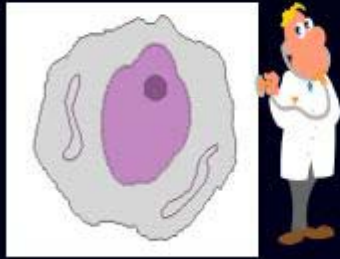


A  
I  
H



*Allogreffe de Cellules Souches Hématopoïétiques du Sang Placentaire*

*Marseille, 30 septembre - 1 octobre*

*Association des Internes et Jeunes Hématologues*



**V Rocha MD, PhD**  
**Unité de Greffe de Moelle Osseuse**  
**Hôpital Saint Louis,**  
**France**



# First cord blood transplant



# Past and Present of Cord Blood Transplants

- 1989 ➡ First Cord blood transplant
- 1989-92 ➡ Clinical observation that GVHD was reduced in HLA incompatible CBT
- 1992-93 ➡ Establishment of Cord blood banks (NY, Paris, Milan and Dusseldorf )
- 1993-95 ➡ Feasibility of HLA incompatible unrelated cord blood transplants
- 1995 ➡ Establishment of Eurocord group
- 1997 ➡ Nucleated cell dose more important factor for engraftment and survival , influence of HLA on engraftment
- 1998 ➡ Large series of UCBT = confirmation of cell dose and HLA
- >2000 ➡ Retrospective comparisons between UBMT and UCBT
- 2002 ➡ Use of cord blood cells in adults with promising results
- 2003 ➡ Criteria of cord blood choice and indications
- 2003-04 ➡ Use of double cord and RIC regimen in adults
- 2004 ➡ Isolation of USSC from umbilical cord blood
- 2004-05 ➡ Comparable results between unrelated CBT and UBMT in adults

# NETCORD-EUROCORD INTERACTIONS

## CORD BLOOD BANKS



## NETCORD

Standards  
Quality Control  
Accreditation FACT-Netcord  
Donor search

## EUROCORD

Registry  
Protocols  
Clinical Studies



**BMDW**  
MUD Registries



**TRANSPLANT CENTERS** (EBMT and non EBMT)



# EUROCORD Registry

**2842 cord blood transplantation performed from 1988 to Sep 2006  
in 39 countries and 318 transplant centers:**

**- 138 EBMT → 1700 cases**

**- 180 Non-EBMT → 742 cases**

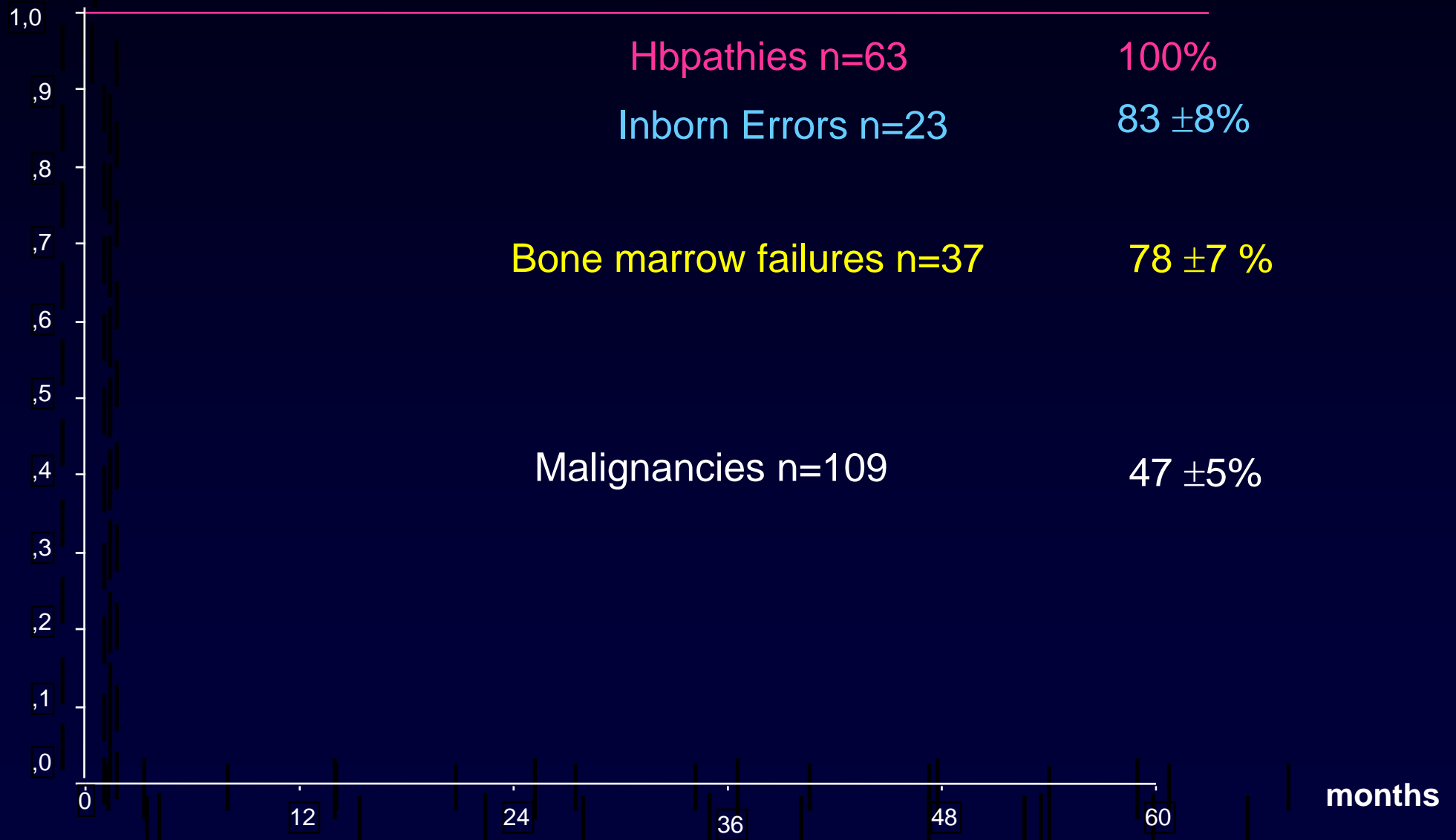
- **Single CB transplant n=2680      Related      n= 267**  
**Unrelated n = 2313**
- **Expanded Unit n= 52**
- **Unit for multi cord n= 150**
- **UCB + BM (haplo) n= 14**
- **CB + BM (genoidentical) n= 18**
- **Autologous or gene therapy n=4**

# ***CLINICAL RESULTS***

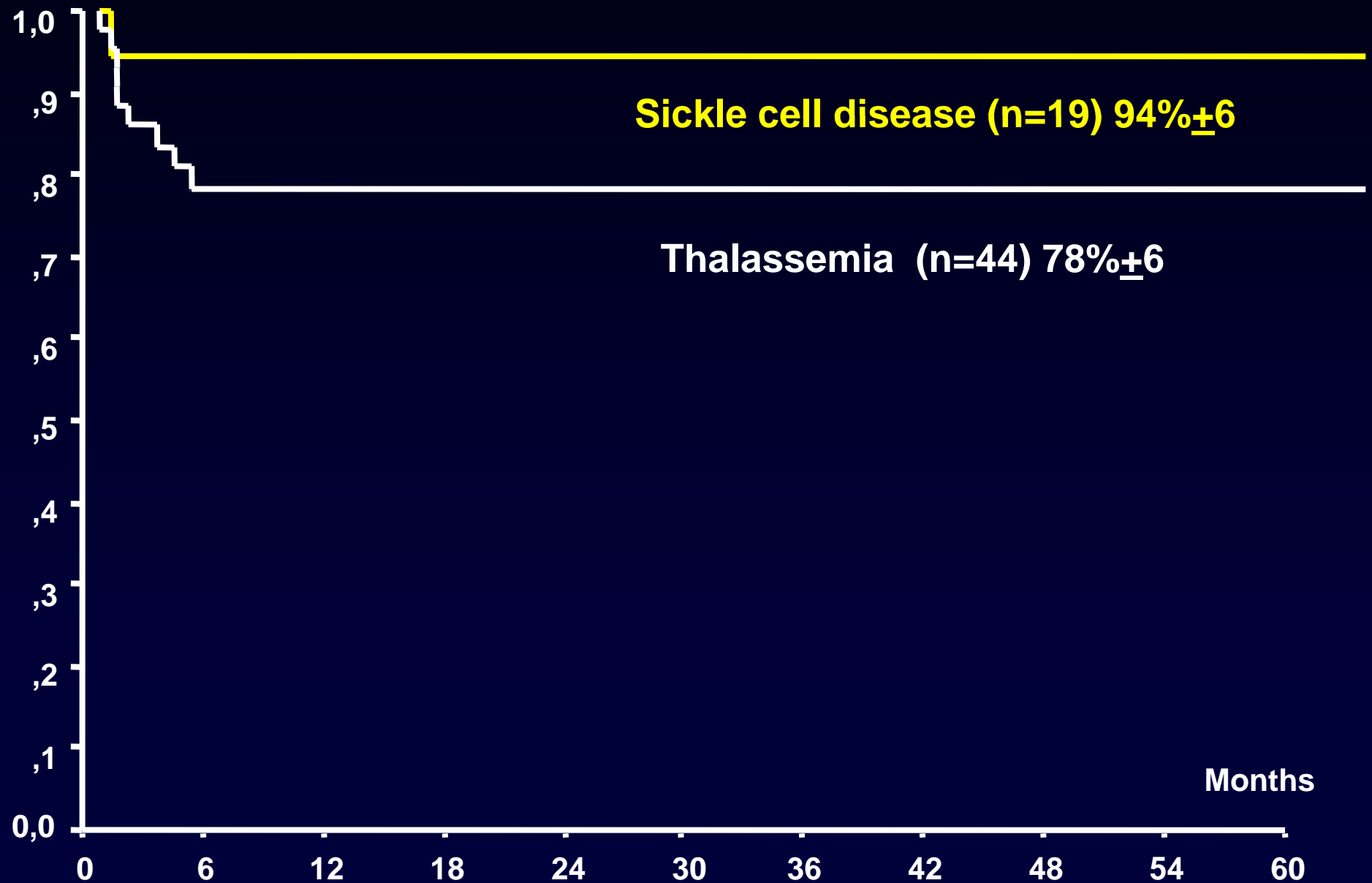
Related Cord Blood Transplantation

# Related Cord Blood Transplantation (n=231)

## Survival according to diagnosis

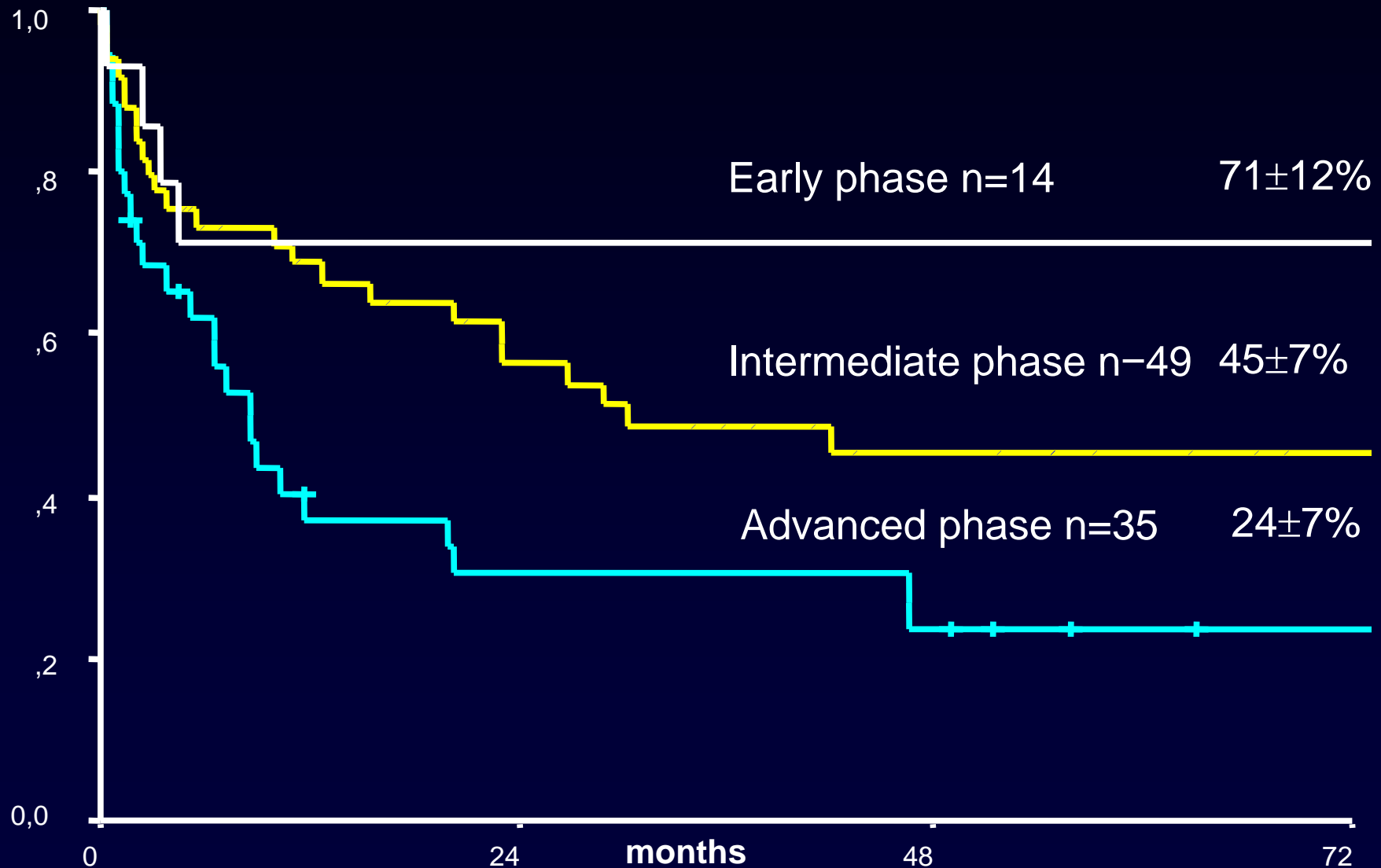


# 5 years EFS according to diagnosis





# Related cord blood transplantation for malignancies (n=109) Survival according to status of the disease at CBT



**COMPARISON OF GVHD AFTER  
HLA-IDENTICAL SIBLING CORD BLOOD  
vs BONE MARROW TRANSPLANTS  
IN CHILDREN**



***International Bone Marrow  
Transplant Registry  
and  
Eurocord***

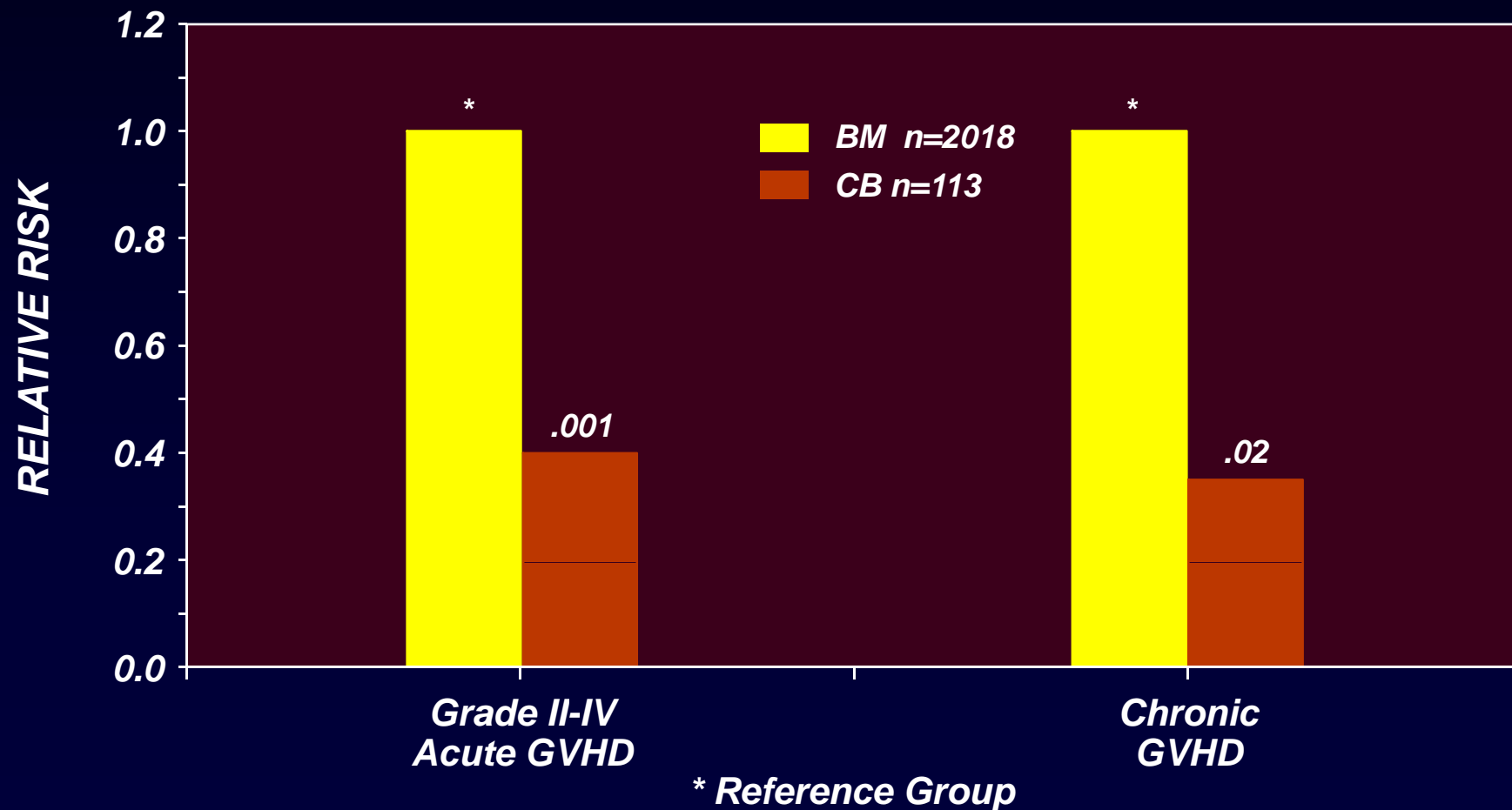


***V Rocha et al***

***NEJM 342: 1846-1854, 2000***

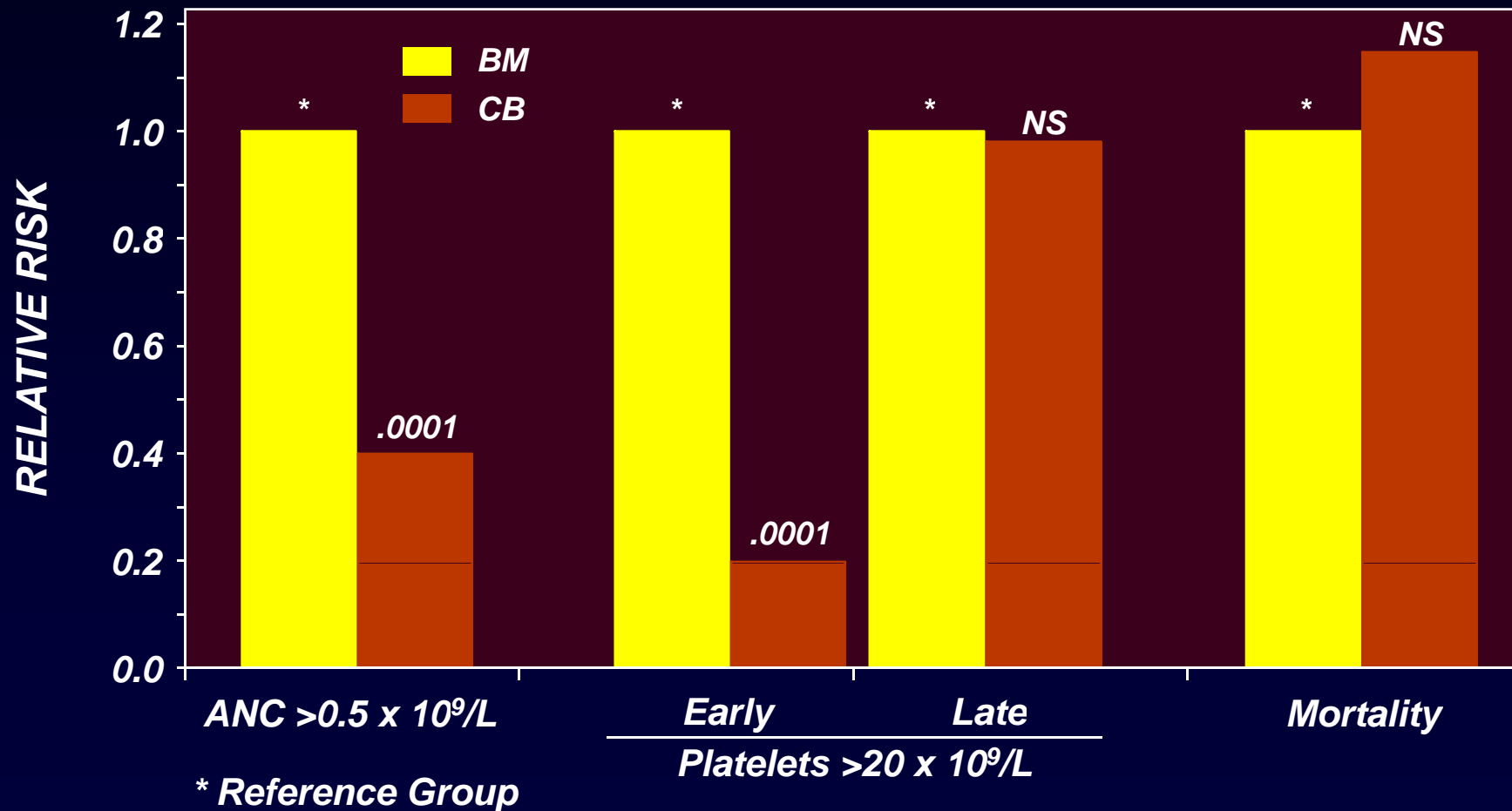
# MULTIVARIATE ANALYSIS

## - GVHD -

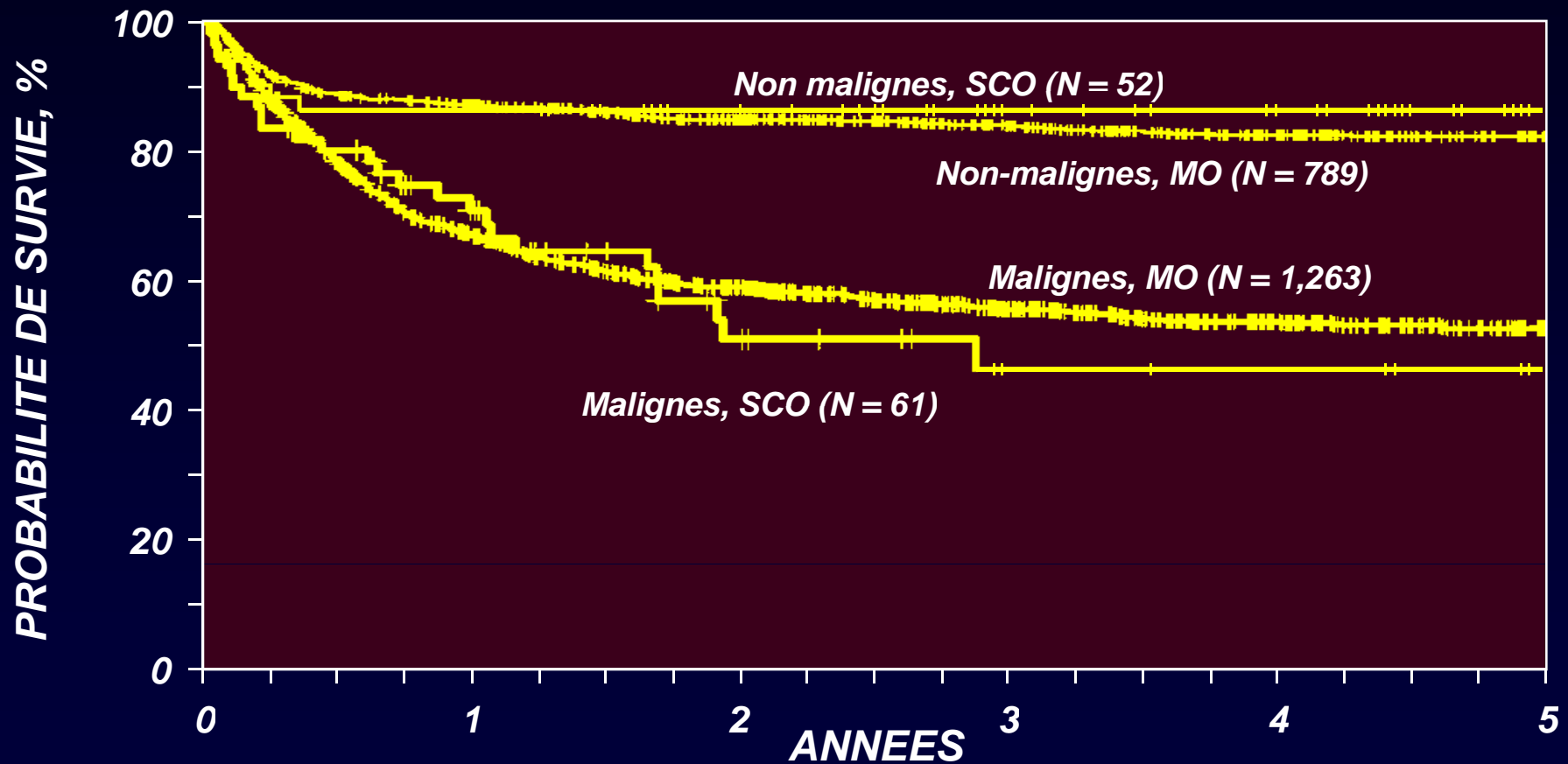


# MULTIVARIATE ANALYSIS

## - Hematopoietic Recovery & Survival -



# Survie Globale après greffes HLA identiques de SCO comparées aux greffes de MO chez les enfants selon les diagnostics



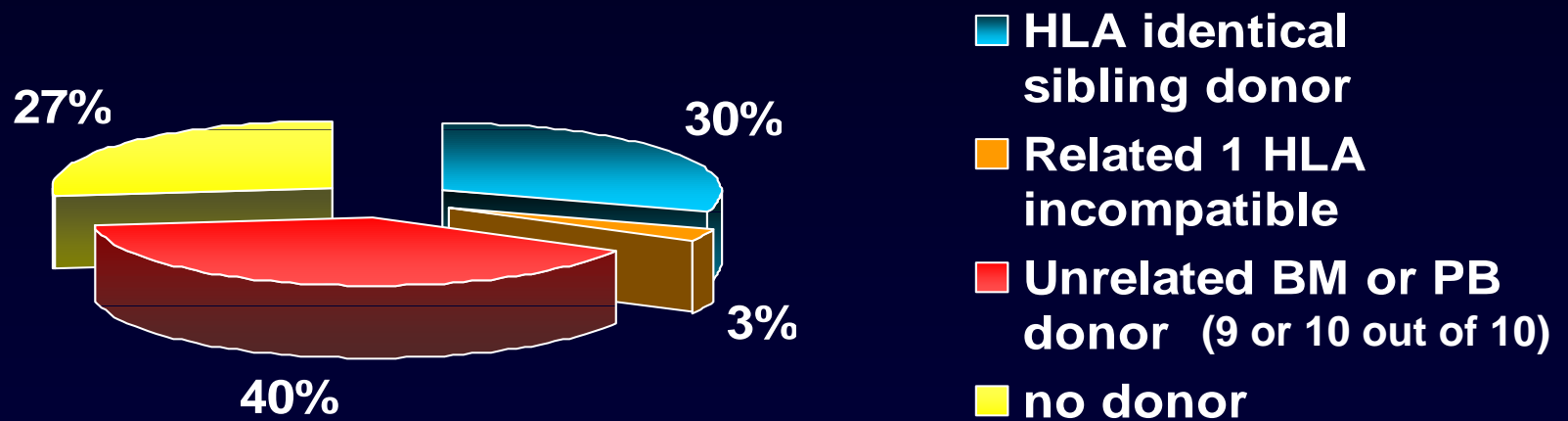
V Rocha, J Wagner, K Sobosinski et al, NEJM 342: 1846-1854, 2000

