



Anticorpi anti HLA e trapianto di Cellule Staminali Emopoietiche

Valeria Miotti

AIBT Summer School-Ercolano, 13-15 giugno 2019

Stato dell'arte

- Anticorpi HLA DSA e PGF
- Meccanismo del danno
- Pazienti a rischio-Impatto sul trapianto
- Metodiche
- MFI (cut off clinico)
- Ab non DSA
- Ab locus specifici
- Ab “de novo”
- Desensibilizzazione
- Protocolli di gestione/monitoraggio
- Studio Gitmo AIBT

Anticorpi anti-HLA e trapianto di cellule staminali emopoietiche

Antibody-Mediated Marrow Failure After Allogeneic Bone Marrow Transplantation

By Alan J. Barge, Gretchen Johnson, Robert Witherspoon, and Beverly Torok-Storb

Marrow graft failure observed in association with histocompatibility differences between donor and recipient is often attributed to rejection mediated by host-derived cytolytic T lymphocytes. The data presented in this report indicate that persistent host antibodies specific for donor antigen may also mediate graft failure, either by antibody-dependent cell-mediated cytotoxicity (ADCC), or complement-mediated cytotoxicity. In the case of HLA Class I disparity, where all donor cells express the target antigen,

the presence of α -donor antibody was associated with complete graft failure and death. In the case of ABO blood group antigen disparity, the presence of α -donor antibody resulted in erythroid hypoplasia. The latter cases proved informative insofar as they established that host antibodies could persist for more than 18 months after chemoradiotherapy and impair marrow function.

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Blood, Vol 74, No 5 (October), 1989: pp 1477-1480



trapianto di cellule staminali emopoietiche

Solo il 30% dei pazienti ha un donatore HLA identico

- **Unrelated Registry Donors**
- **HLA-haploidentical family members**
- **Umbilical Cord Blood stem cells (UCB)**

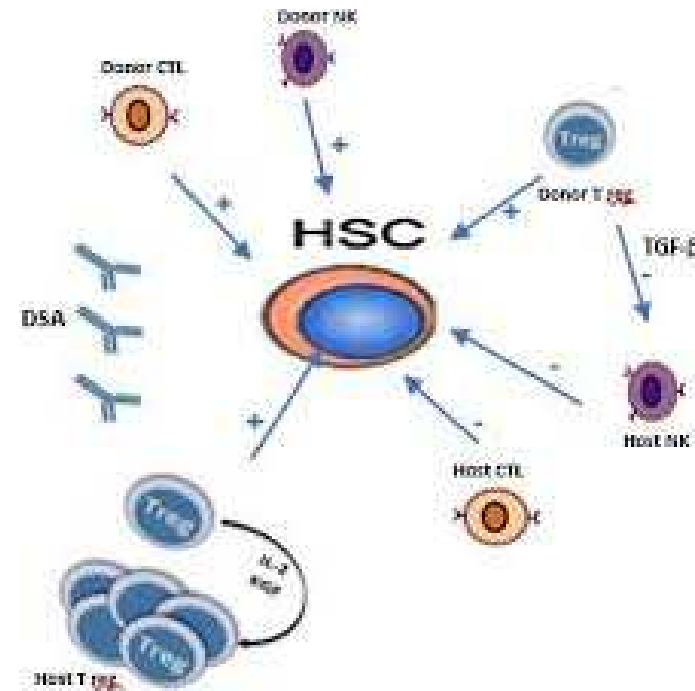
partially HLA
mis/matched

Anticorpi anti-HLA e trapianto di cellule staminali emopoietiche

Graft Failure

4% matched unrelated donor

20% donatore alternativo (cordone e aploidentico)



Anticorpi anti-HLA e trapianto di cellule staminali emopoietiche

❑ **Graft Rejection:**

failure to engraft neutrophils (ANC $< 500/\mu\text{L}$)
for 3 consecutive days by day +28 in the **absence of donor hematopoiesis**

❑ **Poor Graft Function:**

failure to achieve adequate blood counts (ANC $> 500/\mu\text{L}$ Hb $> 8\text{g/dl}$ or PLT $> 20,000/\mu\text{L}$)
for 3 consecutive days beyond day +28 in the **presence of complete donor hematopoiesis**

Anticorpi anti-HLA e trapianto di cellule staminali emopoietiche

TABLE 1 | Studies of DSA impact in different settings in AHSCT.

Reference	Patients (n)	Stem cell source	Conditioning	Anti-HLA%	DSA%	Graft failure with/without DSA
Spellman et al. (34)	115	Mismatched unrelated	RIC	ND	9	24 versus 1%
Ciurea et al. (36)	592	10/10 and 9/10 unrelated	MACorRIC	19.6	1.4	37.5 versus 2.7%
Yoshihara et al. (39)	79	Haplo-identical	RIC	20.2	14	27 versus 3%
Ciurea et al. (36)	24	Haplo-identical	RIC	ND	21	60 versus 5%
Chang et al. (40)	345	Haplo-identical	MAC	25.2	11.3	61% (MFI, 10,000) versus 3.2%
Ciurea et al. (36)	122	Haplo-identical	Non-specified	ND	18	32 versus 4%
Takanashi et al. (41)	386	Single CBU	MAC	23.1	5	83 versus 32%
Cutler et al. (42)	73	Double CBU	MACorRIC	ND	24	57 versus 5.5%
Ruggeri et al. (43)	294	Single and double CBU	RIC	23	5	81 versus 44%
Yamamoto et al. (44)	175	Single CBU	MACorRIC	39.4	ND	50% if anti-HLA-C, DP, DQ, DRB1/2/3 versus 16%

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Anticorpi anti-HLA e trapianto di cellule staminali emopoietiche

Table 4. Incidence and impact of HLA-specific antibodies in HSCT

Reference	HSCT type	N	HLA-Ab N (%)	DSA N (%)	Significant impact of DSA and comments
(154)	Unrelated	115	NG	10 (8.7)	Associated with graft failure
(155)	Unrelated	592	116 (19.6)	8 (1.4)	Associated with graft failure; All DSA were anti-HLA-DP
(156)	sUCB	386	89 (23.1)	20 (5.2)	Associated with graft failure; reduced OS and EFS
(157)	dUCB	126	50 (39.7)	18 (14.3)	No difference in engraftment with and without DSA
(158)	dUCB	73	NG	18 (24.7)	Associated with graft failure; excess 100 day mortality or relapse
(160)	d,sUCB	293	62 (21.2)	14 (4.8)	Associated with graft failure and OS
(159)	sUCB	70	31 (44.3)	12 (17.1)	Both DSA and any HLA-Ab associated with reduced engraftment; DSA associated with reduced OS
(165)	Haplo-ID	24	NG	5 (20.8)	Associated with high rate of graft failure
(161)	Haplo-ID	79	16 (20.3)	11 (13.9)	Associated with graft failure
(162)	Haplo-ID	296	68 (23)	43 (14.5)	None observed; DSA was avoided or reduced by treatment

The incidence and impact of HLA-specific antibodies on outcomes of HSCT are given from recent studies that used current sensitive and specific solid phase immunoassays for detection and characterization of donor HLA-specific antibodies. HLA-Ab, the presence of any HLA-specific antibody; DSA, donor HLA-specific antibody; HLA-ID, HLA-identical donor; OS, overall survival; EFS, event-free survival; sUCB, single umbilical cord blood unit; dUCB, double UCB units; Haplo-ID, HLA-haploidentical donor.

