The 4th WBMT Congress and Workshop

Riyadh, Saudi Arabia

Current indications for HCT in pediatrics

Adriana Seber

Hospital Samaritano São Paulo

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Current indications for HCT in pediatrics

Pediatric Hematology Committee

ABHH Associação Brasileira de Hematologia, Hemoterapia e Terapia Celular

Pediatric HCT Working Group

SBTMO

sobope

Adriana Seber

Hospital Samaritano São Paulo

WBMT worldwide network for blood and marrow transplantation WWW.WBMT.ORG

AMEO Associação da Medula Óssea

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SPECIAL SEMINARS

2007: Retinoblastoma Conference - One World, One Vision (In collaboration with The Hamilton Eye Institute, University of Tennessee Health Science Center)

Jordan: Building a Center of Excellence, the King Hussein Cancer Center Model

by **Ibrahim Qaddoumi, MD, MS**

Presented: JANUARY 25, 2007 Released: APRIL 28, 2007

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Abstract

Ibrahim Qaddoumi, MD, presents the model of the collaborative efforts between King Hussein Cancer Center and St. Jude Children's Research Hospital for the care of children with retinoblastoma. He discusses the challenges and the steps taken by both institutions to

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Abstract by: *Ayda G. Nambayan, RN, DSN*

Seminar is part of:

- 2007: Retinoblastoma Conference -

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17 JANUARY 2017 RIYADH, SAUDI ARABIA

Current indications for HCT in pediatrics

Biology of Blood and Marrow Transplantation

journal homepage: www.bbmt.org

Guideline

Indications for Autologous and Allogeneic Hematopoietic Cell Transplantation: Guidelines from the American Society for Blood and Marrow Transplantation

Navneet S. Majhail [1,*], Stephanie H. Farnia [2], Paul A. Carpenter [3], Richard E. Champlin [4], Stephen Crawford [5], David I. Marks [6], James L. Omel [7], Paul J. Orchard [8], Jeanne Palmer [9], Wael Saber [10], Bipin N. Savani [11], Paul A. Veys [12], Christopher N. Bredeson [13], Sergio A. Giralt [14], Charles F. LeMaistre [15]

Biol Blood Marrow Transplant 21 (2015) 1863

Current indications for HCT in pediatrics

- … foundation for discussion among patients, providers, payers, and policymakers.
- Whether or not to proceed with transplantation in an individual patient is a clinical decision, best made after a careful consideration of the alternatives, risks, and benefits of the procedure.

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Current indications for HCT in pediatrics

- The medical decision-making process for a transplant is complex and includes several factors besides the underlying indication, e.g.
  - patient's overall health
  - performance status
  - comorbidities
  - disease risk (remission, responsiveness to treatment)
  - graft and donor source

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Current indications for HCT in pediatrics

- Review of published recommendations for HCT indications:
  - European Group for Blood and Marrow Transplantation (EBMT)
  - British Society of Blood and Marrow Transplantation (BSBMT)
- Public comments

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Current indications for HCT in pediatrics

- Clinical trials and observational studies
  - specific questions
  - extrapolating the evidence to broad indication categories is challenging

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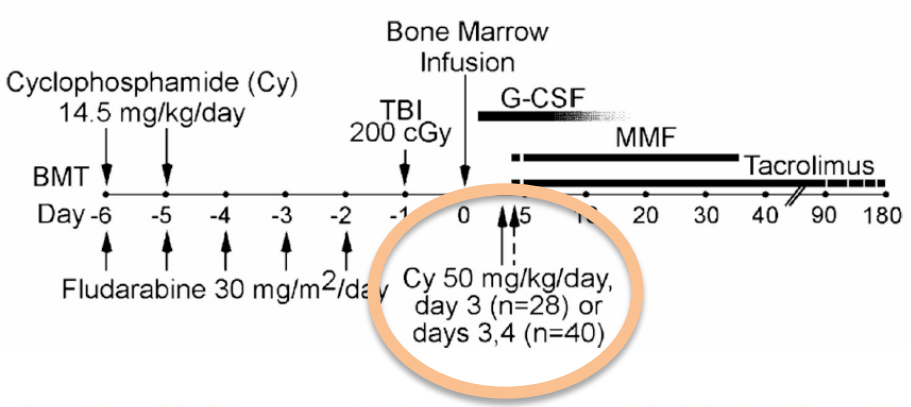
Current indications for HCT in pediatrics

- A suitable donor source can be found for most patients who may benefit from HCT
  - HLA-identical sibling donor
  - matched unrelated donor
  - unrelated umbilical cord blood
  - haploidentical donor



