Focus su anticorpi anti HLA e impatto sull'outcome post-trapianto

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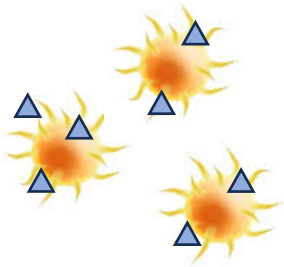
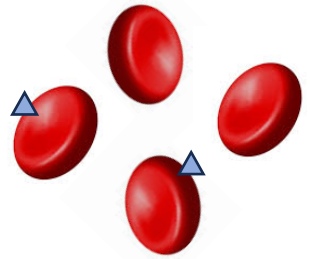
SIMT - Fondazione IRCCS Policlinico S. Matteo
Pavia

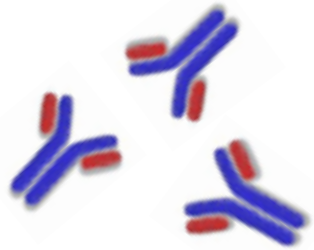
Roma, 8 maggio 2026

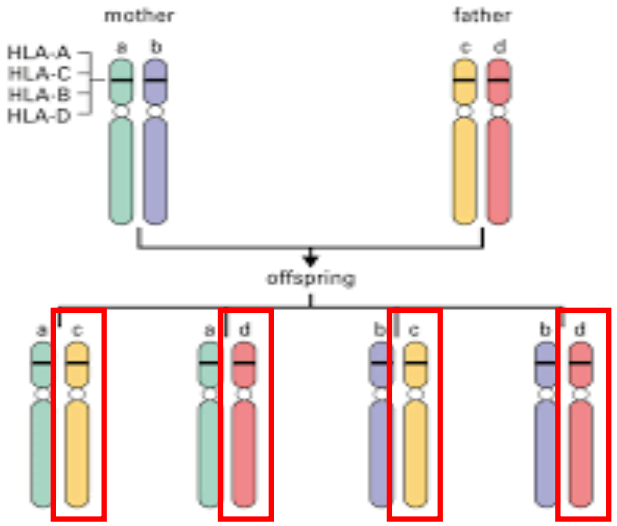
Assenza di conflitti di interesse

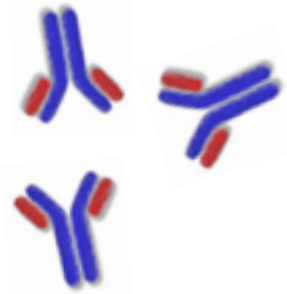
- Trasfusioni
- Trapianto
- Gravidanze

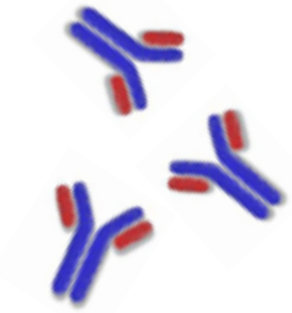












"Natural" Human Leukocyte Antigen Antibodies Found in Nonalloimmunized Healthy Males

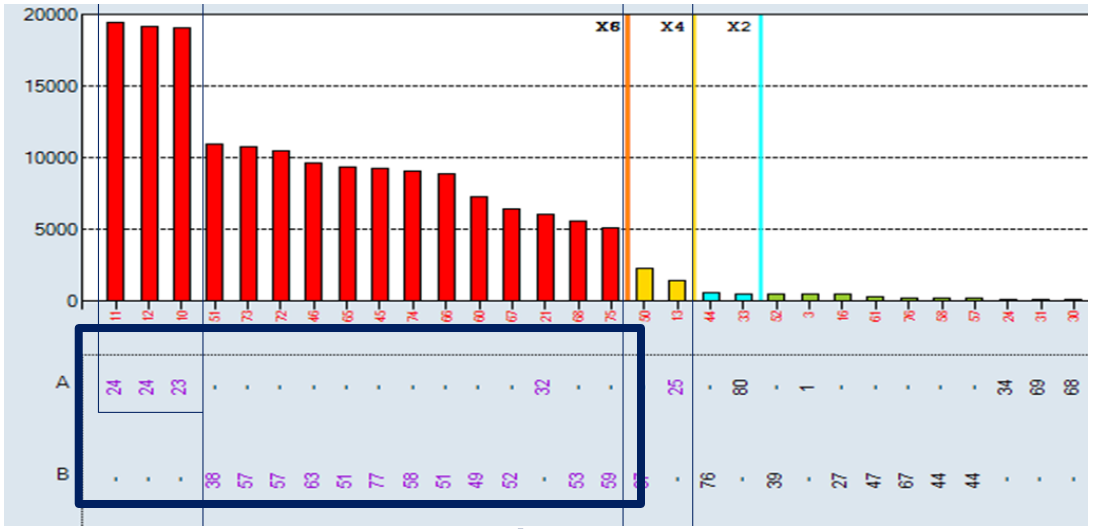
Luis E. Morales-Buenrostro,[1,2] Paul I. Terasaki,[2,5] Lluvia A. Marino-Vázquez,[1] Jar-How Lee,[3] Nadim El-Awar,[3] and Josefina Alberú[4]