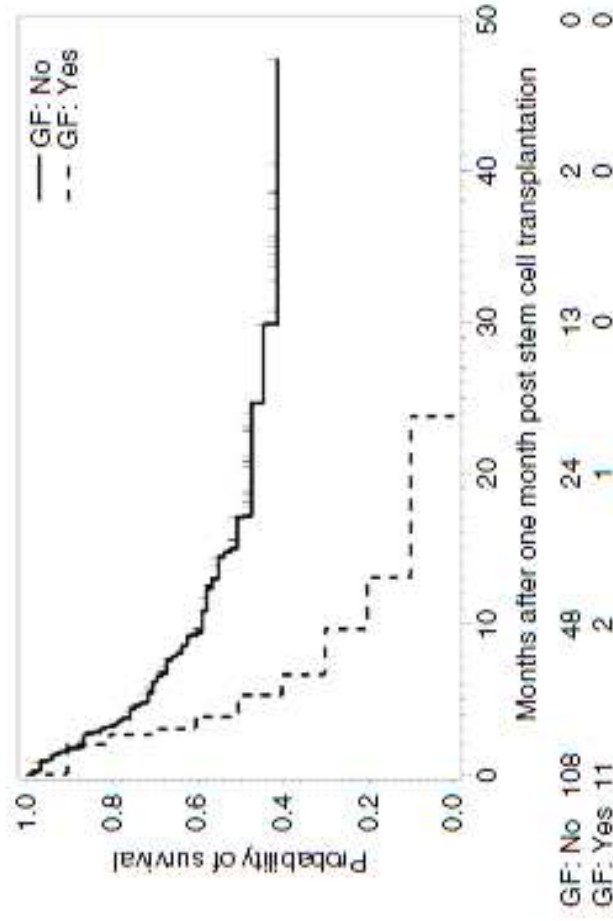


Fig. 1 Survival of haploidentical transplants for patients who experience primary graft failure as compared with those who engrafted the donor cells (Reproduced with permission from Ciurea SO, et al.) [34]

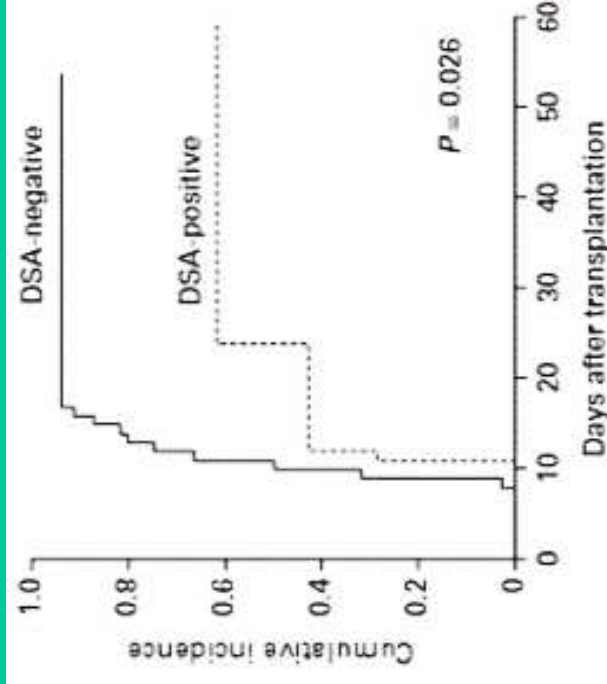
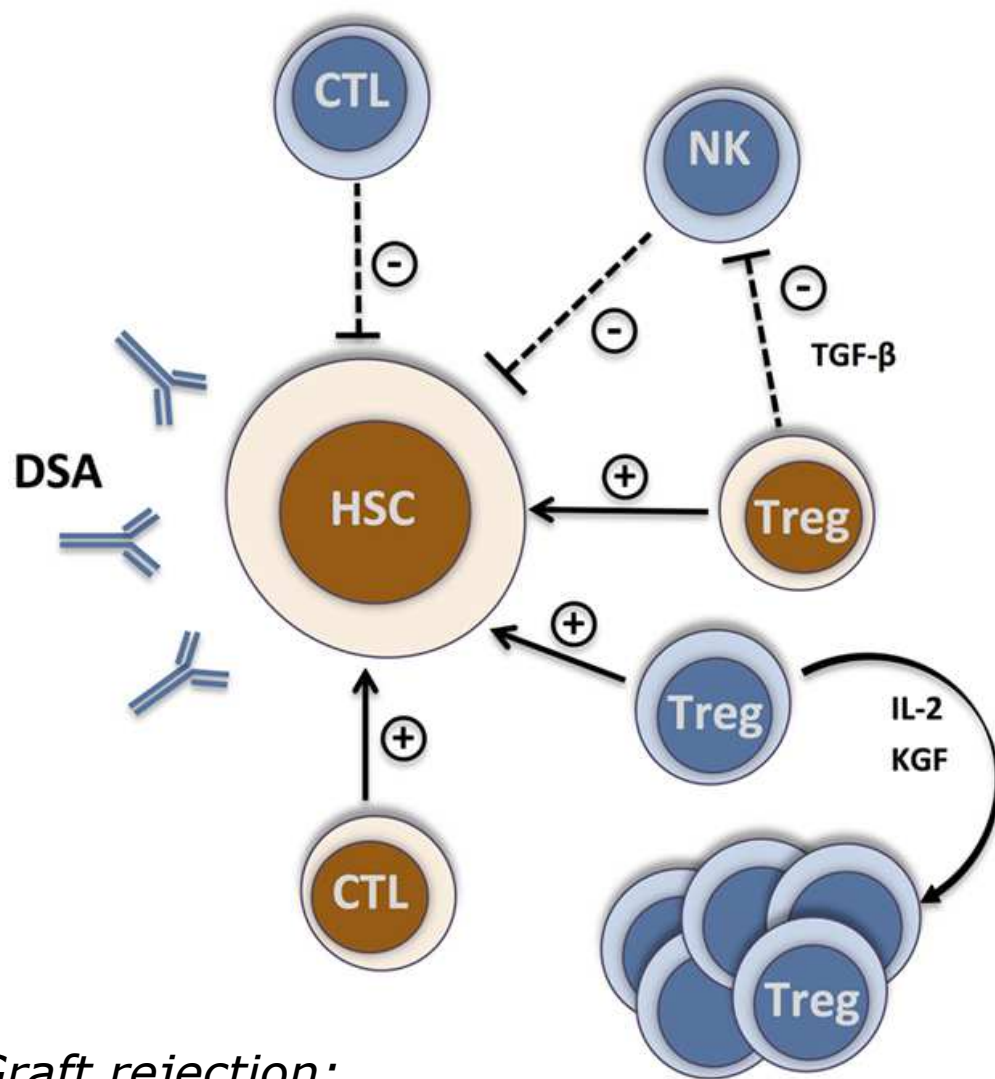


Figure 2 Pretransplant DSA and cumulative incidence of neutrophil engraftment. The cumulative incidences of donor neutrophil engraftment in pretransplant DSA-negative patients ($n = 72$, solid line) and DSA-positive patients ($n = 7$, dotted line). DSA-positive patients had a significantly lower incidence 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.