# Indications of cord blood banking for family use

- **Sibling with a disease which can be cured by hematopoietic stem cell transplantation: Poor risk leukemia, aplastic anemia, hereditary disorders.**
- **HLA mismatched transplants with 1, 2 or full haplotype (?)**
- **Familial predisposition to malignancies**
- **Genetic disease (autologous use for gene therapy)**

# **Unrelated Cord Blood Transplantation**

# Estimate number of patients with an indication of an allogeneic hematopoietic stem cell transplants





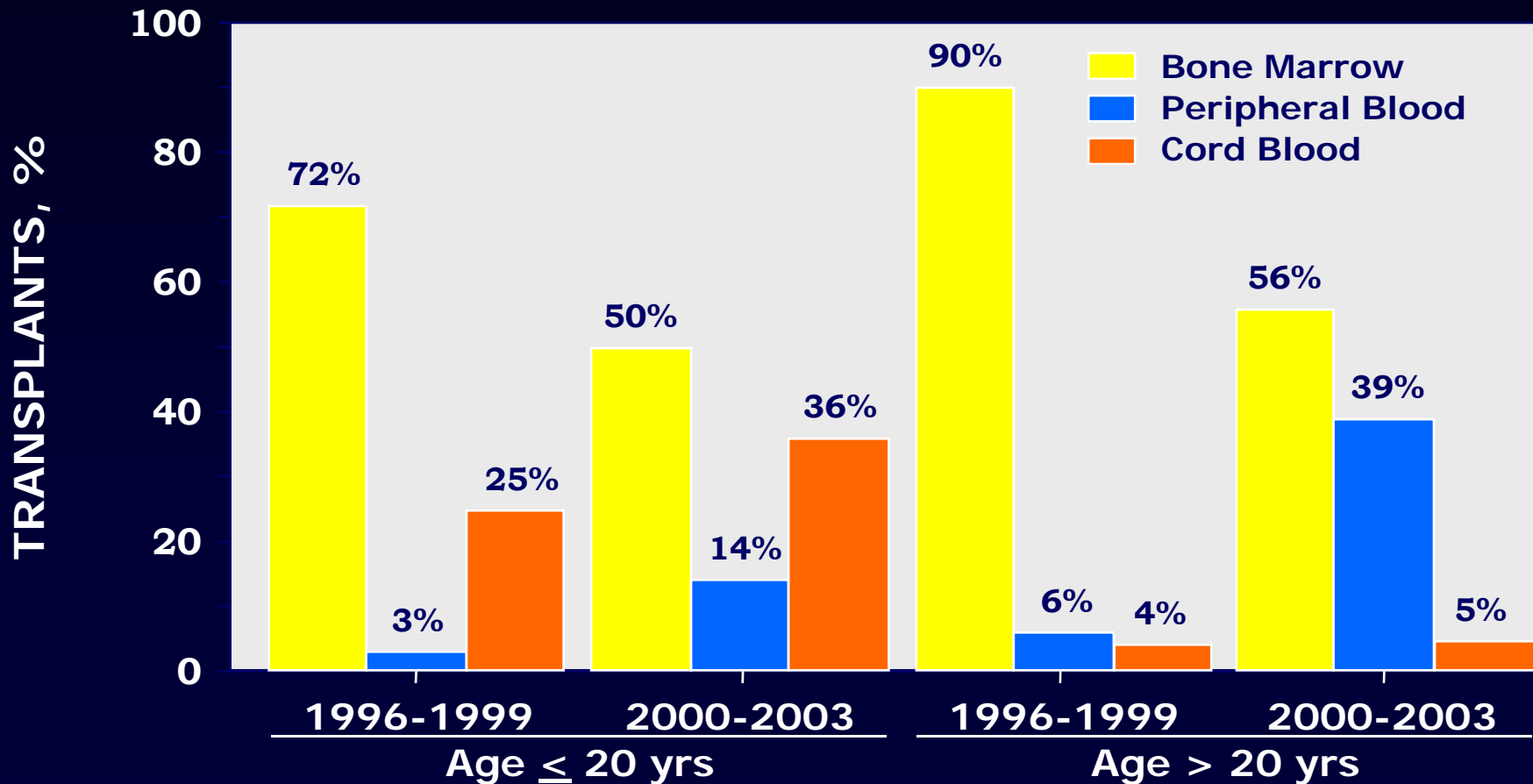
## Advantages and disadvantages

### Searching and identifying an unrelated stem cell donor

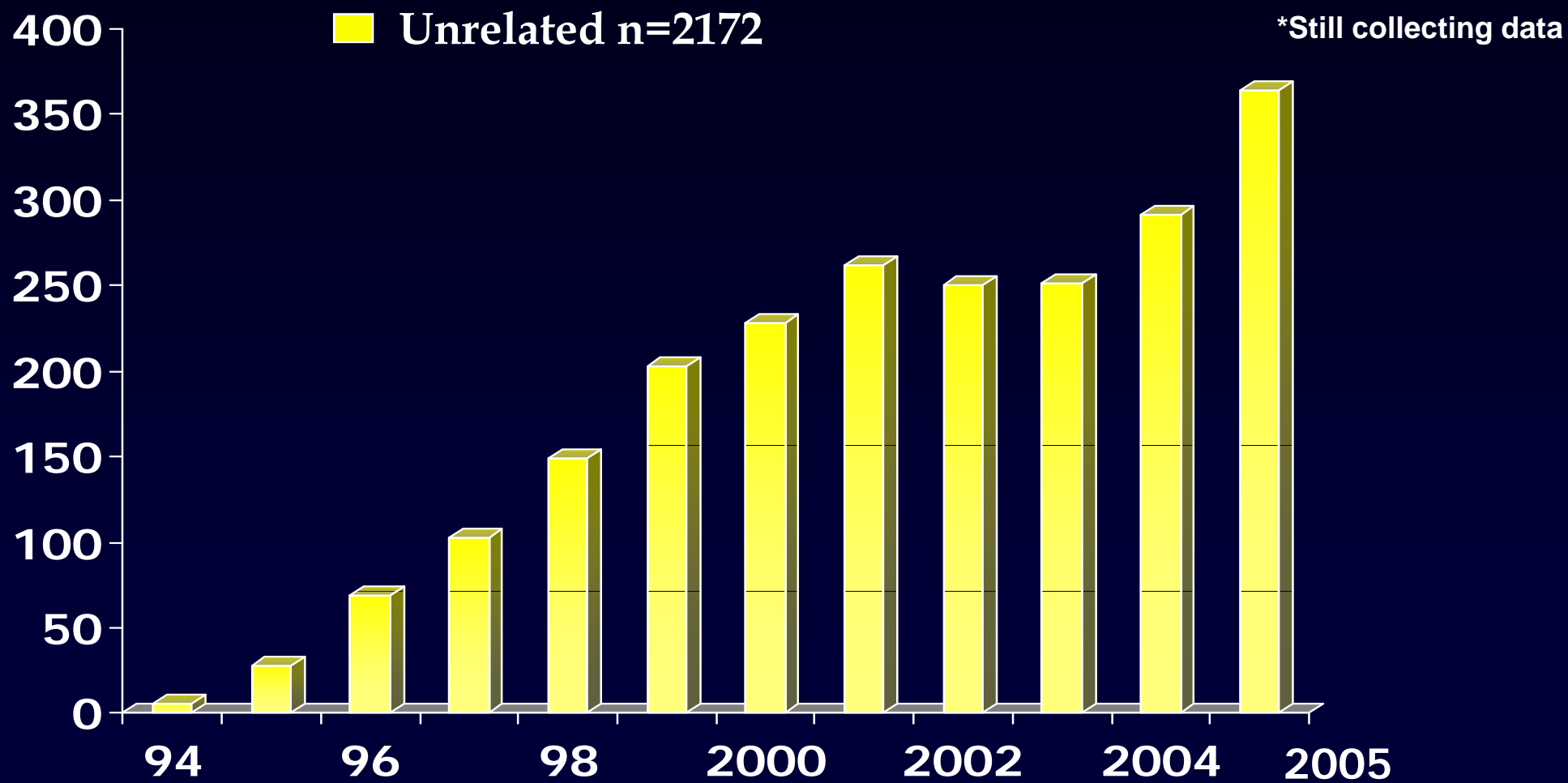
	BM	CB
Information of A+B (serology) +DRB1(DNA) typed	16-56%	40-80%
Median search time	3-6 mon	<1mon
Donors identified but not available	30%	~1(?)%
Rare Haplotypes represented	2-10%	20%
Major limiting factors to graft acquisition	HLA match	Cell Dose
Ease of rearranging date of cell infusion	Difficult	Easy
Potential for second HSC graft or DLI from the same donor	Yes	No
Potential for viral transmission to recipient	Yes	No
congenital diseases	No	Yes
Risk to donor	Yes	No

# UNRELATED TRANSPLANTS BY RECIPIENT AGE

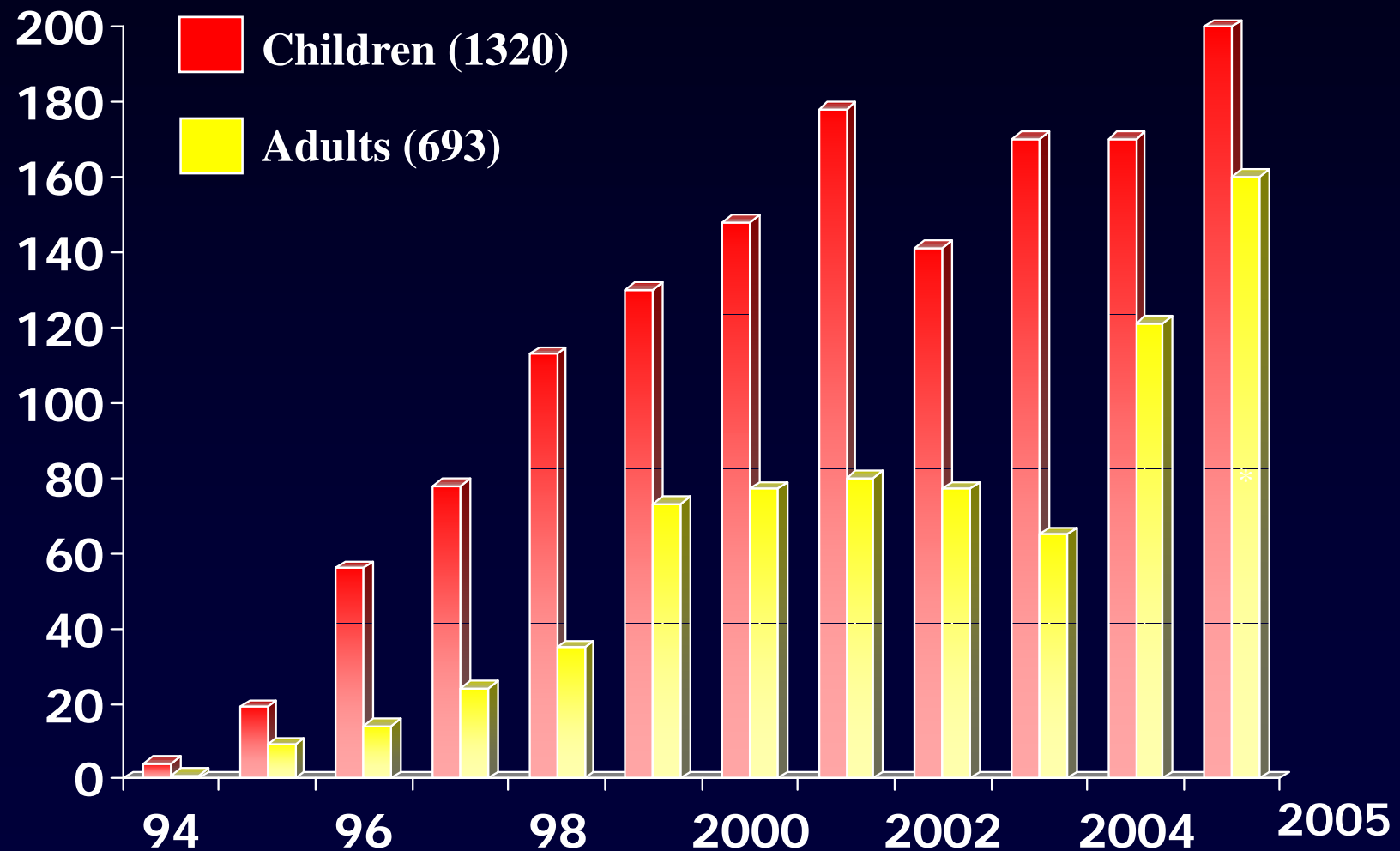
- Registered with CIBMTR, 1996 to 2003 -



## Number of Unrelated CBT / year reported to Eurocord



# Number of Unrelated Donor CBT according to the recipient age/year reported to Eurocord



# ***UNRELATED CORD BLOOD TRANSPLANT IN CHILDREN***

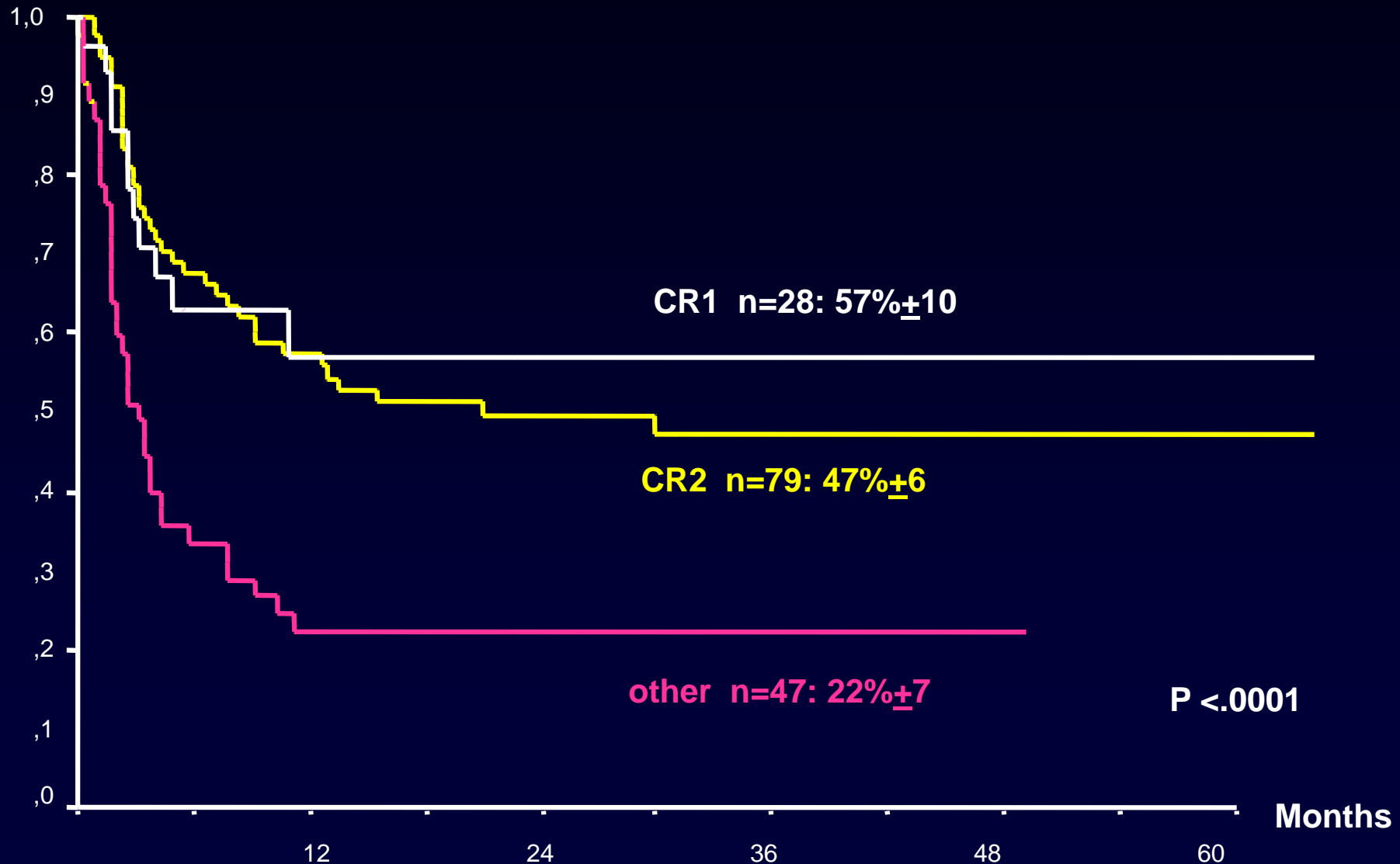
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***Eurocord Registry***



# UCBT in children with AML (n=154)

Leukemia free survival according to the status of the disease at transplant



# **Outcome after Unrelated Umbilical Cord Blood Transplants for Children with Acute Lymphoblastic Leukemia**

**V Rocha, M Labopin, G Michel, N Kabbara, W Arcese, J Ortega, A P Iori, L Madero K-  
W Chan, F Locatelli, F Garnier, I Ionescu, P Wernet, E Gluckman**

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**Eurocord and Acute Leukemia Working Party of EBMT**

*Hôpital Saint-Louis, Paris*

## Patient and disease characteristics (n=361)

	<b>CR1</b>	<b>CR2</b>	<b>Advanced</b>
N	<b>87</b>	<b>152</b>	<b>122</b>
Median age at UCBT	<b>4.7</b> (0.4-16)	<b>6.7</b> (0.7-16)	<b>8.0</b> (0.5-16)
< 1 year	<b>18%</b>	<b>&lt;1%</b>	<b>&lt;1%</b>
+CMV Recipient	<b>43%</b>	<b>44%</b>	<b>58%</b>
Previous autograft	<b>0</b>	<b>2%</b>	<b>10%</b>
Duration of first CR	<b>-</b>	<b>21 mo</b>	<b>23 mo</b>



# Disease Characteristics

**CR1 (n= 87)**      **CR2 (n=152)**      **Advanced (n=122)**

---

Pre-B	<b>47%</b>	<b>56%</b>	<b>66%</b>
B	<b>21%</b>	<b>19%</b>	<b>12%</b>
T	<b>17%</b>	<b>16%</b>	<b>14%</b>
Null	<b>7%</b>	<b>3%</b>	<b>6%</b>
Biphenotypic	<b>8%</b>	<b>6%</b>	<b>2%</b>

Poor risk	<b>89%</b>	<b>38%</b>	<b>39%</b>
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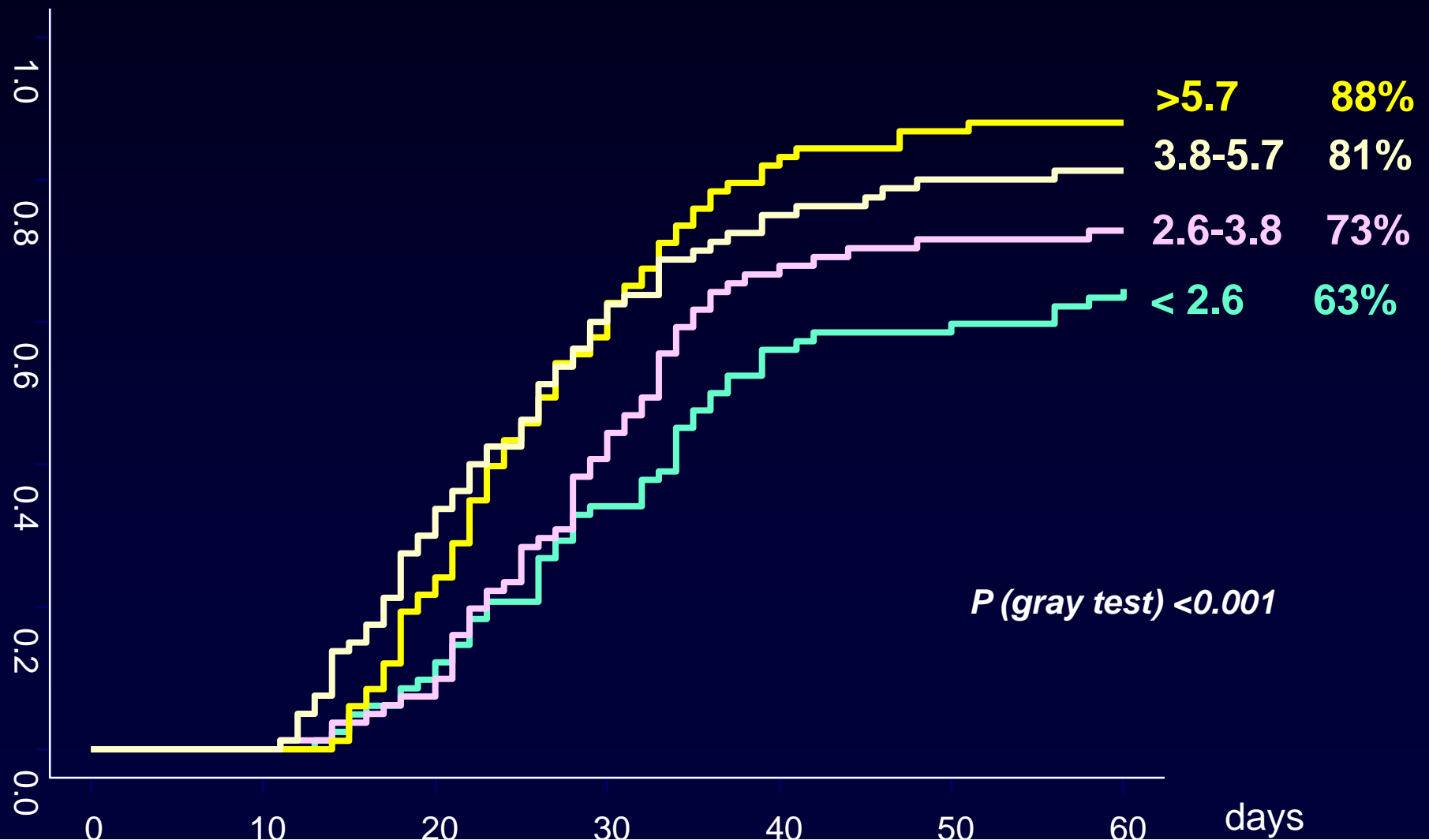
Cytogenetics  
t (9;22), t (4;11)

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# Outcomes after UCBT for children with ALL (n=361)

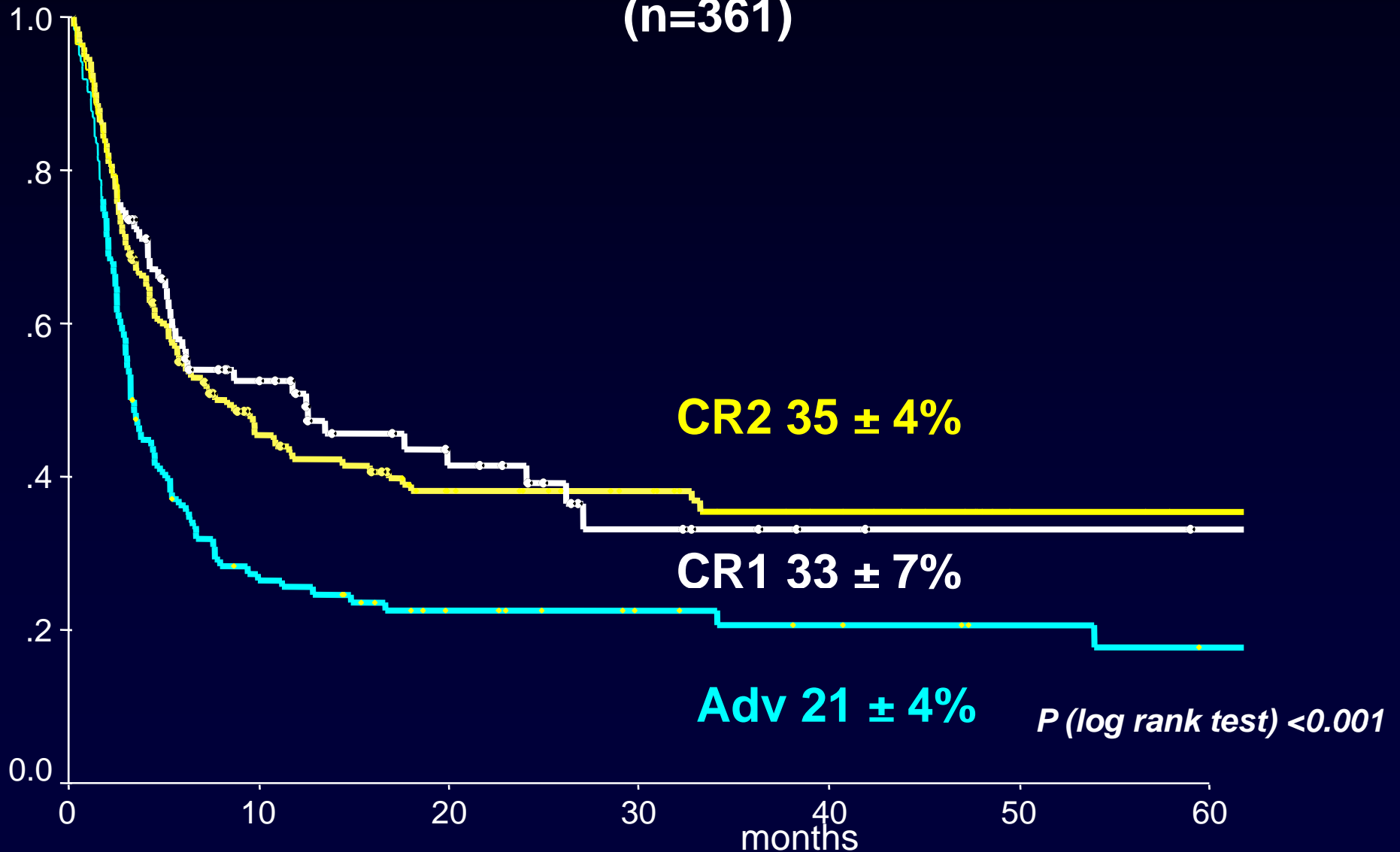
## UCBT for Children with ALL

Cumulative incidence of neutrophil recovery according to number of cells infused ( $10^7/\text{kg}$ ) (per quartiles) (n=361)



