



## Patient Search

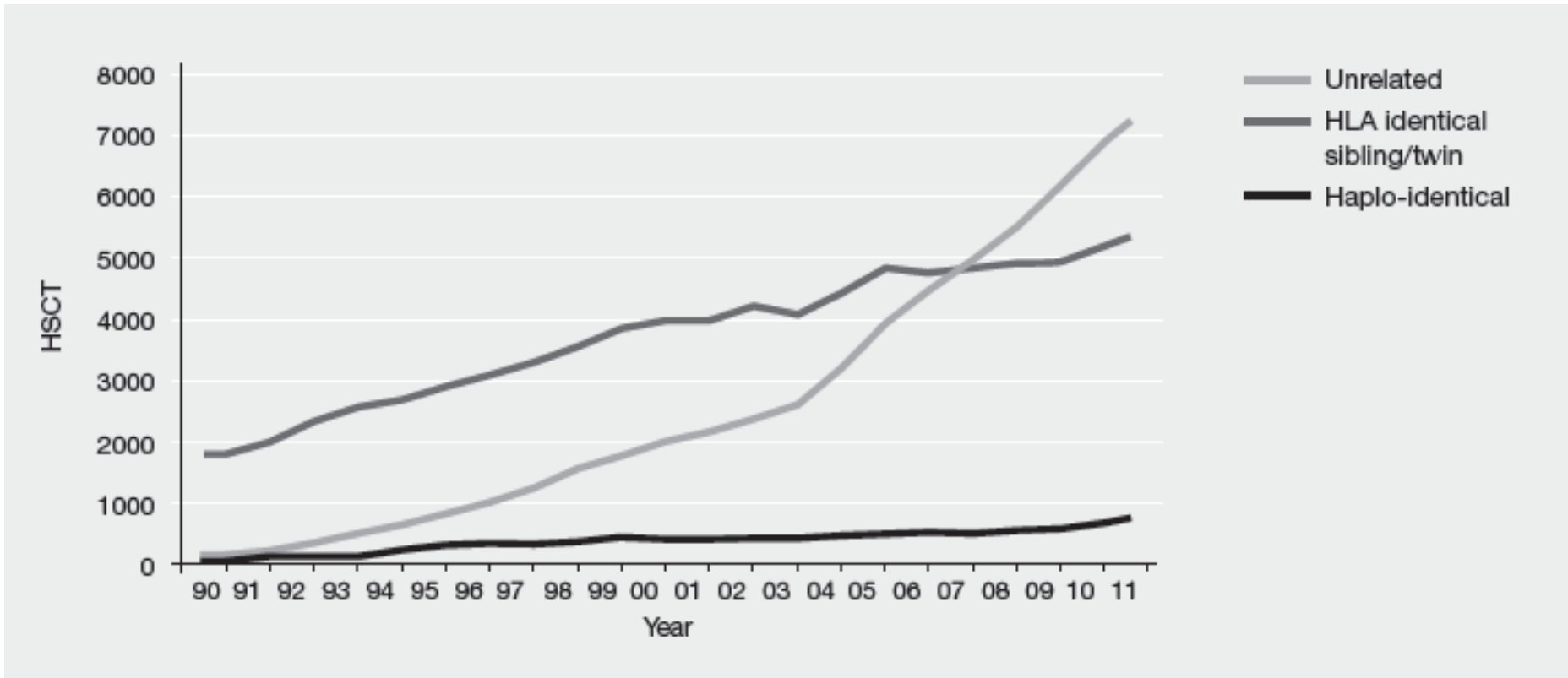
Prof. Dr. P. Zachée  
Internist Nefrolog & Hematoloog

# What shall we learn?

- Introduction
- Related donor searches
- Unrelated donor searches
- The overlooked Donor
- Patient eligibility



# Major changes in indications and use of transplant techniques over the years.



## CASUS:

- AA, female, 28 years old
- 2011 AML, M2 or M5, Treated in Irak, after induction 10% blasts. After 4 cycli chemotherapy CR
- 12/11/2012: relapse. Cytogenetic: inv 16, reinduction with Dauno-AraC → CR
- On day 1 HLA A B DRB1 : PCR-SS0. Low resolution
- On Day 2 HLA A B C DRB1 DQB1. High resolution

# Transplant comité



# Transplant indications

## SIBLING DONORS

<u>Disease</u>	<u>disease status</u>	<u>sibling donor</u>
----------------	-----------------------	----------------------

### Leukaemia

AML	CR1 (low risk)	C0
	CR1 (intermediate)	S
	CR (high risk)	S
	CR2	S
	CR3, incipient relapse	S
	M3 molecular persistence	S
	M3 molecular CR2	S
	Relapse or refractory	C0

# Transplant indications

## SIBLING DONORS

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	CR3, incipient relapse	S
	M3 molecular persistence	S
	M3 molecular CR2	S
	Relapse or refractory	C0

# Minimal and ideal compatibility

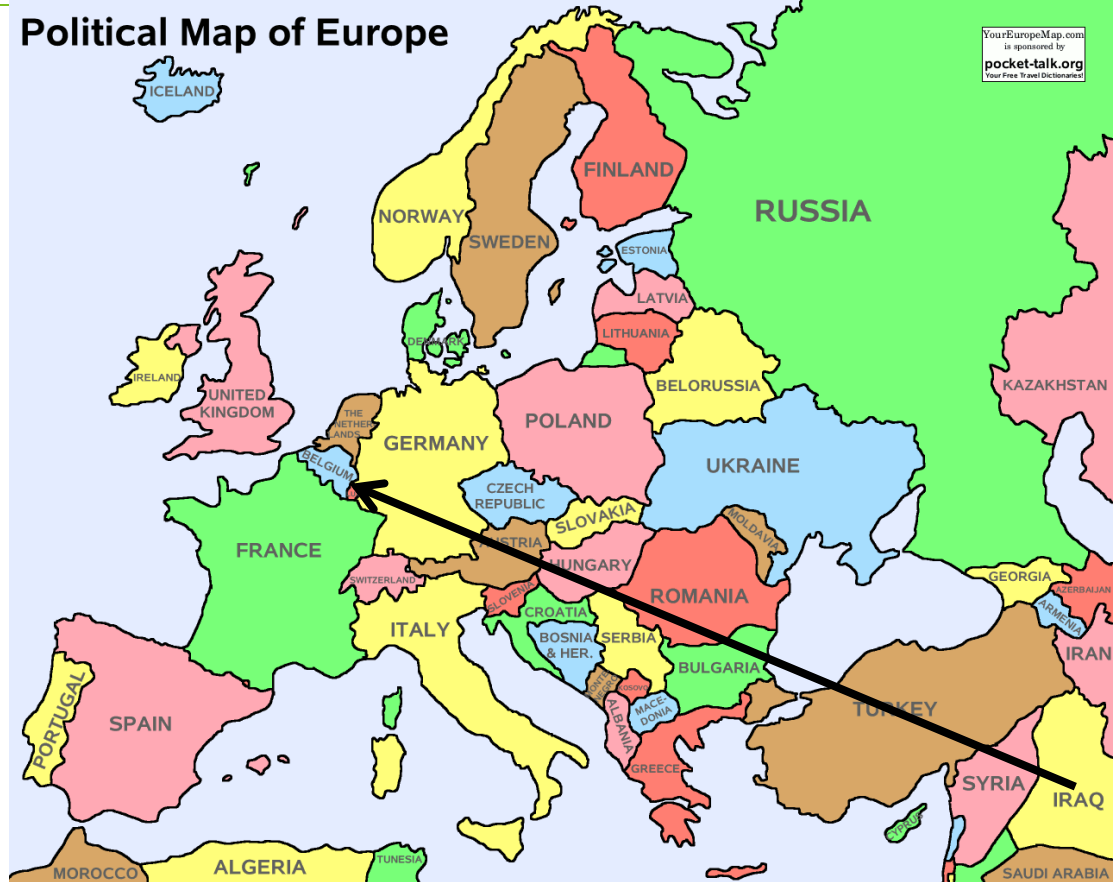
DONOR TYPE	MATCH LEVEL		REMARK
	IDEAL	MINIMUM	
Identical twin	By definition genotypically identical		
Sibling or other family donor	<b>6/6</b>	<b>5/6 IF one haplotype is genotypically identical. If not , see MUD</b>	




# SECONDARY CRITERIA

<b>AGE</b>	<b>Weight</b>	<b>Sex</b>	<b>Transfusion</b>	<b>CMV</b>	<b>ABO</b>	<b>KIR</b>	<b>Anti-HLA</b>
<u>Risk</u> survival	<u>Risk</u> engraftment	<u>Risk</u> CGVHD	<u>Risk</u> VOD	<u>Risk</u> CMV AGVHD	<u>Risk</u> PRCA TRM	<u>Risk</u> relapse	<u>Risk</u> Engraftment
<u>Best</u> young	<u>Best</u> Don > rec	<u>Best</u> Male Don (Haplo mother)	<u>Best</u> No transfusion	<u>Best</u> Don = rec	<u>Best</u> ABO compt	<u>Best</u> KIR misM  → GVH	<u>Best</u> No Against Don
<u>Avoid</u> >75 Y	<u>Avoid</u> Don < < Rec	<u>Avoid</u> F - > M	<u>Avoid</u> transfusion	<u>Avoid</u> CMV +/- CMV -/+	<u>Avoid</u> ABO misM	<u>Avoid</u> KIR M	<u>Avoid</u> Against Don

# Familial screening



**DHL & 3 months  
RED CROSS**

# Familial screening

Abraheem Areg Dheya(1)

## FAMILIALE ZOEKTOCHT

Naam & Voornaam Patient

~~Abraheem Areg Dheya~~

Geboortedatum

~~20/05/1988~~

Aanvrager

Dr. Zachoo

Versie

1

Datum

01/08/2013

Trigram

hhi

Ziekenhuis, Dienst en Adres

ZNA Stier Camp, Stulvenberg  
Lange Besidekensstr.267  
2060 Antwerpen

HAPLOTYPES (afgeleid)

A	C	D
A* 03	A* 24	A* 03
B* 35	B* 55	B* 08
Cw*	Cw*	Cw*
DRB1* 11	DRB1* 13	DRB1* NT
DQB1*	DQB1*	DQB1*

HAPLOTYPES (afgeleid)

B
A* 03
B* 51
Cw*
DRB1* NT
DQB1*

Moeder getypeerd		Vader getypeerd	
A	B	C	D
A* 03	A* 03	A*	A*
B* 35	B* 51	B*	B*
Cw*	Cw*	Cw*	Cw*
DRB1*11		DRB1*	DRB1*
DQB1*	DQB1*	DQB1*	DQB1*

Patient	
A	C
A* 03	A* 24
B* 35	B* 55
Cw*	Cw*
DRB1* 11	DRB1* 13
DQB1*	DQB1*

Broer/Zus	
D	B
A* 03	B* 08
B* 08	B* 51/52/78
Cw*	Cw*
DRB1* NT	DRB1* NT
DQB1*	DQB1*

Broer/Zus	
D	B
A* 03	B* 08
B* 08	B* 51/78
Cw*	Cw*
DRB1* NT	DRB1* NT
DQB1*	DQB1*

Broer/Zus	
B	C
A* 03	A* 24
B* 51	B* 55
Cw*	Cw*
DRB1* NT	DRB1* NT
DQB1*	DQB1*

Broer/Zus	
D	B
A* 03	B* 08
B* 08	B* 51/78
Cw*	Cw*
DRB1* NT	DRB1* NT
DQB1*	DQB1*

Broer/Zus	
D	B
A* 03	B* 51
B* 08	B* 51
Cw*	Cw*
DRB1* NT	DRB1* NT
DQB1*	DQB1*

KIND 1	
A	B
A*	A*
B*	B*
Cw*	Cw*
DRB1*	DRB1*
DQB1*	DQB1*

KIND 2	
A	B
A*	A*
B*	B*
Cw*	Cw*
DRB1*	DRB1*
DQB1*	DQB1*

KIND 3	
A	B
A*	A*
B*	B*
Cw*	Cw*
DRB1*	DRB1*
DQB1*	DQB1*

KIND 4	
A	B
A*	A*
B*	B*
Cw*	Cw*
DRB1*	DRB1*
DQB1*	DQB1*

echtgenote/je	
A	B
A*	A*
B*	B*
Cw*	Cw*
DRB1*	DRB1*
DQB1*	DQB1*

tante	
x	y
A* 01	A* 02
B* 35	B* 53
Cw*	Cw*
DRB1* 11	DRB1* 03
DQB1*	DQB1*

nonkel	
x	B
A* 01	A* 03
B* 35	B* 51
Cw*	Cw*
DRB1*11	
DQB1*	DQB1*

**Result:** Deze patient is mogelijk haplo identiek met ~~Abraheem Areg Dheya~~ & haar moeder. Haar tante & nonkel zijn niet haplo identiek met patiente.

