

Use of the HLA-B leader to optimize cord blood transplantation

Effie W. Petersdorf,^{1,2} Ted Gooley,¹ Fernanda Volt,³ Chantal Kenzey,³ Alejandro Madrigal,⁴ Caroline McKallor,¹ Sergio Querol,⁵ Hanadi Rafii,³ Vanderson Rocha,^{3,6} Ryad Tamouza,^{3,7} Christian Chabannon,^{8,9} Annalisa Ruggeri^{3,9,10} and Eliane Gluckman^{3,11}

¹Division of Clinical Research, Fred Hutchinson Cancer Research Center, Seattle, WA, USA; ²Department of Medicine, University of Washington, Seattle, WA, USA; ³Eurocord, Hôpital Saint Louis APHP, Institut de Recherche de Saint-Louis (IRSL) EA3518, Université de Paris, Paris, France; ⁴University College London Cancer Institute, Royal Free Campus, London, UK; ⁵Cell Therapy Services, Catalan Blood and Tissue Bank, Barcelona, Spain; ⁶Hospital das Clínicas and LIM31, Faculty of Medicine University of São Paulo, Brazil; ⁷INSERM U955, CHU Henri Mondor, Créteil, France; ⁸Institut Paoli-Calmettes, INSERM CBT1409, Marseille, France; ⁹Cellular Therapy and Immunobiology Working Party of the European Society for Blood and Marrow Transplantation, Leiden, the Netherlands; ¹⁰Hematology and Bone Marrow Transplant Unit, IRCCS San Raffaele Scientific Institute, Milan, Italy and ¹¹Monacord, International Observatory on Sickle Cell Disease, Centre Scientifique de Monaco, Monaco

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Correspondence: *EFFIE W. PETERSDORF* - epetersd@fredhutch.org

Supplementary Materials

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Effie W. Petersdorf, M.D., Ted Gooley, Ph.D., Fernanda Volt, M.S., Chantal Kenzey, C.R.A., Alejandro Madrigal, M.D., Ph.D, Caroline McKallor, M.S., Sergio Querol, M.D., Hanadi Rafii, M.D., Ph.D., Vanderson Rocha, M.D., Ph.D., Ryad Tamouza, M.D., Ph.D., Christian Chabannon, M.D., Annalisa Ruggeri, M.D., Ph.D., and Eliane Gluckman, M.D., F.R.C.P.

Table of Contents

Supplemental Table 1. Participating transplant centers

Supplemental Table 2. Patient and cord-blood unit leader genotype and outcome among 4822 transplants

Supplemental Table 3. Patient and cord-blood unit leader genotype and outcome among 2178 transplants mismatched for one HLA-B

Supplemental Table 4. Patient and cord-blood unit leader genotype among 1013 single HLA-B-mismatched cord-blood transplants who are matched at HLA-A and HLA-DRB1

Supplemental Table 1. Participating transplant centers

Algeria
Alger - Centre Pierre et Marie Curie
Argentina
Buenos Aires - Fundacion Favaloro
La Plata - Instituto de Trasplante de Médula Osea
Australia
Perth Western Australia - RP Group Royal Perth Hospital
Randwick - Sydney Children's Hospital
Sydney - The Children's Hospital at Westmead
Austria
Linz - Elisabethinen-Hospital
Graz - Medical University
Graz - Medical University Graz
Vienna - Medizinische Universitaet Wien
Vienna - St. Anna Kinderspital
Belarus
Minsk - Belorussian Centre for Paediatric Oncology and Hematology
Belgium
Brussels - Children`s University Hospital BMT Unit
Brussels - Cliniques Universitaires St. Luc
Brussels - Universitair Ziekenhuis Brussel
Gent - University Hospital Gent
Hasselt - Jessa Ziekenhuis Dept. of Hematology
Leuven - University Hospital Gasthuisberg Dept. of Hematology
Liege - University of Liege
Brazil
Jaú - Hospital Amaral Carvalho
São Paulo - Hospital Sírio-Libanês Hematology Bone Marrow Transplant Unit
Canada
Montréal - Ste-Justine Hospital
Croatia
Zagreb - University Hospital Center Rebro
Czech Republic
Prague - Institute of Hematology and Blood Transfusion
Prague - University Hospital Motol
Denmark
Copenhagen - Rigshospitalet
Finland
Helsinki - University of Helsinki - Hospital for Children & Adolescents
Turku - Turku University Central Hospital
France
Angers - Centre Hospitalier Universitaire (CHU) Angers
Besançon - CHU Saint Jacques
Bordeaux - CHU Pellegrin-Enfants
Bordeaux - CHU Haut-Lévêque
Brest - Augustin Morvan

