

*Ercolano, 13-14 giugno 2019*  
*Summer School AIBT 2019*

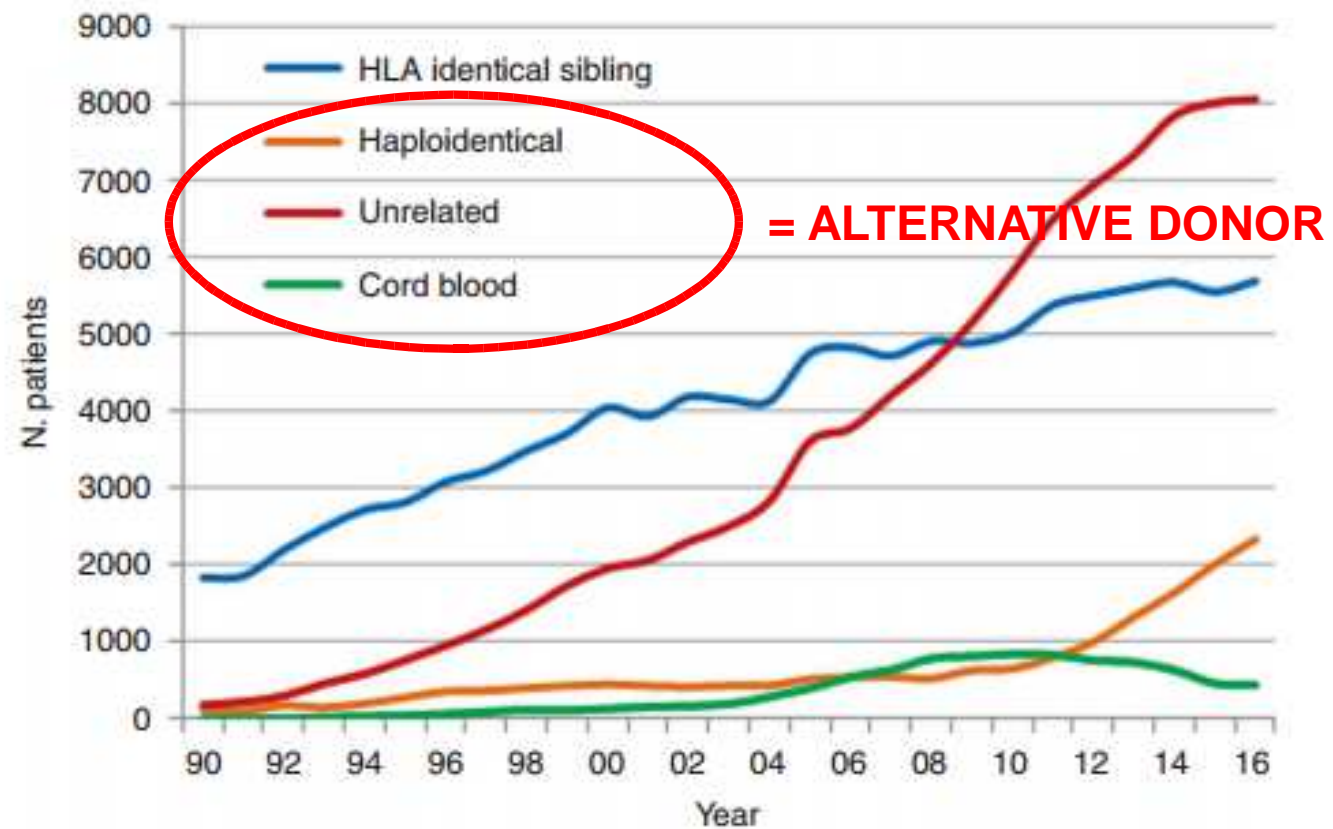
## **La selezione del donatore alternativo di CSE: il punto di vista del cli**

**Alessandra Picardi**  
**UOC Ematologia con Trapianto di CSE e Terapia Intens**



# The 2016 European Society for Blood and Marrow Transplantation Transplant Activity Survey

## Trend in the absolute numbers of SCT in Europe 1990-2016



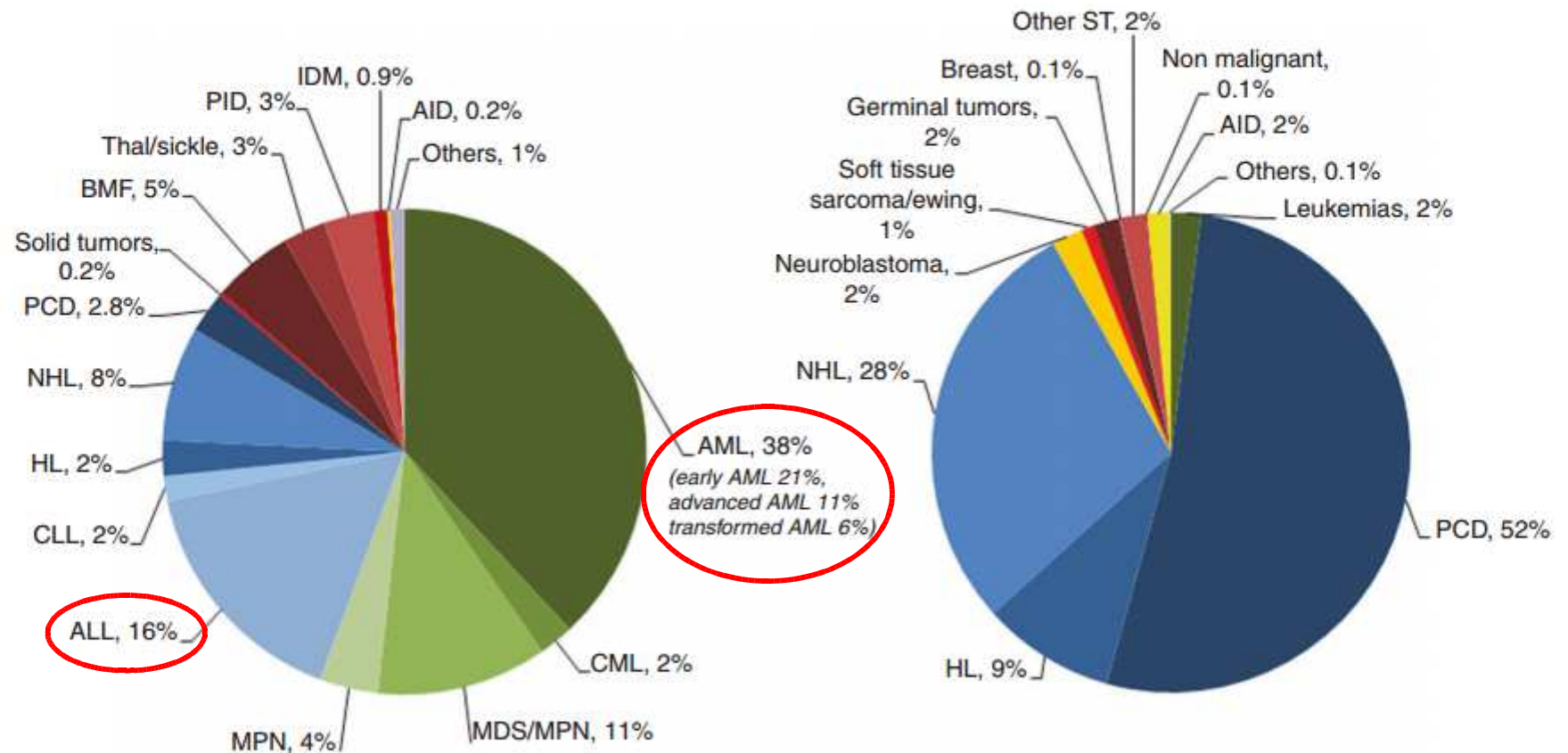
# Which factors do you consider during the alternative donor search process?

- Strategy in alternative donor selection:
  - Timing
  - Donor Availability
  - Stem Cell Source
  - Type of Donor & HLA matching
  - Clinical factors

**Transplant Centre  
Policy**

# The 2017 European Society for Blood and Marrow Transplantation Transplant Activity Survey

## Disease indications for hematopoietic stem cell transplantation



**Allogeneic SCT**

**Autologous SCT**

# Timing of HLA Typing in Acute Leukem

*Risk-adapted, MRD-directed therapy for young adults  
with newly diagnosed acute leukemia*



**HLA typing at diagnosis : patients of 18 - 70 years**  
Aim: selection of best donor

# HSCT: Team-work and operative synergy

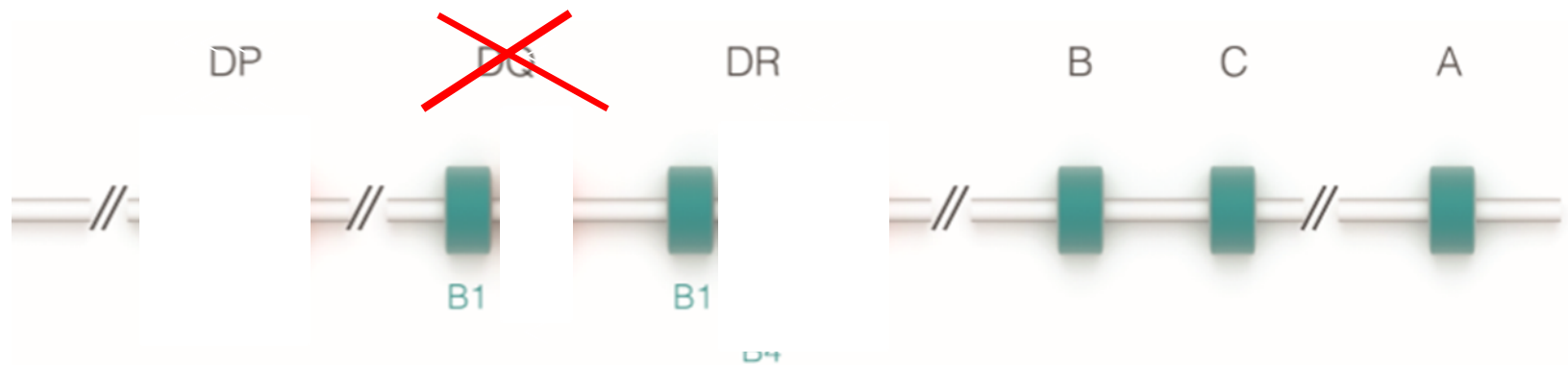


**Family involvement for HLA typing at diagnosis of AML: both parents and siblings**

- ✓ Haplotype segregation
- ✓ Knowledge of family composition
- ✓ Clinical evaluation before HLA typing of parents and siblings
- ✓ Offsprings