**Belangrijke opmerking:** Dit document is enkel een aanvulling ter verduidelijking van de haplotypes en meestal gebaseerd op 1 typering van zowel donors als patient. Voor definitieve selectie van een donor (hetzij HLA identisch, hetzij Haplo-identisch) zijn 2 onafhankelijke typeringen en een bijkomende evaluatie van het dossier vereist. De volledige HLA typeringen zijn enkel beschikbaar via het standaard rapport zoals aangemaakt via het labo informatica systeem GLIMS.

*Handwritten signature and date:*  
A. Dheya  
05/08/2013

## CASUS:

- AA, female, 28 years old
- 2011 AML, M2 or M5, Treated in Irak, after induction 10% blasts. After 4 cycli chemotherapy CR
- 12/11/2012: relapse. Cytogenetic: inv 16, reinduction with Dauno-AraC → CR
- Indication for MUD?

# TRANSPLANT INDICATION

## ALLOGENEIC

<u>Disease</u>	<u>disease status</u>	<u>Well_matched</u>
		<b>unrelated</b>

### Leukaemia

AML	CR1 (low risk)	D
	CR1 (intermediate)	C0
	CR (high risk)	S
	CR2	S
	CR3, incipient relapse	C0
	M3 molecular persistence	C0
	M3 molecular CR2	C0
	Relapse or refractory	D

# TRANSPLANT INDICATION

## ALLOGENEIC

<u>Disease</u>	<u>disease status</u>	<u>Well_matched</u>
		unrelated

### Leukaemia

AML	CR1 (low risk)	D
	CR1 (intermediate)	C0
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	M3 molecular persistence	C0
	M3 molecular CR2	C0
	Relapse or refractory	D



Mechelen, 07/08/2013

ME130118-015

Bloedgroep: B neg  
Rhesus: C- E- c+ e+

dr. Janssens Ann

RBC antistoffen :

Pagina : 2 van 2

18/01/2013

#### Commentaar bij de bepalingen

» patiënte heeft het zeldzame A\*24:02:01:02L dat laag tot expressie komt. A\*24:02:01:02L komt voor in een haplotype met HLA-B55, HLA-Cw01. Ongeveer 20% van de donoren die het haplotype A24, B55, Cw1 heeft is A\*24:02:01:02L.

Er zijn weinig gegevens over patiënten met laag expressie HLA varianten met betrekking tot een stamceltransplantatie met onverwante donor. In afwezigheid van een 10/10 MUD zal gezocht worden naar een donor met HLA-A\*24:02. Gezien de minder voorkomende HLA typering van deze patiënte zal het zowieso niet eenvoudig zijn een 10/10 MUD te vinden.

In geval van een mismatch MUD zal men rekening moeten houden met de aanwezige HLA antistoffen.

In geval van vafrekeritelt ...

# College of directors of RIZIV/INNAM

## NIEUW FORMULIER

COLLEGE VAN GENEESHEREN-DIRECTEURS  
R.I.Z.I.V.  
Guffenslaan 33 te 3500 Hasselt  
Fax: 011/45 77 50

**INSCHRIJVING VAN DE RECHTHEBBENDE ALS TRANSPLANTATIEKANDIDAAT BIJ HET COLLEGE VAN GENEESHEREN-DIRECTEURS (art.14m), van de nomenclatuur van de geneeskundige verstrekkingen.**

**Vak voorbehouden voor de geneesheer die de transplantatie voorschrijft**

Naam en voornaam van de  
rechthebbende (receptor):  
Aard van de transplantatie: **Stamcellen/beenmerg**

als behandelingsindicatie vastgesteld  
tijdens het verblijf van: \_\_\_\_\_ tot \_\_\_\_\_  
in de verpleeginrichting: A.Z. Stuijvenberg  
De voorschrijvende geneesheer: Prof. Dr. P. Zachée  
Internist – Nefroloog – Hematoloog  
Naam: Prof. Dr. P. Zachée  
R.I.Z.I.V.-Identificatienummer: 1-13711-70-598

In geval van stamcellen-/beenmergtransplantatie verklaar ik dat het nationaal register van de kandidaten beenmergdonors het niet mogelijk heeft gemaakt een compatibele beenmergdonor te selecteren.

Datum:  
Handtekening:

### In te vullen door de coördinator van het transplantatiecentrum

Geboortedatum van de rechthebbende  
Identificatienummer van het  
Rijksregister :  
Nationaliteit:  
Verzekeringsinstelling:  
Buitenlandse bevoegde instelling:  
(1) Datum van uitreiking van het formulier E111  
of E112 (2):  
Naam en adres van de gerechtigde:

Erkenningsnummer: **71000931221**  
Benaming: Stuijvenberg EBMT Centr. 3391  
Adres: Lange Beeldekensstraat 267, 2060 Antwerpen

- Naam en adres van de coördinator van het transplantatiecentrum: **Prof. Dr. P. Zachée**  
Telefoon: 03/217 74 18

(1) IN TE VULLEN INGEVAL HET GAAT OM EEN BUITENLANDSE TRANSPLANTATIE  
(2) DOORHALEN WAT NIET PAST



# Initial search

Prometheus - Stem Cell Donor Registry

Donor Patient Search EMDIS Service Help

Select New Reports History Stack Active Analytic Tool Validate Records to be validated (HLA/DNA) Records to be validated (Other info) Patient Commands Patient Tools Patient Validation

Patient BE [REDACTED]

Edit Patient ABRAHEEM AREG DHEYA / BEKULAA210785 OK Esc

E/DNA

A\* 03:01 24:02:01:02L ...

B\* 35:08 55:01 ...

C\* 01:02 04:JKTU ...

DRB1\* 11:03 13:01 ...

DRB3\* ...

DRB4\* ...

DRB5\* ...

DQB1\* 03:01 06:03 ...

DQA1\* ...

DPB1\* ...

DPA1\* ...

Date of typing 1 08.02.2013

Date of typing 2

Laboratory BELABHILA1

Record changed on 31.07.2  
Record inserted on 11.02.2  
HLA/DNA validated on 29.03.2  
Medical data validated on 29.03.2

HUB	State	Watch	Search result	Reason
ALL	Stopped	<input type="checkbox"/>		
BE	Stopped	<input type="checkbox"/>	8/10/2013	UCT
AT	Stopped	<input type="checkbox"/>	23/04/2013	OTH
AU	Stopped	<input type="checkbox"/>	16/07/2013	OTH
SE	Stopped	<input type="checkbox"/>	24/04/2013	OTH
CH	Stopped	<input type="checkbox"/>	25/04/2013	OTH
CZ	Stopped	<input type="checkbox"/>	2/06/2013	OTH
DE	Stopped	<input type="checkbox"/>	13/07/2013	OTH
ES	Stopped	<input type="checkbox"/>	17/07/2013	OTH
FR	Stopped	<input type="checkbox"/>	4/09/2013	UCT
GB	Stopped	<input type="checkbox"/>	23/04/2013	OTH
IT	Stopped	<input type="checkbox"/>	15/05/2013	OTH
NL	Stopped	<input type="checkbox"/>	5/08/2013	UCT
NO	Stopped	<input type="checkbox"/>	23/04/2013	OTH
GL	Stopped	<input type="checkbox"/>	23/04/2013	OTH
WA	Stopped	<input type="checkbox"/>	23/04/2013	OTH
US	Stopped	<input type="checkbox"/>	8/04/2013	OTH

OK Cancel ? F1

5 / 5

Previous / next page

Change status in selected HUBs

D: allow all DCs T: BETRAANS1 allow all TCs

Logged user: Marie-Paule Emonds Group: CENTER

start Inbox - Micr... Vodafone M... Presentaties HAPLO Haplomeetin... MJD educat... Presentatie... MetaFrame ... Prometheus... NL 21:08

# Confirmation of MDP-B on donor search in Belgium



Marrow Donor Program Belgium - Registry  
Motstraat 40  
2800 Mechelen  
Tel: (32) - 15 44 33 96 Fax: (32) - 15 44 36 56

## NOTIFICATION OF UNRELATED DONOR (URD) SEARCH BY THE REGISTRY

Mechelen,

Dear Prof. Zachée,

We confirm the receipt of your request to start an URD search in the Belgian Bone Marrow Donor Registry for your patient

D.O.B.

After validation of the patient's registration, you will receive the Belgian search results through the search software application PROMETHEUS.