A

GRAFT FAILURE

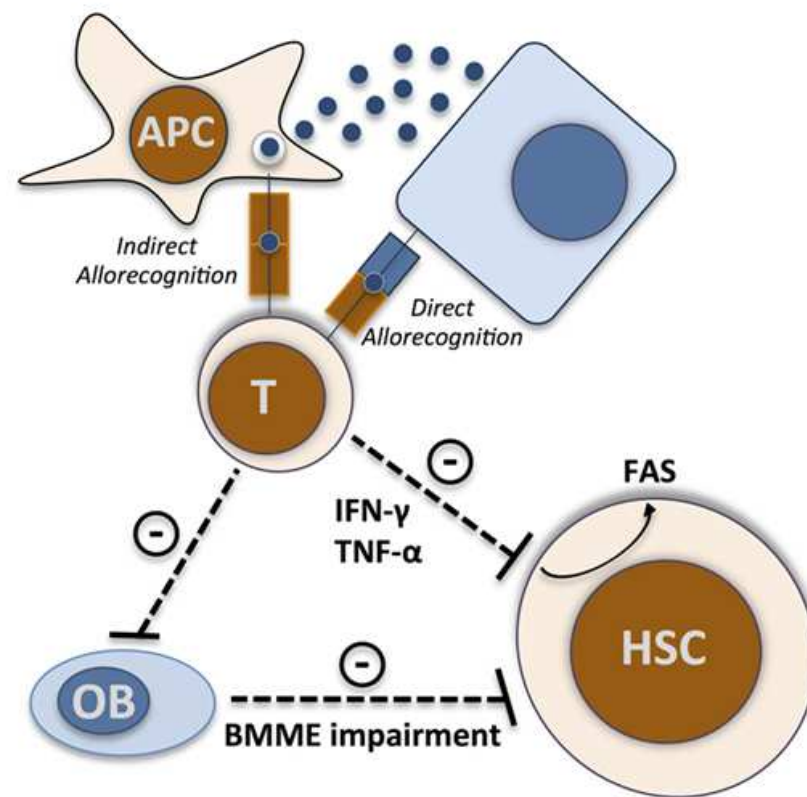


Graft rejection:

azione citolitica mediata dalle cellule T e/o NK sopravvissute al condizionamento e dagli anticorpi

B

POOR GRAFT FUNCTION



Anticorpi anti-HLA e trapianto di cellule staminali emopoietiche

- **ANTIBODY-DEPENDENT CELL-MEDIATED CITOTOXICITY (ADCC)**

Nevertheless, the molecular bases underlying T cell-mediated graft rejection remain incompletely defined.

- **COMPLEMENT DEPENDENT CITOTOXICITY(CDC)**

Antibody-mediated BM failure after AHSCT can occur either by antibody-dependent cell-mediated cytotoxicity or by complement mediated cytotoxicity [41]. Evidence from

Prevention of the homing of stem cells to the niches in the recipient marrow

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Patient Group (N)	Any HLA-Specific Abs	Donor HLA-Specific Abs
All candidates (296)	68 (23.0%)	43 (14.5%)
Males (185)	20 (10.8%)	9 (4.9%)
Females (111)	48 (43.2%)	34 (30.6%)
Parous females (63)	33 (52.4%)	27 (42.9%)
Nulliparous females (48)	15 (31.3%)	6 (12.5%)

Gladstone, BBMT 2013



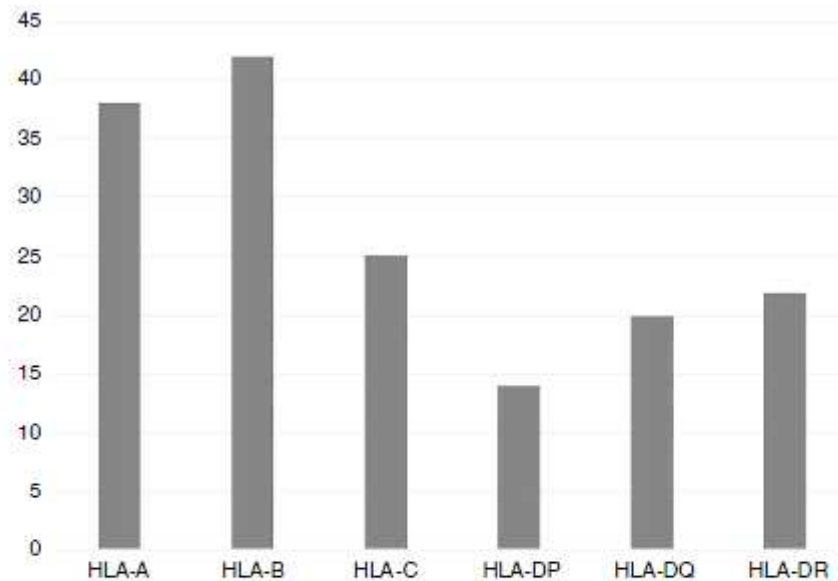
Pazienti a rischio:
genere femminile e gravidanza

- ✓ middle age multi-parous females
- ✓ transplant setting “child-to-mother”

Origine degli anticorpi anti HLA

- ✓ gravidanza
- ✓ trasfusioni
- ✓ trapianti
- ✓ Anticorpi naturali

Fig. 1 Frequency and mean fluorescence intensity (MFI) of anti-HLA antibodies against each HLA antigen coded by the different HLA loci, including HLA-A, B, C, DP, DQ, and DR in 486 pediatric patients



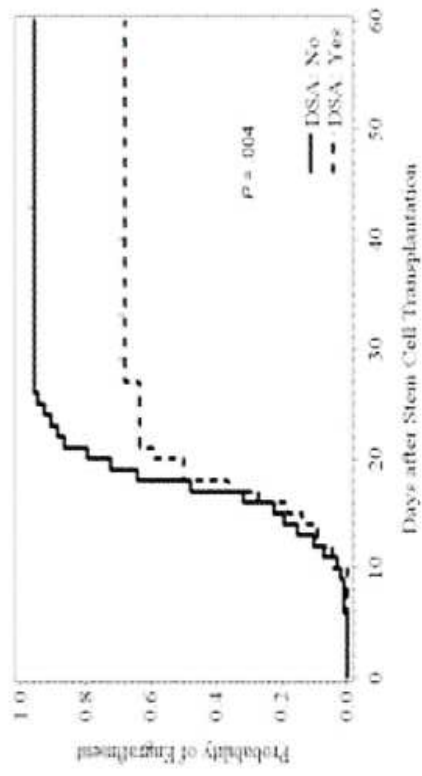
Locus specifici

Loci	A	B	C	DP	DQ	DR
Positive DSA Numbers (Percent)	38 (7.8%)	42 (8.6%)	25 (5.1%)	14 (2.9%)	20 (4.1%)	22 (4.5%)
Positive DSA MFI median	1678	1514	1148	1067	2139	1372
Total patients MFI Median (Range)	175 (7-21491)	186 (8-20119)	186 (14-15833)	201 (30-19994)	290 (19-20095)	274 (27-21848)