# Donor's Availability

HLA Typing for Unrelated Donor Search



**Which donor do you search? 10/10 or 8/8 HLA matched?**

# Donor's Availability

**Table 2.** Overall probabilities of identifying a 7/8, 8/8, 9/10 and 10/10 matched unrelated donor.

Ethnic origin (country) <sup>a</sup>	Match 8/8	Match ≥7/8	Match 9/10	Match 10/10	Match 9-10/10	Reference
European (NL)					69% <sup>e</sup>	62
European (UK)					72%	63
European (A)					80% <sup>f</sup>	64
European (D)			20%	61%		17
European (CH)			24%	58%		7
European (NL)			31%	48%		46
European (IT)			32%	43%		65
European (HR)			30%	65%		66
European (USA)	75%	97%				18
African (USA)	18%	71%				18
ME/NA (USA) <sup>b</sup>	46%	90%				18
Asian (USA) <sup>c</sup>	27-42%	76-88%				18
Hispanic (USA) <sup>d</sup>	34%	80%				18

<sup>a</sup>NL: the Netherlands; UK: United Kingdom; A: Austria; D: Germany; CH: Switzerland; HR: Croatia; USA: United States of America; <sup>b</sup>ME: Middle Eastern; NA: North African; <sup>c</sup>Chinese, Korean, South Asian, Japanese, Southeast Asian, Vietnamese; <sup>d</sup>Hispanic: South/Central American; <sup>e</sup><9/10 in 13% patients; <sup>f</sup>exceptionally 8/10 matched donors.

*Tiercy et al, Haematol*

# Donor's Availability

Cattura rettangolare

Table 2. Adult-Donor Availability in 2010, According to Broad Racial and Ethnic Category.				
Racial and Ethnic Category*	Confirmatory Typing Available†	Typing Not Discrepant‡	Workup Available§	Available Overall
	percentage of donors			
White	62	98	83	51
Black	36	95	69	23
Asian or Pacific Islander	42	97	73	29
Hispanic	44	96	68	29
Native American	45	98	63	28

## ORIGINAL ARTICLE

# Ethnicity, length of time on the register and sex predict donor availability at the confirmatory typing stage

RN Lown<sup>1,2</sup>, SGE Marsh<sup>1,2</sup>, GE Switzer<sup>3,4,5,6</sup>, KA Latham<sup>1</sup>, JA Madrigal<sup>1,2</sup> and BE Shaw<sup>1,2,7</sup>

Despite over 20 million unrelated donors being listed worldwide, donor attrition at the confirmatory typing (CT) stage acquisition is a key source of delay. Anthony Nolan undertook a study of CT requests from 2010 to 2011 to identify factors associated with attrition. Of 7541 CT requests, 38.2% were cancelled for donor reasons. Of these, 19.4% were personal, medical, 36% no contact, 7.9% emigrated and 2.6% others. African (odds ratio (OR) 2.78,  $P < 0.001$ ), African-Caribbean ( $P < 0.001$ ), Asian (OR 2.65,  $P < 0.001$ ), Jewish (OR 1.54,  $P = 0.009$ ) and Mediterranean (OR = 2.38,  $P < 0.001$ ) donors were more likely not to be available compared to Caucasian donors. Female donors were also more likely not to be available (OR = 1.32,  $P = 0.001$ ) primarily due to pregnancy. Older donors were less likely to be available in univariate analysis, but this association was not significant after controlling for other factors. Blood donors and those recruited within the past five years had lower rates of attrition. Accumulation of additional attrition-associated characteristics for a given donor was associated with progressively greater attrition (OR 1.99, 2.52, 3.4 and 5.53, respectively, for 1, 2, 3 and 4 risk factors,  $P < 0.001$ ). Donor registries must develop driven strategies to recruit and retain the most reliable donors.

*Bone Marrow Transplantation* (2014) **49**, 525–531; doi:10.1038/bmt.2013.206; published online 13 January 2014

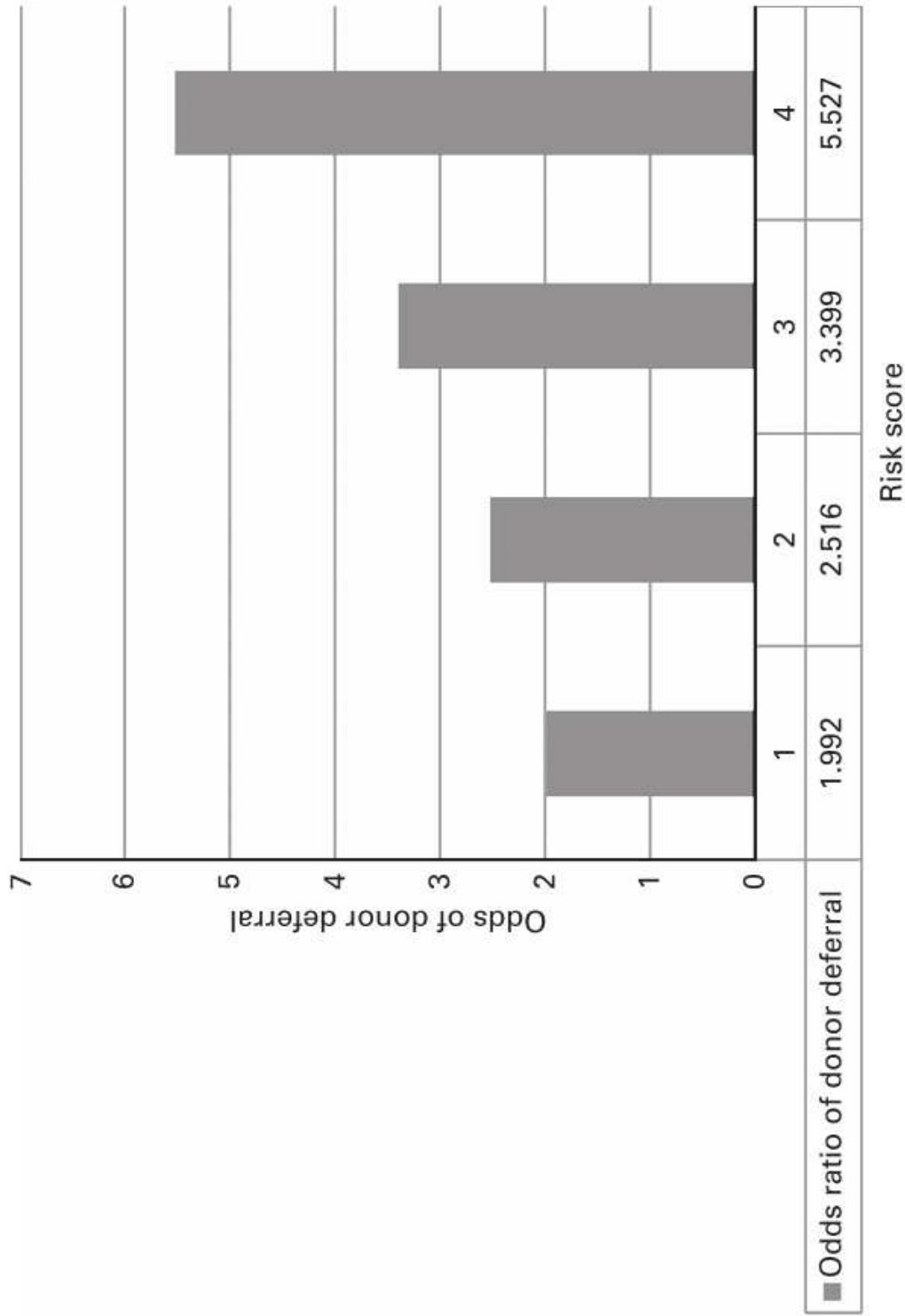
**Keywords:** marrow and SCT; allogeneic transplantation; donor attrition; unrelated donor; ethnicity

**Table 3.** Multivariate logistic regression analysis of donor characteristics influencing donor attrition

<i>Donor characteristic</i>	<i>Odds ratio for donor cancellation</i>	<i>95% Confidence interval</i>	<i>P-value</i>
<i>Age</i>			
18–30 <sup>a</sup>	1.00	—	—
31–45	1.01	0.87–1.17	0.95
46–60	0.89	0.70–1.13	0.33
<i>Sex</i>			
Male <sup>a</sup>	1.00	—	—
Female	1.22	1.07–1.38	0.003
<i>Ethnicity</i>			
White N European <sup>a</sup>	1.00	—	—
African	2.39	1.35–4.2	0.003
African Caribbean	1.50	0.97–2.32	0.07
Asian	2.64	1.94–3.60	< 0.001
Eastern European	0.78	0.24–2.51	0.68
Hispanic	0.96	0.10–9.28	0.97
Jewish	1.20	0.79–1.82	0.39
Mediterranean	2.55	1.50–4.34	0.001
Middle Eastern	2.20	0.70–6.89	0.18
Mixed race	1.47	0.81–2.67	0.20
Oriental	1.30	0.21–7.87	0.80
Other	2.20	1.04–4.66	0.04
<i>Blood donor</i>			
No <sup>a</sup>	1.00	—	—
Yes	0.68	0.60–0.78	< 0.001
<i>Duration on register</i>			
Less than 1–5 years <sup>a</sup>	1.00	—	—
6–10 years	1.53	1.32–1.78	< 0.001
11–15 years	1.47	1.18–1.79	< 0.001
16 years +	1.29	1.02–1.64	0.038

<sup>a</sup>Reference category.





