

Corso di Formazione **GITMO**
**Trapianto e
terapie cellulari:
cellule, donatori e
condizionamenti**

Udine, 8-9 Ottobre 2026

Aula Polifunzionale Ospedale di Udine

Come e quando desensibilizzare in caso di DSA?
Iori Anna Paola



SISTEMA SANITARIO REGIONALE

**AZIENDA OSPEDALIERO-UNIVERSITARIA
POLICLINICO UMBERTO I**



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Disclosures

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Roche					x	
Alexion					x	x
SOBI					x	x
Novartis					x	x

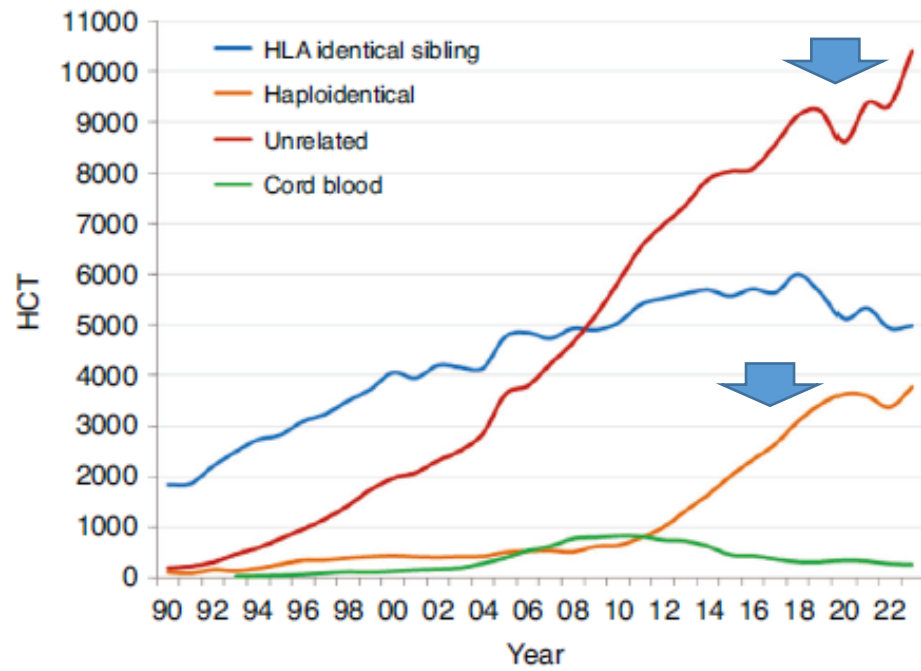
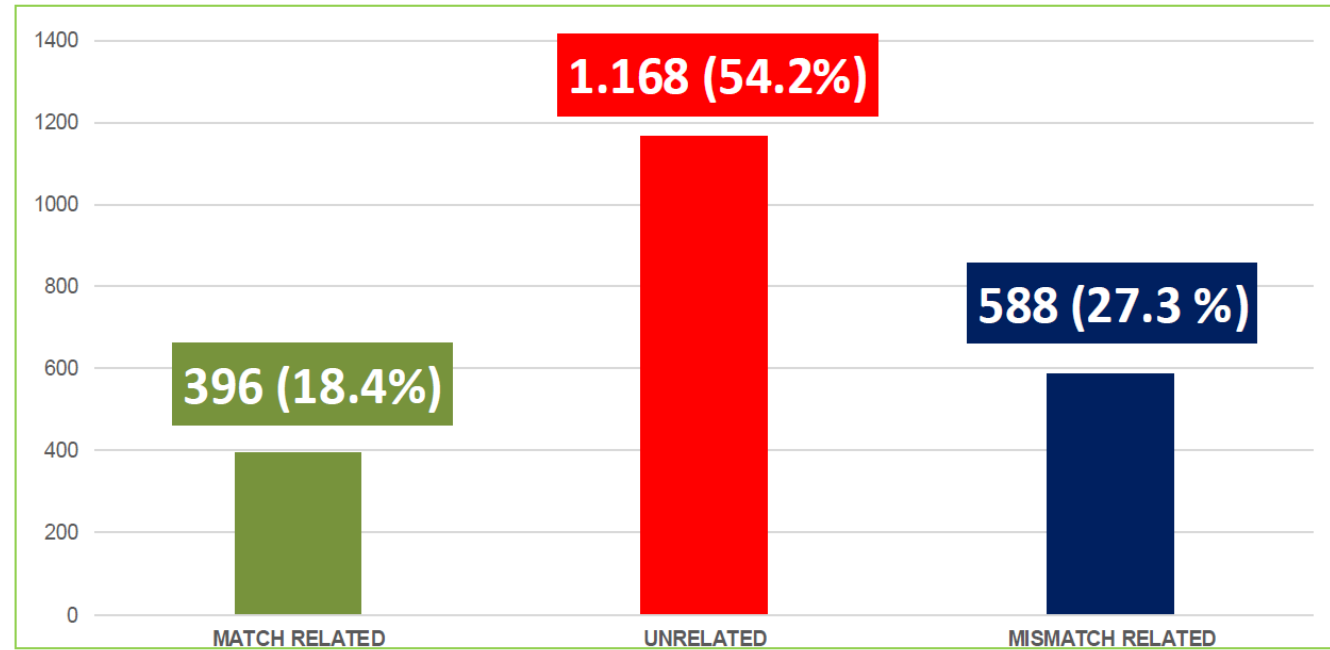


Fig. 4 Change in type of donor for first allogeneic HCT from 1990 to 2023.

2025: Allogeneic Transplants (n. 2.152) – Donor Type



“Alloimmunization”

the immune response to alloantigens, antigens from individuals of the same species that are genetically different

“HLA antibodies can form through multiple mechanisms that activate HLA-specific humoral immunity.

- **Pregnancies**

The risk of allo-sensibilization ↑ pregnancies number
Multiparous women vs. males: 30% vs 12% ($p < 0.0001$)

- **Previous transfusion**

Risk > in pts receiving leukodepleted blood products pre-storage blood products with leucodepletion vs pts receiving leukodepleted blood products pre e post storage (19% vs 7%).

- **Natural antibodies**

inflammatory events such as vaccination, infection, or trauma can result in the formation of HLA antibodies, potentially due to cross reactivity or bystander activation



ANTIBODIES



**ANTIGENS/ALLELES HLA
EXPRESSED BY THE DONOR**

*Approximately 30% of transplant candidates are positive for HLA antibody

DSA Prevalence : 3-30% Haplo; 1-10% MUD, 3-7% CBU



Published in final edited form as:

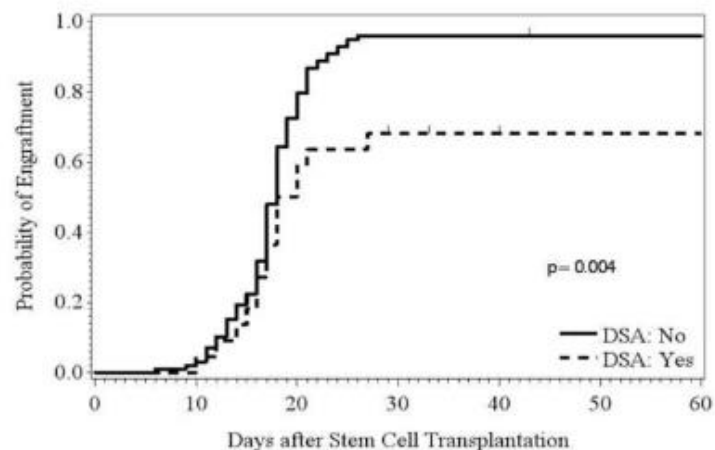
Biol Blood Marrow Transplant. 2015 August ; 21(8): 1392–1398. doi:10.1016/j.bbmt.2015.05.001.

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

Stefan O. Ciurea¹, 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, and Kai Cao³

We hypothesized that complement-binding DSA are associated with GF
122 haploidentical transplant recipients tested prospectively for DSA

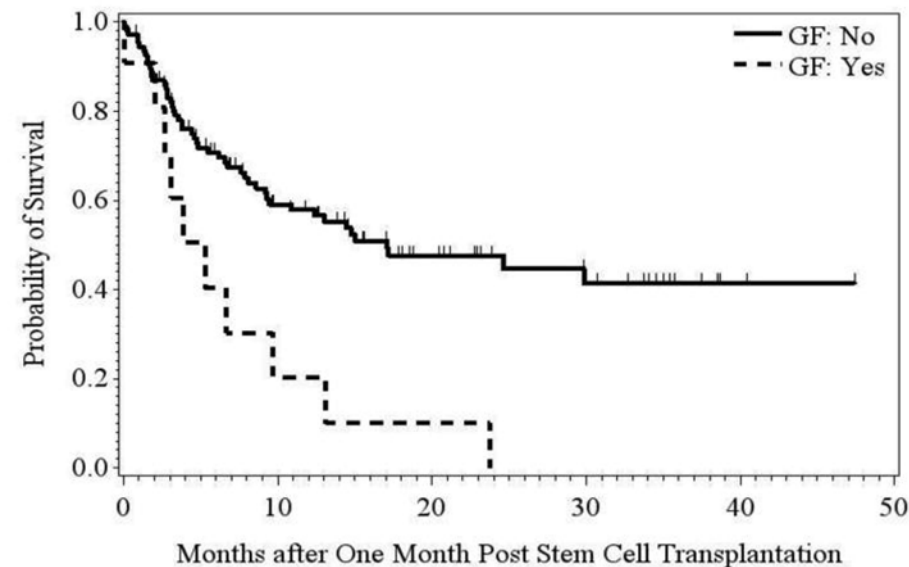
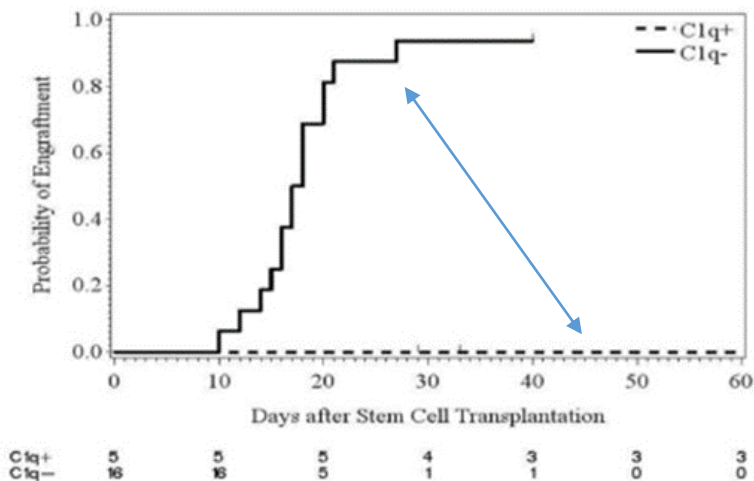
A.