# UCBT for Children with ALL

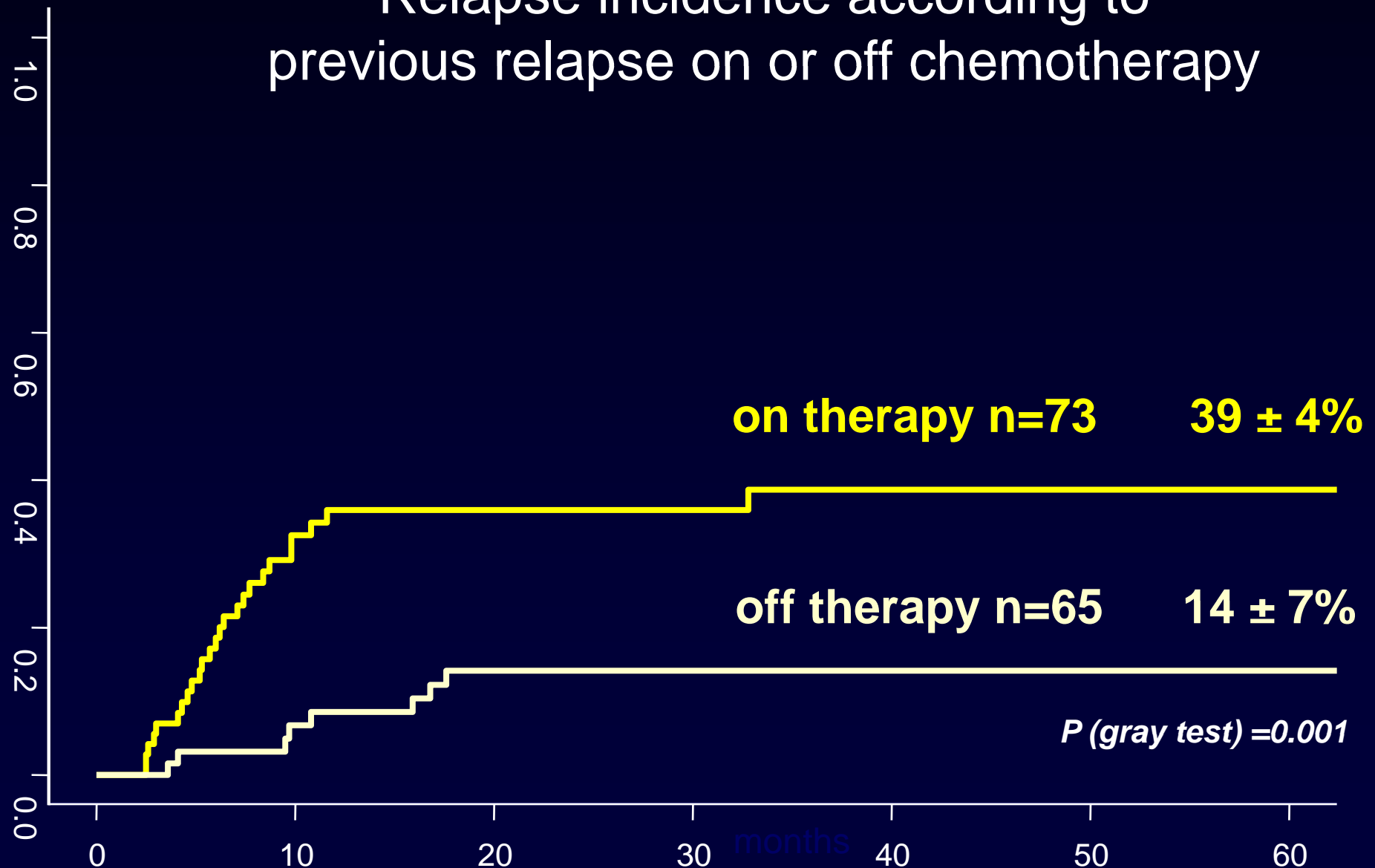
Leukemia Free Survival according to disease status  
(n=361)



# **Risk factors of outcomes after UCBT for children with ALL in 2<sup>nd</sup> CR (n=152)**

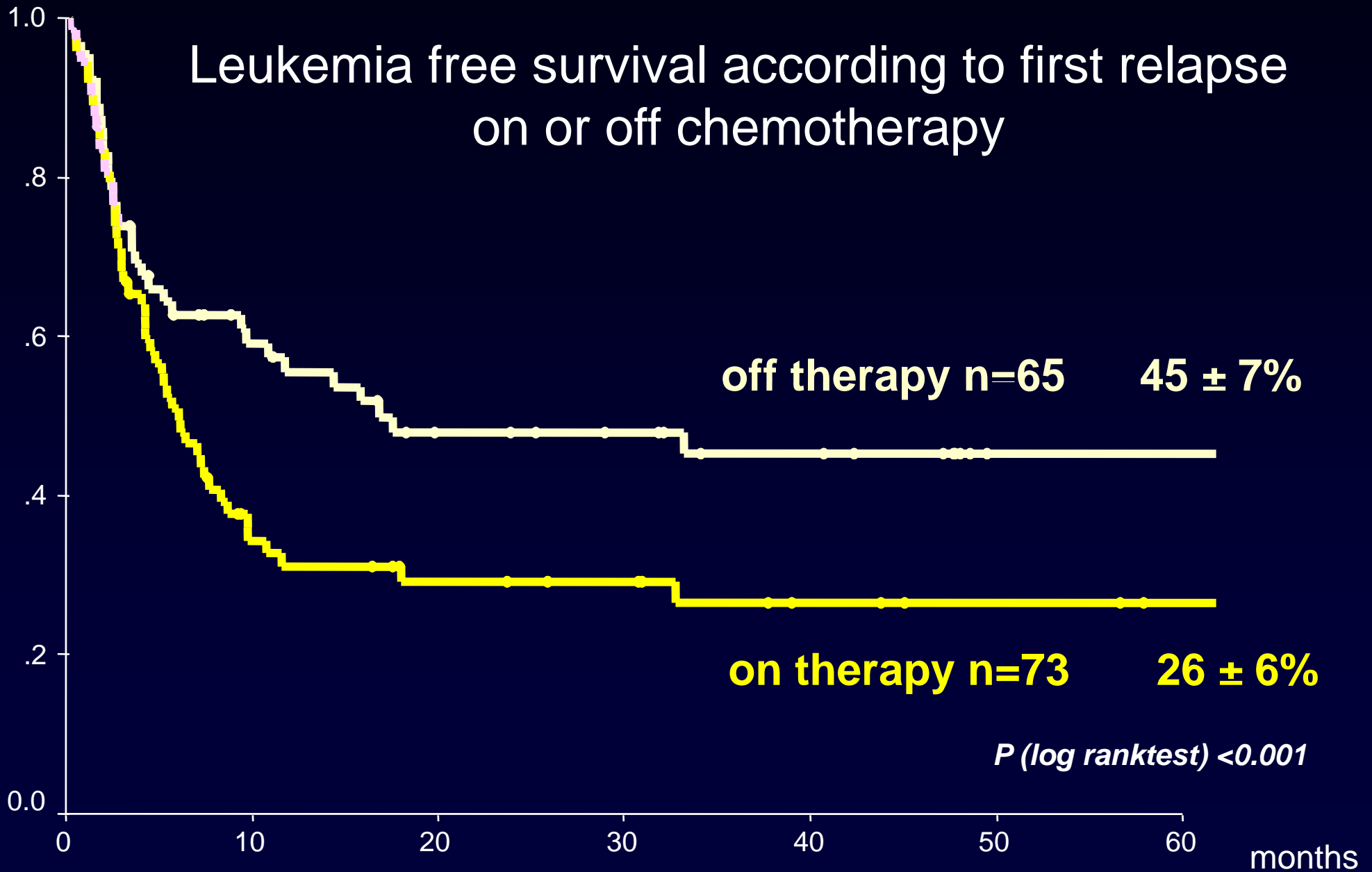
## UCBT for Children with ALL in CR2 (n=152)

Relapse incidence according to  
previous relapse on or off chemotherapy



# UCBT for Children with ALL in CR2 (n=152)

Leukemia free survival according to first relapse on or off chemotherapy



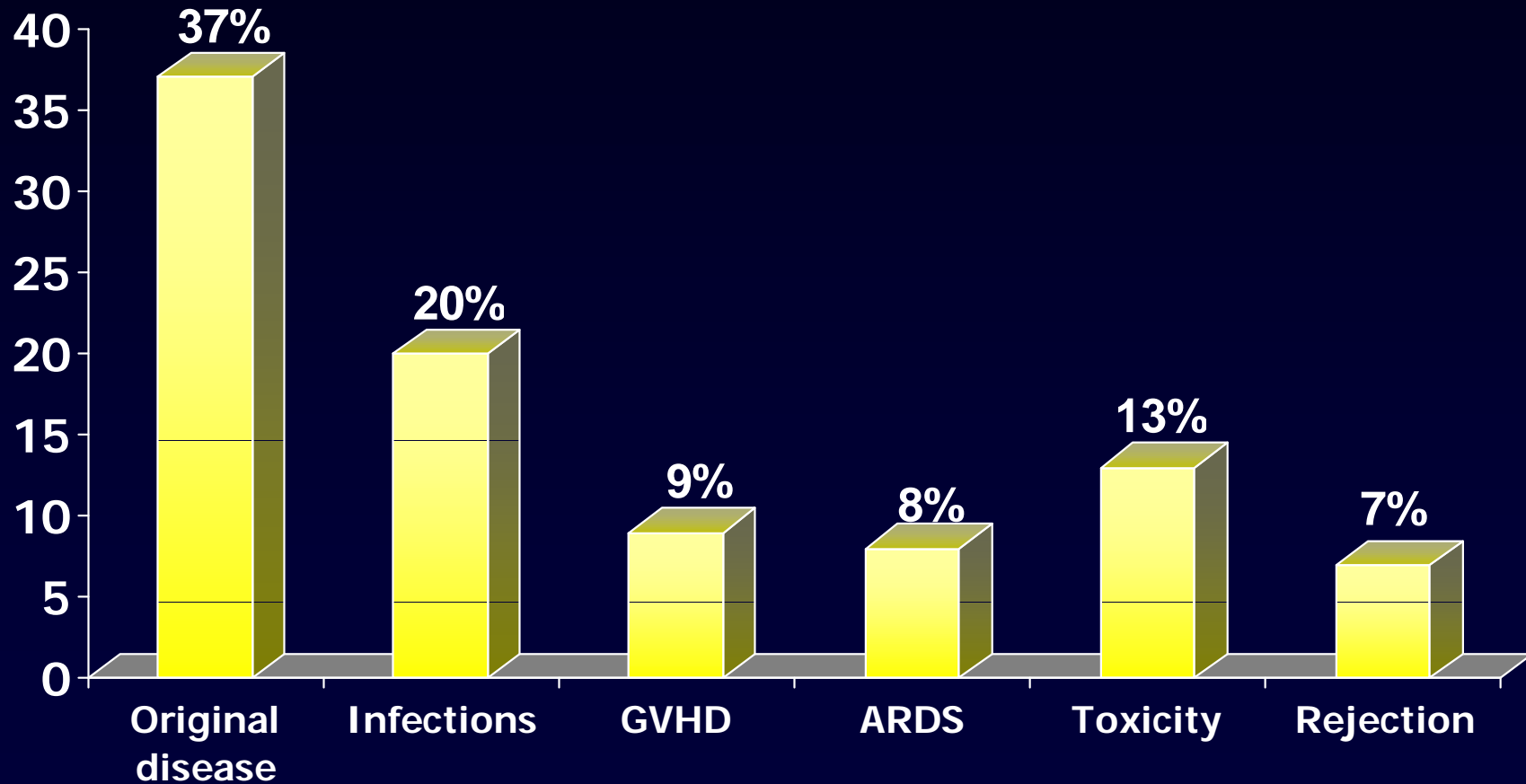
## Results of multivariate analysis in CR2 patients

	p value	RR	95%CI
<b><i>Acute GVHD (II-IV)</i></b>			
Use of Serotherapy	0,03	0,42	0.19-0.93
<b><i>TRM</i></b>	no factor		
<b><i>Relapse</i></b>			
Off therapy	0,03	0,33	0.12-0.92
<b><i>LFS</i></b>			
Off therapy	0,02	0,57	0.36-0.92



*UCBT for Children with ALL in CR2 (n=152)*

**Causes of death (n=86)**



# Comparative studies between UCBT and UBMT in children

(V Rocha Blood 2001, J Barker Blood 2001, H Dalle BMT 2004, Jacobson BMT 2004, P Rubinstein ASH 2005)

**Cord blood vs Bone Marrow**

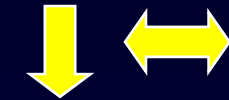
**ENGRAFTMENT**



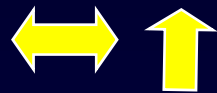
**ACUTE GVHD**



**CHRONIC GVHD**



**EARLY TRM**



**RELAPSE**

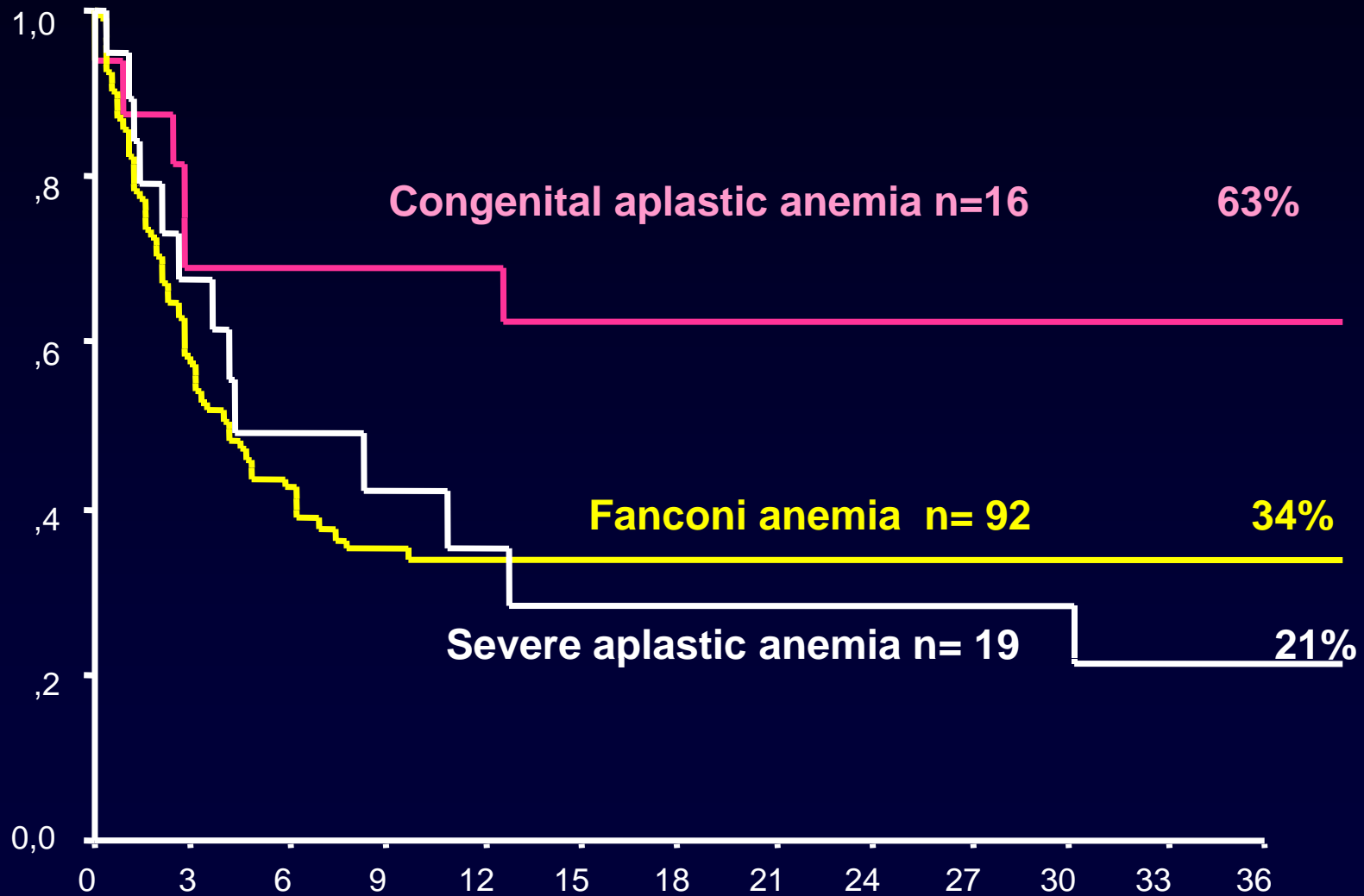


**SURVIVAL**

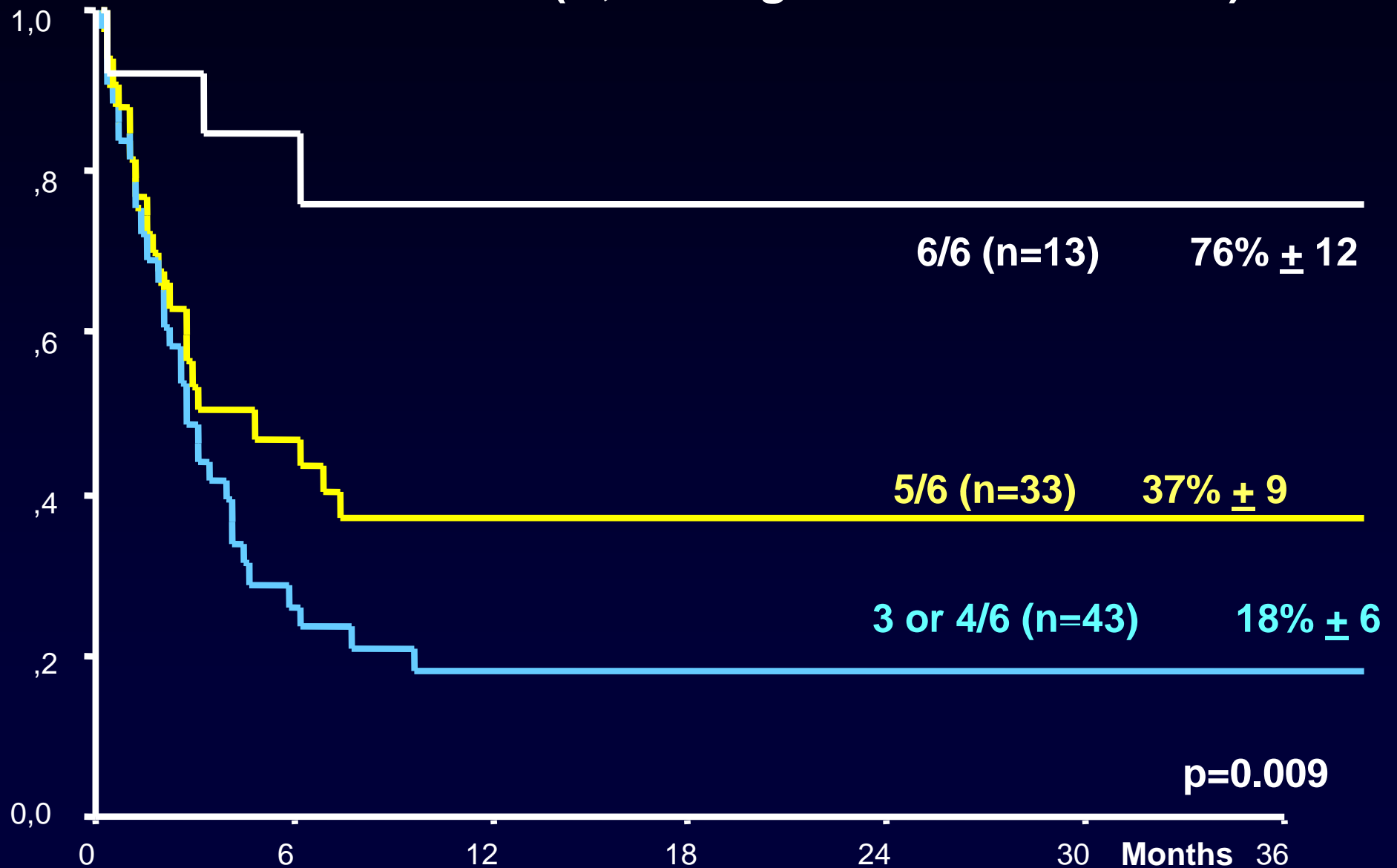


# Non malignant diseases in children

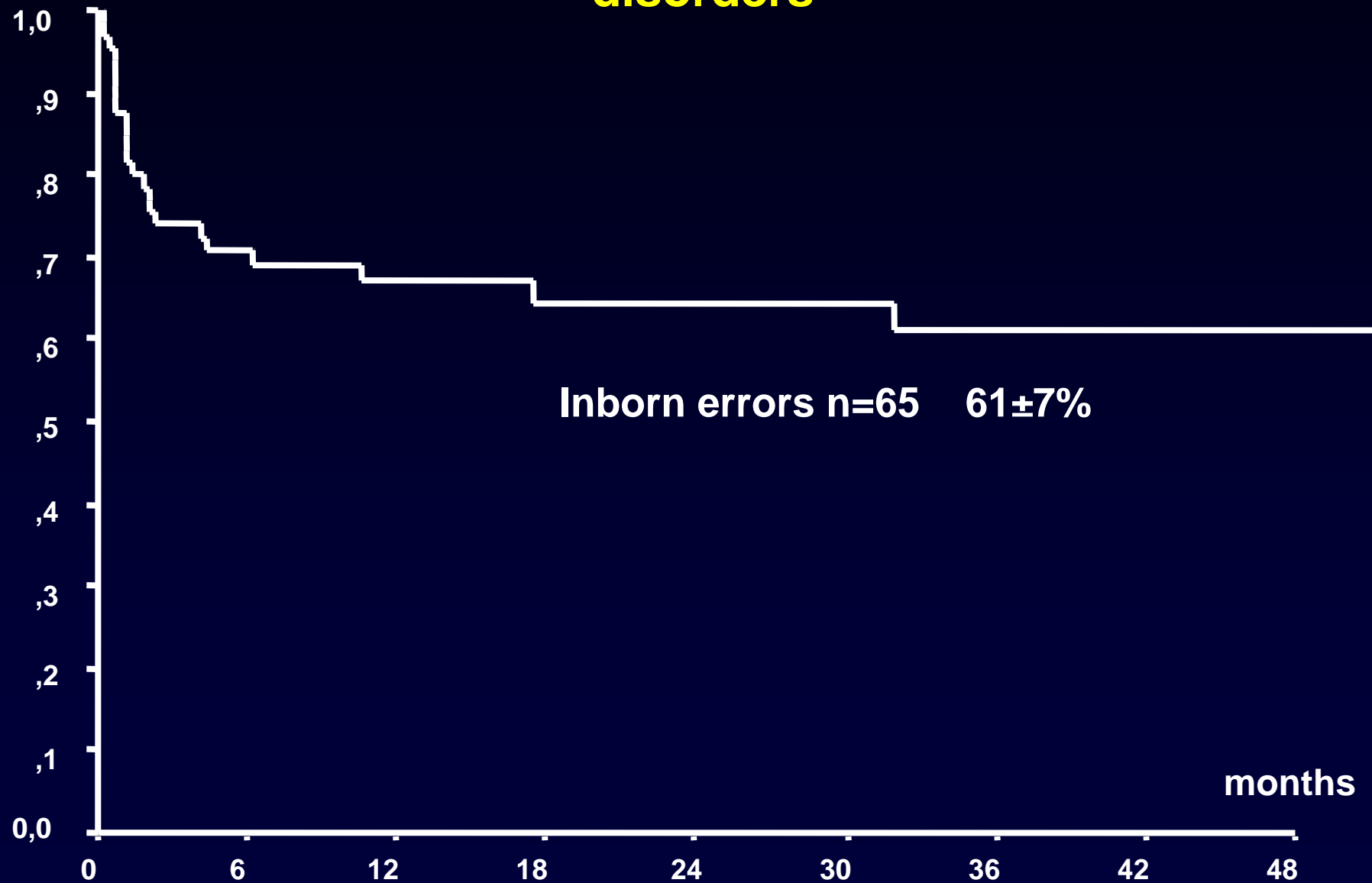
# Overall survival after UCBT in patients with bone marrow failure syndromes



