ERITRO-EXCHANGE PRE-TRAPIANTO ALLOGENICO DI CELLULE STAMINALI EMOPOIETICHE NELLA DREPANOCITOSI: UN' INDICAZIONE AGGIUNTIVA?

Piero Marson[1], Tiziana Tison[1], Laura Sainati[2], Raffaella Colombatti[2], Manuela Tumino[2], Chiara Messina[2], Giustina De Silvestro[1]

[1]Unità di Aferesi Terapeutica, U.O. Immunotrasfusionale;

[2]U.O. Oncoematologia Pediatrica

Azienda Ospedale Università di Padova

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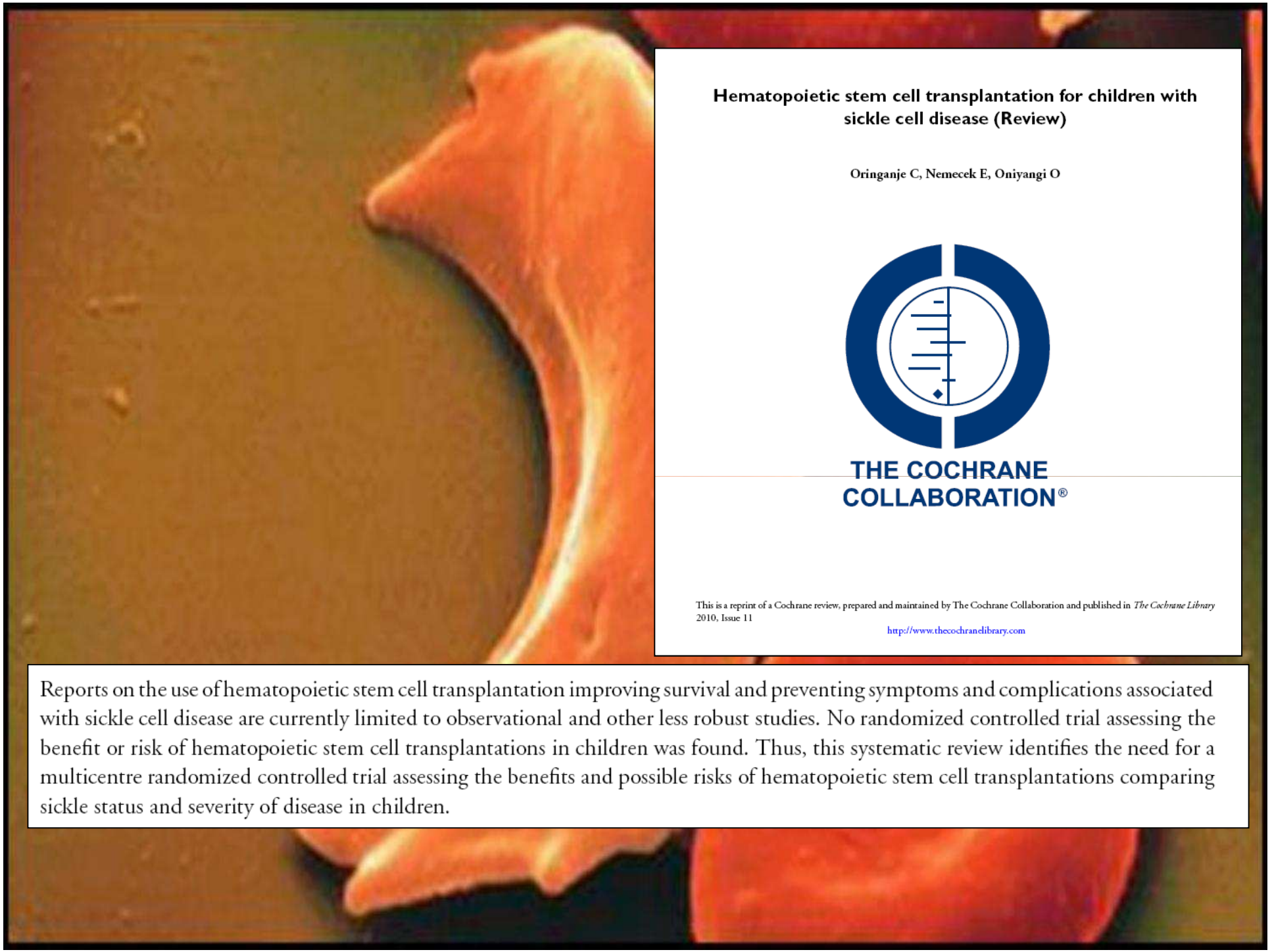
Allogeneic hematopoietic stem cell transplantation for sickle cell disease: the time is now

