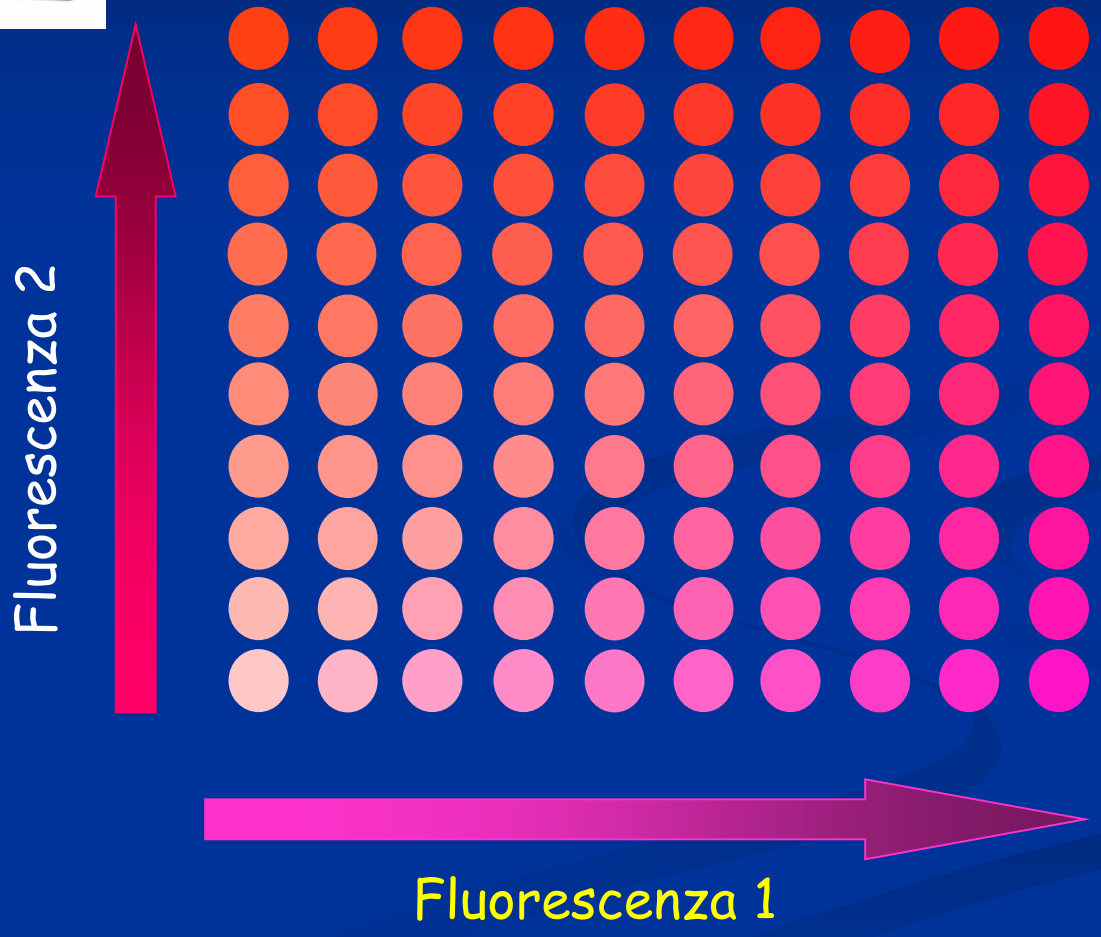
Anticorpi anti-HLA nel trapianto di cellule staminali emopoietiche

A. Bontadini

Summer School
AIBT
Pesaro, 9-11 giugno 2016

La tecnologia Luminex ha modificato la vita degli anticorpi, dei trapianti .....e la nostra.



L'evoluzione delle tecniche

Dal 1964 nuove tecniche emergenti vengono utilizzate nel laboratorio in combinazione determinando discrepanze di risultato a causa della loro differenza in sensibilità e specificità che stanno aumentando continuamente.

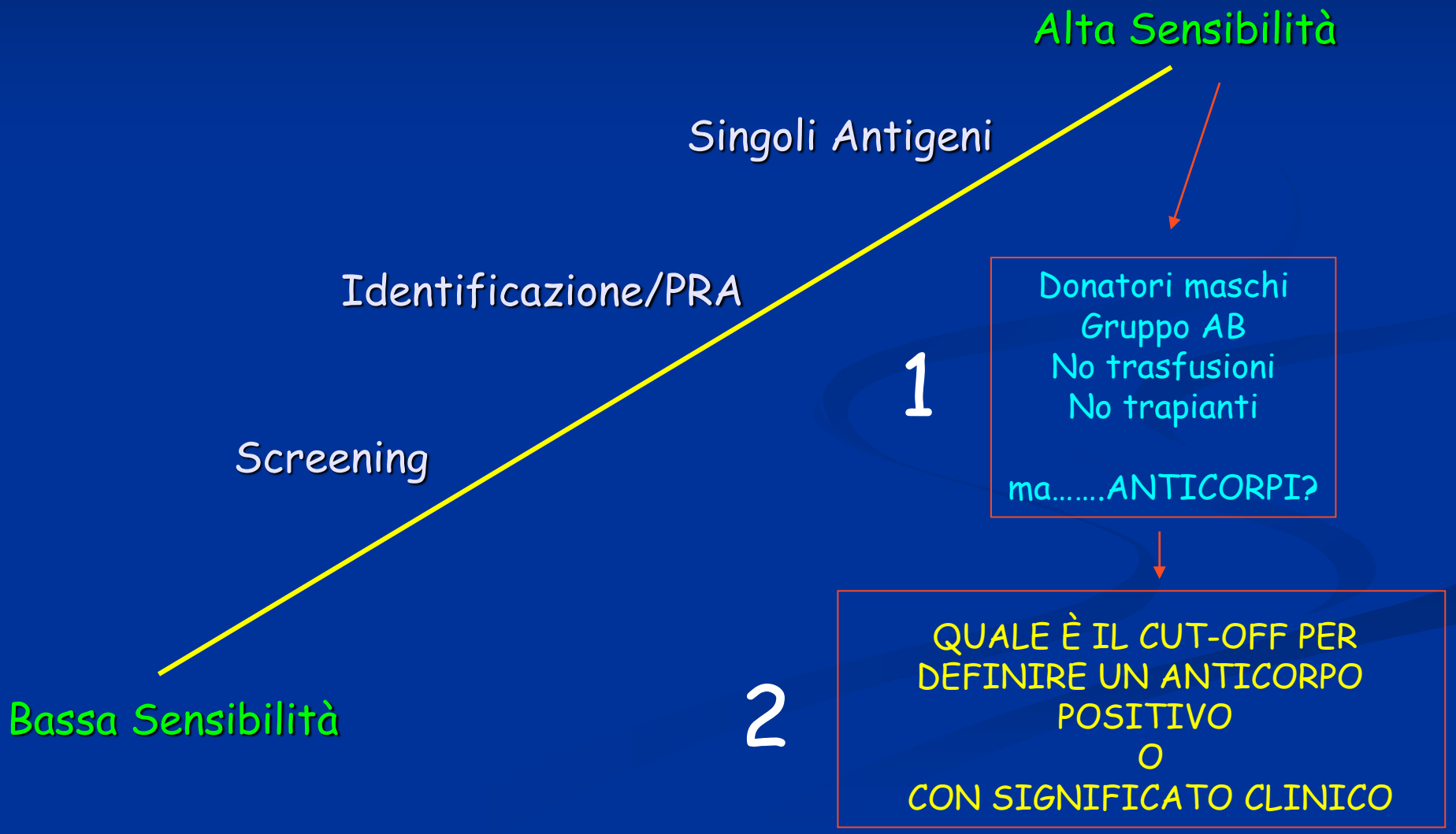
	CDC positiva N.	CDC negativa N.	Totale
Luminex positivo	112	21	133
Luminex negativo	2	176	178
Totale	114	197	311