Class I and II human leukocyte antibodies in pediatric haploidentical allograft candidates: prevalence and risk factors

Meng Lv¹ · Shu-Zhen Zhai¹ · Yu Wang¹ · Lan-Ping Xu¹ · Xiao-Hui Zhang¹ · Huan Chen¹ · Yu-Hong Chen¹ · Feng-Rong Wang¹ · Wei Han¹ · Yu-Qian Sun¹ · Yi-Fei Cheng¹ · Chen-Hua Yan¹ · Xiao-Dong Mo¹ · Kai-Yan Liu¹ · Ying-Jun Chang¹ · Xiao-Jun Huang^{1,2} · Xiang-Yu Zhao¹

A



B

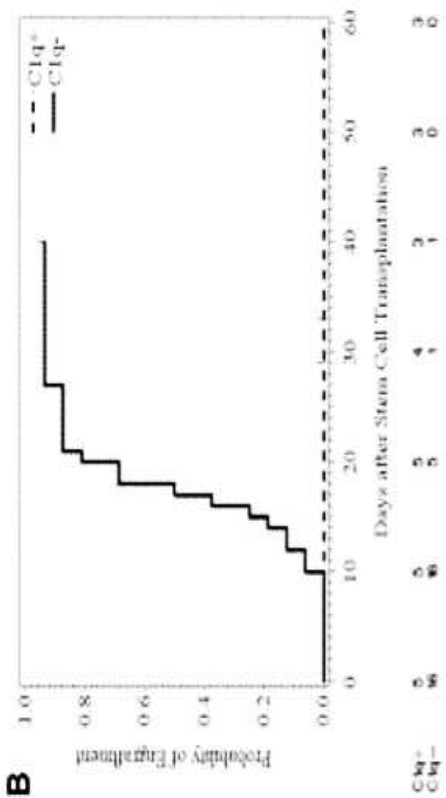


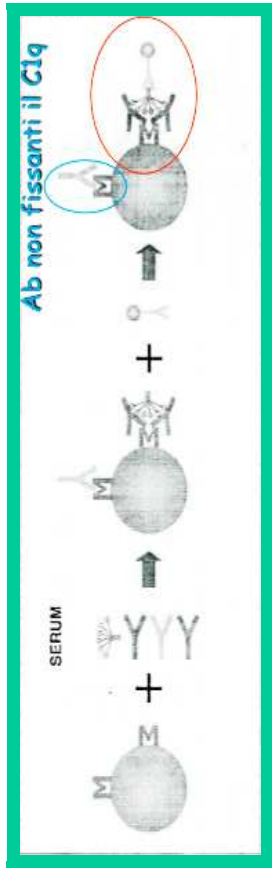
Figure 1. Probability of engraftment in patients by DSA status (A) and C1q status (B).

Table 2

Associations between Gv, C1q Status, and Treatment

Covariate	Gv		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)	

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



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

Stefan O. Ciurea^{1,2}, Peter F. Thall², Denái R. Milton², Titus H. Barnes³, Piyanuch Kongtim¹, Yudith Carmazzi³, Asdrúbal A. López³, Dianne Y. Yap³, Uday Popat¹, Gabriela Rondon¹, Benjamin Lichtiger³, Fleur Aung³, Vahid Afshar-Kharghan⁴, Qing Ma¹, Marcelo Fernández-Viña⁵, Richard E. Champlin¹, Kai Cao³



Anticorpi anti-HLA e trapianto di cellule staminali emopoietiche



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'attecchimento.**
- 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

Anticorpi de novo

Table 1
HLA typing of the recipient and donor.

	HLA-A	HLA-B	HLA-C	HLA-DRB1	HLA-DQB1	HLA-DQA1	HLA-DPB1
Patient	01:01, 11:01	08:01, 35:03	04:01, 07:01	01:01, 03:02	02:01, 03:02	03:01, 05:01	04:01, 04:01
Donor	01:01, 11:01	08:01, 35:03	04:01, 07:01	01:01, 03:02	02:01, 03:02	03:01, 05:01	<u>01:01</u> , 04:01

The mismatched donor allele is underlined.

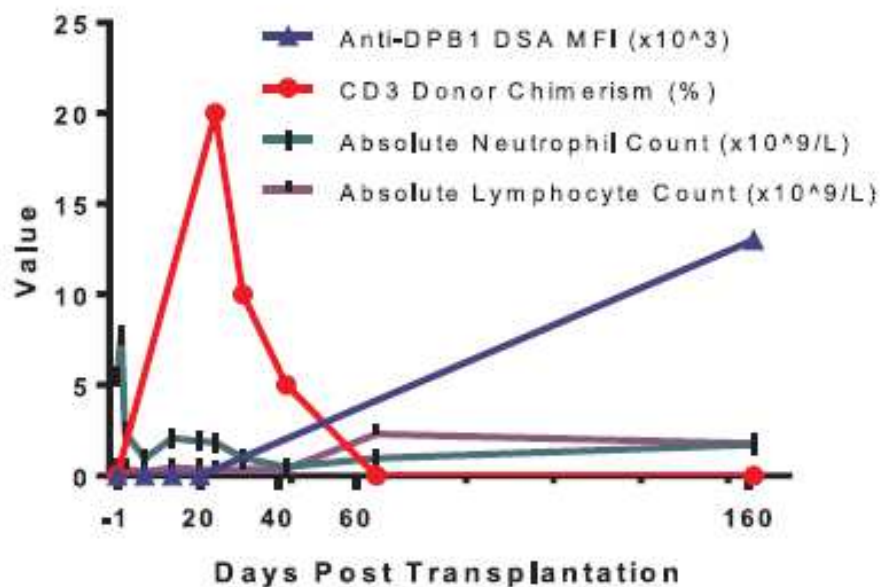


Fig. 1. Temporal association of anti-DPB1 DSA MFI, CD3 chimerism, absolute neutrophil count and absolute lymphocyte count after transplantation.



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The association of de novo anti-HLA-DPB1 donor-specific antibody formation and primary graft failure after allogeneic hematopoietic cell transplantation

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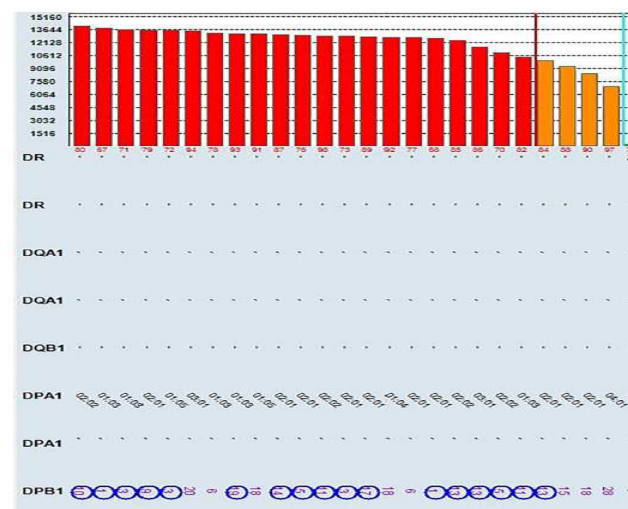


Fig. 2. The mean fluorescent intensity of anti-HLA antibodies against HLA-DPB1 alleles that share the 85–87 EAV epitope.

