BMT: survival infertility and other complications

Eurobloodnet Patient Session Series
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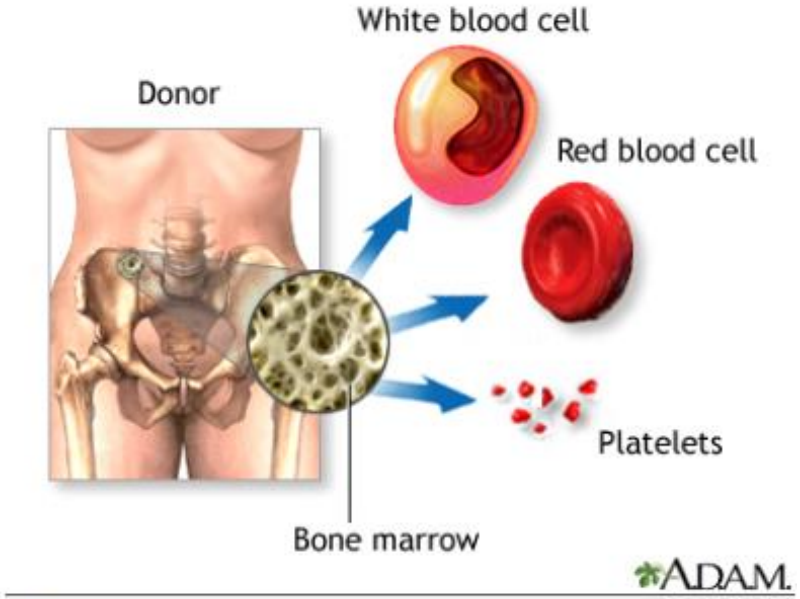
What is a bone marrow transplant