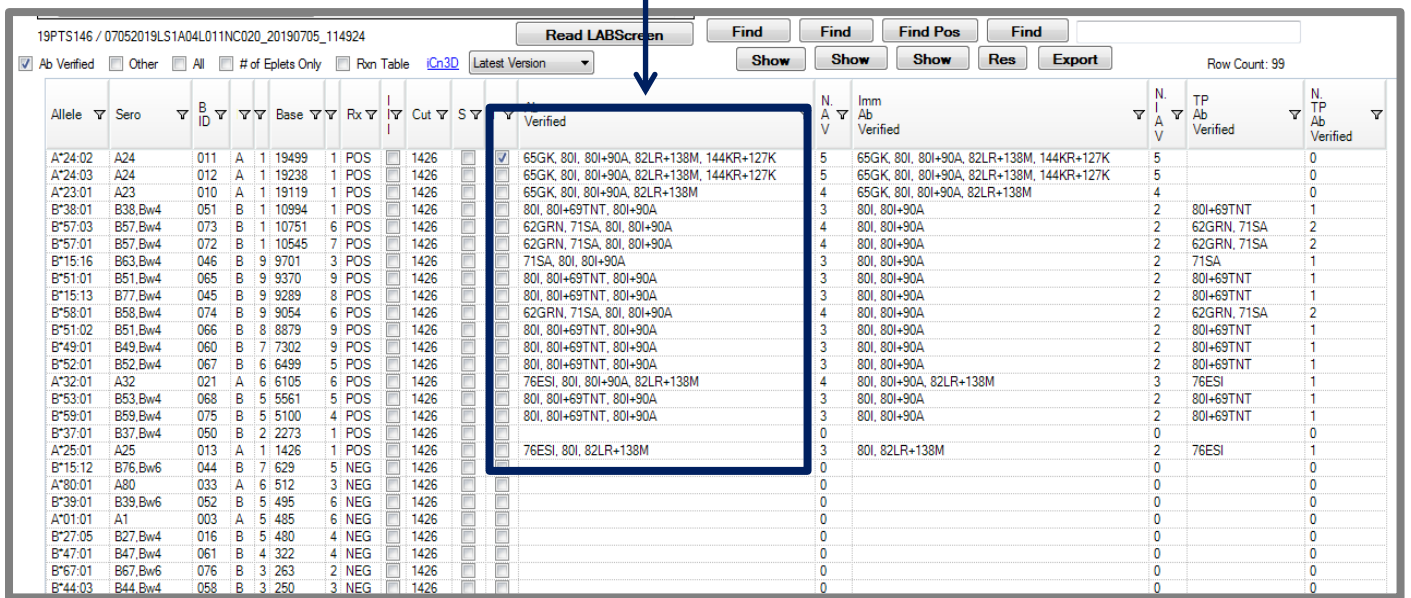
Conclusions. Normal males were found to have HLA antibodies to infrequent HLA specificities. It is likely that these HLA antibodies are produced to cross-reactive epitopes found in microorganisms, ingested proteins and allergens—making them natural antibodies.