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

..... e il donatore?

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



Florent Delbos¹, Walid Barhoumi², Ludovic Cabanne³, Florence Beckerich², Christine Robin², Rabah Redjoul², Safae Astaty², Andréa Toma⁴, Cécile Pautas², Hélène Ansart-Pirenne¹, Catherine Cordonnier², Philippe Bierling^{1,3}, Sébastien Maury^{2,3,4,*}

¹ Etablissement Français du Sang, Ile de France, HLA Laboratory, Clitell, France

² Department of Hematology, AP-HP, Hôpital Henri Mondor, DHU Virus-Immunity Cancer, Clitell, France

³ INSERM, University Paris Est Clitell, INSERM U1155, Clitell, France

⁴ Center for Clinical Investigation in Biotechnology, Clitell, France

Table 2

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

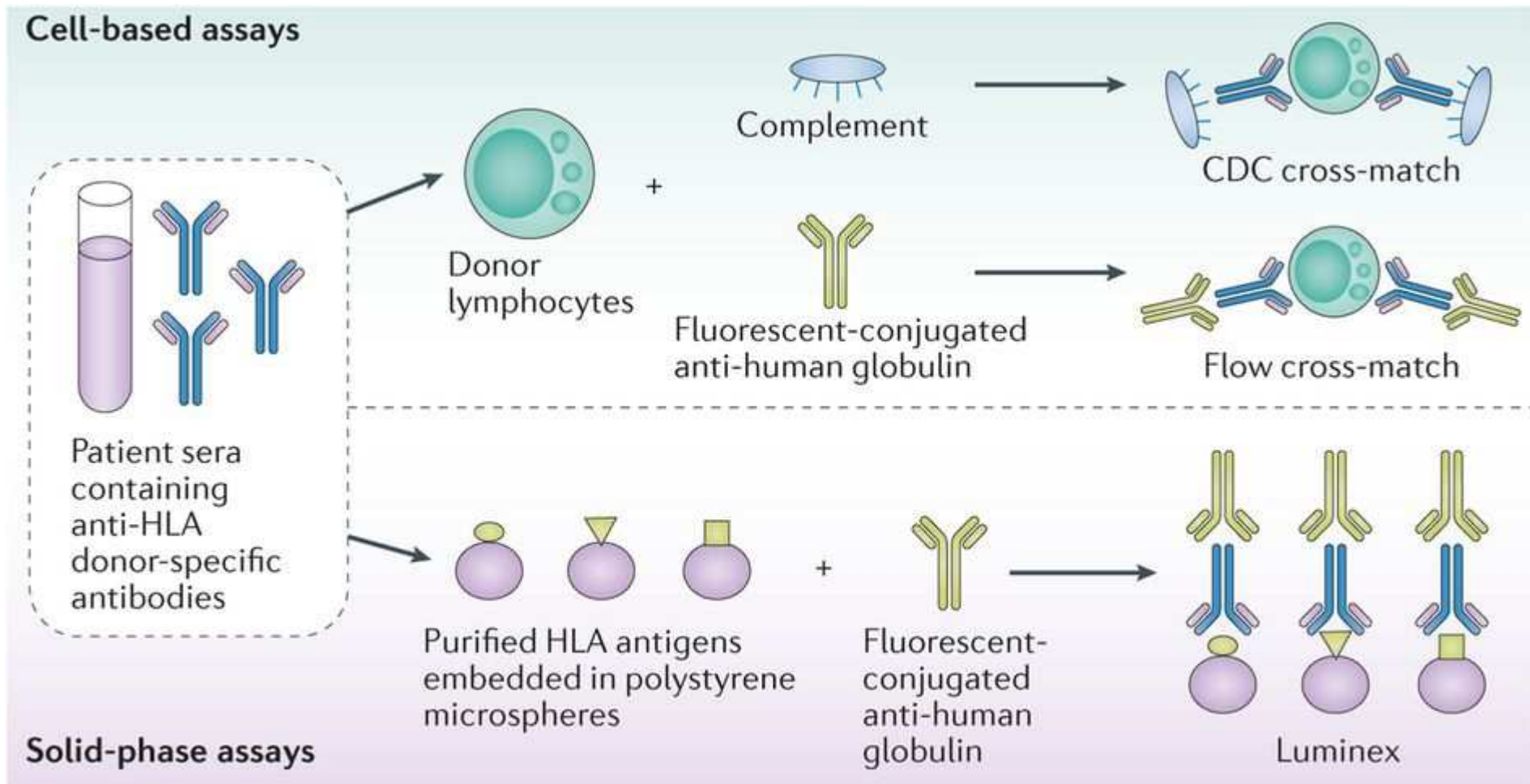
D/R Pair	Stem Cell Source	Donor Sex	Maximal NBG Ratio	Average NBG Ratio	RSA Specificity	MF of RSA	GVHD	Outcome	Follow Up, Mo
1	BM	Male	4	3.7	DPB1*11:01	650	No	Alive	28+
2	PB	Male	5	2.7	DPB1*01:01	1232	No	Dead	9
3	BM	Male	4	3.1	DPB1*01:01	1368	aGVHD grade II	Alive	3+
4	PB	Male	3	3.0	DPB1*03:01	543	aGVHD grade IV	Dead	3
					DPB1*04:02	509			
5	PB	Male	4	2.5	DPB1*03:01	914	aGVHD grade IV	Dead	7
							cGVHD		
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	Dead	12
							cGVHD		
8	BM	Female	6	5.4	DPB1*01:01	1374	aGVHD grade II	Alive	12+
					DPB1*04:01	619	cGVHD		
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	DRB1*02:02	580	aGVHD grade III	Dead	5

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

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 optimum 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.

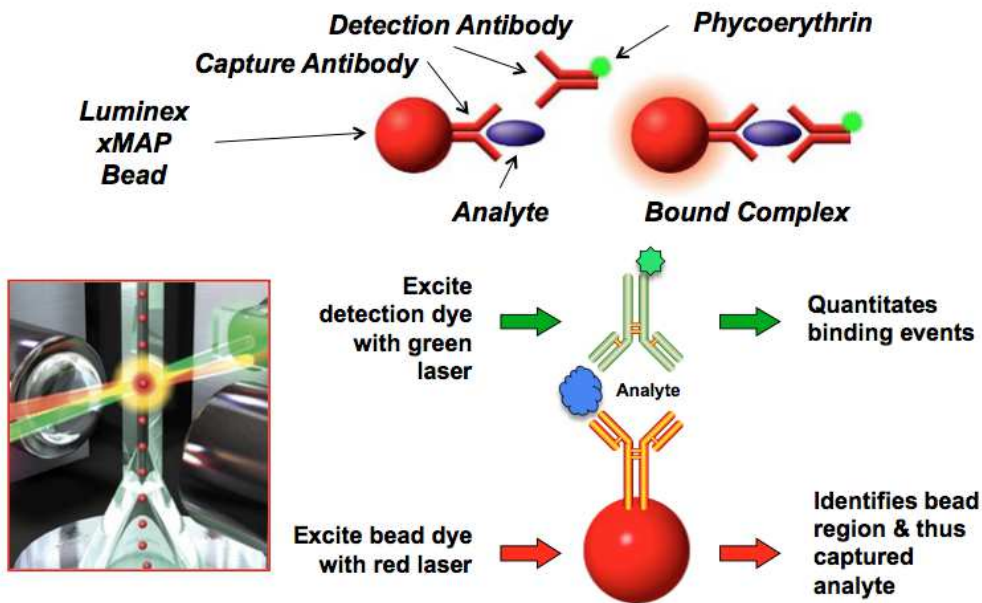
metodiche



metodiche

Luminex-based assay

Mean Fluorescence Intensity (MFI)