DSA: No	96	96	27	4	4	3	3
DSA: Yes	22	22	11	6	5	4	4

Ciurea SO, et al. Biol Blood Marrow Transplant. 2015

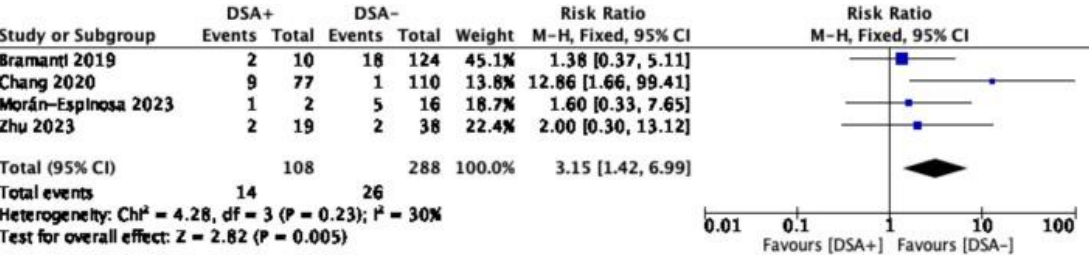
Retrospective C1q testing was done on 22 allosensitized recipients.



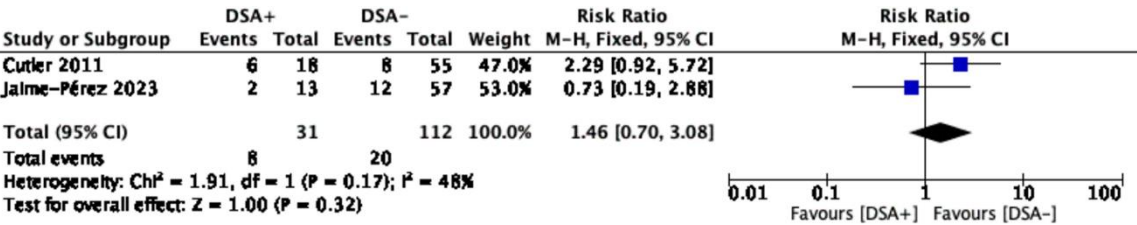
Impacts of donor-specific anti-HLA antibodies on post-transplant clinical outcomes in hematopoietic stem cell transplantation: A systematic review and meta-analysis

Muchen Liu^a, Zhongyu Kang^b, Huan Zhang^{c,*}

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^b Department of Blood Transfusion, Tianjin First Central Hospital, School of Medicine, Nankai University, Tianjin, Nankai, China
^c Department of Hematology, Tianjin First Central Hospital, School of Medicine, Nankai University, Tianjin, Nankai, China



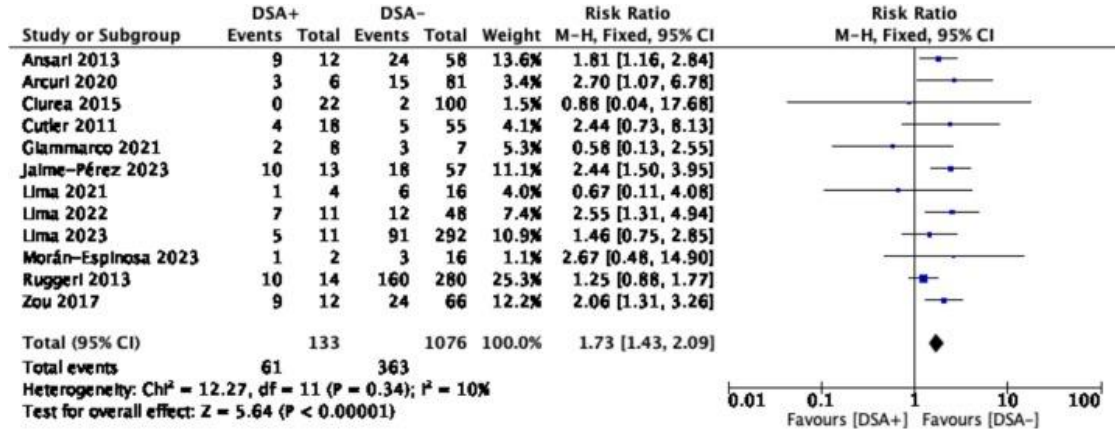
Patients with DSA-positive had a significantly higher risk of **Poor Graft Function** compared to patients with DSA-negative (RR 3.15, 95 % CI 1.42–6.99, $p < 0.05$).



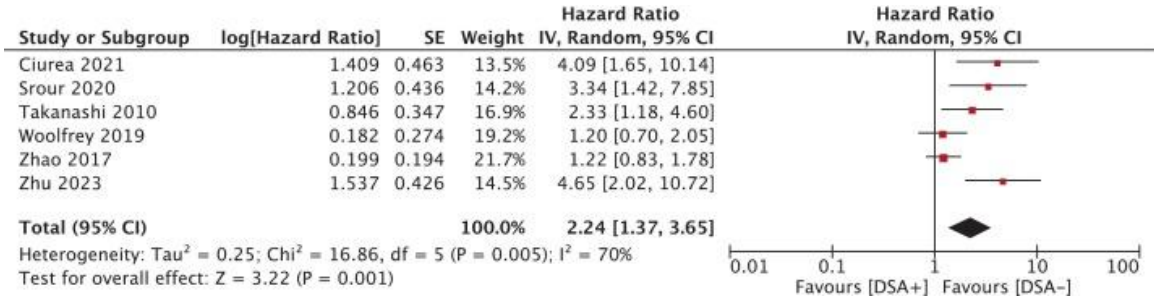
Patients with DSA-positive had a significantly higher risk of **Graft Failure** compared with patients with DSA-negative (RR 3.92, 95 % CI 2.75–5.59, $p < 0.00001$).

The findings demonstrate that patients with DSA positive have a significantly **higher risk of PGF, GF, increased mortality, and reduced OS**. These results underscore the detrimental role of DSAs in HSCT outcomes and highlight the need for effective strategies to mitigate their impacts.

- Comprehensive dataset of 32 studies involving 5555 patients, including 557 DSA-positive and 4998 DSA-negative cases, published between 2009 and 2024 from ten countries.
- Broad age range, with median ages spanning from 0 to 74 years.



Patients with DSA-positive had a higher risk of **death** compared with patients with DSA-negative (RR 1.73, 95 % CI 1.43–2.09, $p < 0.00001$).



The pooled analysis revealed that patients with DSA-positive had significantly lower **OS** compared with patients with DSA-negative (HR = 2.24, 95 % CI 1.37–3.65, $p = 0.001$; Fig. 11).

EDITORIAL

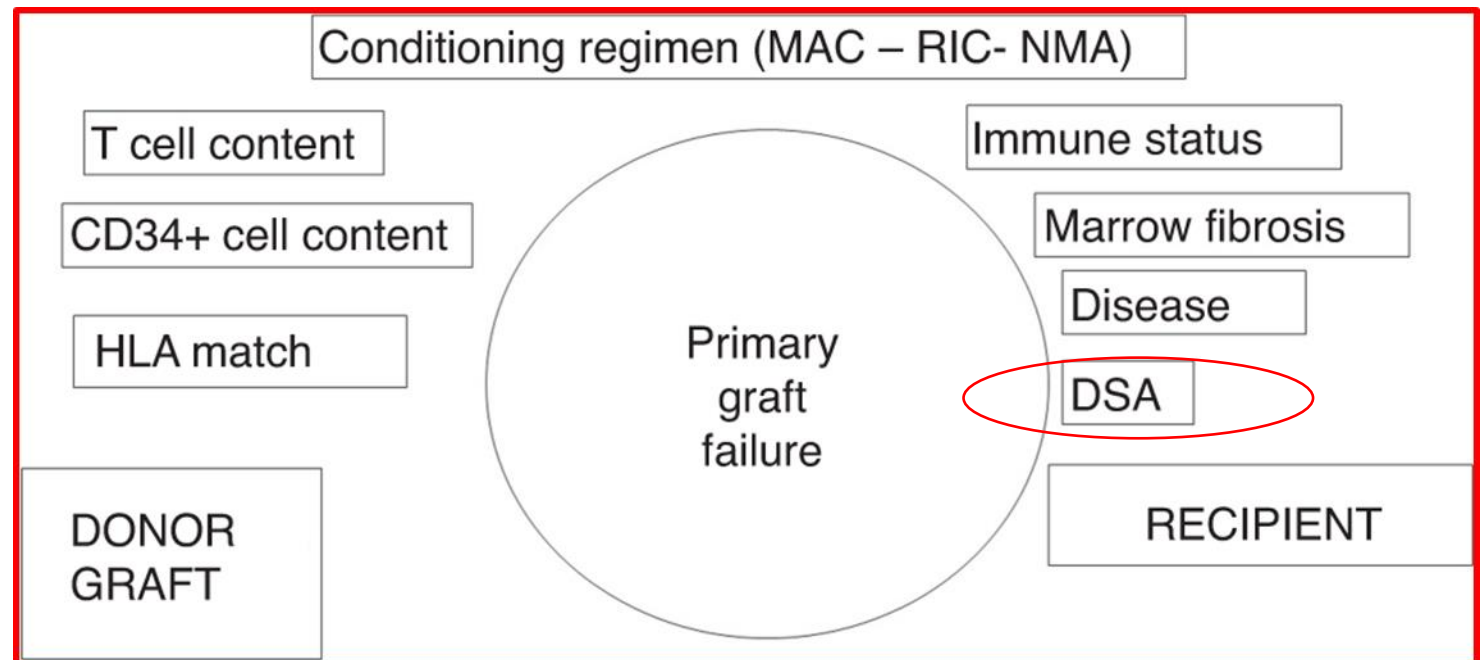
 Check for updates

Donor specific antibodies (DSA): the only risk factor for primary graft failure?

