

Table 1: Indications for HSCT Procedures in Children (See page 4 for footnotes)

Disease	Disease status	Allogeneic matched related	Allogeneic Unrelated	Haploidentical related	Autologous blood or marrow
<b>Donor specifics</b> <sup>a,b</sup>		10/10 sibling other 10/10 related other 9/10 related	10/10 adult 9-10/10 adult 4-6/6 cord	<9/10 related	
<b>Stem Cell Source</b>		BM/PBPCs/cord	BM/PBPCs/cord	PBPCs/BM	PBPCs/BM
<b>AML</b>	High risk CR1 <sup>c</sup>	S <sup>c</sup>	S <sup>c</sup>	CO	GNR
	CR≥2 <sup>d</sup>	S	S	S <sup>e</sup>	CO <sup>f</sup>
	Relapse/refractory	CO	CO	CO <sup>g</sup>	GNR
<b>ALL</b>	High risk CR1 <sup>h</sup>	S <sup>h</sup>	S <sup>h</sup>	CO	GNR
	CR2 <sup>i</sup>	S <sup>i</sup>	S <sup>i</sup>	S <sup>i</sup>	GNR
	CR3	S	S	S	GNR
	Relapse/refractory	GNR	GNR	GNR	GNR
<b>CML</b>	Chronic phase	S <sup>j</sup>	S <sup>j</sup>	CO <sup>j</sup>	GNR
	Accelerated phase	S	S	CO	GNR
	Blast crisis	S <sup>k</sup>	S <sup>k</sup>	CO <sup>k</sup>	GNR
<b>T-NHL</b>	As per ALL <sup>l</sup>				
<b>Lymphoblastic (non-Burkitt) B-NHL</b>	As per ALL <sup>l</sup>				
<b>ALCL</b>	CR2	S <sup>m</sup>	S <sup>m</sup>	CO	S <sup>n</sup>
	CR≥3	S	S	CO	GNR
	Refractory	S	S	CO	GNR
<b>Burkitt NHL</b>	CR2	CO	CO	CO	S
	Refractory	CO	CO	CO	S

Disease	Disease status	Allogeneic matched related	Allogeneic Unrelated	Haploidentical related	Autologous blood or marrow
<b>Donor specifics</b> <sup>a,b</sup>		10/10 sibling other 10/10 related other 9/10 related	10/10 adult 9-10/10 adult 4-6/6 cord	<9/10 related	
<b>Stem Cell Source</b>		BM/PBPCs/cord	BM/PBPCs/cord	PBPCs/BM	PBPCs/BM
<b>Hodgkin's Disease</b>	CR1 <sup>o</sup>	GNR <sup>p</sup>	GNR <sup>p</sup>	GNR	GNR
	CR2 <sup>o</sup>	CO <sup>p</sup>	CO <sup>p</sup>	GNR	S <sup>q</sup>
	CR3 <sup>o</sup>	CO <sup>p</sup>	CO <sup>p</sup>	GNR	CO
	Refractory	CO <sup>p</sup>	CO <sup>p</sup>	GNR	CO
<b>Myelodysplasia</b>	RC <sup>r</sup> , RfAEB, secondary MDS	S	S	S	GNR
	JMML	S	S	S	GNR
<b>IMMUNODEFICIENCIES</b> <sup>s</sup>		S	S	S	Gene therapy may be considered in appropriate clinical trials
<b>INBORN ERRORS</b> <sup>t</sup>		S	S	S	
<b>HAEMOGLOBINOPATHIES</b> <sup>u</sup>					
Thalassaemia		S	CO	CO	N/A
Sickle cell disease		S <sup>v</sup>	CO <sup>v</sup>	CO <sup>v</sup>	N/A
<b>BONE MARROW FAILURE</b>					
Acquired aplastic anaemia <sup>w</sup>		S	S	CO <sup>y</sup>	N/A
Constitutional monocytopenia <sup>x</sup>		S	S <sup>y</sup>	CO <sup>y</sup>	N/A
Fanconi anaemia		S <sup>y</sup>	S <sup>y</sup>	CO <sup>y</sup>	N/A
Dyskeratosis congenita		S	CO	CO	N/A
Diamond-Blackfan anaemia		S <sup>z</sup>	S <sup>aa</sup>	GNR	GNR

