Principles of Care for Primary Immunodeficiencies

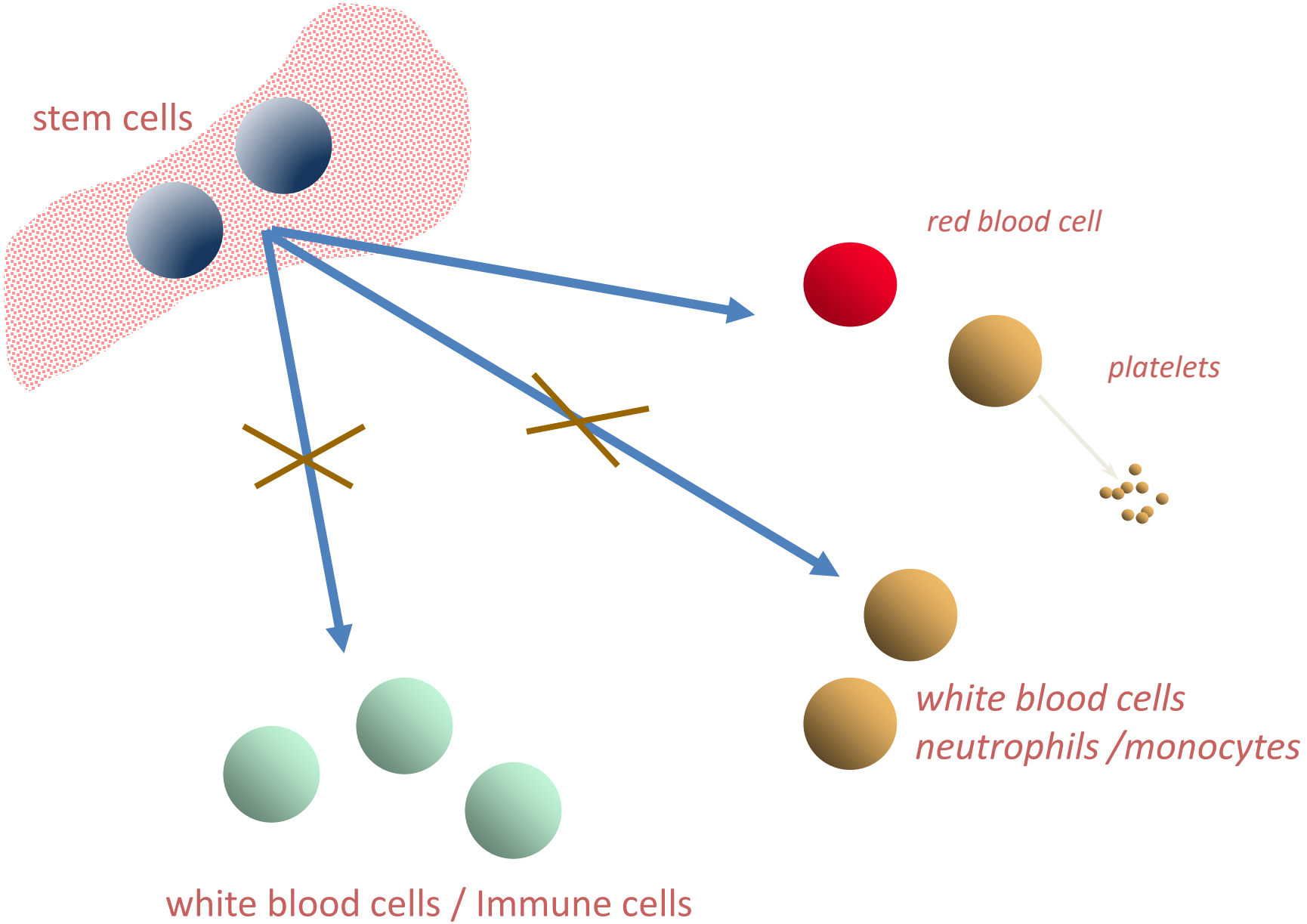
EU Parliament Brussels 2015

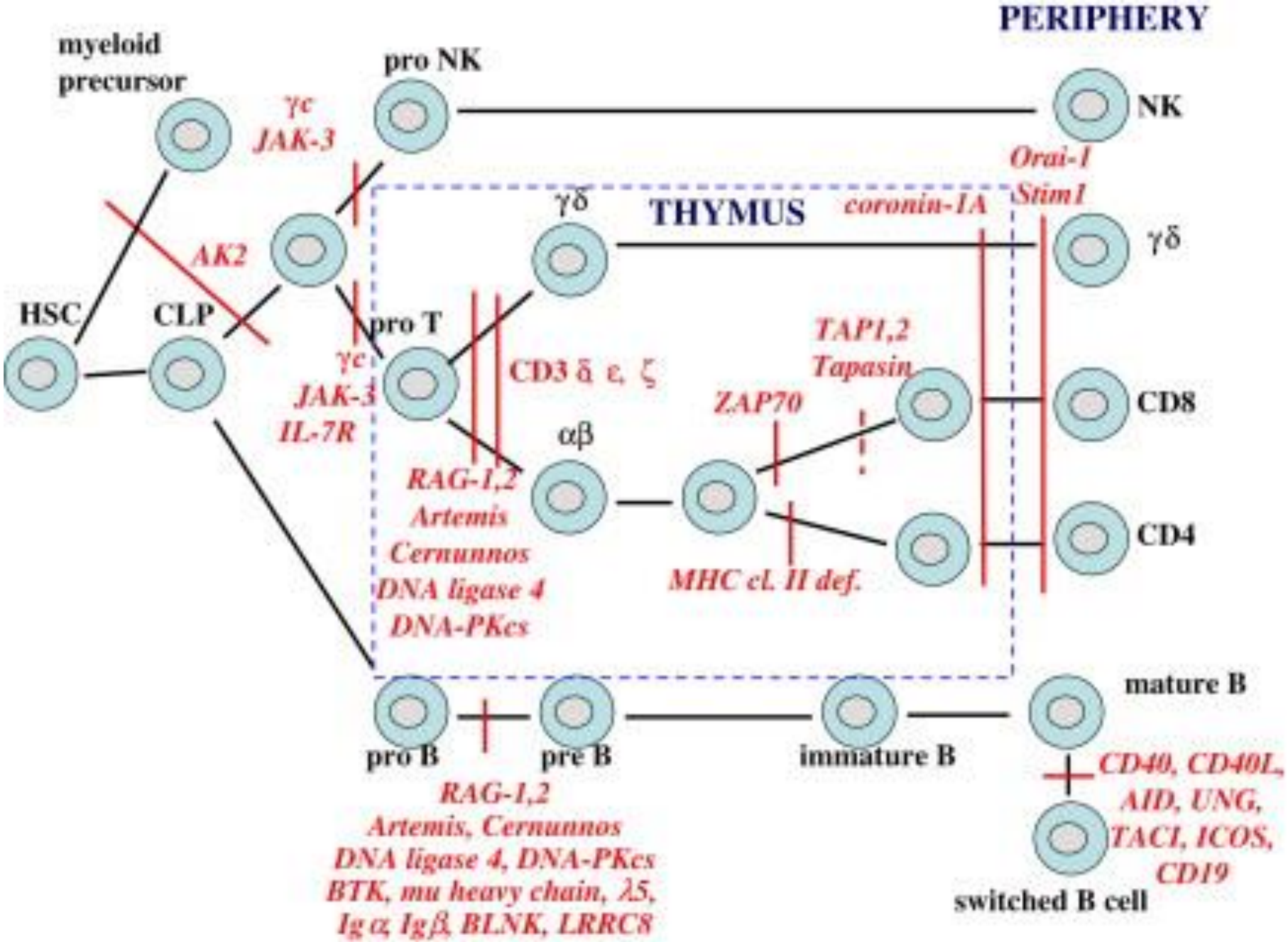
Bobby Gaspar

Centre for Immunodeficiency

UCL Institute of Child Health/Great Ormond Street NHS Trust

Primary Immunodeficiency




PERIPHERY
myeloid precursor
pro NK
NK
γc
JAK-3
Orai-1
Stim1
THYMUS
coronin-1A
γδ
γδ
AK2
HSC
CLP
pro T
TAP1,2
Tapasin
γc
JAK-3
IL-7R
CD3 δ, ε, ζ
ZAP70
CD8
αβ
RAG-1,2
Artemis
Cernunnos
DNA ligase 4
DNA-PKcs
CD4
MHC cl. II def.
mature B
pro B
pre B
immature B
CD40, CD40L,
AID, UNG,
TACI, ICOS,
CD19
RAG-1,2
Artemis, Cernunnos
DNA ligase 4, DNA-PKcs
BTK, mu heavy chain, λ5,
Igα, Igβ, BLNK, LRRC8
switched B cell