Kind regards,

Dr Bob Moldenhauer  
Medical director MDPB Registry

# MDPB-REGISTRY

7 donor centers  
➤ 63.000 donors

5 cord blood banks  
> 18.000 CBUs

9 Transplant Centers  
(national)

EMDIS

65 international Registries

44 CB Banks

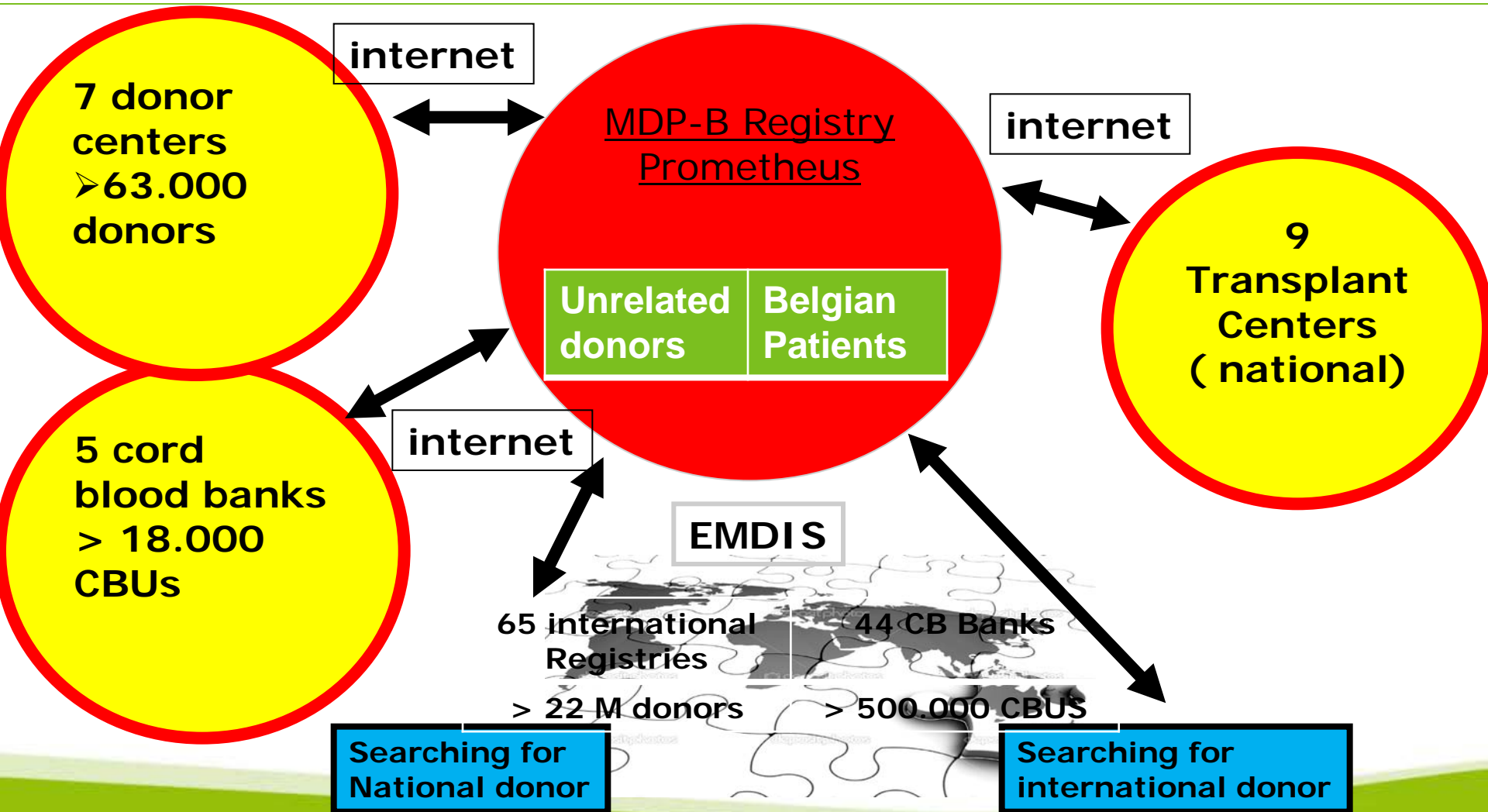
> 22 M donors

> 500.000 CBUS

Searching for National donor

Searching for international donor

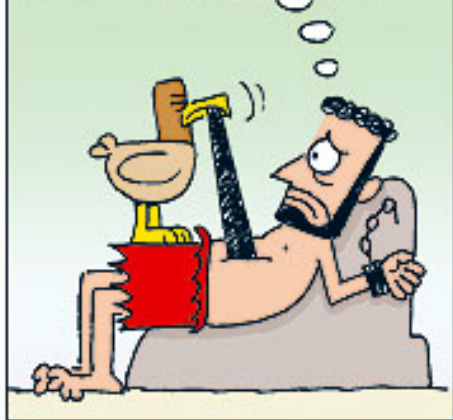
# MDP-B-REGISTRY



# Prometheus

## PROMETHEUS

EVERY DAY THIS EAGLE  
EATS MY LIVER...



...AND ALL BECAUSE  
ZEUS IS ANGRY WITH ME  
FOR GIVING **FIRE**  
TO MANKIND.



OH, WELL, MY SUFFERING  
IS WORTH IT—I'M SURE  
MANKIND HAS MADE  
GOOD USE OF MY GIFT!



MEANWHILE...



©2007 Mark Weinstein

# Minimal and ideal compatibility

DONOR TYPE	MATCH LEVEL		REMARK
	IDEAL	MINIMUM	
Identical twin	By definition genotypically identical		
Sibling or other family donor	<b>6/6</b>	<b>5/6 IF one haplotype is genotypically identical. If not , see MUD</b>	
Unrelated	<b>10/10</b>	<b>8/10 allelic*</b>	

## (\*) minimum 8/10 allelic:

- |                         |   |
|-------------------------|---|
| • 1 antigenic MM (9/10) | • 1 allelic + 1 Antigenic MM (8,5/10)   |
| • 2 allelic MM (9/10)   | • 1 antigenic + 1 antigenic DQB1 (8/10) |

# Search results

EMDIS Search Results: ABRAHEEM, BEKULAA210785

Patient | Summary of Donors | List of Donors | Donor - Details

Sorting | Multiple Allele Codes | Report | Show/Hide Report Maker | Custom Report | Typing Request | Sample Request | CBU Report Request

TC A 03:01 B 35:08 C 01:02 DRB1 11:03 DQB1 03:01  
 BETRAANS1 24:02:0 55:01 04:JKTL 13:01 06:03

Msg	Donor Update	Validity	Record Update	HUB	ID	State	Type	Sex	DOB	Match Grade	Match h	A.1 [03:01]	A.2 [24:02]	B.1 [35:08]	B.2 [55:01]	C.1 [01:02]	C.2 [04:JKT]	DR.1 [11:03]	DR.2 [13:01]	DQ.1 [03:01]	DQ.2 [06:03]
Old	New	Latest	3/04/2013	BE	BEANT000137	AV	MD	M	1959	5/6 Antigen Match	9/10	3	9	35	44			11	6	3	1
Old	New	Latest	3/04/2013	BE	BEANT000371	AV	MD	M	1959	5/6 Antigen Match	9/10	3	9	7	22			11	6	3	1
Old	Dupl	Latest	8/10/2013	BE	BEANT0004698	AV	MD	F	1955	6/6 Antig.Match - Allele MM	9/10	3	9	35	22			11:MS	13:XJ		
Old	New	Latest	3/04/2013	BE	BEANT0005132	AV	MD	F	1955	5/6 Antigen Match	9/10	3	24	35	22			11:GX	01:AD		
Old	New	Latest	3/04/2013	BE	BEANT0005618	AV	MD	M	1971	5/6 Antigen Match	9/10	3	24	35	7			11	13		
Old	New	Latest	3/04/2013	BE	BEANT0007108	AV	MD	M	1964	5/6 Antigen Match	9/10	3	24	35	22			01:AD	13:XJ		
Old	New	Latest	3/04/2013	BE	BEBT000069806	AV	MD	M	1971	5/6 Antigen Match	9/10	3	24	35	55			01:XX	13:XX		
Old	New	Latest	3/04/2013	BE	BEKUL11314	AV	MD	M	1970	5/6 Antigen Match	9/10	3	24	35	27	1	4	11	13	7	6
Old	New	Latest	3/04/2013	BE	BEKUL18228	AV	MD	M	1962	5/6 Antigen Match	9/10	3	24	35	51	1		11	13	7	6
Old	New	Latest	3/04/2013	BE	BEUCL0320636	AV	MD	M	1971	5/6 Antigen Match	9/10	3	24	35	62			11:03	13:01	7	1
Old	New	Latest	3/04/2013	BE	BEULBCM003762	AV	MD	F	1966	5/6 Antigen Match	9/10	11	24	35	55			11:XX	13:XX	7	6
Old	New	Latest	3/04/2013	BE	BEULBDV005492	AV	MD	F	1975	5/6 Antigen Match	9/10	3	24	35	49			11:XX	13:XX		
Old	New	Latest	3/04/2013	BE	BEULBV8003972	AV	MD	F	1957	5/6 Antigen Match	9/10	3	24	35	7			11	6	7	1
Old	New	Latest	3/04/2013	BE	BEVUB00000692	AV	MD	M	1963	5/6 Antigen Match	9/10	3	24	35	7	4	1	11:XX	13:XX		
Old	New	Latest	3/04/2013	BE	BECB030008001882	AV	CB	F	2008	5/6 Antigen Match	9/10	03:XX	24:XX	35:XX	55:XX			16:XX	13:XX		
Old	New	Latest	3/04/2013	BE	BECB030009000954	AV	CB	F	2009	5/6 Antigen Match	9/10	03:XX	24:XX	35:XX	55:XX			11:XX	04:XX		
Old	New	Latest	3/04/2013	BE	BECB030010001768	AV	CB	F	2010	5/6 Antigen Match	9/10	03:XX	24:XX	35:XX	15:XX			11:XX	13:XX		
Old	New	Latest	3/04/2013	BE	BECBLVCB002095	AV	CB	F	2001	5/6 Antigen Match	9/10	03:XX	24:XX	35:XX	55:XX			01:MV	13:GVA		
Old	New	Latest	3/04/2013	BE	BECBLVCB002411	AV	CB	F	2001	5/6 Antigen Match	9/10	03:XX	24:XX	35:XX	55:XX			14:MX	13:GVA		
Old	New	Latest	3/04/2013	BE	BECBLVCB012158	AV	CB	F	2012	5/6 Antigen Match	9/10	03:XX	24:XX	35:XX	55:XX			15:AB	13:AB		
Old	Dupl	Latest	23/04/2013	GL	GL9005855	AV	MD	M	1959	3/4 AB Antigen Match	9/10	11	24	35	55						
Old	Dupl	Latest	24/04/2013	SE	SELU-5809	AV	MD	M	1955	3/4 AB Antigen Match	9/10	11	24	35	55						
Old	New	Latest	23/04/2013	CZ	CZ22150	AV	MD	M	1964	3/4 AB Antigen Match	9/10	11	9	35	22	3	4				
Old	New	Latest	3/04/2013	DE	DEFRB.....11424	AV	MD	M	1967	6/6 Antig.Match - Allele MM	9/10	3	24	35	55	3	4	11:01	13:01		
Old	New	Latest	23/04/2013	CZ	CZ91520	AV	MD	F	1959	3/4 AB Antigen Match	9/10	3	24	7	55	9	7				
Old	Upd	Latest	15/04/2013	DE	DEDKM.....901524	AV	MD	M	1967	6/6 Antig.Match - Allele MM	9/10	03:XX	24:XX	35:XX	55:XX			11:PAZ	13:XX		
Old	Upd	Latest	15/04/2013	DE	DEULM.....50424	AV	MD	F	1960	6/6 Antig.Match - Allele MM	9/10	03:XX	24:XX	35:XX	55:XX			11:XX	13:02		
Old	Dupl	Latest	24/04/2013	SE	SELU-5021	AV	MD	F	1973	3/4 AB Antigen Match	9/10	3	24	7	55						
Old	Dupl	Latest	24/04/2013	SE	SEHU-13110	AV	MD	M	1971	3/4 AB Antigen Match	9/10	3	24	7	55						
Old	Dupl	Latest	24/04/2013	SE	SESA-836	AV	MD	F	1967	3/4 AB Antigen Match	9/10	3	24	7	55						
Old	Dupl	Latest	24/04/2013	SE	SEHU-7494	AV	MD	M	1966	3/4 AB Antigen Match	9/10	3	24	7	55						
Old	Dupl	Latest	24/04/2013	SE	SEHU-15280	AV	MD	M	1966	3/4 AB Antigen Match	9/10	3	24	7	55						
Old	Upd	Latest	10/05/2013	IT	ITBA01104900	AV	MD	M	1976	6/6 Antig.Match - Allele MM	9/10	3	24	35	55	3	4	11:04	13:01	7	6

Filter: ((Match Grade = 9) or (Match Grade = 8) or (Match Grade = 7))

Count: 763



# Search results

EMDIS Search Results: ABRAHEEM, BEKULAA210785

Patient | Summary of Donors | List of Donors | Donor - Details

Sorting | Multiple Allele Codes | Report | Show/Hide Report Maker | Custom Report | Typing Request | Sample Request | CBU Report Request