Disease	Disease status	Allogeneic matched related	Allogeneic Unrelated	Haploidentical related	Autologous blood or marrow
<b>Donor specific<sup>a,b</sup></b>		10/10 sibling other 10/10 related other 9/10 related	10/10 adult 9-10/10 adult 4-6/6 cord	<9/10 related	
<b>Stem Cell Source</b>		BM/PBPCs/cord	BM/PBPCs/cord	PBPCs/BM	PBPCs/BM
<b>SOLID TUMOURS<sup>bb</sup></b>					
<b>Neuroblastoma</b>	High risk	GNR	GNR	GNR	S
	Relapsed intermediate risk	GNR	GNR	GNR	S
<b>PNET (medulloblastoma)</b>	High risk/relapse	GNR	GNR	GNR	CO
<b>ATRT (CNS)</b>	High risk/relapse	GNR	GNR	GNR	CO
<b>Germ cell tumour (GCT)</b>	High risk CNS GCT (1 <sup>st</sup> line treatment)	GNR	GNR	GNR	S
	Relapsed CNS GCT	GNR	GNR	GNR	S
	Relapsed extracranial GCT	GNR	GNR	GNR	S
<b>Ewing's sarcoma</b>	1 <sup>st</sup> line, poor histological response or pulmonary metastases	GNR	GNR	GNR	S
	1 <sup>st</sup> line, extrapulmonary metastases	GNR	GNR	GNR	GNR
	2 <sup>nd</sup> remission	GNR	GNR	GNR	S
<b>Wilms tumour</b>	Defined groups of relapse (as per CCLG guidelines)	GNR	GNR	GNR	S
<b>Multisystem LCH</b>	Relapse/refractory	S	S	GNR	GNR
<b>Autoimmune disease</b>	Refractory	CO	CO	GNR	CO

**Indications for HSCT in children recommended by UK Paediatric BMT group (modified from Cornish et al. 1998\*)**

This document indicates when HSCT is indicated but is not intended to dictate how a transplant should be performed (eg conditioning strategy).

S = standard of care, generally indicated in suitable patients and/or in context of clinical trial

D = developmental, further trials needed

CO = clinical option, requires careful assessment of the risks and benefits

GNR = generally not recommended

**a** = 10 antigens: HLA-A, B, C, DRB1, DQB1. High resolution typing generally recommended (low resolution may be sufficient for sibling donors in non-consanguineous families with straightforward haplotypes)

**b** = 6 antigens (cords): HLA-A, B, DRB1. High resolution typing recommended for HLA-DRB1, intermediate resolution for HLA-A, B. NCC dose is important, minimum requirement 6/6 >3, 5/6 >4, 4/6 >5 x 10<sup>7</sup>/kg; double cord transplants may be considered

**c** = according to UK Treatment guideline for acute myeloid leukaemia or high risk myelodysplastic syndrome in children (B Gibson, D Webb, 13/10/11). Also applicable to secondary AML in remission

**d** = see Figure 2

**e** = if relapse <1 year from diagnosis

**f** = if relapse >1 year from diagnosis

**g** = worth considering if KIR mismatched donor available due to GVL effect of NK cells, reduced intensity conditioning may be an option

**h** = according to relevant clinical trial, currently UK CYP ALL Interim Guideline, July 2011 (UK ALL 2011 when introduced), EsPhALL and Interfant-06

**i** = according to UK R3 trial

**j** = if intolerant of TK inhibitor or failure to obtain and maintain a very good TK inhibitor response (according to LeukaemiaNet criteria)

**k** = transplant after achieving 2<sup>nd</sup> chronic phase using TK inhibitor +/- chemotherapy

**l** = according to UK CYP ALL Interim Guideline, July 2011 (UK ALL 2011 when introduced)

**m** = in early relapse (<12 months)

**n** = in late relapse (>12 months)

**o** = CR includes good PR by conventional imaging and FDG-PET negativity

**p** = allografting may be used after relapse following an autograft, in refractory disease at relapse or where mobilisation of autologous PBPCs has failed

**q** = the first transplant approach in children who achieve CR2 should usually be an autograft, assuming adequate autologous harvest has been achieved

**r** = if cytogenetics abnormal or blood product dependent

**s** = see Table 2

**t** = see Table 3

**u** = PBPCs not recommended for haemoglobinopathy due to significantly higher GvHD and decreased survival. Unrelated cord has a high rate of rejection with current protocols.

