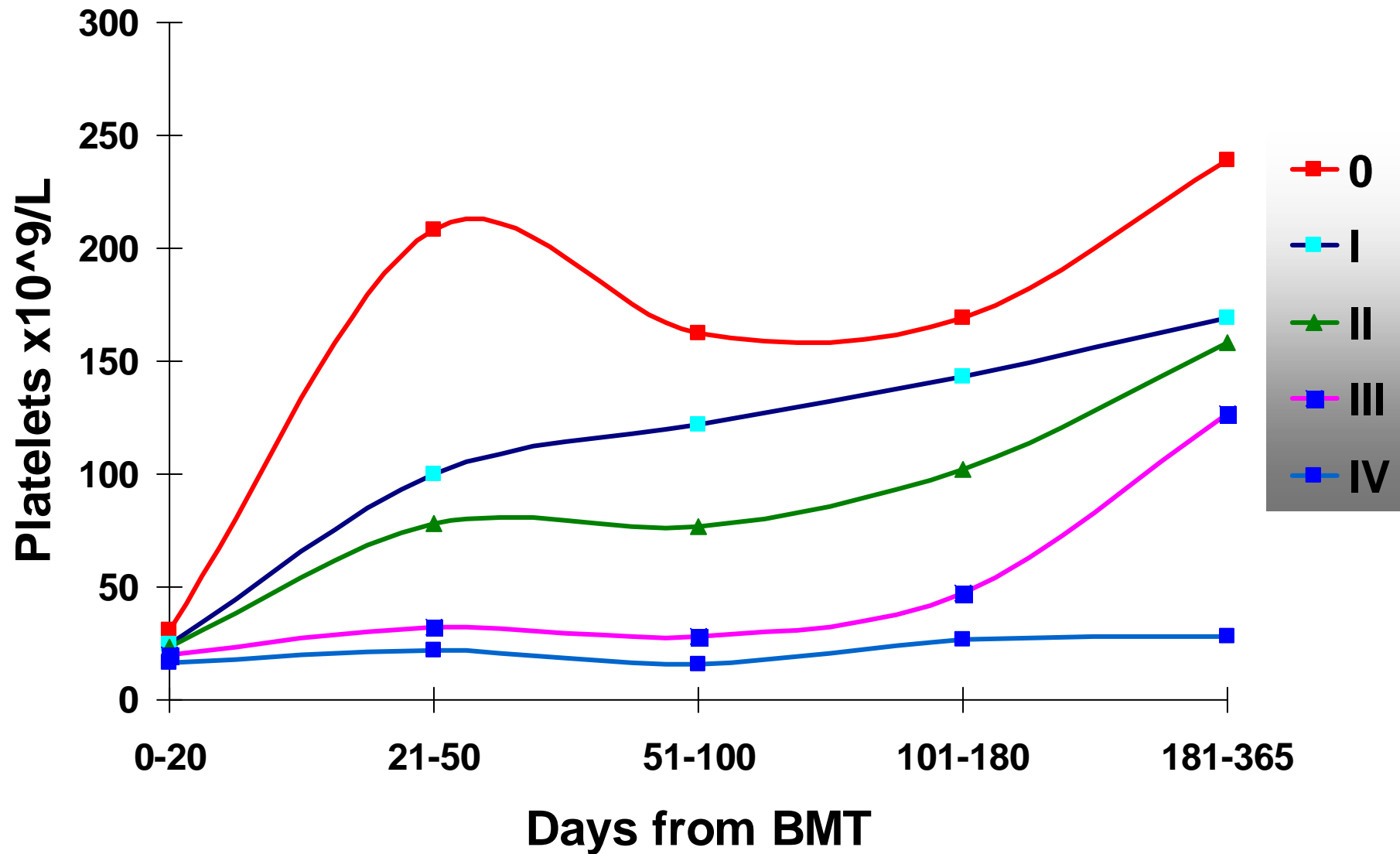
Bacigalupo 1998 97 faster faster fewer =