TC BETRAANS1 A 03:01 B 35:08 C 01:02 DRB1 11:03 DQB1 03:01  
24:02:0 55:01 04:JKTL 13:01 06:03

Msg	Donor Update	Validity	Record Update	HUB	ID	State	Type	Sex	DOB	Match Grade	Match h	A.1 [03:01]	A.2 [24:02]	B.1 [35:08]	B.2 [55:01]	C.1 [01:02]	C.2 [04:JKT]	DR.1 [11:03]	DR.2 [13:01]	DQ.1 [03:01]	DQ.2 [06:03]
Old	New	Latest	3/04/2013	BE	BEANT000137	AV	MD	M	1959	5/6 Antigen Match	9/10	3	9	35	44			11	6	3	1
Old	New	Latest	3/04/2013	BE	BEANT000371	AV	MD	M	1959	5/6 Antigen Match	9/10	3	9	7	22			11	6	3	1
Old	Dupl	Latest	8/10/2013	BE	BEANT0004698	AV	MD	F	1955	6/6 Antig.Match - Allele MM	9/10	3	9	35	22			11:MS	13:KJ		
Old	New	Latest	3/04/2013	BE	BEANT0005132	AV	MD	F	1955	5/6 Antigen Match	9/10	3	24	35	22			11:GX	01:AD		
Old	New	Latest	3/04/2013	BE	BEANT0005618	AV	MD	M	1971	5/6 Antigen Match	9/10	3	24	35	7			11	13		
Old	New	Latest	3/04/2013	BE	BEANT0007108	AV	MD	M	1964	5/6 Antigen Match	9/10	3	24	35	22			01:AD	13:KJ		
Old	New	Latest	3/04/2013	BE	BEBT000069806	AV	MD	M	1971	5/6 Antigen Match	9/10	3	24	35	55			01:XX	13:KJ		
Old	New	Latest	3/04/2013	BE	BEKUL11314	AV	MD	M	1970	5/6 Antigen Match	9/10	3	24	35	27	1	4	11	13	7	6
Old	New	Latest	3/04/2013	BE	BEKUL18228	AV	MD	M	1962	5/6 Antigen Match	9/10	3	24	35	51	1		11	13	7	6
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Old	New	Latest	3/04/2013	BE	BEULBCM003762	AV	MD	F	1966	5/6 Antigen Match	9/10	11	24	35	55			11:XX	13:XX	7	6
Old	New	Latest	3/04/2013	BE	BEULBDV005492	AV	MD	F	1975	5/6 Antigen Match	9/10	3	24	35	49			11:XX	13:XX		
Old	New	Latest	3/04/2013	BE	BEULBV8003972	AV	MD	F	1957	5/6 Antigen Match	9/10	3	24	35	7			11	6	7	1
Old	New	Latest	3/04/2013	BE	BEVU800000692	AV	MD	M	1963	5/6 Antigen Match	9/10	3	24	35	7	4	1	11:XX	13:XX		
Old	New	Latest	3/04/2013	BE	BECB030008001882	AV	CB	F	2008	5/6 Antigen Match	9/10	03:XX	24:XX	35:XX	55:XX			16:XX	13:XX		
Old	New	Latest	3/04/2013	BE	BECB030009000954	AV	CB	F	2009	5/6 Antigen Match	9/10	03:XX	24:XX	35:XX	55:XX			11:XX	04:XX		
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Old	New	Latest	3/04/2013	BE	BECBLVCB																
Old	New	Latest	3/04/2013	BE	BECBLVCB																
Old	Dupl	Latest	23/04/2013	GL	GL9005855	AV	MD	M	1959	3/4 AB Antigen Match	9/10	11	24	35	55						
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Old	New	Latest	23/04/2013	CZ	CZ22150	AV	MD	M	1964	3/4 AB Antigen Match	9/10	11	9	35	22	3	4				
Old	New	Latest	3/04/2013	DE	DEFRB.....11424	AV	MD	M	1967	6/6 Antig.Match - Allele MM	9/10	3	24	35	55	3	4	11:01	13:01		
Old	New	Latest	23/04/2013	CZ	CZ91520	AV	MD	F	1959	3/4 AB Antigen Match	9/10	3	24	7	55	9	7				
Old	Upd	Latest	15/04/2013	DE	DEDKM.....901524	AV	MD	M	1967	6/6 Antig.Match - Allele MM	9/10	03:XX	24:XX	35:XX	55:XX			11:PAZ	13:XX		
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Old	Dupl	Latest	24/04/2013	SE	SELU-5021	AV	MD	F	1973	3/4 AB Antigen Match	9/10	3	24	7	55						
Old	Dupl	Latest	24/04/2013	SE	SEHU-13110	AV	MD	M	1971	3/4 AB Antigen Match	9/10	3	24	7	55						
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Old	Dupl	Latest	24/04/2013	SE	SEHU-15280	AV	MD	M	1966	3/4 AB Antigen Match	9/10	3	24	7	55						
Old	Upd	Latest	10/05/2013	IT	ITBA01104900	AV	MD	M	1976	6/6 Antig.Match - Allele MM	9/10	3	24	35	55	3	4	11:04	13:01	7	6

Count: 763

start | Inbo - Micr... | Vodafone M... | Presentaties | HAPLO | Hsplmeetin... | MUD educat... | Presentatie... | MetaFrame ... | Prometheus... | NL | 21:09

Two donors for confirmatory typing



# Search results

EMDIS Search Results: ABRAHEEM, BEKULAA210785

Patient | Summary of Donors | List of Donors | Donor - Details

Sorting | Multiple Allele Codes | Report | Show/Hide Report Maker | Custom Report | Typing Request | Sample Request | CBU Report Request

TC BETRAANS1 A 03:01 B 35:08 C 01:02 DRB1 11:03 DQB1 03:01  
24:02:0 55:01 04:JKTL 13:01 06:03

Msg	Donor Update	Validity	Record Update	HUB	ID	State	Type	Sex	DOB	Match Grade	Match	A.1 [03:01]	A.2 [24:02]	B.1 [35:08]	B.2 [55:01]	C.1 [01:02]	C.2 [04:JKT]	DR.1 [11:03]	DR.2 [13:01]	DQ.1 [03:01]	DQ.2 [06:03]	
Old	New	Latest	3/04/2013	BE	BEANT000137	AV	MD	M	1959	5/6 Antigen Match	9/10	3	9	35	44			11	6	3	1	
Old	New	Latest	3/04/2013	BE	BEANT000371	AV	MD	M	1959	5/6 Antigen Match	9/10	3	9	7	22			11	6	3	1	
Old	Dupl	Latest	8/10/2013	BE	BEANT0004698	AV	MD	F	1955	6/6 Antig.Match - Allele MM	9/10	3	9	35	22			11:MS	13:KJ			
Old	New	Latest	3/04/2013	BE	BEANT0005132	AV	MD	F	1955	5/6 Antigen Match	9/10	3	24	35	22			11:6X	01:AD			
Old	New	Latest	3/04/2013	BE	BEANT0005618	AV	MD	M	1971	5/6 Antigen Match	9/10	3	24	35	7			11	13			
Old	New	Latest	3/04/2013	BE	BEANT0007108	AV	MD	M	1964	5/6 Antigen Match	9/10	3	24	35	22			01:AD	13:KJ			
Old	New	Latest	3/04/2013	BE	BEBT000069806	AV	MD	M	1971	5/6 Antigen Match	9/10	3	24	35	55			01:XX	13:KJ			
Old	New	Latest	3/04/2013	BE	BEKUL11314	AV	MD	M	1970	5/6 Antigen Match	9/10	3	24	35	27	1	4	11	13	7	6	
Old	New	Latest	3/04/2013	BE	BEKUL18228	AV	MD	M	1962	5/6 Antigen Match	9/10	3	24	35	51	1		11	13	7	6	
Old	New	Latest	3/04/2013	BE	BEUCL0320636	AV	MD	M	1971	5/6 Antigen Match	9/10	3	24	35	62			11:03	13:01	7	1	
Old	New	Latest	3/04/2013	BE	BEULBCM003762	AV	MD	F	1966	5/6 Antigen Match	9/10	11	24	35	55			11:XX	13:XX	7	6	
Old	New	Latest	3/04/2013	BE	BEULBDV005492	AV	MD	F	1975	5/6 Antigen Match	9/10	3	24	35	49			11:XX	13:XX			
Old	New	Latest	3/04/2013	BE	BEULBV8003972	AV	MD	F	1957	5/6 Antigen Match	9/10	3	24	35	7			11	6	7	1	
Old	New	Latest	3/04/2013	BE	BEVU800000632	AV	MD	M	1963	5/6 Antigen Match	9/10	3	24	35	7	4	1	11:XX	13:XX			
Old	New	Latest	3/04/2013	BE	BECB030008001882	AV	CB	F	2008	5/6 Antigen Match	9/10	03:XX	24:XX	35:XX	55:XX			16:XX	13:XX			
Old	New	Latest	3/04/2013	BE	BECB030009000954	AV	CB	F	2009	5/6 Antigen Match	9/10	03:XX	24:XX	35:XX	55:XX			11:XX	04:XX			
Old	New	Latest	3/04/2013	BE	BECB030009000954	AV	CB	F	2009	5/6 Antigen Match	9/10	03:XX	24:XX	35:XX	55:XX			11:XX	04:XX			
Old	New	Latest	3/04/2013	BE	BECB030009000954	AV	CB	F	2009	5/6 Antigen Match	9/10	03:XX	24:XX	35:XX	55:XX			11:XX	04:XX			
Old	New	Latest	3/04/2013	BE	BECBLVCB	AV	MD	M														
Old	New	Latest	3/04/2013	BE	BECBLVCB	AV	MD	M														
Old	New	Latest	3/04/2013	BE	BECBLVCB	AV	MD	M														
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Old	Dupl	Latest	24/04/2013	SE	SELU-5809	AV	MD	M	1955	3/4 AB Antigen Match	9/10	11	24	35	55							
Old	New	Latest	23/04/2013	CZ	CZ22150	AV	MD	M	1964	3/4 AB Antigen Match	9/10	11	9	35	22	3	4					
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Old	Upd	Latest	15/04/2013	DE	DEDKM.....901524	AV	MD	M	1967	6/6 Antig.Match - Allele MM	9/10	03:XX	24:XX	35:XX	55:XX			11:PAZ	13:XX			
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Old	Upd	Latest	10/05/2013	IT	ITBA01104900	AV	MD	M	1976	6/6 Antig.Match - Allele MM	9/10	3	24	35	55	3	4	11:04	13:01	7	6	

NO donor

Count: 763

# TRANSPLANTATION INDICATION

## ALLOGENEIC

<u>Disease</u>	<u>disease status</u>	mm unrelated
		> 1Ag mm related

## Leukaemia

AML	CR1 (low risk)	GNR
	CR1 (intermediate)	D
	CR (high risk)	C0
	CR2	C0
	CR3, incipient relapse	D
	M3 molecular persistence	GNR
	M3 molecular CR2	GNR
	Relapse or refractory	D

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	CR2	C0
	CR3, incipient relapse	D
	M3 molecular persistence	GNR
	M3 molecular CR2	GNR
	Relapse or refractory	D

# MAC TRANSPLANT INDICATIONS D or GNR



Marrow Donor Program Belgium - Registry  
 Motstraat 40 2800 Mechelen  
 Tel: (32) - 15 44 33 96 Fax: (32) - 15 44 36 56  
 Email : MDPB-registry@rodekruis.be

## REQUEST MEDICAL ADVISORY COMMITTEE

SECTION A: TO BE COMPLETED BY TRANSPLANT CENTER OR DONOR CENTER  
 REQUESTING MAC APPROVAL  
 PLEASE EMAIL OR FAX TO THE REGISTRY 0032 15 44 36 56

Reply within 1 week

Urgent request (within 48 hours)   
 Please specify reason of urgency:

Patient ID:

DOB:

Donor code (if applicable):

- a.  Patient's disease is not generally recommended : GNR.  
Please submit the MAC request, incl. full description of the patient's disease history and reason for an URD transplant by completing section B "request for review" for review by the Medical Advisory Committee.
- b.  Patient's disease belongs to category "developmental".  
Please submit the MAC request, incl. full description of the patient's disease history and reason for an URD transplant by completing section B "request for review" for review by the Medical Advisory Committee.
- c.  Indications for a second BM or PBSC donation (HPC.M or HPC.A) for the same recipient, same Belgian donor.  
Please submit "MDPB006 second donation request v1 2010" for review by the Medical Advisory Committee.
- d.  In case of a significant mismatch (<B>10), please submit the IRB approved Protocol for review by the Medical Advisory Committee.
- e.  Results of the blood test doesn't comply to the blood donor requirements.  
Please submit "MDPB016 donor clearance v1 2010" for review by the Medical Advisory Committee.
- f.  In case of cryopreservation of cells of voluntary donor (HPC.M or HPC.A), please submit reason and clinical condition of patient and expected date of transplant.
- g.  Other:

MOTIVATION:

Name of physician:  
 Signature:

STAMP:

MDPB036 MAC request for review v2 2011

Fig. 10



Marrow Donor Program Belgium - Registry  
 Motstraat 40 2800 Mechelen  
 Tel: (32) - 15 44 33 96 Fax: (32) - 15 44 36 56  
 Email : MDPB-registry@rodekruis.be

## MAC APPROVAL

### MEDICAL ADVISORY COMMITTEE (MAC)

For patients not fulfilling the eligibility criteria as described in the SOP as well as for any request not clearly covered by the SOPs, the Registry must contact all MAC members individually by email. The members of the MAC must reply within 1 week (48 hours if urgent). A minimum of 50% of the members has to approve the request prior to proceeding. A MAC member cannot vote on a request from his/her own center. The decision will be considered final. In general, deviations from the SOPs will only be accepted in exceptional situations.

