ACCADEMIA di FORMAZIONE

SIMTI

Il significato della titolazione degli anticorpi in Medicina Trasfusionale: aggiornamento

Il ruolo della titolazione degli anticorpi anti-AB nel trapianto di CSE: impatto sulla gestione del pz e del graft

Francesca Monochio

U.O.C. Immunoematologia e Medicina Trasfusionale,

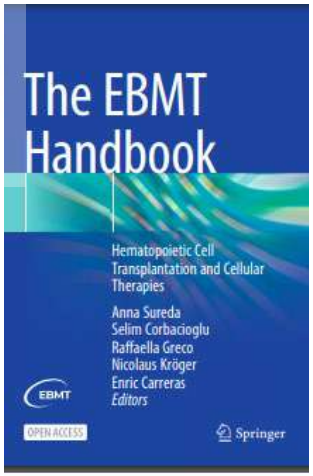
San Giuseppe Moscati - Avellino
Azienda Ospedaliera di Rilievo Nazionale e di Alta Specialità

La sottoscritta, in qualità di Relatrice
dichiara che

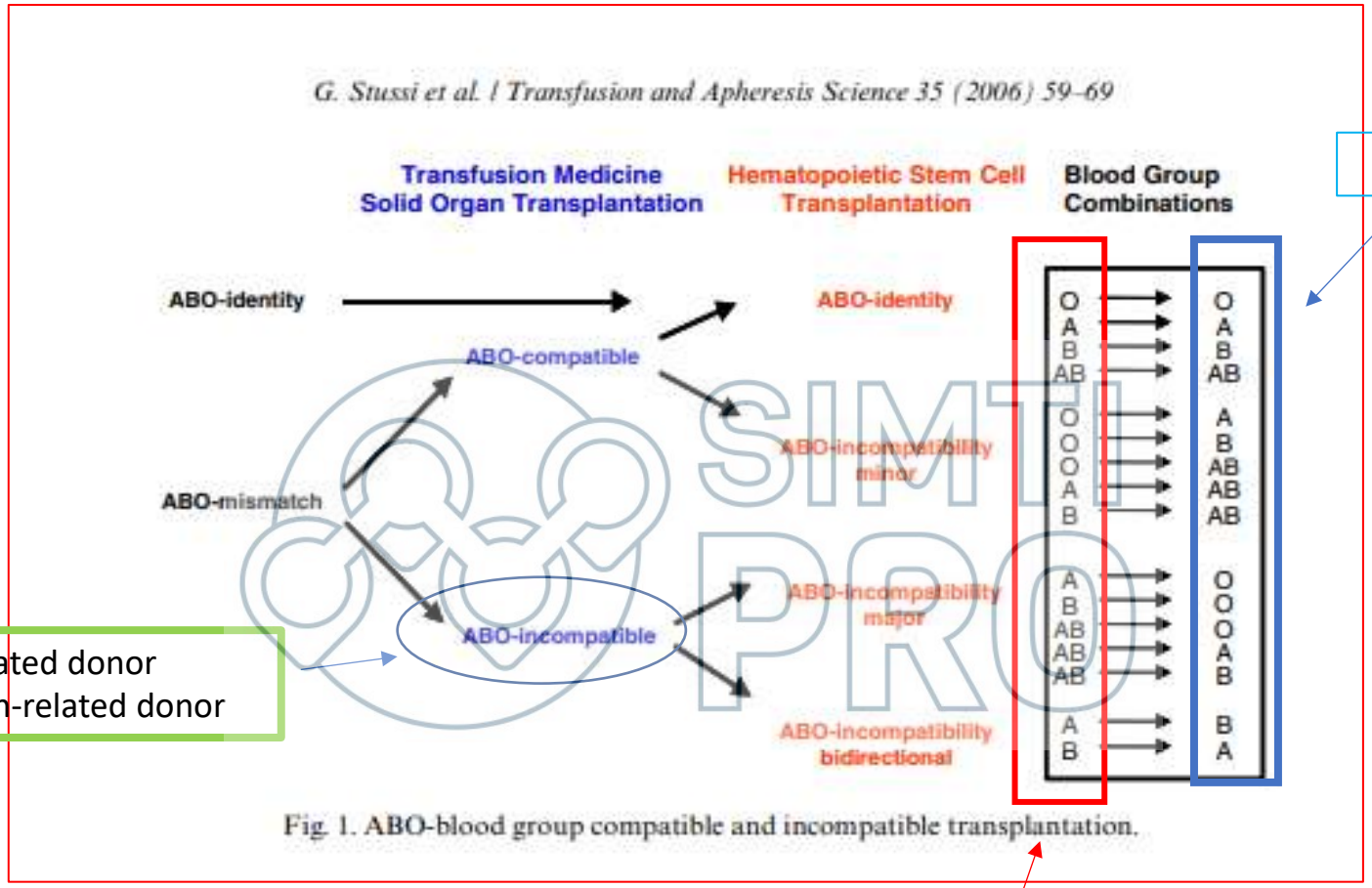
nell'esercizio della Sua funzione e per l'evento in oggetto, NON È in alcun modo portatrice di interessi commerciali propri o di terzi; e che gli eventuali rapporti avuti negli ultimi due anni con soggetti portatori di interessi commerciali non sono tali da permettere a tali soggetti di influenzare le mie funzioni al fine di trarne vantaggio.

Francesca Monochio

Sorgenti CSE		
	BM	PBSC
CD34+	2,4 10^6/Kg	7,3 10^6/Kg
CD3+CD4+	26 10^6/Kg	393 10^6/Kg
CD3+CD8+	18 10^6/Kg	236 10^6/Kg
Recupero PMN >0,5x10^6	21 gg	14 gg
Recupero PLT >20x10^6	22 gg	16 gg
Reticolocitosi > 1%	22 gg	15 gg
GVHDa	+	+++
GVL	+	+++
OS	=	=
FDS	=	=
GVHDc	+	+++
RBC	200-450ml	20-50 ml
Plasma	≥1000 ml	200-500 ml
Raccolta Vantaggi Svantaggi	 Anche Donatore pediatrico Procedura invasiva, autodonazione	Aferesi Mobilizzazione con GCSF + cort ↓T degenza ↓ complicanze infettive Accessi venosi Doppia raccolta No pediatrici
Utilizzo	20%	80%
Malattia	NMD (AA)	MD



Hematopoietic Cell Transplantation and Cellular Therapies



ricevente

30% related donor
50% non-related donor

donatore

Management trapianto CSE ABO INCOMPATIBILE

- Outcome e Complicanze
- Trattamento Graft /Paziente
- Monitoraggio IEM : Metodiche Titolazione IHAs e significato variazione titolo IHAs
- Strategia trasfusionale adeguata

0041-1337/88/4506-1091$02.00/0
TRANSPLANTATION
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Vol. 45, 1091-1094, No. 6, June 1988
Printed in U.S.A.

ABO COMPATIBILITY AND ACUTE GRAFT-VERSUS-HOST DISEASE FOLLOWING ALLOGENEIC BONE MARROW TRANSPLANTATION[1]

A. BACIGALUPO,[2] M. T. VAN LINT, D. OCCHINI, M. MARGIOCCO, G. FERRARI, P. A. PITTALUGA, F. FRASSONI, J. PERALVO, G. LERCARI, F. CARUBIA, AND A. M. MARMONT

Department of Hematology, Ospedale San Martino, and Department of Mathematics, University of Genoa, Genoa, Italy

Original Article

Impact of ABO-blood group incompatibility on the outcome of recipients of bone marrow transplants from unrelated donors in the Japan Marrow Donor Program

Fumihiko Kimura,[1] Ken Sato,[1] Shinichi Kobayashi,[1] Takashi Ikeda,[1,2] Hiroshi Sao,[3] Shinichiro Okamoto,[4] Koichi Miyamura,[5] Shin-ichiro Mori,[6] Hideki Akiyama,[7] Makoto Hirokawa,[8] Hitoshi Ohto,[9] Hiroshi Ashida,[10] and Kazuo Motoyoshi[1] for The Japan Marrow Donor Program

Controverso se incompatibilità ABO possa influenzare outcome trapianto

Engrafment e Recovery leucociti e Plt, **Relapse**, non-relapse mortality **NMR**, GVHD acuta e cronica, Overall Survival **OS** , disease free survival **DFS**, graft failure.