Ustun 1999 80 faster faster fewer =

Russell 1999 87 faster faster fewer =

Champlin 2000 824 faster faster fewer =

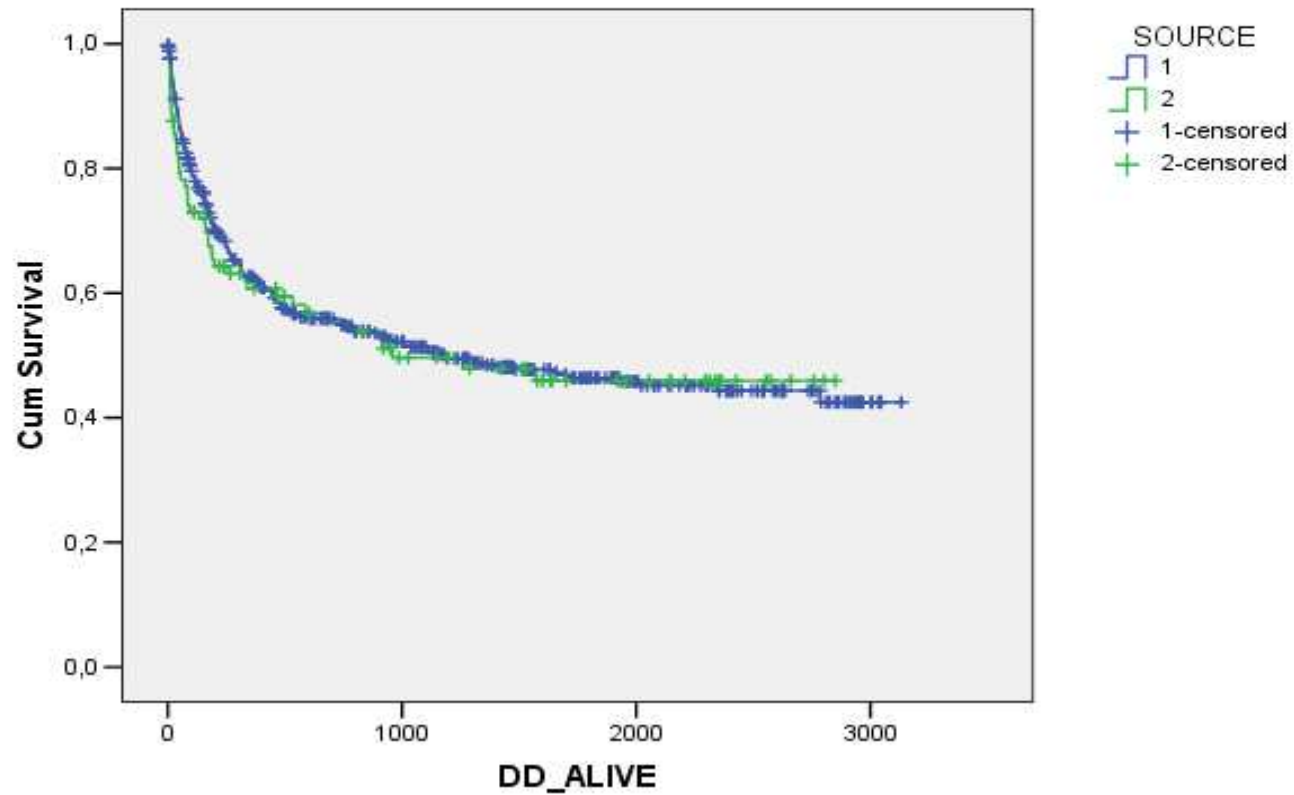
# The effect of aGvHD on platelets reconstitution: 351 pts; CY-TBI; hem.malignancies; =/alt don