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Current indications for HCT in pediatrics

- A suitable donor source can be found for most patients who may benefit from HCT
- Consider:
  - underlying disease
  - disease stage
  - urgency

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Definitions for classifying indications

- **Standard of Care** (**S**): well defined and generally supported by evidence in the form of high quality clinical trials and/or observational studies (e.g., through the CIBMTR or EBMT).
- Standard of Care, **Clinical Evidence Available** (**C**): large clinical trials and observational studies are not available. However, HCT has been shown to be an effective therapy with acceptable risk of morbidity and mortality in sufficiently large studies. HCT can be considered as a treatment option for individual patients after careful evaluation of risks and benefits.

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Definitions for classifying indications

- Standard of Care, **Rare Indication** (**R**): rare diseases for which clinical trials and observational studies with sufficient number of patients are not feasible because of their very low incidence.
  However, studies in small cohorts of patients have shown HCT to be effective treatment with acceptable risks of morbidity and mortality.

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Definitions for classifying indications

- **Developmental (D**) indications: preclinical and/or early phase clinical studies show HCT to be a promising treatment option. HCT is best pursued for these indications as part of a clinical trial.
- **Not Generally Recommended** (**N**): evidence and clinical practice do not support the routine use of HCT; transplantation may be pursued for these indications within the context of a clinical trial.

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Current indications for HCT in pediatrics

S - Standard of Care
C - Standard, Clinical Evidence Available
R - Standard, Rare Indication
D - Developmental
N - Not Generally Recommended

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Table 2

Indications for HCT in Pediatric Patients (Generally Age < 18 years)

Indication and Disease Status	Allogeneic HCT	Autologous HCT
Acute myeloid leukemia		
CR1, low risk	N	N
CR1, intermediate risk	C	N
CR1, high risk	S	N
CR2+	S	N
Not in remission	C	N
Acute promyelocytic leukemia, relapse	R	R
Acute lymphoblastic leukemia		
CR1, standard risk	N	N
CR1, high risk	S	N
CR2	S	N
CR3+	C	N
Not in remission	C	N

Table 2

Indications for HCT in Pediatric Patients (Generally Age < 18 years)

Indication and Disease Status	Allogeneic HCT	Autologous HCT
Chronic myeloid leukemia		
Chronic phase	C	N
Accelerated phase	C	N
Blast phase	C	N
Myelodysplastic syndromes		
Low risk	C	N
High risk	S	N
Juvenile myelomonocytic leukemia	S	N
Therapy related	S	N

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Table 2

Indications for HCT in Pediatric Patients (Generally Age < 18 years)

Indication and Disease Status	Allogeneic HCT	Autologous HCT
T cell non-Hodgkin lymphoma		
CR1, standard risk	N	N
CR1, high risk	S	N
CR2	S	N
CR3+	C	N
Not in remission	C	N
Lymphoblastic B cell non-Hodgkin lymphoma (non-Burkitt)		
CR1, standard risk	N	N
CR1, high risk	S	N
CR2	S	N
CR3+	C	N
Not in remission	C	N

Table 2

Indications for HCT in Pediatric Patients (Generally Age < 18 years)

Indication and Disease Status	Allogeneic HCT	Autologous HCT
Burkitt's lymphoma		
First remission	C	C
First or greater relapse, sensitive	C	C
First or greater relapse, resistant	C	N
Hodgkin lymphoma		
CR1	N	N
Primary refractory, sensitive	C	C
Primary refractory, resistant	C	N
First relapse, sensitive	C	C
First relapse, resistant	C	N
Second or greater relapse	C	C

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Table 2

Indications for HCT in Pediatric Patients (Generally Age < 18 years)

Indication and Disease Status	Allogeneic HCT	Autologous HCT
Anaplastic large cell lymphoma		
CR1	N	N
Primary refractory, sensitive	C	C
Primary refractory, resistant	C	N
First relapse, sensitive	C	C
First relapse, resistant	C	N
Second or greater relapse	C	C

Table 2

Indications for HCT in Pediatric Patients (Generally Age < 18 years)

Indication and Disease Status	Allogeneic HCT	Autologous HCT
Nonmalignant diseases		
Severe aplastic anemia, new diagnosis	S	N
Severe aplastic anemia, relapse/refractory	S	N
Fanconi's anemia	R	N
Dyskeratosis congenita	R	N
Blackfan-Diamond anemia	R	N
Sickle cell disease	C	N
Thalassemia	S	N

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Table 2
(*continued*)