Morales-Buenrostro LE et al., Transplantation 2008

Solid Phase (BEAD) Antibody Testing

Meet Luminex





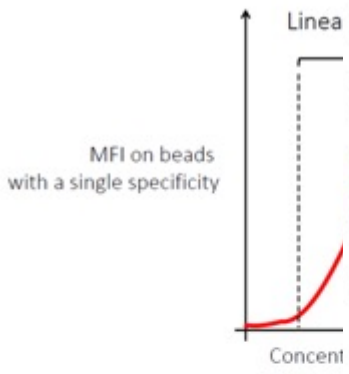
Allele	Sero	B ID			Base		Rx	I I	Cut	S		Verified	N. A V	Imm Ab Verified	N. I A V	TP Ab Verified	N. TP Ab Verified
A*24:02	A24	011	A	1	19499	1	POS		1426		☑	65GK, 80I, 80I+90A, 82LR+138M, 144KR+127K	5	65GK, 80I, 80I+90A, 82LR+138M, 144KR+127K	5		0
A*24:03	A24	012	A	1	19238	1	POS		1426			65GK, 80I, 80I+90A, 82LR+138M, 144KR+127K	5	65GK, 80I, 80I+90A, 82LR+138M, 144KR+127K	5		0
A*23:01	A23	010	A	1	19119	1	POS		1426			65GK, 80I, 80I+90A, 82LR+138M	4	65GK, 80I, 80I+90A, 82LR+138M	4		0
B*38:01	B38,Bw4	051	B	1	10994	1	POS		1426			80I, 80I+69TNT, 80I+90A	3	80I, 80I+90A	2	80I+69TNT	1
B*57:03	B57,Bw4	073	B	1	10751	6	POS		1426			62GRN, 71SA, 80I, 80I+90A	4	80I, 80I+90A	2	62GRN, 71SA	2
B*57:01	B57,Bw4	072	B	1	10545	7	POS		1426			62GRN, 71SA, 80I, 80I+90A	4	80I, 80I+90A	2	62GRN, 71SA	2
B*15:16	B63,Bw4	046	B	9	9701	3	POS		1426			71SA, 80I, 80I+90A	3	80I, 80I+90A	2	71SA	1
B*51:01	B51,Bw4	065	B	9	9370	9	POS		1426			80I, 80I+69TNT, 80I+90A	3	80I, 80I+90A	2	80I+69TNT	1
B*15:13	B77,Bw4	045	B	9	9289	8	POS		1426			80I, 80I+69TNT, 80I+90A	3	80I, 80I+90A	2	80I+69TNT	1
B*58:01	B58,Bw4	074	B	9	9054	6	POS		1426			62GRN, 71SA, 80I, 80I+90A	4	80I, 80I+90A	2	62GRN, 71SA	2
B*51:02	B51,Bw4	066	B	8	8879	9	POS		1426			80I, 80I+69TNT, 80I+90A	3	80I, 80I+90A	2	80I+69TNT	1
B*49:01	B49,Bw4	060	B	7	7302	9	POS		1426			80I, 80I+69TNT, 80I+90A	3	80I, 80I+90A	2	80I+69TNT	1
B*52:01	B52,Bw4	067	B	6	6499	5	POS		1426			80I, 80I+69TNT, 80I+90A	3	80I, 80I+90A	2	80I+69TNT	1
A*32:01	A32	021	A	6	6105	6	POS		1426			76ESI, 80I, 80I+90A, 82LR+138M	4	80I, 80I+90A, 82LR+138M	3	76ESI	1
B*53:01	B53,Bw4	068	B	5	5561	5	POS		1426			80I, 80I+69TNT, 80I+90A	3	80I, 80I+90A	2	80I+69TNT	1
B*59:01	B59,Bw4	075	B	5	5100	4	POS		1426			80I, 80I+69TNT, 80I+90A	3	80I, 80I+90A	2	80I+69TNT	1
B*37:01	B37,Bw4	050	B	2	2273	1	POS		1426				0		0		0
A*25:01	A25	013	A	1	1426	1	POS		1426			76ESI, 80I, 82LR+138M	3	80I, 82LR+138M	2	76ESI	1
B*15:12	B76,Bw6	044	B	7	629	5	NEG		1426				0		0		0
A*80:01	A80	033	A	6	512	3	NEG		1426				0		0		0
B*39:01	B39,Bw6	052	B	5	495	6	NEG		1426				0		0		0
A*01:01	A1	003	A	5	485	6	NEG		1426				0		0		0
B*27:05	B27,Bw4	016	B	5	480	4	NEG		1426				0		0		0
B*47:01	B47,Bw4	061	B	4	322	4	NEG		1426				0		0		0
B*67:01	B67,Bw6	076	B	3	263	2	NEG		1426				0		0		0
B*44:03	B44,Bw4	058	B	3	250	3	NEG		1426				0		0		0

IN-VITRO ANTIGENIC ANALYSIS

↓

IN-SILICO EPITOPE ANALYSIS

Courtesy of G. Rombolà



Contents lists available at ScienceDirect

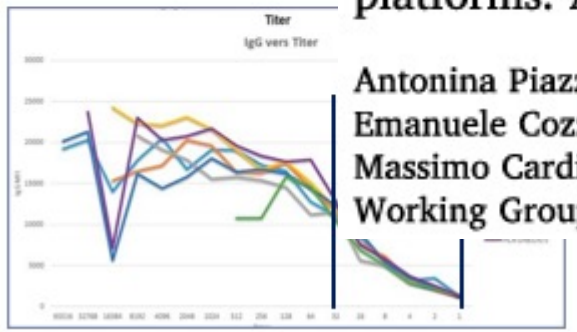
Human Immunology

journal homepage: www.elsevier.com/locate/humimm

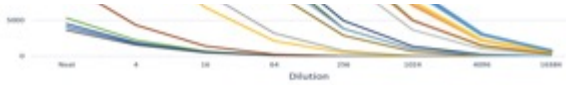
Research article

A comprehensive comparative assessment of mean fluorescence intensity of luminex single antigen bead tests between laboratories and commercial platforms: A report from the Italian Histocompatibility Network

Antonina Piazza [a], Giovanni Rombolà [b,*], Umberto Maggiore [c], Dario Ciappi [d], Emanuele Cozzi [e], Maria Chiara de Stefano [f], Roberto Crocchiolo [g], Andrea Ricci [f], Massimo Cardillo [h], Valeria Miotti [i], Giuseppe Feltrin [f], Franco Papola [j], on behalf of AIBT Working Group