**Figure 4.** Odds of donor deferral by risk score. The risk score is assigned according to the presence of certain attrition-related factors each assigned a score of 1. These factors include: female sex, African, African-Caribbean, Asian or Mediterranean ethnicity, blood donor and duration on the register > 5 years.

# Policy to face the Donor work up cancellation

- Back up donor: request of at least 2 confirmatory HLA typing for unrelated donor
- Considering Alternative Source at the start up of the search process: CB – Haplo for unrelated and matched related donor
- Autologous stem cell back up

# Stem Cell Sources

## **Bone Marrow**

**HSC = 0.01% out of Bone Marrow cells**

## **Peripheral Blood Stem Cells**

**HSC = 0.05 – 0.04% out of nucleated cells**

## **Cord Blood**

**HSC = 0.1 – 1% out of nucleated cells**

# CELL DOSE ACCORDING TO STEM CELL SOURCE

	Med CD34+ Content	Med CD3+ Content	Target Cell Dose
BONE MARROW	$2-3 \times 10^6/\text{kg}^*$	$25 \times 10^6/\text{kg}$	$\text{TNC} > 2 \times 10^8/\text{kg}$
PERIPHERAL BLOOD	$8 \times 10^6/\text{kg}$	$250 \times 10^6/\text{kg}$	$\text{CD34+} = 4-8 \times 10^6/\text{kg}$
UMBILICAL CORD BLOOD	$2 \times 10^5/\text{kg}$	$25 \times 10^5/\text{kg}$	$\text{TNC} > 3 \times 10^7/\text{kg}$

\*= recipient body weight

# STEM CELL SOURCE

**Matched Unrelated Donor**

# The NEW ENGLAND JOURNAL of MEDICINE

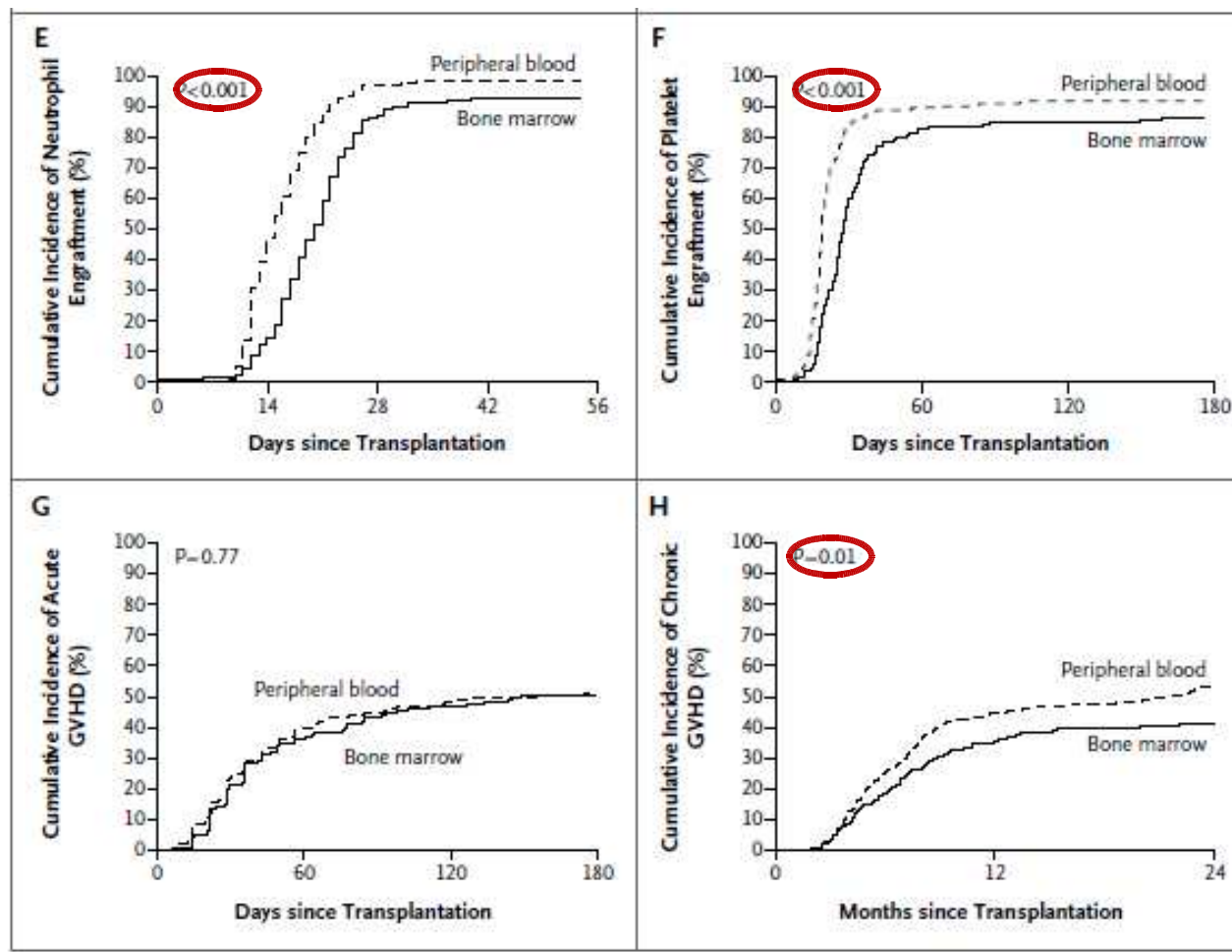
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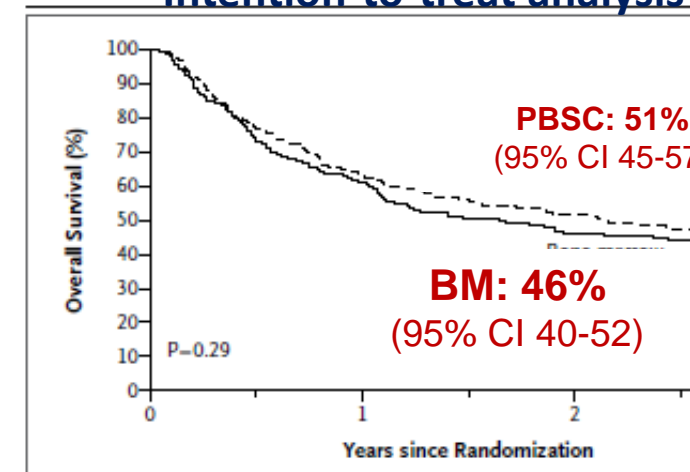
VOL. 367 NO. 16

## Peripheral-Blood Stem Cells versus Bone Marrow from Unrelated Donors

Claudio Anasetti, M.D., Brent R. Logan, Ph.D., Stephanie J. Lee, M.D., M.P.H., Edmund K. Waller, M.D., Ph.D.,



### Intention-to-treat analysis



**Failure: BM > PB**  
**Engraftment: PB > BM**  
**cGVHD PB > BM**  
**No difference in OS, DFS, Rel**

# STEM CELL SOURCE

**Unrelated Cord Blood Unit**

# Cord Blood source: summary

## How?

- Minimum **TNC  $3 \times 10^7/\text{kg}$**  : increasing the dose did not lower NRM (except for 4 mismatching HLA)
- Allele-level HLA matching lowers NRM risks (*Eapen, Blood 2014; Eapen Lancet & Haematol. 2016*)
  - Lowest risks after 8/8 allele-matched transplants
  - Risks were lower after 6-7/8 HLA-matched compared to 3-5/8 HLA-matched transplants
  - Warning for Cw + DRB1 mismatching association
  - Worst outcome for single A, Cw, DRB1 versus B mismatching

## When?

- In the absence of well HLA matched unrelated donor
- Minor ethnicity
- Urgent situations: delayed time to identify unrelated adult donor graft
- Anti-leukemic effect (*Milano, NEJM 2016*)
- Low body weight & Patient's CMV negative
- Specific diseases and center preference
- **Look at CB for emergency plan**

# STEM CELL SOURCE

**In Haploidentical Setting**

## It depends on Haplo-platform for GVHD prophylaxis

- T-cell repleted ATG based: BM G-CSF primed (Huang et al 2006, Di Bartolomeo et al 2013)
- T-cell repleted PT-CY based: BM (Lunzyk et al 2006) or PBSC in advanced disease (Bashey et al 2017)
- T-cell depletion/alfa-beta depletion : PBSC (Aversa et al 2006, Bertaina et al 2014)