Indication and Disease Status	Allogeneic HCT	Autologous HCT
Congenital amegakaryocytic thrombocytopenia	R	N
Severe combined immunodeficiency	R	N
T cell immunodeficiency, SCID variants	R	N
Wiskott-Aldrich syndrome	R	N
Hemophagocytic disorders	R	N
Lymphoproliferative disorders	R	N
Severe congenital neutropenia	R	N
Chronic granulomatous disease	R	N
Other phagocytic cell disorders	R	N
IPEX syndrome	R	N

Table 2
(*continued*)

Indication and Disease Status	Allogeneic HCT	Autologous HCT
Mucopolysaccharoidoses (MPS-I and MPS-VI)	R	N
Other metabolic diseases	R	N
Osteopetrosis	R	N
Globoid cell leukodystrophy (Krabbe)	R	N
Metachromatic leukodystrophy	R	N
Cerebral X-linked adrenoleukodystrophy	R	N

Leukodystrophies	
X-ALD with cerebral involvement	S
Infantile MLD	CO (only early and/or asymptomatic) Offer gene therapy if available as 1st option
Juvenile MLD	CO (only early and/or asymptomatic) Offer gene therapy if available as 1st option
Late onset MLD	CO (only early and/or asymptomatic)
Glycoprotein metabolic & miscellaneous disorders	
Alpha-mannosidosis	S
Aspartylglucosaminuria	CO
Osteopetrosis	
TCIRG1 mutation (47%)	S
CLCN7 mutation (15%)	CO (if no neuropathic form)
OSTM1 mutation (5%)	GNR
RANK mutation (2%)	S
RANK Ligand mutation (1%)	GNR
Genetically undefined	CO (severe phenotype, no neuropathic form)

Table 2 Indications for HSCT in immunodeficiencies

** not all patients proceed to HSCT*

I. Combined Immunodeficiency (CID)

SCID

Functional	Genetic
T- B- NK-	ADA
	Reticular dysgenesis (AK2)
T- B- NK+	RAG 1/2
	DCLRE1C
	Cernunnos
T- B+ NK-	DNA Ligase 4
	DNA PKcs
T- B+ NK+	yc (X linked)
	Jak 3 kinase
	IL7 Ra
	CD3γδε,
	CD45,
	ZAP70 kinase,
	Coronin 1A

Other/undefined

CID
- CD40 Ligand Deficiency
- CD4 lymphopenia
- MHC class II
- PNP
- Omenn syndrome
- Leaky SCID
- MALT1
- LCK
- MST1(STK4)
- CTPS1
- Other/undefined

II. CID with associated features

- WAS
- DiGeorge (22q11 del, Tbx1), CHARGE (CHD7).
- CID with skeletal dysplasia
- Cartilage hair hypoplasia (RMRP)
- Njmegen breakage syndrome*
- DOCK 8
- Tyk2
- ICF
- DKC
- PI3Kδ activating mutant
- LRBA
- ORAI-1
- STIM1
- Other/undefined

III. Antibody Deficiencies

- Severe CVID
- MDS with hypogammaglobulinaemia

IV. Immune Dysregulation

Haemophagocytic disorders
- Familial HLH with genetic diagnosis (*PRF1*, *UNC13D*, *MUNC18-2*, *STX11)*
- HLH without genetic diagnosis but with: recurrent/refactory disease, affected sibling, absent NK function, CNS disease
- Griscelli syndrome type 2 (RAB27A)
- Chediak-Higashi syndrome (LYST)
- Other/undefined

Lymphoproliferative disorders*
- XLP1 (SH2D1A) & 2 (XIAP)
- Chronic Active EBV (with or without lymphoma or HLH)*
- ITK
- CD27
- MAGT1
- Other/undefined

Autoimmune
- ALPS (homozygotes)
- STAT3 GOF
- CTLA4
- Other/undefined

Early Onset Inflammatory Bowel Disease
- IPEX syndrome
- IL10
- IL10 receptor
- immunodeficiency with multiple intestinal atresia (TTC7a).
- Other/undefined

V. Phagocytic cell disorders

- LAD 1-3
- X linked CGD
- AR-CGD
- GATA2 (Mono MAC syndrome)
- other/undefined

VI. Innate Defects

- NEMO
- STAT1
- STAT5
- IFN-γ receptor
- IL12 receptor
- other/undefined

NB:
- *Not all patients listed require HSCT*
- *Criteria such as T cell numbers/function, infectious and non-infectious complications and geno/phenotype correlation indicative for severe immune deficiency and expected dismal outcome without HSCT need to be taken into account.*