Tambur, Transplantation 2018

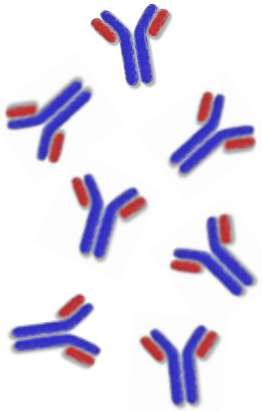


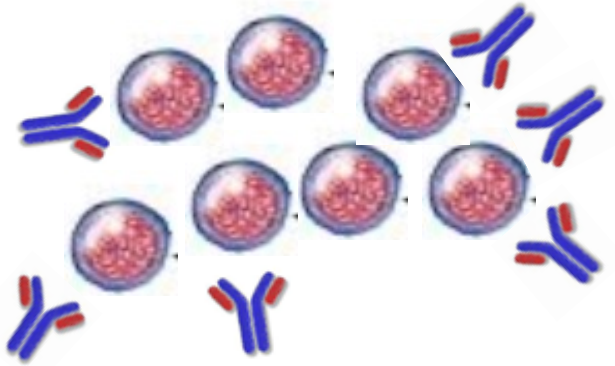
Tambur, HLA 2022

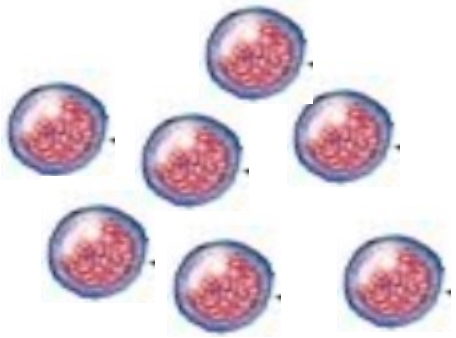
NON LINEAR CORRELATION ACROSS ALL MFI VALUES

Courtesy of G. Rombolà

DSA: 1 - 18%



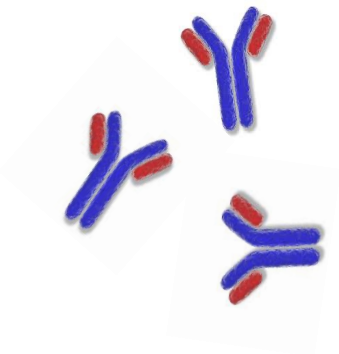




non-DSA: 16 - 55%

DSA → fattore prognostico riconosciuto ed indipendente

non-DSA → perché potrebbero interessare:



- **la maggior parte dei pazienti è politrasfusa**
- **donne multipare**
- **cambio di donatore se DSA**
- **refrattarietà piastrinica immuno-mediata**

ELSEVIER
Transplantation and Cellular Therapy
Volume 30, Issue 12, December 2024, Pages 1139-1154

Guideline

ASTCT Consensus Recommendations on Testing and Treatment of Patients with Donor-specific Anti-HLA Antibodies

Piyanuch Kongtim [1], Pongthep Vittayawacharin [1], Jun Zou [2], Samer Srour [3], Brian Shaffer [4], Roman M. Shapiro [5], Ankur Varma [6], Joseph McGuirk [7], Bhagirathbhai R. Dholaria [8], Shannon R. McCurdy [9], Amy E. DeZern [10], Nelli Bejanyan [11], Asad Bashey [12], Sabine Furst [13], Luca Castagna [14], Jacopo Mariotti [15], Annalisa Ruggeri [16], Rebeca Bailen [17], Takanori Teshima [18], Huang Xiao-Jun [19]...Stefan O. Ciurea [1] *

non-DSA

"Until new evidence emerges, pre-transplant desensitization is not recommended for recipients with non-donor specific anti-HLA antibodies and non-HLA antibodies (Grade of recommendation: C, Levels of evidence 2)"

Non-DSA: letteratura

Reference	N.	Tx	Outcome	Comments	
Takanashi 2008	41(8) on 250	CBT	No impact on ENG.		N
Takanashi 2010	89(20) on 386	CBT	73% vs. 83% ENG.		Y
Ciurea 2011	116(20) on 592	MUD, mMUD	94% vs. 97.5% ENG.	p=0.07	Y
Detrait 2012	24 on 107	HLA-id sib, MUD, mMUD	HR for OS = 2.04	DSA?	Y
Zhu 2014	28 on 51	All	78.6 vs. 100% OS	Pediatric, AA; DSA?	Y
Andolina 2020	45(1) on 157	HLA-id sib, MUD, mMUD	No difference in OS		N
Wei 2024	111 on 402	HLA-id sib	HR for ENG. = 1.42	HR for 6m-OS =2.32 (only F)	Y
Milano 2024	15(5) on 64	Haplo, mMUD	mOS 21 vs.61months	No specific death cause found	Y
Hagino 2025	137(8) on 3,657	HLA-mismatched related	60% vs. 65% PLT ENG.	p=0.047	Y
La Rocca 2025	68(23) on 804	HLA-mismatched related and unrelated	HR for OS = 2.37	DSA?	Y

HEMATOPOIETIC STEM CELL TRANSPLANTATION AND CORD BLOOD BANKING

Original article

Donor-specific anti-HLA antibodies (DSAs) in patients undergoing allogeneic hematopoietic stem cell transplantation from mismatched donors on behalf of GITMO and AIBT