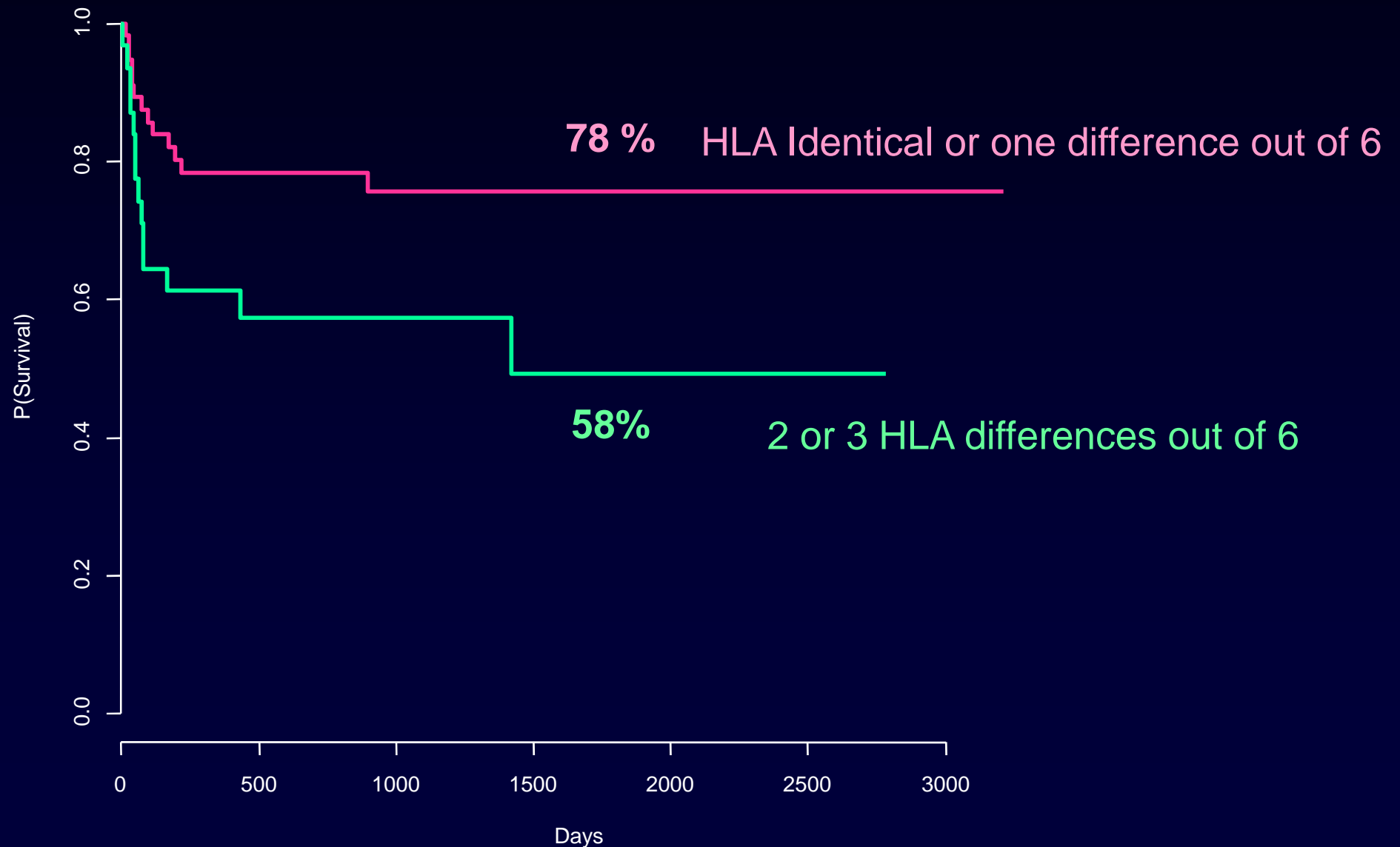
# Survival after UCBT for Fanconi anemia (n=92) according to number of HLA differences (A, B antigen and DRB1 allelic)



# Overall survival after UCBT in children with metabolic disorders



# Overall survival of children with Primary Immunodeficiencies according to Number of HLA differences (n=93)



# ***UNRELATED CORD BLOOD TRANSPLANT IN ADULTS***

## ***Results***

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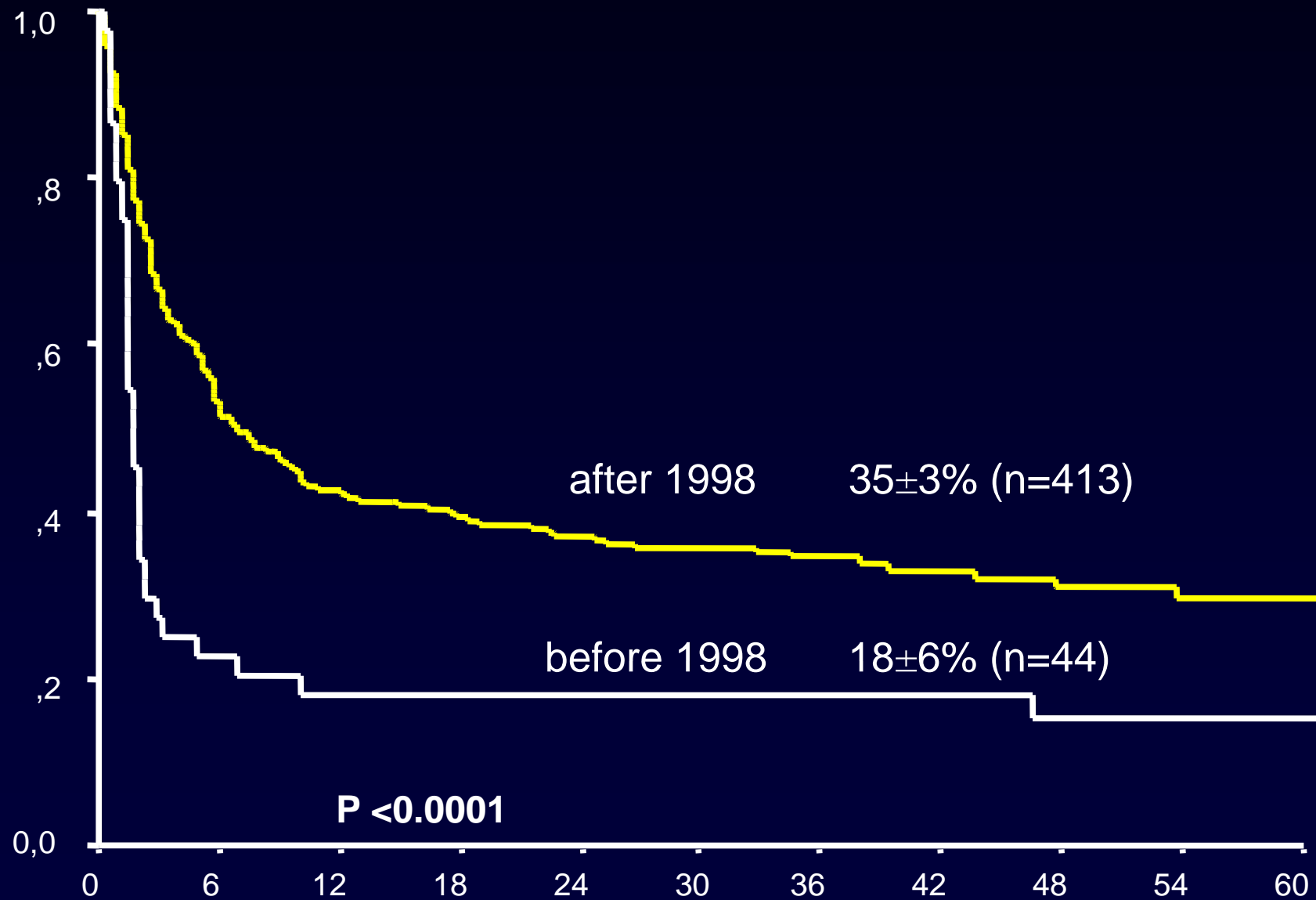


***Eurocord Registry***

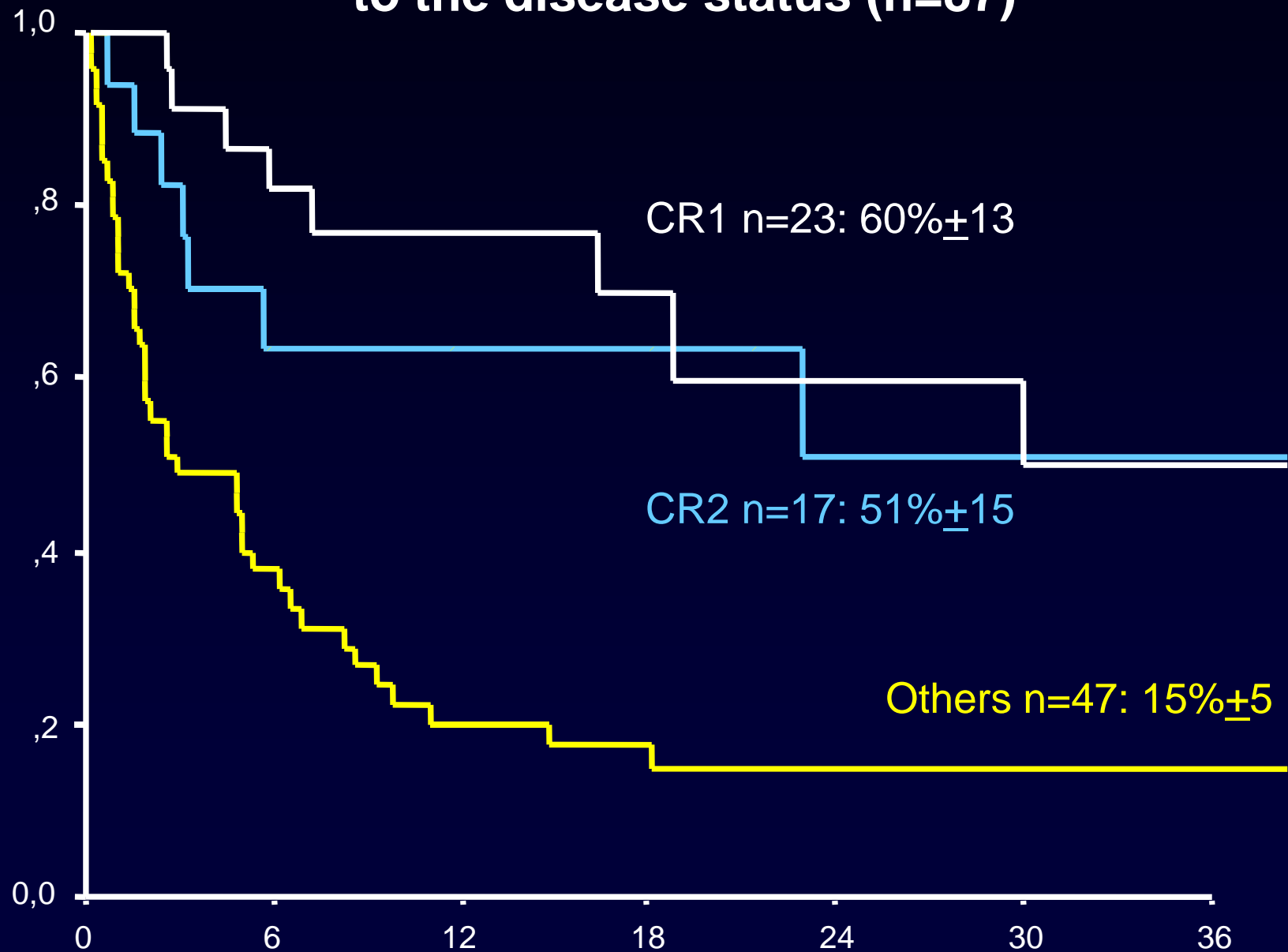




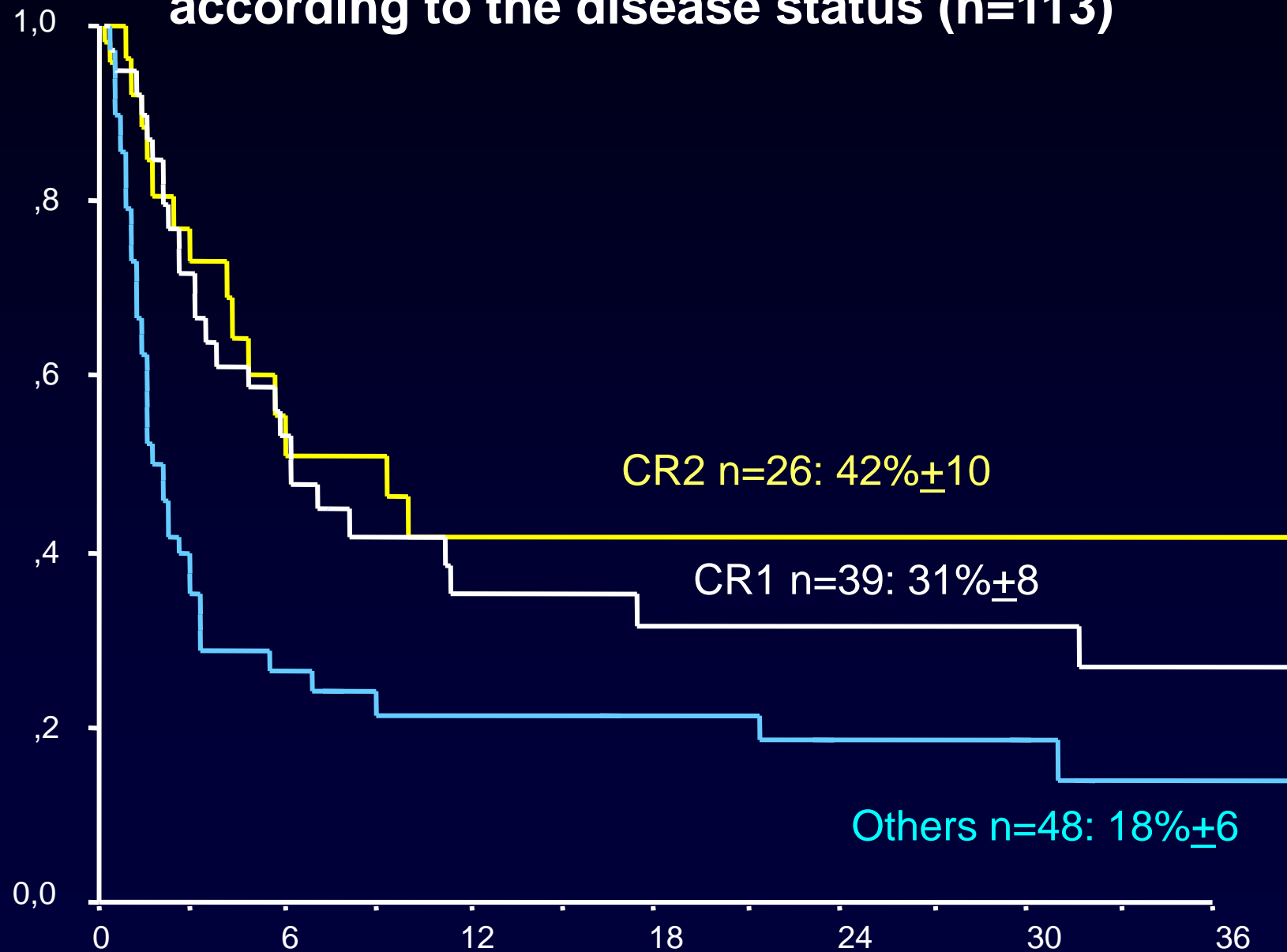
# Overall Survival after UCBT for adults with hematologic malignancies n= 457



# Leukemia Free Survival after UCBT for adults with AML according to the disease status (n=87)



# Leukemia Free Survival after UCBT for adults with ALL according to the disease status (n=113)



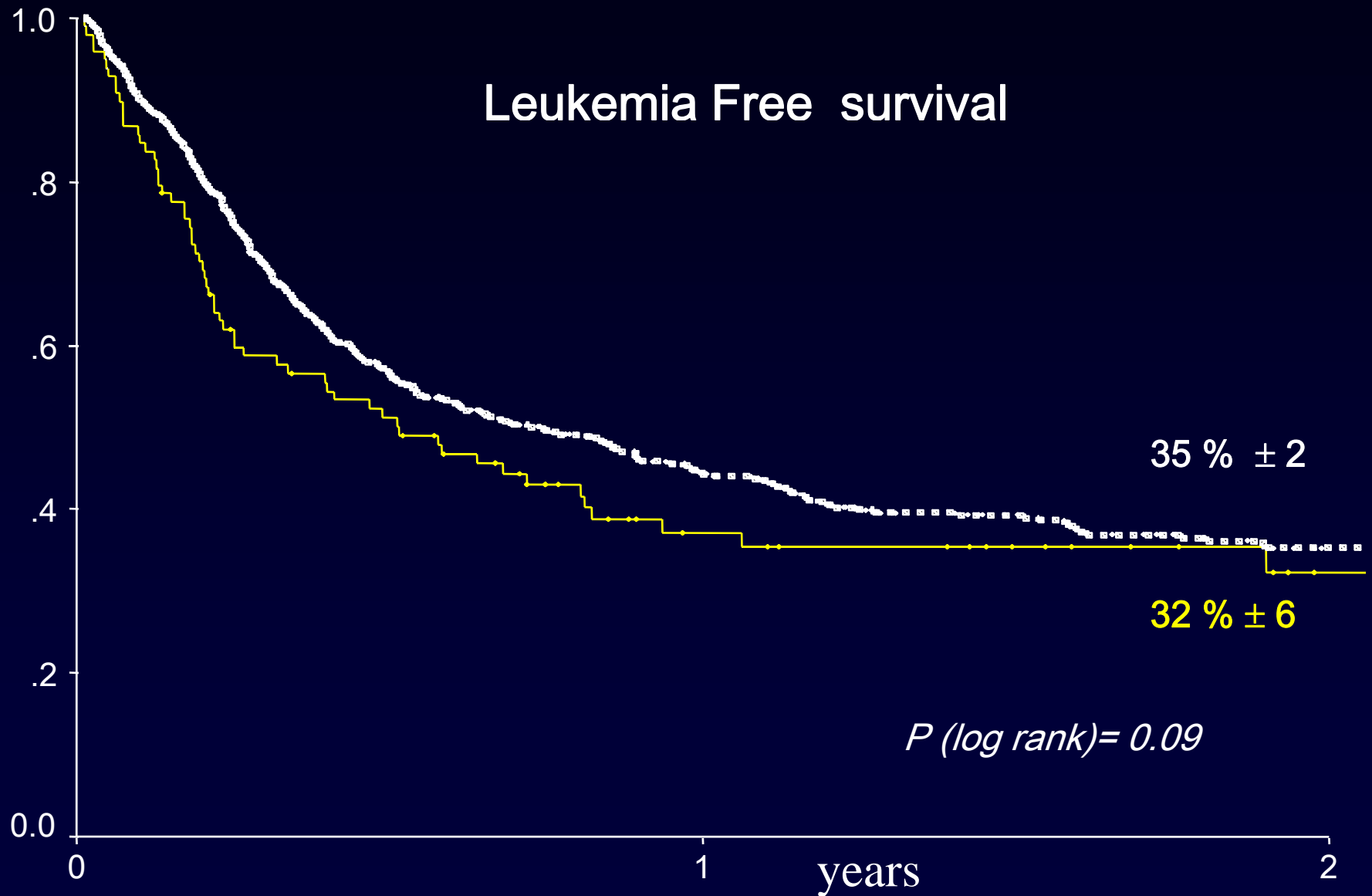
***Outcomes of Unrelated Cord Blood Transplants  
compared to Unrelated Bone Marrow Transplants in  
Adults with Acute Leukemia***

***A retrospective based registry study***



***V Rocha on behalf of Eurocord and Acute Leukemia Working Party-EBMT  
New England Journal of Medecine , Nov 2004***

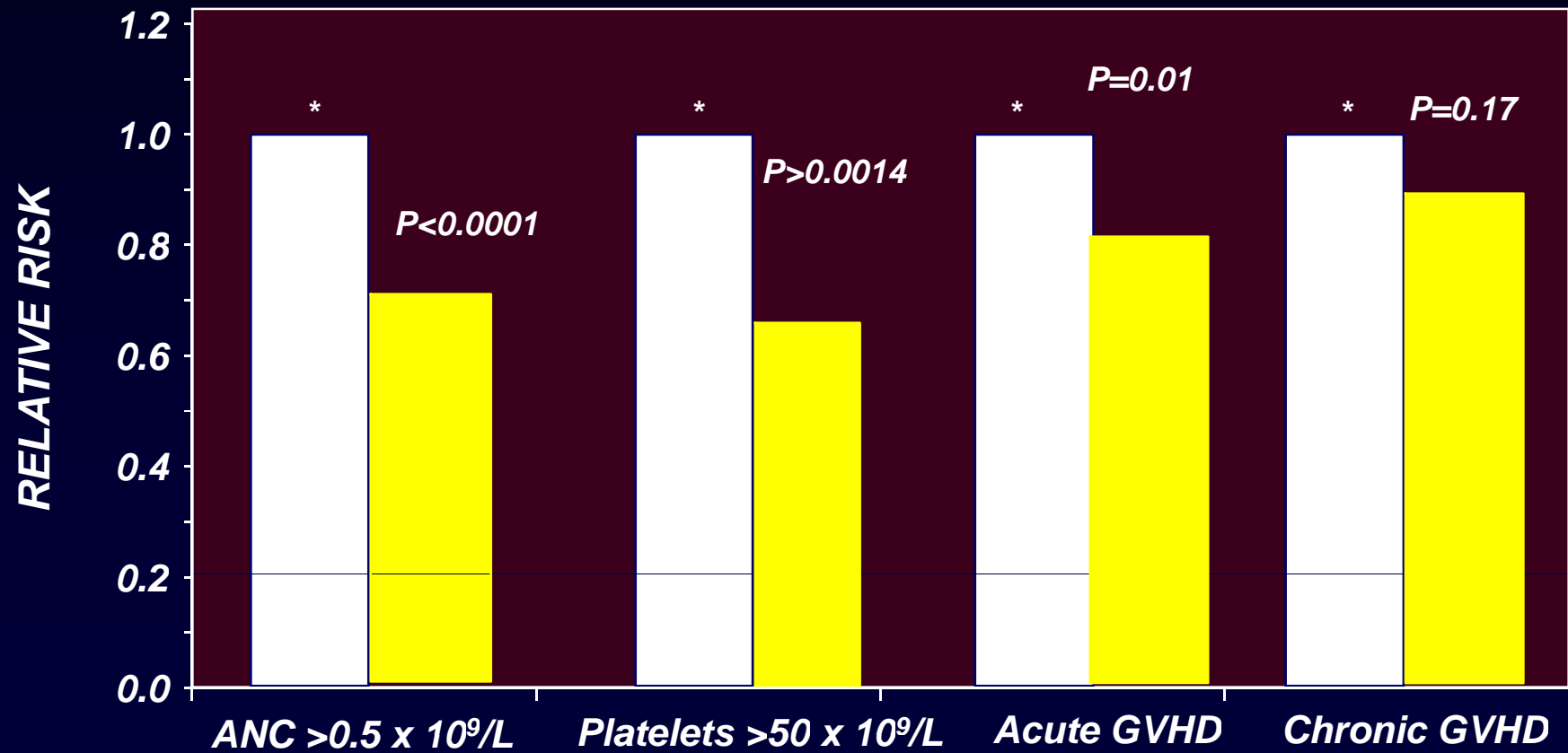
# UCBT versus UBMT in adults with acute leukemias



# MULTIVARIATE ANALYSIS

## - Hematopoietic Recovery & GVHD -

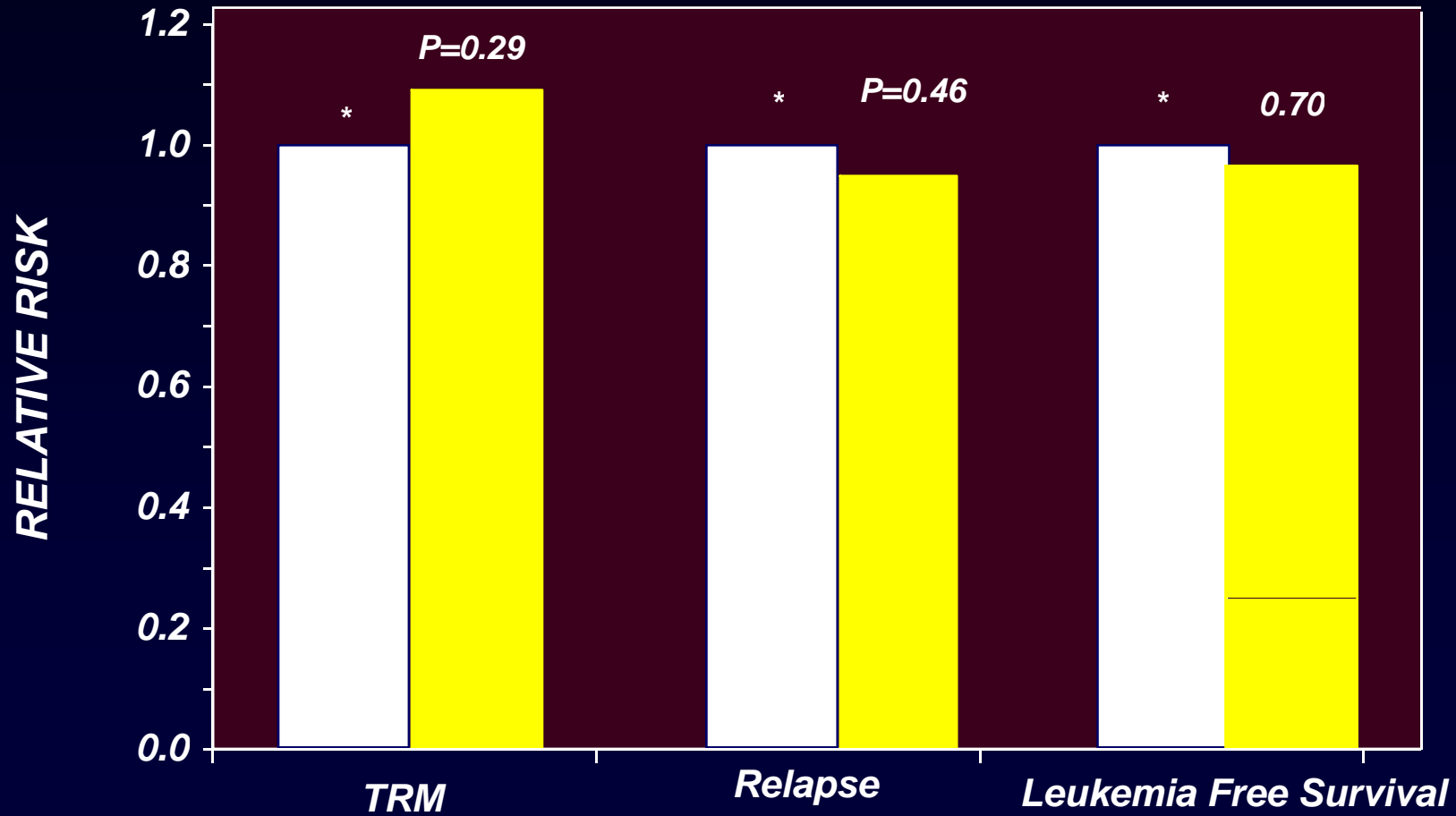
UBMT  
UCBT



\* Reference Group

# MULTIVARIATE ANALYSIS - TRM , RELAPSE AND LFS -

■ UBMT  
■ UCBT



\* Reference Group

# Indication for allogeneic HSCT

NO HLA identical sibling

NO HLA matched unrelated donor



Unrelated Cord Blood



Haplo Identical T-cell depleted  
PBSC





# Comparison of outcomes after Unrelated Cord Blood or



# Haploidentical T-cell depleted Peripheral Blood Stem Cells in Adults with High Risk Acute Leukemia

V Rocha, F Aversa, M Labopin, G Sanz, F Ciceri, W Arcese, D Bunjes, J Rowe, P Di Bartolomeo, F Frassoni, M Martelli and E Gluckman on behalf of the Eurocord-Netcord and Acute Leukemia Working Party  
EBMT