Your request was reviewed by the Medical Advisory Committee.

Patient ID:

DOB:

Donor code (if applicable):

(In attachment a copy of "MDPB036 mac request for review" signed by the MAC members).

MAC approval: you may proceed with the request.

NO MAC approval: you may not proceed with the request.

Date:

Kind regards,

Dr Anne Vanhosebrouck  
 Director  
 MDPB-Registry  
 Motstraat 40  
 2800 MECHELEN

# The Overlooked Donor

Haploidentical stem cell donor

Cord Blood

## Third party transplantation (definition)

**Co-infusion of cells from two different donors**

**cord blood + cord blood**

**MSC + cord blood**

**MSC + HLA (8/10 matched) stem cells**

**Haplo + cord**

**The goal is to enhance engraftment**

## Minimal and ideal compatibility

DONOR TYPE	MATCH LEVEL		REMARK
	IDEAL	MINIMUM	
Identical twin	By definition genotypically identical		
Sibling or other family donor	<b>6/6</b>	<b>5/6 IF one haplotype is genotypically identical. If not , see MUD</b>	
Unrelated	<b>10/10</b>	<b>8/10 allelic*</b>	
Cord Blood	<b>6/6</b>	<b>4/6</b>	<b>Allelic MM DRB1?</b>
Haploidentical	<b>1 haplotype identical</b>		

### (\*) minimum 8/10 allelic:

- |                         |   |
|-------------------------|---|
| • 1 antigenic MM (9/10) | • 1 allelic + 1 Antigenic MM (8,5/10)   |
| • 2 allelic MM (9/10)   | • 1 antigenic + 1 antigenic DQB1 (8/10) |

# Guidelines for CBU unit choice

## Eurocord criteria for malignant disorders

- UCB unit with 5/6 or 6/6 HLA match  
Collected TNC >  $2.5 \times 10^7/\text{kg}$   
Collected/infused CD34+ cells >  $1.2 \times 10^5/\text{kg}$
  
- UCB unit with 4/6 HLA match  
Collected TNC >  $3.5 \times 10^7/\text{kg}$   
Collected/infused CD34+ cells >  $1.7 \times 10^5/\text{kg}$

# Recommendation For selection of a single Cord for transplantation

- A 6/6 HLA matched (HLA-A, -B, -DR) cord blood unit should be selected as the donor source with TNC  $>2.5 \times 10^7/\text{kg}$
- If there is no 6/6 HLA matched cord blood unit, select the largest unit (TNC  $\geq 5.0 \times 10^7/\text{kg}$ ) with 1 (preferably) or 2 HLA Mismatches
- If there is no 5-6/6 HLA matched cord blood unit with TNC  $\geq 5.0 \times 10^7/\text{kg}$ , select the largest unit (TNC  $\geq 2.5 \times 10^7/\text{kg}$ ) with 1 (preferably) or 2 HLA mismatches
- If possible, avoid units with TNC  $\leq 2.5 \times 10^7/\text{kg}$  and or 3-4 HLA mismatches In this case double CBT should be considered
- Testing for HLA-DQ are recommended
- Avoid HLA mismatches at loci in which patients have preformed HLA antibodies



# Double CBU transplantation

## Primeur in ZNA-Stuivenbergziekenhuis: Leukemiepatiënt gered

ANTWERPEN – René Vranckaert (57) stond vorig jaar nog ten dode opgeschreven, maar dankzij een revolutionaire behandeling in het Antwerpse ZNA-Stuivenbergziekenhuis is zijn leukemie bijna volledig genezen. Op 6 januari onderging René met succes een transplantatie van bloedcellen afkomstig uit 2 navelstrengen. «Deze transplantatie in Antwerpen is de eerste succesvolle behandeling in Vlaanderen», vertelt arts Prof. Zachée.

«Bij René's laatste controle waren er geen leukemiecellen meer te vinden», zegt professor Zachée. «Het risico bij deze operatie was nochtans zeer groot: de patiënt kon de cellen afstoten en andersom. René had er meer dan een jaar chemotherapie opzitten. Toen duidelijk bleek dat de conventionele manier niet werkte, volgde een lange zoektocht naar geschikte bloeddonors. Zonder resultaat. Op het eerste zicht was dit het doodvonnis voor René. Onze laatste hoop was de transplantatie van navelstrengbloed. Deze behandeling is courant bij



Professor Zachée kon leukemiepatiënt René Vranckaert (57) redden dankzij een unieke operatie in Vlaanderen. Foto Klaas Die Scheider

kinderen, maar voor een volwassene heb je onvoldoende stamcellen in één enkele navelstreng. Uiteindelijk vonden we twee geschikte navelstrengen, één in Gent en één in New York. Op 6 januari werden dan 1,8 miljard stamcellen uit de twee navelstrengen bij René ingeplant. Drie weken later bleek dat ingreep -

gelukt was.» René kan terug fietsen, zwemmen, wandelen. «Prof. Zachée heeft me geweldig goed geholpen. Mijn grootste droom is verre reizen te maken, maar dat valt nog eventjes af te wachten». «Het unieke is dat René nu met 2 verschillende DNA-profielen rondloopt, zonder dat die elkaar afstoten», licht Zachée toe. (AVT)

## Comparison between CBU and other sources of stem cells

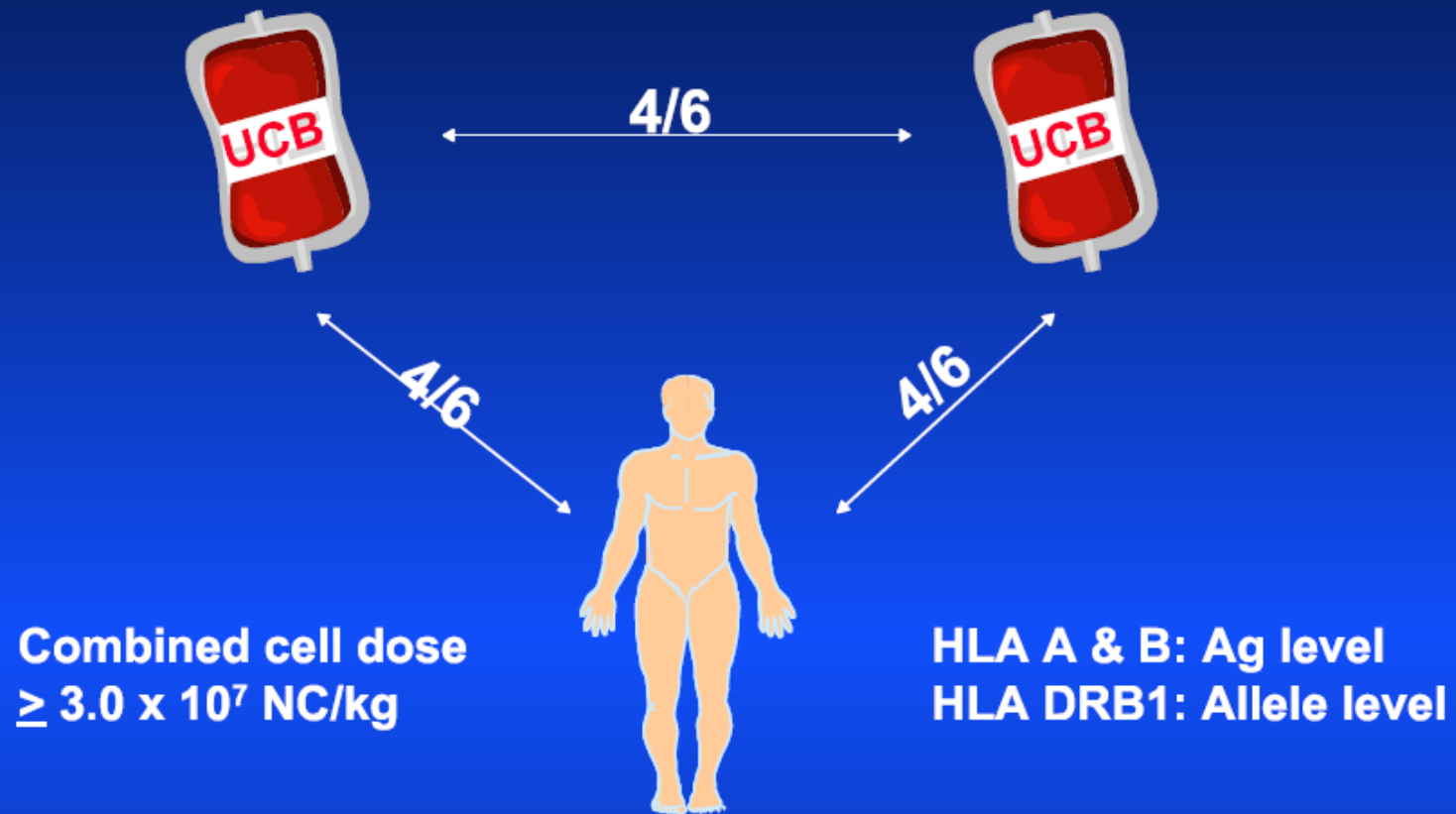
- **Same survival and leukemia free survival**
- **Engraftment is delayed**
- **Higher incidence of infections and early TRM**
- **Less acute and chronic GVHD**