Bacigalupo A; BMT (2024) 59:299–300

Primary graft failure appears to have a multifactorial pathogenesis, and DSA may play a role

Patterson J, Br J Haematol. **1986**;63:221–30
Storb R, Blood. **1989**;74:1139–43.
Solh H, Pediatr Hematol Oncol. **1997**;14:73–7.
Haddad EJ Allergy Clin Immunol. **2013**;131:994–1000.



When to desensitize:

- TEST to use to detect DSA
- Role of MFI value, crossmatch, and C1q complement

How to desensitize

- Possible desensitization strategies

HLA antibodies identification strategies



HLA Antibody Detection Method	Features
Single-antigen bead (SAB) assay	Multiplexed detection of antibodies against ~100 HLA Class I and Class II antigens simultaneously.
Flow cytometric crossmatch	Detection of antibodies that bind to donor HLA present on the cell surface.
CDC crossmatch	Detection of antibodies that bind to donor HLA present on the cell surface and can mediate cell lysis in the presence of complement.

Solid phase immune- assays (Luminex)

Mean Fluorescence intensity

Solid-phase assays may be completed with the addition of Cd4, C3d or Cq1 tests, with the aim to assess antibodies' functions and distinguish complement-fixing from non-complement fixing antibodies.

MFI: Mean fluorescence intensity



Reference	Donor	Test	N	% Anti-HLA+	%DSA+	Graft Outcome (DSA +/DSA -)
Ciurea et al. Transplantation 2009	TCD Haplo SCT Prospective	Luminex SA	24	NA	21 MFI > 500	GF 75 vs 5% (P= 0.0008)
Spellman et al. Blood 2010	MMUD	Flow PRA Luminex SA	115	37	8.7 MFI > 2000	GF 24% vs 1%
Takanashi et al Blood. 2010	Single UCB	Flow PRA Luminex SA	386	23.1	5 MFI ≥800	Patients with DSA had significantly lower EFS and OS compared with no DSA
Brunstein et al. BBMT 2011	Double UCB	Luminex SA	126	41	24% DSA 1 UCB, 12% DSA 2 UCB MFI ≥ 500	GF 17% VS 22%
Cutler et al Blood. 2011	Double UCB	Luminex SA	73	NA	24.6 MFI ≥1000	GF: 18.2 % and 57% in pts with DSAs against 1 and 2 UCB respectively, versus 5.5% in patients without DSAs (P=0.01)
Yoshihara et al. BMT 2012	HaploSCT Prospective	Lab Screen Pra Luminex SA	79	20	14 MFI > 5000	GF 27% vs 4% CI of neutrophil engraftment was 61.9% vs 94.4% (P=0.026)
Ruggeri et al. Blood 2013	SUCB DUCB	Elisa (lamda Antigen Tray Mixed Class I-II) Luminex SA	294	21	4.7 MFI > 1000	GF :56 % vs 23%
Ciurea et al BBMT 2015	HaploSCT Prospective	Luminex SA	122	NA	18 MFI Continuous variable	GF 32% vs 4% (P< 0.001)
Chang et al. J H O 2015	HaploSCT Prospective	NA	345	25.2	11.3 MFI > 500	Primary graft rejection was 20 vs 0.3% (P=0.002) Primary poor graft function was 27.3% vs 1,9% (P=0.003)

26 OCTOBER 2021 • VOLUME 5, NUMBER 20

Treatment of allosensitized patients receiving allogeneic transplantation

Stefan O. Ciurea,^{1,2*} Monir M. Al Malki,^{3,*} Piyannuch Kongtim,² Jun Zou,⁴ Fleur M. Aung,⁴ Gabriela Rondon,¹ Julianne Chen,¹ Michiko Taniguchi,⁵ Salman Otoukesh,² Ausyorn Nademanee,⁶ Stephen J. Forman,² Richard Champlin,¹ Ketevan Gendzekhadze,¹ and Kai Cao^{4,7}

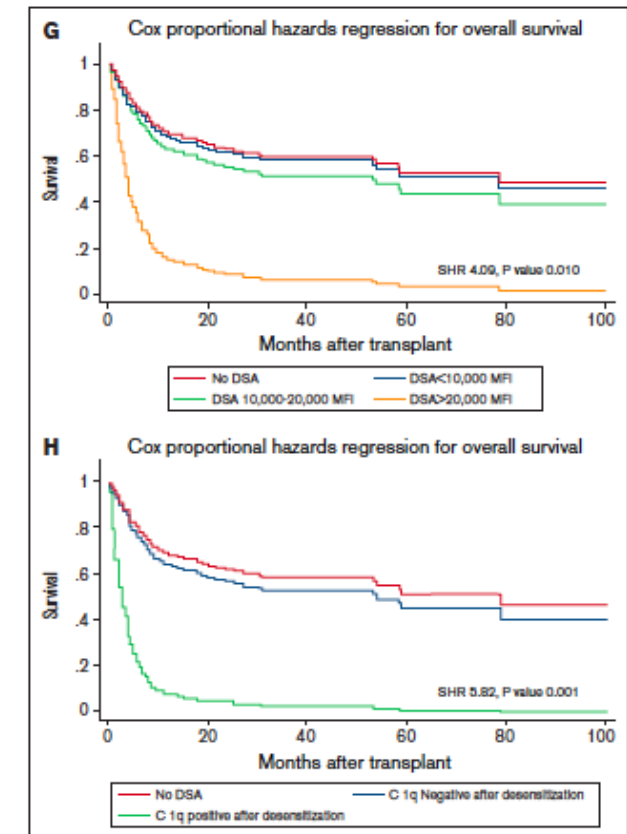
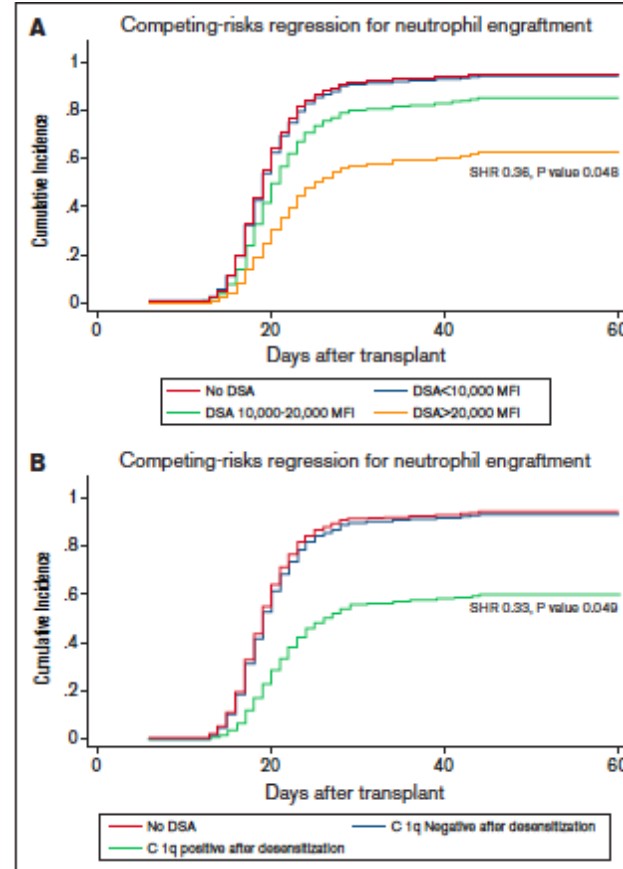
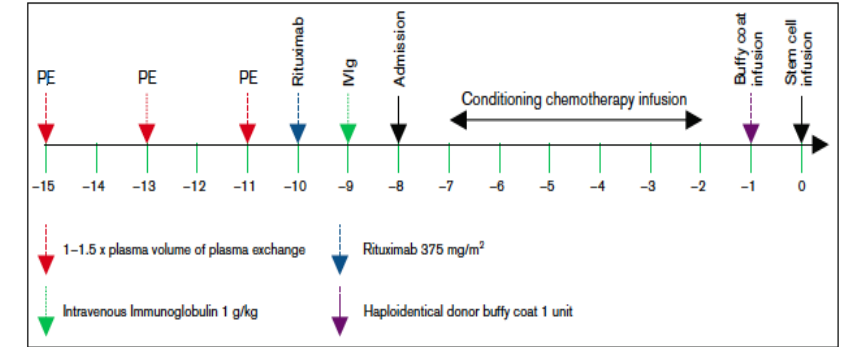
¹Department of Stem Cell Transplantation and Cellular Therapy, The University of Texas MD Anderson Cancer Center, Houston, TX; ²Hematopoietic Cell Transplantation and Cell Therapy Program, Division of Hematology-Oncology, The University of California Irvine, Irvine, CA; ³Department of Hematology and Hematopoietic Cell Transplantation, City of Hope, CA; ⁴Department of Pathology, The University of Texas MD Anderson Cancer Center, Houston, TX; and ⁵HLA Laboratory, City of Hope, Duarte, CA

37 pts, median age 51 yrs

DESENSITIZATION: PE, rituximab, IGEV, irradiated donor buffy coat.