## *Patients*

**From 1998-2002**

**229 haplo and 139 UCBT were performed for adults with high risk acute leukemia (AML and ALL)**

**Two different analysis were performed**

**AML patients      Haplo= 154**

**UCBT= 66**

**ALL patients      Haplo= 75**

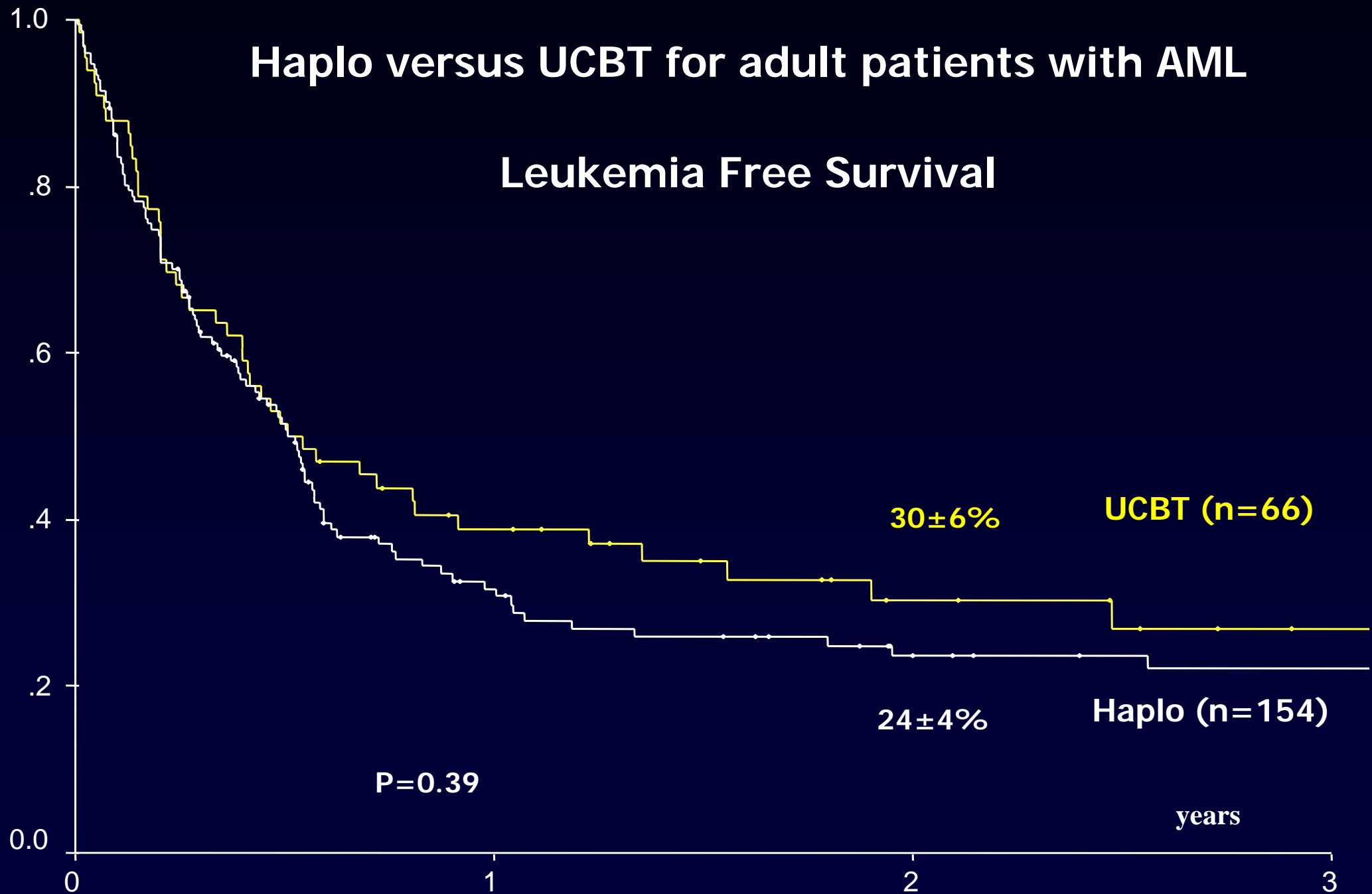
**UCBT= 73**

## *AML Patients and Disease characteristics*

	Haplo	UCBT	P
<b>N</b>	<b>154</b>	<b>66</b>	
<b>Status at transplant</b>			<b>0.9</b>
<b>CR1</b>	<b>33 (21%)</b>	<b>15 (23%)</b>	
<b>CR2</b>	<b>32 (21%)</b>	<b>12 (18%)</b>	
<b>More advanced</b>	<b>89 (58%)</b>	<b>39 (59%)</b>	
<b>Previous autologous transplant</b>	<b>21%</b>	<b>25%</b>	<b>0.61</b>
<b>Interval from diag-transplant</b>	<b>333 d</b>	<b>384 d</b>	<b>0.16</b>
<b>Median year of transplantation</b>	<b>2000</b>	<b>2000</b>	<b>0.21</b>

# Haplo versus UCBT for adult patients with AML

## Leukemia Free Survival



## Haplo versus UCBT for adult patients with AML

2 year-LFS according to status of the disease

	Haplo	UCBT	P
CR1	48±9%	48±14%	0.94
CR2	42±10%	44±16%	0.70
Advanced	8±3%	20±6%	0.29

## *ALL Patients and Disease characteristics*

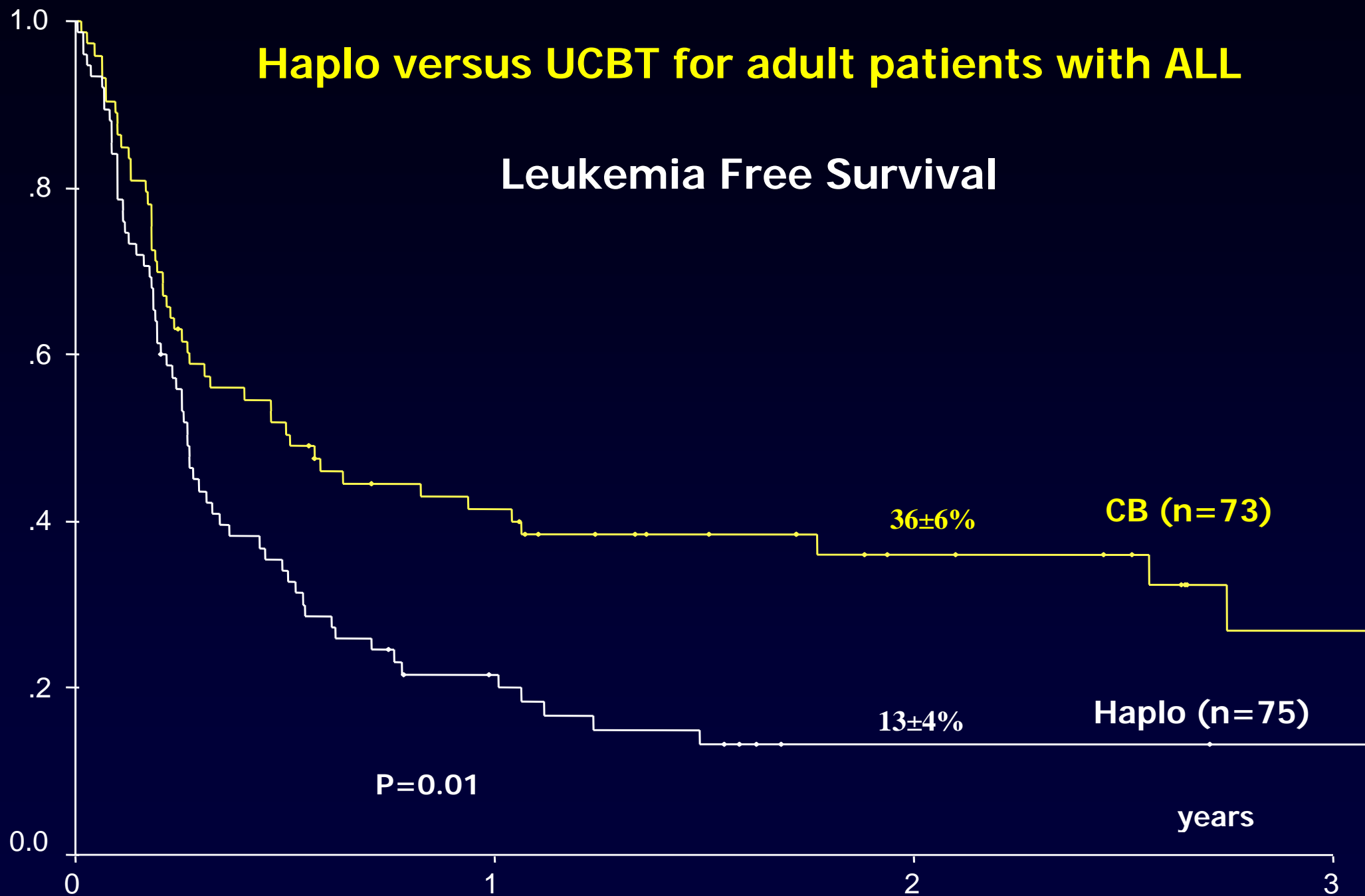
	<b>Haplo</b>	<b>UCBT</b>	<b>P</b>
<b>N</b>	<b>75</b>	<b>73</b>	
<b>Age (y) Median</b>	<b>27</b>	<b>20</b>	<b>0.007</b>
<b>Range</b>	<b>15-56</b>	<b>15-55</b>	
<b>CMV+</b>	<b>65%</b>	<b>62%</b>	<b>0.76</b>
<b>Cytogenetics abnormality</b>			
<b>t (9;22)</b>	<b>41%</b>	<b>34%</b>	<b>0.57</b>

## *ALL Patients and Disease characteristics*

	Haplo	UCBT	P
<b>N</b>	<b>75</b>	<b>73</b>	
<b>Status at transplant</b>			<b>0.79</b>
CR1	23 (31%)	15 (29%)	
CR2	18 (24%)	12 (20%)	
More advanced	34 (45%)	39 (51%)	
<b>Previous autologous transplant</b>	<b>13%</b>	<b>14%</b>	<b>0.90</b>
<b>Interval from diag-transplant</b>	<b>419 d</b>	<b>415 d</b>	<b>0.10</b>
<b>Median year of transplantation</b>	<b>2000</b>	<b>2000</b>	<b>0.23</b>

# Haplo versus UCBT for adult patients with ALL

## Leukemia Free Survival





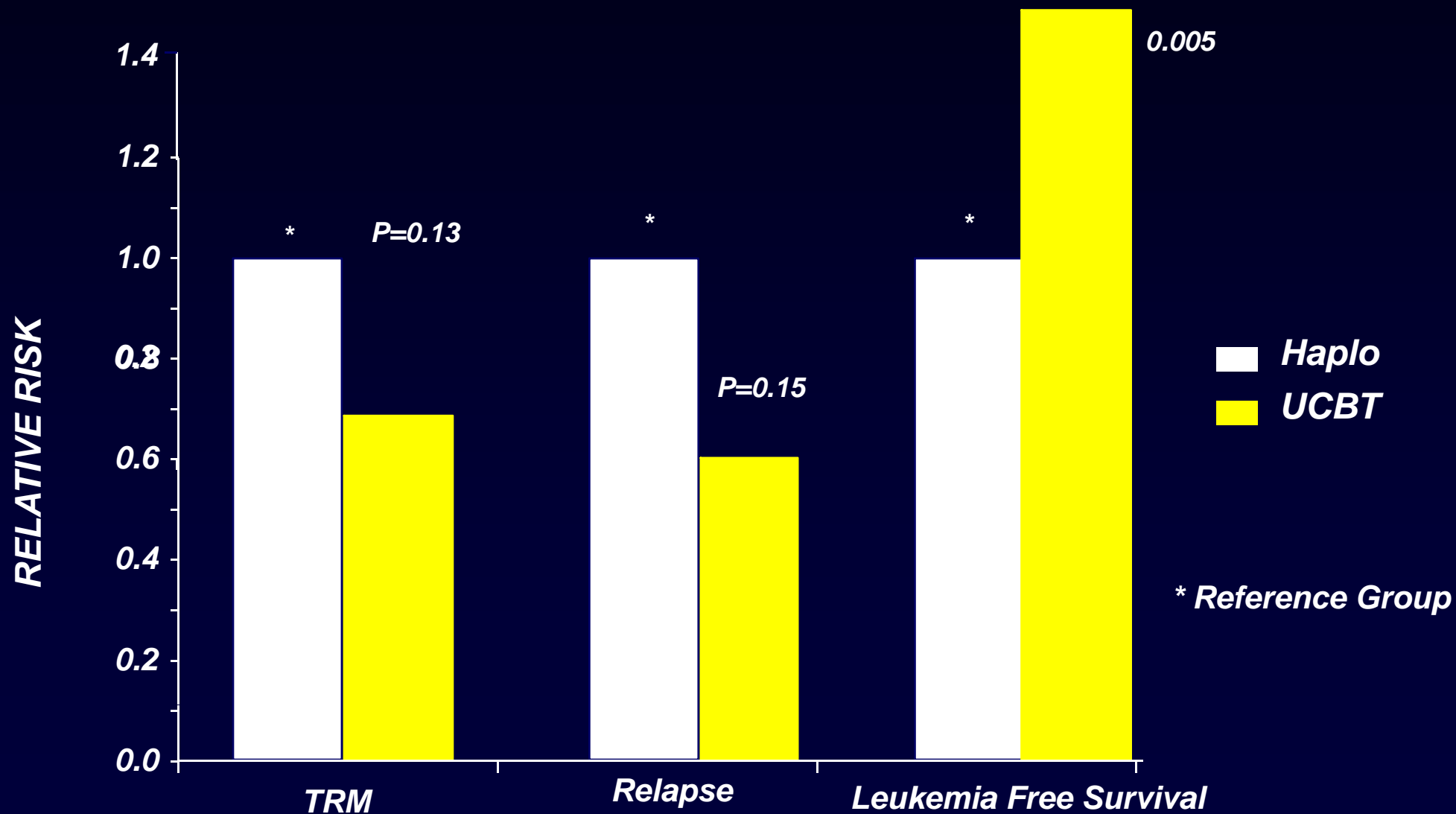
## Haplo versus UCBT for adult patients with ALL

Unadjusted 2 year-LFS according to status of the disease

	<b>Haplo</b>	<b>UCBT</b>	<b>P</b>
<b>CR1</b>	<b>32±10%</b>	<b>38±11%</b>	<b>0.92</b>
<b>CR2</b>	<b>15±9%</b>	<b>40±13%</b>	<b>0.16</b>
<b>Advanced</b>	<b>0%</b>	<b>33±8%</b>	<b>0.0004</b>

## Haplo versus UCBT for adult patients with ALL

Multivariate analysis –TRM, Relapse and LFS



## *Conclusions*

- In this retrospective registry-based analysis in adults patients with high risk acute leukemia, outcomes of HLA mismatched UCBT compared to T-cell depleted Haploidentical PBSC have shown
  - Delayed neutrophil recovery
  - Increased incidence of acute GVHD
  - Same incidence of chronic GVHD in ALL and increased incidence in AML
- In patients **with AML**, TRM, relapse rate and LFS were similar between UCBT and Haplo transplants.
- In patients **with ALL**, LFS is increased in UCBT recipients compared to Haplo transplants

# How to improve engraftment?

## Donor choice

How to choose the best unit?

## Strategies of Cord Blood Banks

Collection of units containing high number of cells

## Under investigation

Use of hematopoietic growth factors at day 0

Ex vivo expansion of cord blood cells

Intrabone injection of cord blood cells

Co-infusion of mesenchymal cells

Reduced intensity conditioning regimen using cord blood cells

Use of double transplants

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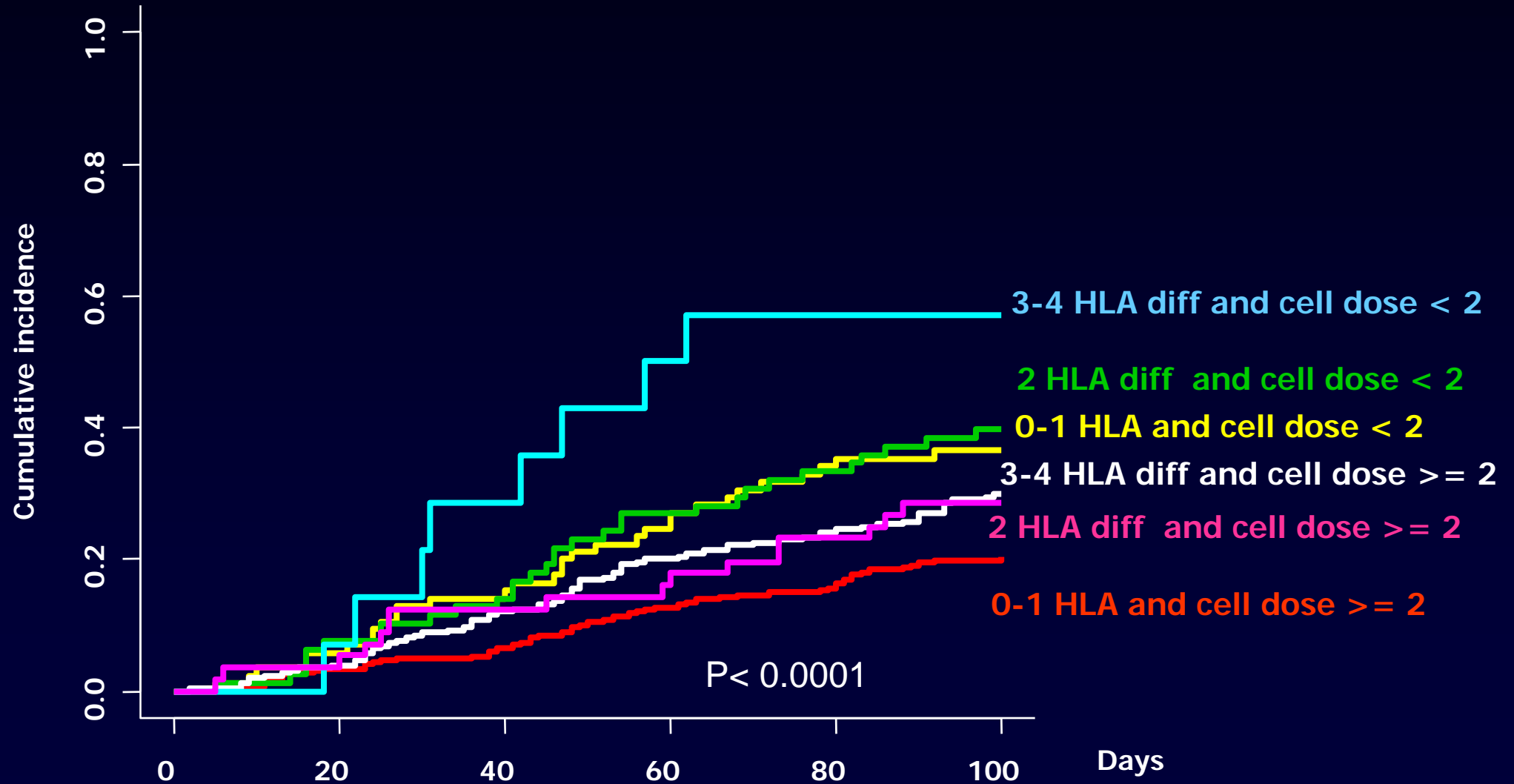
Use of double transplants

**Impact of number and type of HLA incompatibilities and cell dose on outcomes of unrelated cord blood transplants for patients with malignant and non-malignant disorders**

**An Eurocord registry analysis**

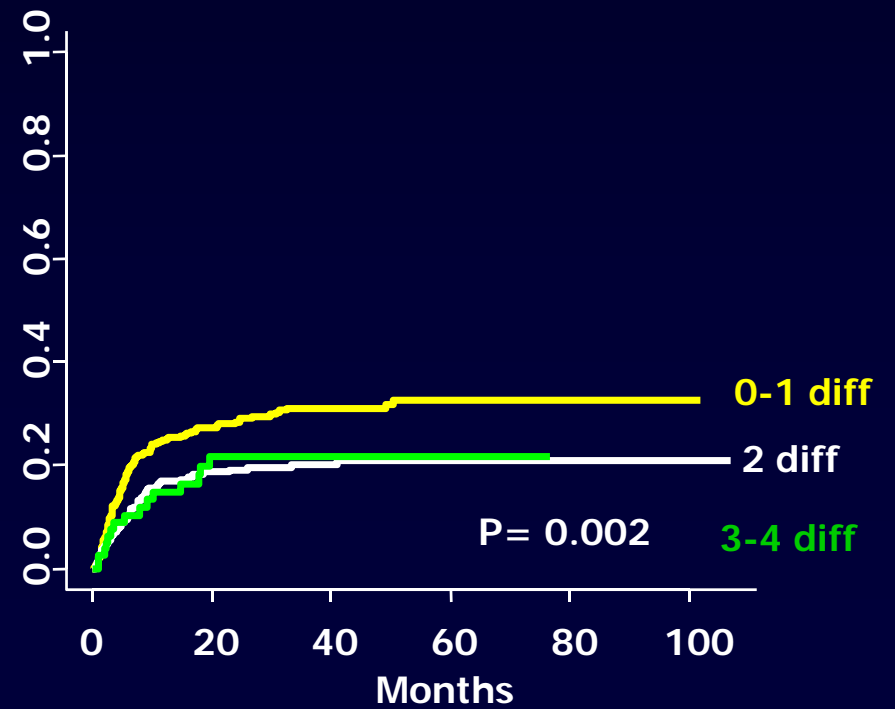
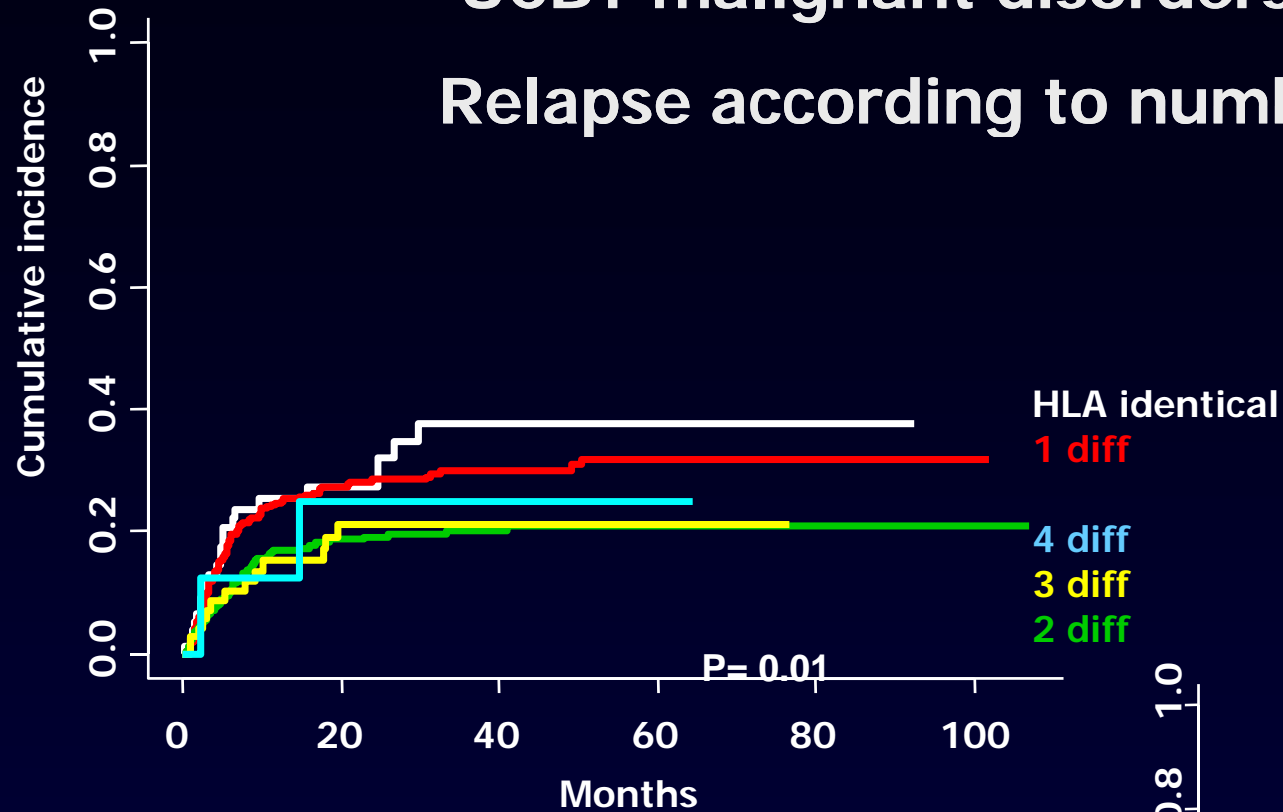
# UCBT malignant disorders (n=929)