Bacigalupo 2021, Kanda 2009, Kimura 2008, Damodar 2017, Worel 2016.

Transfusion Medicine and Hemotherapy

Review Article

Transfus Med Hemother 2016;43:3–12
DOI: 10.1159/000441507

Received: March 16, 2015
Accepted: July 6, 2015
Published online: October 29, 2015

TRANSPLANTATION AND CELLULAR ENGINEERING

Impact of ABO mismatching on the outcomes of allogeneic related and unrelated blood and marrow stem cell transplantations for hematologic malignancies: IPD-based meta-analysis of cohort studies

Junya Kanda, Tatsuo Ichinohe, Keitaro Matsuo, Richard J. Benjamin, Thomas R. Klumpp, Primoz Rozman, Neil Blumberg, Jayesh Mehta, Sang-Kyun Sohn, and Takashi Uchiyama

ABO-Mismatched Allogeneic Hematopoietic Stem Cell Transplantation

Nina Worel

Department for Blood Group Serology and Transfusion Medicine, Medical University of Vienna, Vienna, Austria

Accepted Manuscript

Title: Donor: Recipient ABO Mismatch Does Not Impact Outcomes of Allogeneic Hematopoietic Cell Transplantation Regardless of Graft Source

Author: Sharat Damodar, Ryan Shanley, Margaret MacMillan, Celalettin Ustun, Daniel Weisdorf

PII: S1083-8791(17)30278-1
DOI: http://dx.doi.org/doi: 10.1016/j.bbmt.2017.02.009
Reference: YBBMT 54582

CSE ABO Incompatibilità	Complicanze	Cause	Misure di prevenzione
Maggiore	Emolisi immediata (durante infusione)	RBC incompatibili IHA ≥32 (2)	RBC deplezione se >20ml (BM no PBSC) PEX albumina/plasma **(2,3,4)**
	Emolisi ritardata (7-14 gg)	Linfociti B residui ricevente	Immunoassorbimento, PEX se titolo IHA anti don ≥ 32
	PRCA (29%) A → 0	Persistenza IHAs anti Don	
Minore	Emolisi immediata	IHA nel plasma donatore	Plasma deplezione BM e PBSC se IHA anti ricevente ≥ 256 RBC exachange group 0 **(2)**
	Emolisi ritardata	Sindrome Linfocita Passeggero **PLS**	
Bidirezionale	Emolisi immediata	IHA Don/Ric	RBC e plasma deplezione
	Emolisi ritardata	IHA Ric. e linf B Don	

1. **Matteocci**, and Luca Pierelli . Review. Immuno-Hematologic Complexity of ABO-Incompatible Allogeneic HSC Transplantation Cells 2024, 13, 814
2. **Worel,** N. ABO-mismatched allogeneic hematopoietic stem cell transplantation. Transfus. Med. Hemotherapy 2016, 43, 3–1
3. **Raimondi**. ABO-incompatible bone marrow transplantation: A GITMO survey of current practice in Italy and comparison with the literature. Bone Marrow Transplant. 2004,34, 321–329.
4**. Balduzzi**. ABO incompatibile graft management in pediatric transplantation. EBMT Pediatric Diseases Working Party. Bone Marrow Transplant. 2021, 56, 84–90.

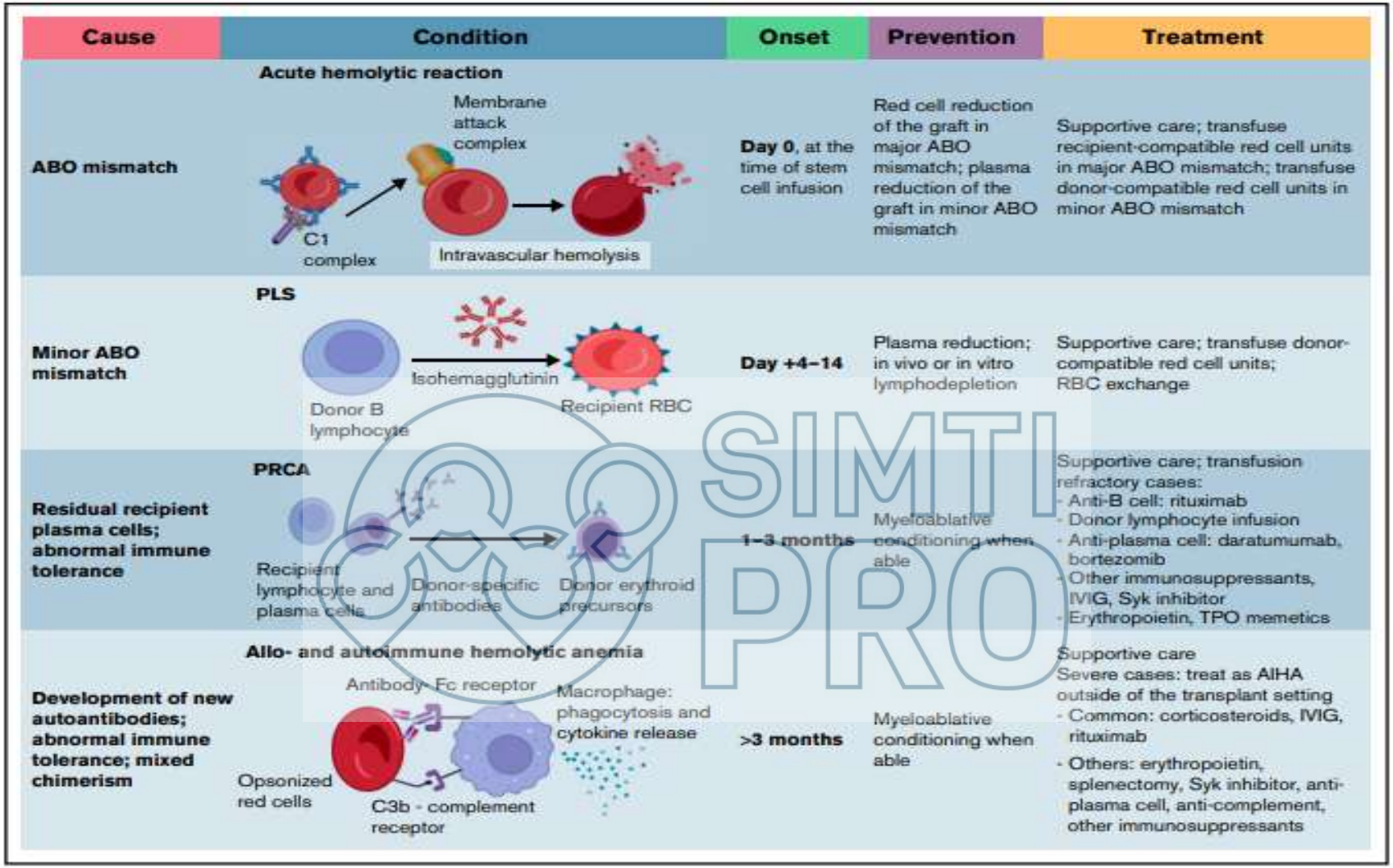


Figure 2. General approach for posttransplantation immune-mediated hemolysis. The graph outlines underlying mechanisms of posttransplantation hemolysis.

Migdady. Posthematopoietic stem cell transplantation immunemediated anemia:. Blood Adv.2022

- **Target Titolo IHAs**

- **Sicuro ricevente < 32**
- **Ricevente ≥ 1:32, deplezione RBC in Graft e PEX ricevente**
- **Donatore 1:256, rimozione plasma nel Graft**

Bone Marrow Transplantation (2004) 34, 321–329

www.nature.com/bmt

ABO-mismatched transplants

ABO-incompatible bone marrow transplantation: a GITMO survey of current practice in Italy and comparison with the literature

R Raimondi[1], M Soli[2], T Lamparelli[3], A Bacigalupo[3], W Arcese[4], M Belloni[2], F Rodeghiero[1], on behalf of the Gruppo Italiano Trapianto di Midollo Osseo (GITMO)

[1]*Department of Haematology, BMT Unit, S Bortolo Hospital, Vicenza, Italy;* [2]*Immunohaematology and Transfusion Service, S Bortolo Hospital, Vicenza, Italy;* [3]*Department of Haematology-Oncology, BMT Unit, S Martino Hospital, Genoa, Italy; and* [4]*Department of Biopathology, University Tor Vergata, Rome, Italy*

Eterogeneità nell'approccio per manipolazione Graft (BM/PBSC) e trattamento ricevente.