- 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





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Anti-HLA antibody testing in hematology patients

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Many studies have used different MFI cut-offs to assign clinical significance to HLA antibodies in HPC transplantation. In one study, patients who failed to engraft had anti-DPB1 antibodies of at least intermediate strength (i.e., MFI > 1,500) [4]. In haploidentical donors, intermediate strength DSA was seen in recipients with graft failure [21]. DSA with MFI > 1,000 was associated with double cord transplant engraftment failure [5] while MFI > 2,000 was associated with graft failure in mismatched donors [6]. One problem with using MFI alone to assign clinical significance is that bead arrays display high variation in MFI values (up to 62%), which can be improved (to about 25%) with inter-laboratory standardization [22]. Sources of this wide variation in MFI are inter-operator technique as well as differences in antigen density on beads. There should be discussion between the clinical team and HLA laboratory regarding MFI cut-offs, if any, to be used in donor selection.

MEAN FLUORESCENCE INTENSITY (MFI)

Level or strength of antibody (semi-quantitative)

DSA: esiste un valore soglia sicuro ?

NO CONSENSUS

positive range from MFI 500 to 5000

categorie

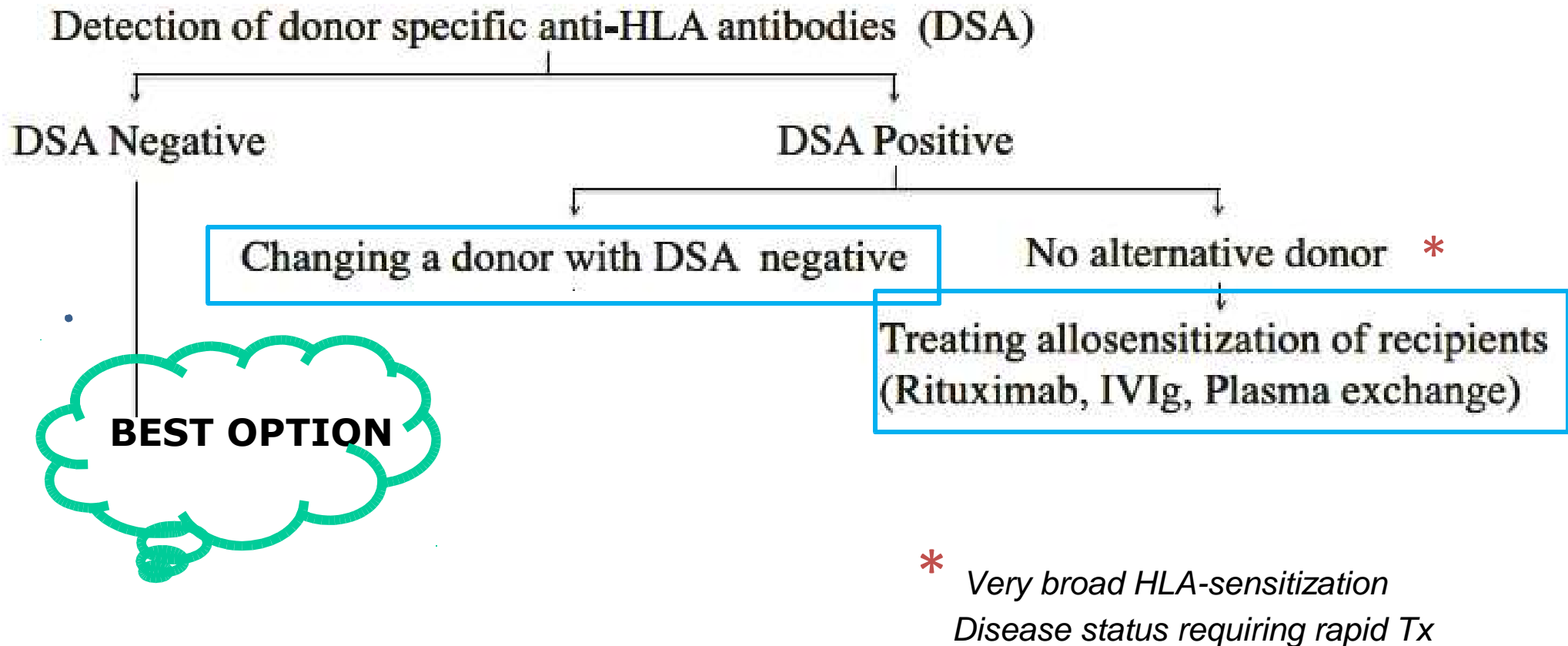
HLA-mismatched HSCT:

- Unrelated
- Haploidentical
- Cord Blood

HLA matched HSCT:

- Unrelated (also in 8/8 or 10/10 HLA matching potential presence of Ab against HLA-DP)

Selezione del donatore



How do we choose the best donor for T-cell-replete, HLA-haploidentical transplantation?
Chang et al., Journal of Hematology & Oncology (2016)

✓ DESENSITIZATION TREATMENTS

Preformed DSA removal

TREATMENT	TARGET	<u>MECHANISMS OF ACTION</u>
PEX	<u>Preformed DSA</u>	Non-selective removal of <u>Immunoglobulins</u> , <u>Immune complexes</u> , <u>complement factors</u> , <u>cytokines</u> , <u>etc</u>
<u>Immunoadsorption</u>	<u>Preformed DSA</u>	<u>Selective IgG removal</u>
Donor platelets transfusion	<u>Preformed DSA</u>	<u>Adsorption DSA Class I</u>