## TRM according to number of HLA and cell dose



# UCBT malignant disorders (n=929)

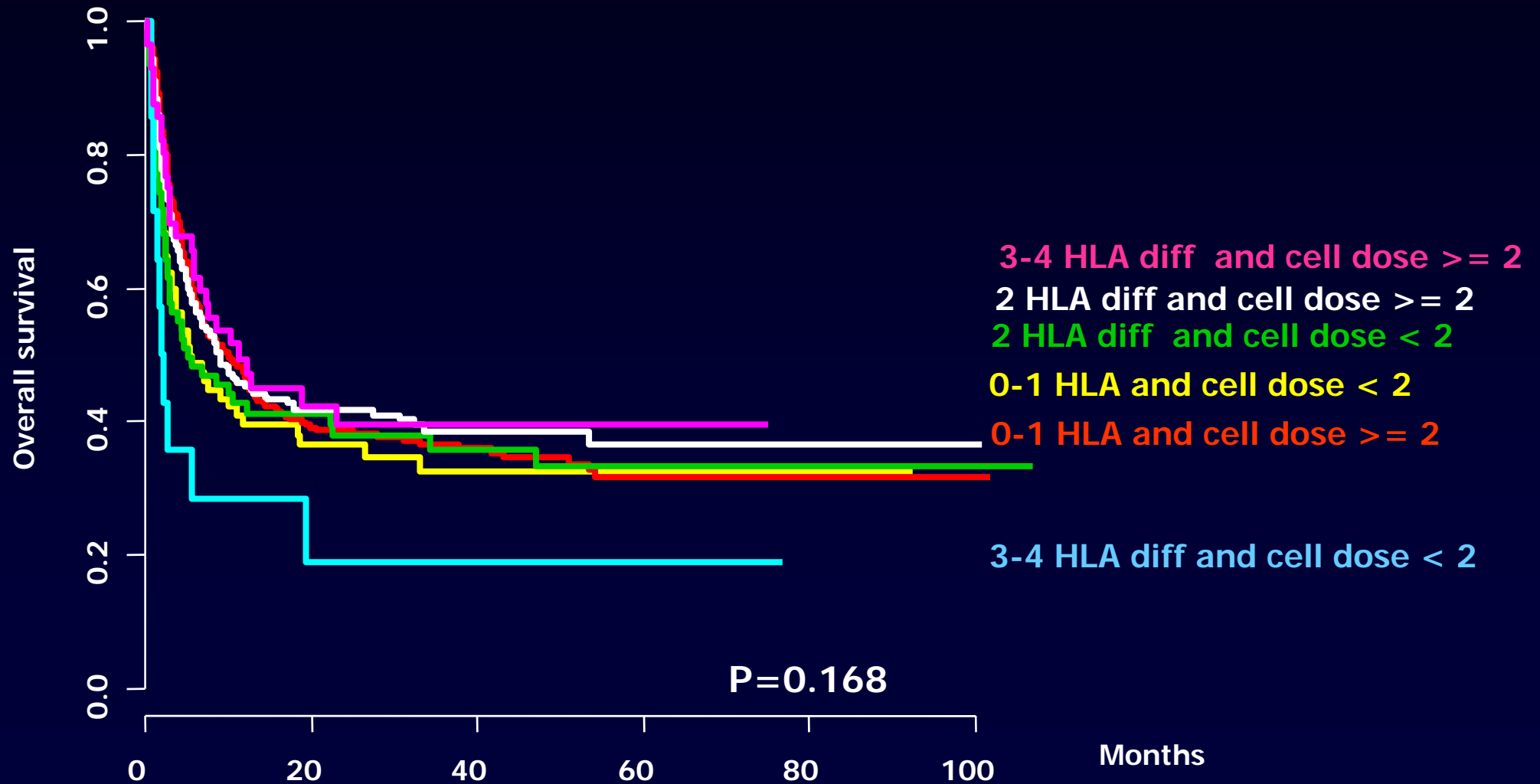
## Relapse according to number of HLA





# UCBT malignant disorders (n=929)

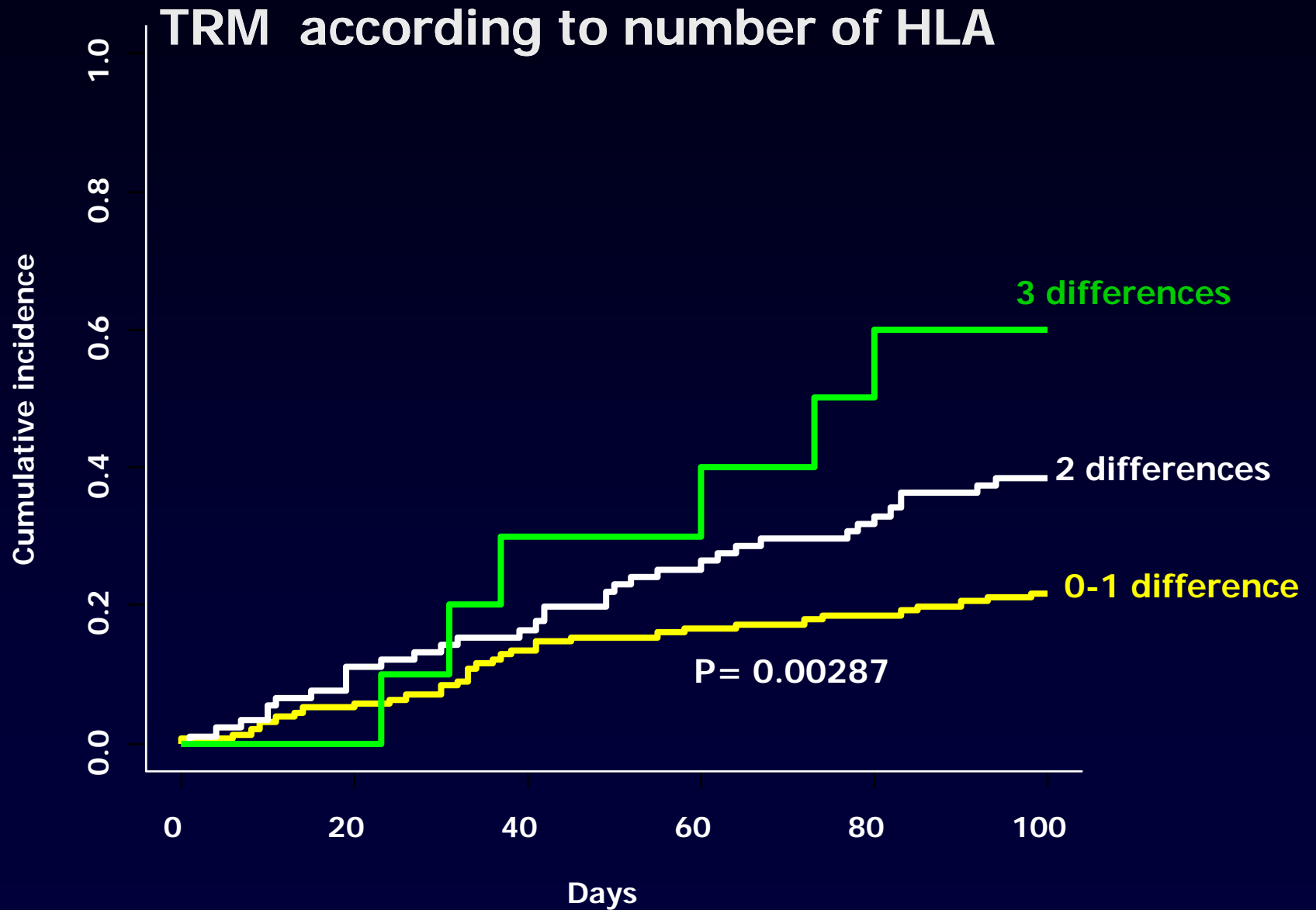
## Overall survival according to number of HLA and cell dose



## Interaction between HLA mismatches, number of cells and outcomes after unrelated CBT for malignant diseases

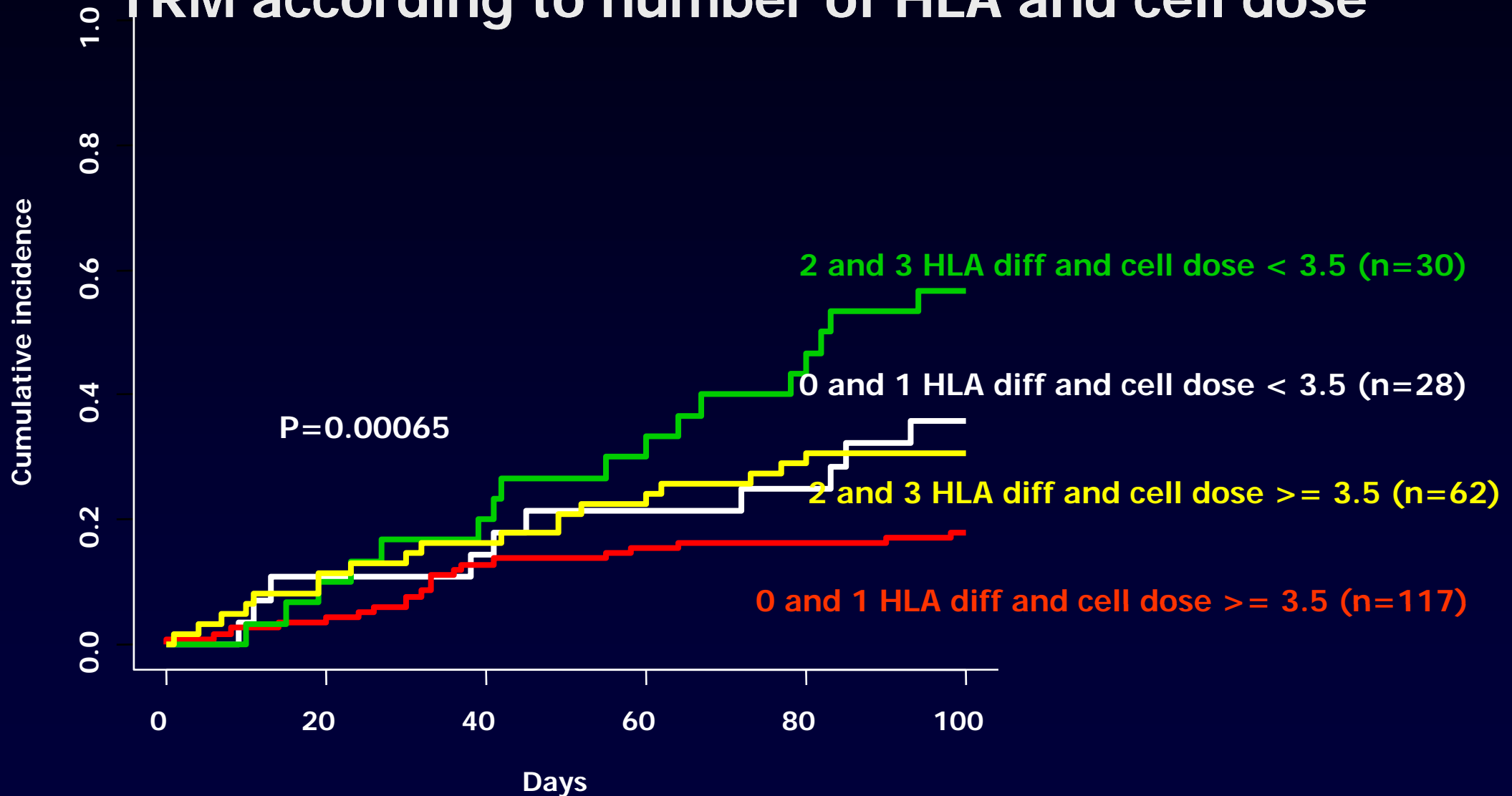
	<b>Number of HLA MM 0-1 vs 2 vs 3-4</b>	<b>Type of HLA MM Class I vs class II</b>	<b>Interaction with number of cells</b>
<b>PMN engraftment</b>	Less	Same	Worse 3-4 MM and <3x10 <sup>7</sup> NC/kg
<b>Platelet engraftment</b>	Less	Same	Worse 3-4 MM and <3x10 <sup>7</sup> NC/kg
<b>TRM</b>	More	More 2 DR MM	Worse 3-4 MM and <3x10 <sup>7</sup> NC/kg
<b>AGVH</b>	More	More 2 DR MM	Same
<b>CGVH</b>	More	Same	Decreased < MM and > cells
<b>Relapse</b>	Less	Less 2 DR MM	Increased < MM and > cells
<b>OS , EFS</b>	Same	Same	Decreased >MM and <cells

# UCBT in non-malignant disorders (n=268)



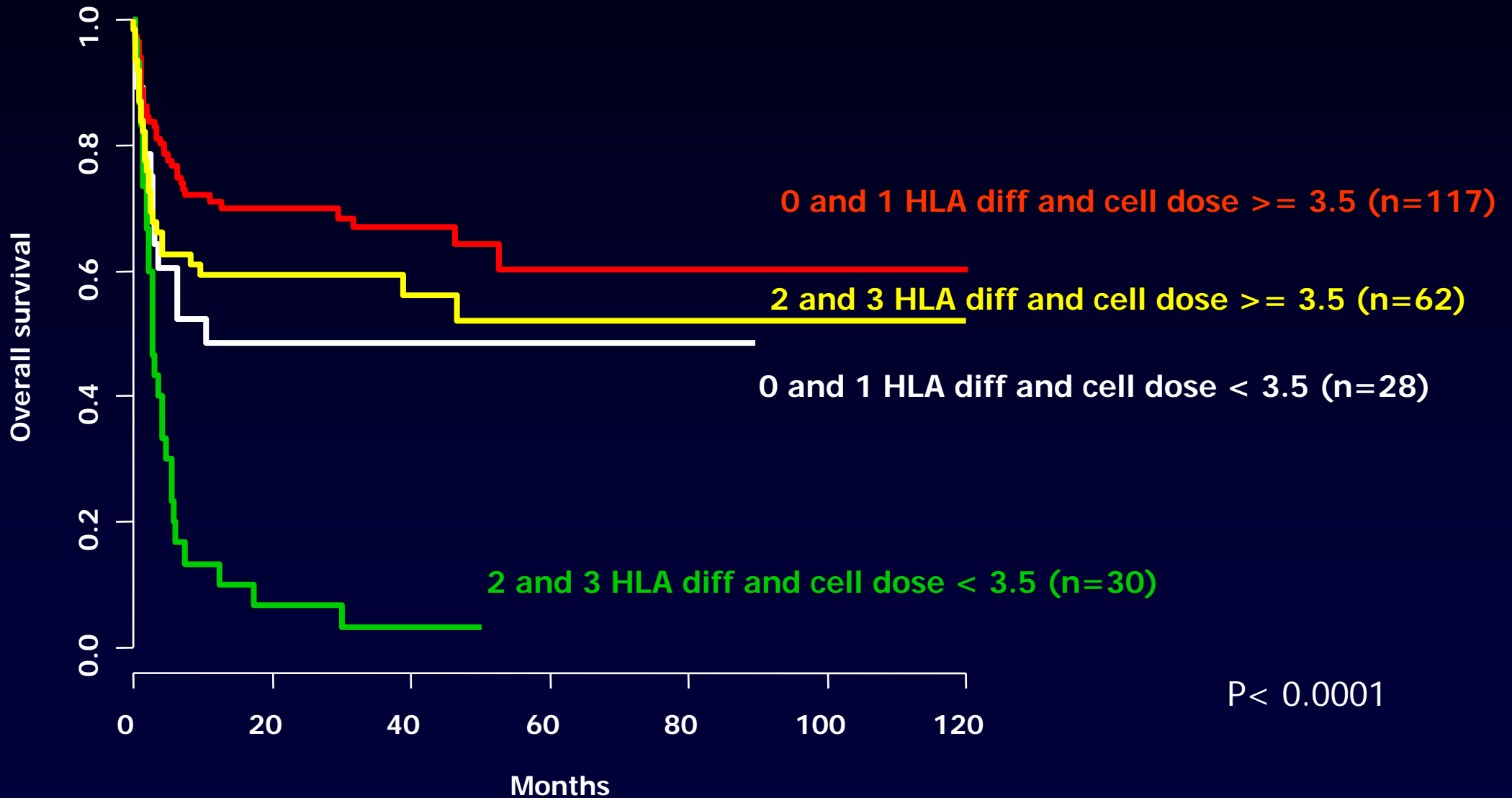
# UCBT in non-malignant disorders (n=268)

## TRM according to number of HLA and cell dose



# UCBT in non-malignant disorders (n=268)

## Overall survival according to HLA and cell dose



## Interaction between HLA mismatches, number of cells and outcomes after unrelated CBT for non malignant diseases

	Number of HLA MM 0-1 vs 2 vs 3-4	Type of HLA MM Class I vs class II	Interaction with number of cells
PMN engraftment	Less	More 1 HLA-B # Less 2 DRB1=	Less <cells and more MM
Platelet engraftment	Less	More 1 HLA-B # Less 2 DRB1=	Less <cells and more MM
TRM	More	More 2 DRB1=	Less <cells and more MM
AGVH	More	Same	More >cells and>MM
CGVH	More	Same	More >cells and>MM
OS , EFS	Less	Less with DRB1	Worse if HLA MM $\geq$ 2 and NC $\leq$ 3.5NC/kg

# How to improve engraftment?

## Donor choice

How to choose the best unit?

## Strategies of Cord Blood Banks

Collection of units containing high number of cells

## Under investigation

Use of hematopoietic growth factors at day 0

Ex vivo expansion of cord blood cells

Intrabone injection of cord blood cells

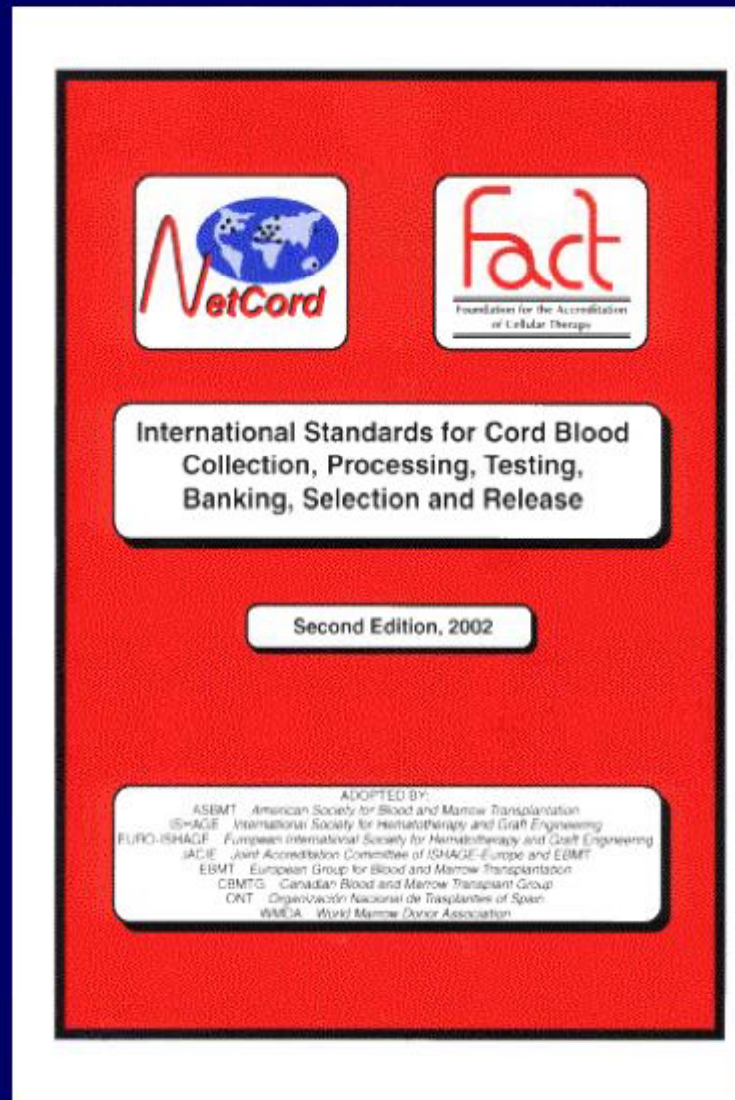
Co-infusion of mesenchymal cells

Use of double transplants

Reduced intensity conditioning regimen using cord blood cells



# NETCORD/FACT Standards



**NETCORD/FACT standards developed in consensus by representatives of NETCORD and FACT**

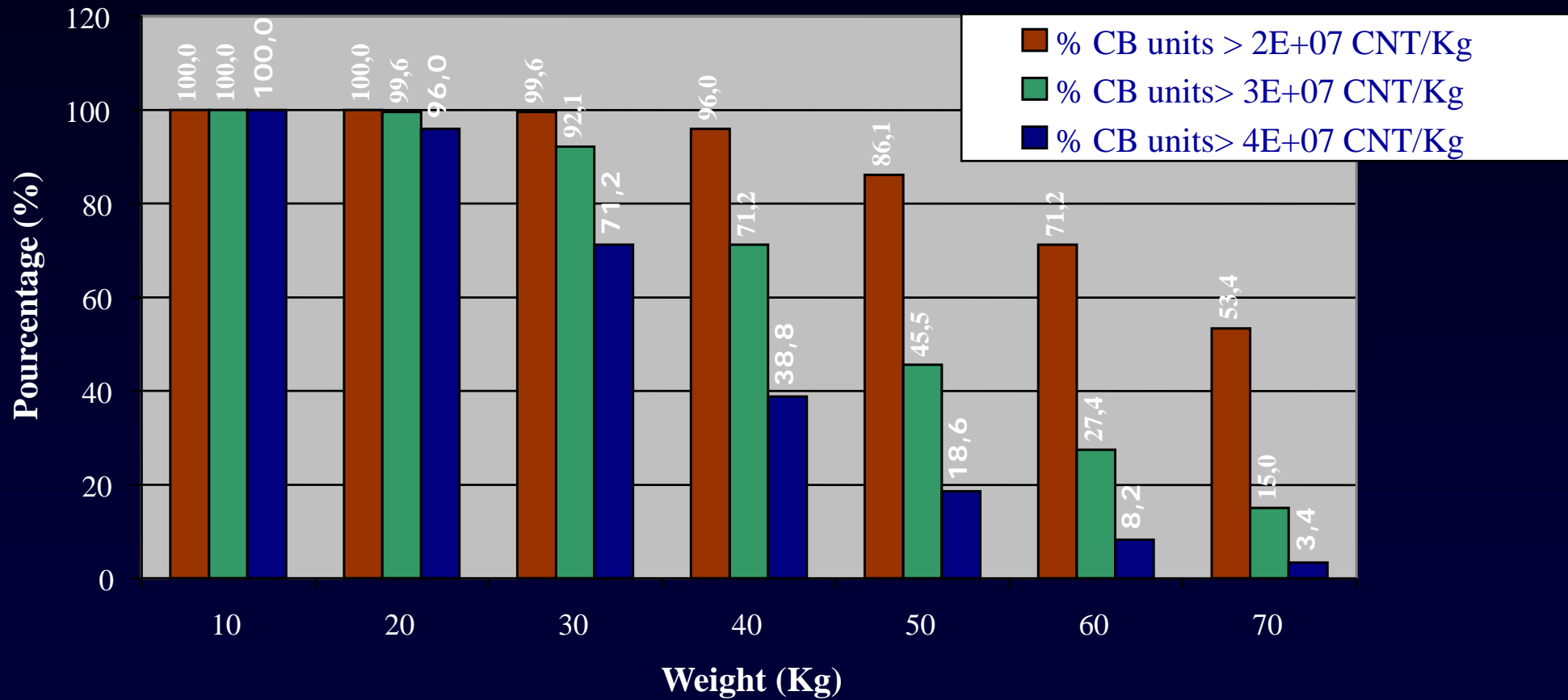


**Accreditation**

**(FACT = Foundation for the Accreditation of Cellular Therapy)**



# % of French CB units according to the number of NC/Kg



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# New Approaches to Adult UCBT

**Problem: Low Cell Dose**



## Solution: Use 2

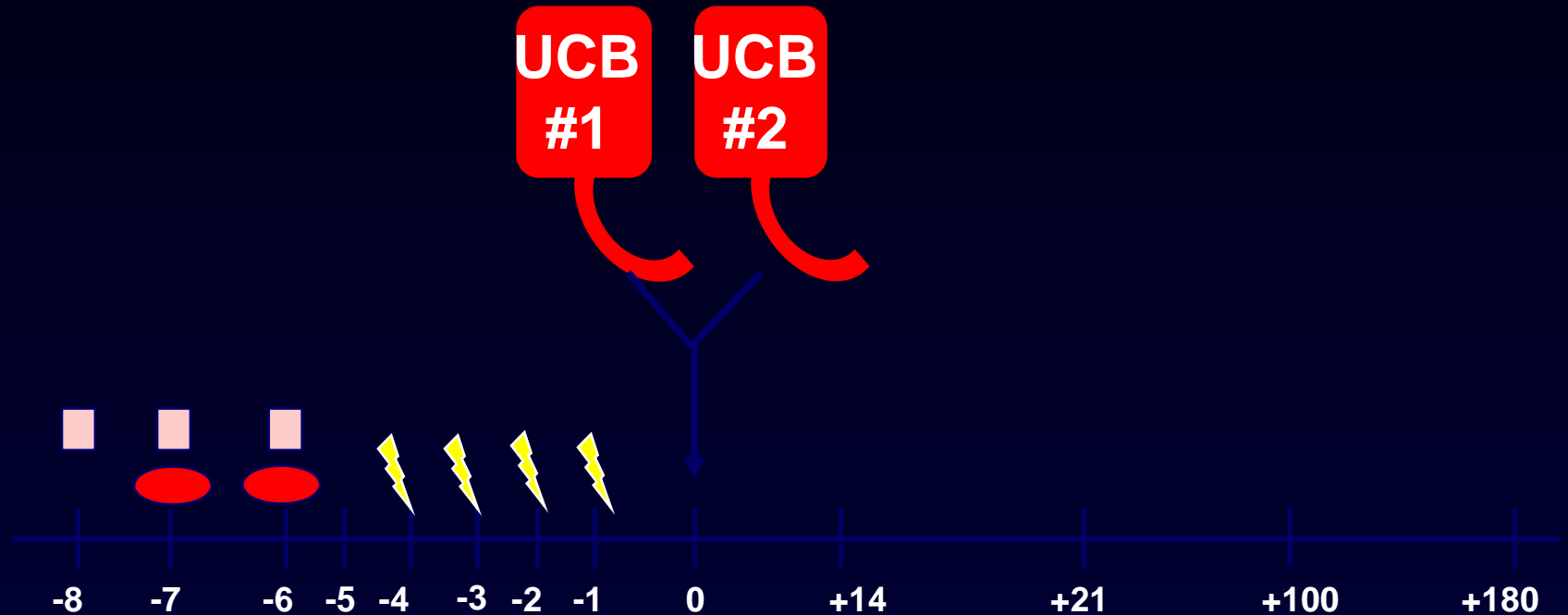
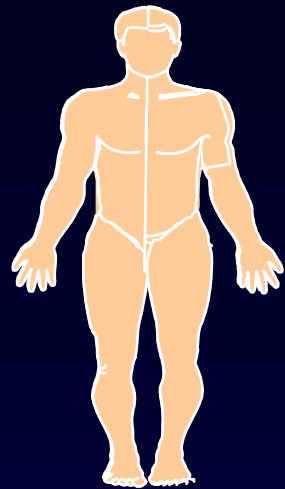