GITMO AIBT

n=1330 identified

Cox multivariate			
Negative Positive- class II	0.74	0.32, 1.70	0.48
Positive – both classes	2.37	1.28, 4.41	0.006
Postive- class I	1.41	0.84, 2.34	0.19
Age at HSCT	1.01	1.00, 1.03	0.020
Full donor engraftment within 28 days after HSCT	0.62	0.43, 0.89	0.010
Early graft loss	2.99	1.42, 6.26	0.004

Multivariate analysis revealed that concomitant positivity of both classes of anti-HLA Abs was a risk factor affecting OS (p=0.006). We cannot explain this finding, but we can speculate that this patient population represents a cohort with a complex immunological status, beyond DSAs, requiring a dedicated strategy of transfusion support and desensitization. However, further studies are needed to analyze these aspects.

n=804 evaluable
26 TC

Courtesy of U. La Rocca

Sistema Socio Sanitario
Ospedale Niguarda
Regione Lombardia

Davide Chizzoniti, MD

Adela Sulejmani, MD PhD

PROTOCOLLO

STUDIO RETROSPETTIVO OSSERVAZIONALE

Titolo dello Studio: Link between non donor-specific anti-HLA Antibodies and Inferior Key outcomes after Allogeneic stem cell transplantation (**The "LAIKA" study**)

•Davide Chizzoniti[1 2], Sabrina Giammarco[3], Barbara Sarina[2], Davide Bernasconi[4 5], Lorenzo Dal Castello[6], Adela Sulejmani[7], Giuliana Lando[7], Giovanni Grillo[7], Stefania Bramanti[2], Elena Longhi[8], Filippo Frioni[9], Luisa Giaccone[10], Silvia Deaglio[10], Cristiana Caorsi[10], Salvatore Leotta[11], Valentina Capuzzo[12], Giovanni Rombolà[13], Patrizia Chiusolo[14], Roberto Crocchiolo[7]