EFI, Tolosa 2008

Studio anti-HLA con Luminex

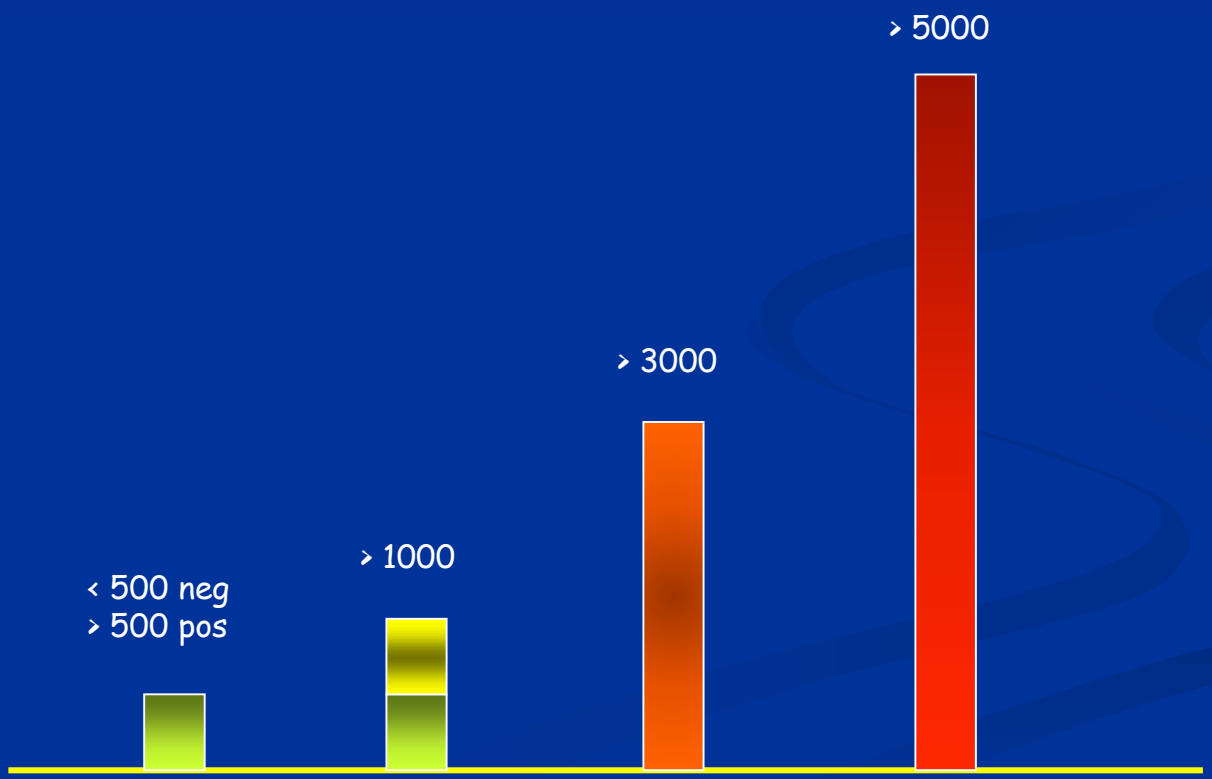
- Ricerca anticorpi anti-HLA:
  - Negativo
  - Positivo
- Identificazione specificità :
  - Specificità dell'anticorpo o degli anticorpi
  - Classe I e/o Classe II
- Biologia dell' anticorpo:
  - distinzione tra anticorpi fissanti e non fissanti il complemento

Differenti sensibilità



MFI: Mean Fluorescence Intensity

$$MFI = \frac{\text{MFI biglia} - \text{MFI medio background biglie}}{\text{MFI controllo positivo} - \text{MFI medio background biglie}} \times 100$$



Rischio immunologico

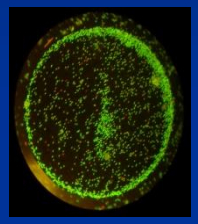
CDC -

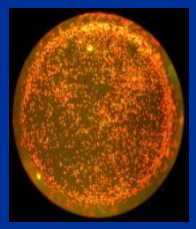
CDC+

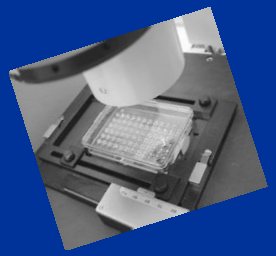
Luminex DSA Classe I Luminex DSA Classe II MFI ?	Luminex DSA Classe I Luminex DSA Classe II MFI ?

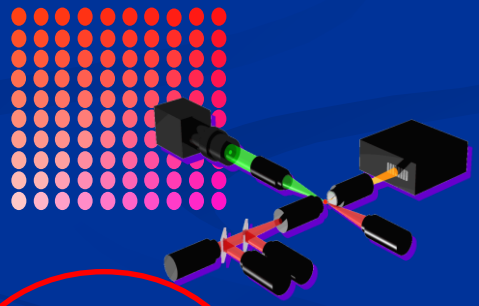
Rigetto iper-acuto/ accellerato	Rischio aumentato Rigetto acuto umorale	Basso rischio

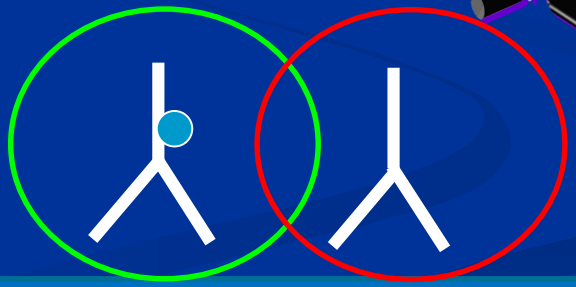
La ricerca degli anticorpi anti-HLA: le tecniche che utilizzano antigeni HLA











Anticorpi anti-HLA fissanti il complemento ⟶ Anticorpi anti-HLA fissanti e NON fissanti il complemento

Epitopes of human leukocyte antigen class I antibodies found in sera of normal healthy males and cord blood

Nadim El-Awar [a,*], Paul I. Terasaki [b], Anh Nguyen [a], Nori Sasaki [a], Luis E. Morales-Buenrostro [c], Hiroh Saji [d], Etsuko Maruya [d], Francesca Poli [e]

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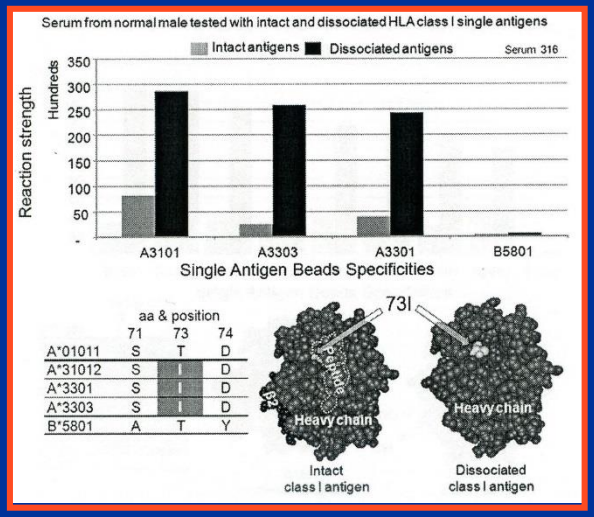
[b] Terasaki Foundation Laboratory, Los Angeles, CA 90064, USA
[c] Department of Nephrology and Mineral Metabolism, National Institute of Medical Sciences and Nutrition Salvador Zubirán, Mexico City DF 14000, Mexico
[d] HLA Laboratory NPO, Kyoto 606-8396, Japan
[e] IRCCS Fondazione Ospedale Maggiore Policlinico, Mangiagalli e Regina Elena, Department of Regenerative Medicine, North Italy Reference Center, Milan, Italy

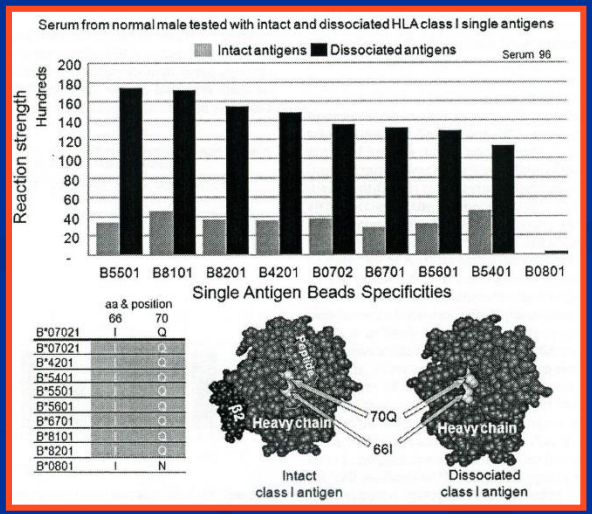
306 Sieri maschi non alloimmunizzati, messicani
95 Sieri maschi non alloimmunizzati, giapponesi
18 Sieri sangue cordonale, italiani

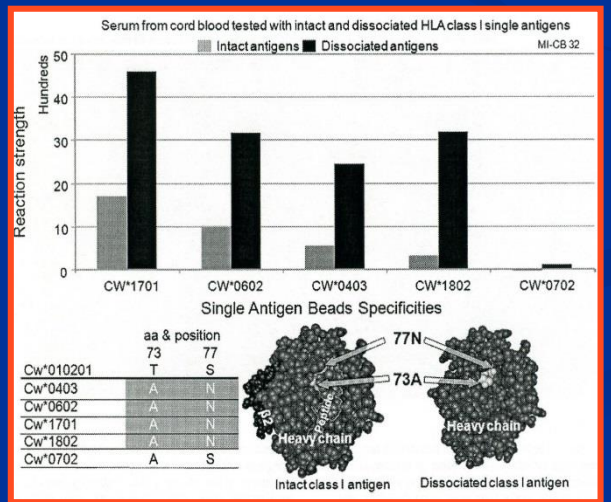
Ab verso antigeni HLA denaturati:
normale sopravvivenza graft