**Transplant Centre  
Expertise**

# How to choose the Stem Cell Source?

- Risk of Infection: PBSC
- Risk of Relapse (GVL effect): PBSC or CB (?)
- Risk of Failure: PBSC & DSA in mm HSCT
- Increased Risk of GVHD: BM
- Non malignant disease: BM
- Ethnic Minority or Caucasian Patient's with New Allele Identification
- Reduced Conditioning Regimen: PBSC
- CMV negative or low body weight: CB

**Donor Safety and Availability  
Transplant Center Policy**

# **TYPE of DONOR**

**Matched and Mismatched Unrelated Donor**

**vs**

**Haploidentical donor**

**vs**

**Cord Blood**



High Resolution Donor/Recipient HLA Matching Level in Unrelated Hematopoietic Stem Cell Transplantation and Impact on the Transplant Outcome: The Italian Experience on Behalf of GITMO, IBMDR and AIBT



**N=1789**

**Promotore:** GITMO

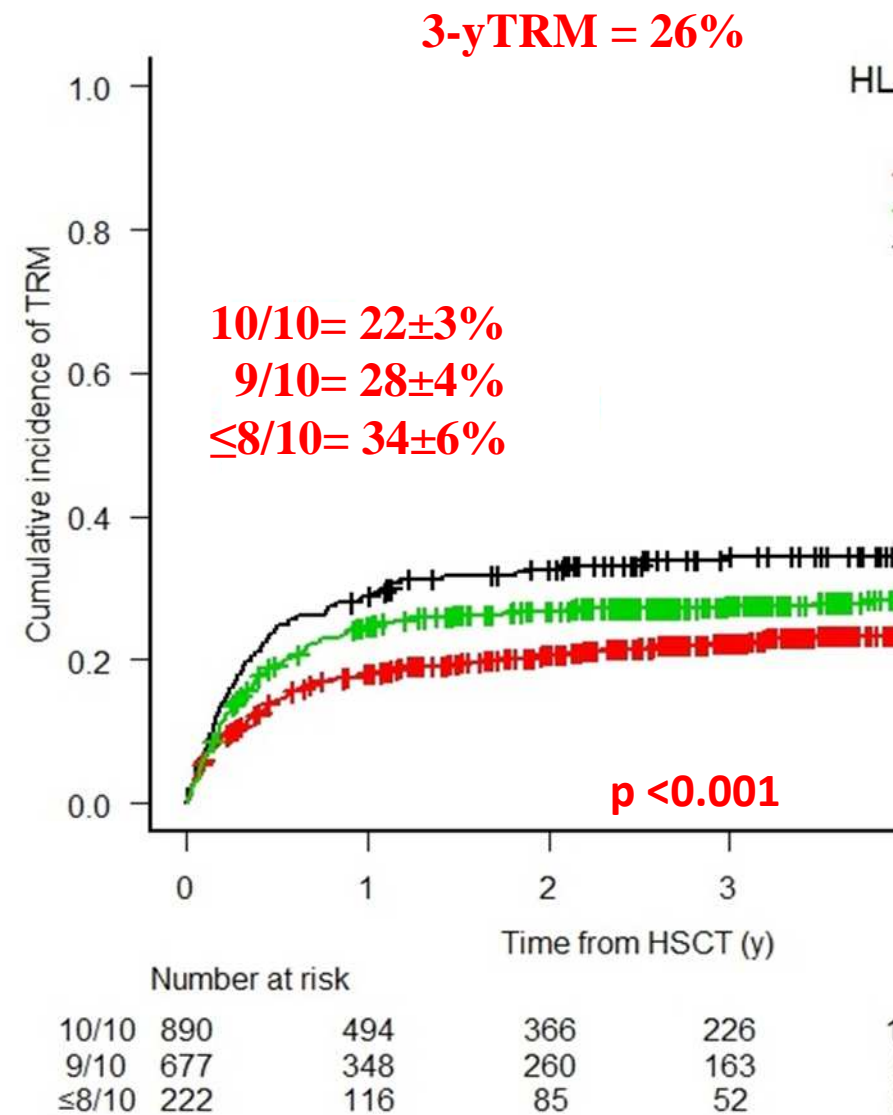
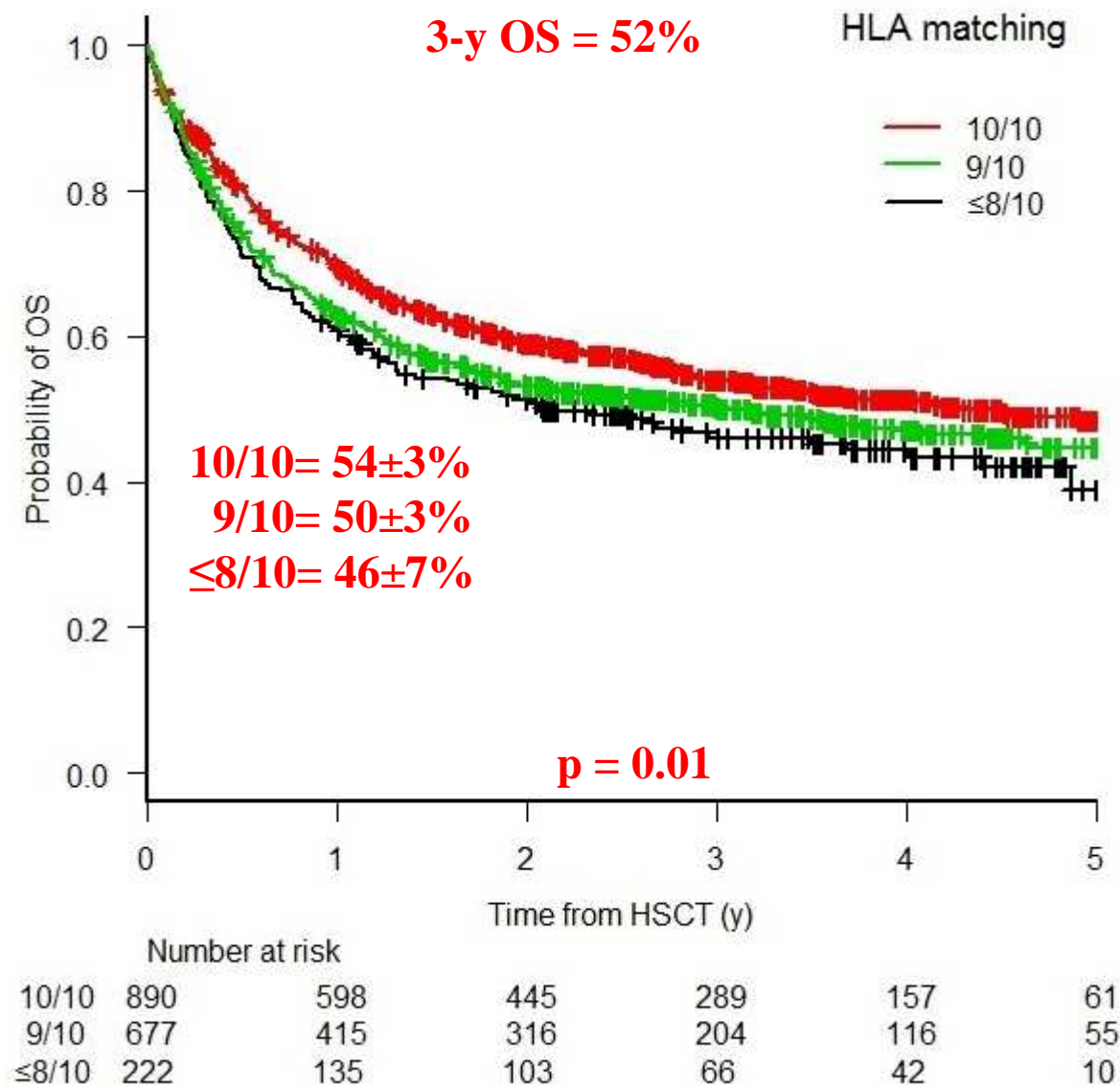
**Principal Investigator Nazionale:** Dott.ssa Alessandra Picardi

**Centro Coordinatore:** Università di Roma Tor Vergata (RM04)

**Collaborazione:** Registro Nazionale Italiano Donatori di Midollo Osseo (IBMDR),  
l'Associazione Italiana di Immunogenetica e Biologia dei Trapianti (AIBT)