Bone Marrow Transplantation
https://doi.org/10.1038/s41409-020-0981-7

EBMT

ARTICLE

ABO incompatibile graft management in pediatric transplantation

Adriana Balduzzi[1] · Halvard Bönig[2] · Andrea Järisch[3] · Tiago Nava[4] · Marc Ansari[4] · Alessandro Cattoni[1] · Giulia Prunotto[1] · Giovanna Lucchini[5] · Gergely Krivan[6] · Toni Matic[7] · Krzyzstof Kalwak[8] · Akif Yesilipek[9] · Marianne Ifversen[10] · Peter Svec[11] · Jochen Büchner[12] · Kim Vettenranta[13] · Roland Meisel[14] · Anita Lawitschka[15] · Christina Peters[15] · Brenda Gibson[16] · Arnaud Dalissier[17] · Selim Corbacioglu[18] · André Willasch[3] · Jean-Hugues Dalle[19] · Peter Bader[3] · on behalf of the EBMT Pediatric Diseases Working Party

Received: 20 June 2019 / Revised: 28 March 2020 / Accepted: 12 June 2020

Monitoraggio immunoematologico IEM e timing ricevente/donatore

Fase pre trapianto 30 gg prima

Incompatibilità maggiore e minore (donatore/ricevente)

ABO/Rh/K

DAT e IAT

Titolo Ab naturali e immuni anti A/B (IHA IgM e IgG)

Ricerca emolisina anti A/B

Incomp. maggiore titolo IHA IgM e IgG pre e post PEX

Fase post trapianto

Incomp. maggiore, ricevente

Titolazione IHA (IgM e IgG) gg +1,+7, +14, +30 ogni 15gg fino 100 gg dall'infusione

Incomp. minore, ricevente

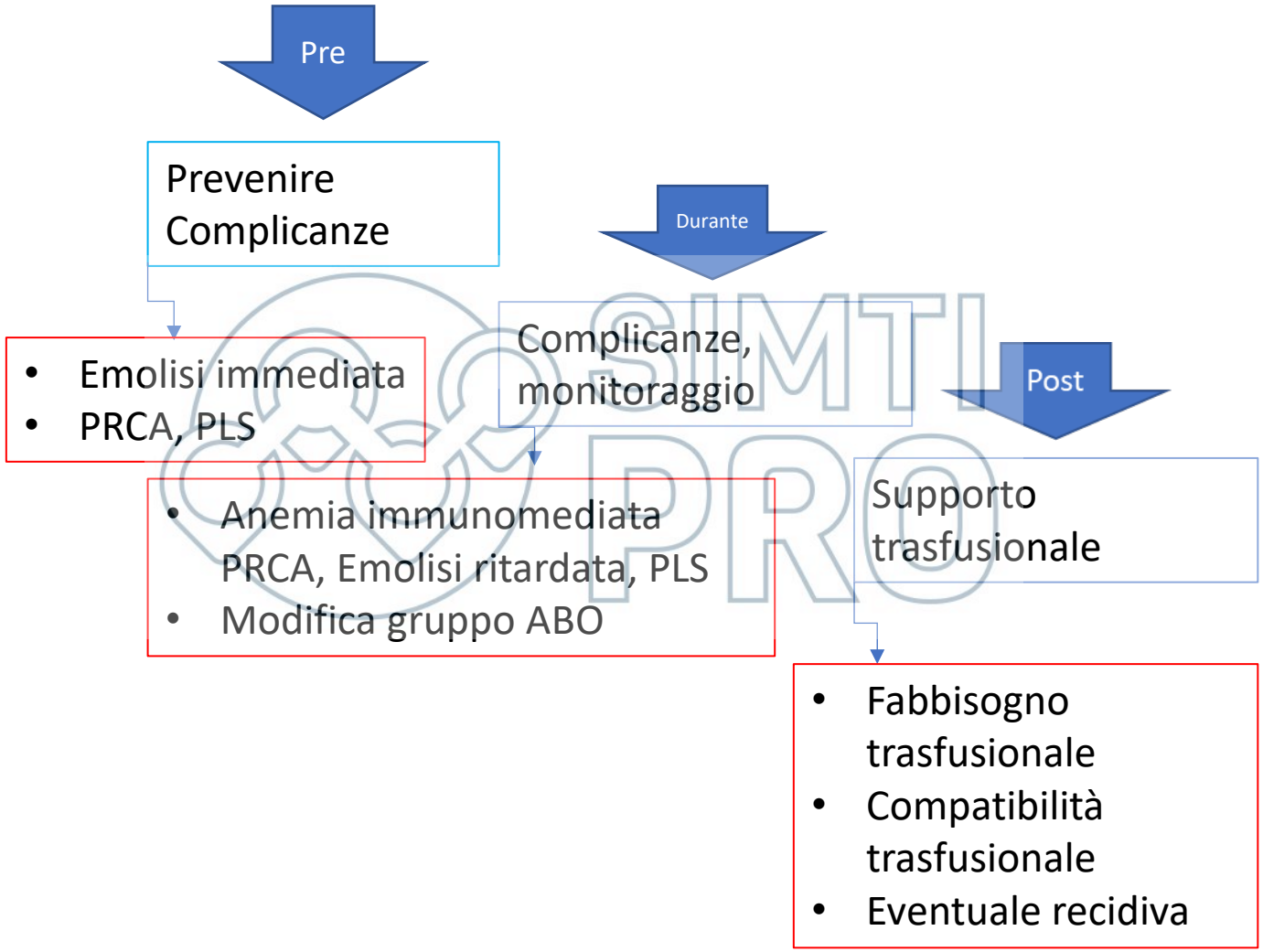
DAT e IAT ogni sett. per 2-3 sett

Se DAT pos, monospecifico ed eluato 1/sett/1mese fino negativizzazione

Tipizzazione ABO/Rh (+30, ogni mese) con corretta valutazione sierologica del campo misto nella tipizzazione diretta e genotipizzazione RBC, ove possibile.

***Matteocci**, and Luca Pierelli . Review Immuno-Hematologic Complexity of ABO-Incompatible Allogeneic HSC Transplantation Cells 2024.*

Titolo IHAs anti-A/B in CSE ABO incompatibile



IMMUNOHAEMATOLOGY

Original article

ABO antibody titres: a multisite comparative study of equivalency and reproducibility for automated solid-phase and haemagglutination titration, and manual dilution with gel column agglutination technology

Dana Schneider[a], Mariangela Vicarioto[a], Serelina Coluzzi[a], Antonella Matteocci[a], Nicoletta Revelli[a], Barbara Foglieni[a], Patrizia Artusi[a], Donatella Londero[a], Anna Quaglietta[a], Giancarla Barrotta[a,b], Domenico Visceglie[a], Giuseppina Portararo[a], Jonella Gilsdorf[a]

[a]Immucor Inc., Norcross, GA, United States of America; [b]Department of Transfusion Medicine, University Hospital of Padua, Padua, Italy; [c]Blood Transfusion Service and Haematology, Umberto I Hospital, Rome, Italy; [d]Transfusion Medicine Unit, San Camillo Forlanini Hospital, Rome, Italy; [e]Department of Transfusion Medicine and Haematology and Lombardy Regional Rare Blood Bank, IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy; [f]Department of Transfusion Medicine and Haematology ASST Lecco, Lecco, Italy; [g]Department of Transfusion Medicine, Azienda Ospedaliera Universitaria Policlinico, Modena, Italy

Background - ABO antibody titres are important in many clinical decisions; however, much variability is observed in titre results. For reliable and reproducible titre results, automated ABO titration methods have been developed. In this 10-site study, we evaluated the equivalency of the automated ABO titration assays on the Galileo NEO, a fully automated blood bank analyzer (Immucor, Inc.) to manual titration with gel Column Agglutination Technology (CAT), as well as the reproducibility of both methods.