Caen – Centre François Baclesse
 Clamart - Hôpital d'Instruction des Armées Percy
 Clermont-Ferrand - CHU Hotel Dieu/Jean Perrin
 Créteil - CHU Henri Mondor
 Grenoble - La Tronche CHU Albert Michallon
 Lille - CHU Claude Huriez
 Lille - Hôpital Jeane de Flandre
 Limoges - CHU Service d'Hématologie Clinique
 Lyon - Debrousse/Institut Hématologie Oncologie Pédiatrique
 Lyon - CHU Edouard Herriot/Lyon Sud
 Marseille - La Timone
 Marseille - Institut Paoli Calmettes
 Marseille - CHU La Conception
 Montpellier - CHU Arnaud de Villeneuve
 Montpellier - CHU Lapeyronie- adulte
 Nancy - CHU Brabois
 Nantes - CHU Hotel Dieu
 Nice - CHU l'Archet
 Paris - Hôpital Saint Louis - Assistance Publique –Hôpitaux de Paris
 Paris - Hôpital Saint-Antoine – Assistance Publique –Hôpitaux de Paris
 Paris - Hôpital Pitié Salpêtrière - Assistance Publique –Hôpitaux de Paris
 Paris - Hôpital Necker - Assistance Publique –Hôpitaux de Paris
 Paris - Hôpital Robert Debré - Assistance Publique –Hôpitaux de Paris
 Poitiers - CHU Jean Bernard
 Rennes - CHU Pontchaillou
 Rouen - Centre Henry Becquerel
 Rouen - CHU Charles Nicolle
 Saint-Etienne - CHU Hôpital Nord / Institut de Cancérologie de la Loire
 Strasbourg - CHU Hôpital Hautepierre
 Toulouse - CHU Purpan
 Villejuif - Institut Gustave Roussy

Germany

Berlin - Charité-CVK University Medicine
 Dresden - Universitaetsklinikum Dresden
 Düsseldorf - Universitaetsklinikum
 Frankfurt am Main - Klinikum der Johann Wolfgang Goethe-Universität
 Halle - Martin-Luther-Univ. Halle-Wittenberg
 Hamburg - University Hospital Eppendorf
 Hannover - Medical School Dept. Haematology/Oncology/Stem Cell Transplantation
 Idar-Oberstein - Klinik Hamatologie/Onkologie
 Munich - Klinikum Schwabing
 Regensburg - University Regensburg
 Tübingen - University Hospital
 Ulm - Universitaet Ulm
 Würzburg - Julius Maximilian University of Würzburg

Greece

Athens - Evangelismos Hospital
 Athens - St. Sophia Children's Hospital
 Patras - University Medical School