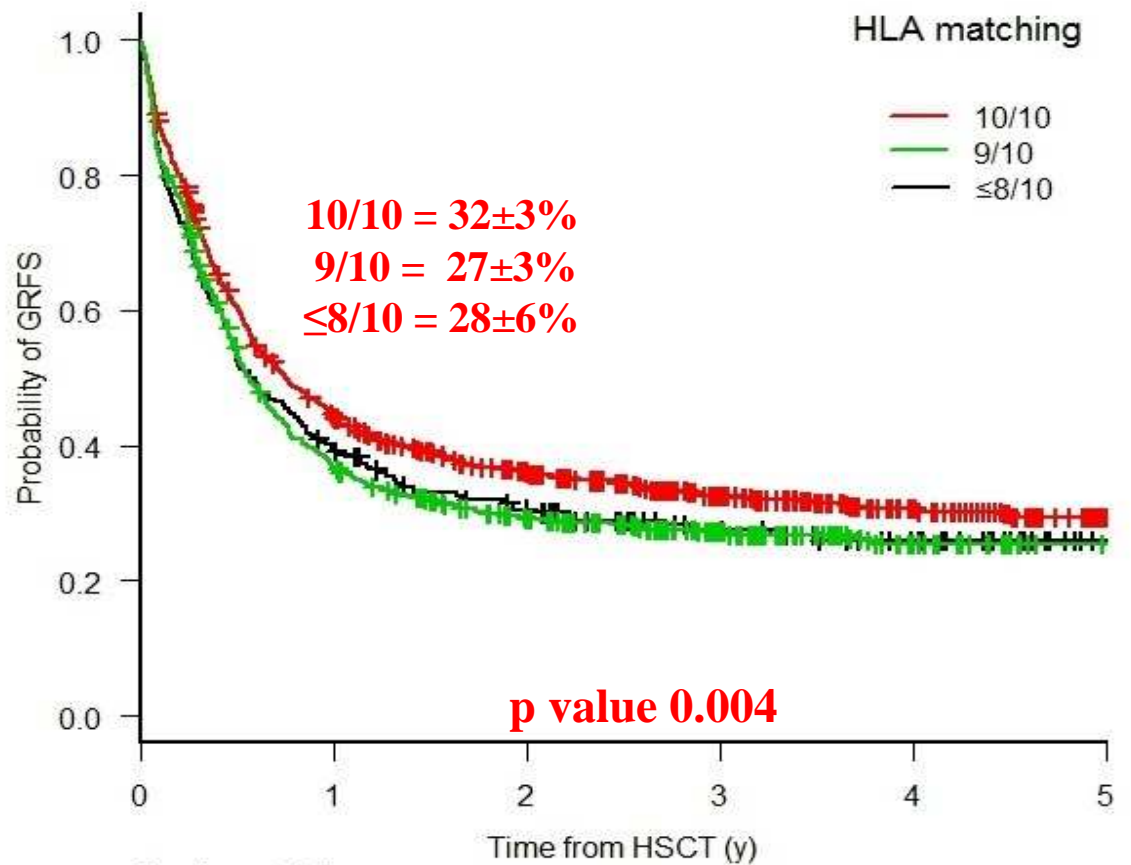
**Tipologia di Studio:** Osservazionale, Retrospettivo, Multicentrico

# OS and TRM according to HLA matching



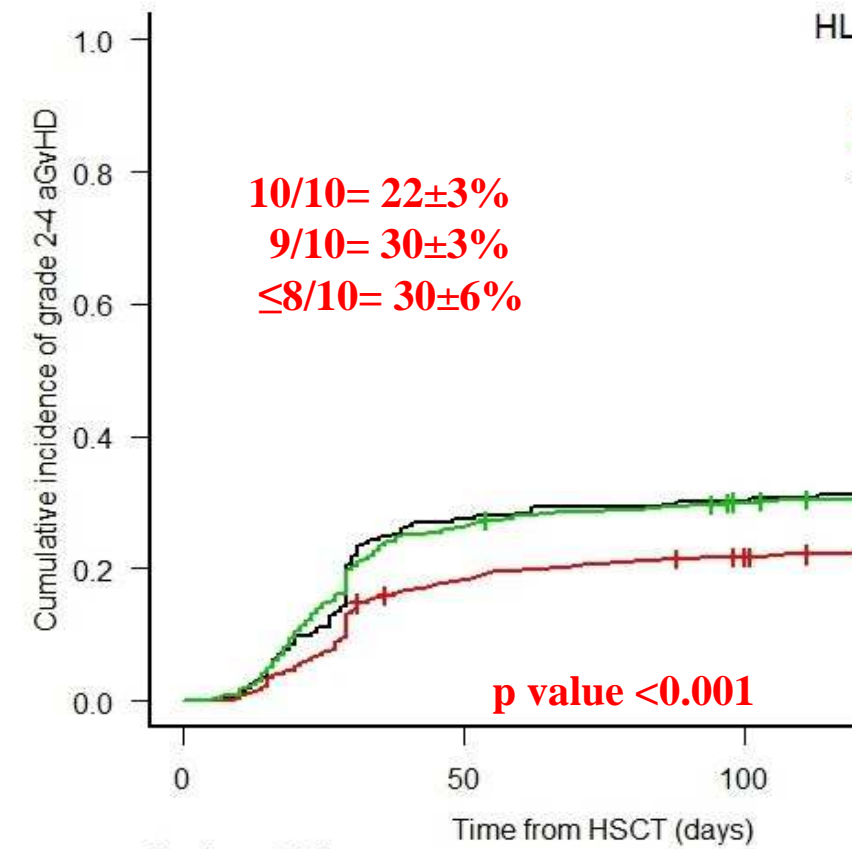
# GRFS and aGVHD according to HLA matching

**3-y GRFS = 30%**



	Number at risk					
	0	1	2	3	4	5
10/10	890	382	269	168	95	35
9/10	677	241	171	107	55	31
≤8/10	222	87	61	38	25	5

**Grade 2-4 aGVHD = 26%**

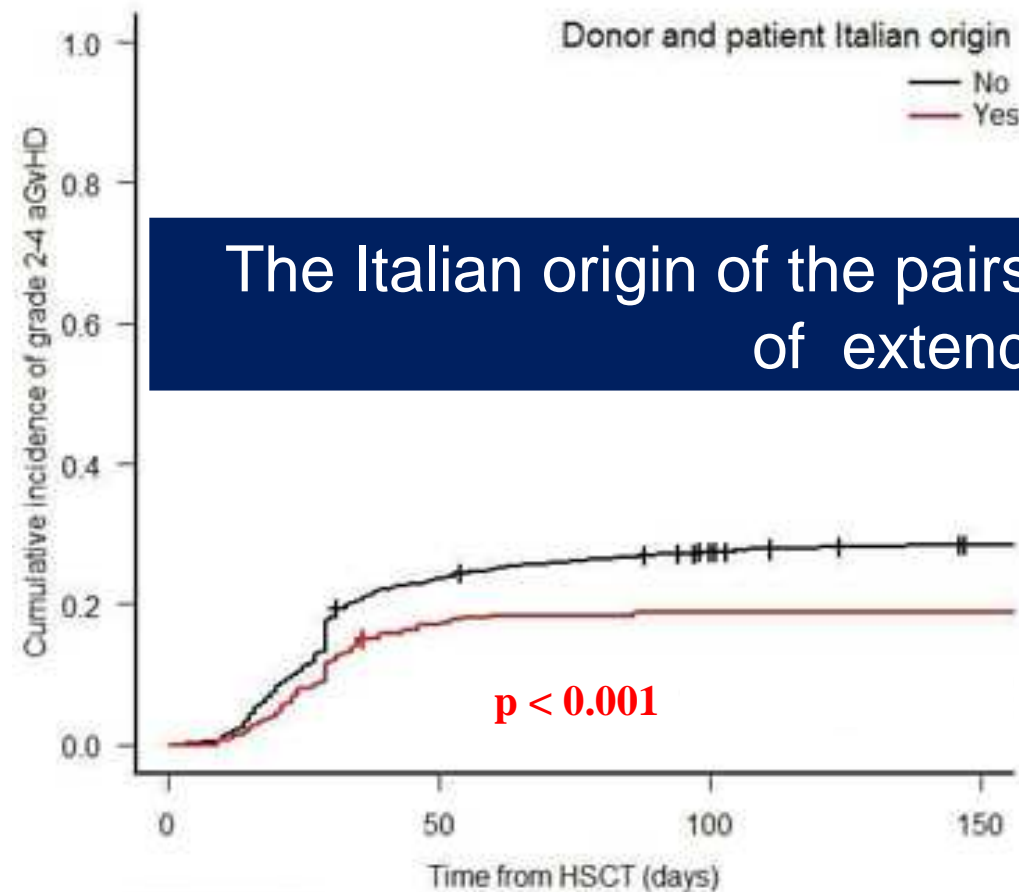


	Number at risk		
	0	50	100
10/10	883	644	561
9/10	670	443	379
≤8/10	222	139	123

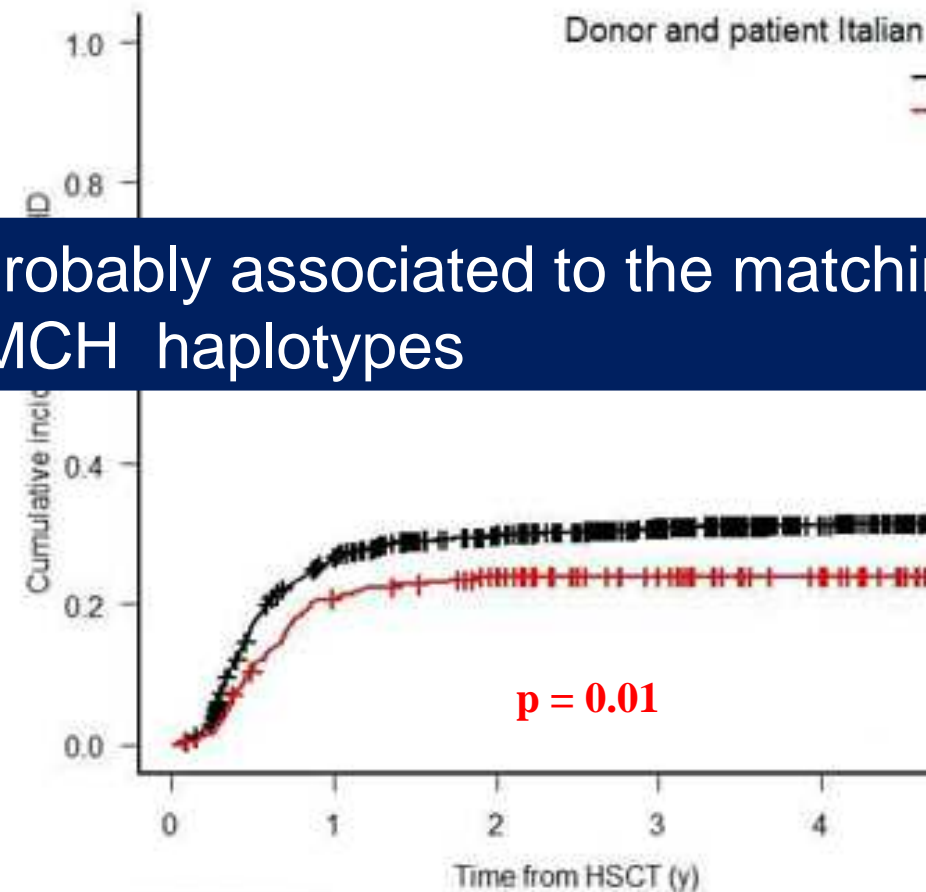
# Acute and chronic GVHD according to pair's origin