Matthew M. Hsieh, Courtney D. Fitzhugh and John F. Tisdale

Table 1. Indications for HSCT or hydroxyurea

Indications to start hydroxyurea	Historical indications for HSCT (patients ≤ 16 y)	NIH indications for HSCT (patients ≥ 16 y)
Three or more VOC requiring hospitalizations	Stroke or CNS event lasting longer than 24 hours	Irreversible end-organ damage
Two or more acute chest syndromes	Abnormal brain MRI	Stroke or clinically significant CNS event
Two or more joints with osteonecrosis	Elevated TCD	Elevated TRV ≥ 2.6 m/s
Symptomatic anemia	ACS with recurrent hospitalizations	Sickle-related renal insufficiency (Cr ≥ 1.5 times the upper limit of normal or biopsy proven)
	Two or more VOC requiring hospitalizations for several years	Sickle hepatopathy (including iron overload)
	Osteonecrosis of multiple joints	Reversible sickle complication not ameliorated by hydroxyurea
	Red cell alloimmunization	Two or more VOC requiring hospitalizations for several years
	Sickle cell lung disease	Any ACS while on hydroxyurea

ACS indicates acute chest syndrome; NIH, National Institutes of Health; MRI, magnetic resonance imaging; TCD, transcranial Doppler; TRV, tricuspid regurgitant velocity; and VOC, vaso-occlusive crises.



Hematopoietic stem cell transplantation for children with sickle cell disease (Review)

Oringanje C, Nemecek E, Oniyangi O

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This is a reprint of a Cochrane review, prepared and maintained by The Cochrane Collaboration and published in *The Cochrane Library* 2010, Issue 11

http://www.thecochranelibrary.com

Reports on the use of hematopoietic stem cell transplantation improving survival and preventing symptoms and complications associated with sickle cell disease are currently limited to observational and other less robust studies. No randomized controlled trial assessing the benefit or risk of hematopoietic stem cell transplantations in children was found. Thus, this systematic review identifies the need for a multicentre randomized controlled trial assessing the benefits and possible risks of hematopoietic stem cell transplantations comparing sickle status and severity of disease in children.

Gruppo di Lavoro "Patologia del globulo rosso"
Coordinatore: Dr. Silverio Perrotta

RACCOMANDAZIONI PER LA GESTIONE DELLA MALATTIA DREPANOCITICA IN ETA' PEDIATRICA IN ITALIA

Autori
Maddalena Casale, Andrea Ciliberti, Raffaella Colombatti, Gian Carlo Del Vecchio, Domenico De Mattia, Benedetta Fabrizzi, Cinzia Favara Scacco, Paola Giordano, Valentina Kiren, Saverio Ladogana, Nicoletta Masera, Agostino Nocerino, Lucia Dora Notarangelo, Giovanni Palazzi, Silvio Perrotta, Anna Pusiol, Anita Regalia, Giovanna Russo, Laura Sainati, Piera Samperi, Paola Saracco, Marco Zecca

Coordinatore
Giovanna Russo

Revisori interni
Giovanna Russo, Piera Samperi, Laura Sainati, Raffaella Colombatti

Revisori esterni (autorevoli esperti di Ematologia Pediatrica)
Gian Luca Forni (Genova), Renzo Galanello (Cagliari)

Revisore esterno (Assoc. Ligure Thalassemici, Thalassemia International Federation)
A. Loris Brunetta (Genova)

DREPANOCITOSI

CRITERI DI ELEGGIBILITA' AL TRAPIANTO ALLOGENICO DI CELLULE STAMINALI EMOPOIETICHE (AIEOP, 2011)