Materials and methods - Ten different locations participated in this study. The equivalency study included 70 random samples at each site. The reproducibility study tested the same blinded 30-sample panel at each study site. Anti-A and anti-B IgM and IgG antibody titres were tested with both the automated and manual methods; additionally, dithiothreitol (DTT) treatment was used to inactivate IgM antibodies in the manual CAT method.

Results - The equivalency between CAT manual method and Galileo NEO automated titres at each site ranged from 38 to 88%; equivalency for each

VoxSanguinis

The International Journal of Transfusion Medicine

ISBT International Society of Blood Transfusion

Vox Sanguinis (2020)

DOI: 10.1111/vox.12893

ORIGINAL PAPER

An exploration of the advantages of automated titration testing: low inter-instrument variability and equivalent accuracy for ABO and non-ABO antibody titres relative to tube testing

Brian D. Adkins,[1] Shanna A. Arnold Egloff,[1,2] Kayla Fahey-Ahrndt,[3] Andrea L. Kjell,[3] Claudia S. Cohn[4] & Pampee P. Young[1,5]

[1]Department of Pathology, Microbiology and Immunology, Vanderbilt University Medical Center, Nashville, TN
[2]Department of Veterans Affairs, Tennessee Valley Healthcare System, Nashville, TN
[3]Blood Bank Laboratory, M-Health, Fairview Hospital, Minneapolis, Minnesota
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[5]American Red Cross, Biomedical Services, Washington, D.C.

Received: 30 March 2021 | Revised: 16 May 2021 | Accepted: 16 May 2021

DOI: 10.1111/vox.13160

Metodo titolazione non standardizzato

VoxSanguinis

The International Journal of Transfusion Medicine

ISBT International Society of Blood Transfusion

Vox Sanguinis (2016)

DOI: 10.1111/vox.12399

ORIGINAL PAPER

A WHO reference reagent to standardize haemagglutination testing for anti-A and anti-B in serum and plasma: international collaborative study to evaluate a candidate preparation

S. J. Thorpe,[1] B. Fox,[1] G. Sharp,[1] J. White[2] & C. Milkins[2]

[1]National Institute for Biological Standards and Control (NIBSC), Medicines and Healthcare Products Regulatory Agency, Potters Bar, Herts, UK
[2]UK NEQAS Blood Transfusion Laboratory Practice, Watford, UK

Vox Sanguinis

Background and Objectives The aim of the study was to evaluate a lyophilized serum preparation, 14/300, for its suitability to serve as a World Health Organization (WHO) Reference Reagent to standardize and control haemagglutination titrations for anti-A and anti-B in serum and plasma, in an international collaborative study.

Vox Sanguinis ISBT International Society of Blood Transfusion

ORIGINAL ARTICLE

Challenges in antibody titration for ABO-incompatible renal transplantation

Htar Kahlyar[1] | David Roxby[2] | Tony Badrick[1] | Thiru Vanniasinkam[3]

[1]Royal College of Pathologists of Australasia, Sydney, New South Wales, Australia
[2]College of Medicine and Public Health, Flinders University, South Australia, Australia
[3]School of Biomedical Sciences, Charles Sturt University, New South Wales, Australia

Correspondence
Thiru Vanniasinkam, School of Biomedical Sciences, Charles Sturt University, NSW 2650, Australia.
Email: tvanniasinkam@csu.edu.au

Abstract

Background and Objectives: Accurate and regular monitoring of anti-A and anti-B titres pre- and post-transplantation plays a crucial role in the clinical management of patients receiving ABO-incompatible renal transplants. There is no standardized protocol or an external quality assurance program (EQA) currently available for this testing in Australia. The aim of this study was to investigate the diversity of techniques, test platforms and reagents that were currently in use in various laboratories with the aim of developing an EQA.

Materials and Methods: An online survey was sent to the participants enrolled with the Royal College of Pathologists of Australasia Quality Assurance Program (RCPAQAP) to assess their interest in participation in the pilot study. A total of 24 participants who expressed interest were sent the group O plasma, A_1, A_2 and B cells to perform ABO titration using their own methods.

Problematica aggiuntiva !!!!!!

Titolazione durante utilizzo DARA per PRCA

Leukemia Research Reports 17 (2022) 100314

Contents lists available at ScienceDirect

Leukemia Research Reports

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

Case report

Daratumumab as a Frontline Immunosuppression for Pure Red Cell Aplasia after Major ABO-mismatched Allogeneic Hematopoietic Stem Cell Transplantation

Thiti Asawapanumas [a,b,*], Chantiya Chanswangphuwana [a,b], Phandee Watanaboonyongcharoen [c], Ponlapat Rojnuckarin [a,b], Udomsak Bunworasate [a,b]

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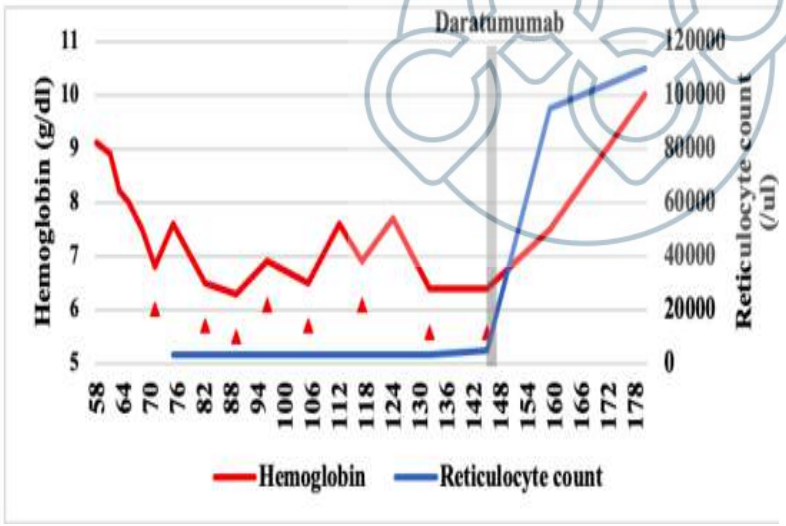
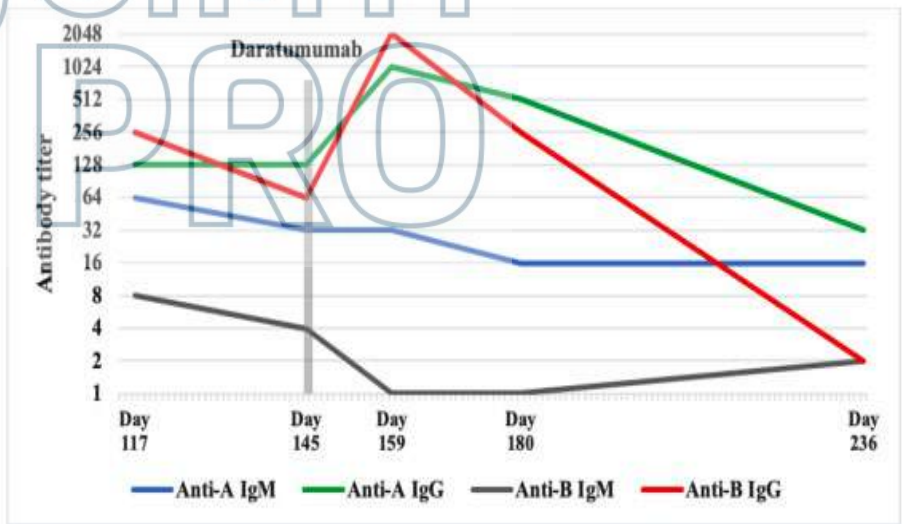
[b] Research Unit in Translational Hematology, Chulalongkorn University, Bangkok, Thailand
[c] Department of Laboratory Medicine, Faculty of Medicine, Chulalongkorn University and Transfusion Medicine Unit, King Chulalongkorn Memorial Hospital, Bangkok, Thailand