WHO / IUIS classification

1. Combined deficiencies
2. Other well-defined syndromes with immunodeficiency
3. Predominantly antibody deficiencies
4. Diseases of immune dysregulation
5. Disorders of phagocyte number, function or both
6. Defects of innate immunity
7. Autoinflammatory disorders
8. Complement deficiencies

Primary immunodeficiency diseases: an update on the classification from the International Union of Immunological Societies Expert Committee for Primary Immunodeficiency

Waleed Al-Herz[1,2], Aziz Bousfiha[3], Jean-Laurent Casanova[4,5], Talal Chatila[6], Mary Ellen Conley[4], Charlotte Cunningham-Rundles[7], Amos Etzioni[8], Jose Luis Franco[9], H. Bobby Gaspar[10], Steven M. Holland[11], Christoph Klein[12], Shigeaki Nonoyama[13], Hans D. Ochs[14], Erik Oksenhendler[15,16], Capucine Picard[5,17], Jennifer M. Puck[18], Kate Sullivan[19] and Mimi L. K. Tang[20,21,22]*

J Clin Immunol
DOI 10.1007/s10875-015-0201-1

ORIGINAL RESEARCH

Primary Immunodeficiency Diseases: an Update on the Classification from the International Union of Immunological Societies Expert Committee for Primary Immunodeficiency 2015

Capucine Picard[1,2] · Waleed Al-Herz[3,4] · Aziz Bousfiha[5] · Jean-Laurent Casanova[1,6,7,8,9] · Talal Chatila[10] · Mary Ellen Conley[6] · Charlotte Cunningham-Rundles[11] · Amos Etzioni[12] · Steven M. Holland[13] · Christoph Klein[14] · Shigeaki Nonoyama[15] · Hans D. Ochs[16] · Eric Oksenhendler[17,18] · Jennifer M. Puck[19] · Kathleen E. Sullivan[20] · Mimi L K. Tang[21,22,23] · Jose Luis Franco[24] · H. Bobby Gaspar[25]

Management and treatment Options

- Antibody (Immunoglobulin- Ig) replacement therapy
- Effective antibiotic prophylaxis and treatment
- Allogeneic haematopoietic stem cell transplant (HSCT)
- Autologous HSC gene therapy
- Appropriate vaccinations