✓ DESENSITIZATION TREATMENTS

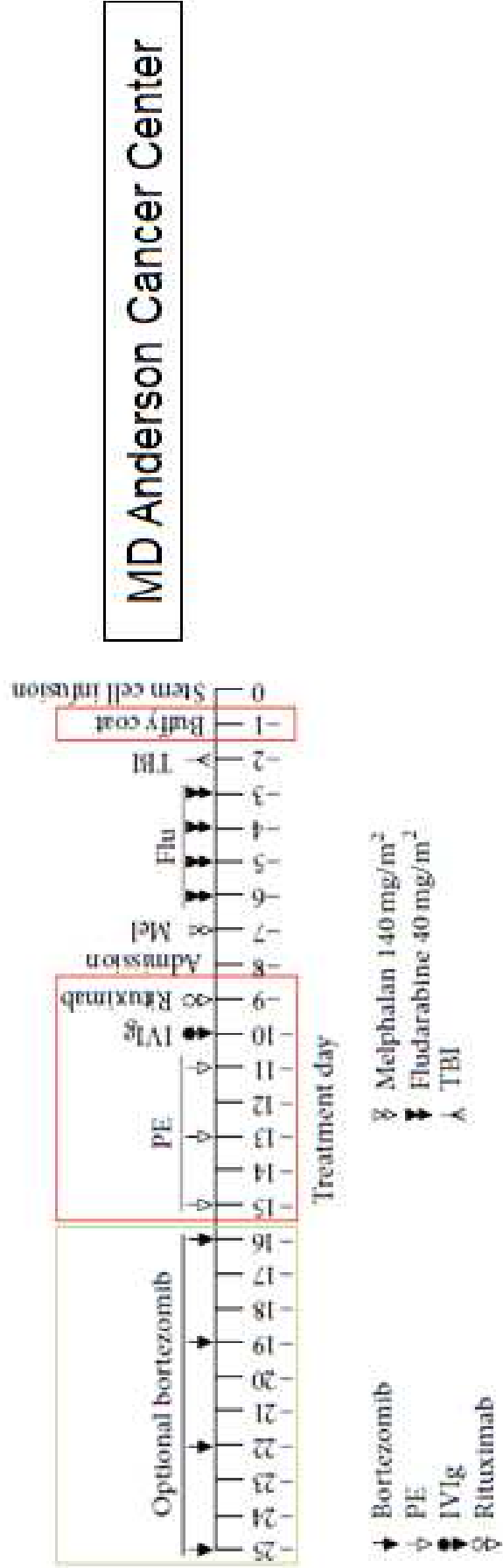
B-lymphocytes/plasma cells depletion

TREATMENT	TARGET	MECHANISMS OF ACTION
<u>RITUXIMAB</u> (Anti CD20)	<u>CD 20+ B cell</u>	Depletion of memory B cell
<u>BORTEZOMIB</u>	<u>Plasma cells</u>	<u>Depletion of Ab-producing cell</u>

Abrogation of Cellular-cytotoxicity

TREATMENT	TARGET	MECHANISMS OF ACTION
IVIG	Multiple	<u>Enhanced clearance of Ab, complement modulation, inhibition of FcR mediated clearance Ab bound cells</u>
<u>ECULIZUMAB</u>	C5a	<u>Prevention of complement dependent cytotoxicity</u>

✓ DESENSITIZATION TREATMENTS



1-2 weeks before conditioning			Conditioning		-1	0	+1/+2
PEX		PEX		IVIg 1gr/Kg	± PEX IVIg	Stem cells infusion	± PEX IVIg
Tacrolimus and Mycophenolate mophetil							

John Hopkins group

Reference	Donor type (N)	Anti-HLA abs test	Desensitization method	MFI after treatment	Graft outcome
Barge et al. 1989 [41]	Haplo (N = 1)	CDC	Plasmapheresis	NA	Graft failure
Maruta et al. 1991 [52]	Mismatched related (N = 1)	AHG-CDC	CyA, methylpred, Plasmapheresis, DLI	Negative XM	Engrafted
Braun et al. 2000 [53]	Haplo (N = 1)	FCXM	Staphylococcal protein A immunoadsorption	Negative XM	Engrafted
Ottinger et al. 2002 [20]	Mismatched related (N = 2)	DTT-CDC	Plasmapheresis, mismatched platelet transfusion	1 patient with negative XM, 1 patient with positive XM	Patient with negative XM after treatment engrafted, while patients with positive XM had GF
Pollack and Ririe 2004 [54]	Mismatched HLA-A68 related (N = 1)	FCXM	Platelet transfusion, plasmapheresis, IVIg	Negative XM	Engrafted
Narimatsu et al. 2005 [55]	Mismatched related (N = 1)	AHG-LCT	Rituximab, platelet transfusion	Negative AHG-LCT	Engrafted
Ciurea et al. 2009 [22]	Haplo (N = 4)	Luminex MFI >500	Rituximab, plasmapheresis	1 negative, 1 low titer, 2 high titers	Patients with DSAs negative and low titer after treatment engrafted; 2 patients with high titer had GF

Yoshihara et al. 2012 [48]	Haplo (N = 5)	Luminex MFI >500	Plasmapheresis + rituximab (N = 2), platelet transfusion (N = 2), bortezomib + dexamethasone (N = 1)	1 patient had temporary DSA reduction and 1 patient had significant reduction after plasmapheresis; 2 patients had a significant reduction post platelet transfusion; 1 patient had moderate DSA reduction after bortezomib and dexamethasone	All patients engrafted
Ciurea et al. 2015 [46]	Haplo (N = 12)	Luminex MFI >500	Plasmapheresis + rituximab + IVIg (N = 5), PE + rituximab + IVIg + donor buffy coat infusion (N = 7)	5 patients with Clq positive after treatment had GF while patients who became Clq negative engrafted	
Leffell et al. 2015 [56]	Haplo (N = 13) MMUD (N = 2)	Luminex MFI >1000	Plasmapheresis + IVIg	Mean reduction of DSAs after treatment was 64.4%. 1 patient failed to reduce DSAs to the level that was thought to be safe for transplant	All 14/14 transplanted patients engrafted

MFI, mean fluorescence intensity; CDC, complement-mediated cytotoxicity; XM, crossmatch; FCXM, flow cytometric crossmatch; GF, graft failure; AHG, LCT.