## **Double Unit UCBT: Hypothesis**

**Increased graft cell dose will improve  
engraftment & survival**

**(Each unit will not reject the other)**

# Myeloablative Treatment Schema



## Eligibility:

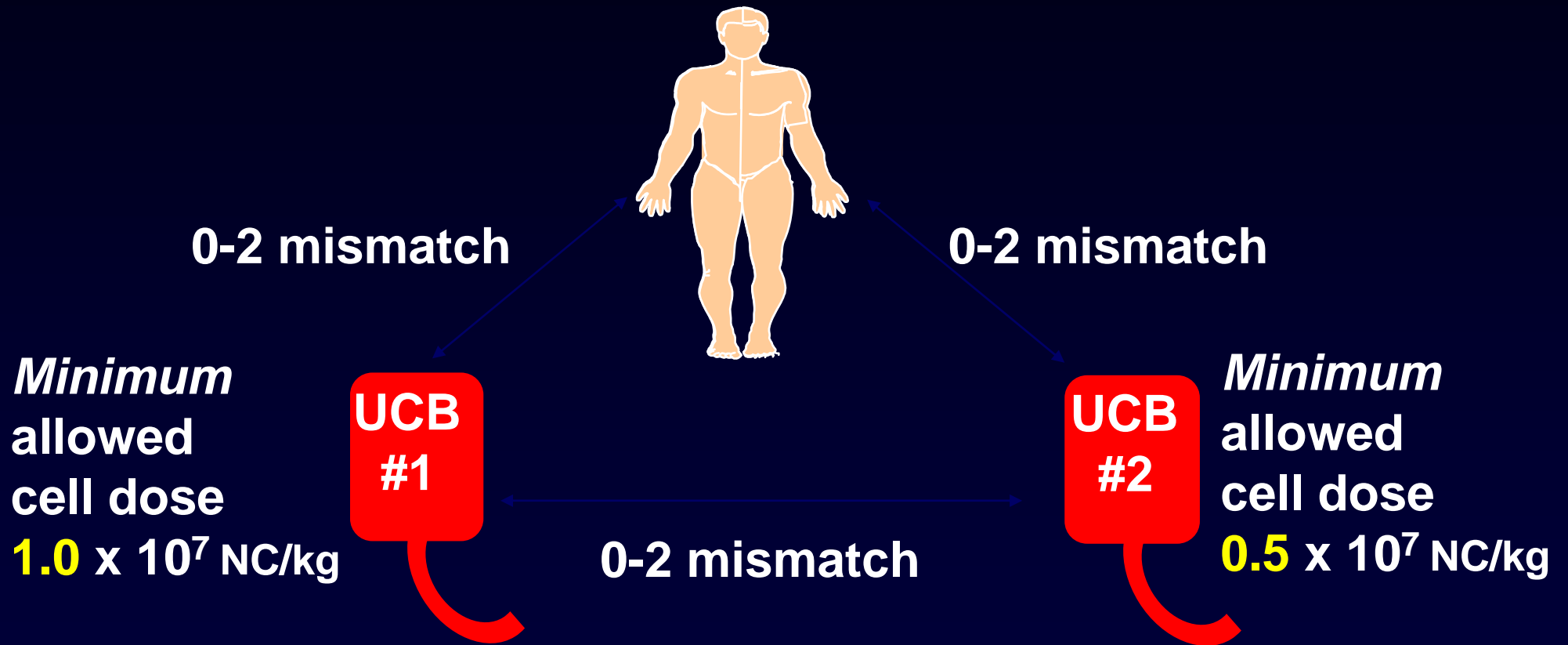
- High-risk hematologic malignancy
- No single 4-6/6 UCB  $\geq 2.5 \times 10^7$  NC/kg (later increased to 3.5)

CSA - 3 to  $\geq$  +100

Mycophenolate - 3 to + 30

G-CSF

# Double Unit Selection



Goal : maximize graft cell dose  
**1° Endpoint: Donor Engraftment**

# Patient Characteristics

<b>Total N</b>	<b>23</b>
<b>Tx date</b>	<b>2000-2003</b>
<b>Age</b>	<b>24 yrs (13-53)</b>
<b>Wt</b>	<b>73 kg (48-120)</b>
<b>Diagnosis</b>	
<b>AML</b>	<b>13 (56%)</b>
<b>CML</b>	<b>2 (9%)</b>
<b>ALL</b>	<b>8 (35%)</b>
<b>Conditioning</b>	
<b>Cy120/ TBI 1320/ ATG</b>	<b>2 (9%)</b>
<b>Cy120/ TBI 1320/ Flu75</b>	<b>21 (91%)</b>
<b>Median Follow-Up</b>	<b>10 months (4 - 30)</b>



# Cell Doses using Double UCB Tx

<b>Infused TNC</b>	<b><math>3.5 \times 10^7</math> /kg (1.1-6.3)</b>
Larger Unit	1.9 (0.6-3.6)
Smaller Unit	1.5 (0.5-2.7)
<b>Infused CD34+</b>	<b><math>4.3 \times 10^5</math> /kg (0.9-14.3)</b>
Larger Unit	2.7 (0.5-10.4)
Smaller Unit	1.2 (0.4-4.7)

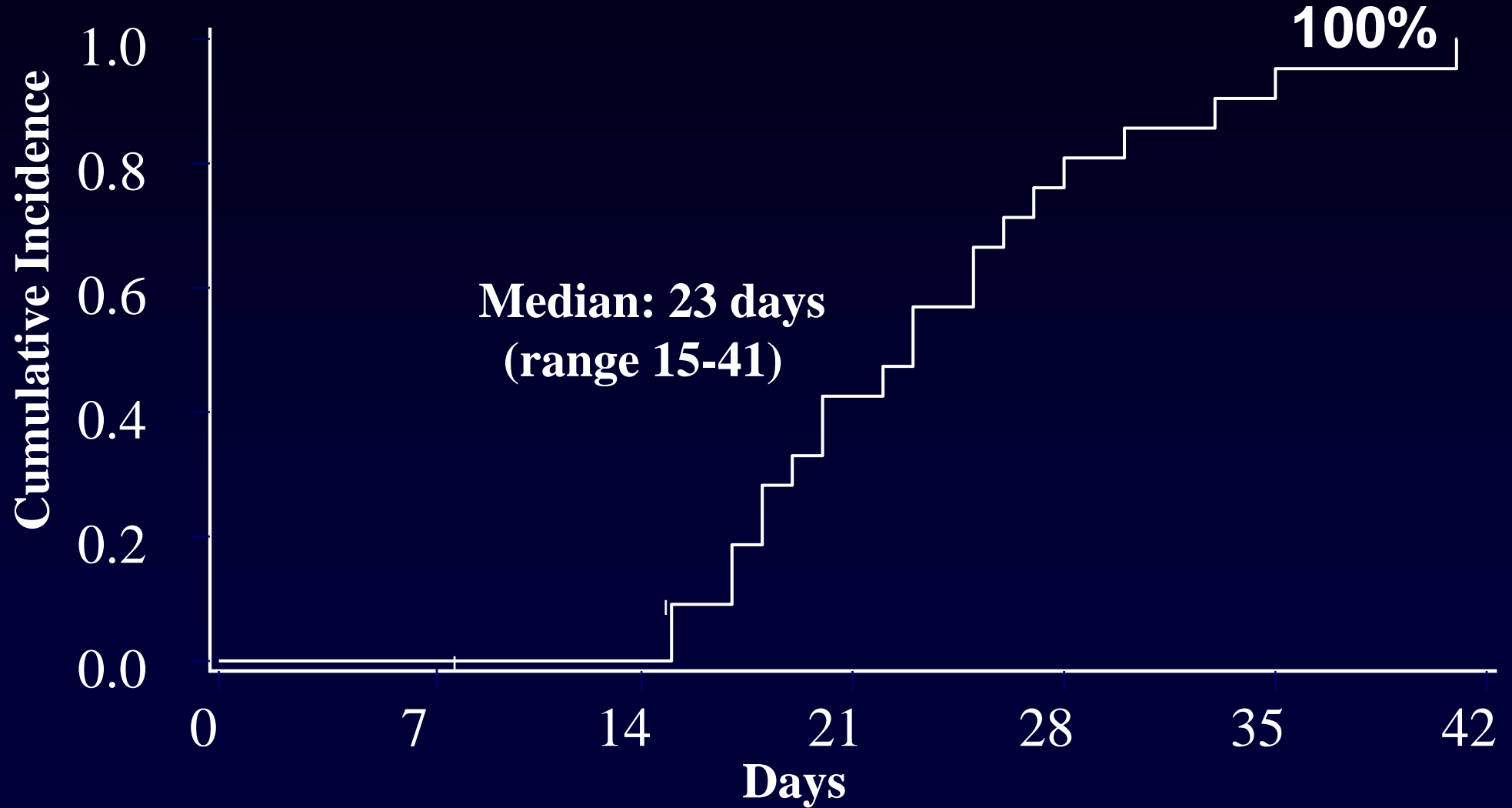
# HLA match in Double UCB Tx

<b>Best Match to Recipient</b>	<b>N = 23</b>
<b>6/6</b>	<b>2 (9%) one 6/6 unit (2nd unit: 6/6 n = 1, 5/6 n = 1)</b>
<b>5/6</b>	<b>11 (48%) one 5/6 unit (2nd unit: 5/6 n = 4, 4/6 n = 7)</b>
<b>4/6</b>	<b>10 (43%) both units 4/6</b>

<b>Match to Each Other</b>	<b>N = 23</b>
<b>6/6</b>	<b>2</b>
<b>5/6</b>	<b>5</b>
<b>4/6</b>	<b>16</b>

# Neutrophil Engraftment (n = 21)



***Do Both Units Contribute to  
Hematopoiesis?***

***Do Both Units Contribute to  
Hematopoiesis?***

NO

Only 1 unit is sustained

# Chimerism

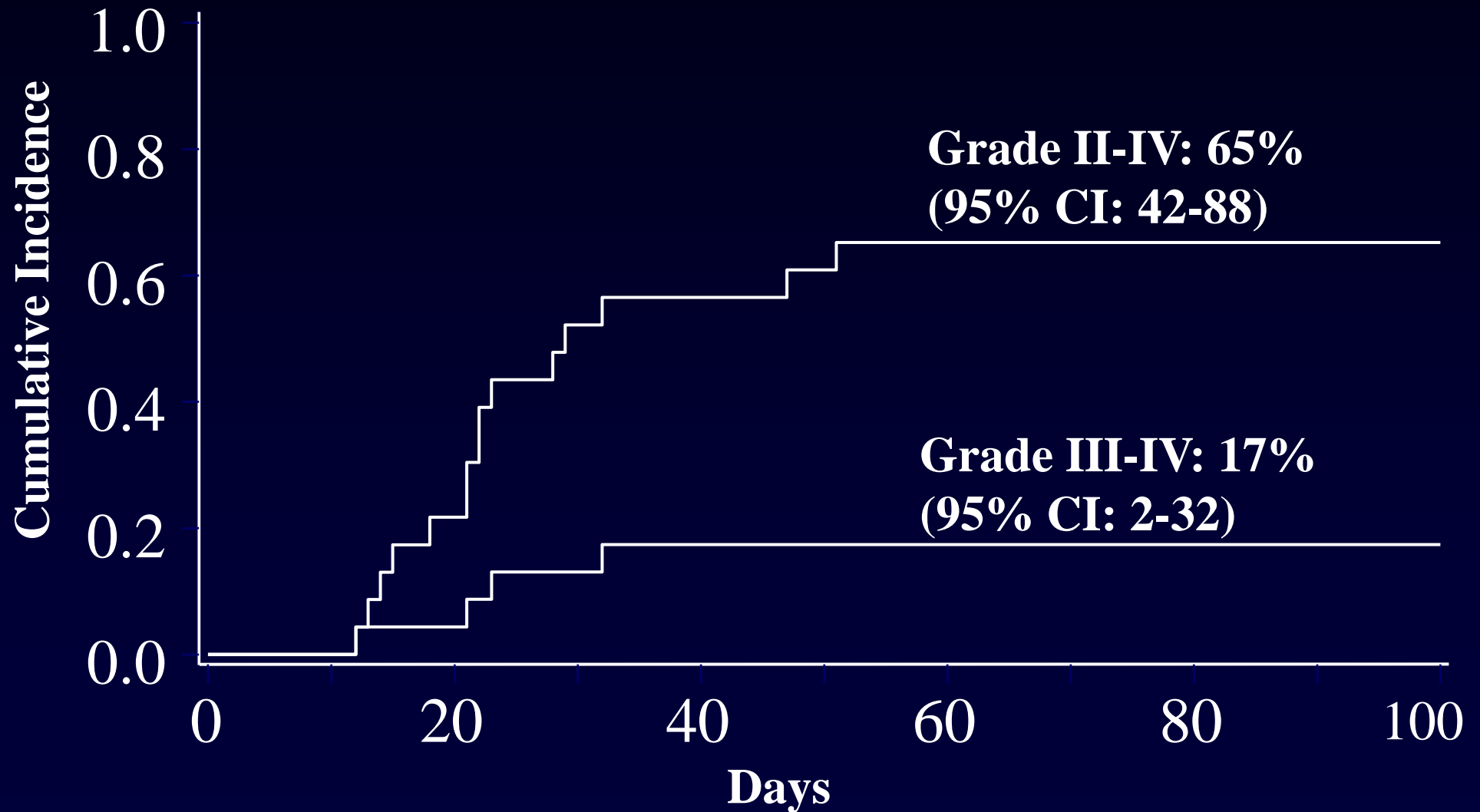
	Double (n = 23)	
Day +21	91% (64-100)	24%: 2 units present 74% (42-85) vs. 20% (15-40)
+100	100%	76%: 1 unit

**Complete donor chimerism was rapid and sustained.  
Sustained hematopoiesis accounted for by only 1 unit.**

# Cell Doses using Double UCB Tx

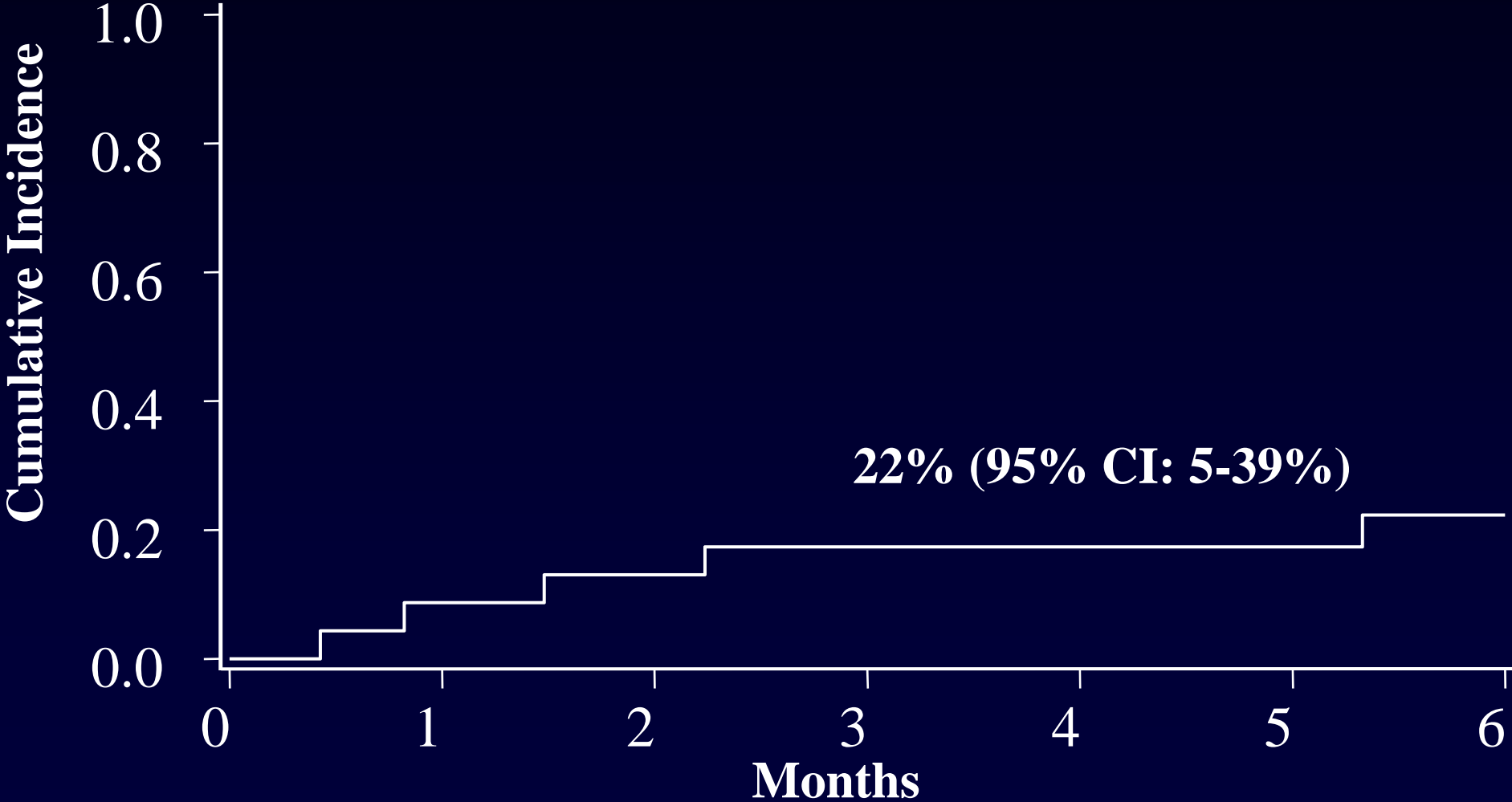
<b>Infused TNC</b>	<b><math>3.5 \times 10^7</math> /kg (1.1-6.3)</b>
Larger Unit	1.9 (0.6-3.6)
Smaller Unit	1.5 (0.5-2.7)
<b>Infused CD34+</b>	<b><math>4.3 \times 10^5</math> /kg (0.9-14.3)</b>
Larger Unit	2.7 (0.5-10.4)
Smaller Unit	1.2 (0.4-4.7)
<b>Infused CD3+</b>	<b><math>1.0 \times 10^7</math> /kg (0.5-2.2)</b>
Larger Unit	0.6 (0.3-1.3)
Smaller Unit	0.4 (0.1-0.9)

# Acute GVHD

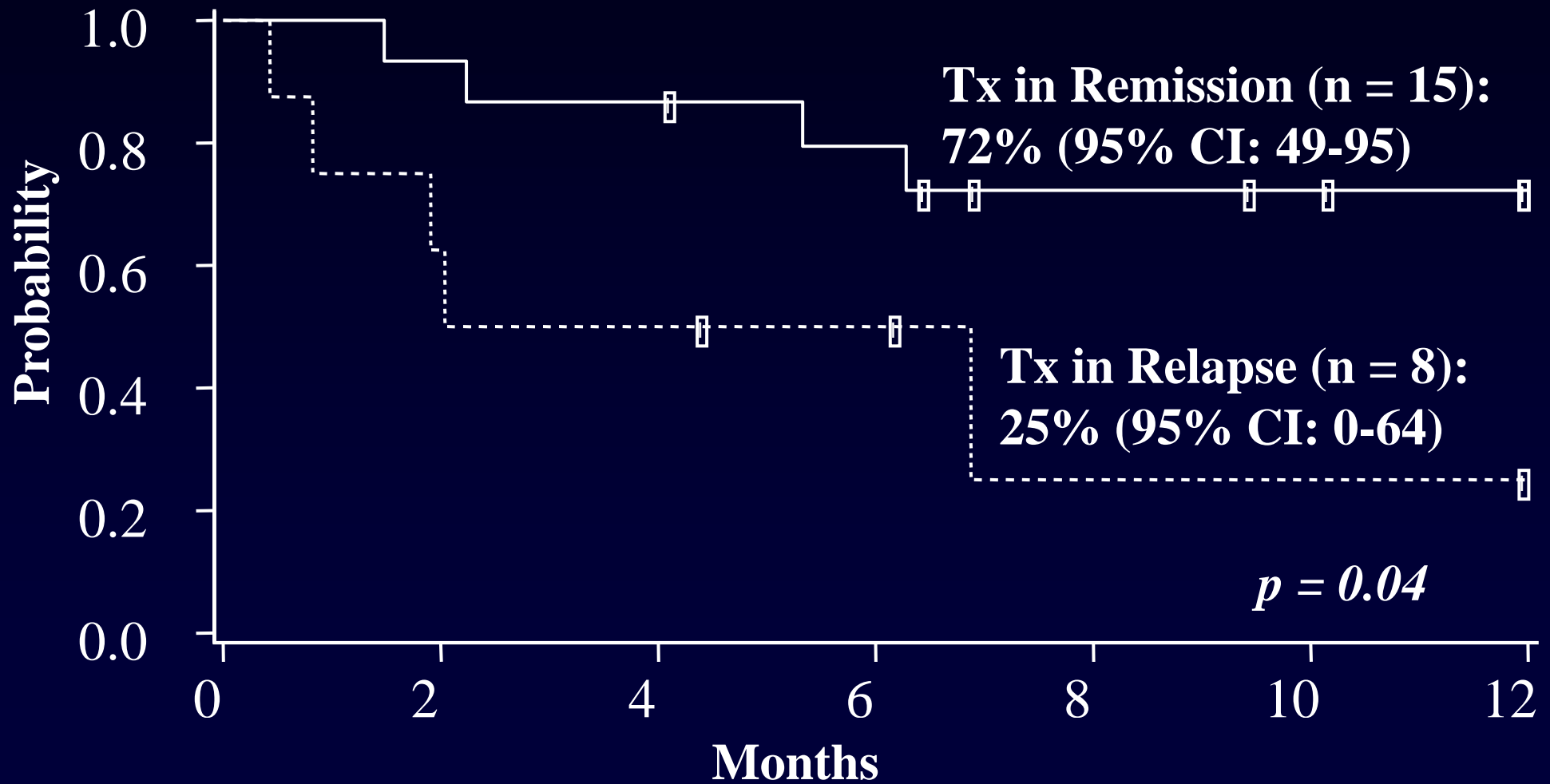




# Transplant Related Mortality



# Disease-Free Survival



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Ex vivo expansion of cord blood cells

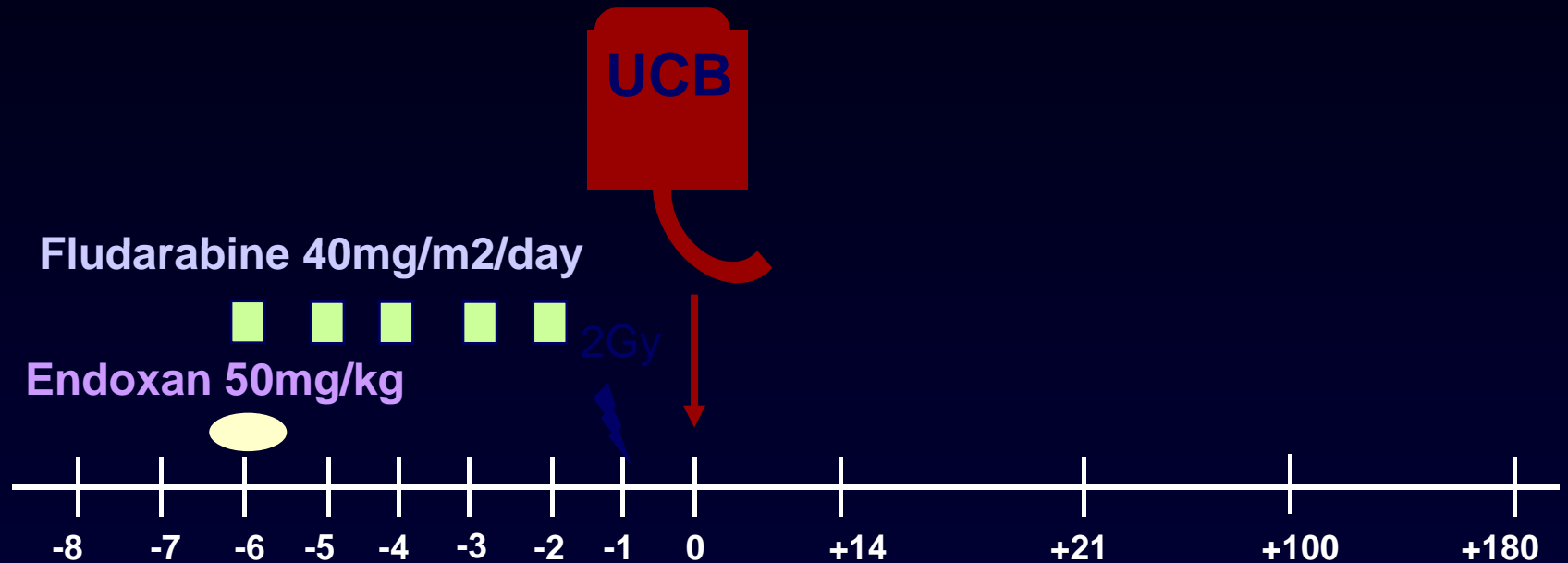
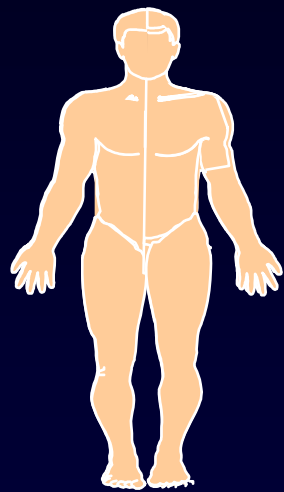
Intrabone injection of cord blood cells

Co-infusion of mesenchymal cells

Use of double transplants

Reduced intensity conditioning regimen using cord blood cells

# Non-myeloablative regimen for UCBT in adults (n=18)



## Eligibility:

- High-risk hematological malignancy
- 4-6/6 UCB  
 $\geq 2.5 \times 10^7$  NC/kg (at collection)

(J Barker and J Wagner)

# Reduced Intensity conditioning regimen in Unrelated cord blood transplants for patients with hematological malignancies (n=65)

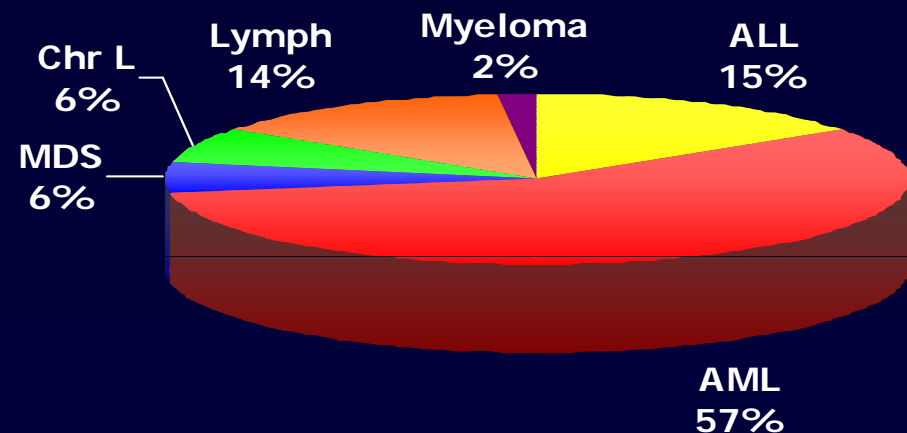
## Patients and disease characteristics

Transplants performed from 1999-2005 (75% in the last 3 years) with single units

Follow-up: 8 months (3-26)  
Median age: 47 years (16-76)  
Median weight: 60 kg (40-110kg)  
CMV+: 63%

## Diagnosis

Previous autologous transplant:  
39% (n=26)