Intravenous Ig replacement

Subcutaneous Ig replacement

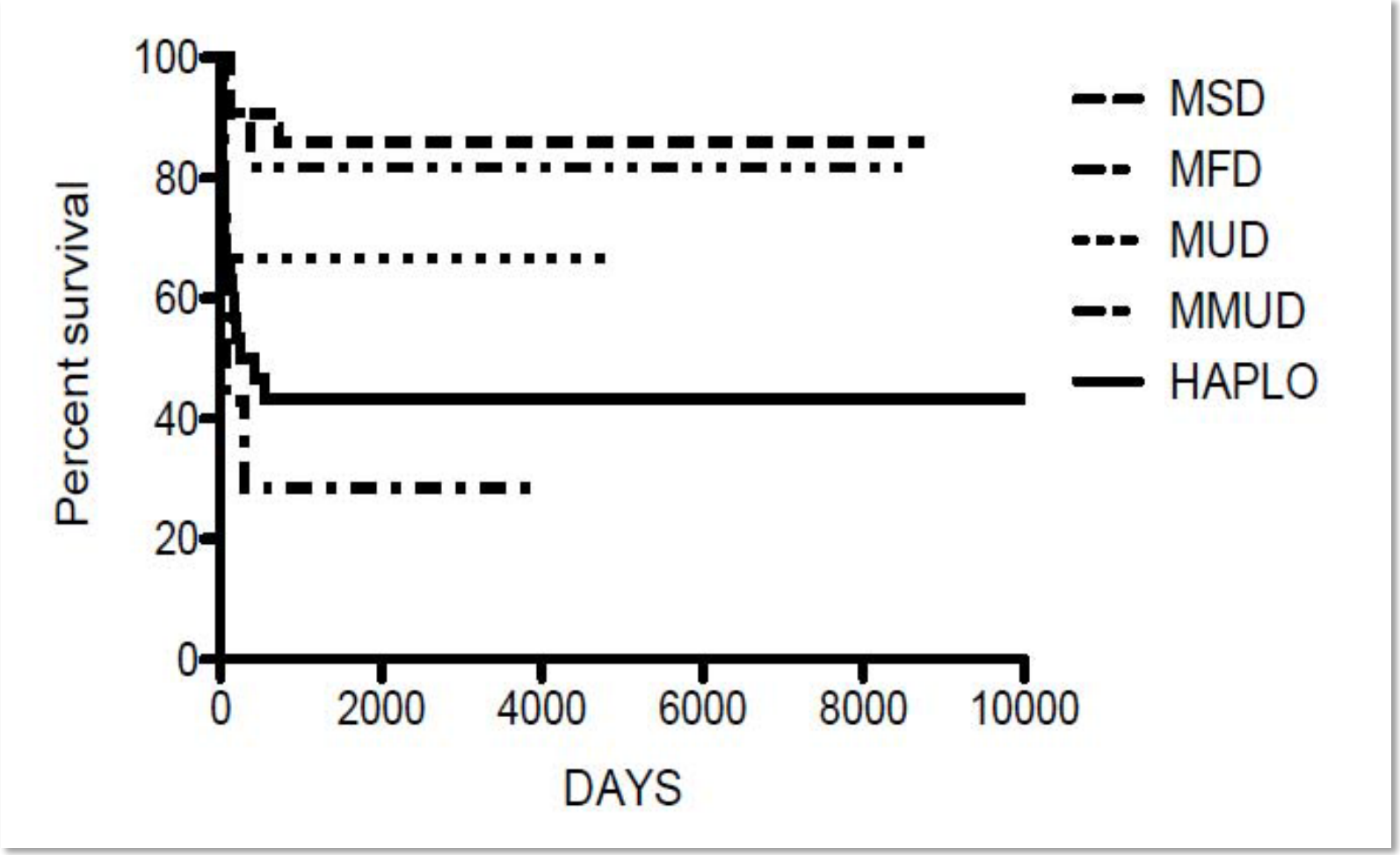
Table 4 | Current challenges to Ig therapy.

- Provision of finances to ensure availability of several Ig products in every country, to enable wide access to appropriate therapies, as per WHO Essential Medicines Lists
- Early diagnosis to prevent infection-related complications such as bronchiectasis
- Selection of optimal therapy and dosage for each patient, with regular medical follow-up to check reduction/abolition of breakthrough infections
- Increasing doses with growth in children
- Expert treatment centers, with dedicated nursing staff, to avoid side effects due to incorrect infusion techniques in first few infusions
- Training for self-infusion by suitable patients at home, with regular follow-up to ensure on-going high standards
- PID patients are prioritized for Ig products in times of restriction (for financial or availability reasons)
- Improvement of outcomes for complex patients by using additional therapies for disease-related complications

Table 5 | Advantages of programs for self-infusion at home.