Hungary

Budapest - St. István & St. Laszlo Hospital of Budapest

Budapest - St. László Hospital

Miskolc - Postgraduate Medical School

India

Chennai - Apollo Specialty Hospital

Iran

Teheran - Shariati Hospital

Ireland

Dublin - Our Lady s Hospital for Sick Children

Israel

Haifa - Rambam Medical Center

Jerusalem - Hadassah University Hospital

Petach-Tikva - Beilinson Hospital

Petach-Tikva - Schneider Children's Medical Center of Israel

Tel Hashomer - Chaim Sheba Medical Center

Tel Hashomer - Edmond & Lily Safra Children`s Hospital, Chaim

Tel Aviv - Sourasky Medical Center

Italy

Ancona-Torrete Ancona - Azienda Ospedali Riuniti di Ancona

Bergamo - Ospedali Riuniti di Bergamo

Bologna - Azienda Ospedaliero-Universitaria di Bologna

Bologna - Bologna University, S.Orsola-Malpighi Hospital

Brescia - Spedali Civili

Brescia - TMO Adulti Brescia

Brescia - Università degli Studi di Brescia

Catania - Ospedale Ferrarotto

Catania - Ospedale Ferrarotto

Cuneo - Azienda Ospedaliera S. Croce e Carle

Florence - Azienda Ospedaliero Universitaria Meyer - Ospedale di Careggi

Genoa - Institute G. Gaslini

Genoa Ospedale San Martino Department of Haematology II

Milan - Ospedale Maggiore di Milano

Milan - San Raffaele Scientific Institute

Milan - University of Milano Istituto Nazionale dei Tumori

Modena - Azienda Ospedaliera-Universitaria

Monza - Ospedale San Gerardo

Monza Ospedale San Gerardo Clinica Pediatrica dell Università di Milano Bicocca

Naples-Hospital Pausilipon

Padua - Clinica di Oncoematologia Pediatrica

Palermo - Ospedale dei Bambini

Palermo - Ospedale La Maddalena

Palermo - Ospedale V. Cervello

Pavia - Fondazione IRCCS Policlinico San Matteo

Pavia - Policlinico San Matteo

Perugia - Università di Perugia

Pesaro - Pesaro Hospital

Pescara - Ospedale Civile Department of Hematology

Pisa - Azienda Ospedaliera Universitaria Pisa

Rome - Ospedale S. Camillo

Rome - Rome Transplant Network

Rome - Universita Cattolica S. Cuore
 Rome - Ospedale Pediatrico Bambino Gesù
 Rome - Universita La Sapienza
 Rozzano - Istituto Clinico Humanitas
 Siena - Azienda Ospedaliera Universitaria Senese Policlinico S.Maria alle Scotte
 Trieste - Istituto per l'Infanzia Burlo Garofolo
 Turin - Ospedale Infantile Regina Margherita Onco-Ematologia Pediatrica
 Turin - Ospedale Universitaria San Giovanni Battista
 Udine - University Hospital
 Verona - Policlinico G.B. Rossi

Jordan

Amman - King Hussein Cancer Centre

New Zealand

Christchurch - Canterbury Health Laboratories

Norway

Rikshospitalet Department of Medicine

Poland

Bydgoszcz - University Hospital Collegium Medicum
 Poznan - Poznan University of Medical Sciences Department of Hematology
 Poznan - University of Medical Sciences
 Wroclaw - Wroclaw Medical University
 Wroclaw DCTK

Portugal

Lisbon - Instituto Portugues de Oncologia
 Porto - Inst. Portugues de Oncologia do Porto

Russia

Moscow - Russian s Children's Hospital
 Saint Petersburg - Saint Petersburg State Medical Pavlov University

Saudi Arabia

Riyadh - King Faisal Specialist Hospital & Research Centre

Singapore

Singapore - Department of Haematology Singapore General Hospital

Slovenia

Ljubljana - University Med. Center

South Africa

Cape Town - University of Cape Town Faculty of Health Sciences
 Pretoria - Netcare Pretoria East Hospital

Spain

Barcelona - Hospital Clinic
 Barcelona - Hospital Santa Creu i Sant Pau
 Barcelona - Hospital Universitari Germans Trias i Pujol
 Barcelona - Hospital Vall d' Hebron
 Barcelona - Hospital Duran i Reynals
 Cadiz Jerez de la Frontera - Hospital del SAS
 Cordova - Hosp. Reina Sofia
 Granada- Hospital Univ. Virgen de las Nieves
 La Coruña - Complejo Hospitalario de A Coruña
 Madrid - Hospital Gregorio Marañón
 Madrid - Hospital Ramon y Cajal
 Madrid - Hospital Universitario La Paz

Madrid - Hospital Universitario Puerta de Hierro
 Madrid - Niño Jesus Children`s Hospital
 Málaga - Hospital Carlos Haya
 Murcia - Hospital Morales Meseguer
 Murcia - Hospital Universitario Virgen de la Arrixaca
 Oviedo - University Hospital of Asturias
 Palma de Mallorca - Hospital Universitari Son Dureta
 Salamanca - Hospital Clínico
 Santander - Hospital U. Marqués de Valdecilla
 Santiago de Compostela - Complejo Hospitalario Universitario de Santiago
 Seville - Hospital Universitario Virgen del Rocío
 Valencia - Hospital Clínico Universitario
 Valencia - Hospital Universitario La Fe
 Valencia Hospital Infantil La Fe
 Vigo-Hospital Álvaro Cunqueiro - Complejo Hospitalario Universitario de Vigo

Sweden

Goeteborg - Sahlgrenska University Hospital
 Lund - University Hospital
 Stockholm - Karolinska University Hospital Children`s Hospital
 Umea - Umea University Hospital
 Uppsala - University Hospital

Switzerland

Basel - University Hospital
 Genève - Hôpitaux Universitaires de Genève
 Zurich - University Hospital
 Zurich - University Children's Hospital