Ab verso antigeni HLA intatti:
ridotta sopravvivenza graft

Cai, Terasaky et al. Transplantation 2009







Anti-HLA immuni: la gravidanza

- 24 out of 61 were Positive (39.3%)

  30% 1 prengnancy

  70% 2 or more pregnancies

- 37 out of 61 were Negative (60.7%)

Antibody Specificity:

- 8 Anti-HLA Class I
- 4 Anti-HLA Class II
- 12 Anti-HLA Class I and II

Anti-HLA immuni: la gravidanza

Strength of the antibody

Antibody anti-HLA	> 500 < 1000	>1000 <5000	> 5000
Class I n. 8	4	2	2
Class II n. 4	2	2	0
Class I Class II n. 12	2 0	5 5	5 7

SIMTI, Milano 2011

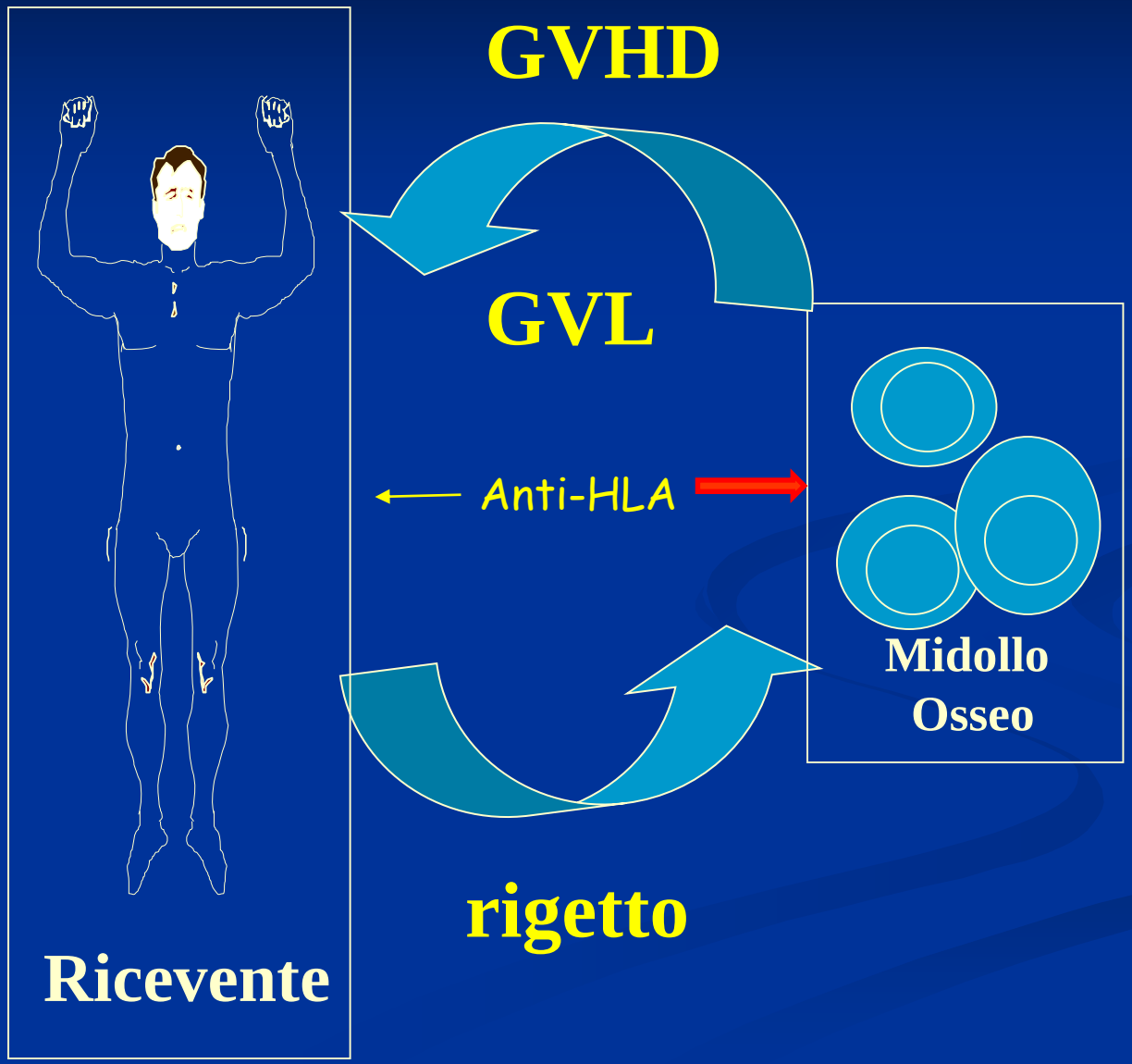
On the role of HLA antibodies in hematopoietic stem cell transplantation

A. Brand[1,2], I. N. Doxiadis[2] & D. L. Roelen[2]

Table 1 Prevalence of HLA antibodies in blood donor populations

			N (% positive HLA antibodies)		
			Males	Females	
References	Cohort (*n*, population)	Technique	Non-transfused (NT) Transfused (T)	Non-parous	Parous
Densmore et al. (13)	322, American	CDC (23 cells)	nt	*N* = 103 (7.8%+)	*N* = 221 (21%+)
Powers et al. (14)	1053, American	Luminex I/II Own NBG	*N* = 26 T (12%+)	*N* = 459 (5.9%+)	*N* = 497 parity ≥ 1 (42.5%+)
Sachs et al. (15)	229, German	EIA I/II	nt	nt	*N* = 59 parity > 2 (26 + %)
Morales-Buenrostro et al. (11)	424, Mexican	Luminex SA MFI 1000	*N* = 424 NT (63%+)	nt	nt
Reil et al. (16)	5332, German	ELISA I/II	*N* = 229 NT (0%+)	nt	*N* = 5332 (8.9%+) *N* = 888 parity >3 (12%+)
Lopes et al. (10)	300, Brazilian	ELISA	nt	nt	*N* = 300 (26.7%+) *N* = 60 parity > 3 (37%+)
		Luminex SA	nt	nt	ELISA & Luminex: *N* = 60 parity > 3 (65%+)
Kakaiya et al. (17)	7920, American	Luminex I/II	*N* = 895 T (1.7%+);	*N* = 45 T (4.4%+)	*N* = 299 T (30.4%+)
		Own NBG	*N* = 1138 NT (1% +)	*N* = 1732 NT (1.8%+)	*N* = 3598 NT (24%+)
Middelburg et al. (18)	6034, Dutch	Luminex I/II MFI 2000	*N* = 3432 (7.1%+)	*N* = 1092 (6.8%+)	*N* = 1994 (33%+) *N* = 368 parity > 3 (38%+)
Vassallo et al. (9)	2432, American	ELISA I/II	*N* = 1522 NT (<1 + %)	*N* = 275 (<1 + %)	*N* = 549 (21 + %)
		Luminex I/II	(32%+)	(33%+)	(52%+)
		Own NBG	(1.7%+)	(5%+)	(21%+)

Il trapianto di midollo osseo: doppia barriera immunologica



Anti-HLA dopo stimolazione con G-CSF

Anti-HLA by CDC: +30 after PBHSCT or BMT

Don neg Ab/Rec neg Ab	PBHSCT	BMT	P
Anti-HLA IgG	4/23 (17%)	0/27	.001
Anti-HLA IgM	8/24 (33%)	0/26	.001

Anti-HLA by flow cytometry: +30 after PBHSCT or BMT

Don neg Ab/Rec neg Ab	PBHSCT	BMT	P
Anti-HLA Class I IgG	7/20 (35%)	0/20	.008
Anti-HLA Class II IgG	1/19 (5%)	0/22	.46

Lapierre V et al. Blood 2002

- Dopo stimolazione con G-CSF vi è una maggiore incidenza di anticorpi anti-HLA post-trapianto
- La maggior parte sono donatrici pluripare
- Concomitante produzione di agglutinine anti-AB nei trapianti ABO incompatibili
- Anticorpi non rilevanti per recupero piastrinico e supporto trasfusionale

0041-1337/02/7308-1280/0
TRANSPLANTATION
Vol. 73, 1280–1285, No. 8, April 27, 2002
Printed in U.S.A.