ok

BM n=504 43%  
PBSC n=97 46%  
P=0.74

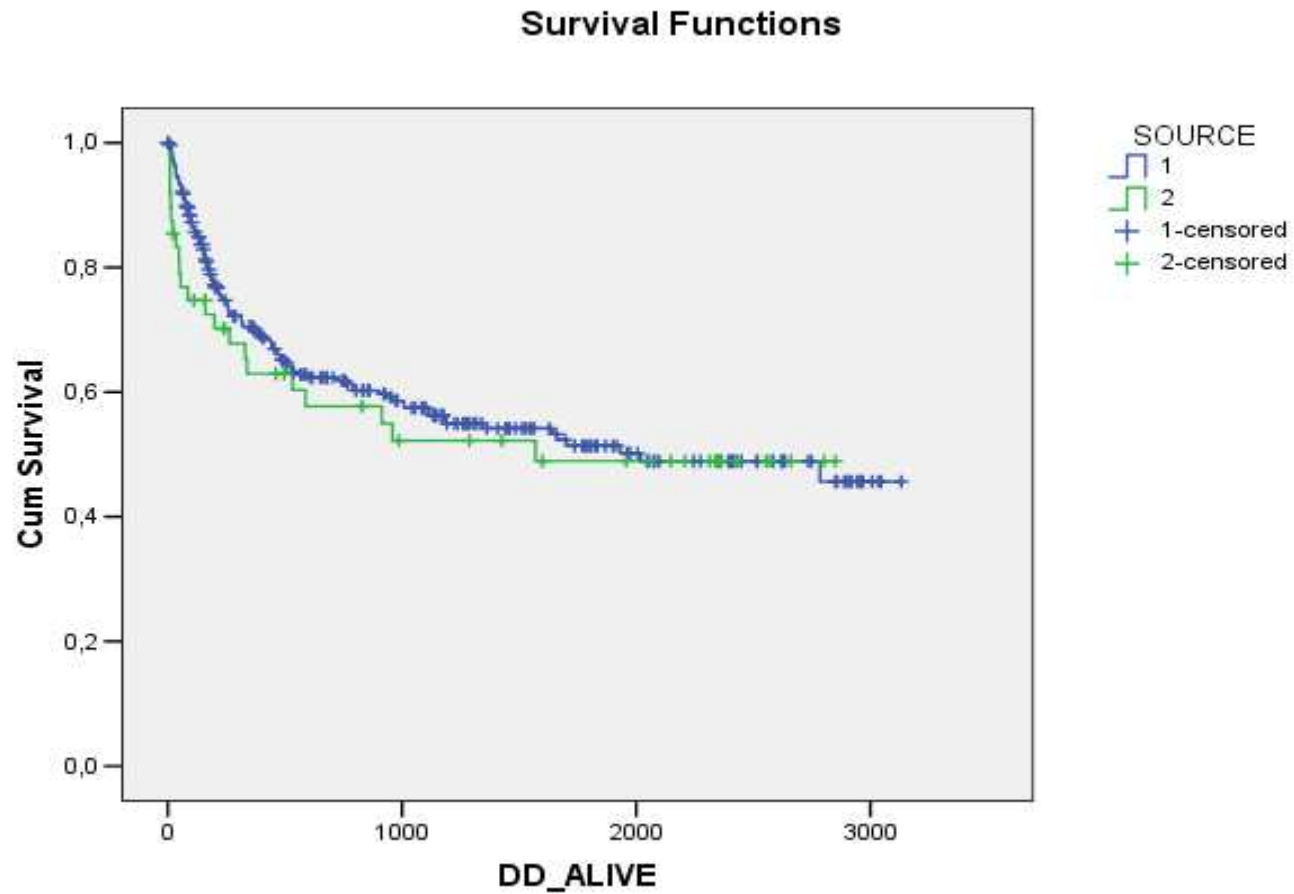
Survival Functions



In HLA id.sib

ok

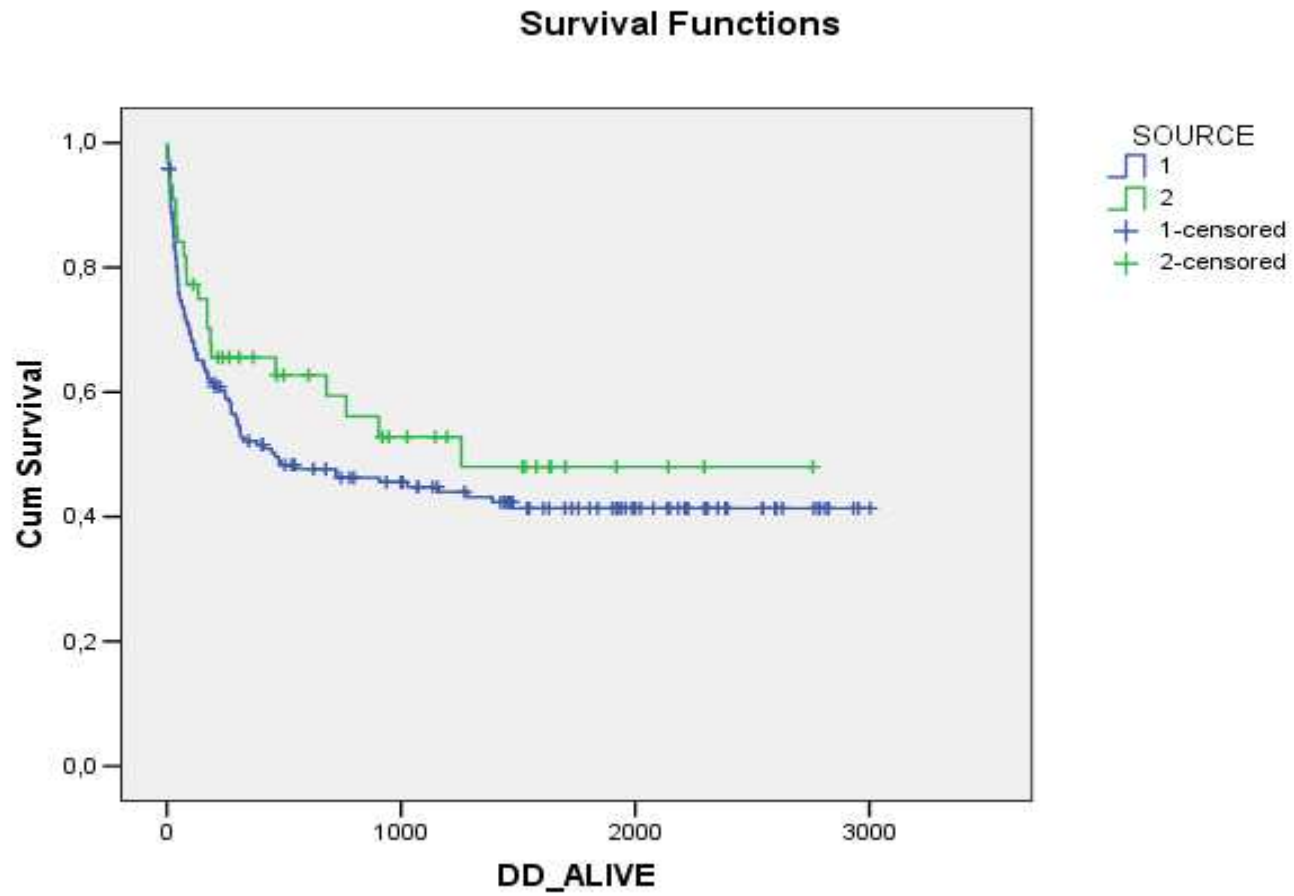