- **stroke**
- **ACS ricorrenti non responsive al trattamento con idrossiurea (HU)**
- **crisi dolorose ricorrenti non responsive al trattamento con HU**
- **retinopatia proliferativa bilaterale o deficit visivo maggiore ad un singolo occhio**
- **osteonecrosi in sedi multiple**
- **altra complicanza d'organo potenzialmente evolutiva e/o invalidante**
- **alloimmunizzazione alle trasfusioni eritrocitarie**
- **impossibilità di aderire ai trattamenti sanitari proposti**

DREPANOCITOSI

TRAPIANTO ALLOGENICO DI CELLULE STAMINALI EMOPOIETICHE

- **SOPRAVVIVENZA GLOBALE: > 90%**
- **EVENT-FREE SURVIVAL: 82-86%**
- **MORTALITA' TRAPIANTO-CORRELATA: 7-8%**
- **RISCHIO DI RIGETTO: 8-10%**
- **RISCHIO DI GVHD ACUTA (GRADO II-IV): 10-20%**
- **RISCHIO DI GVHD CRONICA ESTESA : < 5%**

Journal of Clinical Apheresis 25:83–177 (2010)

Guidelines on the Use of Therapeutic Apheresis in Clinical Practice–Evidence-Based Approach from the Apheresis Applications Committee of the American Society for Apheresis

Zbigniew M. Szczepiorkowski,[1*†] Jeffrey L. Winters,[2*] Nicholas Bandarenko,[3*] Haewon C. Kim,[4*] Michael L. Linenberger,[5*] Marisa B. Marques,[6*] Ravindra Sarode,[7*] Joseph Schwartz,[8*] Robert Weinstein,[9*] and Beth H. Shaz[10*]

SICKLE CELL DISEASE

	Procedure	Recommendation	Category
Incidence: 289 per 100,000 African-Americans, 89.8 per 100,000 Hispanics primarily from Caribbean islands (1 in 375 for Hb SS, 1 in 835 for Hb SC, 1 in 1,667 for Hb S/β-thalassemia among African-American live births)	RBC exchange	Grade 1C	I (Acute stroke)
			II (Acute chest syndrome)
	RBC exchange	Grade 1C	II (Prophylaxis for primary or secondary stroke prevention of transfusional iron load)
	RBC exchange	Grade 1C	
	RBC exchange	Grade 2C	III (Multiorgan failure)

# of reported patients*: >300

	RCT	CT	CS	CR	Type of evidence
Acute stroke	0	0	7 (160)	7 (9)	Type II-3
Acute chest syndrome	0	0	12 (142)	8 (8)	Type II-3
Prophylaxis for primary or secondary stroke prevention of transfusional iron load	0	0	18 (310)	3 (3)	Type II-3
Multiorgan failure	0	0	3 (10)	2 (2)	Type II-3

DREPANOCITOSI

INDICAZIONI AL TRATTAMENTO ACUTO CON ERITRO-EXCHANGE

(AIEOP, 2011)

- **INDICAZIONI RICONOSCIUTE IN LETTERATURA**
  - stroke
  - ACS (casi con importante compromissione respiratoria)
  - preparazione ad intervento di chirurgia “maggiore” od oftalmica
  - multiorgan failure
  - esami con mezzi di contrasto e.v. ad alte dosi

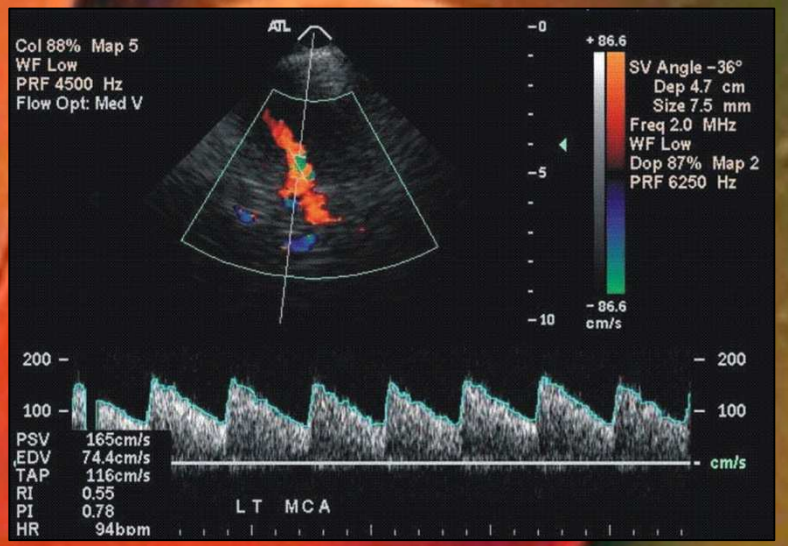
- **INDICAZIONI CONTROVERSE**
  - crisi dolorose severe non responsive a terapia reidratante ed antalgica
  - priapismo