POSITIVE SERUM CROSSMATCH AS PREDICTOR FOR GRAFT FAILURE IN HLA-MISMATCHED ALLOGENEIC BLOOD STEM CELL TRANSPLANTATION

HELLMUT D. OTTINGER,[1,2] VERA REBMANN,[1] KERSTIN A. PFEIFFER,[1] DIETRICH W. BEELEN,[2] BERNHARD KREMENS,[3] VOLKER RUNDE,[2] ULRICH W. SCHAEFER,[2] AND HANS GROSSE-WILDE[1,4]

30 pazienti trapiantati di CSE (26 adulti e 4 pazienti pediatrici)
Periodo: dal 1985 al 2000

Tipizzazione HLA

Periodo dal 1985-1990:	Tipizzazione sierologica e MLC
Periodo dal 1990-1996:	Tipizzazione sierologica Classe I e Biologia molecolare Bassa risoluzione Classe II
Periodo dal 1996:	Biologia molecolare bassa risoluzione Classe I e alta risoluzione Classe II

Cross-match (XM)
XM positivo per i linfociti B: 30 pazienti
XM positivo per i linfociti T: 14 pazienti

Cross-match
Rigetto del graft

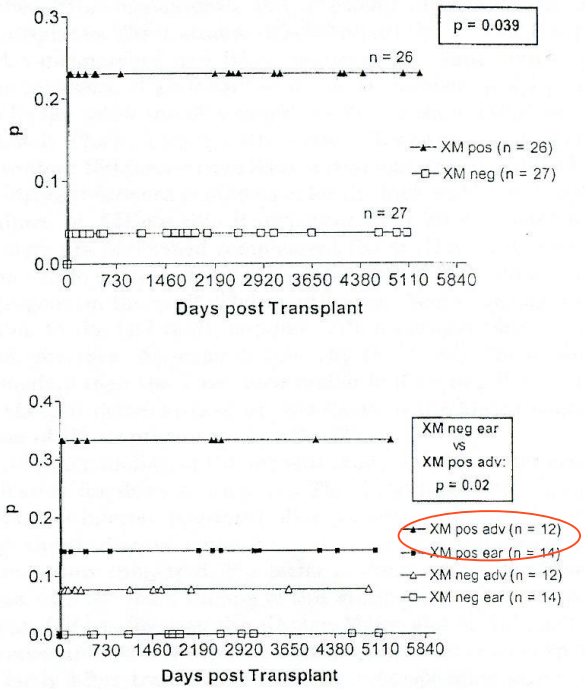


FIGURE 2. Risk of graft failure after hematopoietic stem cell transplantation (Kaplan-Meier plots) for patients with a positive serum crossmatch (XM pos) and controls (XM neg). Study patients and controls were evaluated without further stratification (top) and after stratification for early (ear) and advanced (adv) disease stage (bottom). Patients not surviving day 28 posttransplant were censured. For statistical analysis, log-rank test was performed.

Cross-match
numero di mismatch

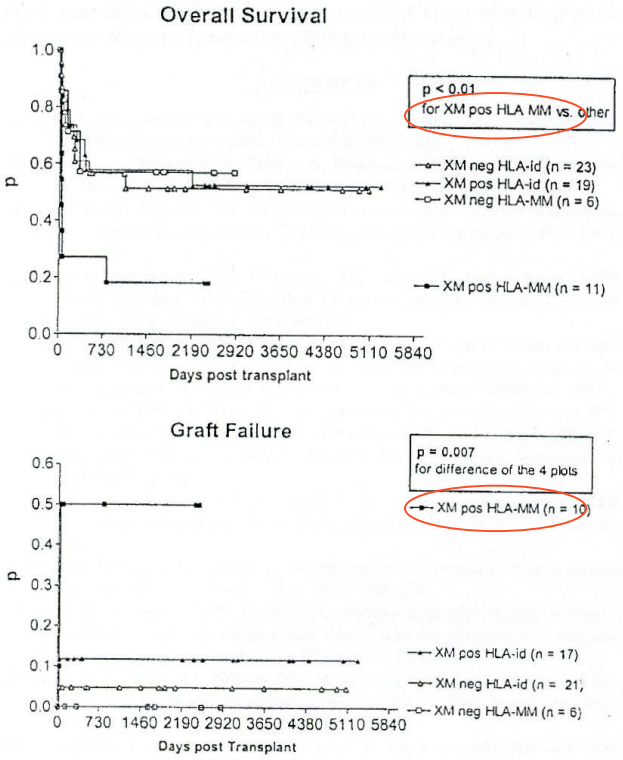


FIGURE 3. Kaplan-Meier plots for overall survival (top) and graft failure (bottom) in patients with a positive (XM pos) and a negative (XM neg) serum crossmatch transplanted with blood stem cells from HLA-identical (HLA-id) and HLA-mismatched (HLA-MM) donors. Patients with early death (not surviving day 27 posttransplant) were censured for graft failure analysis.

Ottinger et al. Transplantation 2002

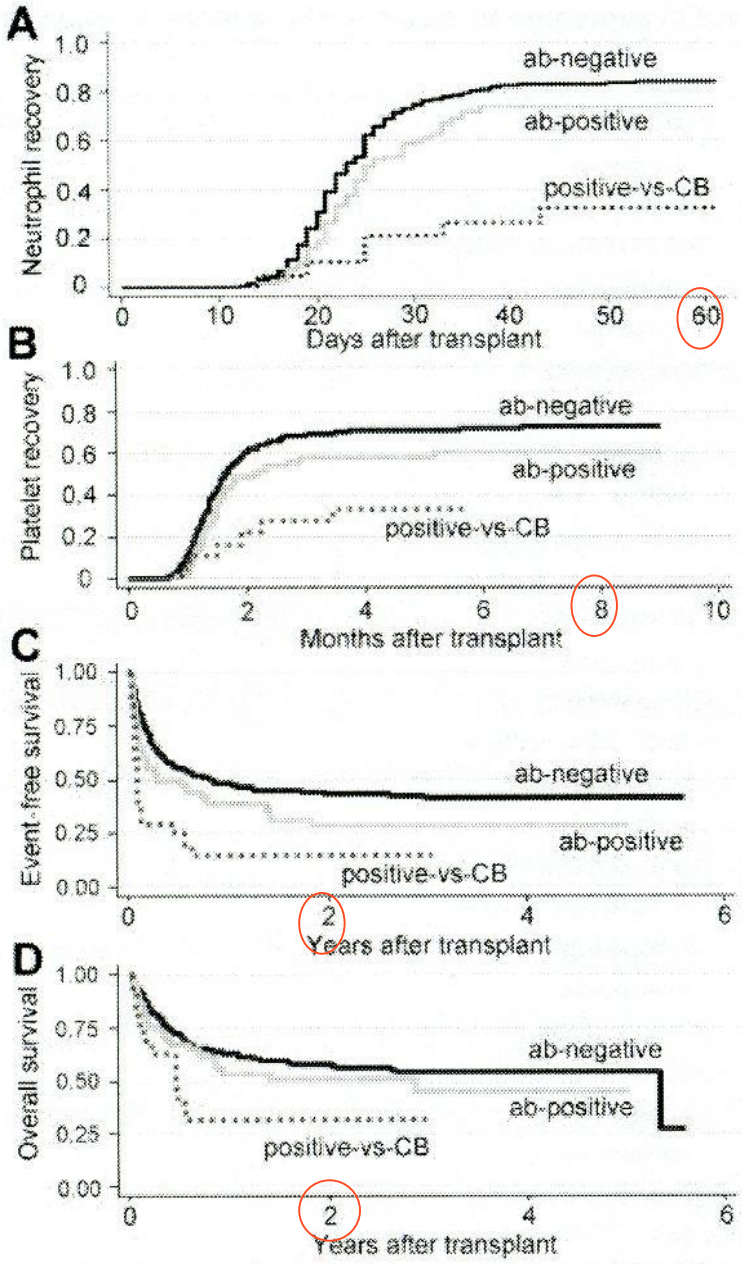
The impact of anti-HLA antibodies on unrelated cord blood transplantations

Minoko Takanashi,[1] Yoshiko Atsuta,[2] Koki Fujiwara,[1] Hideki Kodo,[3] Shunro Kai,[4] Hiroyuki Sato,[5] Masatoshi Kohsaki,[6] Hiroshi Azuma,[7] Hidenori Tanaka,[1] Atsuko Ogawa,[1] Kazunori Nakajima,[1] and Shunichi Kato[8]

[1]Japanese Red Cross Tokyo Blood Center, Tokyo, Japan; [2]Department of HSCT Data Management, Nagoya University School of Medicine, Nagoya, Japan; [3]Tokyo Cord Blood Bank, Tokyo, Japan; [4]Department of Transfusion Medicine, Hyogo College of Medicine, Nishinomiya, Japan; [5]Japanese Red Cross Fukuoka Blood Center, Fukuoka, Japan; [6]Japanese Red Cross Osaka North Blood Center, Osaka, Japan; [7]Japanese Red Cross Hokkaido Blood Center, Sapporo, Japan; and [8]Department of Cell Transplantation & Regenerative Medicine, Tokai University School of Medicine, Isehara, Japan

Blood, 2010

- 386 casi studiati
  - 89 positivi per anticorpi anti-HLA (23,1%)
    - 69 positivi per anticorpi NON diretti verso il Cordone
      - 45 casi positivi per anticorpi anti HLA Classe I
      - 10 casi positivi per anticorpi anti HLA Classe II
      - 14 casi positivi per anticorpi anti HLA Classe I e II
    - 20 positivi per anticorpi diretti verso il Cordone
      - 15 casi positivi per anticorpi anti HLA Classe I
      - 5 casi positivi per anticorpi anti HLA Classe II