- Pts with DSA > 20 000 MFI and C1q pos, persistent after desensitization minor probability of engraftment, increased mortality and reduced OS
- Pts with DSA < 20.000 MFI e C1q - after desensitization similar outcome to control group

Optional Bortezomid D -25; -22; -19; -16



In conclusion, treatment with PE, rituximab, IVIg, and donor buffy coat is effective in promoting engraftment in patients with DSAs $\leq$ 20 000 MFI



Haploidentical

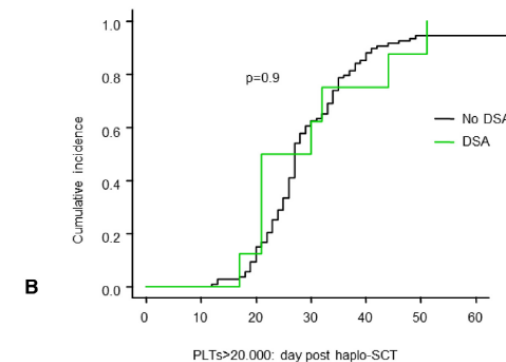
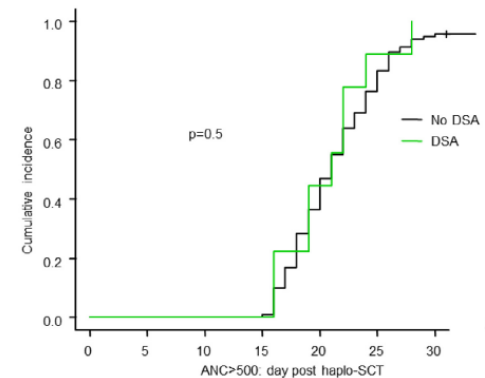
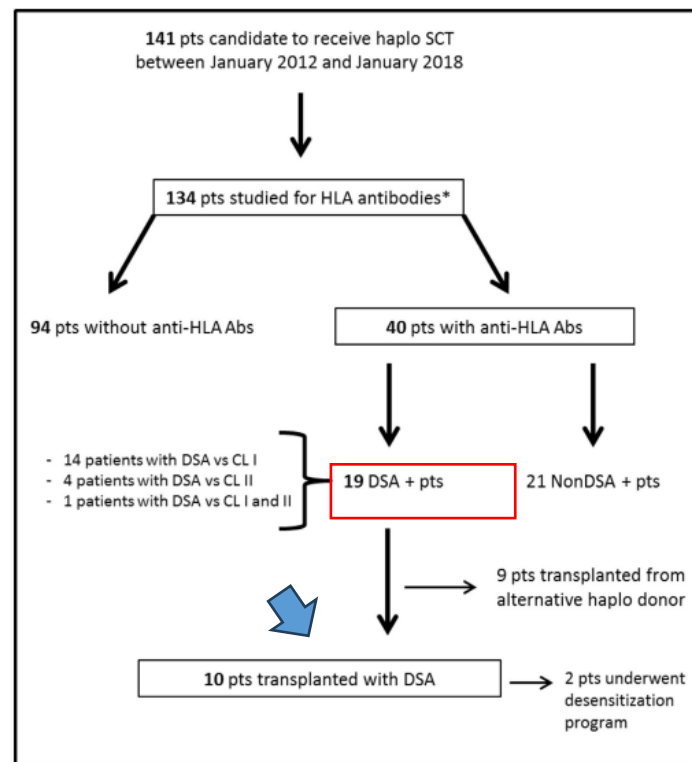
Donor-Specific Anti-HLA Antibodies in Haploidentical Stem Cell
Transplantation with Post-Transplantation Cyclophosphamide: Risk of
Graft Failure, Poor Graft Function, and Impact on Outcomes

Stefania Bramanti^{1,*}, Valeria Calafiore^{1,*}, Elena Longhi², Jacopo Mariotti¹, Loretta Crespiatico²,
Barbara Sarina¹, Chiara De Philippis¹, Angela Nocco², Armando Santoro¹, Luca Castagna¹

¹ Bone Marrow Unit, Humanitas Cancer Center, Rozzano, Milan, Italy

² Laboratory of Transplant Immunology, IRCCS Ca' Granda Foundation Maggiore Policlinico Hospital Milan, Italy

- Desensitization treatment was performed in 2 patients with MFI values > 10,000 (1 positive CDCXM): 1 obtained MFI reduction; 1 no reduction, early death.
- 8 patients who were not desensitized despite DSA positivity:
6 had an MFI between 1000 and 3000
2 had a moderate/high DSA level between 3000 and 10,000 MFI, with negative CDCXM results. Notably, only 2 of these patients had received a MAC regimen before transplantation.



*The presence of low-level DSA in the absence of desensitization did not correlate
with the risk of developing graft failure and poor graft function.*



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

Stefan O. Ciurea¹, Kai Cao¹, Marcelo Fernandez-Vina², Piyanuch Kongtim³, Monzr Al Malki⁴, Ephraim Fuchs⁵, Leo Luznik⁵, Xiao-Jun Huang⁶, Fabio Ciceri⁷, Franco Locatelli⁸, Franco Aversa⁹, Luca Castagna¹⁰, Andrea Bacigalupo¹¹, Massimo Martelli¹², Didier Blaise¹³, Rupert Handgretinger¹⁴, Denis-Claude Roy¹⁵, Paul O'Donnell¹⁶, Asad Bashey¹⁷, Hillard M. Lazarus¹⁸, Karen Ballen¹⁹, Bipin N. Savani²⁰, Mohamad Mohty²¹, Arnon Nagler²²

We recommend:

1. DSA testing (by **Luminex platform and/or cell-based assays**) be performed in all candidate patients for haploidentical (or HLA mismatched) donor transplants;
2. If DSA >1,000 MFI, **C1q testing and/or cell-based assays must be done to further assess the risk to the allograft**
3. DSA testing should be **incorporated in donor selection prior to transplantation**; if DSA >1,000 MFI in the absence of an alternative suitable donor, it is recommended that patients undergo **desensitization** therapy, especially with high DSA levels (>5,000 MFI) and/or C1q positive, which pose a very high risk to the allograft;
4. The choice of desensitization protocol may be based on **prior local experience**.

American Society of transplantation and cell therapy



Transplantation and
Cellular Therapy

journal homepage: www.astctjournal.org



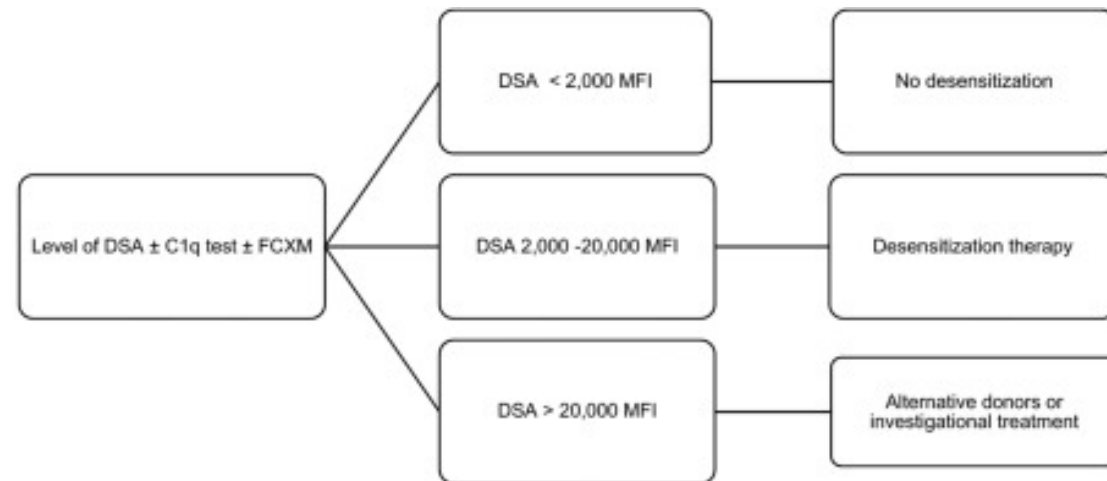
Guideline

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

Piyanuch Kongtim¹, Pongthep Vittayawacharin¹, Jun Zou², Samer Srour³, Brian Shaffer⁴, Roman M. Shapiro⁵, Ankur Varma⁶, Joseph McGuirk⁷, Bhagirathbhai R. Dholaria⁸, Shannon R. McCurdy⁹, Amy E. DeZern¹⁰, Nelli Bejanyan¹¹, Asad Bashey¹², Sabine Furst¹³, Luca Castagna¹⁴, Jacopo Mariotti¹⁵, Annalisa Ruggeri¹⁶, Rebeca Bailen¹⁷, Takanori Teshima¹⁸, Huang Xiao-Jun¹⁹, Carmen Bonfim²⁰, Fleur Aung²¹, Kai Cao²¹, Paul A. Carpenter²², Mehdi Hamadani²³, Medhat Askar^{24,25}, Marcelo Fernandez-Vina²⁶, Alin Girnita²⁷, Stefan O. Ciurea^{1,*}

Kongtim P, et al. Transplant Cell Ther. 2024

- To optimize donor cell engraftment, graft function and survival, a donor without corresponding HLA is preferred for a recipient with anti-HLA antibodies, in addition to other donor-related factors affecting transplant outcomes. (Grade of recommendation: B, Levels of evidence 2++)
- While the optimal strategy requires further study, DSA desensitization therapy is required to promote hematopoietic engraftment and may lead to improved survival for recipients with DSA, when a suitable alternative donor without the corresponding HLA is unavailable. (Grade of recommendation: C, Levels of evidence 2+)
- Higher DSA levels are associated with poor graft function, graft failure, and worse survival. A DSA level >1,000 MFI for CBT and >2,000 MFI for haploidentical and unrelated HSCT might serve as a threshold to initiate desensitization. (Grade of recommendation: C, Levels of evidence 2+)