## Grade 2-4 aGVHD

## cGVHD



Number at risk					
No	Yes	0	50	100	150
1476	299	1006	870	767	
		220	193	181	



Number at risk						
No	Yes	0	1	2	3	4
1482	302	506	336	207	113	
		112	79	50	32	

The Italian origin of the pairs is probably associated to the matching of extended MCH haplotypes

# Alternative donors for allogeneic hematopoietic stem cell transplantation in poor-risk AML in CR1

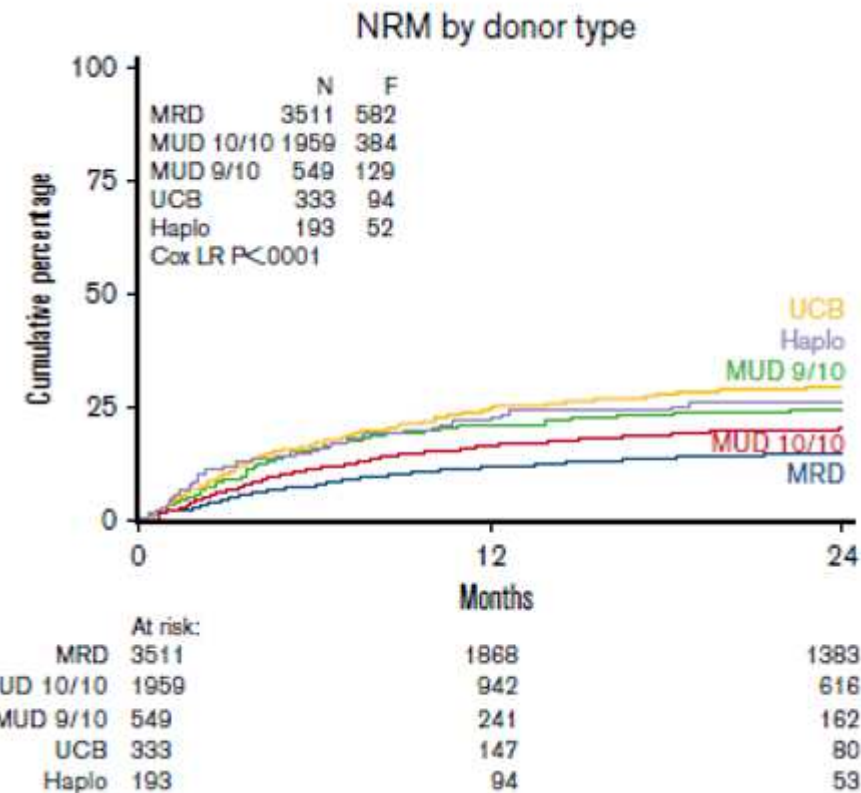
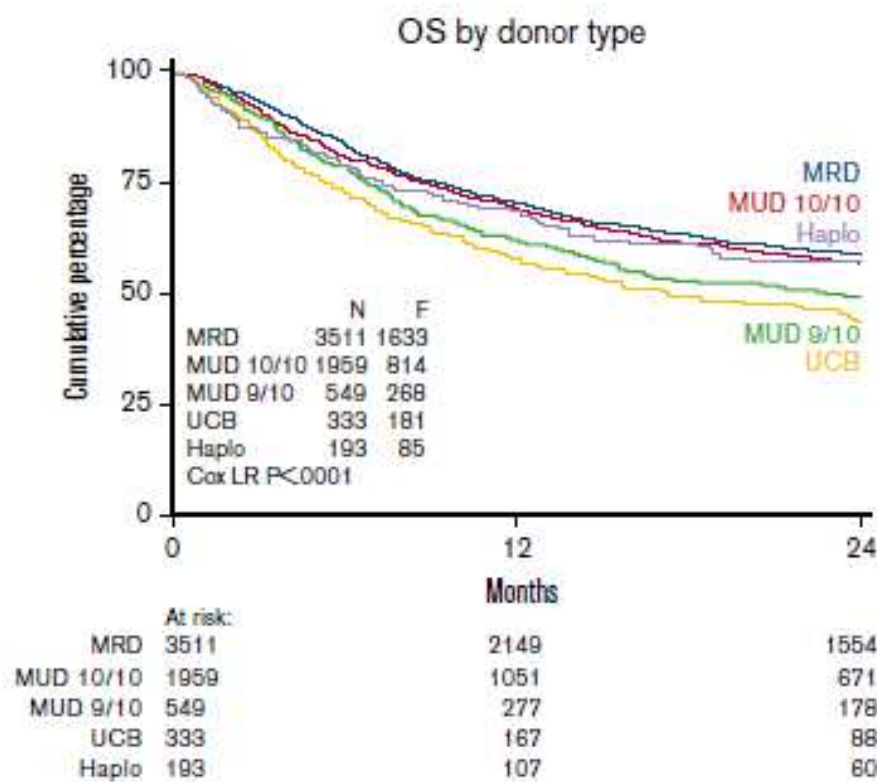
Jurjen Versluis,<sup>1</sup> Myriam Labopin,<sup>2-5</sup> Annalisa Ruggeri,<sup>4,6</sup> Gerard Socie,<sup>7,8</sup> Depei Wu,<sup>9</sup> Liisa Volin,<sup>10</sup> Didier Blaise,<sup>11</sup> Noel Milpied,<sup>12</sup>

## Key Points

- The preferred donor for patients with poor-risk AML in CR1 proceeding to alloHSCT include MRD or 10/10 MUD.
- Alternative donors are 9/10 MUD, UCB grafts, and especially haplo, but sufficient numbers and follow-up to define a hierarchy are lacking.

Allogeneic hematopoietic stem cell transplantation (alloHSCT) remains the treatment of choice to consolidate remission in patients with poor-risk acute myeloid leukemia (AML). With increasing alternative donors available, the preferred donor or stem cell source is debated. We set out to study outcome in recipients of alloHSCT with poor-risk AML in first complete remission (CR1) by donor type. A total of 6545 adult patients with poor-risk AML in CR1 receiving an alloHSCT using matched related donor (MRD,  $n = 3511$ ) or alternative donors, including 10/10 ( $n = 1959$ ) or 9/10 matched unrelated donors (MUDs,  $n = 549$ ), umbilical cord blood (UCB) grafts ( $n = 333$ ), or haplo-identical (haplo) donors ( $n = 193$ ) were compared. Overall survival (OS) at 2 years following MRD alloHSCT was an estimated  $59 \pm 1\%$ , which did not differ from 10/10 MUD ( $57 \pm 1\%$ ) and haplo alloHSCT ( $57 \pm 4\%$ ). OS, however, was significantly lower for 9/10 MUD alloHSCT ( $49 \pm 2\%$ ) and UCB grafts ( $44 \pm 3\%$ ), respectively ( $P < .001$ ). Nonrelapse mortality (NRM) depended on donor type and was estimated at  $26 \pm 3\%$  and  $29 \pm 3\%$  after haplo alloHSCT and UCB grafts at 2 years vs  $15 \pm 1\%$  following MRD alloHSCT. Multivariable analysis confirmed the impact of donor type with OS following MRD, 10/10 MUD, and haplo alloHSCT not being statistically significantly different. NRM was significantly higher for alternative donors as compared with MRD alloHSCT. Collectively, these results suggest that alloHSCT with MRDs and 10/10 MUDs may still be preferred in patients with poor-risk AML in CR1. If an MRD or 10/10 MUD is not available, then the repertoire of alternative donors includes 9/10 MUD, UCB grafts, and haplo-identical donors. The latter type of donor is increasingly applied and now approximates results with matched donors.