Ab-neg vs Ab-pos p=.024

Ab-pos vs pos-CB p=.005

Ab-neg vs Ab-pos p=.05

Ab-pos vs pos-CB p=.062

Ab-neg vs Ab-pos p=.037

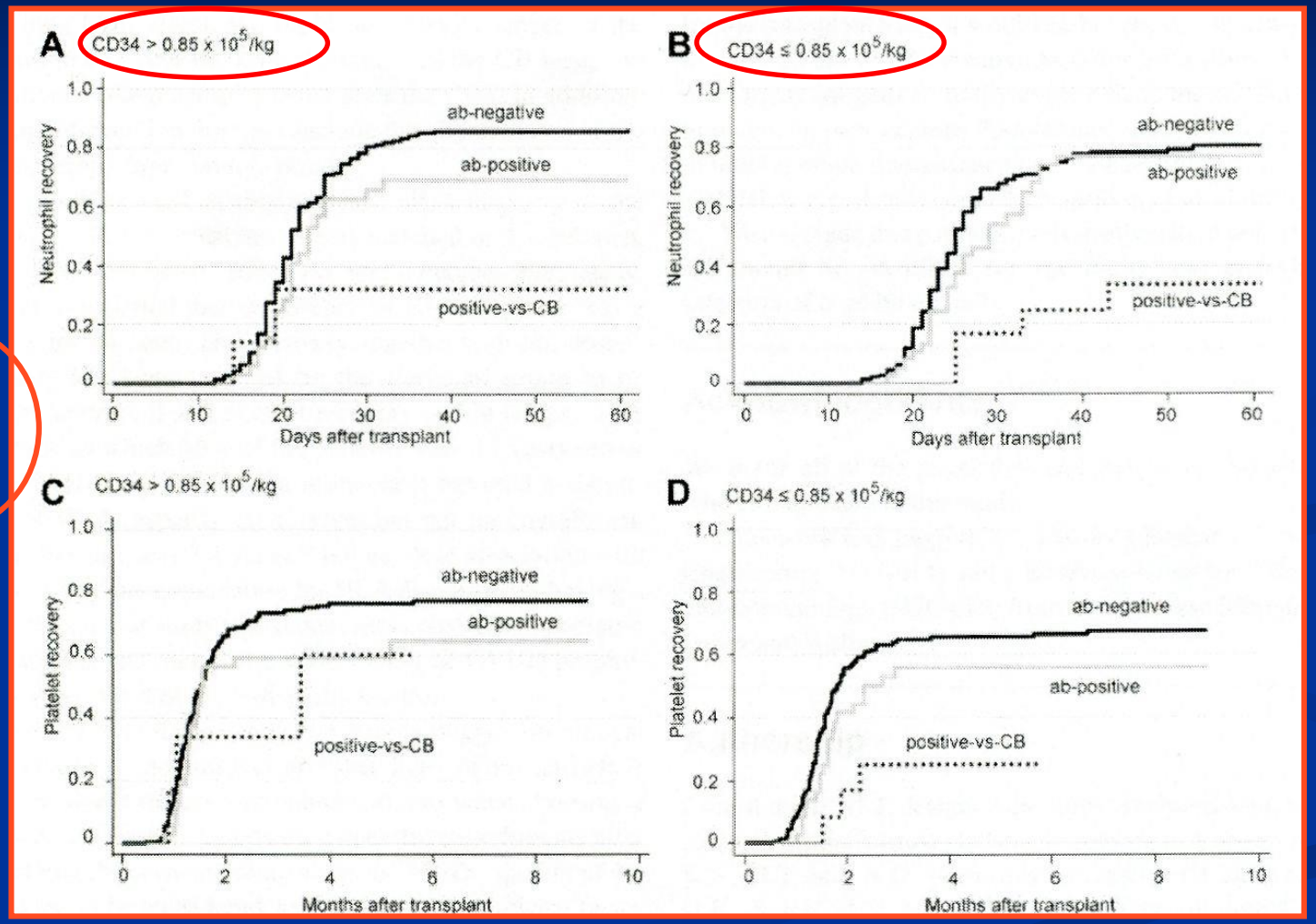
Ab-pos vs pos-CB p=.016

Ab-neg vs Ab-pos p=.25

Ab-pos vs pos-CB p=.13

Takanashi et al. Blood 2010

Dose CD34+ e anticorpi anti-HLA



A-C
p=n.s

p=.0061

p=.020

Takanashi et al. Blood 2010

Risk and prevention of graft failure in patients with preexisting donor-specific HLA antibodies undergoing unmanipulated haploidentical SCT

S Yoshihara[1], E Maruya[2], K Taniguchi[1], K Kaida[1], R Kato[1], T Inoue[1], T Fujioka[1], H Tamaki[3], K Ikegame[1], M Okada[1], T Soma[1], K Hayashi[2], N Fujii[2], T Onuma[2], Y Kusunoki[2], H Saji[2] and H Ogawa[1]

Bone Marrow Transplantation 2012

Studio prospettico: n 79 trapianti aploidentici

n. 63 pazienti HLA negativi

n. 5 pazienti HLA positivi non-DSA

n. 11 pazienti HLA positivi DSA

n. 5/11 pazienti GF

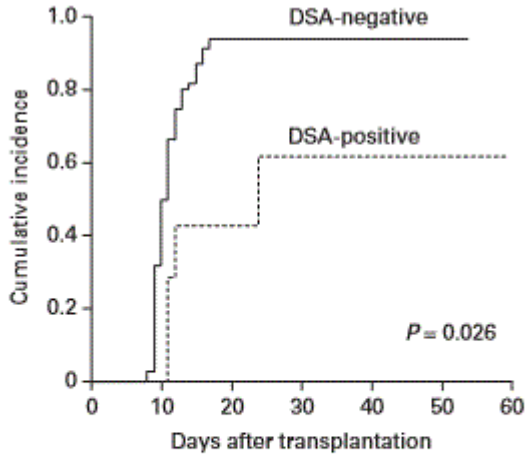


Figure 2 Pretransplant DSA and cumulative incidence of neutrophil engraftment. The cumulative incidences of donor neutrophil engraftment in pretransplant DSA-negative patients ($n = 72$, solid line) and DSA-positive patients ($n = 7$, dotted line). DSA-positive patients had a significantly lower incidence of neutrophil engraftment than DSA-negative patients (61.9 vs 94.4%, $P = 0.026$). Three of both DSA-positive and DSA-negative patients developed graft failure.