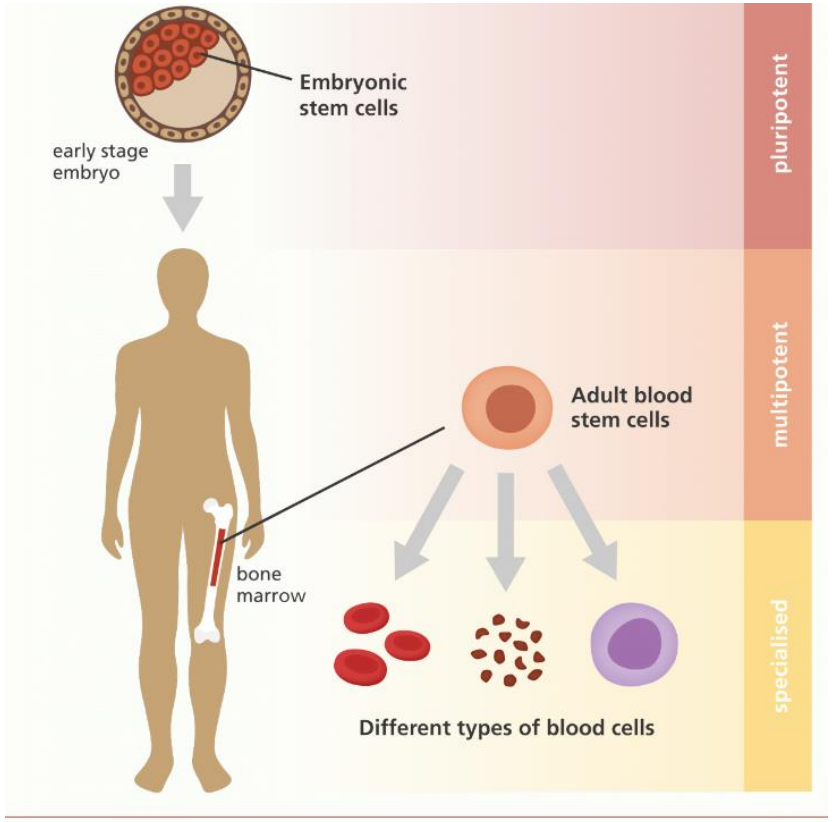


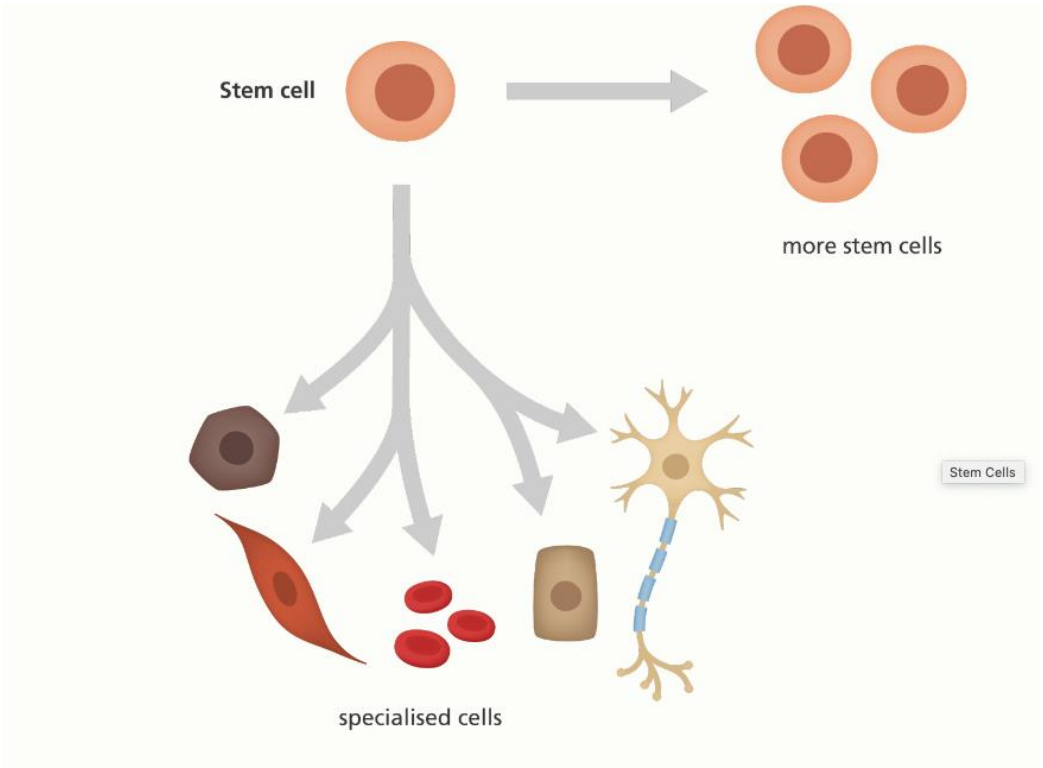
Normal anatomy

Bone-marrow is a soft, fatty tissue found inside of bones that produces blood cells (red blood cells, white blood cells, and platelets). Red blood cells carry oxygen throughout the body. White blood cells act to ward off infection. Platelets aid in blood-clotting.