STRATEGIE DI DESENSIBILIZZAZIONE

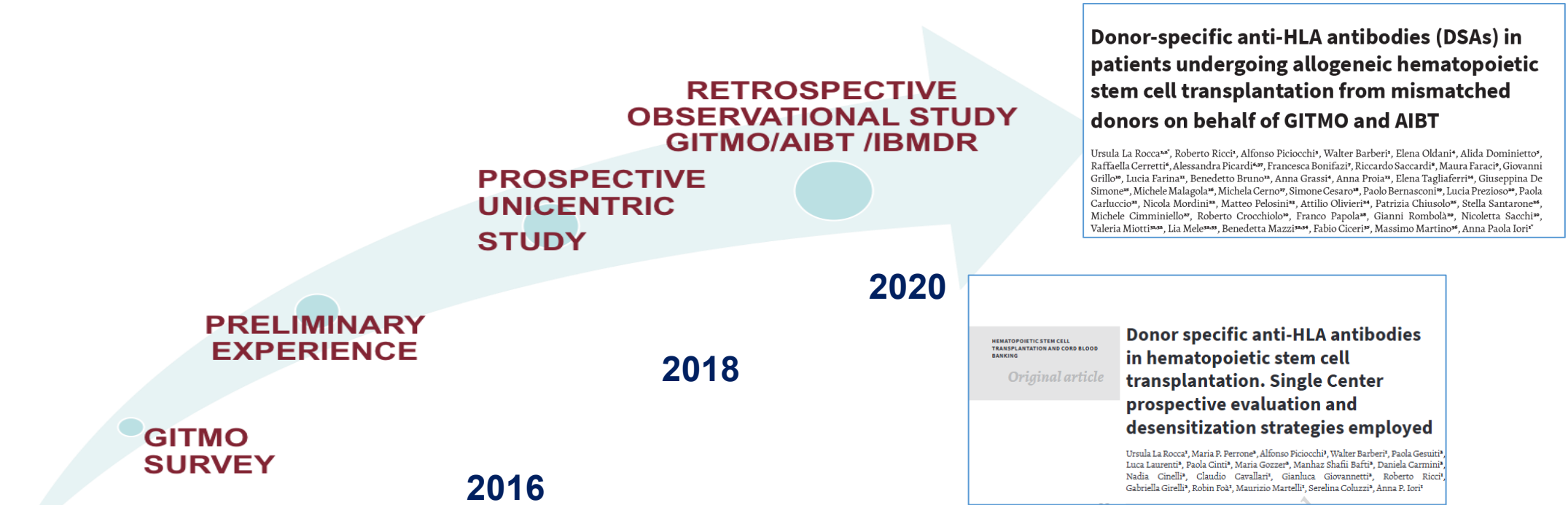
REFERENCE	DONOR TYPE (Nr. of cases)	ANTI-HLA TEST	DESENSITIZATION	DSA POST-DT	OUTCOME
Barge et al. 1989	HAPLO (1)	CDC	PP (2 cycles)	NA	GF
Maruta et al. 1991	MMRD (1)	AHG-CDC	CyA /Methylprednisolone 1 week PP DLI	Negative XM	Engraftment
Ottinger et al. 2002	MMRD (2)	DTT-CDC	PP dedicated PLTs transfusion	1 pt -> negative XM 1 patient positive XM	Engraftment GF
Pollack et al. 2004	MMRD (1)	FCXM	PLTs transfusion PP IVIG	Antibodies disappearance at 86 days after HSCT	Engraftment after II HSCT
Norimatsu et al. 2005	MMRD (1)	AHG-LCT	Rituximab (weekly- 4 administrations) dedicated PLTs transfusions (40 units)	Negative AHG-LCT	Engraftment
Ciurea et al. 2009	HAPLO (4)	Luminex MFI > 500	2 weekly doses Rituximab (375 mg/mq) PP (2 cycles)	1 negative 1 low titer 2 high titer	DSA negative and low titer engraftment 2 pt with high titer GF
Yoshihara et al. 2012	HAPLO (5)	Luminex MFI > 500	PP + Rituximab (2) PLTs Transfusions (2) Bortezomib + Dexamethasone (1)	Reduction (2) Reduction (2) Moderate Reduction (1)	All engrafted
Ciurea et al. 2015	HAPLO (12)	Luminex MFI >500	3 PP + Rituximab (1 dose 375 mg/mq) + IVIG 1 g/Kg Kg + donor's buffy coat infusion (5) PP+ Rituximab (1 dose 375 mg/mq) + IVIG 1 g/ (7)	All Pts cleared DSAs after HSCT 5 Pts were C1q positive after treatment	Pts C1q positive after treatment -> GF Pts C1q negative after treatment engrafted
Leffell et al. 2015	HAPLO (13) MMUD (2)	Luminex MFI>1000	PP + IVIG 100 mg/Kg	Mean DSAs Reduction 64.4% 1 pt did not reduce DSAs	All Pts engrafted

STRATEGIE DI DESENSIBILIZZAZIONE

REFERENCE	DONOR TYPE (Nr. of cases)	ANTI-HLA TEST	DESENSITIZATION	DSA POST-DT	OUTCOME
Zhang R et al. 2020	Haplo (N=5)	MFI > 500	2 U of donor apheresis PLT D-1 + R 375 mg/m2 single dose 1-2 weeks prior to conditioning regimen (if DSA class II positive)	Significant decrease in 5/5	5/5 (100%)
Bailen et al. 2021	Haplo (N=19)	> 1,000	Varied between pts; included R 375 mg/m2, IVIG 0.4 mg/kg/day, MMF 5-10 mg/kg/bid, tacrolimus, PEX, PLT, buffy coat, steroids	Mean reduction 74%	17/19 (89%)
Ciurea S et al. 2021	Haplo (N=37); controls (N=345) - 100% for MFI20,00	> 1,000	PEX 1-1.5 TPV QOD for 3 sessions, starting 1-week prior to conditioning regimen, + R 375 mg/m2 single dose 1 day after PEX completion, + IVIG 1 g/kg 1 dose 1 day after R & donor irradiated buffy coat on	D-1 Mean pre tx DSA - 10,198, Mean DSA post-tx - 5,937 (42% reduction)	100% for MFI < 20,000
Hashem H et al. 2022	Haplo (N=8)	> 3,000	DSA > 8000 MFI: IVIG + R + PEX DSA 3000-8000 MFI: IVIG + R	NA	4/8 (50%)
Shen Y et al. 2023	Haplo (N=13)	> 4,000	IVIG 0.4 g/kg within 72 hours prior to stem cell infusion + R 375 mg/m2 1-2 doses D-16, -9+ HLA-selected PLT infusion 48 hours prior to stem cell infusion DSA reduction	48.3%	13/13 (100%) NE
Altareb M et al. 2023	Haplo (N=5)	> 500	- PEX 1-1.5 TPV for 3 sessions, starting 1-week prior to conditioning regimen, + R 375 mg/m2 single dose 1 day after PEX completion. + IVIG 1 g/kg 1 dose 1 day after R + donor irradiated buffy coat on D-1	Significant decreased in 3/3	5/5 (100%)

Nel corso degli anni, i diversi gruppi hanno iniziato a porre maggiore attenzione al valore di MFI, riservando trattamenti ridotti a condizioni caratterizzate da MFI più bassi,

DSAs : A STEPWISE PROJECT TO ESTABLISH A BETTER DEFINITION OF THEIR ROLE AND A DESENSITIZATION STRATEGY



GITMO SURVEY

2015

PRELIMINARY EXPERIENCE

2016

PROSPECTIVE UNICENTRIC STUDY

2018

**RETROSPECTIVE OBSERVATIONAL STUDY
GITMO/AIBT /IBMDR**

2020

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

Ursula La Rocca^{1,2}, Roberto Ricci³, Alfonso Piciocchi⁴, Walter Barberi⁵, Elena Oldani⁶, Alida Dominiotto⁷, Raffaella Cerretti⁸, Alessandra Picardi^{9,10}, Francesca Bonifazi¹¹, Riccardo Saccardi¹², Maura Faraci¹³, Giovanni Grillo¹⁴, Lucia Farina¹⁵, Benedetto Bruno¹⁶, Anna Grassi¹⁷, Anna Proia¹⁸, Elena Tagliaferri¹⁹, Giuseppina De Simone²⁰, Michele Malagola²¹, Michela Cerno²², Simone Cesaro²³, Paolo Bernasconi²⁴, Lucia Prezioso²⁵, Paola Carluccio²⁶, Nicola Mordini²⁷, Matteo Pelosini²⁸, Attilio Olivieri²⁹, Patrizia Chiusolo³⁰, Stella Santaroni³¹, Michele Cimminiello³², Roberto Crocchiolo³³, Franco Papola³⁴, Gianni Rombola³⁵, Nicoletta Sacchi³⁶, Valeria Miotti^{37,38}, Lia Mele^{39,40}, Benedetta Mazzi^{41,42}, Fabio Ciceri⁴³, Massimo Martino⁴⁴, Anna Paola Iori⁴⁵

HEMATOPOIETIC STEM CELL TRANSPLANTATION AND CORD BLOOD BANKING

Original article

Donor specific anti-HLA antibodies in hematopoietic stem cell transplantation. Single Center prospective evaluation and desensitization strategies employed

Ursula La Rocca¹, Maria P. Perrone², Alfonso Piciocchi³, Walter Barberi⁴, Paola Gesuiti⁵, Luca Laurenti⁶, Paola Cinti⁷, Maria Gozzer⁸, Manhaz Shafii Bafti⁹, Daniela Carmini¹⁰, Nadia Cinelli¹¹, Claudio Cavallari¹², Gianluca Giovannetti¹³, Roberto Ricci¹⁴, Gabriella Girelli¹⁵, Robin Foà¹⁶, Maurizio Martelli¹⁷, Serelina Coluzzi¹⁸, Anna P. Iori¹⁹