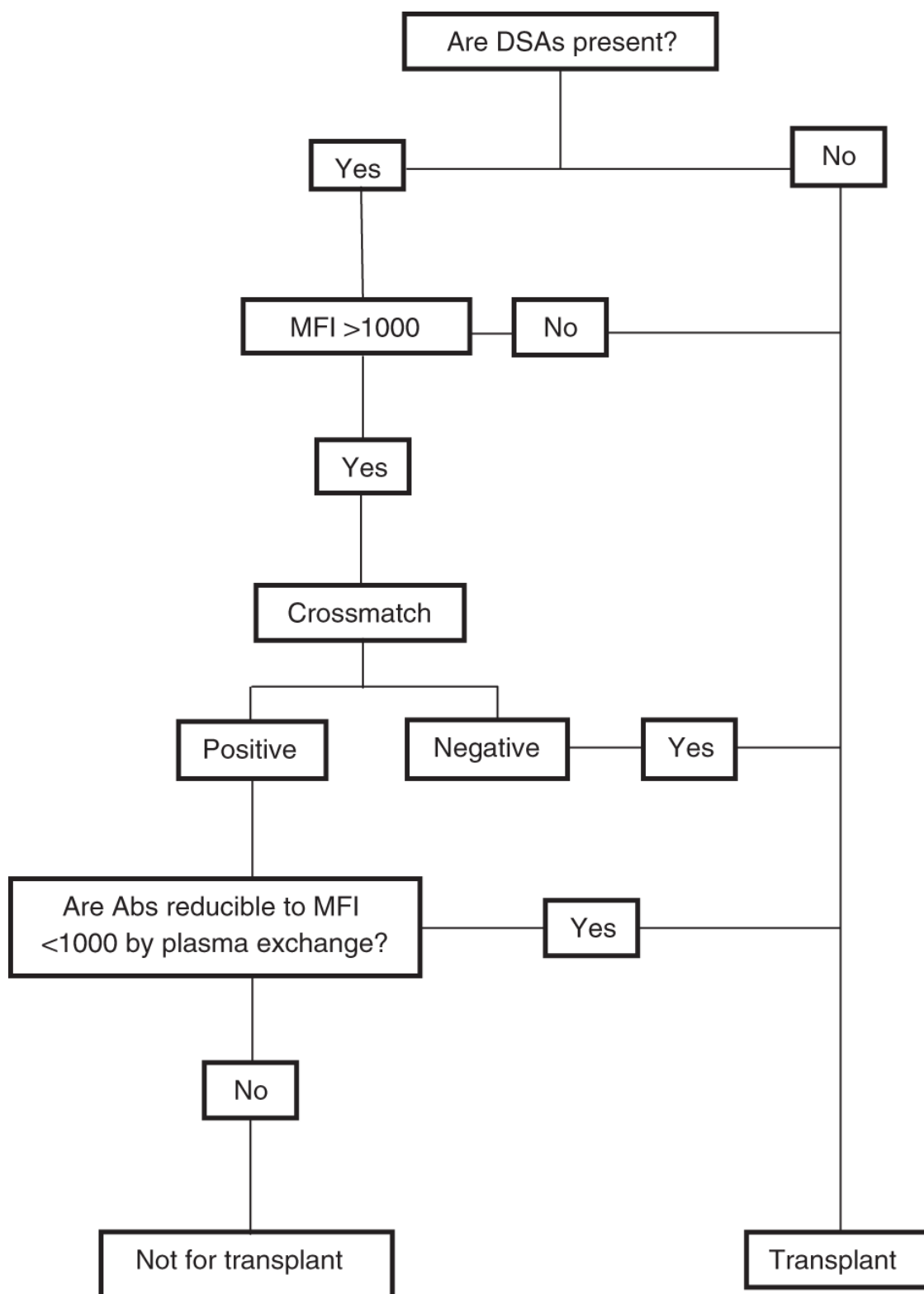
Indicazioni trattamento di desensibilizzazione

Fattori di rischio aggiuntivi:

- ☐ Alti livelli di DSA
- ☐ DSA multipli
- ☐ HLA mismatch da precedente trapianto
- ☐ Trapianto figlio-madre
- ☐ Aumento DSA prima del trattamento
- ☐ Eventi pro-infiammatori (infezioni, chirurgia)

- MFI 1000 – 3000 (5000, Yoshihara S, 2012)
- Cross match negative level (Leffell MS. 2015)
- C1q negativity (Ciurea S, 2015)

**Desensitization
End Points**



Comportamento condiviso
CT-Lab HLA-Aferesi
Udine



The European Society for Blood and Marrow Transplantation (EBMT) Consensus Guidelines for the Detection and Treatment of Donor- specific Anti-HLA Antibodies (DSA) in Haploidentical Hematopoietic Cell Transplantation

Published online: 15 January 2018

Recommendations for DSA positive HSCT recipients on:

- testing (C1q testing)
- monitoring
- treatment

Titolo

Anticorpi anti HLA donatore specifici (DSAs**) nei pazienti candidati a trapianto allogenico mismatched**

Acronimo Protocollo

GITMO/AIBT DSAs

Promotore

GITMO/AIBT

Disegno

Studio osservazionale, retrospettivo, multicentrico

Gruppo di studio

GITMO/AIBT

Obiettivo Primario

Indagine conoscitiva sulla pratica del monitoraggio degli anticorpi anti HLA DSAs nei centri trapianto italiani:

- 1) cut off impiegati nei vari centri ed il loro impatto clinico
- 2) politica di selezione del donatore sulla base della presenza dei DSAs
- 3) strategie di desensibilizzazione impiegate per la rimozione dei DSAs nei vari centri

Obiettivi Secondari

Valutare l'outcome trapiantologico in termini di attecchimento, tempi di attecchimento, poor graft , graft failure, rigetto, overall survival in relazione alla presenza e al livello di DSAs

Popolazione in studio

Tutti i pazienti sottoposti a trapianto allogenico mismatched, indipendentemente dalla fonte di cellule staminali nel periodo 2014-2017 indipendentemente dalla ricerca dei DSAs

Anticorpi anti-HLA donatore-specifici (DSAs) nei pazienti candidati a trapianto allogenico mismatched
Italiano, Osservazionale, Retrospektivo, Multicentrico, Spontaneo, Non-interventistico, Non-farmacologico

Report sullo stato dell'arruolamento al 30/05/2019

First name	Last name	CIC	Arruolamento	Accesso alla piattaforma software
Michele	Malagola	141	25	si
Daniele	Vallisa	163	0	no
Alida	Dominietto	217	0	no
Benedetto	Bruno	231	42	si
Anna Paola	Iori	232	89	si
Francesca	Bonifazi	240	79	si
Lucia	Prezioso	245	53	si
Stella	Santarone	248	0*	si
Elena	Tagliaferri	265	25	si
Maura	Faraci	274	57	si
Sonia	Bonanomi	279	0	no
Paolo	Bernasconi	286	0	no
Anna	Proia	287	26	si
Giovanni	Grillo	294	0	no
Irene	Donni	304	51	si
Patrizia	Chiusolo	307	6	si
Giuseppina	De Simone	341	0	no
Stefania	Bramanti	354	0	no
Angelo Michele	Carella	526	0	no
Marco	Zecca	557	0	no
Massimo	Martino	587	25	si
Nicola	Mordini	606	10	si
Lucia	Farina	616	53	si
Giorgina	Specchia	649	10	si
Vincenzo	Pavone	652	0	no
Anna	Grassi	658	37	si
Michela	Cerno	705	0	no
Alessandra	Picardi	756	93	si
Irene	Federici	788	1	si
Matteo	Pelosini	795	0	no
Fabio	Ciceri	813	16	si
Michele	Cimminiello	861	0	si
Luca	Crotto	305.2	0	no
Angelo	Andreini	623.1	0	no
Simone	Cesaro	623.2	15	si
Totale			713	

**35
Centri Trapianto**

**713
Pazienti Arruolati**

Conclusioni

- ✓ La ricerca degli anticorpi anti HLA deve essere parte fondamentale del pre trapianto nella scelta del donatore
- ✓ La presenza di DSA è associata ad alto rischio di **graft failure**, ma non è una controindicazione assoluta al trapianto
- ✓ **I protocolli di desensibilizzazione possono ridurre i livelli di DSA per permettere l'attecchimento a quei pazienti che non hanno alternative**

Da definire:

- ❑ ***MFI clinicamente rilevante***
- ❑ ***Migliore approccio terapeutico***

Stretta collaborazione tra Centro Trapianti,
Laboratorio HLA ed ambulatorio Aferesi

Grazie per l'attenzione