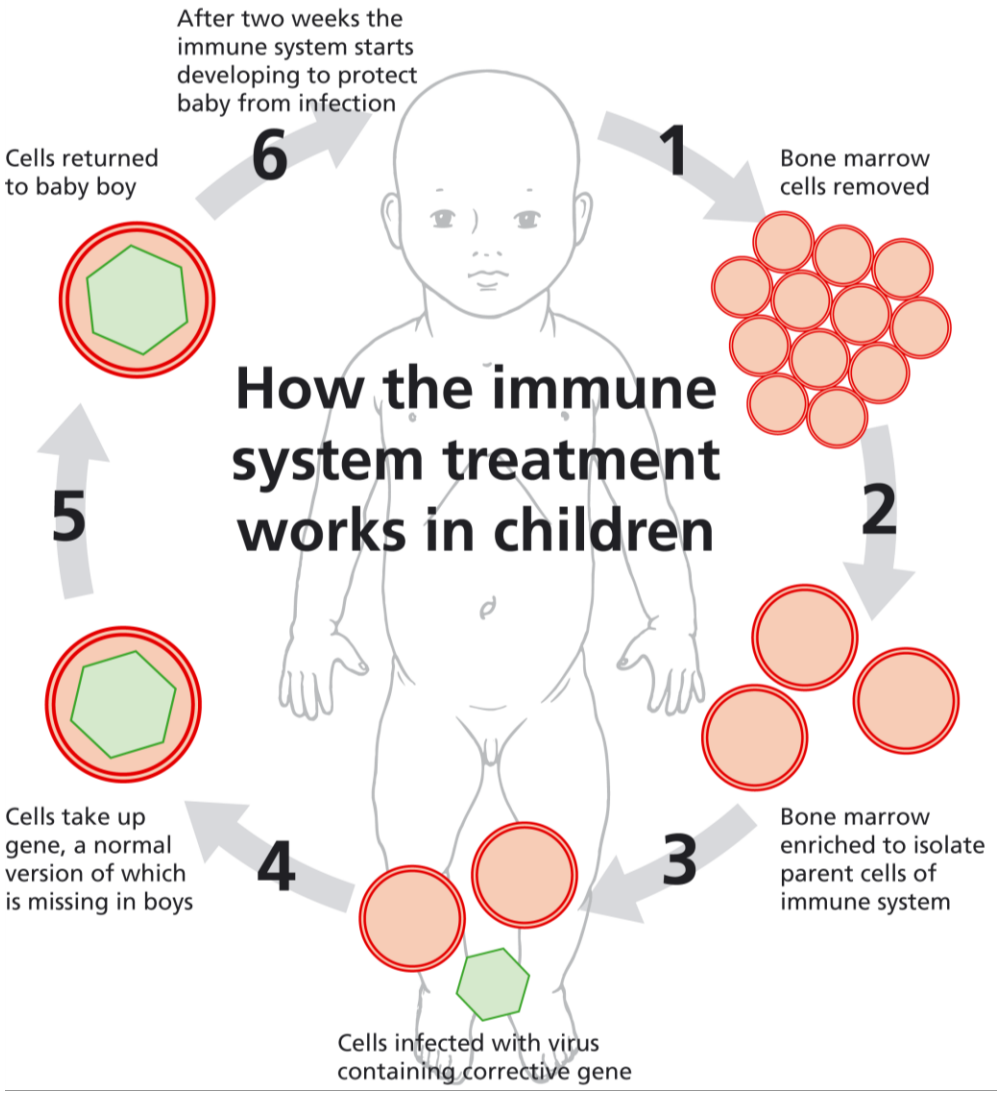
- Adult patients report that they are less tired, can plan their lives and do not have to miss work to attend treatment sessions
- Parents report that home-therapy keeps the child healthier due to regular treatment, enabling participation in school activities
- Participation in family/social and leisure activities for adults and playing with friends for children allow them to feel and act like others
- Parents themselves report less worry for the future of their child, fewer restrictions or sudden changes in plans in relation to family activities (e.g., holiday trips), less tension at home and more time for own needs and therefore have a higher quality of life