# Advantages and disadvantages of alternative donor HSCT

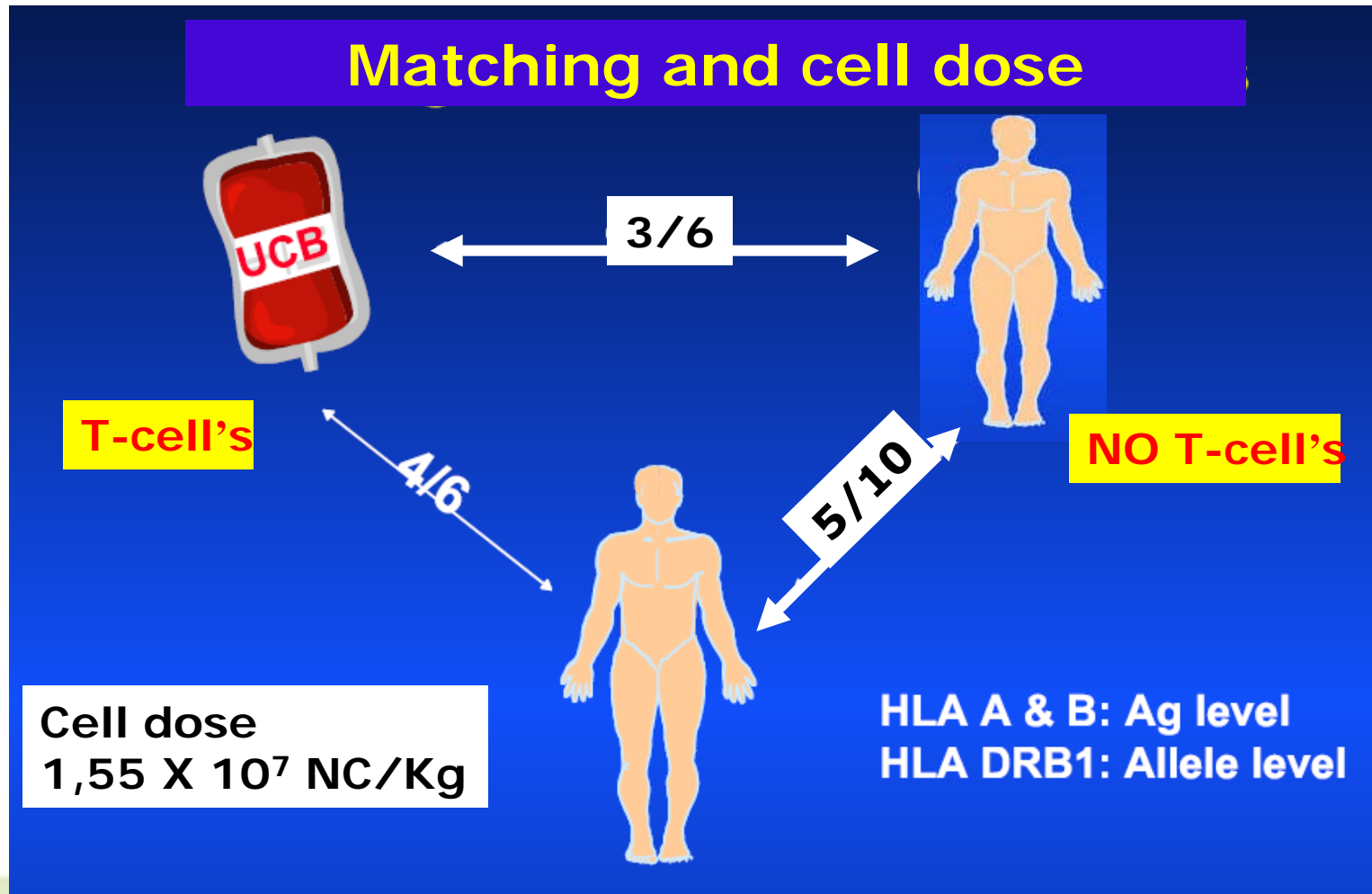
	Unrelated BMT	Unrelated UCB	CD34 selected related haplo-identical PBSC
Available pool	> 11 ME	>250 000	-
Likelihood of suitable donor	10/10=40% >9/10=70% Ethnic minority= 20%	>5/6=40% >4/6=70%	> 90%
Speed of access	3-4 months	2-3 weeks	Immediate
Cost of obtaining graft	High	High	Low
Risk to donor	low	None	Low
Ability to re-arrange infusion date	May be difficult	Easy	Easy
Re-access	Possible	No	Yes
Quality of product	Assured	Variable	Assured
Speed of engraftment	Moderate	Slow	Fast
Graft rejection	low	Moderate	Moderate
GVHD risk	High	Moderate	Low
Speed of immune reconstitution	Moderate	Moderate	Very slow
Speed to GVL effect	Moderate	Moderate	Very slow
Risk of viral transmission	Yes	No	Yes
Risk of transmission of congenital disease	No	Yes	No

## Double cord

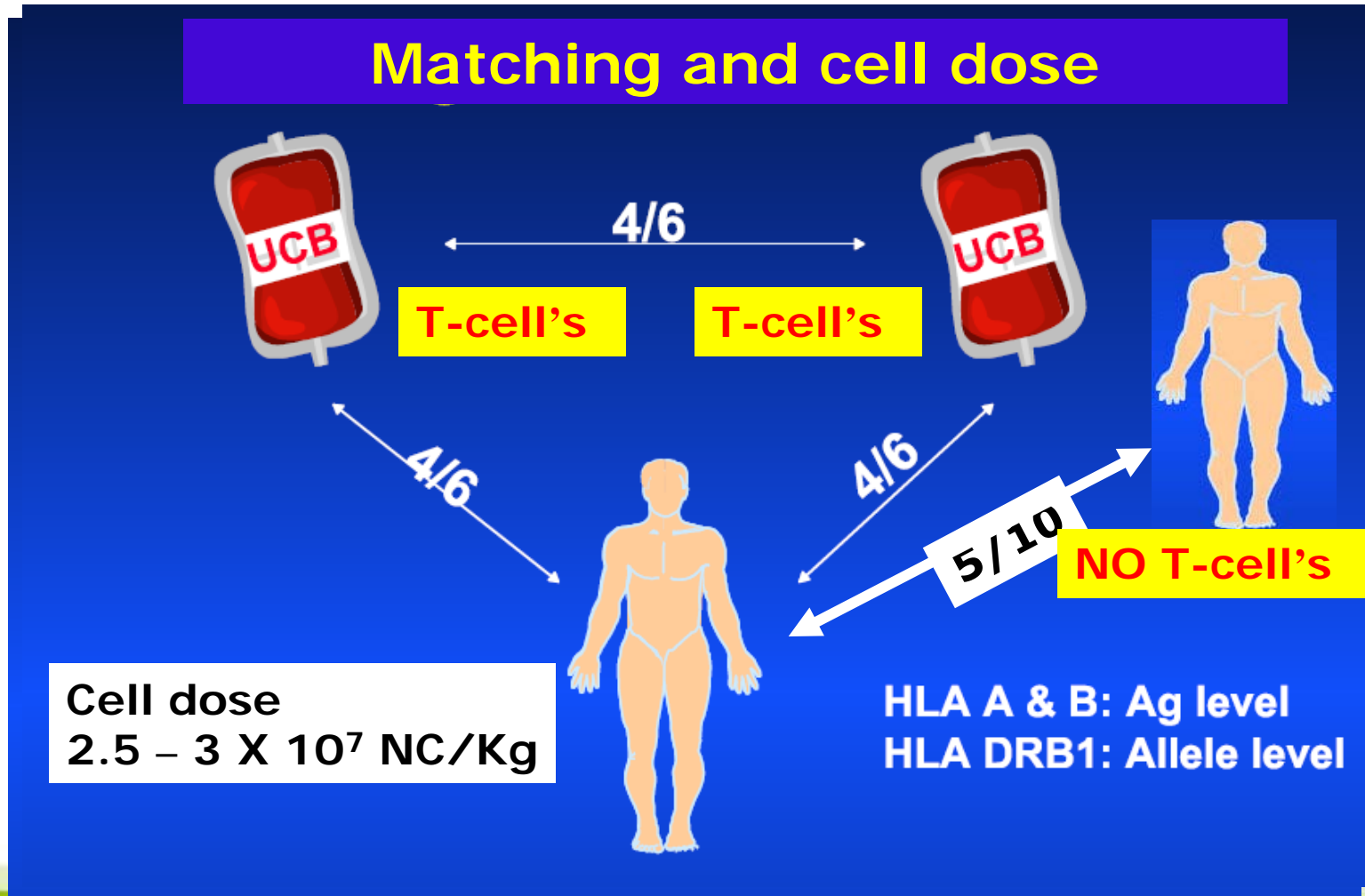
### Matching of Double UCB Unit Grafts



# Haplo & cord



# Haplo & cord: Manhattan version



# Conclusions



- ❑ GVHD is low
- ❑ Neutrophil recovery is quick → less neutropenia –related infections, thus favoring engraftment
- ❑ Low disease relapse
- ❑ The strategy of co-infusion of haplo and CB make a rapidly available transplant possible as in the situation of graft failure.
- ❑ The strategy of co-infusion of haplo and CB can contribute to making CB –transplant as first choice option for a large number of wide age range who lack a HLA compatible donor or when total cord blood cell dose of  $> 3 \times 10^7/\text{Kg}$  NC could not be reached.
  
- ❑ T cell Immune reconstitution is slow
- ❑ High cost



# What shall we learn?

- Introduction
- Related donor searches
- Unrelated donor searches
- The overlooked Donor
- Patient eligibility





## CASUS:

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- Patient eligibility?
  - Intake Consultation
  - Risks and benefits
  - Possible adverse events
  - LAB
  - ECG & Echo cardio & lung function & eye fundus & RX Thorax & sinuses

## Eligibility of the Patient

- **Performance: ECOG: WHO < 2. Karnofsky >75%.**
- **Lung function: VC, FEV1, DLCO all >50%.**
- **Cardiac function: ejection fraction > 45%.**
- **Liver enzymes: < 2.5 x upper limit of bilirubine and transaminases.**
- **Renal function: Creatinine clearance > 40 ml/min.**
- **Do the SOROR score**
- **Do the EBMT score**

# SOROR INDEX

Sorror index	NRM - 2jaar	OS -2jaar
<b>0</b>	<b>14%</b>	<b>71%</b>
<b>1</b>	<b>21%</b>	<b>60%</b>
<b>2</b>	<b>21%</b>	<b>60%</b>
<b>3</b>	<b>41%</b>	<b>34%</b>
<b>4</b>	<b>41%</b>	<b>34%</b>

Comorbiditeit	Definitie van comorbiditeit	Score
Arythmie	Atriale fibrillatie of flutter, sick sinus syndroom en ventriculaire aritmie	1
Cardiaal	Coronaire arteriële ziekte, aangeboren hartfalen, myocard infarct of EF - 50%	1
Inflammatoire intestinale ziekten	Ziekte van Crohn of ulceratieve colitis	1
Diabetes	Behandeling met insuline vereist of orale medicatie, niet enkel dieet	1
Cerebrovasculaire ziekten	TIA of CVA	1
Psychiatrische stoornis	Depressie of angst episodes welke een psychiatrisch consult of behandeling vereisen	1
Lever, milt	Chronische hepatitis, bilirubine > NL tot 1.5 x NL, of AST/ALT > NL tot 2.5 x NL	1
Obesitas	Patiënten met een BMI > 35 kg/m <sup>2</sup>	1
Infecties	Vereist een onafgebroken toediening van een antimicrobiële behandeling na dag 0	1
Reumatologie	SLE, RA, polymyositis, gemengde CTD of polymyalgia rheumatica	2
Peptisch ulcus	Behandeling vereist	2
Gematigde of ernstige renale aandoeningen	Serum creatinine >2 mg/dl, op dialyse of eerdere niertransplantatie	2
Gematigd longlijden	DLCO en/of FEV <sub>1</sub> , 66% - 80% of dyspnoe bij de minste inspanning of activiteit	2
Eerste solide tumor	Behandeld op gelijk tijdstip in de voorgeschiedenis van de patiënt, met uitsluiting van niet-melanoom huidtumor	3
Hartkleplijden	Met de uitzondering van een mitralisklep prolaps	3
Ernstig pulmonaal lijden	DLCO en/of FEV <sub>1</sub> <65% of dyspnoe bij rust en zuurstof afhankelijk	3
Gematigd of ernstig leverlijden	Levercirrhose, bilirubine >1,5x ULN of AST/ALT > 2,5 x ULN	3

# EBMT SCORE

			Score
<b>Leeftijd van de patiënt</b>	<20 jaar	0	
	20-40 jaar	1	
	>40 jaar	2	
<b>Histocompaibiliteit</b>	HLA identieke sib	0	
	Andere	1	
<b>Donor geslacht combinatie</b>	Andere	0	
	Vrouwelijke donor voor mannelijke receptor	1	
<b>Ziekte stadium*</b>	Vroeg	0	
	Tussen	1	
	Laat	2	
<b>Tijd vanaf de diagnose**</b>	< 12 maand	0	
	> 12 maand	1	
			Totale score

\*Ziekte stadium:

0= Acute leukemie 1<sup>ste</sup> CR, MDS onbehandeld of 1 CR, CML 1<sup>ste</sup> chronische fase, NHL en MM onbehandeld of 1<sup>ste</sup> CR