# RESULTS



**Haplo: no ex-vivo T-cell depletion**

# CLINICAL FACTORS

✓ Donor's Age and Gender

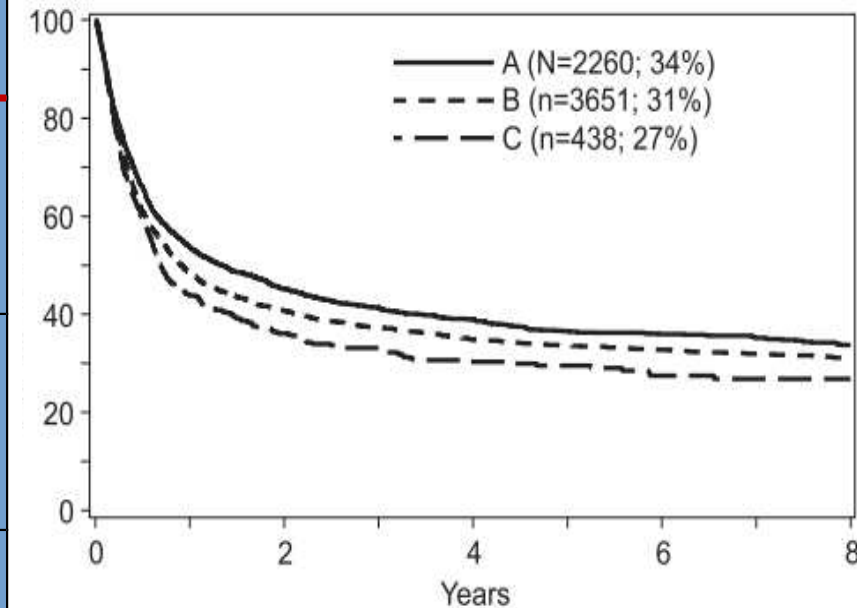
✓ CMV

✓ ABO

# Donor age and donor/recipient HLA predict outcome after hematopoietic cell transplantation from Unrelated Donor

**CIBMTR Registry: training cohort 1988-2006 (n=6349); validation cohort 2007-2011 (n=4690)**

Donor characteristics	%	Pts and HSCT characteristics	%
Age, y		Age, y	
18-32	36	<18	17
33-50	57	18-45	49
>50	7	>45	34
HLA match		Disease	
8/8	59	AML	39
7/8	25	ALL	24
<7/8	16	Other	37
ABO mismatch		Disease status	
Minor	25	1 <sup>st</sup> - 2 <sup>nd</sup> CR	71
Major	31	Relapse/refractory	29
Donor sex and parity		Conditioning regimen	
M	62	MA	87
F, nulliparous	15	RIC	13
F, parity≥1	21	Graft source	
Donor/recipient CMV serostatus		BM	62
Neg/Neg	31	PB	38
Neg/Pos	33		
Pos/Pos	20		
Pos/Neg	14		



**8-years risk adjusted overall survival probability according to age of donor**

**A: 18-32y 34%**

**B: 33-50y 31%**

**C: > 50 y 27%**

# Donor age and donor/recipient HLA predict outcome after hematopoietic cell transplantation from Unrelated Donor

CIBMTR Registry: training cohort 1988-2006 (n=6349); validation cohort 2007-2011 (n=4690)

Overall survival	P value
Donor age (10-y increments)	.01
HLA match: 8/8 vs 7/8	<.001
<b>Non relapse mortality</b>	
Donor age, years: ≤32 vs 33-50 vs >50	.03
HLA match: 8/8 vs 7/8 vs 6/8 or lower	<.001
Donor sex : male vs female nulliparous vs female ≥ 1 parity	< .001
<b>Relapse</b>	
Donor age, years: ≤32 vs 33-50 vs >50	.29
Donor sex : male vs female nulliparous vs female ≥ 1 parity	.06
<b>Grade 2 to 4 acute GVHD</b>	
Donor age, years: ≤32 vs 33-50 vs >50	.01
HLA match: 8/8 vs 7/8 vs 6/8	<.001
<b>Chronic GVHD</b>	
Donor sex and parity	<.001
Male	
Female, no pregnancies	.88
Female, ≥ 1 pregnancies	<.001

Adjusted multivariate analysis

Kollman C & E  
C

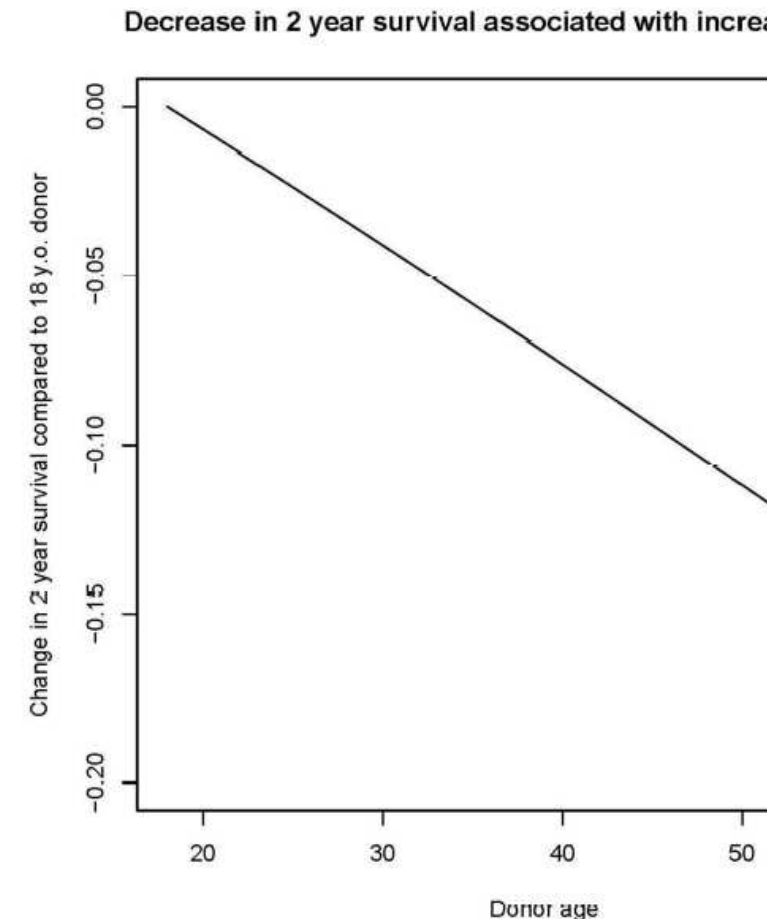
# Development of an Unrelated Donor Selection Score Predictive of Survival after HCT: Donor Age Matters Most

## Key Points

- Younger age is the only donor characteristic consistently associated with survival after HLA-matched unrelated hemopoietic cell transplant

## Research Highlights

- Younger age is associated with better survival after HLA-matched unrelated hemopoietic cell transplant
- Other donor characteristics tested were not consistently associated with survival
- In the HLA-matched setting the youngest donor should be prioritized



# Male or Female?

- Previous pregnancy = alloimmunization risk
- Development of Ab anti-Rh and anti HLA
- Female Donor/ Male Recipient = worst recognized pair
- Y encodes minor HLA – Ag at high polymorphism, recognized by specific T cells of female donor



**Increased risk  
of GVHD**

- Deferrals for inadequate access venous
- Cancellation for pregnancy

# The role of cytomegalovirus serostatus on outcome of hematopoietic stem cell transplantation

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*Per Ljungman*

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## **Purpose of review**

The aim of this review is to discuss recent developments regarding the impact of cytomegalovirus (CMV) serological status of hematopoietic stem cell transplantation recipients and their donors on transplant outcome.

## **Recent findings**

CMV seropositivity of the recipient is still a negative factor for transplant outcome. The use of a CMV seropositive donor has a negative impact on survival in patients receiving unrelated but not human leukocyte antigen-identical sibling grafts. In CMV seropositive patients, the donor serological status influences outcome in patients receiving unrelated donor grafts after myeloablative but not reduced-intensity conditioning. Early CMV replication reduces the risk for leukemia relapse but does not improve survival. The use of leukocyte depleted blood products is sufficient to prevent primary CMV infection.

## **Summary**

Despite major advances in management of CMV infections, CMV serologic status remains an important risk factor for transplant-related complications and mortality after allogeneic hematopoietic stem cell transplantation.

**Curr Opin Hematol** 2014, 21:000–000

**Table 2. Impact of Using a Cytomegalovirus (CMV)–Seropositive Donor for Survival, Transplant-Related Mortality, Nonrelapse Mortality, and Relapse in CMV-Seronegative and CMV-Seropositive Patients Receiving Sibling or Unrelated Donor Transplants Adjusted for Covariates**

Impact	Sibling Donor			Unrelated Donor		
	HR	95% CI	P Value	HR	95% CI	P Value
<u>CMV-seronegative patients</u>						
Overall survival	1.07	1.00–1.14	.06	1.13	1.06–1.21	<.0001
Relapse-free survival	1.05	.99–1.12	.10	1.10	1.03–1.19	.003
Nonrelapse mortality	0.97	.87–1.09	.65	1.13	1.04–1.24	.005
Relapse incidence	1.07	.98–1.16	.12	1.06	.96–1.16	.14
CMV-seropositive patients						
Overall survival	0.99	.94–1.05	.84	0.96	.91–1.01	.11
Relapse-free survival	1.01	.96–1.05	.73	0.98	.93–1.03	.52
Nonrelapse mortality	1.02	.95–1.10	.57	0.94	.87–1.00	.05
Relapse incidence	1.00	.94–1.07	.93	1.05	.97–1.13	.21

Abbreviations: CI, confidence interval; CMV, cytomegalovirus; HR, hazard ratio.