Table 2
(*continued*)

Indication and Disease Status	Allogeneic HCT	Autologous HCT
Juvenile rheumatoid arthritis	D	R
Systemic sclerosis	D	R
Other autoimmune and immune dysregulation disorders	R	N

Table 2

Indications for HCT in Pediatric Patients (Generally Age < 18 years)

Indication and Disease Status	Allogeneic HCT	Autologous HCT
Germ cell tumor, relapse	D	C
Germ cell tumor, refractory	D	C
Ewing's sarcoma, high risk or relapse	D	S
Soft tissue sarcoma, high risk or relapse	D	D
Neuroblastoma, high risk or relapse	D	S
Wilms' tumor, relapse	N	C
Osteosarcoma, high risk	N	C
Medulloblastoma, high risk	N	C
Other malignant brain tumors	N	C

Bone Marrow Transplantation (2015) **50,** 1037–1056

www.nature.com/bmt

SPECIAL REPORT

Indications for allo- and auto-SCT for haematological diseases, solid tumours and immune disorders: current practice in Europe, 2015

A Sureda[1], P Bader[2], S Cesaro[3], P Dreger[4], RF Duarte[1], C Dufour[5], JHF Falkenburg[6], D Farge-Bancel[7], A Gennery[8], N Kröger[9], F Lanza[10], JC Marsh[11], A Nagler[12], C Peters[13], A Velardi[14], M Mohty[15,17] and A Madrigal[16,17] for the European Society for Blood and Marrow Transplantation

Disease	Sibling donor allo-HSCT	Well-matched URD allo-HSCT /CBT	Alternative donor allo-HSCT	ASCT
Germ cell tumour	CO/II	CO/II	CO/II	CO/II
Ewing's sarcoma (high risk or >CR1)	D/II	D/III	D/III	S/II
Soft tissue sarcoma (high risk or >CR1)	D/II	D/II	D/III	CO/II
Neuroblastoma (high risk)	CO/II	D/III	D/III	S/II
Neuroblastoma >CR1	CO/II	D/III	D/III	S/II
Wilm's tumour >CR1	GNR/III	GNR/III	GNR/III	CO/II
Osteogenic sarcoma	GNR/III	GNR/III	GNR/III	D/II
Brain tumours	GNR/III	GNR/III	GNR/III	CO/II

Germ cell tumour

Ewing's sarcoma (high risk or >CR1)

Soft tissue sarcoma (high risk or >CR1)

Neuroblastoma (high risk)

Neuroblastoma >CR1

Wilm's tumour >CR1

Osteogenic sarcoma

Brain tumours

Bone Marrow Transplantation (2015) 1037

special research report

Hematopoietic stem cell transplantation in the Eastern Mediterranean Region (EMRO) 2011–2012: A comprehensive report on behalf of the Eastern Mediterranean Blood and Marrow Transplantation group (EMBMT)

Mahmoud Aljurf [a], Amr Nassar [b,*], Amir Ali Hamidieh [c], Alaa Elhaddad [d], Rose-Marie Hamladji [e], Ali Bazarbachi [f], Ahmed Ibrahim [g], Tarek Ben Othman [h], Fawzi Abdel-Rahman [i], Amal Alseraihy [a], Omar Fahmy [d], Ayad Ahmed Hussein [i], Abdulaziz Alabdulaaly [j], Salman Adil [k], Salam Salim Amur Alkindi [l], Mohamed Bayoumy [m], David Dennison [l], Mohamed Amine Bekadja [n], Ahmed Nacer Redhouane [e], Walid Rasheed [a], Ahmed AlSagheir [o], Reem Alsudairy [p], Saloua Ladeb [h], Said Benchekroun [q], Mani Ramzi [r], Parvez Ahmed [s], Hassan ElSolh [a], Syed Osman Ahmed [a], Fazal Hussain [a], Ardeshir Ghavamzadeh [c]

Hematol Oncol Stem Cell Ther 2015; 8(4): 167–175

Bone Marrow Transplantation (2016), 1–6

www.nature.com/bmt

ORIGINAL ARTICLE

First report of pediatric hematopoietic stem cell transplantation activities in the eastern mediterranean region from 1984 to 2011: on behalf of the pediatric cancer working committee of the eastern mediterranean blood and marrow transplantation group