Variazione titolo IHA dopo trapianto allogenico CSE ABO-incompatibile

IHA	ABO maggiore A/B/AB→O AB→A/B	ABO minore O→A/B/AB	ABO bidirezionale A↔B
Anti A	Scomparsa 82% 38-138 gg Più lenta nelle mieloidi	Comparsa anti A 11%, 13gg	Scomparsa 82% 38-138 gg Comparsa anti A 11%, 13gg
Anti B	Scomparsa 96% 16-29 gg	Nessuna comparsa	Scomparsa 96% 16-29 gg Nessuna comparsa
Persistenza IHAs ricevente: Resistenza plasmacellule al condizionamento	**Scomparsa** più rapida in unrelated , GVHDa, T cell Graft erytroid cell **Ridotta Comparsa** • Immunosoppressione • Presenza di antigeni ABO su tessuti	↑IHAs ricevente predice PRCA Eventuale recidiva ↑IHAs donatore GVHD	

British Journal of Haematology, 2003, 120, 702–710

Changes of isoagglutinin titres after ABO-incompatible allogeneic stem cell transplantation

Je-Hwan Lee,[1] Jung-Hee Lee,[1] Seong-Jun Choi,[1] Shin Kim,[1] Miee Seol,[1] Seog-Woon Kwon,[2] Chan-Jeoung Park,[2] Hyun-Sook Chi,[2] Jung-Shin Lee,[1] Woo-Kun Kim[1] and Kyoo-Hyung Lee[1]
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Received 26 June 2002; accepted for publication 25 September 2002

ARTICLE OPEN

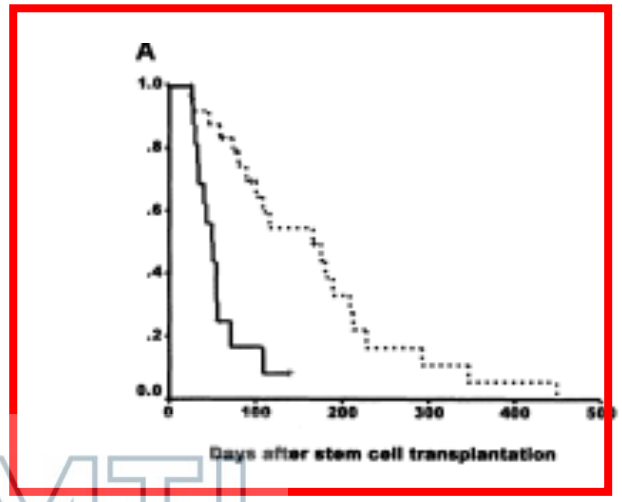
Kinetics of disappearance and appearance of isoagglutinins A and B after ABO-incompatible hematopoietic stem cell transplantation

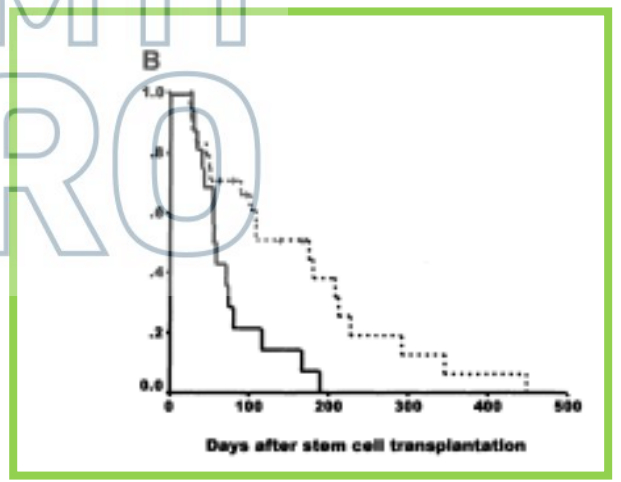
Baptiste Lemaire[1,2✉], Christophe Combescure[3], Yves Chalandon[4], Nicolas Vuilleumier[1] and Sophie Waldvogel Abramowski[1,2]

ABO-incompatible allogeneic hematopoietic stem cell transplantation (HSCT) can be complicated by poor red cell engraftment and hemolysis, both mediated by isoagglutinins. Anecdotally, isoagglutinins indicates an activation of donor's immunity or even relapse. Consequently, the routine monitoring of isoagglutinins could help physicians to predict the risk of complications. The purpose of this study is to investigate the time to disappearance and appearance of isoagglutinins after ABO-incompatible allogeneic HSCT. In a one-year follow-up, data of 136 ABO-incompatible hematopoietic stem cell (HSC) allogeneic transplanted patients were studied, of which 60 had major, 61 minor and 15 bidirectional incompatibility. Survival analyses were conducted and association with hematological diseases, HLA-compatibility and transplantation strategy was investigated. We observed a disappearance of isoagglutinin A in 82.0% of cases at one year with a median and 75th percentile of 38.4 and 138.6 days, respectively. For isoagglutinin B, these same values were 96.4%, 15.9 and 29.1 days, respectively. The appearance of isoagglutinin A occurred in 10.7% of cases. Disappearance of isoagglutinin A was significantly slower in patients with myeloid diseases compared to other diseases. The results of this study provide useful values to detect early risks of preventable immunohematological complications and possibly, in exceptional cases, relapse.

Bone Marrow Transplantation (2022) 57:1405–1410; https://doi.org/10.1038/s41409-022-01737-z

Variables	No. of patients	Time to isoagglutinin disappearance against donor RBCs (median day)	P-value*
Sex			
Male	21	56	0·171
Female	19	109	
Age (years)			
< 35	25	71	0·747
≥ 35	15	116	
Type of stem cell donor			
Sibling	24	166	< 0·001
Unrelated	16	49	
Source of stem cells			
Bone marrow	32	80	0·986
Peripheral blood	8	116	
Conditioning regimen			
BuCy	27	89	0·545
Cy-ATG	5	56	
Bu-Fludara-ATG	8	116	
GVHD prophylaxis			
Cyclosporine plus methotrexate	29	74	0·602
Cyclosporine only	11	116	
ABO incompatibility			
Major	26	116	0·02
Major plus minor	14	51	
Type of isoagglutinins			
Anti-A	21	109	0·151
Anti-B	18	71	
Chimaerism on d 30			
Mixed chimaerism	14	71	0·275
Complete chimaerism	22	74	
Chimaerism on d 60			
Mixed chimaerism	8	80	0·702
Complete chimaerism	25	74	
Chimaerism on d 90			
Mixed chimaerism	10	71	0·381
Complete chimaerism	20	80	
G-CSF administration			
Starting on d 0	4	181	0·473
Starting on d 5	36	80	
Acute GVHD			
No	24	175	0·005
Yes	16	56	
Chronic GVHD			
No	20	109	0·157
Yes	14	56	

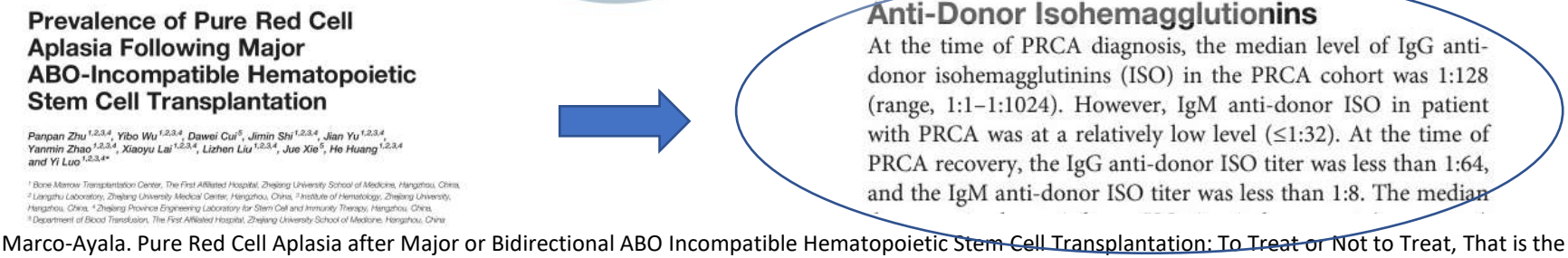




British Journal of Haematology, 2003, 120, 702–710
Changes of isoagglutinin titres after ABO-incompatible allogeneic stem cell transplantation