EBMT

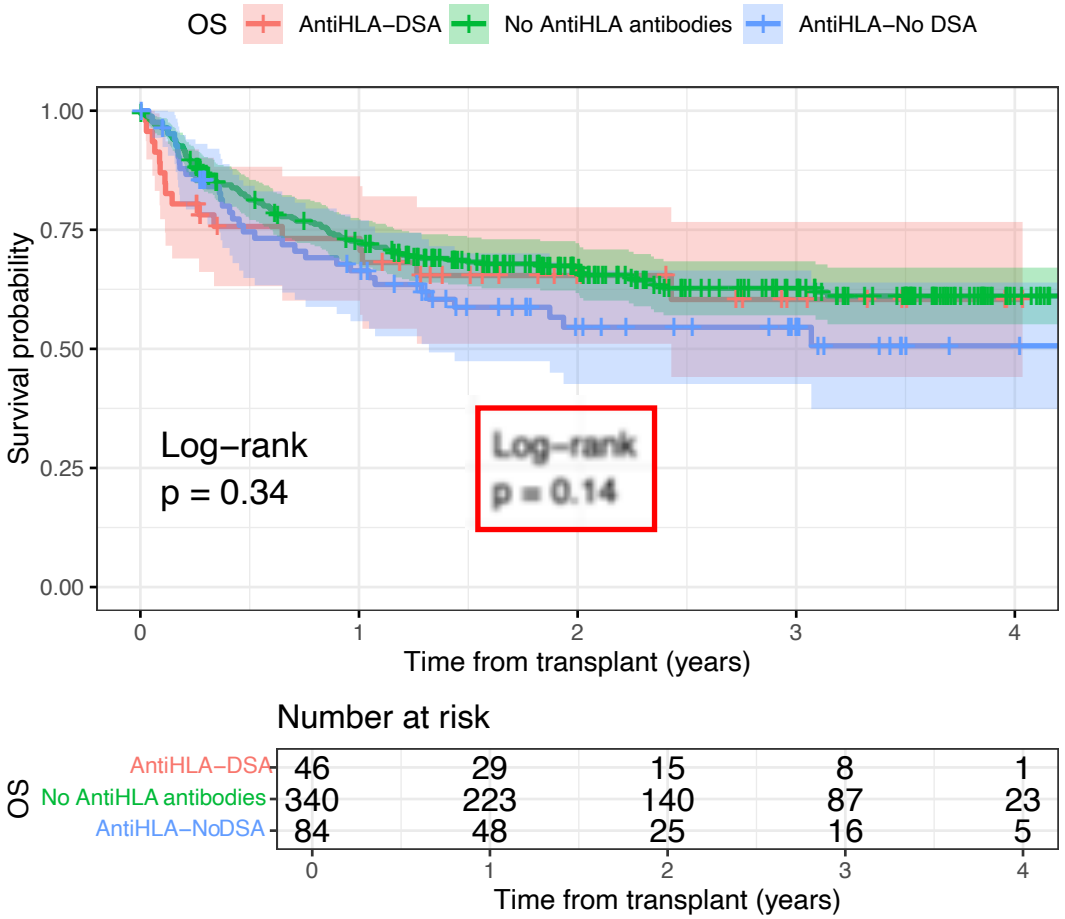
The LAIKA study

Characteristic	Overall N = 425[1]	No anti-HLA antibodies N = 341[1]	No DSA N = 84[1]	Difference[2]	95% CI[2,3]	p-value[4]
Age	54 (14), 58 (46-65), 19, 75	54 (14), 58 (46-65), 19, 75	53 (14), 57 (45-64), 22, 74	0.02	-0.22, 0.25	0.7
Sex				0.51	0.27, 0.75	<0.001
Female	226 (53%)	165 (48%)	61 (73%)			
Male	199 (47%)	176 (52%)	23 (27%)			
Pregnancy and/or Abortion				0.29	0.05, 0.53	0.015
No	371 (88%)	304 (90%)	67 (80%)			
Yes	51 (12%)	34 (10%)	17 (20%)			
Unknown	3	3	0			
Blood type incompatibility				0.32	0.08, 0.56	0.041
No	191 (45%)	143 (42%)	48 (57%)			
Minor	72 (17%)	63 (19%)	9 (11%)			
Major/Bidirectional	158 (38%)	131 (39%)	27 (32%)			
Unknown	4	4	0			

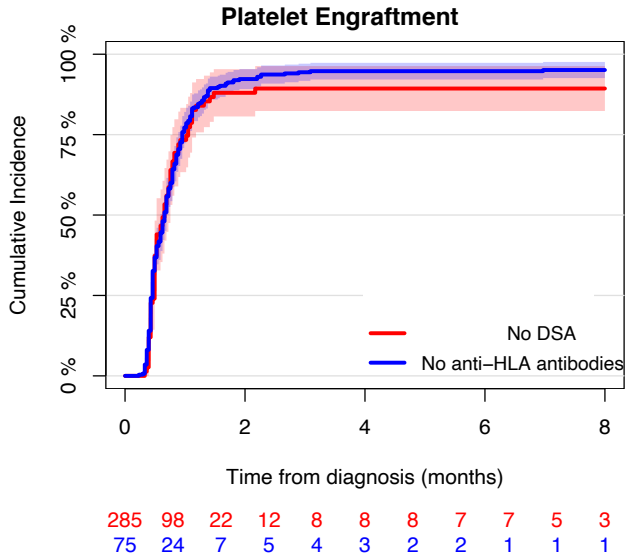
Characteristic	Overall N = 425[1]	No anti-HLA antibodies N = 341[1]	No DSA N = 84[1]	Difference[2]	95% CI[2,3]	p-value[4]
Platelet refractoriness				0.47	0.22, 0.71	<0.001
No	396 (95%)	327 (97%)	69 (84%)			
Si	22 (5.3%)	9 (2.7%)	13 (16%)			
Unknown	7	5	2			
RBCs transfused before transplant				0.19	-0.05, 0.43	0.3
< 10	190 (45%)	154 (45%)	36 (43%)			
> 20	138 (33%)	105 (31%)	33 (39%)			
10-20	95 (22%)	80 (24%)	15 (18%)			
Unknown	2	2	0			
PLTs transfused before transplant				0.29	0.05, 0.53	0.057
< 10	209 (50%)	175 (52%)	34 (40%)			
>20	117 (28%)	85 (25%)	32 (38%)			
10-20	96 (23%)	78 (23%)	18 (21%)			
Unknown	3	3	0			

Unpublished data

The LAIKA study



	S(t)	low	up
DSA	65.4%	51.1%	79.7%
No AntiHLA	67.0%	61.7%	72.2%
No DSA	54.5%	42.6%	66.4%