The Netherlands

Amsterdam - Academisch Ziekenhuis bij de Universiteit
 Leiden - University Hospital
 Rotterdam - Erasmus MC-Daniel den Hoed Cancer Centre
 Utrecht - University Medical Centre
 Utrecht - Princess Máxima Center

Turkey

Ankara - University Faculty of Medicine
 Antalya - Akdeniz University Medical School
 Antalya - Medical Park Antalya Hospital
 Izmir - Ege University

United Kingdom

Birmingham - Birmingham Children's Hospital
 Birmingham - Queen Elizabeth Hospital
 Bristol - Royal Hospital for Children
 Cambridge - Addenbrookes Hospital Department of Haematology
 Cardiff Wales - University of Wales
 Glasgow - Royal Hospital for Sick Children
 Leeds - Mid Yorkshire Hospitals NHS Trust
 Leicester - Leicester Royal Infirmary
 Liverpool - Alder Hey Children`s NHS Foundation Trust
 London - Great Ormond Street Hospital
 London - King`s Denmark Hill Campus School of Medicine
 London - Royal Free and University College Medical School

London - St. George's Hospital

London - St. Mary's Hospital Division of Paediatrics

London Surrey Royal Marsden Hospital

Manchester - Christie NHS Trust Hospital

Manchester - Department of Paediatric Haematology

Manchester - Manchester Royal Infirmary Haematology

Newcastle-Upon-Tyne - Newcastle General Hospital Dept. of Paediatric Immunology

Nottingham - Nottingham City Hospital

Oxford - Churchill Hospital

Sheffield - Royal Hallamshire Hospital

Supplemental Table 2. Patient and cord-blood unit leader genotype and outcome among 4822

transplants

All cord-blood transplants regardless of HLA match status are included in models that examine the risks of MT and MM genotypes relative to TT in patients separately from units, for acute GVHD, relapse, non-relapse mortality and overall mortality.

Clinical endpoint	Group*		Odds ratio or hazard ratio	95% Confidence interval	P value (Global P value)
Grades II-IV acute GVHD	Patient genotype	TT (911/2735=33%)	1	-	(Global P 0.46)
		MT (532/1695=31%)	0.92	0.81-1.05	0.23
		MM (89/288=31%)	0.93	0.71-1.21	0.58
Relapse		TT (576/2217=26%)	1	-	(Global P 0.09)
		MT (366/1303=28%)	1.06	0.93-1.21	0.40
		MM (43/208=21%)	0.73	0.52-1.02	0.06

Non-relapse mortality		TT (741/2217=33%)	1	-	(Global P 0.46)
		MT (405/1303=31%)	0.93	0.82-1.05	0.22
		MM (68/208=33%)	0.95	0.74-1.22	0.68
Mortality		TT (1435/2804=51%)	1	-	(Global P 0.37)
		MT (850/1723=49%)	0.96	0.88-1.05	0.36
		MM (132/293=45%)	0.89	0.75-1.07	0.22
Grades II-IV acute GVHD	Cord-blood unit genotype	TT (874/2635=33%)	1	-	(Global P 0.49)
		MT (563/1791=31%)	0.92	0.81-1.05	0.24
		MM (95/292=33%)	0.98	0.76-1.28	0.91
Relapse		TT (528/2121=25%)	1	-	(Global P 0.13)

		MT (395/1397=28%)	1.15	1.00-1.31	0.04
		MM (62/210=30%)	1.03	0.77-1.37	0.85
Non-relapse mortality		TT (709/2121=33%)	1	-	(Global P 0.28)
		MT (445/1397=32%)	0.94	0.83-1.06	0.28
		MM (60/210=29%)	0.83	0.64-1.09	0.18
Mortality		TT (1360/2698=50%)	1	-	(Global P 0.48)
		MT (920/1827=50%)	1.00	0.92-1.08	0.92
		MM (137/295=46%)	0.90	0.75-1.07	0.23

*The numbers refer to the number of patients who developed the clinical endpoint out of the total number of evaluable patients (for whom data for the clinical endpoint was available).

Supplemental Table 3. Patient and cord-blood unit leader genotype and outcome among 2178

transplants mismatched for one HLA-B

Study pairs have one mismatch at HLA-B without consideration of match status at other HLA loci.

Models examine the risks of MT and MM genotypes relative to TT in patients separately from units, for acute GVHD, relapse, non-relapse mortality and overall mortality.