Pure Red Cell Aplasia (PRCA)

- **Etiologia**: IHA bloccano CFU-E a livello midollare (ABO early presenti)
- **Esordio** :29% Tx incomp. maggiore, +30+120 gg post, ↓ reticolociti, anemia normocitica, assenza di eritroblasti nel midollo
- **Fattori di rischio**: Trapianto A vs O (Incomp. Maggiore), IHA ≥ 64 IgG, Presenza di linfociti B residui o plasmacellule del ricevente RIC (condizionamento intensità ridotta), Donatori fratelli e presenza **IHAs anti-A elevati**
- **IEM**: DAT pos IgG/C3d, eluato pos antiA/B IHAs, Titolazione IHAs
- **Prevenzione**: Riduzione pre-trapianto IHAs anti-donatore. Pex o immunoad. *(Se IHAs anti-donatore presenti 60 gg post-trapianto, la probabilità di eliminazione spontanea è basso).*
- **Trattamento**: supporto trasfusionale, Riduzione graduale farmaci immunosoppressori, Infusioni di leucociti del donatore (DLI), Rituximab (Ab monoclonale diretto contro cellule B CD20+), ATG, DARA



Prevalence of Pure Red Cell Aplasia Following Major ABO-Incompatible Hematopoietic Stem Cell Transplantation

Panpan Zhu[1,2,3,4], Yibo Wu[1,2,3,4], Dawei Cui[5], Jimin Shi[1,2,3,4], Jian Yu[1,2,3,4], Yanmin Zhao[1,2,3,4], Xiaoyu Lai[1,2,3,4], Lizhen Liu[1,2,3,4], Jue Xie[5], He Huang[1,2,3,4]* and Yi Luo[1,2,3,4]*

[1] Bone Marrow Transplantation Center, The First Affiliated Hospital, Zhejiang University School of Medicine, Hangzhou, China, [2] Liangzhu Laboratory, Zhejiang University Medical Center, Hangzhou, China, [3] Institute of Hematology, Zhejiang University, Hangzhou, China, [4] Zhejiang Province Engineering Laboratory for Stem Cell and Immunity Therapy, Hangzhou, China, [5] Department of Blood Transfusion, The First Affiliated Hospital, Zhejiang University School of Medicine, Hangzhou, China

Anti-Donor Isohemagglutinins

At the time of PRCA diagnosis, the median level of IgG anti-donor isohemagglutinins (ISO) in the PRCA cohort was 1:128 (range, 1:1–1:1024). However, IgM anti-donor ISO in patient with PRCA was at a relatively low level (≤1:32). At the time of PRCA recovery, the IgG anti-donor ISO titer was less than 1:64, and the IgM anti-donor ISO titer was less than 1:8. The median

Marco-Ayala. Pure Red Cell Aplasia after Major or Bidirectional ABO Incompatible Hematopoietic Stem Cell Transplantation: To Treat or Not to Treat, That is the Question. Bone Marrow Transpl. 2020, 56, 769–778
Worel. ABO-mismatched allogeneic hematopoietic stem cell transplantation. Transfus. Med. Hemotherapy 2016, 43, 3–1

PLS sindrome linfocita passeggero

Eziologia: produzione IHAs linfociti B donatore
Esordio : +5+21 gg, ↓HCT, Aptoglobina, ↑Hb libera e LDH
Fattori Rischio: unrelated donors, ricevente gruppo A, RIC ,ciclosporina per GVHD, RBC ricevente/ produzione di IHA linfociti B donatore (PBSC)
Linfociti B sfuggono controllo T-cell
Prevenzione: riduzione plasma nel graft, inibitore calcineurina
IEM: DAT pos IgG/C3d, eluato pos antiA/B IHAs, Titolazione IHAs
Trattamento: PEX, supporto trasfusionale donatore compatibile, Rituximab

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Taylor & Francis

CASE REPORT

OPEN ACCESS

Passenger lymphocyte syndrome after ABO-incompatible allogeneic hematopoietic stem cell transplantation; dynamics of ABO allo-antibody and blood type conversion

Haruka Teshigawara-Tanabe[a], Maki Hagihara[a], Ayako Matsumura[a], Hiroyuki Takahashi[a], Yuki Nakajima[a], Takuya Miyazaki[a], Aki Kamijo[b], Etsuko Yamazaki[c], Katsumichi Fujimaki[d], Kenji Matsumoto[a] and Hideaki Nakajima[a]

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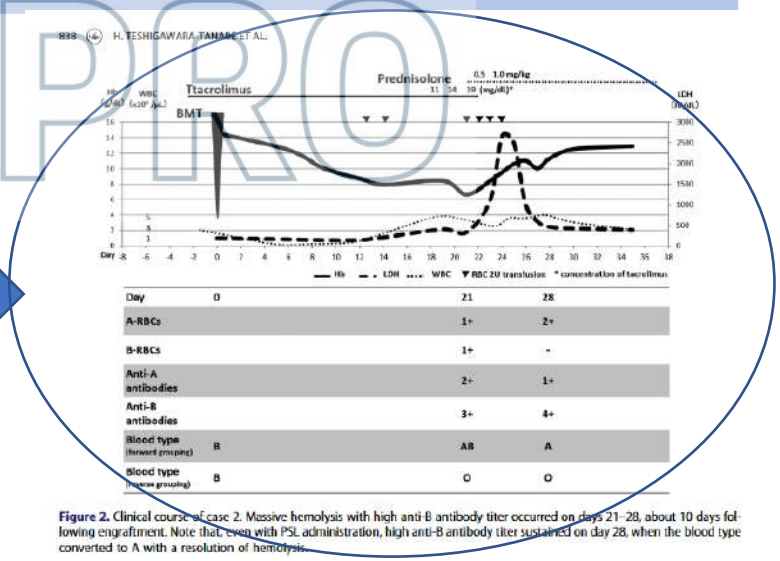
ABSTRACT
Passenger lymphocyte syndrome (PLS) is a specific subtype of graft versus host disease (GVHD) following allogeneic hematopoietic stem cell transplantation (allo-HSCT) characterized by an immune-mediated hemolysis caused by donor-derived B cells. However, precise nature of PLS has not been well characterized due to its rarity. We herein report two cases of PLS following ABO-incompatible HSCT whose clinical course and dynamics of anti-ABO allo-

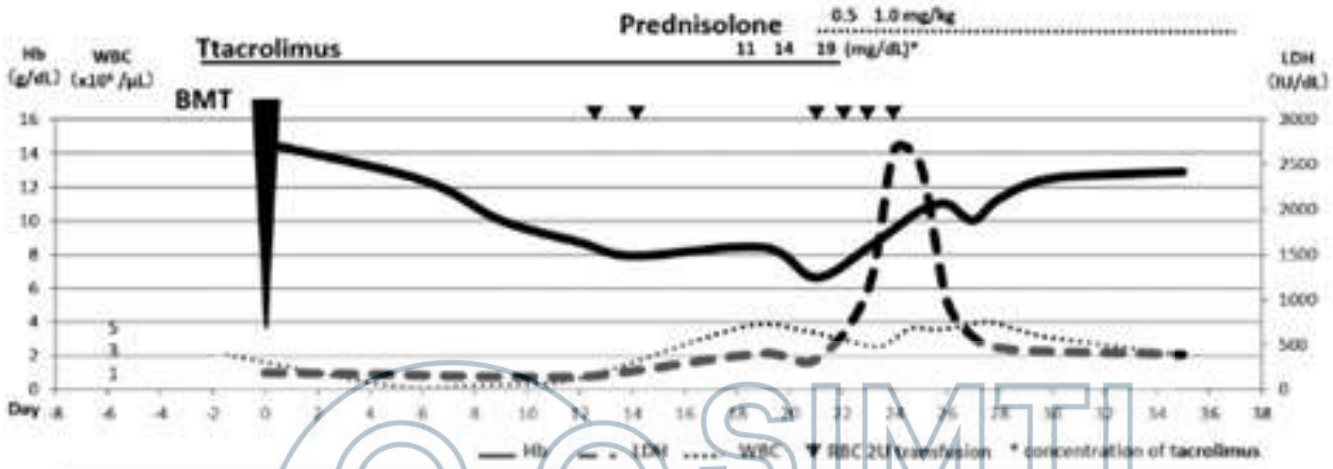
KEYWORDS
Passenger lymphocyte syndrome; hemolysis; hematopoietic stem cell transplantation; graft-versus-host disease

A→B



Day	0	21	28
A-RBCs		1+	2+
B-RBCs		1+	-
Anti-A antibodies		2+	1+
Anti-B antibodies		3+	4+
Blood type (forward grouping)	B	AB	A
Blood type (reverse grouping)	B	O	O

Figure 2. Clinical course of case 2. Massive hemolysis with high anti-B antibody titer occurred on days 21–28, about 10 days following engraftment. Note that, even with PSL administration, high anti-B antibody titer sustained on day 28, when the blood type converted to A with a resolution of hemolysis.