BM n=271 46%  
PBSC n=48 49%  
P=0.55



MUD

ok

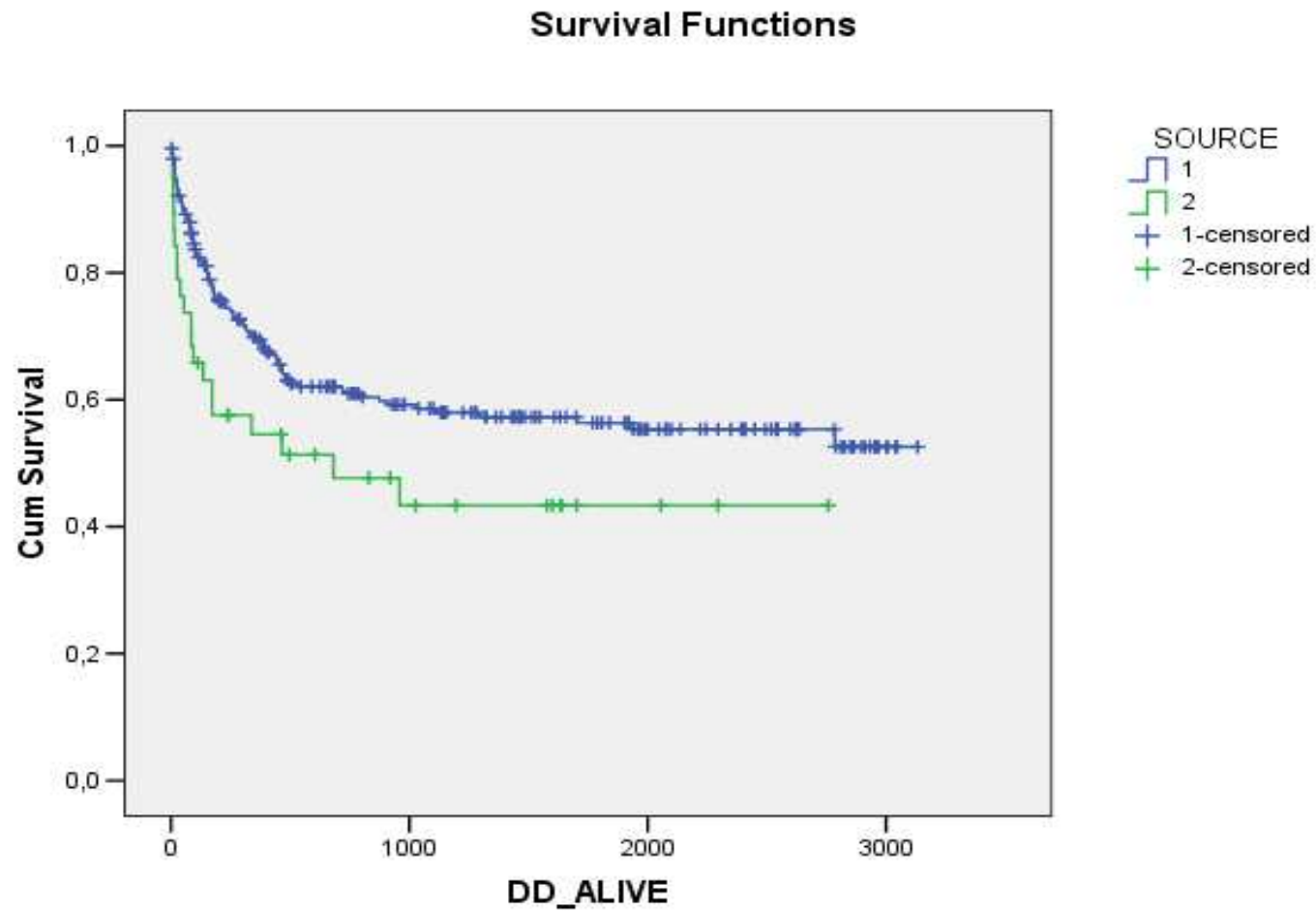
BM n=168 41%  
PBSC n=44 48%  
P=0.28