AA Hussein[1], AA Hamidieh[2], A Elhaddad[3], M Ramzi[4], TB Othman[5], F Hussain[6], D Dennison[7], P Ahmed[8], M Abboud[9], A Al-Ahmari[6], A Wahadneh[10], J Fathy[3], M-A Bekadja[11], S Al-Kindi[7], S Benchekroun[12], A Ibrahim[13], M Behfar[2], M Samra[3], S Ladeb[5], S Adil[14], H El-Solh[6], M Ayas[6], M Aljurf[6], A Ghavamzadeh[2], A Al-Seraihy[6] and Pediatric Cancer Working Committee of the Eastern Mediterranean Blood and Marrow Transplantation (EMBMT) Group

Table 1. Pediatric HSCT activities and related logistics indices in the EM region

Countries	*Population in millions*	*GNI per Capita US$ (WHO income category)*	*Total pediatric HSCT performed in major centers*	*Teams performing HSCT*	*HSCT team density*	*HSCT/10 million population*
Saudi Arabia	24.175	14 740	1977	1	0.42	820.33
Iran	70.270	8050	1197	1	0.14	166.25
Egypt	74.166	4440	811	1	0.13	109.44
Pakistan	160.943	2350	325	2	0.12	19.23
Tunisia	10.215	7900	249	1	0.98	207.50
Jordan	5.729	5280	361	2	3.51	633.33
Oman	2.546	1468	162	1	3.93	648.00
Lebanon	4.055	5740	105	2	4.94	262.50
Morocco	30.853	4360	NA	NA	NA	NA
Afghanistan	26.088	⩾1000	NA	NA	NA	NA
Bahrain	0.739	15 110	NA	NA	NA	NA
Djibouti	0.819	2540	NA	NA	NA	NA
Iraq	28.506	⩾3600	NA	NA	NA	NA
Kuwait	2.779	23 080	NA	NA	NA	NA
Libya	6.039	⩾12 300	NA	NA	NA	NA
Qatar	0.821	⩾80 900	NA	NA	NA	NA
Somalia	8.445	⩾600	NA	NA	NA	NA
Sudan	37.707	2160	NA	NA	NA	NA
Syria	19.408	3930	NA	NA	NA	NA
United Arab	4.248	22 630	NA	NA	NA	NA
Emirates Yemen	21.732	920	NA	NA	NA	NA

Abbreviations: EM = Eastern Mediterranean; GNI = gross national income; HSCT = hematopoietic stem cell transplantation; NA = not available.