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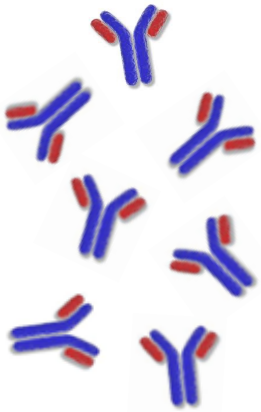
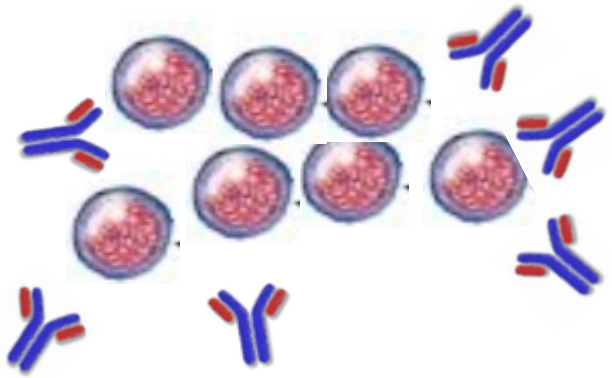
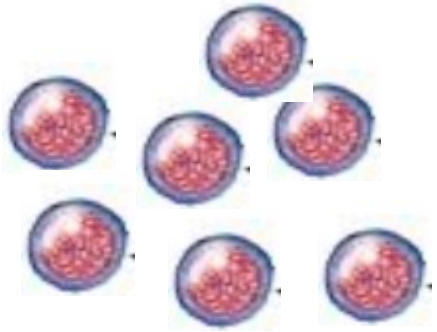
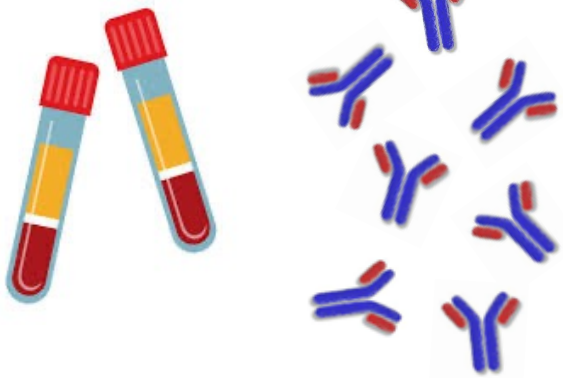
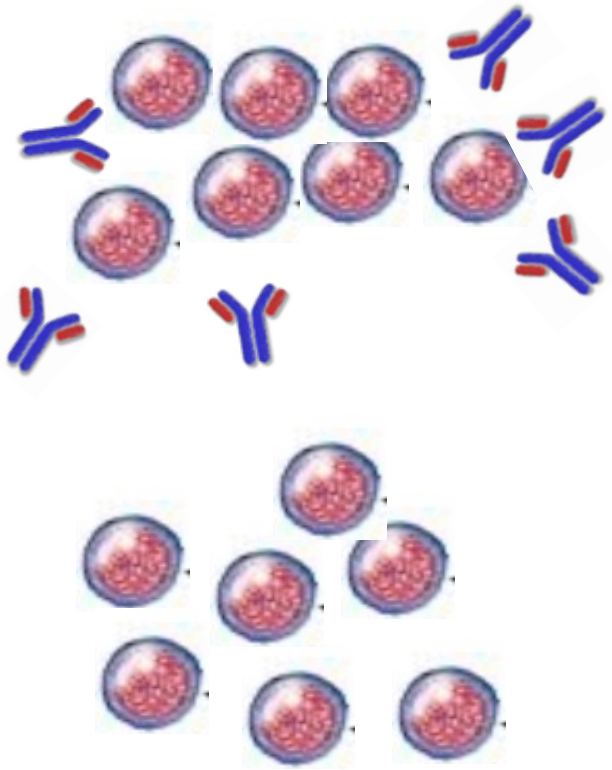






Recipient-specific antibodies



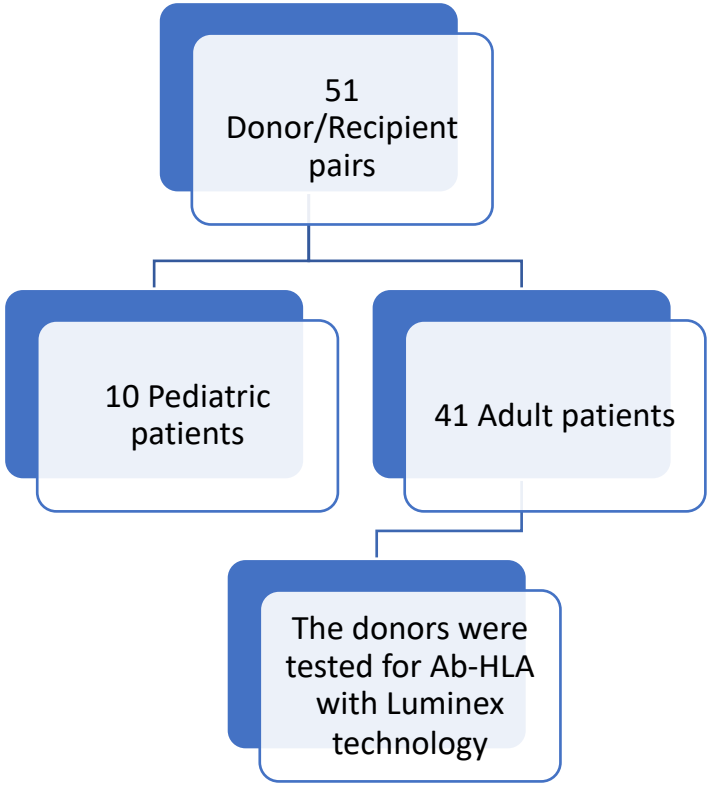


The role of Recipient Specific Antibodies (RSA) in transplant outcome. Analysis of a group of family donors selected for patients undergoing haploidentical transplantation.

Cacciatore R., **Pasi A.**, Bergamaschi P., Giorgiani G., Caldera D., Comoli P., Colombo A. Sbarsi I. Chiesa L., Troletti D., Cornella E., Hoffmann M., Monti C., Perotti C., Bernasconi P., Arcaini L., Zecca M.