In patients under 40 years

BM n=243 53%  
PBSC n=38 43%  
P=0.046

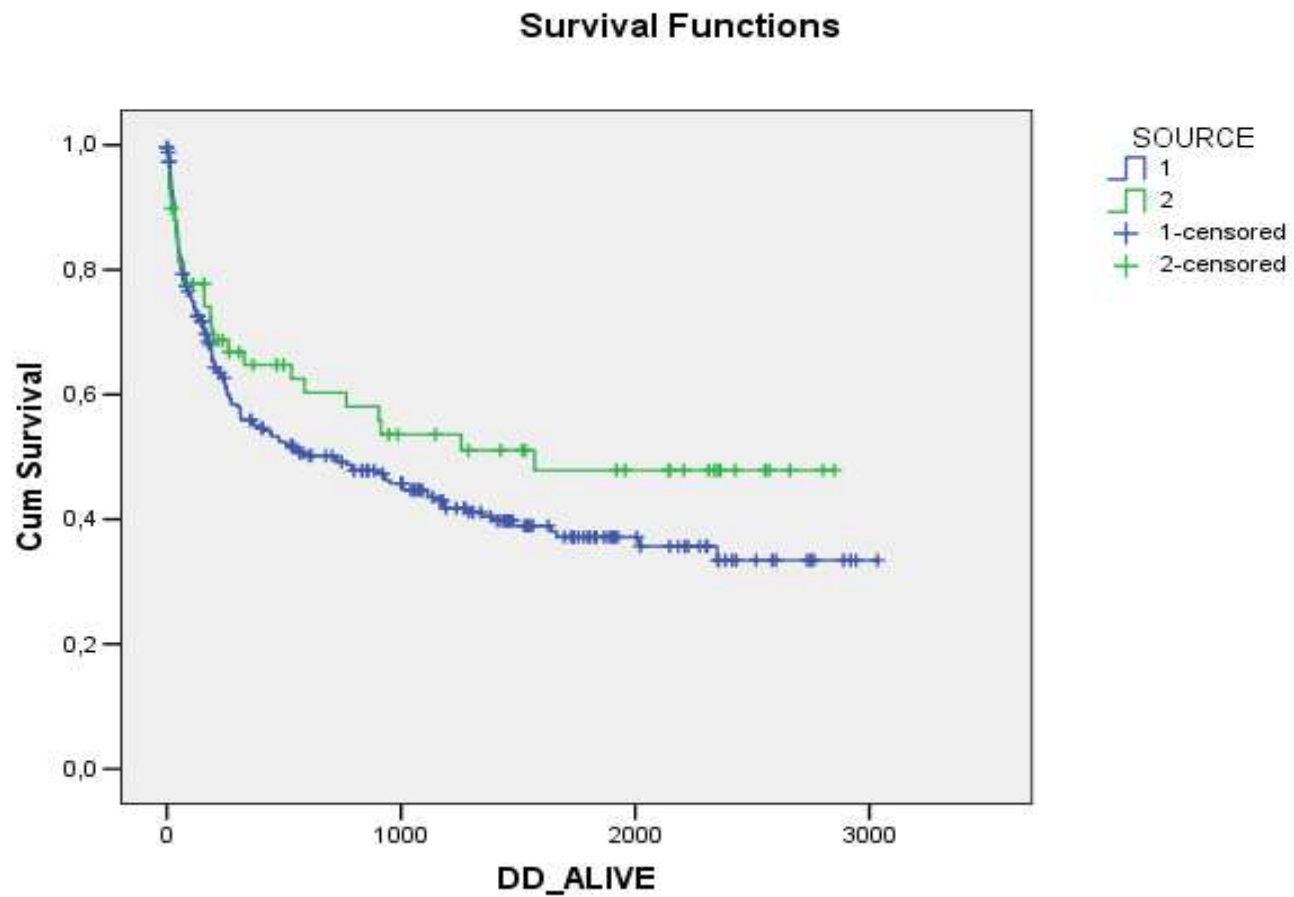
ok



In patients  $\geq 40$  years

BM n=261 33%  