Overall Survival by BMT Type



EBMT/ESID GUIDELINES FOR HAEMATOPOIETIC STEM CELL TRANSPLANTATION FOR PRIMARY IMMUNODEFICIENCIES

Gene therapy



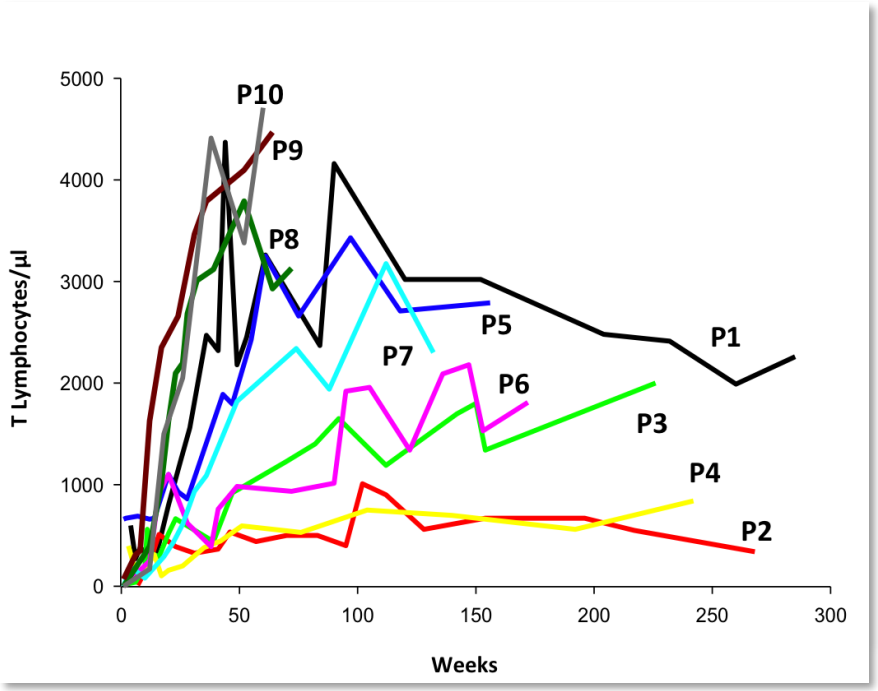
Gene therapy avoids GvHD

For some SCIDs, little or no conditioning

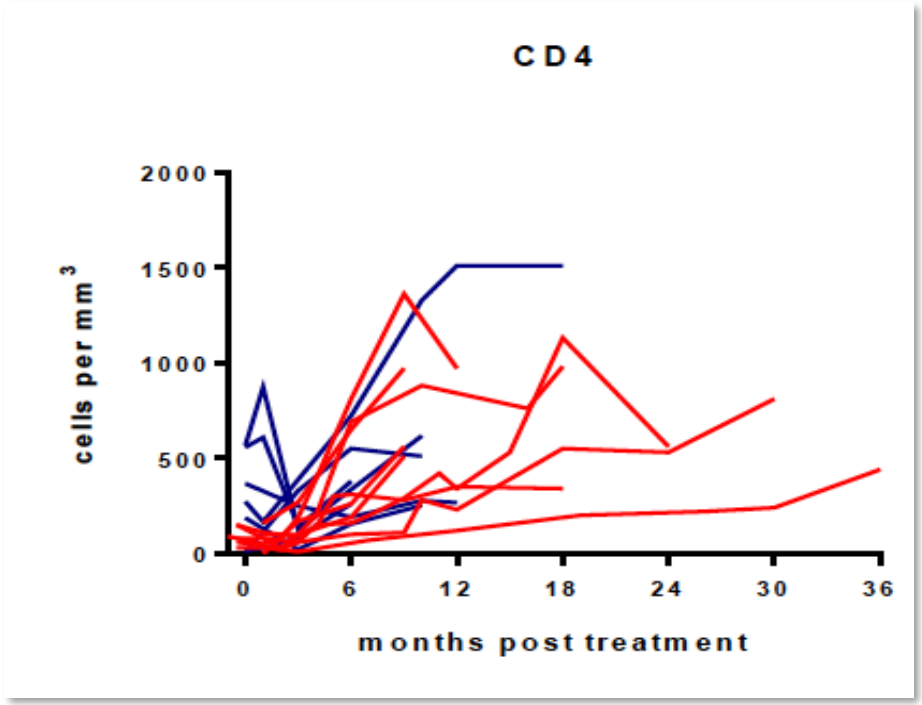
Autologous HSC Stem Cell Gene Therapy

T lymphocyte counts increase after postnatal stem cell gene therapy

SCID X1



ADA SCID



Stem Cell Gene Therapy With Lentiviral Vectors Cures Severe Combined Immunodeficiency


LUMC


EUROPEAN COMMISSION


UCL


IPOPI
INTERNATIONAL
PATIENT ORGANISATION
FOR PRIMARY IMMUNODEFICIENCIES


Unil
UNIL | Université de Lausanne


gene
WERK


SCIDNET


MACS


Miltenyi Biotec


Instituts
thématiques
Inserm
Institut national
de la santé et de la recherche médicale