Pasi Annamaria

IRCCS Policlinico San Matteo-Pavia- ITALY



Courtesy of A. Pasi

HLA antibodies were present in 23 donors

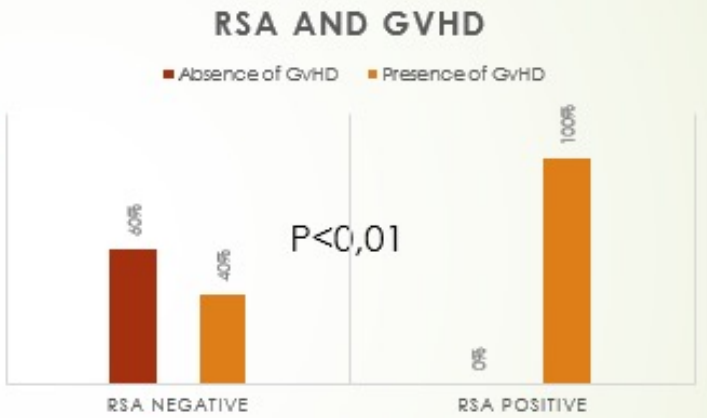
- 21 had HLA class I antibodies
- 11 had HLA class II antibodies
- 9 were positive for class I and class II.

8 donors (35%) were RSA positive

15% of all donors

RSA	Absence of GvHD	Presence of GvHD	
Negative	24 (60%)	16 (40%)	n=40
Positive	0	8 (100%)	n=8

100% of RSA pos recipients (8/8) exhibited acute or chronic GvHD vs 40% of RSA neg recipients (p<0.01).



The analysis of our study group shows that the presence of RSA in the donors correlates with both acute and chronic GvHD.

EFI 2023

Courtesy of A. Pasi

ELSEVIER
Biology of Blood and Marrow Transplantation
journal homepage: www.bbmt.org
ASBMT American Society for Blood and Marrow Transplantation

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,*]

[1] *Etablissement Français du Sang, Ile de France, HLA Laboratory, Créteil, France*
[2] *Department of Hematology, AP-HP, Hôpital Henri Mondor, DHU Virus-Immunity-Cancer, Créteil, France*
[3] *IMRB, University Paris Est Créteil, INSERM U955, Créteil, France*
[4] *Center for Clinical Investigation in Biotherapy, Créteil, France*

- Rischio complessivo di un primo episodio di GVHD acuta o cronica: 88% nelle coppie D/R immunizzate con anti-HLA rispetto al 67% nelle coppie D/R non immunizzate; $P = .03$

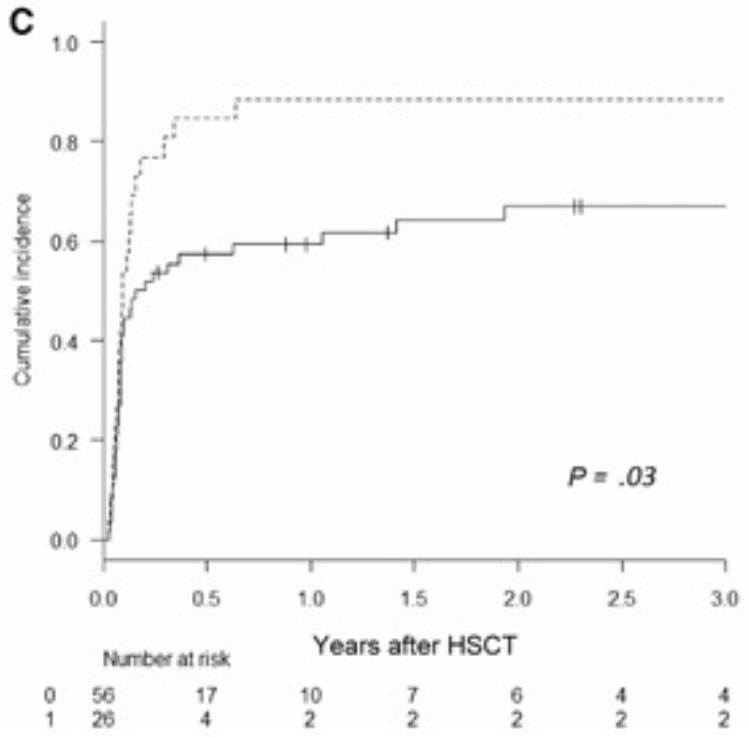


Figure 3. Cumulative incidence of acute GVHD (A), chronic GVHD (B), and first episode of either acute or chronic GVHD (C) according to the presence of at least 1 anti-HLA class II antibody in the donor (dashed line) or not (solid line).

Delbos F et al., BBMT 2016

Conclusioni

- La misurazione (MFI) ed interpretazione (epitopi) degli anticorpi anti-HLA è fondamentale per gli studi di correlazione clinica
- La presenza di anticorpi anti-HLA non donatore-specifici potrebbe rappresentare un «marcatore» dello status immunologico del paziente
- Lo studio degli anticorpi anti-HLA diretti contro il ricevente (RSA) merita interesse ed ulteriori approfondimenti

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