PBSC n=59 48%  
P=0.16

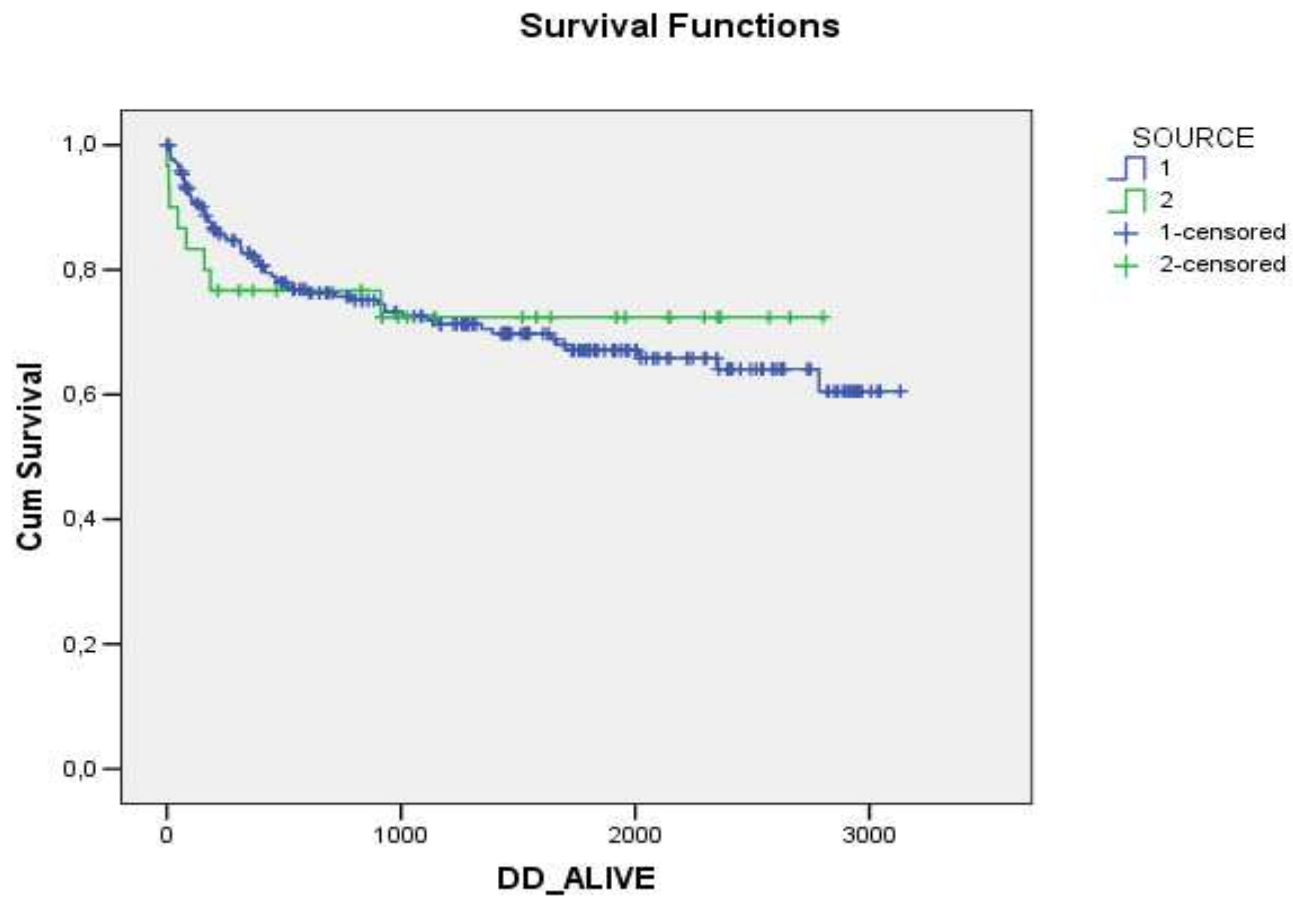
ok



## Fase precoce

BM      n=217    60%  
PBSC    n=30      72%  
P=0.9