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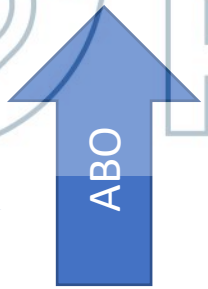
«Per la Conversione del gruppo sanguigno ABO sono essenziali alcuni aspetti diagnostici e clinici: definizione sierologica ABO completa (tipizzazione diretta e inversa) con due prelievi di sangue consecutivi ed indipendenti, DAT negativo, valutazione della corretta presenza/assenza di anti-A /B, IHA a TA e IAT e indipendenza dalle trasfusioni. Può essere utile la genotipizzazione per confermare la presenza di alleli ABO convertiti.»



cells

MDPI

Review

Immuno-Hematologic Complexity of ABO-Incompatible Allogeneic HSC Transplantation

Antonella Matteocci [1,*] and Luca Pierelli [1,2]

Conversione completa del gruppo sanguigno

- Incompatibilità maggiore: gruppo sanguigno ABO coerente diretto-inverso e IHA anti-donatore non rilevabili. (1)
- Incompatibilità minore: gruppo diretto completo del donatore, inverso originale del ricevente, DAT negativo per assenza di IHA anti-ricevente.(2)
- Incompatibilità bidirezionale: gruppo completo del donatore nella tipizzazione diretta. (2)
- La ricostituzione completa del gruppo sanguigno ABO avviene entro 90-110 giorni

Esiste la possibilità di un'espressione persistente dell'antigene ABO del ricevente nel sangue periferico dopo HSCT con incompatibilità ABO (Chimerismo) (3)

- 1. Zhu. ABO-incompatible allogeneic hematopoietic stem cell transplantation. Blood Genom. 2023, 7, 1–12.
- 2. Li. A study of blood group conversion in patients with ABO incompatible hematopoietic stem cell transplantation—A decade survey. Transfus. Apher. Sci. 2023, 62, 103576. [
- 3. Liu. ABOchimerismdeterminedbyreal-time polymerase chain reaction analysis after ABO-incompatible haematopoietic stem cell transplantation. Blood Transfus. 2013,

Fabbisogno trasfusionale in trapianto CSE

-

PROLONGED RBC TRANSFUSION REQUIREMENT AFTER HCT

TABLE 1. Patient and transplant characteristics (group differences in univariate analysis)

Characteristic	Total of patients	Number (%) of patients with PRTR	p Value
Overall	487	48 (9.9)	
Recipient age (years) at transplant			0.002
0-12	101	2 (2.0)	
13-54	315	33 (10.5)	
≥55	71	13 (18.3)	
Median (range)	37 (0-70)	46 (1-67)	
ABO incompatibility			0.003
Major	128	21 (16.4)	
Minor	105	3 (2.9)	
None	254	24 (9.4)	
Conditioning			0.006
Myeloablative	329	24 (7.3)	
Reduced intensity	158	24 (15.2)	
Diagnosis			0.27
Malignant	409	43 (10.5)	
Nonmalignant	78	5 (6.4)	
Stem cell source			0.66
Marrow	138	12 (8.7)	
Peripheral blood stem cells	344	35 (10.2)	
Cord blood	5	1 (20.0)	
Donor type			0.024
Related, HLA-matched	194	11 (5.7)	
Unrelated, HLA-matched	219	29 (13.2)	
Related, HLA-mismatched	15	0 (0)	
Unrelated, HLA-mismatched	59	8 (13.6)	
GVHD prophylaxis			0.91
Standard (CsA + MTX)	256	24 (9.4)	
T-cell reduction	62	6 (9.7)	
Other	169	18 (10.7)	
aGVHD			0.046
Yes	239	17 (7.1)	
No	248	31 (12.5)	
Chronic GVHD			0.98
Yes	163	16 (9.8)	
No	324	32 (9.9)	
Mixed chimerism			0.28
Yes	238	27 (11.3)	
No	249	21 (8.4)	
RBC antibodies*			1.00
Yes	48	4 (8.3)	
No	439	44 (10.0)	

* Positive DCT or irregular antibodies or isoagglutinin titer of greater than 128 within 60 days posttransplant.
CsA = cyclosporine; MTX = methotrexate; DCT = direct Coombs test.

- Incompatibilità maggiore ABO
- Disparità genetica
- GVHD II-IV
- Malattia ad alto rischio
- Età avanzata
- Livelli Hb pre-trapianto

Dhal D, Transfusion 2010

DAHL ET AL.

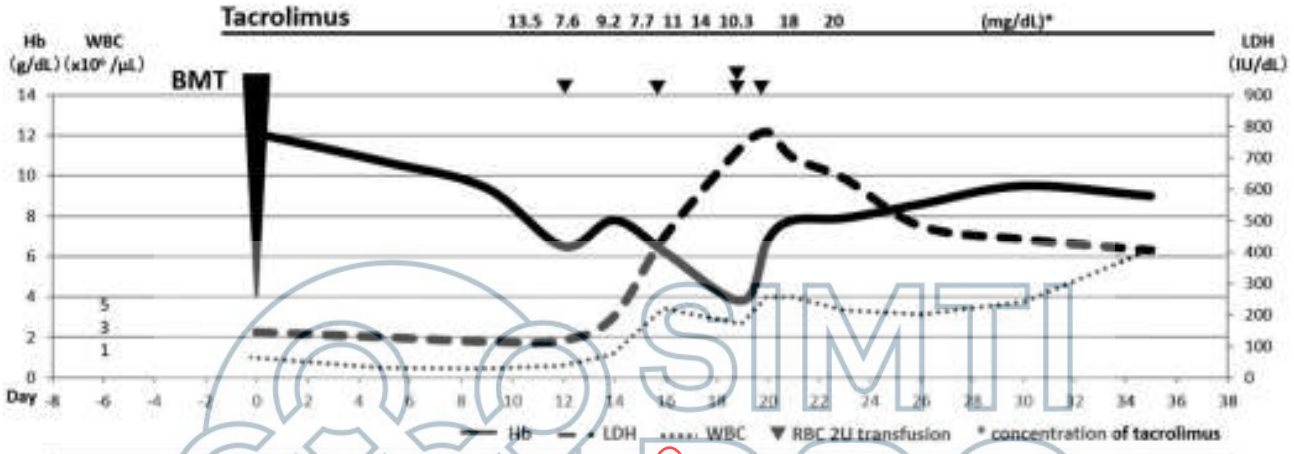
TABLE 2. Factors associated with PRTRs: logistic regression analysis

Factor	OR (95% CI) of PRTR	p Value
Recipient age (years) at transplant		
0-12	0.1 (0.03-0.7)	0.02
13-54*	1.0	
≥55	1.6 (0.7-3.7)	0.31
ABO incompatibility		
Major	1.6 (0.8-3.1)	0.18
Minor	0.2 (0.1-0.7)	0.01
None*	1.0	
Conditioning		
Myeloablative*	1.0	
Reduced intensity	1.7 (0.8-3.8)	0.20
Diagnosis		
Malignant*	1.0	
Nonmalignant	0.7 (0.2-2.2)	0.55
Stem cell source		
Marrow*	1.0	
Peripheral blood stem cells	0.5 (0.2-1.2)	0.12
Cord blood	4.5 (0.2-92.4)	0.33
Donor type		
Related, HLA-matched	0.4 (0.2-0.9)	0.02
Unrelated, HLA-matched*	1.0	
Related, HLA-mismatched	0 (no cases of PRTR observed)	1.0
Unrelated, HLA-mismatched	1.3 (0.5-3.3)	0.62
GVHD prophylaxis		
Standard (CsA + MTX)*	1.0	
T-cell reduction	1.6 (0.5-4.6)	0.40
Other	0.8 (0.3-1.7)	0.50
aGVHD		
Yes	0.6 (0.3-1.2)	0.12
No*	1.0	
Chronic GVHD		
Yes	1.0 (0.5-2.0)	0.99
No*	1.0	
Mixed chimerism		
Yes	1.5 (0.7-3.0)	0.26
No*	1.0	

* Reference group.
CsA = cyclosporine; MTX = methotrexate.