**v** = if vaso-occlusive crisis despite hydroxycarbamide (≥4 episodes / year requiring hospitalisation or impacting schooling), recurrence of acute chest syndrome despite hydroxycarbamide, CNS disease (stroke, abnormal transcranial Doppler [TCD] ultrasound and silent infarct or abnormal psychometric tests / poor school performance on formal assessment, silent infarcts with cognitive deficiency, significant abnormalities in MRA despite transfusions, abnormal TCD and generation of red cell alloantibodies, CNS disease requiring transfusions leading to significant iron overload despite optimum chelation treatment), or suboptimal medical care

**w** = HSCT with a 10/10 unrelated donor may be considered either at initial presentation or after failure of one course of immunosuppressive therapy

**x** = eg Kostmann syndrome, congenital amegakaryocytic thrombocytopenia, Schwachman-Diamond syndrome

**y** = if transfusion-dependent and unsuitable for / losing response to androgens, worrying clonal change or myelodysplasia

**z** = if transfusion-dependent

**aa** = if additional cytopenia (as well as anaemia) or progression to aplasia, transformation to myelodysplasia or leukaemia, or transfusion-dependent and inability to control iron overload despite adequate chelation

**bb** = indications for autologous HSCT agreed in collaboration with appropriate NCRI CCL CSG and / or CCLG sub-group. S applies to suitable patients and/or in context of clinical trial

\* Cornish. J., Goulden. N., Potter. M. (1998) Unrelated donor bone-marrow transplantation. *The Clinical Practice Of Stem Cell Transplantation*. Eds: Barrett. Treleaven. JG. pp 363-391. Follow adult HSCT indications list for adult-type diseases that occur extremely rarely in children (eg myelofibrosis, diffuse large B-cell lymphoma)

**Table 2 Indications for HSCT in immunodeficiencies**

- Severe combined immunodeficiency (SCID)
 

<u>Functional</u>	<u>Genetic</u>	
T- B- NK-	ADA deficiency	}
	reticular dysgenesis	
T- B- NK+	RAG deficiency	}
	SCID with Artemis	
	Cernunnos	}
	DNA Ligase 4	
	DNA PK	
T- B+ NK-	$\gamma$ c deficiency (X linked)	
	Jak 3 kinase deficiency (AR)	
T- B+ NK+	IL7 R $\alpha$ deficiency	
  - CD40 ligand deficiency
  - WASP deficiency
  - XLP
  - Phagocytic cell disorders
    - Familial HLH
    - Osteopetrosis \*
    - Griscelli disease
    - Immunodeficiency with partial albinism
    - IFN- $\gamma$  receptor deficiency
    - Kostmann disease \*
    - Shwachman's syndrome \*
    - Granule deficiency
    - LAD
    - X-linked CGD \*
    - AR-CGD \*
    - Chediak-Higashi syndrome
  - Autoimmune lymphoproliferative syndrome (homozygotes)\*
  - IPEX syndrome
- \* not all patients proceed to HSCT
- T cell immunodeficiency / SCID variants
    - CD4 lymphopenia
    - Zap 70 kinase deficiency
    - MHC class II deficiency
    - PNP deficiency
    - Omenn's syndrome
    - Severe Di George complex (22q 11 del)
    - CID with skeletal dysplasia
    - Cartilage hair hypoplasia
    - Nijmegen breakage syndrome
    - other
  - unspecified
  - other

Donor choice in order of preference MFD, 0-1 antigen-mismatched UD and haploidentical related donor.

These patients should be referred to a Supraregional Centre for HSCT procedure.

**Table 3 Indications for HSCT in metabolic diseases**

Standard	Clinical option	Developmental	Contraindicated
MPS type I (Hurler)	NP type C(2)	MPS type III	NP types B & C
Mannosidosis	Aspartylglucosaminuria	MPS types I HS, I S, II, VI (where antibody attenuates efficacy of ERT)	Infantile TSD
	Late infantile MLD	Juvenile Sandhoff	Infantile Sandhoff
	Wolman	Pompe	GM1 gangliosidosis

ERT = enzyme replacement therapy  
 MLD = metachromatic leukodystrophy  
 MPS = mucopolysaccharodosis  
 NP = Niemann-Pick disease  
 TSD = Tay-Sachs disease