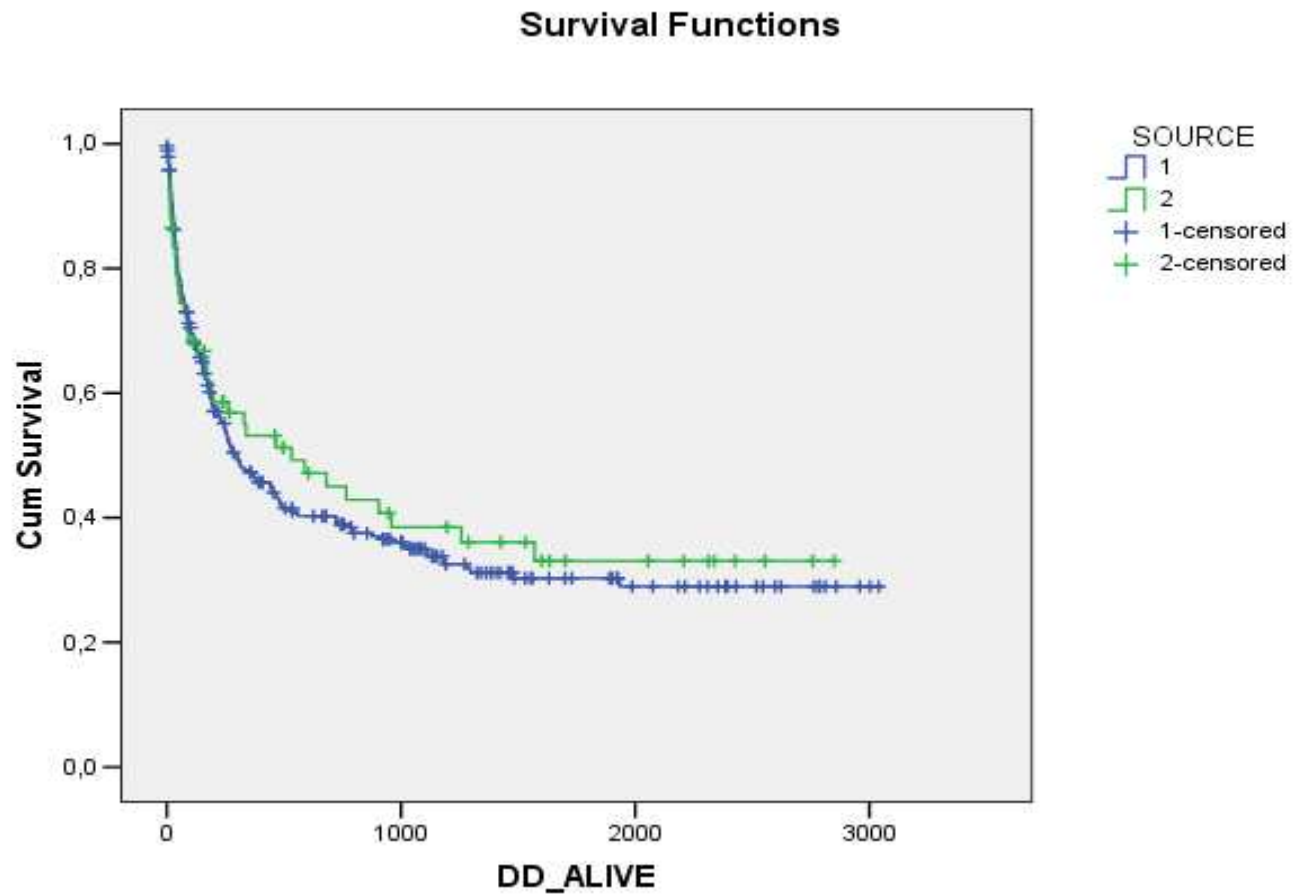
ok



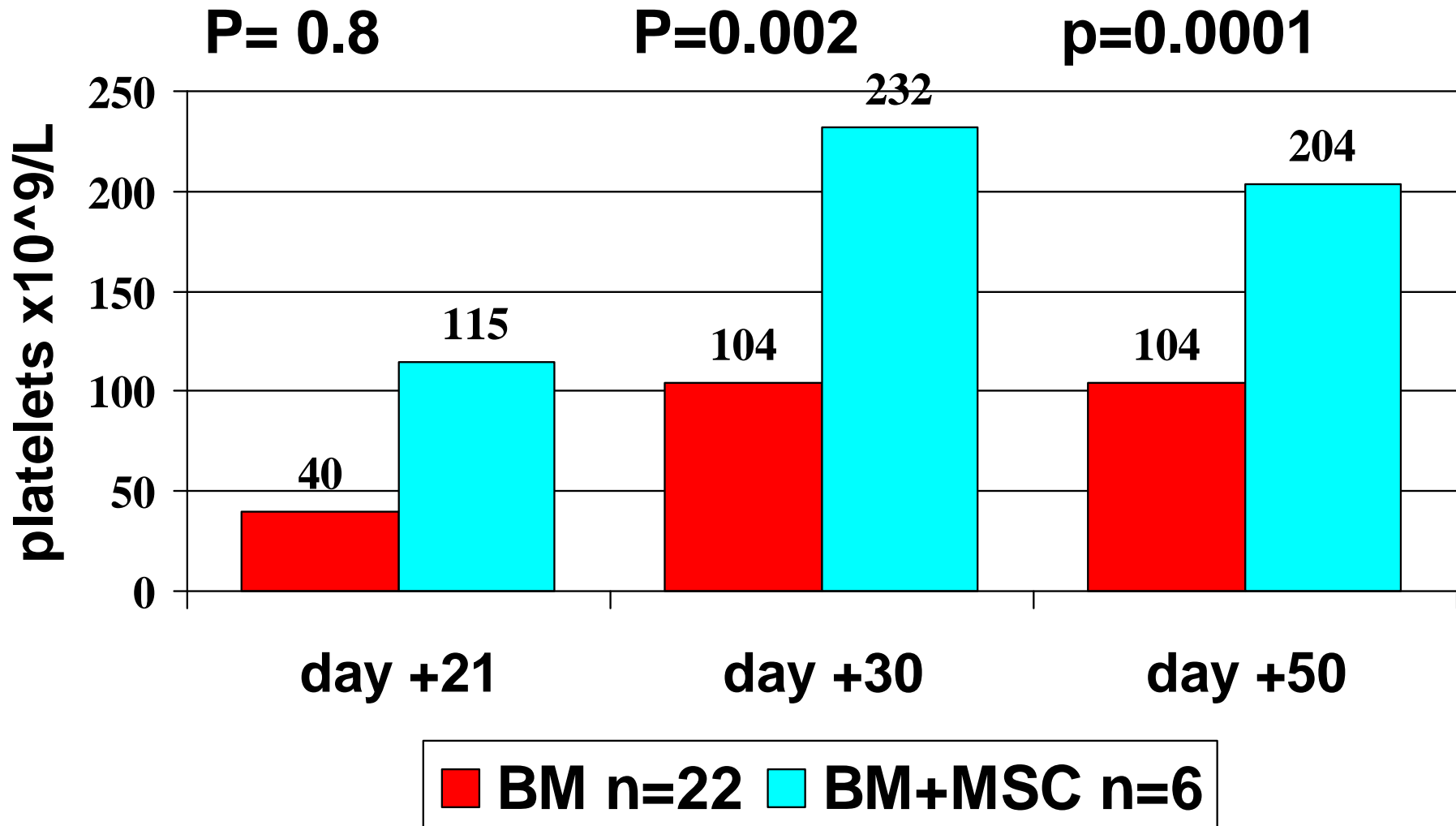
## Fase avanzata

BM n=287 29%  
PBSC n=67 33%  
P=0.55

ok



# Plt after allo-BMT; HLA id sibs; THIO-CY; BM vs BM+expanded MSC (1-5x10<sup>6</sup>/kg)



# Hemopoietic stem cell transplantation Peripheral Blood versus Bone Marrow