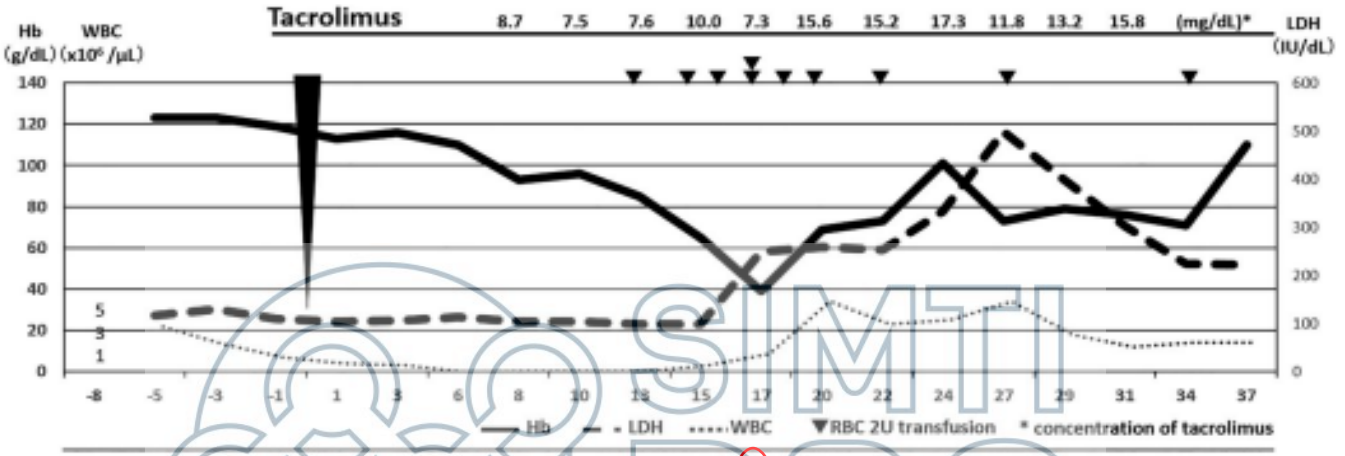
A vs B PLS

A



Day	0	12	16	19	21	26	28	30	33
A-RBCs	-	-	-	-	-	1+	1+	1+	1+
B-RBCs	4+	4+	1+	-	-	-	-	-	-
Anti-A Antibodies	3+	2+	1+	Weak	1+	Weak	Weak	Weak	Weak
Anti-B Antibodies	-	-	2+	4+	4+	4+	4+	4+	4+
Blood type (forward grouping)	B	B	B	O	O	A	A	A	A
Blood type (reverse grouping)	B	B	O	O	O	O	O	O	O

O vs A PLS



Day	0	13	17	20	27
A-RBCs	4+	4+	-	-	-
B-RBCs	-	-	-	-	-
Anti-A antibodies	-	-	3+	4+	4+
Anti-B antibodies	1+	Weak	3+	4+	4+
Blood type (forward group)	A	A	O	O	O
Blood type (reverse group)	A	A	O	O	O

Indicazioni alla trasfusione di emocomponenti nell'incompatibilità ABO.

Pre | Durante | Post

Table 2. Transfusion strategy for peritransplantion.

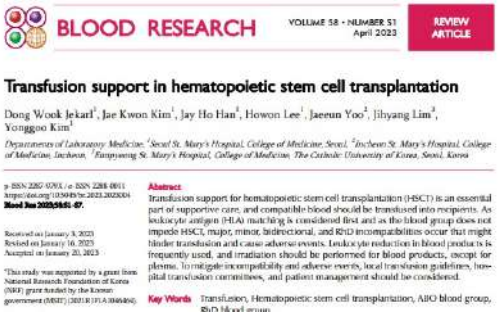
ABO incompatibility	Recipient	Donor	Phase I	Phase II				Phase III
			All product	RBC	PLT 1st	PLT 2nd	Plasma	All product
Major	O	A	Recipient	O	A	AB, B, O	A	Donor
	O	B	Recipient	O	B	AB, A, O	B	Donor
	O	AB	Recipient	O	AB	A, B, O	AB	Donor
	A	AB	Recipient	A	AB	A, B, O	AB	Donor
	B	AB	Recipient	B	AB	B, A, O	AB	Donor
Minor	A	O	Recipient	O	A	AB, B, O	A	Donor
	B	O	Recipient	O	B	AB, A, O	B	Donor
	AB	O	Recipient	O	AB	A, B, O	AB	Donor
	AB	A	Recipient	A	AB	A, B, O	AB	Donor
	AB	B	Recipient	B	AB	B, A, O	AB	Donor
Bidirectional	A	B	Recipient	O	AB	B, A, O	AB	Donor
	B	A	Recipient	O	AB	A, B, O	AB	Donor

This table was modified based on previous studies [1-3].

Blood Res 2023;58:S1-S7. bloodresearch.or.kr

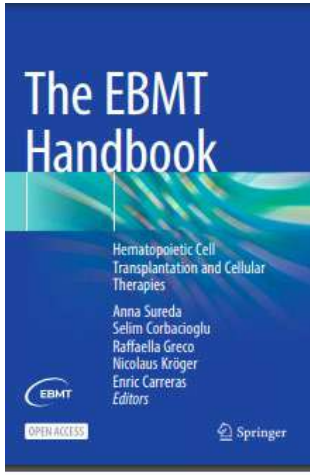
- IHA vs progenitori e PLT trasfuse
- Plt da aferesi Pls ↓
- Corretto fenotipo per stato Ag/Ab
- Compatibilità Ag Sistema Rh e K

*IRRADIAZIONE
Auto, almeno 2 week prima Tx , almeno 3 mesi dopo Tx
ALLO, prima condizionamento , 6 mesi dopo Tx o ricostituzine immunitaria
Alcuni centri per tutta la vita


BLOOD RESEARCH VOLUME 58 • NUMBER S1 April 2023 REVIEW ARTICLE

Transfusion support in hematopoietic stem cell transplantation

Dong Wook Jekarl[1], Jae Kwon Kim[1], Jay Ho Han[1], Howon Lee[1], Jaeeun Yoo[2], Jihyang Lim[3], Yonggoo Kim[1]



Auspicabile

Implementazione di linee guida IEM per gestione del trapianto di CSE ABO incompatibile

Compatibilità ABO per attuare migliore strategia di prevenzione e corretto supporto trasfusionale

Programma per gestione IEM basato su decisioni condivise per la prevenzione delle complicanze precoci e tardive

Requisiti minimi attività trapiantologica
DELIBERAZIONE DELLA GIUNTA REGIONALE n. 757 del 15 giugno 2021

ALLEGATO A

Requisiti minimi organizzativi, strutturali e tecnologici del Programma di trapianto (PT) di CSE e delle Unità ad esso afferenti.

Premessa

L'attività di trapianto di CSE è definita e regolata all'interno di un Programma di Trapianto che dipende dall'azione coordinata di 4 unità operative, rappresentate da:

1. Unità clinica;
2. Unità di raccolta di CSE da sangue periferico (PB- Peripheral Blood);
3. Unità di raccolta di CSE da sangue midollare (BM-Bone Marrow);
4. Unità di Processazione.

UNITA' CLINICA

UNITA' DI RACCOLTA CSE
PB e BM

UNITA' DI PROCESSAZIONE

Grazie per l'attenzione