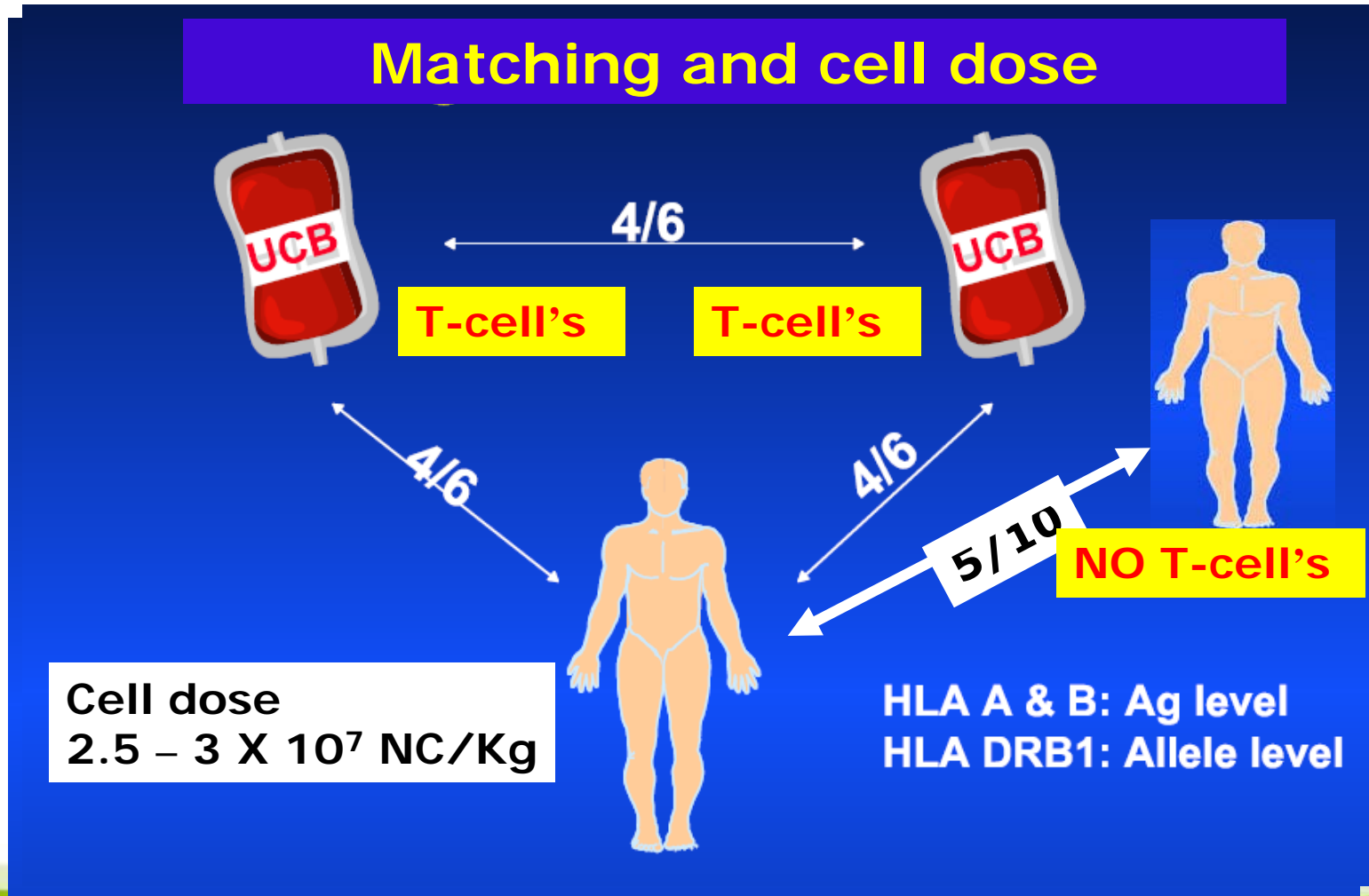
1= Acute leukemie 2<sup>de</sup> CR, CML alle andere stadia dan chronische of blastencrisis, MDS 2<sup>de</sup> CR of PR, NHL en MM 2<sup>de</sup> CR & PR & stabiele ziekte

2= Acute Leukemie al andere stadia, CML blastencrisis, MDS in alle andere stadia, MM en NHL in alle andere ziekte stadia 0 en 1.

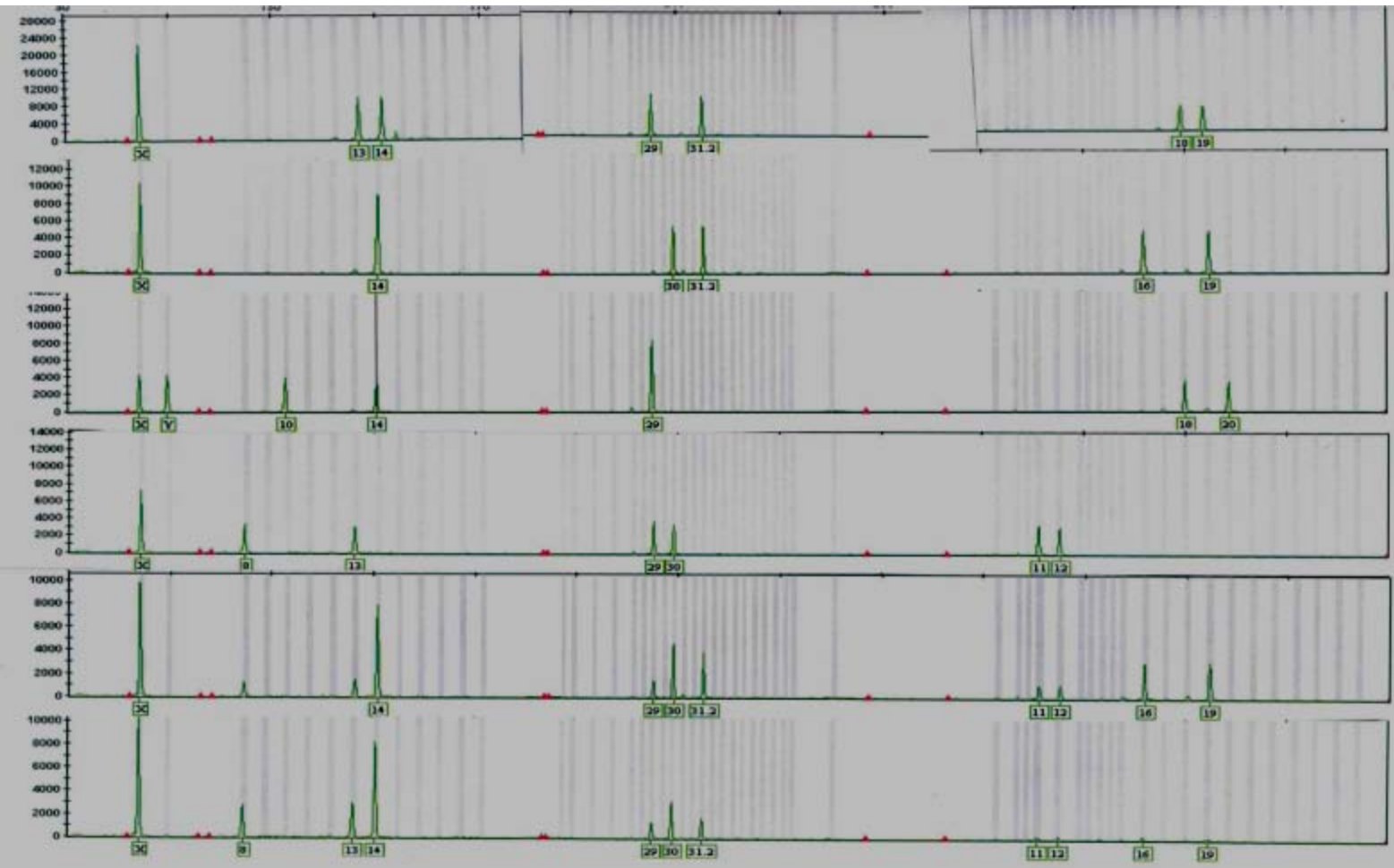
\*\* niet van toepassing in CR1

Prognostische groep	EBMT-score
Goed ( NRM: 10-15%)	0 punten
Intermediair (NRM: 15-25%)	1-2 punten
Slecht ( NRM: 30-40%)	>2 punten