**CMV mismatched  
worst outcome**



# Recipient/donor HLA and CMV matching in recipients of T-cell-depleted unrelated donor haematopoietic cell transplants

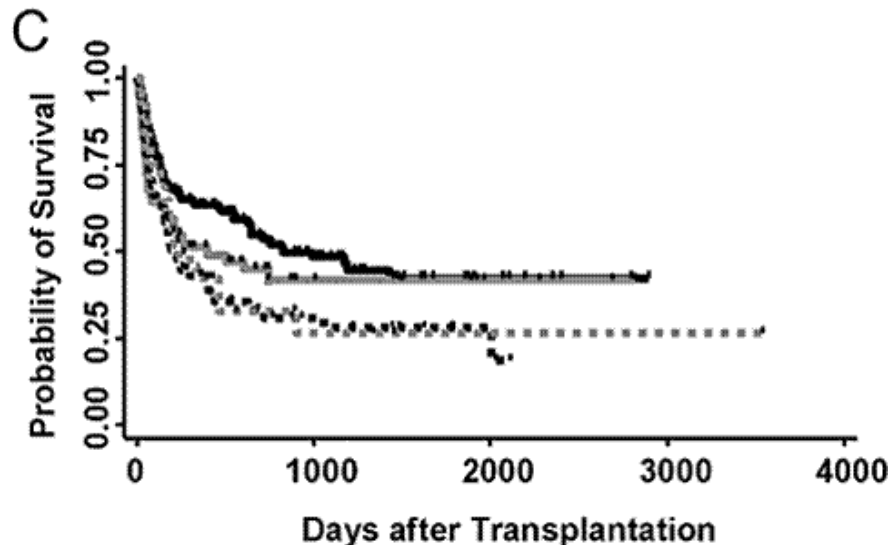
**Table 3.** Multivariate analysis of survival and NRM

	Overall survival			Non-relapse mortality		
	N	RR (95% CI)	P-value	N	RR (95% CI)	P-value
<i>HLA match</i>						
10/10 match	878	1.00		871	1.00	
1 mismatch	239	1.21 (1.1–1.5)	0.042	239	1.24 (0.9–1.6)	0.14
> 1 mismatch	77	1.43 (1.1–1.9)	0.016	83	1.59 (1.1–2.4)	0.028
<i>Recipient/donor CMV</i>						
Match	863	1.00		861	1.00	
Mismatch	331	1.40 (1.2–1.6)	< 0.001	332	1.63 (1.3–2.1)	< 0.001
<i>Recipient age (years)</i>						
< 20	221	1.00				
20–39	351	1.07 (0.8–1.4)	0.57			
40–59	497	1.26 (1.0–1.6)	0.047			
≥ 60	125	1.71 (1.3–2.3)	0.001			
<i>Previous autos</i>						
0	1014	1.00				
> 0	180	1.42 (1.2–1.8)	0.001			
<i>Donor age, years</i>						
< 30	372	1.00				
> 30	822	1.17 (0.98–1.4)	0.078			
<i>Era</i>						
1996–1999	142	1.00		143	1.00	
2000–2003	421	0.84 (0.7–1.1)	0.18	418	0.57 (0.4–0.8)	0.002
2004–2007	345	0.76 (0.6–1.0)	0.049	343	0.54 (0.4–0.9)	0.002
2008–2011	286	0.77 (0.6–1.1)	0.078	289	0.60 (0.3–0.7)	0.001
<i>Disease risk—EBMT</i>						
Good	557	1.00				
Intermediate	444	1.37 (1.2–1.6)	< 0.001			
Poor	193	1.33 (1.1–1.7)	0.013			
<i>Recipient/donor sex</i>						
Other combination				1061	1.00	
Male/female				132	1.38 (0.99–1.9)	0.063

# Impact of ABO mismatching on the outcomes of allogeneic related and unrelated blood and marrow stem cell transplantations for hematologic malignancies: IPD-based meta-analysis of cohort studies

*Junya Kanda, Tatsuo Ichinohe, Keitaro Matsuo, Richard J. Benjamin, Thomas R. Klumpp, Primoz Rozman, Neil Blumberg, Jayesh Mehta, Sang-Kyun Sohn, and Takashi Uchiyama*

**TRANSFUSION** 2009;49:624-635.



Kaplan-Meier survival estimates of OS in patients who received an unrelated graft. (—) ABO-matched transplantation; (---) major mismatched; (···) minor mismatched; (- · -) bidirectional mismatched.

**TABLE 2. Impact of ABO mismatching on OS**

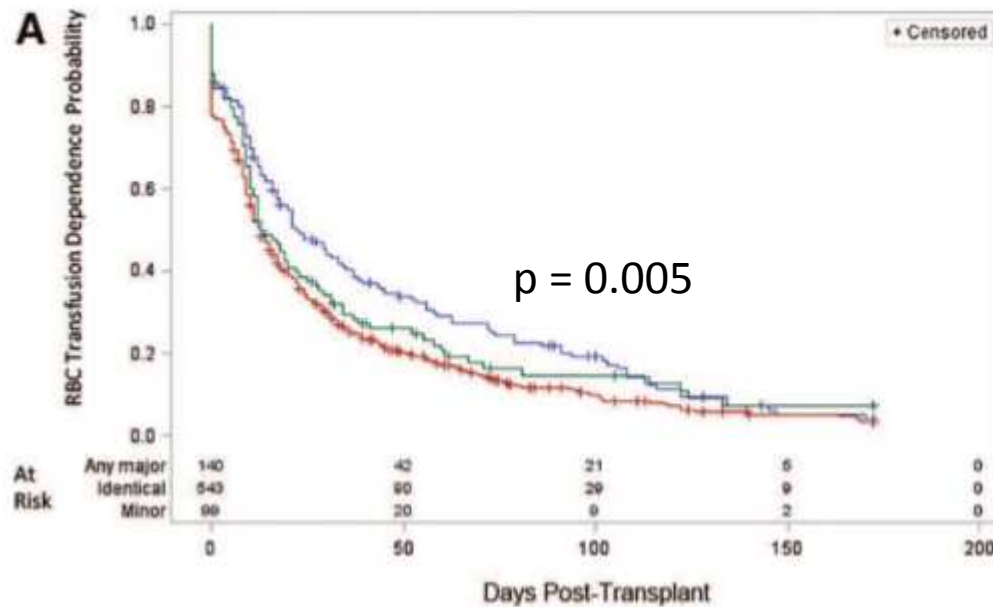
Category	OS (n = 1208)	
	HRs (95% CI)*	p Value
Overall		
Match	1.00	
Major	1.03 (0.82-1.30)	0.81
Minor	1.19 (0.97-1.47)	0.10
Bidirectional	1.25 (0.91-1.72)	0.17
Related SCT		
Match	1.00	
Major	0.93 (0.70-1.23)	0.62
Minor	1.02 (0.79-1.32)	0.88
Bidirectional	1.09 (0.71-1.68)	0.70
Unrelated SCT		
Match	1.00	
Major	1.38 (0.87-2.17)	0.17
Minor	1.68 (1.12-2.51)	0.012
Bidirectional	1.81 (1.08-3.00)	0.023

\* HRs were adjusted for age, sex, diagnosis, risk, stem cell source, conditioning regimen, GVHD prophylaxis, transplant year, transplant centers, and donor, if appropriate.

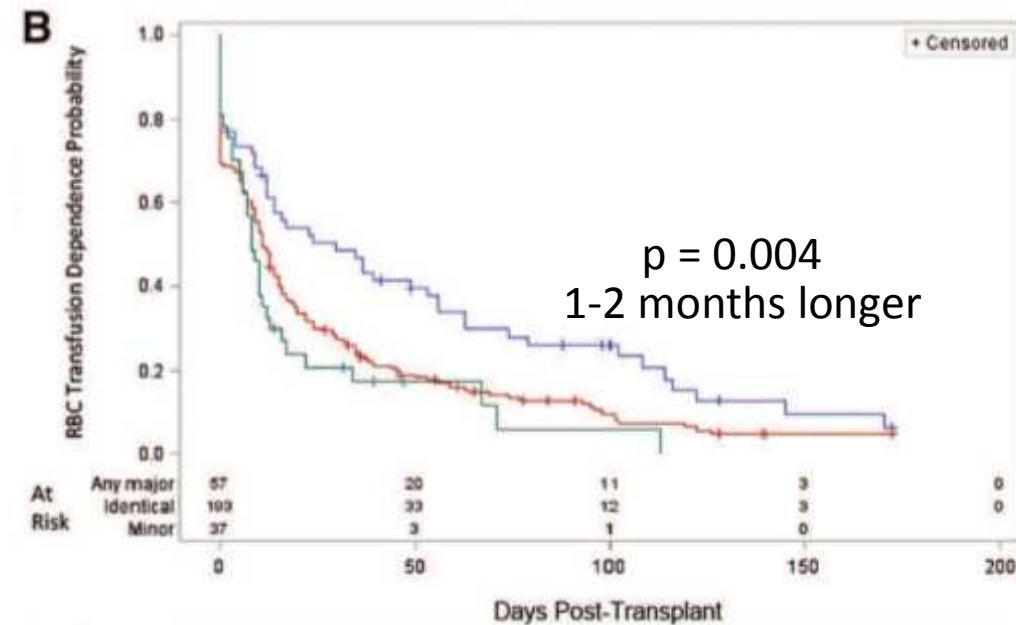
# Transfusion support for matched sibling allogeneic hematopoietic stem cell transplantation (1993–2010): factors that predict intensity and time to transfusion independence

N= 800 (Bethesda Group)

## Overall Transfusion Idpendence



## RIC – PBSC: Transfusion Idpendence



Major & Bidirectional Mismatch  
Minor Mismatch  
Identical

# Algorithm for Donor Selection

HLA- identical sibling



HLA-10/10 matched unrelated donor  
Beyond HLA, consider Donor Age>CMV matching, sex, ABO matching



HLA-9/10 matched unrelated donor, Haploidentical related donor, Cord Blood:  
Beyond HLA, consider DSA and specific Centre Experience

# Take Home Messages

- Fully matched unrelated donor (10/10) represents the best alternative donor
- For children and patients with non malignant disorders, Bone Marrow is preferred stem cell source
- In Unrelated Donor Transplantation, donor age is probably the most relevant non-HLA donor factor
- The choice of mismatched donors depends on centre experience, urgency and detection of specific anti-HLA antibodies
- Defined Alternative Donor Search Strategy is necessary for a better Transplant Efficiency