Clinical endpoint	Group/model*		Odds ratio or hazard ratio	95% Confidence interval	P value (Global P Value)
Grades II-IV acute GVHD	Patient genotype	TT (448/1290=35%)	1	-	(Global P 0.82)
		MT (240/724=33%)	0.95	0.78-1.16	0.60
		MM (41/115=36%)	1.05	0.70-1.58	0.81
	Unit genotype	TT (419/1196=35%)	1	-	(Global P 0.20)
		MT (262/814=32%)	0.87	0.72-1.06	0.16
		MM (48/119=40%)	1.18	0.80-1.75	0.41

Relapse	Patient genotype	TT (301/1118=27%)	1	-	(Global P 0.27)
		MT (176/625=28%)	1.00	0.82-1.21	>0.99
		MM (17/100=17%)	0.67	0.41-1.09	0.11
	Unit genotype	TT (256/1035=25%)	1	-	(Global P 0.13)
		MT (205/709=29%)	1.21	1.00-1.47	0.05
		MM (33/99=33%)	1.17	0.79-1.73	0.43
Mortality	Patient genotype	TT (733/1322=55%)	1	-	(Global P 0.83)
		MT (404/738=55%)	0.97	0.85-1.09	0.57
		MM (63/118=53%)	0.96	0.74-1.25	0.76
	Unit genotype	TT (664/1222=54%)	1	-	(Global P 0.46)

		MT (473/836=57%)	1.04	0.93-1.18	0.47
		MM (63/120=53%)	0.89	0.69-1.16	0.39
Non-relapse mortality	Patient genotype	TT (391/1118=35%)	1	-	(Global P 0.83)
		MT (212/625=34%)	0.95	0.80-1.12	0.56
		MM (38/100=38%)	1.01	0.72-1.42	0.96
	Unit genotype	TT (366/1035=35%)	1	-	(Global P 0.24)
		MT (248/709=35%)	0.98	0.83-1.15	0.78
		MM (27/99=27%)	0.71	0.48-1.06	0.09

*The numbers refer to the number of patients who developed the clinical endpoint out of the total number of evaluable patients (for whom data for the clinical endpoint was available).

Supplemental Table 4. Patient and cord-blood unit leader genotype among 1013 single HLA-B-mismatched cord-blood transplants who are matched at HLA-A and HLA-DRB1

A total of 814 patients are evaluable for relapse and non-relapse mortality.

Clinical endpoint	Group/model*		Odds ratio or hazard ratio	95% Confidence interval	P value (Global P Value)
Grades II-IV acute GVHD	Patient genotype	TT (219/616=36%)	1	-	(Global P 0.77)
		MT (122/328=37%)	1.09	0.82-1.45	0.55
		MM (17/44=39%)	1.18	0.62-2.27	0.61
	Unit genotype	TT (205/555=36%)	1	-	(Global P 0.17)
		MT (124/372=33%)	0.87	0.65-1.15	0.33
		MM (29/61=48%)	1.48	0.85-2.55	0.16
Relapse	Patient genotype	TT (139/508=27%)	1	-	(Global P 0.25)
		MT (79/272=29%)	1.08	0.80-1.44	0.62

		MM (6/34=18%)	0.51	0.22-1.21	0.13
	Unit genotype	TT (111/468=24%)	1	-	(Global P 0.06)
		MT (91/294=31%)	1.29	0.96-1.73	0.09
		MM (22/52=42%)	1.69	1.03-2.75	0.04
Mortality	Patient genotype	TT (328/636=52%)	1	-	(Global P 0.31)
		MT (168/332=51%)	0.97	0.80-1.17	0.73
		MM (18/45=40%)	0.68	0.42-1.11	0.13
	Unit genotype	TT (286/572=50%)	1	-	(Global P 0.58)
		MT (198/379=52%)	1.07	0.89-1.29	0.48
		MM (30/62=48%)	0.89	0.61-1.30	0.55

Non-relapse mortality	Patient genotype	TT (158/508=31%)	1	-	(Global P 0.11)
		MT (82/272=30%)	0.99	0.76-1.30	0.94
		MM (7/34=21%)	0.59	0.27-1.28	0.18
	Unit genotype	TT (150/468=32%)	1	-	(Global P 0.11)
		MT (89/294=30%)	0.99	0.75-1.30	0.93
		MM (8/52=15%)	0.46	0.23-0.95	0.03

*The numbers refer to the number of patients who developed the clinical endpoint out of the total number of evaluable patients (for whom data for the clinical endpoint was available).