Bone Marrow Transplantation (2019) 54:1717–1720
<https://doi.org/10.1038/s41409-019-0497-1>

EBMT

CORRESPONDENCE

Anti-HLA donor-specific antibodies in allogeneic stem cell transplantation: management and desensitization protocol

Ursula La Rocca¹ · Maria Paola Perrone² · Alfonso Piciocchi³ · Paola Cinti² · Walter Barberi¹ · Maria Gozzer² · Mahnaz Shafii Bafti² · Giovanni Fernando Torelli¹ · Luisa Quattrocchi¹ · Paola Gesuiti² · Roberto Lattanzi² · Claudio Cavallari² · Roberto Ricci¹ · Luca Laurenti² · Robin Foà¹ · Gabriella Girelli² · Anna Paola Iori¹

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Anti-HLA donor-specific antibodies in allogeneic stem cell transplantation: management and desensitization protocol

Ursula La Rocca¹ · Maria Paola Perrone² · Alfonso Piciocchi³ · Paola Cinti² · Walter Barberi¹ · Maria Gozzer² · Mahnaz Shafii Baftii² · Giovanni Fernando Torelli¹ · Luisa Quattrocchi¹ · Paola Gesuiti² · Roberto Lattanzi² · Claudio Cavallari² · Roberto Ricci¹ · Luca Laurenti² · Robin Foà¹ · Gabriella Girelli² · Anna Paola Iori¹

Received: 4 September 2018 / Revised: 5 December 2018 / Accepted: 2 February 2019
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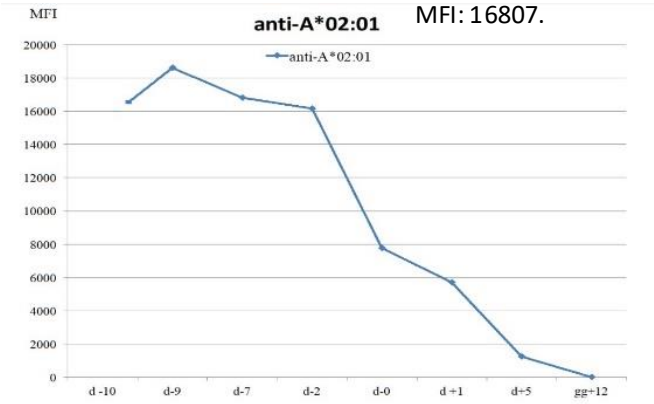
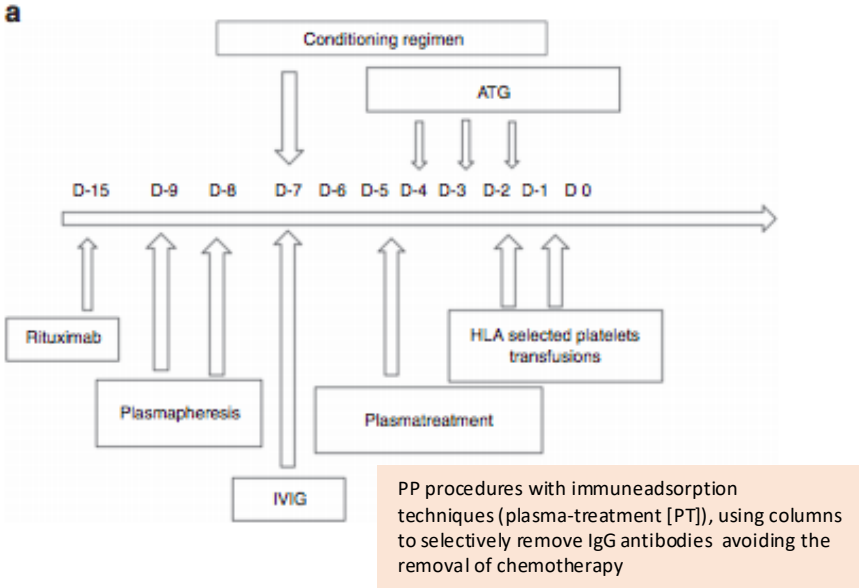
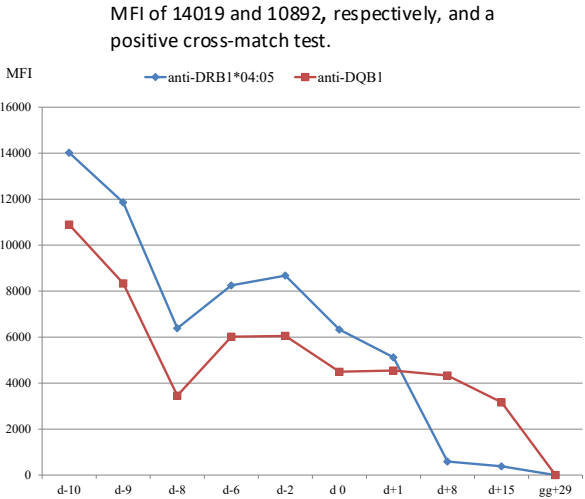
From August 2014 to January 2017, prospectively screened for anti-HLA antibodies **65 consecutive patients** who were candidates for a MMHST MFI > 1000 was considered positive.

Anti-HLA Ab: **20 pz (30%)**
DSA: 4 pz (6.15%) → 2/4 pz: selezione D alternativo
2/4 pz: DESENSIBILIZZAZIONE

La Rocca et al. BMT 2019

IMMUNIZZAZIONE ANTI-HLA IN BASE ALLE TRASFUSIONI

		NO	SI	p
TOTALE (%)		6 (9.2)	59 (90.8)	1.000
Anti-HLA Ab (%)	NEG	4 (66.7)	41 (69.5)	
	POS	2 (33.3)	18 (30.5)	

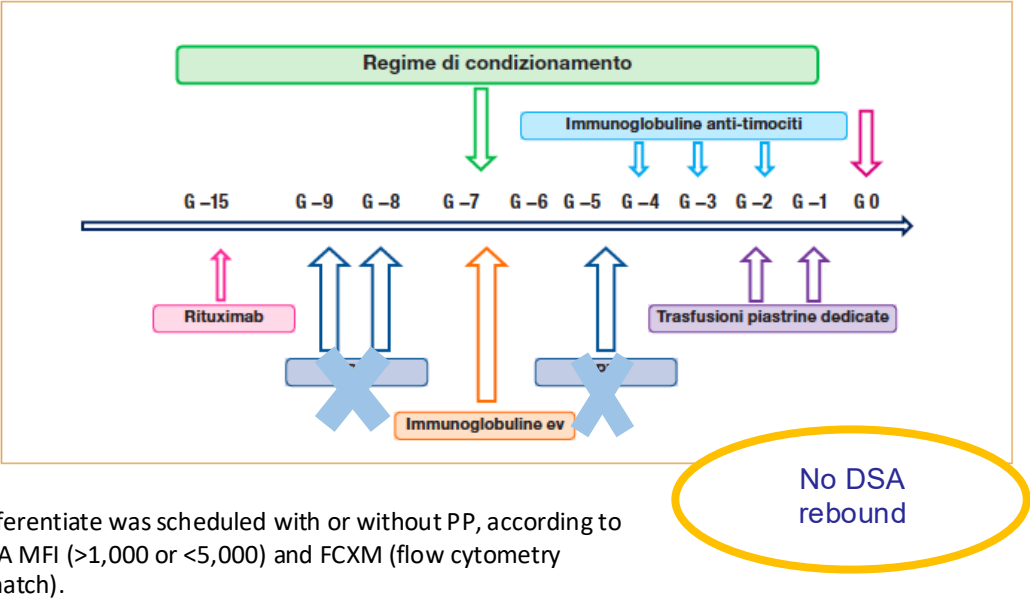
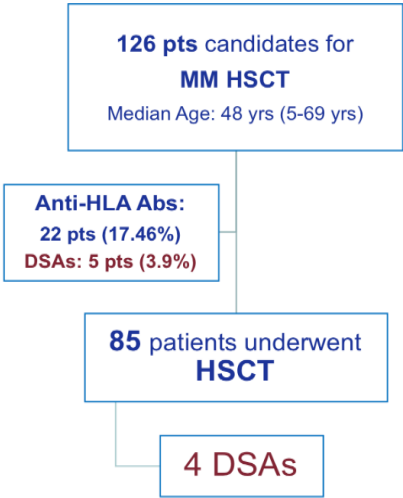


Donor specific anti-HLA antibodies
in hematopoietic stem cell
transplantation. Single Center
prospective evaluation and
desensitization strategies employed

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Aim : efficacy of our strategy for testing DSAs and the
efficacy of the desensitization strategy (DS) employed
between November 2017 and November 2020.