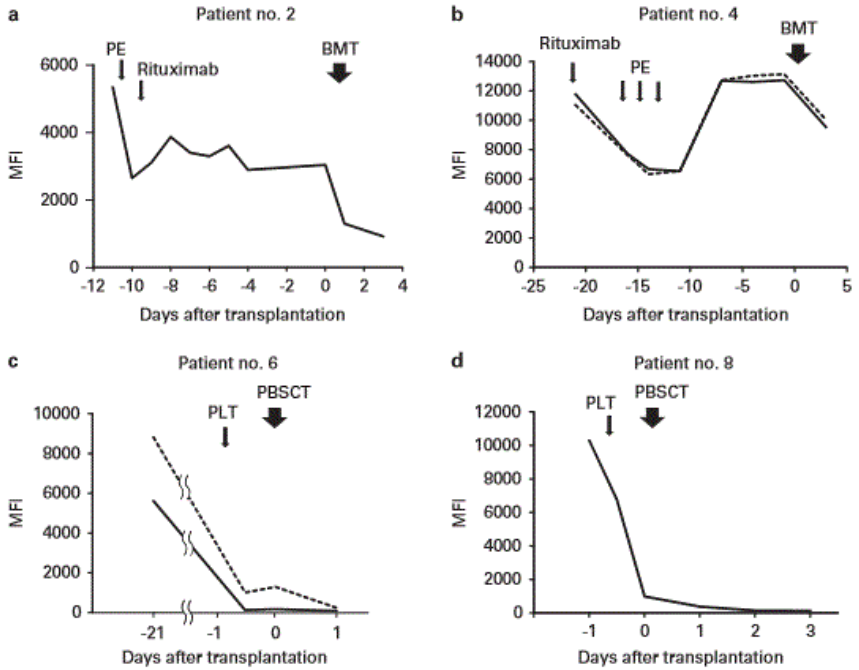
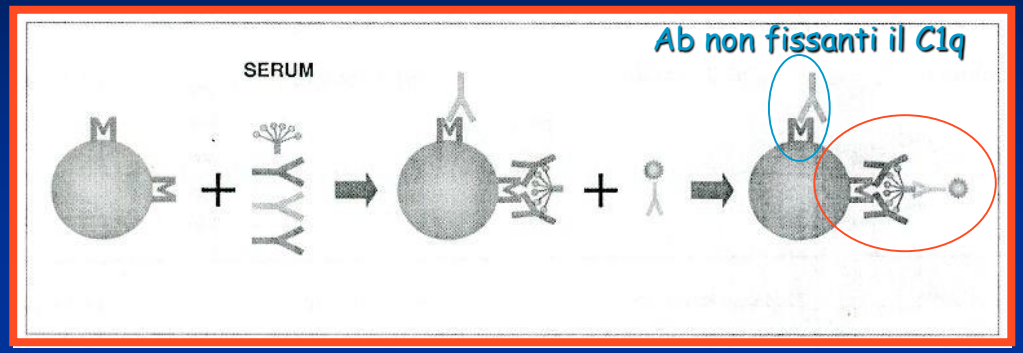
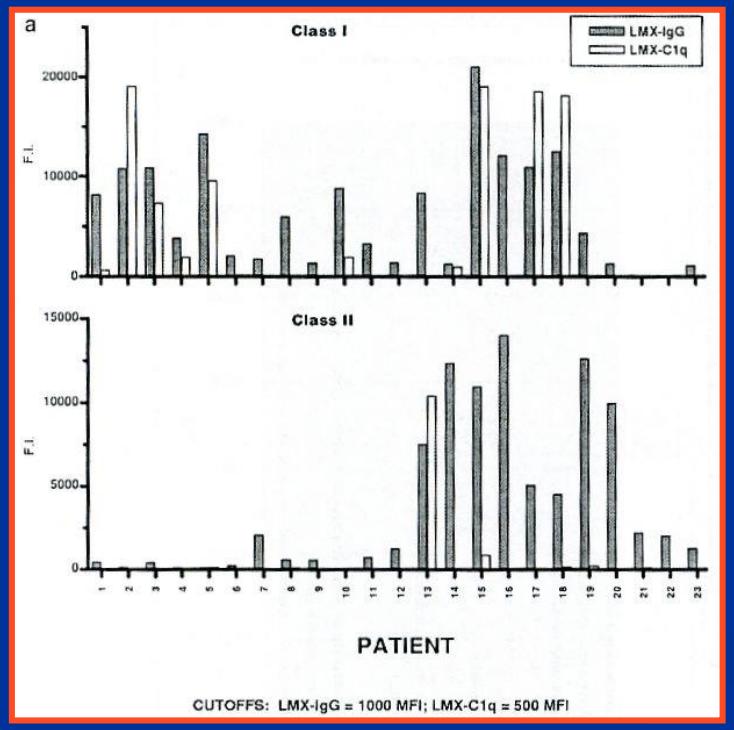


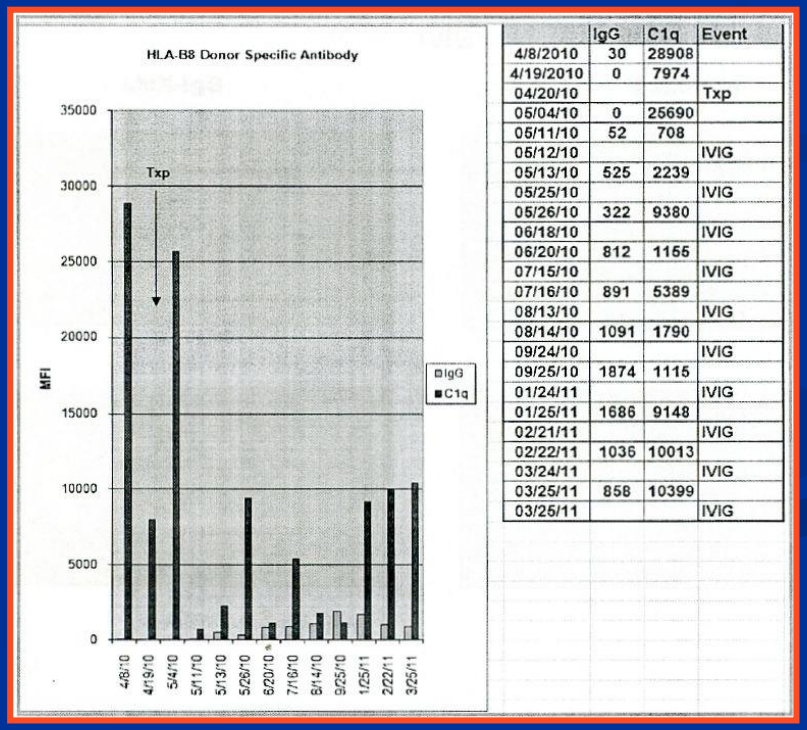
Figure 1 Effect of treatments for DSA. The kinetics of DSA levels in patients who received plasma exchange (PE) plus rituximab (**a**, **b**), and in patients who received platelet transfusion (PLT) from healthy-related donors having DSA-corresponding HLA antigens (**c**, **d**).

Anticorpi anti-HLA in Luminex: anticorpi fissanti il complemento

115 sieri: 22 uomini non trasfusi, 20 sieri positivi per anti-HLA, 6 EPT, 67 trapianti







	IgG	C1q	Event
4/8/2010	30	28908	
4/19/2010	0	7974	
04/20/10			Txp
05/04/10	0	25690	
05/11/10	52	708	
05/12/10			IVIG
05/13/10	525	2239	
05/25/10			IVIG
05/26/10	322	9380	
06/18/10			IVIG
06/20/10	812	1155	
07/15/10			IVIG
07/16/10	891	5389	
08/13/10			IVIG
08/14/10	1091	1790	
09/24/10			IVIG
09/25/10	1874	1115	
01/24/11			IVIG
01/25/11	1686	9148	
02/21/11			IVIG
02/22/11	1036	10013	
03/24/11			IVIG
03/25/11	858	10399	
03/25/11			IVIG

Chen at al. Human Immunology 2011

Complement-Binding Donor-Specific Anti-HLA Antibodies and Risk of Primary Graft Failure in Hematopoietic Stem Cell Transplantation

Stefan O. Ciurea[1,*], Peter F. Thall[2], Denái R. Milton[2], Titus H. Barnes[3], Piyanuch Kongtim[1], Yudith Carmazzi[3], Asdrúbal A. López[3], Dianne Y. Yap[3], Uday Popat[1], Gabriela Rondon[1], Benjamin Lichtiger[3], Fleur Aung[3], Vahid Afshar-Kharghan[4], Qing Ma[1], Marcelo Fernández-Viña[5], Richard E. Champlin[1], Kai Cao[3]

Biology of Blood and Marrow Transplantation 2015

Studio retrospettivo: 22/122 con DSA, MFI medio=6500

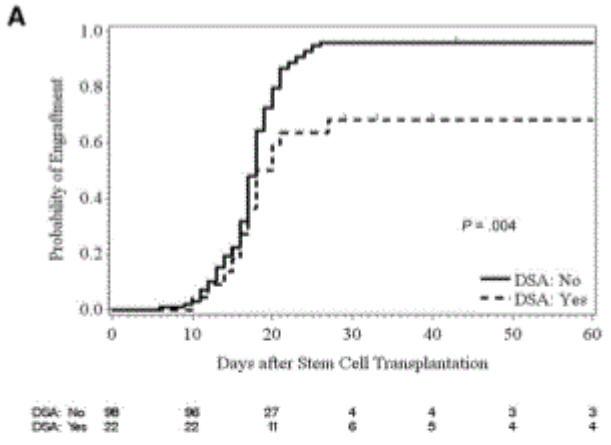


Figure 1. Probability of engraftment in patients by DSA status (A) and C1q status (B).

Desensibilizzazione pre-trapianto nei pazienti C1q+:

n.10 no trattamento ---- n.2/6 C1q+ Trapianto--GF

n.7 PEX/Rit/IVIG ----- n.3/5 C1q+ Trapianto--GF

n.5 PEX/Rit/IVIG + BC ----- n.0/2 C1q+ Trapianto

Table 2
Associations between GF, C1q Status, and Treatment

Covariate	GF		Fisher's Exact Test *P*
	Yes (n = 7)	No (n = 15)	
C1q at transplant, n (%)			.0003
Positive	5 (100)	0	
Negative	1 (6)	15 (94)	
Nonassessable	1	0	
DSA levels at transplant, n (%)			.0039
>5000	7 (64)	4 (36)	
≤5000	0	11 (100)	
Treatment, n (%)			.14
None	3 (30)	7 (70)	
Desensitization alone	4 (57)	3 (43)	
Desensitization with buffy coat	0	5 (100)	

GF indicates graft failure; DSA, donor-specific anti-HLA antibodies.