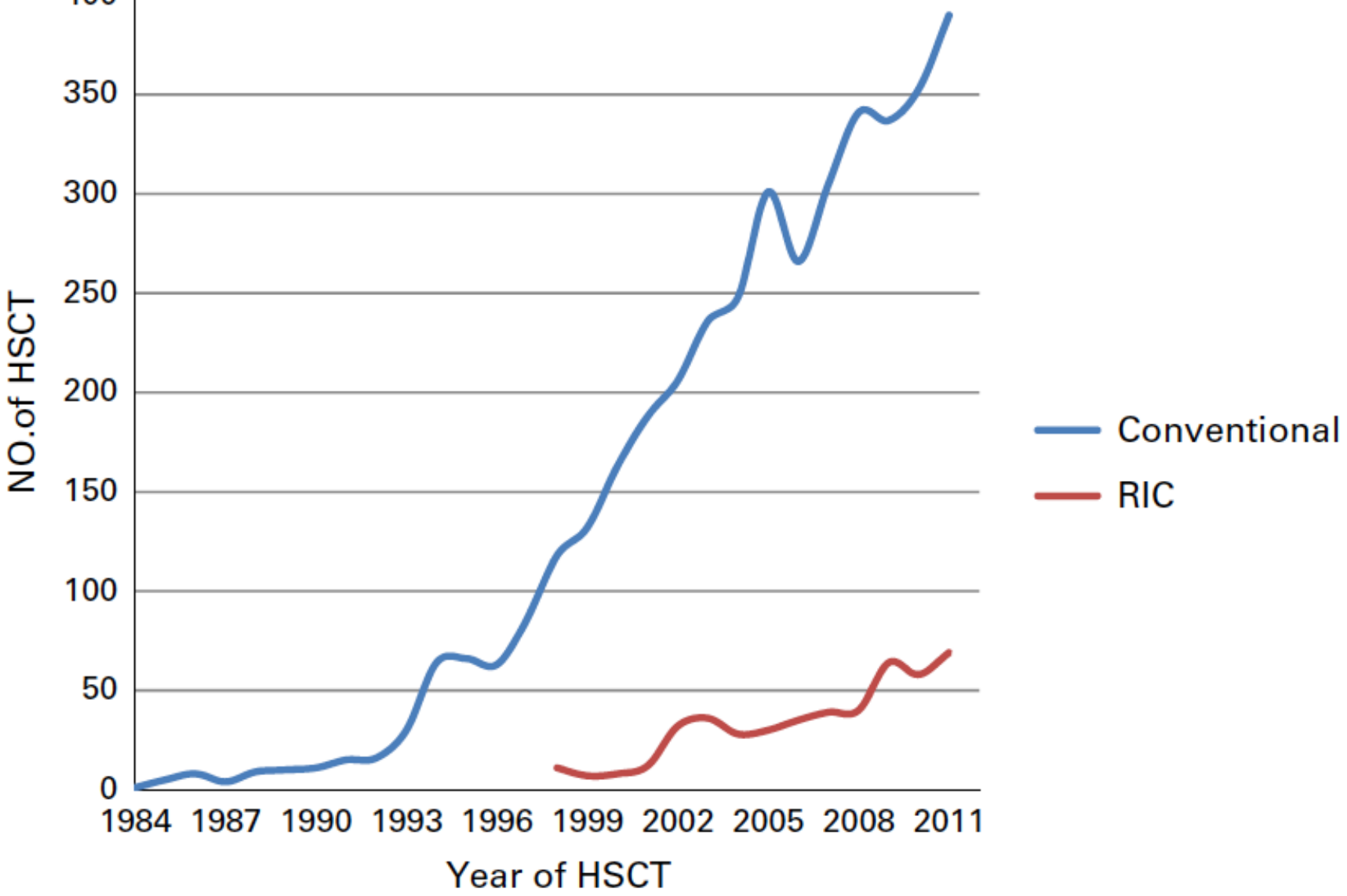


Figure 2. Trends in the use of conventional and RIC for pediatric allogeneic HSCT in the EM region from 1984 to 2011.

Because of limited resources and high cost, the use of alternative donors is very limited in the EM region. In addition, the infrastructure needed for unrelated HSCT such as CB banks, donor registries and regulations for unrelated stem cell donations is still underdeveloped and sparely distributed in the EM countries.[19] Developing haplo-identical transplant protocols using post-transplantation cyclophosphamide is likely to facilitate the performance of HSCT for patients with no related family donor.