UNIVERSITÄTS
KLINIKUM
FREIBURG

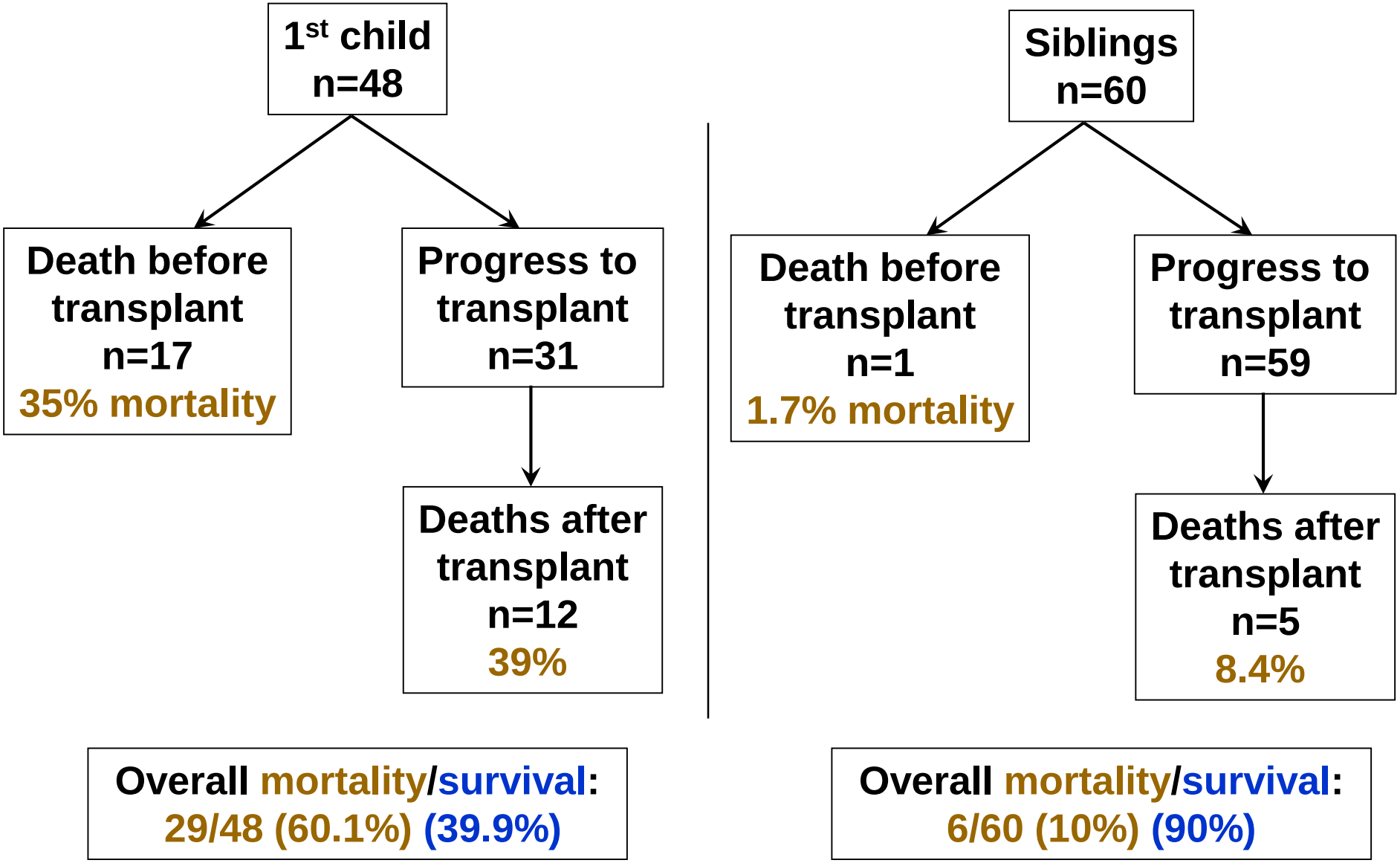

OSPEDALE
SAN RAFFAELE


MHH
Hannover Medical School


GENETHON
CURE THROUGH INNOVATION


Great Ormond Street
Hospital for Children
NHS Trust
NHS

Comparison of outcomes in families with SCID



J Clin Immunol
DOI 10.1007/s10875-014-0029-0

KEY REVIEW ARTICLE

The Case for Mandatory Newborn Screening for Severe Combined Immunodeficiency (SCID)

H. B. Gaspar · L. Hammarström · N. Mahlaoui · M. Borte · S. Borte

IPOPI
INTERNATIONAL
PATIENT ORGANISATION
FOR PRIMARY IMMUNODEFICIENCIES