Il cross-match virtuale…

Clinical Relevance of Pretransplant Donor-Specific HLA Antibodies Detected by Single-Antigen Flow-Beads

Patrizia Amico,[1] Gideon Hönger,[1] Michael Mayr,[1] Jürg Steiger,[1] Helmut Hopfer,[2] and Stefan Schaub[1,3]

Transplantation 2009

334 trapianti di rene

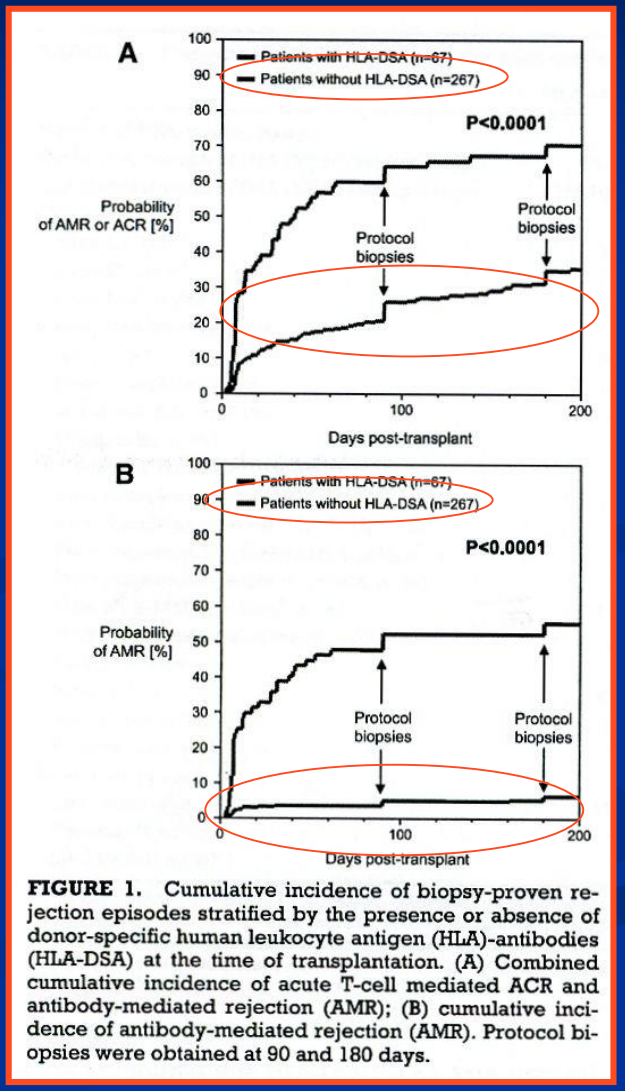


FIGURE 1. Cumulative incidence of biopsy-proven rejection episodes stratified by the presence or absence of donor-specific human leukocyte antigen (HLA)-antibodies (HLA-DSA) at the time of transplantation. (A) Combined cumulative incidence of acute T-cell mediated ACR and antibody-mediated rejection (AMR); (B) cumulative incidence of antibody-mediated rejection (AMR). Protocol biopsies were obtained at 90 and 180 days.

Cross-match virtuale e CSE da cordone

Prospective Monitoring for Alloimmunization in Cord Blood Transplantation: "Virtual Crossmatch" can be Used to Demonstrate Donor-Directed Antibodies

Jonathan A. Gutman,[1,2,4] Susan K. McKinney,[3] Shalini Pereira,[1,3] Sandra L. Warnock,[3] Anajane G. Smith,[1,3] Ann E. Woolfrey,[1,2] John A. Hansen,[1,2] and Colleen Delaney[1,2]

Transplantation 2009

46 pazienti studiati per lo screening anticorpale
4/46 (9%) pazienti con PRA+
Proposto algoritmo di selezione unità di SCO

Paziente n.1 anti-HLA B49: due unità di SCO B49 scartate, selezionato donatore 1 mm/locus B +26 attecchimento neutrofili

Paziente n.2 anti-HLA DR 1: selezionata una unità compatibile, +16 attecchimento neutrofili

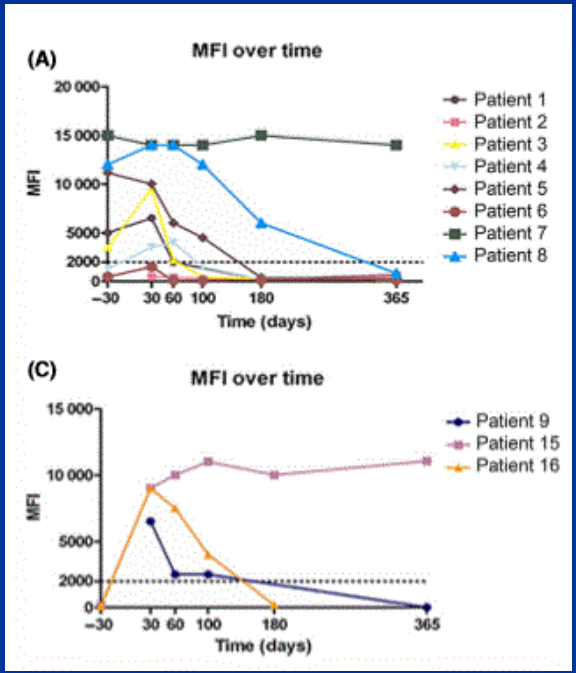
Paziente n.3 anti-DQ7: unità di SCO DQB1*0301, Xm in CDC-, Xm in CF±, Leucemia resistente, infezione, +12 decesso senza evidenza di attecchimento

Paziente n.4 anti-Bw6: nessuna alternativa a unità SCO Bw6+, +21 attecchimento

Persistenza degli anticorpi HLA e produzione de novo nel TMO a ridotta intensità di condizionamento

RM Fasano, Br J Haematol 2014,166,425-434

N. 16 pazienti
Ridotto regime di condizionamento



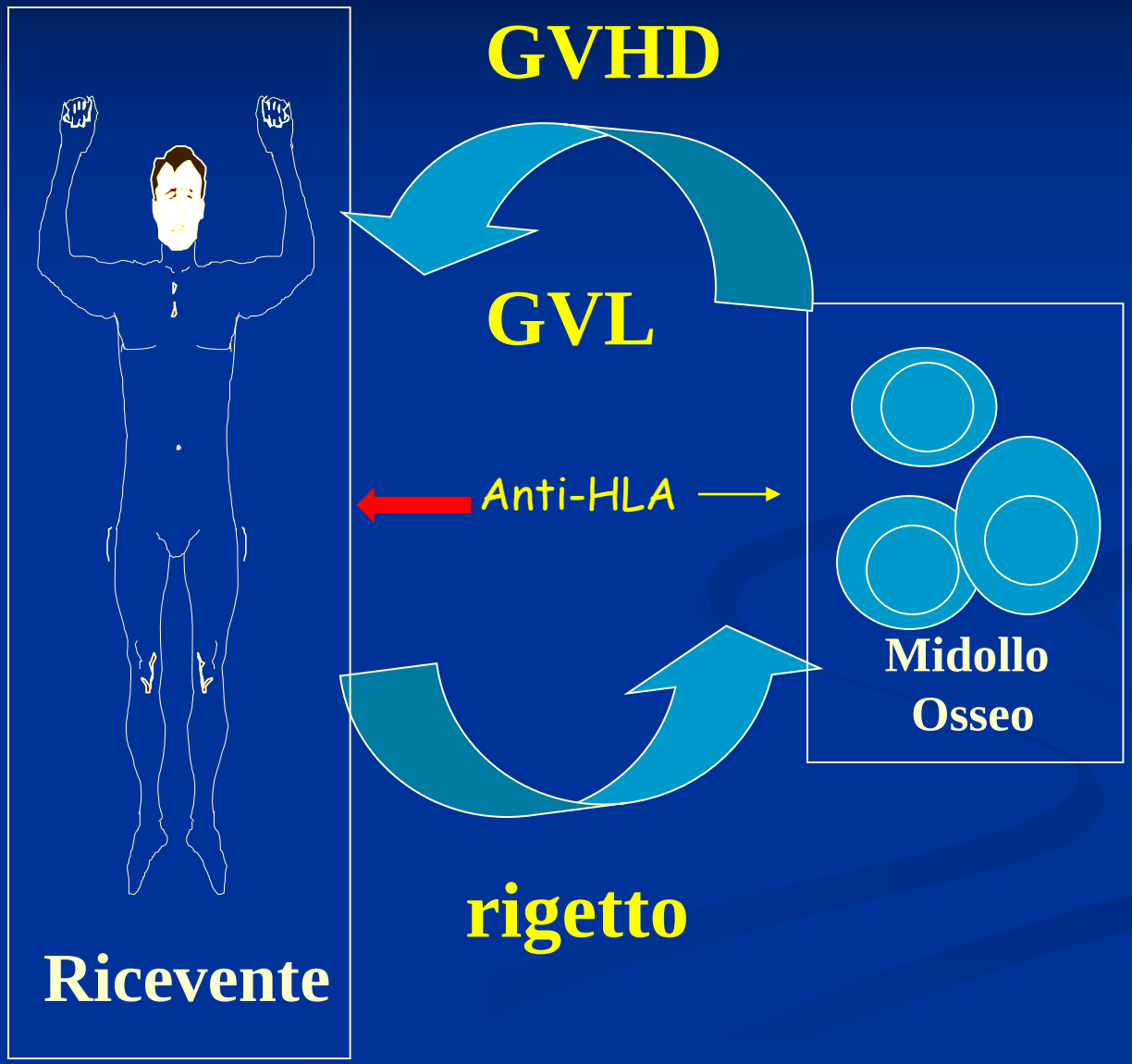
Valutazione dell'effetto degli anticorpi anti-HLA nel trapianto di CSE a ridotto regime di condizionamento.