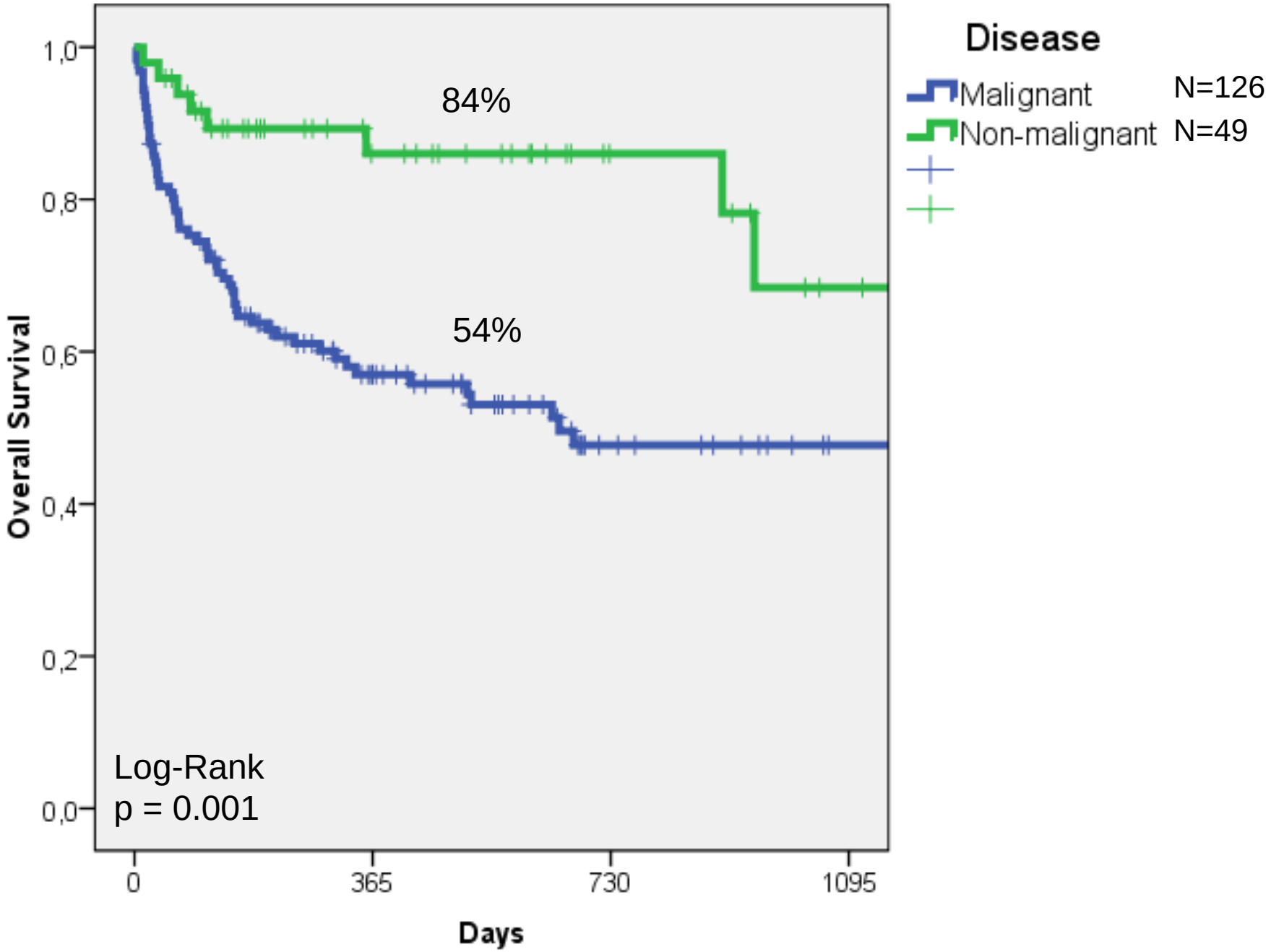
Brazil – Haploidentical Transplants

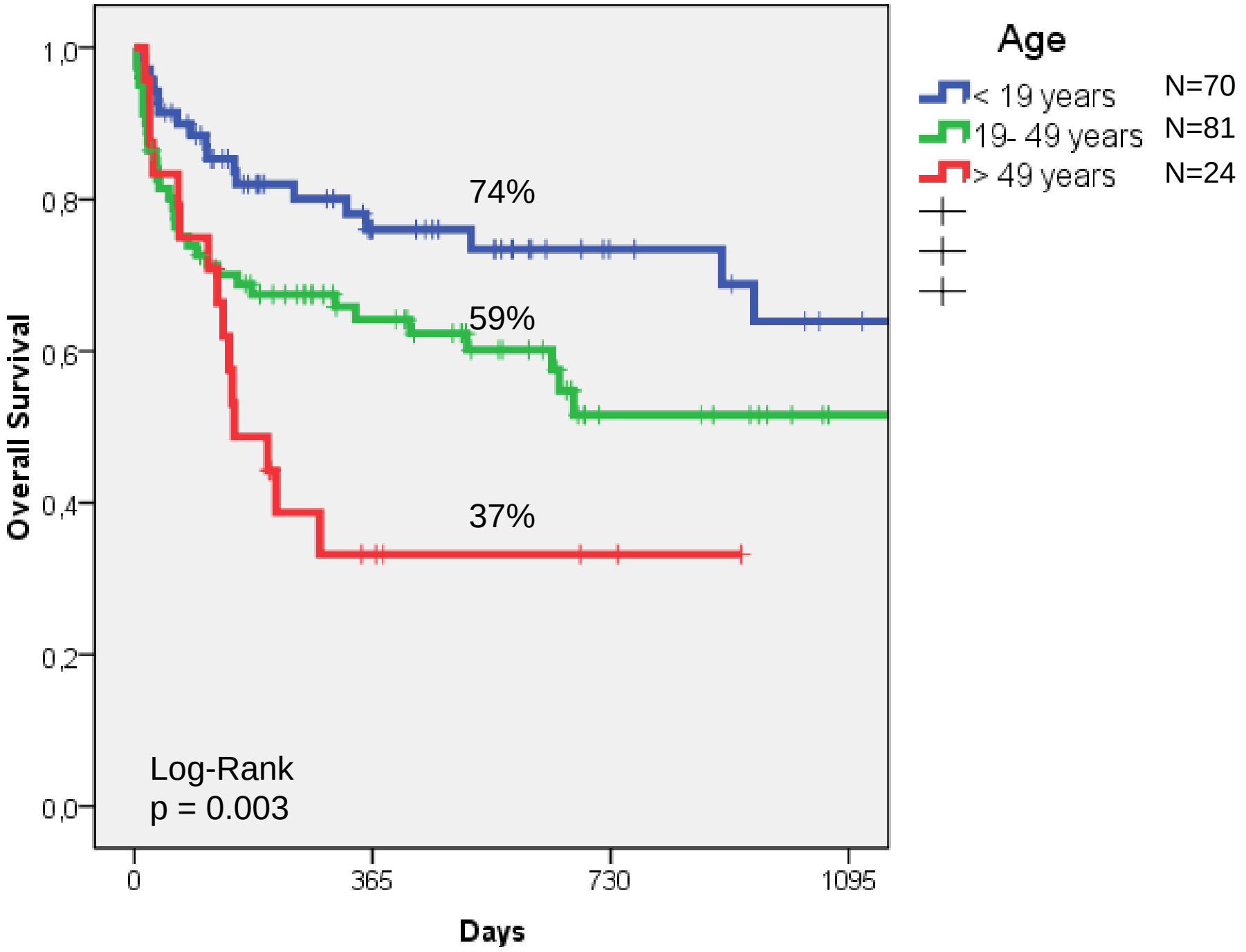
Malignant N = 128

- Acute leukemia – 80
- CLL - 1
- Hodgkin lymphoma – 19
- MDS – 7
- MPS – 12
- Non-Hodgkin lymphoma – 1

Non-malignant N = 52

- Aplastic anemia – 20
- Adrenoleukodystrophy – 10
- Blackfan-Diamond – 2
- Congenital disceratosis – 1
- Fanconi anemia – 4
- Krabbe – 1
- Immunodeficiency – 14


Disease
Malignant N=126
Non-malignant N=49
84%
54%
Log-Rank
p = 0.001
Overall Survival
1,0
0,8
0,6
0,4
0,2
0,0
0
365
730
1095
Days


Age
< 19 years
19- 49 years
> 49 years
N=70
N=81
N=24
74%
59%
37%
Log-Rank
p = 0.003
Overall Survival
1,0
0,8
0,6
0,4
0,2
0,0
0
365
730
1095
Days

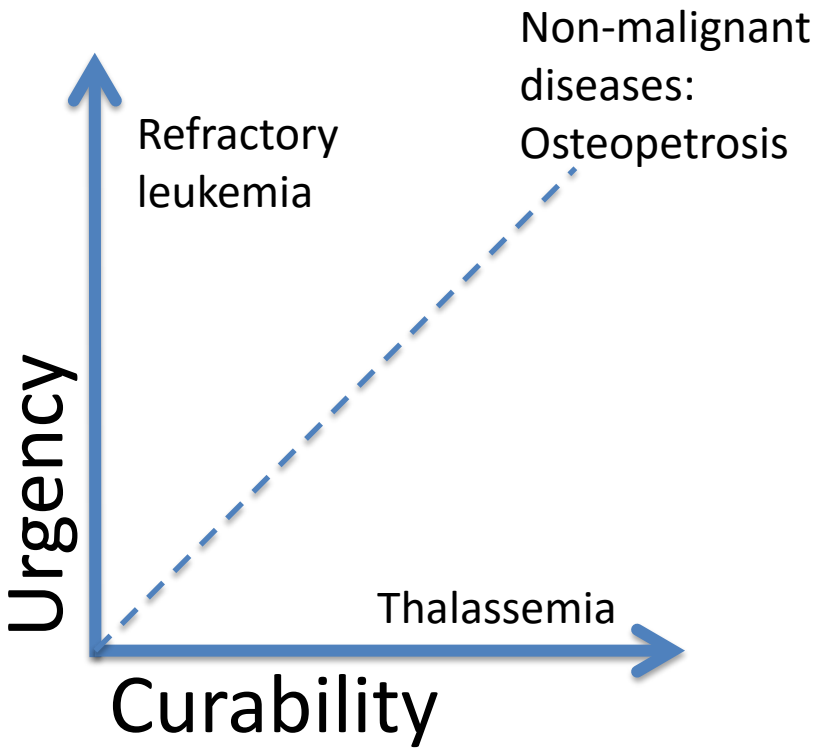
Brazilian Protocols/Guidelines

Non-malignant diseases – Carmem Bonfim

Malignant diseases – Nelson Hamerschlak

Current indications for HCT in pediatrics

- A suitable donor source can be found for most patients who may benefit from HCT
- Consider:
  - underlying disease
  - disease stage
  - urgency



collaboration
success
people
partnership
teamwork
team
business
cooperation
support
group
together
work
cooperate
project
join
person
solution
united
company
executive
presentation
companionship
interact
challenge
meeting
strategy
strong
professional
businessman
colorful
connection
communication
network
companion
unity
leadership
strength
management
trust
seminar
gesture
symbol
friendship
corporate
hands
connect
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Obrigada!

adrianaseber@gmail.com