Reduced Intensity conditioning regimen in Unrelated cord blood transplants for patients with hematological malignancies  
(n=65)

Conditioning

Fludarabine+TBI (2Gy)	3
Fludarabine+Endoxan (or mephalan)	11
Fludarabine+Endoxan+TBI (2y)	33
Fludarabine+Bussulfan(<8mg/kg) ± other	9
Fludarabine+Bussulfan(<8mg/kg)+TBI (<5y)	4
Other	5
Anti T antibodies (ATG/ALG or MonoAb)	26%
Hematopoietic growth factors (<Day 8)	87%

## RESULTS

Neutrophils recovery

Median days: 20 days (0-56)

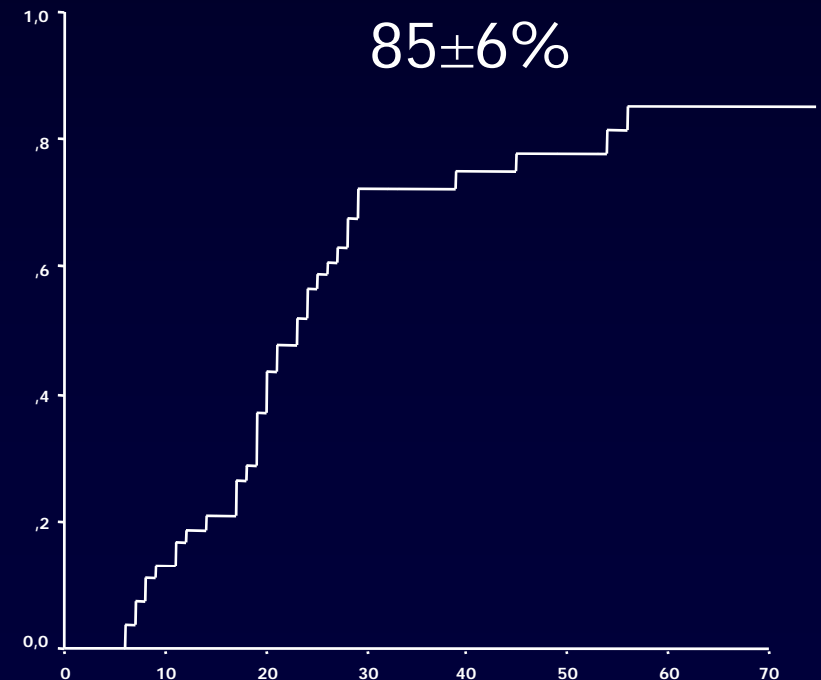
Chimerism at 3 months (available in 71% of the patients)

Full donor 67%

Mixte chimerism 9%

Autologous reconstitution 24%

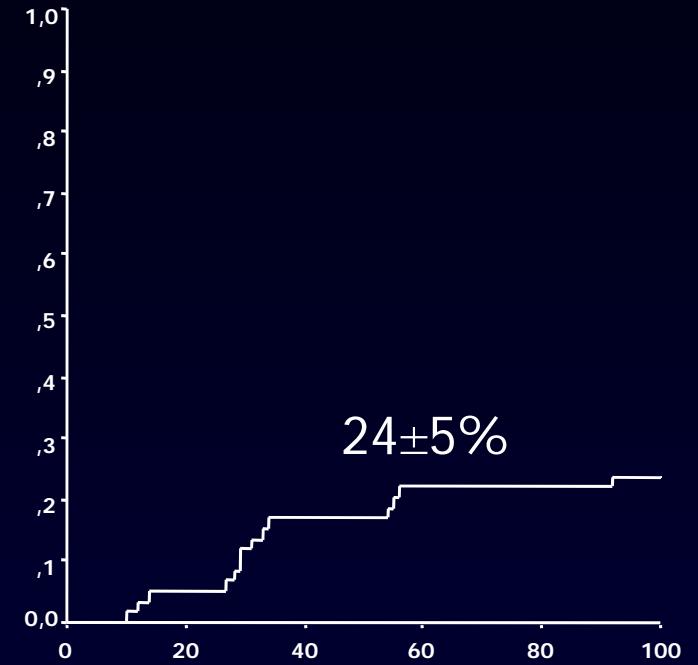
Platelets recovery 35 days (9-63)



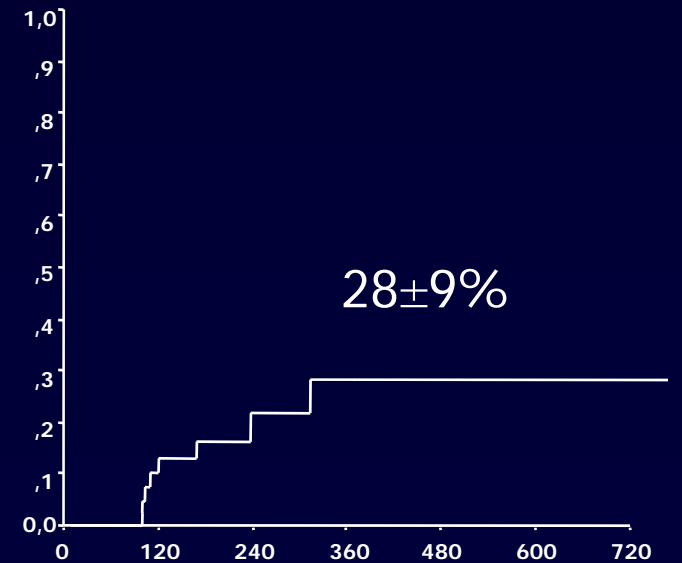
# RESULTS

## Acute GVHD

Grade 2	8 (13%)
Grade 3	4 (7%)
Grade 4	4 (7%)

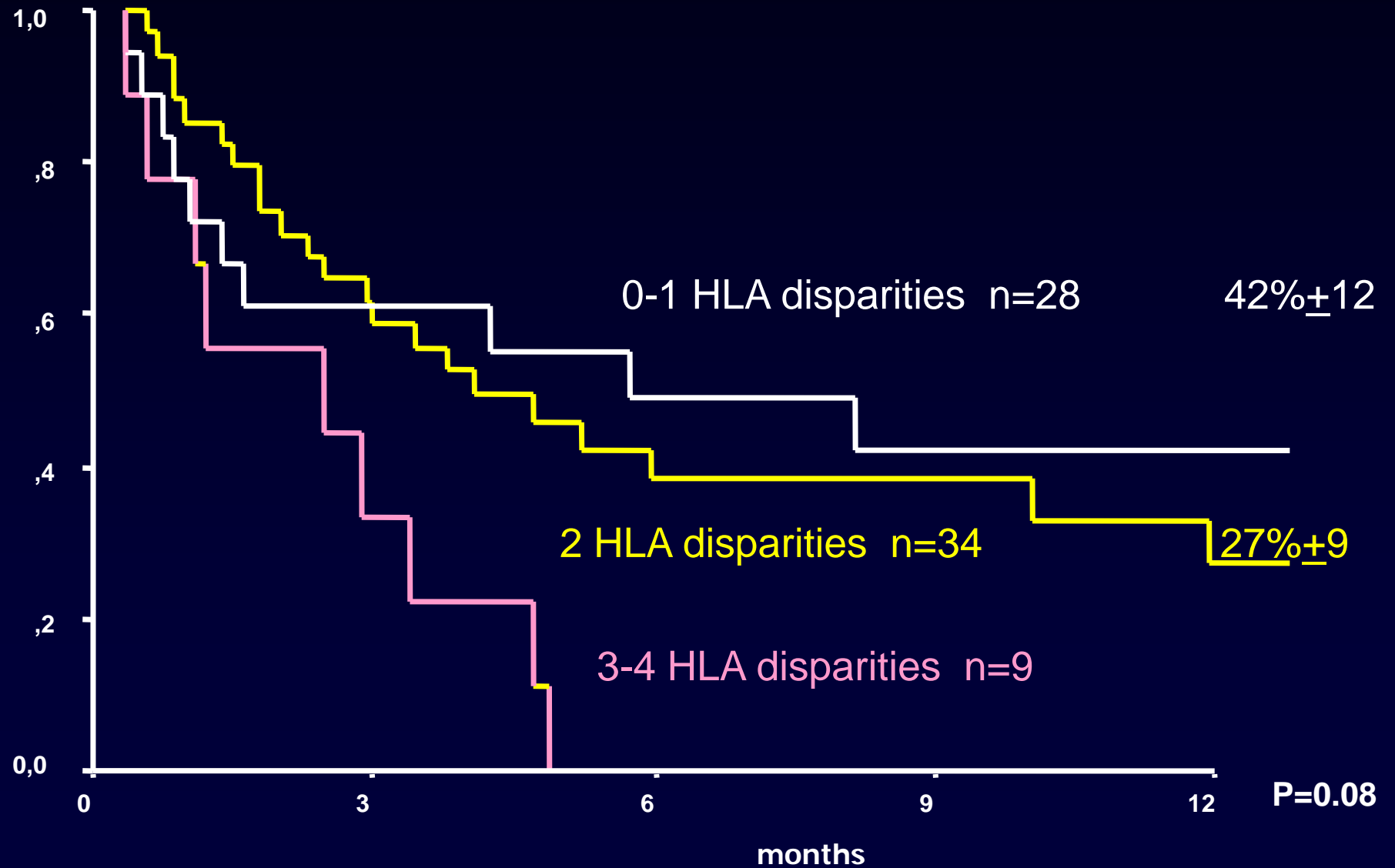


## Chronic GVHD

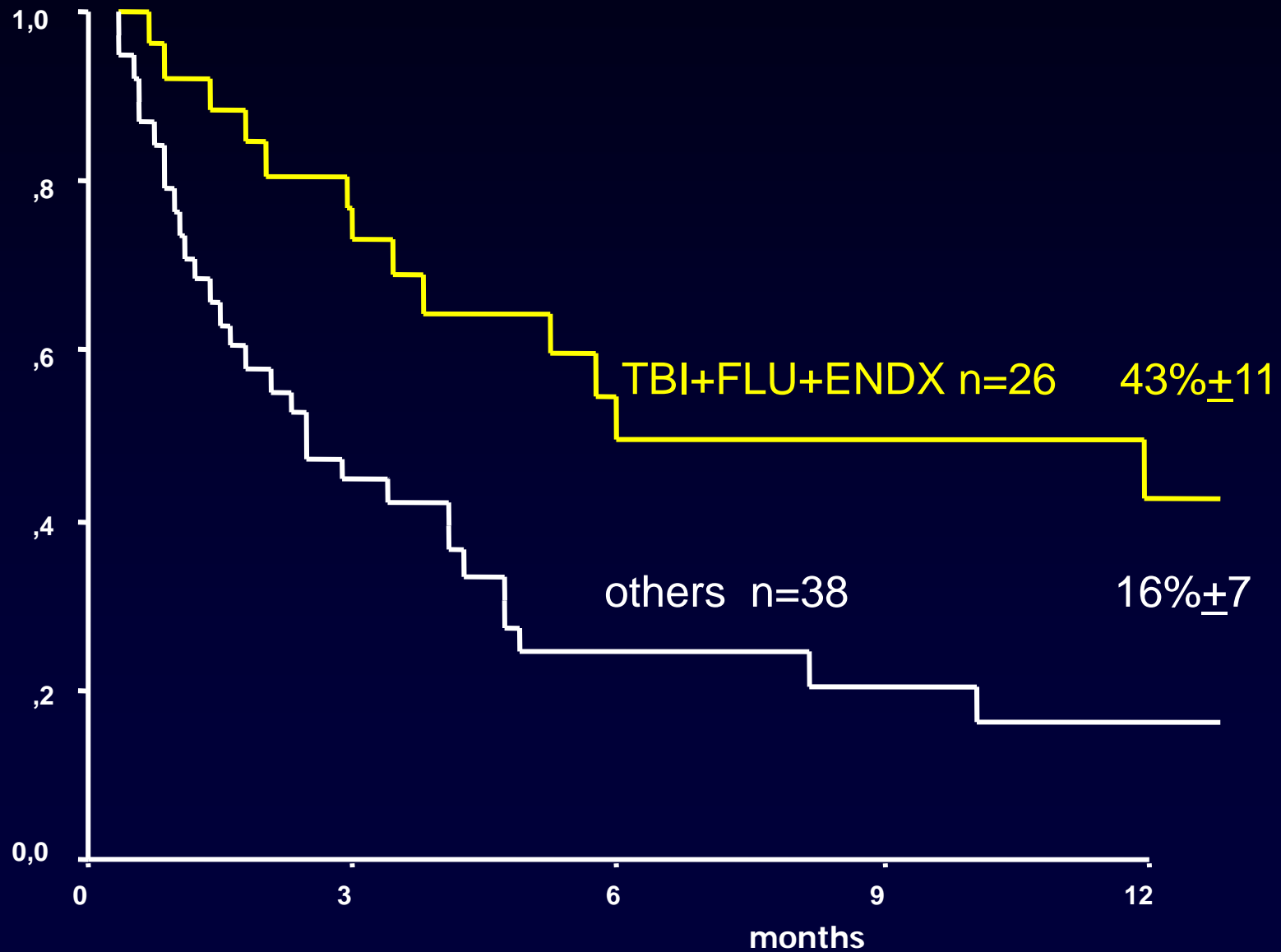




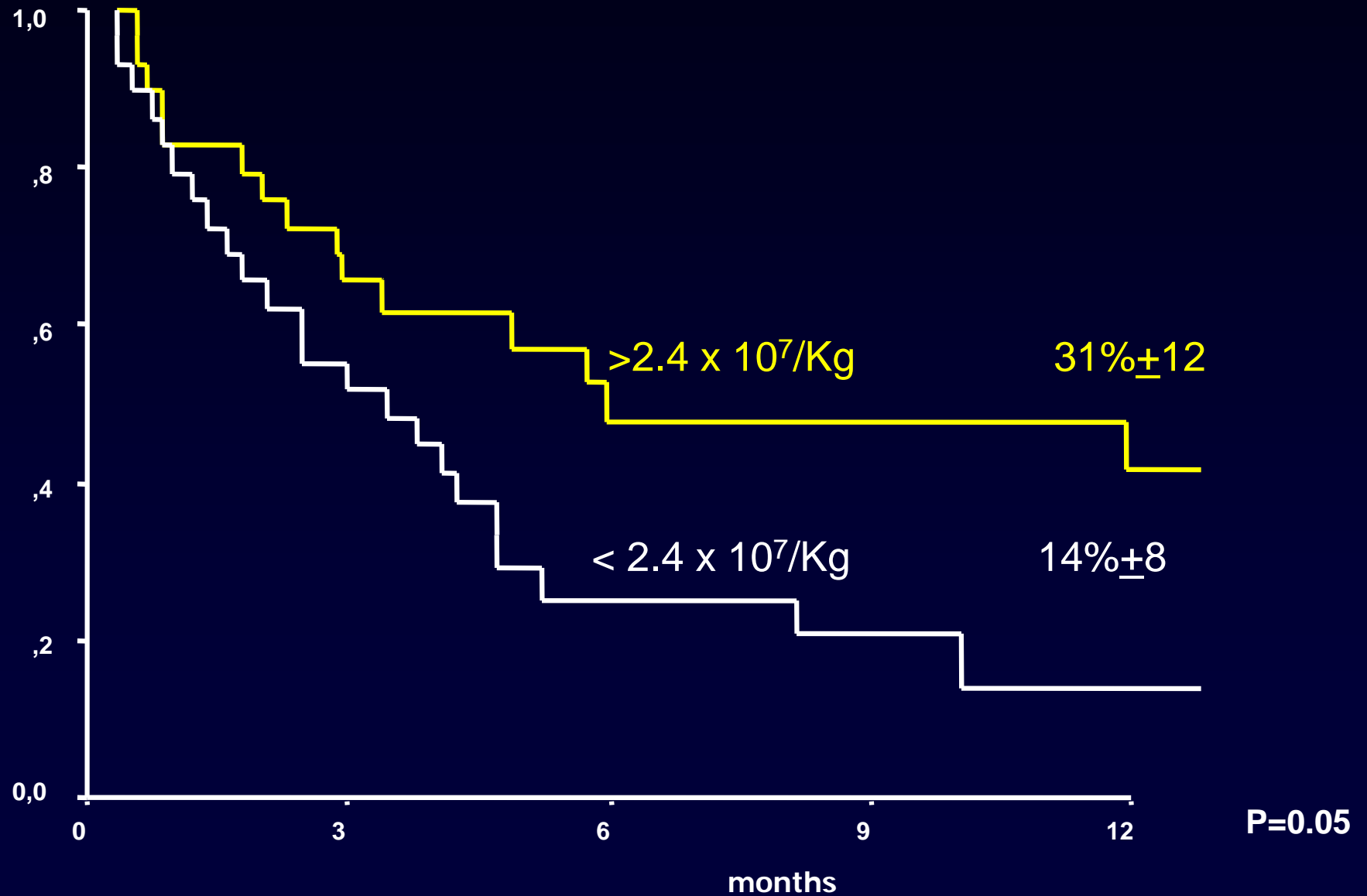
# DFS after RIC UCBT according to number of HLA disparities



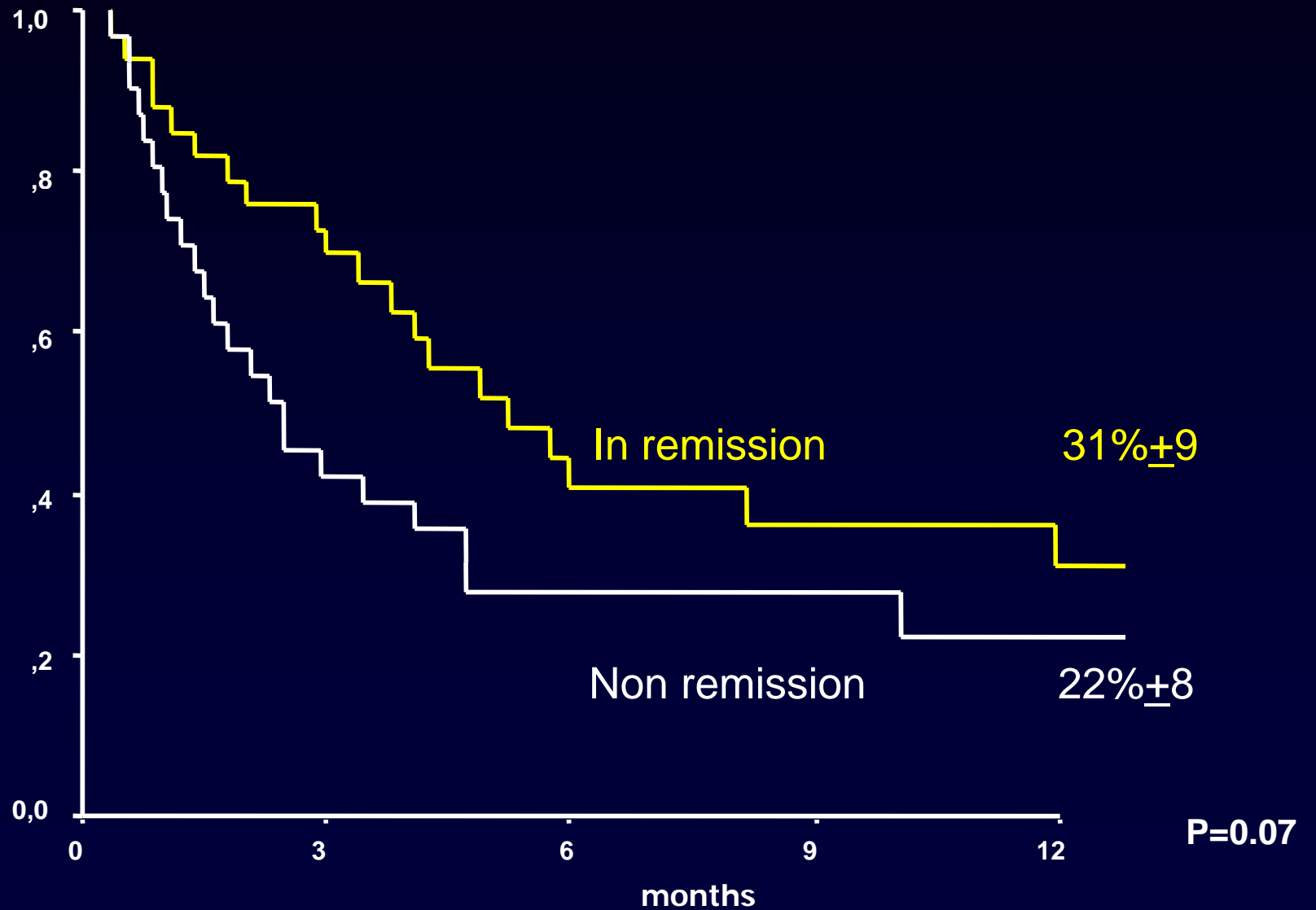
# DFS after RIC UCBT according to conditioning



# DFS after RIC UCBT according to number of cells infused



# DFS after RIC UCBT according to status of disease

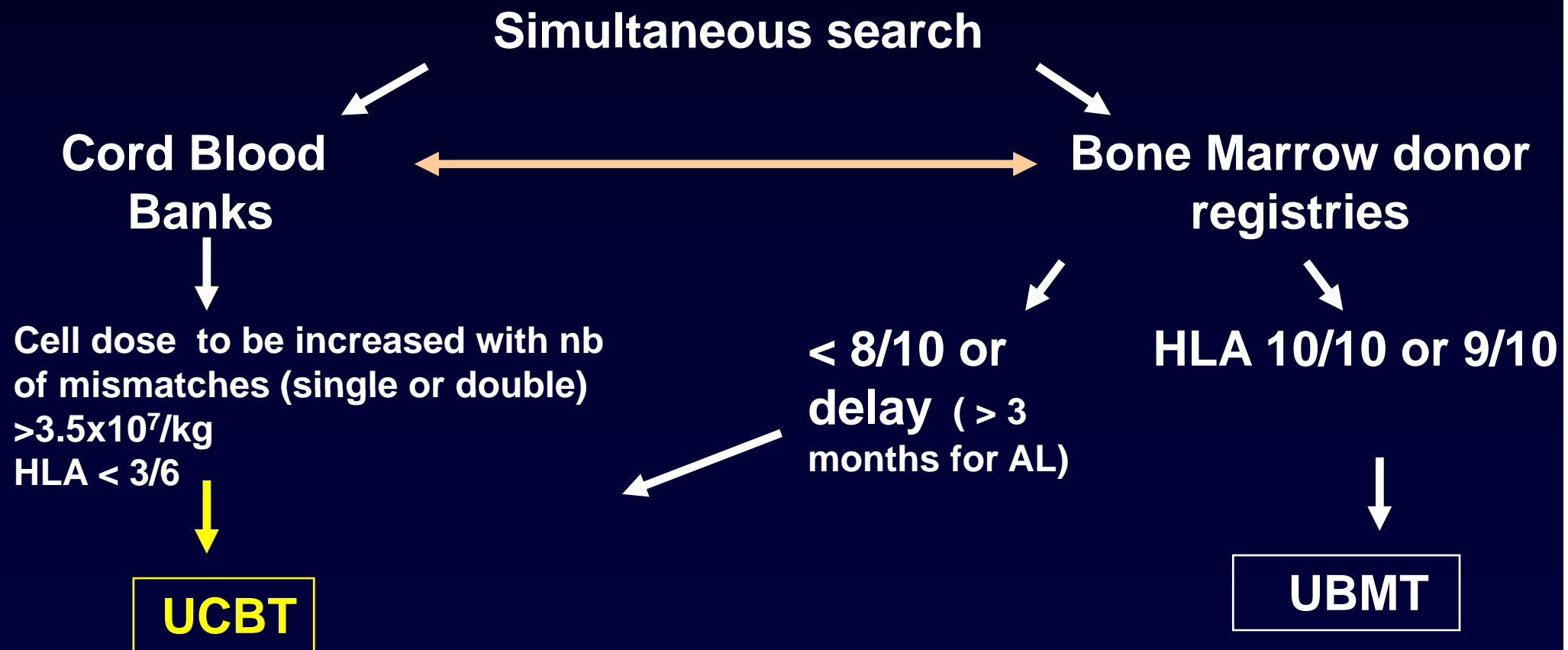


HOW TO CHOOSE AN ALTERNATIVE STEM CELL TRANSPLANT DONOR ??

# Strategy of alternative stem cell donor for patients with malignant disorders

High resolution HLA typing of the patient (adults and children)

↓ To be considered Haplo T-depleted in AML?



# Strategy of alternative stem cell donor for non malignant disorders

High resolution HLA typing of the patient (mostly children)

↓ To be considered Haplo T-depleted?  
↓ Yes for PID

Simultaneous search ( metabolic disorders , PID, BMFS)

Cord Blood  
Banks

Bone Marrow donor  
registries

Cell dose to be increased with nb  
of mismatches (double systematically?)  
>4.5x10<sup>7</sup>/kg (?)  
HLA < 2/6

< 8/10 or  
urgency

HLA 10/10 or 9/10

**UCBT**

**UBMT**

## Conclusions

- **Cord Blood is an established source of hematopoietic stem cell for allogeneic transplantation in children and adults with malignant and non malignant disorders**
- **Nowadays, an alternative HSC donor can be found for almost all patients**
- **The indication of using UCB cells will depend on the urgency of transplantation, number of cells in a unit and number of HLA disparities**
  - **Main questions to be answered :**  
**the immune reconstitution (mainly for adults) and long term follow up**
- **New technologies using cord blood cells such as RIC and double transplants are still in an investigational phase**





# EUROCORD CENTERS

ABECASIS M  
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BAKER D  
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BEKASSY A  
BEKSAC M  
BENGT S  
BENOIT Y  
**BERNAUDIN F**  
**BERTRAND Y**  
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FAVRE C  
FERNANDEZ MN  
FERREIRA E  
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FISCHER S  
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GRAFAKOS S

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GRANENA A  
**GRATECOS N**  
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**JOUET JP**  
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KEESLER C  
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KOBYLKA P  
KOZINER B  
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MESSINA C  
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**MILPIED N**  
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MUÑOZ VILLA A  
NAGLER A  
NIGEL P  
NURNBERGER W  
O'MARCAIGH A  
ORTEGA J  
PASQUINI R  
PEREZ-OYTEZA J  
PESSION A  
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PETRYGA D  
PIHKALA U  
PIMENTEL P  
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PRITCHARD D

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RAJA T  
**REIFFERS J**  
**RIO B**  
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ROSSBACH F  
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RUBIN A  
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SADOUN A  
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SCHULTZ A  
SCIME R  
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SIEVERS E  
SMITH F  
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TAKAHASHI T

TIEDEMANN K  
TOREN A  
UDERZO C  
URBAN C  
VERDEGUER A  
VERDONCK L  
VEYS P  
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WILL A  
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ZANDER A  
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