Pazienti alloimmunizzati: la persistenza degli anticorpi per lungo tempo (>100 gg) era associata ad MFI > 10000.

Anticorpi de-novo post-trapianto: refrattarietà piastrinica e dimostrazione di anticorpi nei donatori

Cut-off utilizzati: Positività Labscreen MFI >500
Positività Single Antigen MFI >2000

Il trapianto di midollo osseo: doppia barriera immunologica



Donor Immunization Against Human Leukocyte Class II Antigens is a Risk Factor for Graft-versus-Host Disease

Florent Delbos[1], Walid Barhoumi[2], Ludovic Cabanne[2], Florence Beckerich[2], Christine Robin[2], Rabah Redjoul[2], Safae Astati[2], Andréa Toma[2], Cécile Pautas[2], Hélène Ansart-Pirenne[1], Catherine Cordonnier[2], Philippe Bierling[1,3], Sébastien Maury[2,3,4,*]

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Biology of Blood and Marrow Transplantation 2015

Table 2
Characteristics of D/R Pairs with Anti-HLA Class II RSAs Detected in the Donor

D/R Pair	Stem Cell Source	Donor Sex	Maximal NBG Ratio	Average NBG Ratio	RSA Specificity	MFI of RSA	GVHD	Outcome	Follow-Up, Mo
1	BM	Male	4	3.7	DPB1*11:01	650	No	Alive	28+
2	PB	Male	5	2.7	DPB1*01:01	1232	No	Dead	9
3	BM	Male	4	3.1	DPB1*01:01	1368	aGVHD grade II	Alive	3+
4	PB	Male	3	3.0	DPB1*03:01 DPB1*04:02	543 509	aGVHD grade IV	Dead	3
5	PB	Male	4	2.5	DPB1*03:01	914	aGVHD grade IV cGVHD	Dead	7
6	PB	Male	14	8.7	DPB1*03:01	1180	cGVHD	Alive	12+
7	BM	Female	188	134.3	DPB1*04:01	2809	aGVHD grade III cGVHD	Dead	12
8	BM	Female	6	5.4	DPB1*01:01 DPB1*04:01	1374 619	aGVHD grade II cGVHD	Alive	12+
9	PB	Female	130	69.7	DPB1*04:02	756	aGVHD grade II	Dead	2
10	BM	Female	6	5.7	DPB1*04:01	582	cGVHD	Alive	25+
11	PB	Female	26	19.4	DPB1*02:01	860	aGVHD grade IV	Dead	1
12	BM	Female	5	3.1	DPB1*03:01	562	aGVHD grade III	Dead	2
13	PB	Female	173	101.3	DRB3*02:02	580	aGVHD grade III	Dead	5

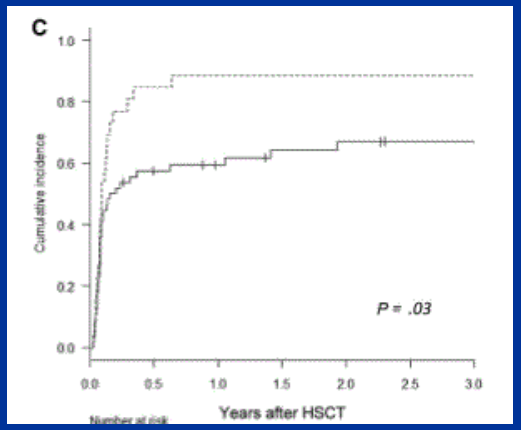
BM indicates bone marrow; PB, peripheral blood; aGVHD, acute GVHD; cGVHD, chronic GVHD.

RSA = Recipient Specific anti-HLA antibodies

n. 12 anti-DPB1
n. 1 anti-DRB3

MFI=509-2809

No studio C1q+



Primo episodio di aGVHD e cGVHD in relazione alla presenza di RSA

In conclusion, donor immunization against foreign HLA antigens is a new parameter to consider for predicting the risk of GVHD after HSCT from an HLA-mismatched unrelated donor, particularly a female donor. Several factors, including (1) the antigenic target of natural antibodies detected in male donors, (2) the potentially different impacts of anti-HLA immunization in male versus female donors, (3) the preferential association with chronic GVHD versus acute or late acute GVHD and level of immunization, (4) the determination of the opotimum threshold of immunization sensitively and specifically correlated to GVHD, and (5) the clinical significance of RSA versus non-RSA, need to be further characterized before this new parameter can be integrated for optimal donor selection.

On the role of HLA antibodies in hematopoietic stem cell transplantation

A. Brand[1,2], I. N. Doxiadis[2] & D. L. Roelen[2]

Tissue Antigens 2012

Table 3 (A) DSA and (non-)engraftment in adult BM or PBSC grafts. (B) DSA and (non-)engraftment in single and double umbilical cord blood transplantation

A

References	Donor/graft type	DSA test	*N* patients design	Conditioning	Rejection DSA-positive (%)	Rejection DSA-negative (%)
Mickelson et al. (34)	1–2MM related BM	AHG-CDC	522 retrospective DSA + $n=21$ DSA − $n=501$	MA	13/21 (62)	31/501 (6)
Spellman et al. (26)	UD BM	FlowPRA, Luminex SA	37 cases/78 controls DSA + $n=10$ DSA − $n=95$	MA 98%	9/10 (90)	28/105 (21)
Ciurea et al. (27)	Haplo T depleted PBSC	Luminex SA, MFI > 500	24 consecutive patients, DSA + $n=5$	RIC	3/5 (60)	1/19 (5)
Ciurea et al. (31)	UD; BM and PBSC	Luminex SA, MFI >500–>7000	592 patients, DSA anti-DPB1 $n=8$	MA and RIC	3/8 (38)	16/584 (3)
Yoshihara et al. (29)	Haplo-id ;61 PBSC 18 BM	Luminex SA, MFI > 500	79 patients DSA + $n=11$	MA 22 RIC 57	3/11 (27)	3/68 (4)
Total					31/55 (56.3)	51/1172[a] (4)

On the role of HLA antibodies in hematopoietic stem cell transplantation

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Tissue Antigens 2012

B

References	Single/ Double UCB	DSA test	*N* patients	Conditioning	Rejection DSA-positive (%)	Rejection DSA-negative (%)
Takanashi et al. (28)	Primary S-UCB	FlowPRA Luminex SA, MFI > 1000	386 patients DSA + *n* = 20 DSA − *n* = 366	MA and RIC	12/20 (60)	62/366 (17)
Uchiyama and Ikeda (35)	S-UCB *n* = 1	CDC-XM	*n* = 1	MA	0/1	
Brunstein et al. (30)	D-UCB	Luminex SA, MFI > 500	126 patients DSA + *n* = 18 DSA − *n* = 108	RIC	4/18 (17)	24/108 (22)
Cutler et al. (36)	D-UCB	Luminex SA, MFI > 1000	73 patients DSA + 1 UCB *n* = 11 DSA + 2 UCB *n* = 7	RIC 75%	6/18 (30) 1 UCB 2/11 2 UCB 4/7	3/55 (5.5)
Ruggeri et al. (33)	S-UCB 40%, D-UCB 60%	Luminex MFI 1620–17629	206 patients DSA + *n* = 16	RIC	9/16 (56)	41/190 (22)
Total					31/72 (43)	130/629 (21)

Anti-HLA non DSA pre-trapianto di CSE

- Eurocord: trapianto singolo o doppio di CSE cordonali. 32 riceventi con anti-HLA non DSA vs 158 pz senza anticorpi: nessuna differenza nel recupero dei granulociti neutrofili

- Detrait et al.: Trapianto di CSE correlato e non correlato. 24 pz anti-HLA non DSA vs 83 pz senza anticorpi: nessuna differenza nell'attechimento.

- Takanashi et al.: trapianto singolo o doppio di CSE cordonali. 35 riceventi con anti-HLA non DSA vs 250 pz senza anticorpi: > 90% attecchimento CSE cordonali

Anti-HLA non DSA: non influenzano l'attecchimento

Punti aperti.....

Definire il cut-off degli anticorpi anti-HLA nel TMO di CSE

Definire le specificità HLA a maggior rischio

Quando studiarli

Anticorpi de-novo, significato clinico

E' importante approfondire le proprietà biologiche dell'anticorpo

Studiare gli anticorpi nel paziente e/o anche nel donatore

Cross-match virtuale

Come e quando desensibilizzare un paziente

Come affrontiamo a Bologna gli anti-HLA nel trapianto di CSE

Summer School AIBT
Pesaro 9-11giugno 2016

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