Anti-HLA antibodies	
Characteristic	p-value ¹
Age, median (range)	0.56
Gender, n (%)	0.033
Pregnancies/ n (%)	0.009
Pre-HSCT Blood Transfusions n (%)	0.39
RBC Transfusions, median (range)	0.69
PLT Transfusions, median (range)	0.87
Plasma Transfusions, median (range)	0.72

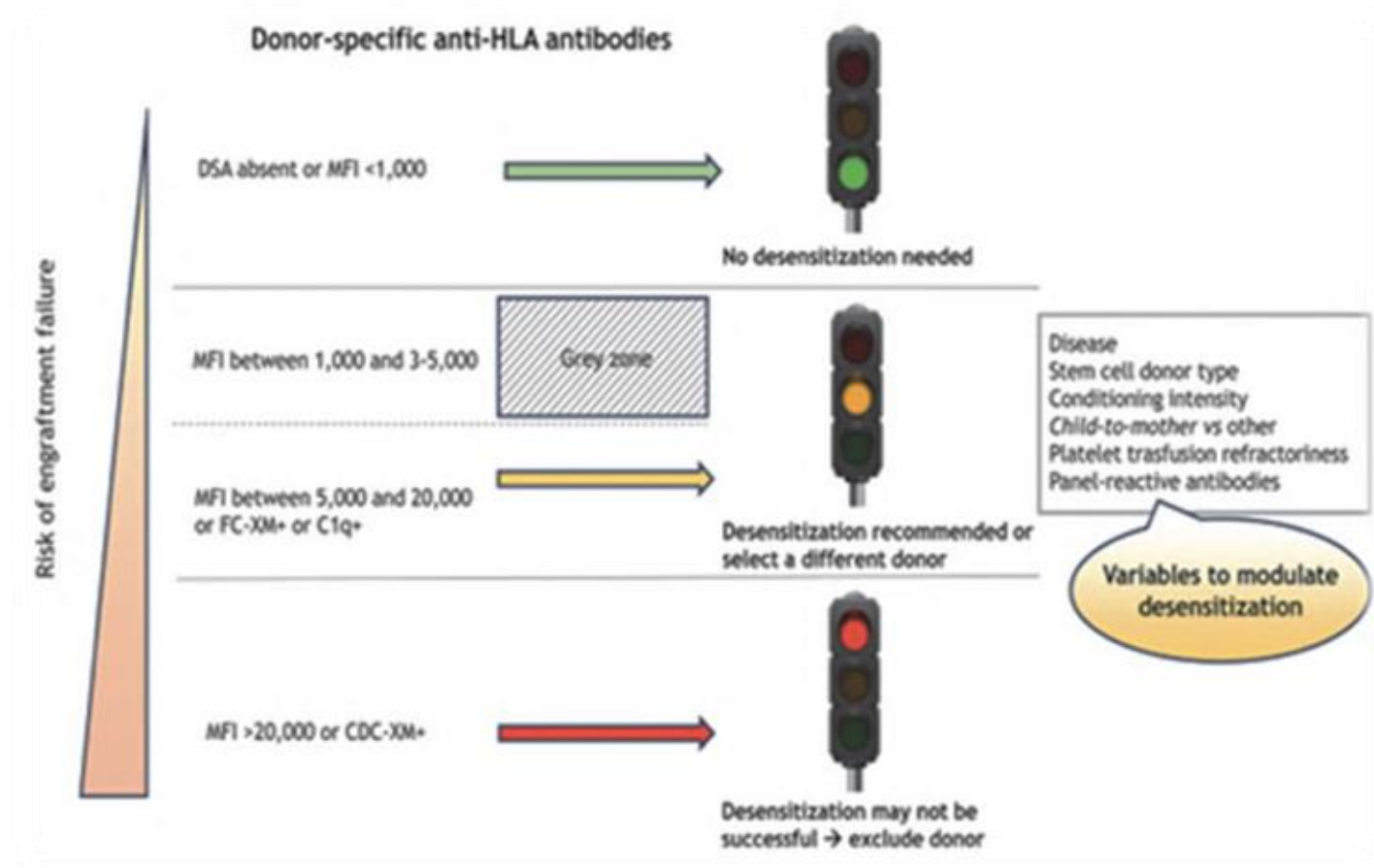


DS differentiate was scheduled with or without PP, according to
the DSA MFI (>1,000 or <5,000) and FCXM (flow cytometry
crossmatch).

GENDER	DONOR	CLASS I DSA MFI	CLASS II DSA MFI	CD34+ X 10 ⁶ /Kg	PMN E	PLTS E	CHIMERIS M D+20	GF	PG F	A- GVHD	F-UP
FEMALE	HAPLO	CW6 1667		3,82	17	25	100,00%	0	0	II	ALIVE
MALE	HAPLO	A2 1109		2,49	18	27	100,00%	0	0	II	ALIVE
FEMALE	HAPLO		DR7 1200	0,58	18	27	100,00%	0	0	0	ALIVE
FEMALE	HAPLO	A2 2263		2,39	15	64	100,00%	0	0	II	ALIVE

Considerazioni

< 1000: No DS
>1000 – 5000: valutare FC-XM/C1q+
>5000: DS
>20.000 DS high intensity



Crocchiolo, Blood Transf 2024

Valutare l'alloimmunizzazione nel contesto clinico specifico, per bilanciare in modo ottimale il rischio di mancato attecchimento con quello di infezioni o recidiva, tenendo in considerazione tutte le variabili.

- ❑ Studio italiano, retrospettivo, osservazionale, multicentrico, spontaneo, non-interventistico, non farmacologico, proposto da GITMO ed AIBT in collaborazione con l'IBMDR
- ❑ Coordinato dalla UOC di Ematologia, Pol. Umberto 1, Università Sapienza .
- ❑ Volto a descrivere gli approcci per la gestione dei pazienti candidati a trapianto con DSA nella realtà dei Centri Trapianto Italiani, e definire una strategia comportamentale propedeutica a studi prospettici.
- ❑ Includente tutti i pazienti sottoposti a TMO di cellule staminali emopoietiche (CSE) mismatched (mm) tra il 2014 ed il 2017.

2014-2017

PERIODO DI ARRUOLAMENTO

804

PAZIENTI VALUTABILI

HSCT da donatori mismatch

CLINICALTRIALS.GOV

NCT04469085

HEMATOPOIETIC STEM CELL TRANSPLANTATION AND CORD BLOOD BANKING

Original article

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Background

Antibodies directed against donor-specific HLA allele(s)/antigen(s) (DSAs) represent a known risk factor for hematopoietic stem cell transplantation (HSCT) engraftment. Still, the overall management needs to be standardized.

Material and methods

GITMO and AIBT ran a survey on DSAs in Italian Transplant Programs including mismatched HSCT performed between January 2014 and June 2017.

Results

One-thousand-thirty-three patients were proposed for the study, 804 were evaluable. Overall, 355 (44%) were screened: 91/355 (25.6%) showed anti-HLA antibodies, 23 DSAs (6.5%). Female gender and at least 4 previous pregnancies showed an impact on alloimmunization. Eleven patients with DSAs underwent desensitization. In seven cases no desensitization was employed. An alternative donor was selected for five patients. Neutrophil and platelet engraftment were obtained in 93.6% and 86.6% of the whole population, respectively, and were statistically associated with the absence of anti-HLA antibodies, ABO match, a higher number of infused nucleated cells and lack of a-GvHD. In addition, significant factors for platelet engraftment were the use of leuco-depleted transfusions, HLA match, younger age of the patient. Graft failure (GF) was associated with bone marrow stem cell source, and a lower number of infused CD34+. The detection of antibodies directed against both HLA classes, donor and patient age, the hematologic and molecular remission at HSCT, HLA match, ANC and PLT engraftment, full donor engraftment within 28 days after HSCT, early and late GF, grade-II a-GVHD showed an impact on OS.

Discussion

Anti-HLA antibodies and DSAs were confirmed as risk factors affecting OS. DSAs were managed with various approaches resulting in stable engraftment in 81.9% of patients. Our study supports the clinical relevance of DSAs detection and management in mmHSCT. A standardized approach of DS is warranted.

Keywords

anti-HLA antibodies, donor selection, engraftment, desensitization strategy.

La Rocca et al. Blood Transfus. 2025

RISULTATI Ricerca anticorpi anti-HLA e DSA, policy di screening

Ricerca anticorpi anti-HLA
355/804

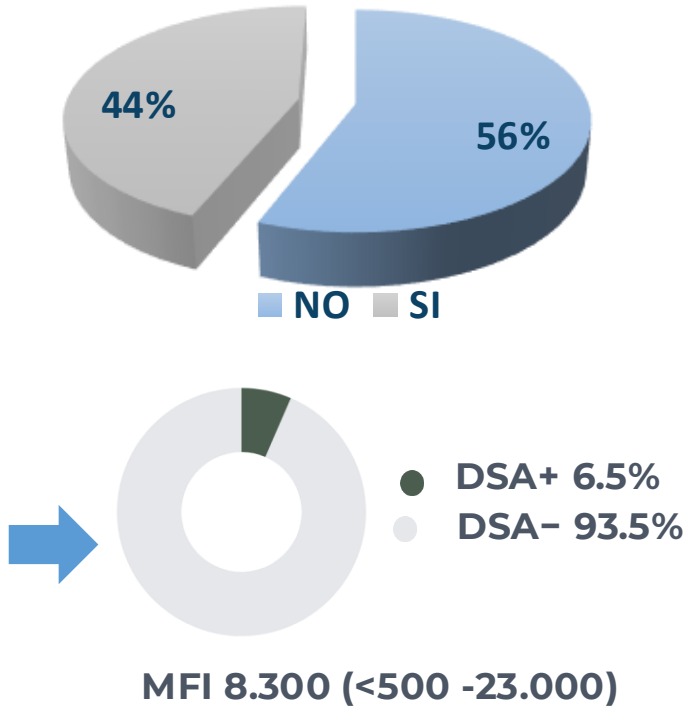
Risultati anti-HLA

Negative 264 (74.3%)
Positive 82 (25%)

- Classe I 42 (12%)
- Classe II 26 (7.3%)
- Entrambe 23 (6.4%)

Metodi utilizzati per la ricerca anticorpale:

- Luminex 335 (94.3%)
- ELISA 17 (4.78%)
- Elisa + Luminex 3 (0.84%)



Complement Activity Evaluation:

- C1q/C3d: 26 (7.6 %)