# Haplo & cord: Manhattan version



# Chimerisme evolution



**PATIENT**

**HAPLO**

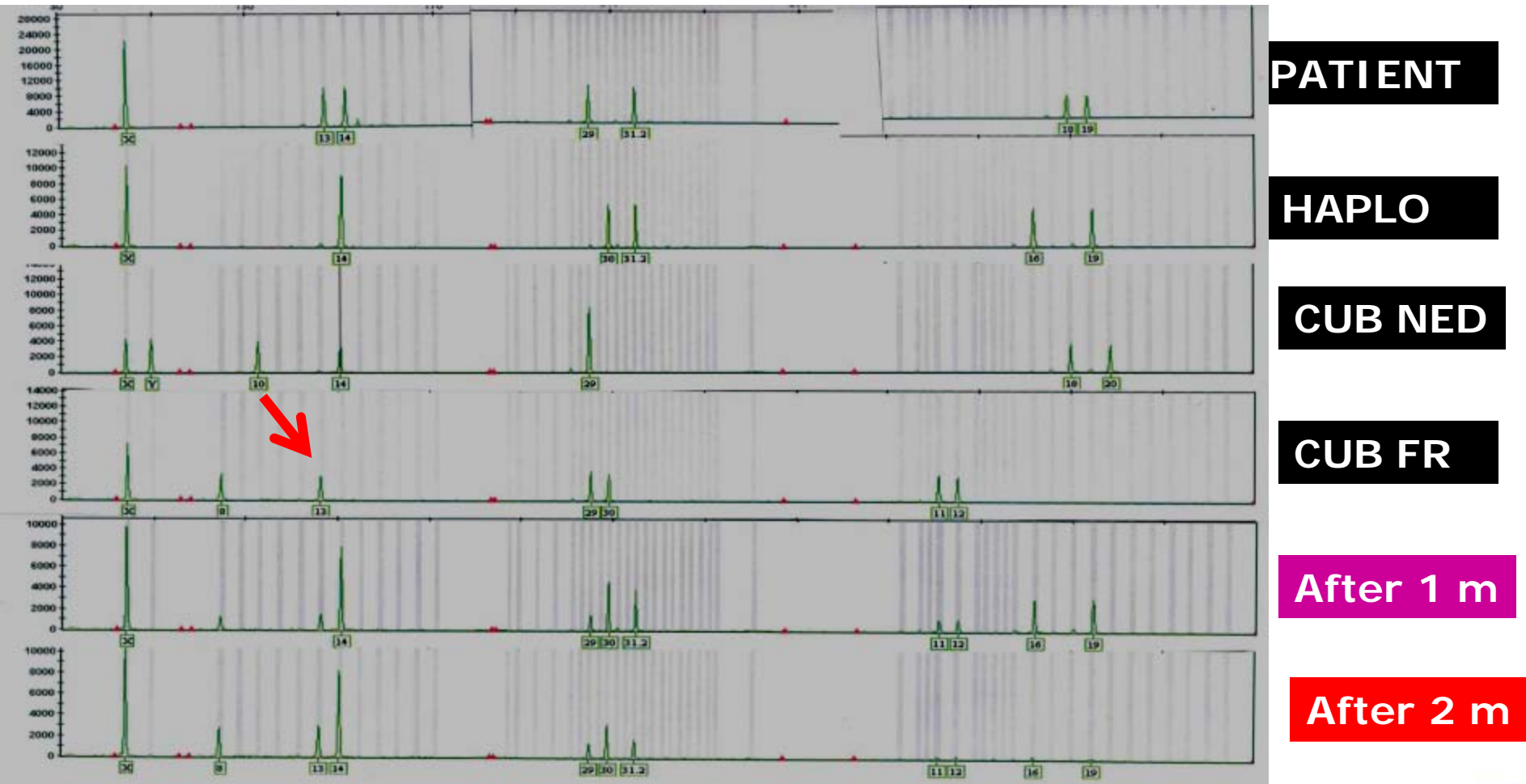
**CUB NED**

**CUB FR**

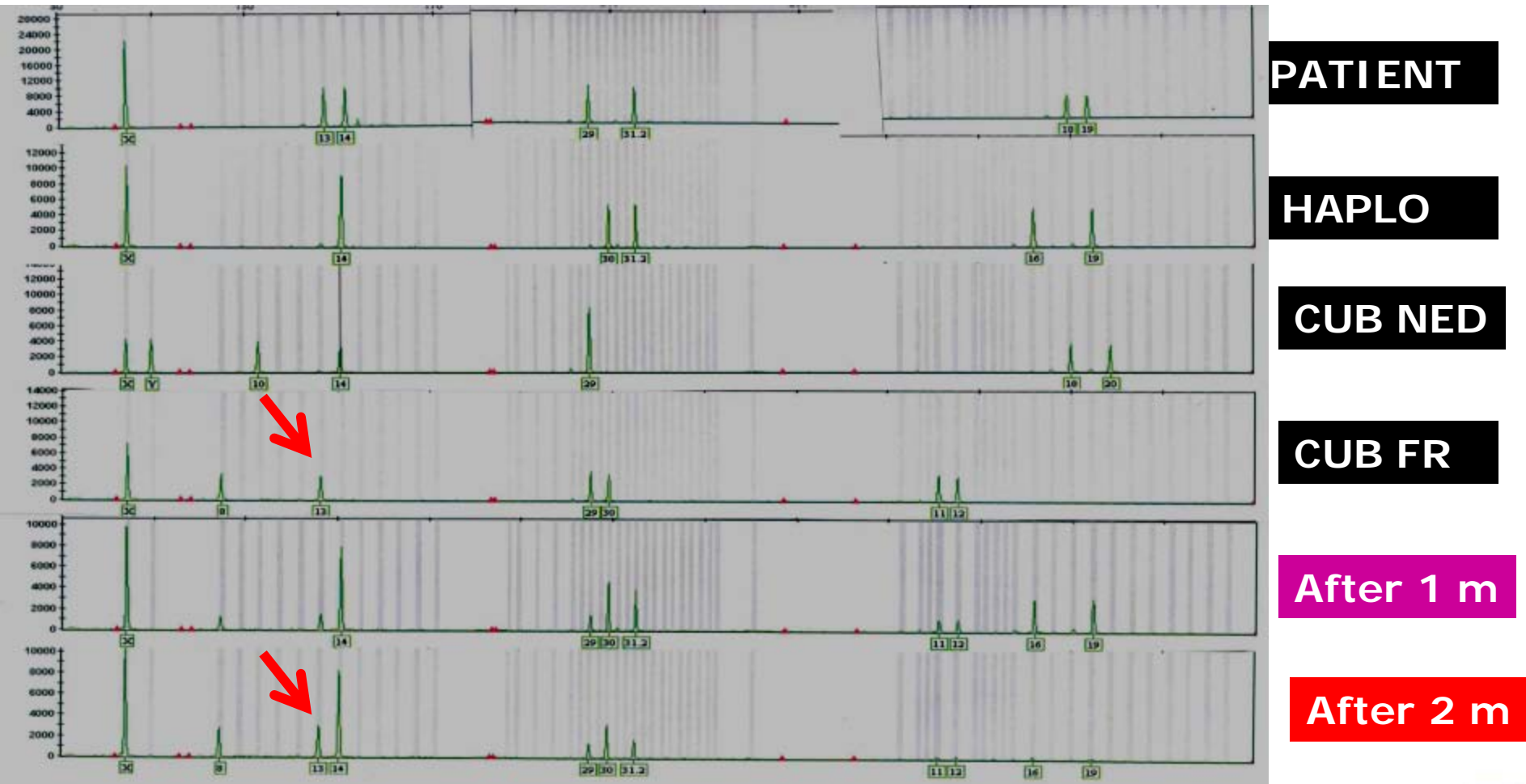
**After 1 m**

**After 2 m**

# Chimerisme evolution

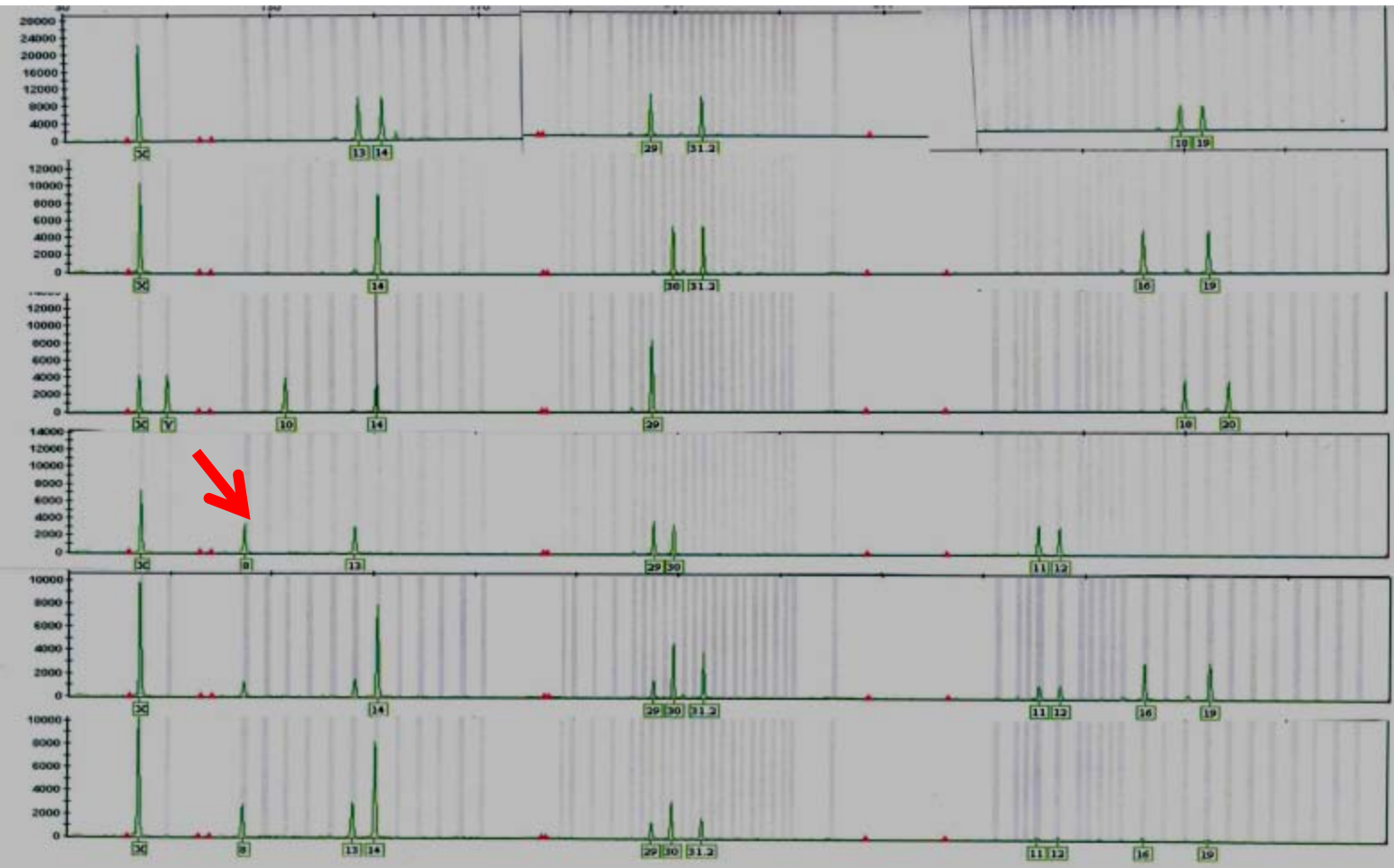


# Chimerisme evolution





# Chimerisme evolution



**PATIENT**

**HAPLO**

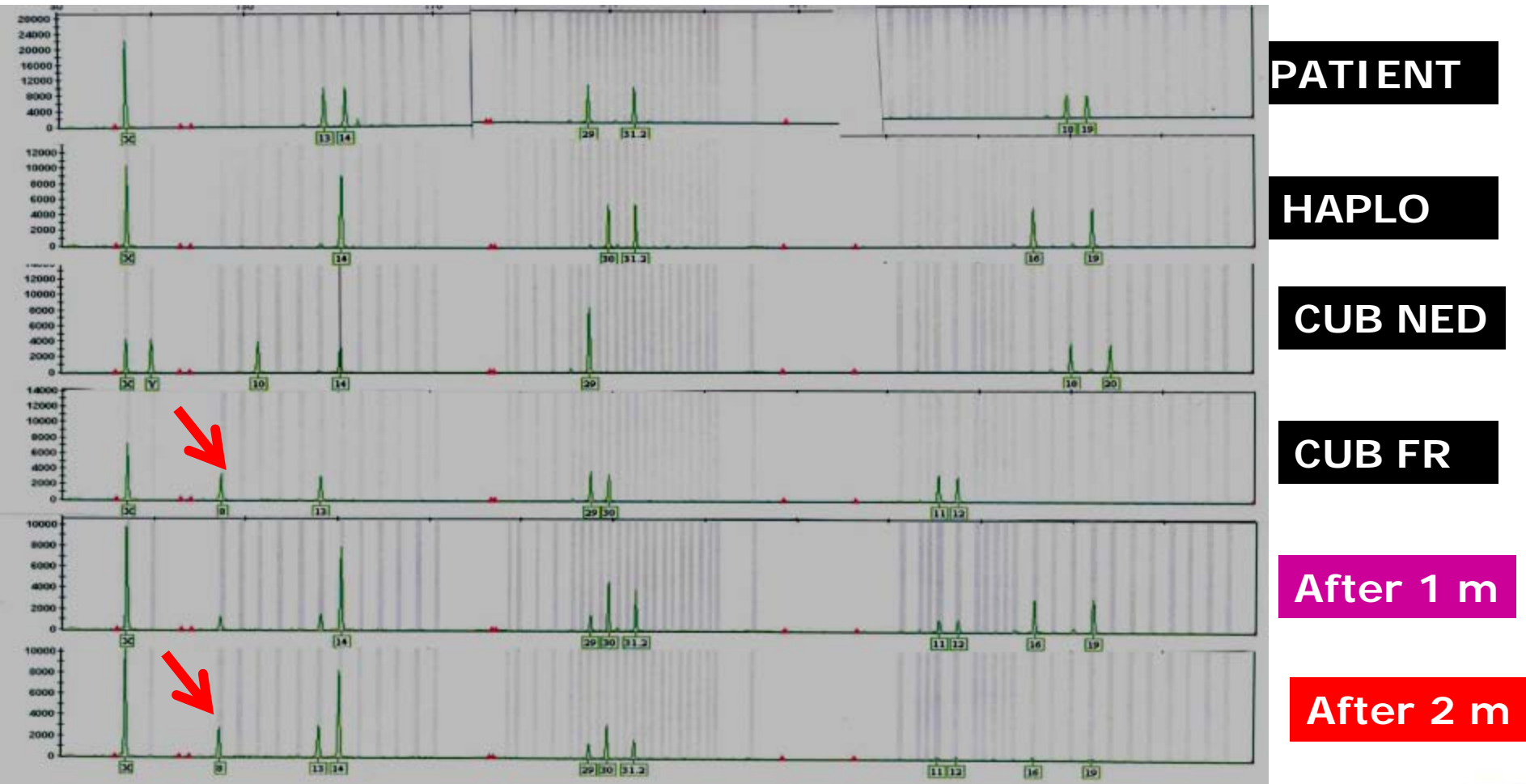
**CUB NED**

**CUB FR**

**After 1 m**

**After 2 m**

# Chimerisme evolution



# Role of the Transplant comité



## INDICATIONS

disease  
disease status  
donor type

## ELIGIBILITY

condition of the patient  
disease status  
donor compatibility