DREPANOCITOSI

INDICAZIONI AL TRATTAMENTO CRONICO CON ERITRO-EXCHANGE

(AIEOP, 2011)

- **INDICAZIONI RICONOSCIUTE IN LETTERATURA**
  - **Prevenzione primaria dello stroke in bambini con TCD patologico**
  - **Prevenzione secondaria dello stroke**



DREPANOCITOSI

ERITRO-EXCHANGE PRE-TRAPIANTO ALLOGENICO DI CELLULE STAMINALI EMOPOIETICHE: REVISIONE DELLA LETTERATURA

AUTORI	PROVENIENZA	NUMERO PAZIENTI	ETA' media – range (in anni)	ERITRO-EXCHANGE PRE-TRAPIANTO
Walters et al. (2000)	USA	50	9 (3-14)	SI
Adamkiewicz et al. (2004)	USA	3	7 (3-12)	NON SPECIFICATO
Horan et al. (2005)	USA	3	22 (9-30)	SI
Panepinto et al. (2007)	USA	67	16 (2-27)	NON SPECIFICATO
Bernaudin et al. (2007)	FRANCIA	87	9 (2-22)	SI
Kriswamurti et al. (2008)	USA	7	11 (6-18)	SI
McPherson et al. (2009)	USA	27	8 (3-17)	NO
Hsieh et al. (2009)	USA	10	26 (16-45)	SI
Majummar et al. (2010)	USA	10	10 (3-16)	NON SPECIFICATO

DREPANOCITOSI

ERITRO-EXCHANGE PRE-TRAPIANTO ALLOGENICO DI CELLULE STAMINALI EMOPOIETICHE

- **I.P.C., M, anni 3, peso kg 16**
  - **Assetto Hb pre-EEx: Hb 82 g/L, HbF 17,7%, HbA2 4,5%, HbA1 8,3%, HbS 69,5%**
  - **EEx: volume eritrocitario di scambio 572 mL, Ht 80%**
  - **Assetto Hb post-EEx: Hb 115 g/L, HbF 4,0%, HbA2 3,0%, HbA1 73,6%, HbS 19,4%**

CASISTICA PERSONALE

A	*B*	*C*	*D*	*E*	*F*	*G*	*H*	*I*	*L*
IPC	M	3	16	69,5	19,4	+20	+22	3	2
CRC	F	6	18	37,2	9,7	+20	+22	4	7
COK	F	9	25	31,9	9,3	+30	+28	5	8

REGIME DI CONDIZIONAMENTO
- *thiotepa*
- *treosulfano*
- *fludarabina*
- *ATG*

PROFILASSI GVHD
- *ciclosporina A*
- *methotrexate*

A	PAZIENTE
B	SESSO
C	ETA' (anni)
D	PESO (kg)
E	HbS PRE-ERITRO-EXCHANGE
F	HbS POST-ERITRO-EXCHANGE
G	ATTECCHIMENTO NEUTROFILI (gg.)
H	ATTECCHIMENTO PIASTRINE (gg.)
I	EPISODI TRASFUSIONALI EMAZIE CONCENTRATE
L	EPISODI TRASFUSIONALI CONCENTRATI PIASTRINICI

Trapianto allogenico
di cellule staminali emopoietiche
Euro 84.000

Eritro-exchange
Euro 500

CONCLUSIONI

eritro-exchange pre-trapianto allogenico
di cellule staminali emopoietiche

procedura di sicurezza nella prevenzione
delle complicanze trapiantologiche