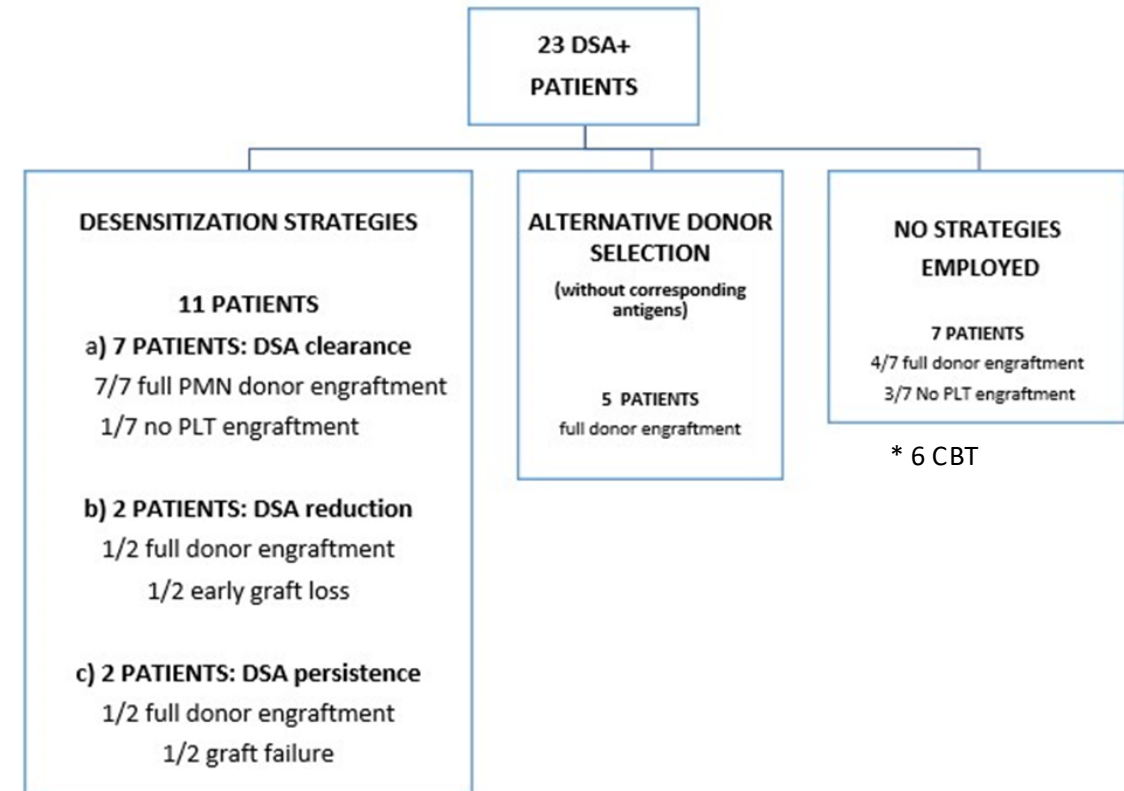
La gestione del paziente positivo a DSA nel trapianto allogenico di CSE

Variabile analizzata	Anti-HLA antibodies screening p-value ¹	Anti-HLA antibodies result p-value ¹
Genere	0.17	0.003
Gravidanze	0.028	0.89
Numero di gravidanze (≥4)	0.25	0.024
Aborti	0.95	0.077
Trasfusioni pre-HSCT	0.007	0.064

¹Pearson's Chi-squared test

Desensitization strategies

- Rituximab (375mg/m²) on day -15, followed by plasmapheresis procedures (PP) on days -9 and -8 and intravenous immunoglobulin (IVIG) on day -7. Selected platelet transfusions were employed in case of antibodies directed against class I HLA.
- PP procedures on days -10, -8, -1.
- PP procedures, using EC30W filters (days not specified).
- Weekly PP procedures and Rituximab 375 mg/m² (repeated for four weeks).
- Rituximab 375 mg/m²/week for 4 weeks, IVIG 1g/Kg/day for 2 consecutive days, followed by the infusion of donor irradiated PLT transfusions.
- Rituximab 375 mg/m² on day -7.
- IVIG followed by selected platelet transfusion in case of antibodies directed against class I HLA.
- PP procedures on two consecutive days followed by IVIG.



We cannot confirm data on DSAs, considering the low number of positive patients included, the low MFI median value observed (8,300; range 257-23,000), and the efficacy of the desensitization strategies used, allowing us to obtain stable engraftment in 9 out of 11 treated patients

CONCLUSIONI



Lo studio GITMO AIBT evidenzia ampia eterogeneità di gestione e di desensibilizzazione dei DSAs nella realtà italiana, seppur i **diversi approcci impiegati** abbiano consentito di ottenere un **attaccamento stabile** nell'81,9% dei pazienti.



Una migliore definizione **patogenetica**, in relazione alle **specificità anticorpali** ed all'**espressione e densità cellulare antigene-specifica** potrebbe consentire la definizione di nuovi, **specifici target terapeutici** per la **desensibilizzazione anticorpale**.



Necessità di **studi prospettici multicentrici**, volti a un miglior **inquadramento** delle risposte ai quesiti ancora aperti, quali l'armonizzazione delle strategie diagnostiche, il **rischio immunologico**, tenendo conto delle altre variabili (**diagnosi, regime di condizionamento e profilassi della GVHD, cut-off MFI**), e la miglior strategia **desensibilizzante** in relazione ai valori di MFI.



E' necessaria una forte collaborazione tra medici **trapiantologi, trasfusionisti e immunogenetisti** per la definizione di schemi di gestione e desensibilizzazione laddove l'**urgenza trapiantologica** e le **caratteristiche della coppia donatore/ricevente prevalgano** sulla possibilità di selezionare un donatore alternativo.



There is a need for prospective multicentric studies to define the role of DSAs in relation to each HLA loci, the MFI cutoff associated with a higher risk of graft rejection, and the efficacy of a desensitization strategy.

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

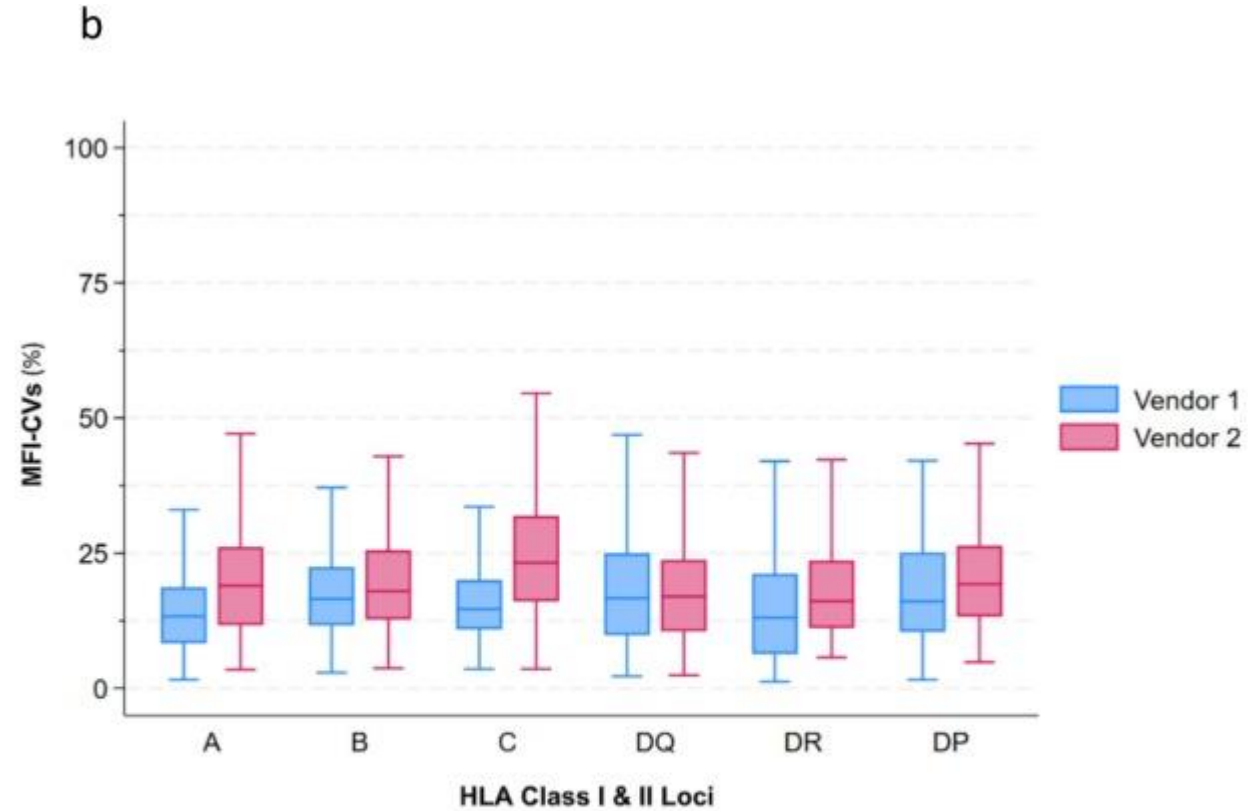
Antonina Piazza^{a,*}, Giovanni Rombolà^{b,*}, Umberto Maggiore^c, Dario Ciappi^d, Emanuele Cozzi^e, Maria Chiara de Stefano^f, Roberto Crocchiolo^g, Andrea Ricci^h, Massimo Cardillo^h, Valeria Miottiⁱ, Giuseppe Feltrinⁱ, Franco Papola^j, on behalf of AIBT Working Group

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Variabilità MFI nei test Luminex tra diversi laboratori e piattaforme commerciali: esiste una **variabilità non trascurabile tra piattaforme commerciali**.

È fondamentale promuovere:

- standard condivisi
- controlli di qualità interlaboratorio
- criteri interpretativi uniformi.



	CVs (%) Vendor 1	CVs (%) Vendor 2
HLA Antigen		
A	13.3	19.0
B	16.5	18.0
C	14.7	23.2
DQ	16.7	17.0
DR	13.1	16.1
DP	16.1	19.3

Studio GITMO: Anticorpi anti HLA donatore specifici (DSAs) nei pazienti candidati a trapianto allogenico mismatched



Associazione Italiana di Immunogenetica e
Biologia dei trapianti

STUDIO GITMO

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

Italiano, Osservazionale, Prospettico, Multicentrico, Spontaneo, Non-interventistico, Non-farmacologico

3w2

Acronimo: GITMO - AIBT DSAs