https://www.stlukes-stl.com/health-content/health-ency-multimedia/1/003009.htm

What is a stem cell



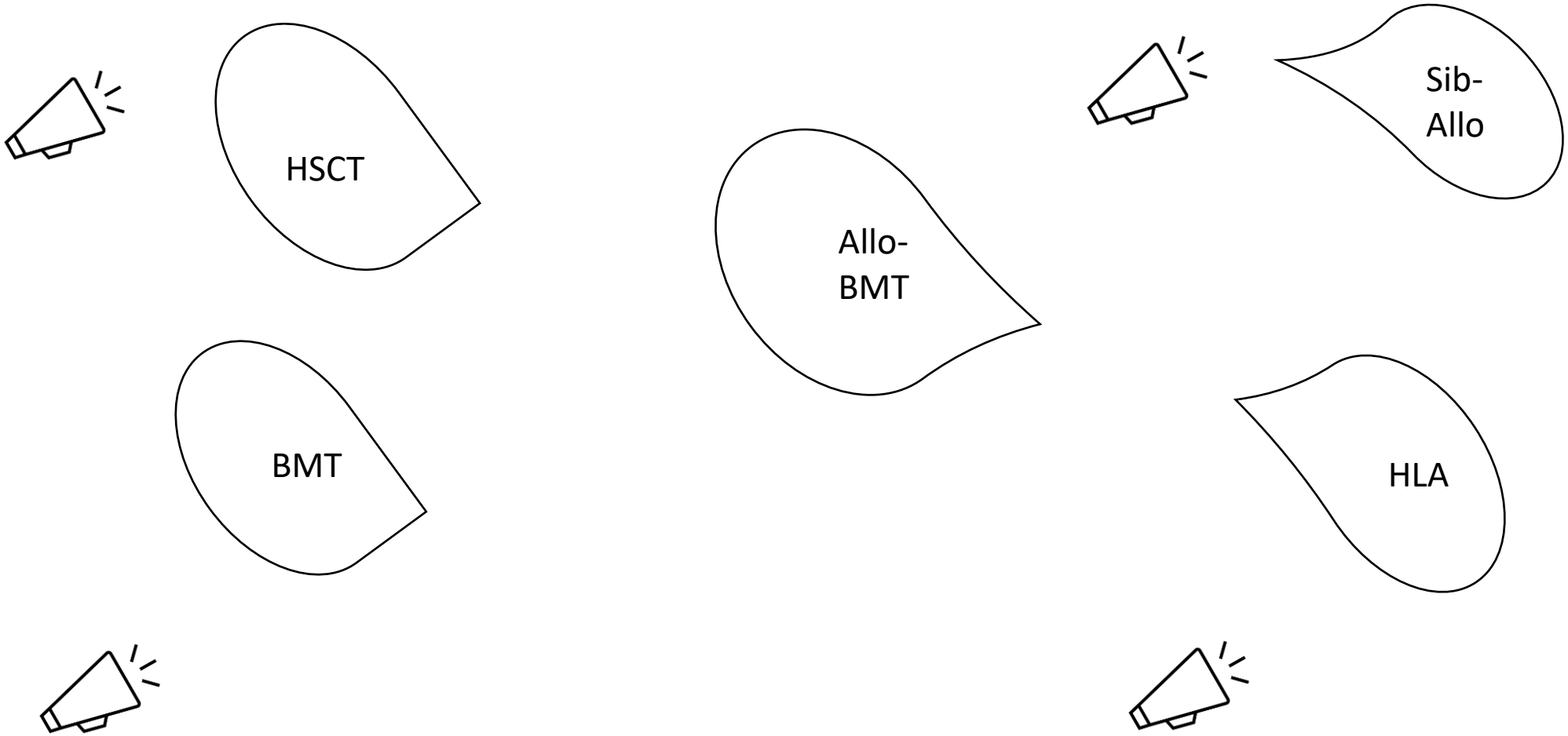


https://www.yourgenome.org/facts/what-is-a-stem-cell/

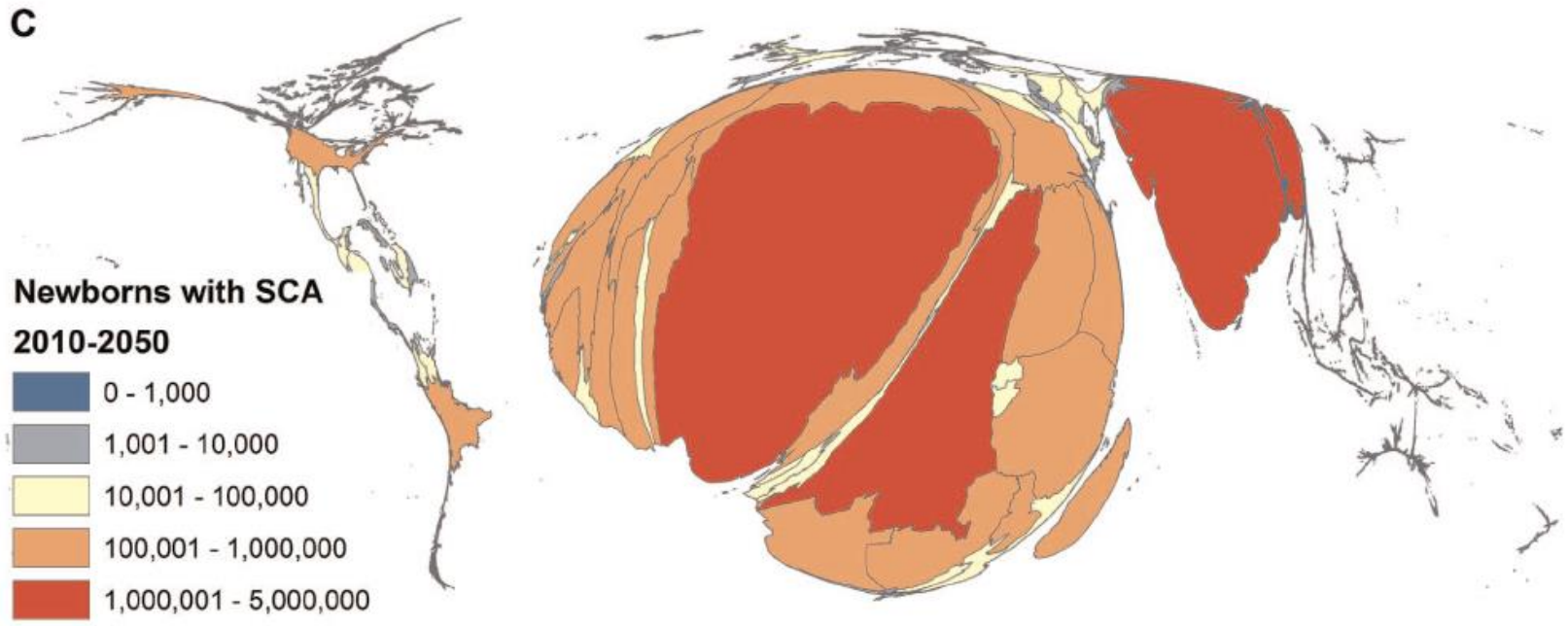
Links to YouTube video form the BMT Charity ‘Be the Match’

- https://www.youtube.com/watch?v=xUtdWWd6yyE&list=PLhHOWoRKO0EWfnunKIJQH8QGfT8gdkShJ&index=1
- https://www.youtube.com/watch?v=BUs4ykI0KNU&list=PLhHOWoRKO0EWfnunKIJQH8QGfT8gdkShJ&index=2

Names/acronyms can be confusing



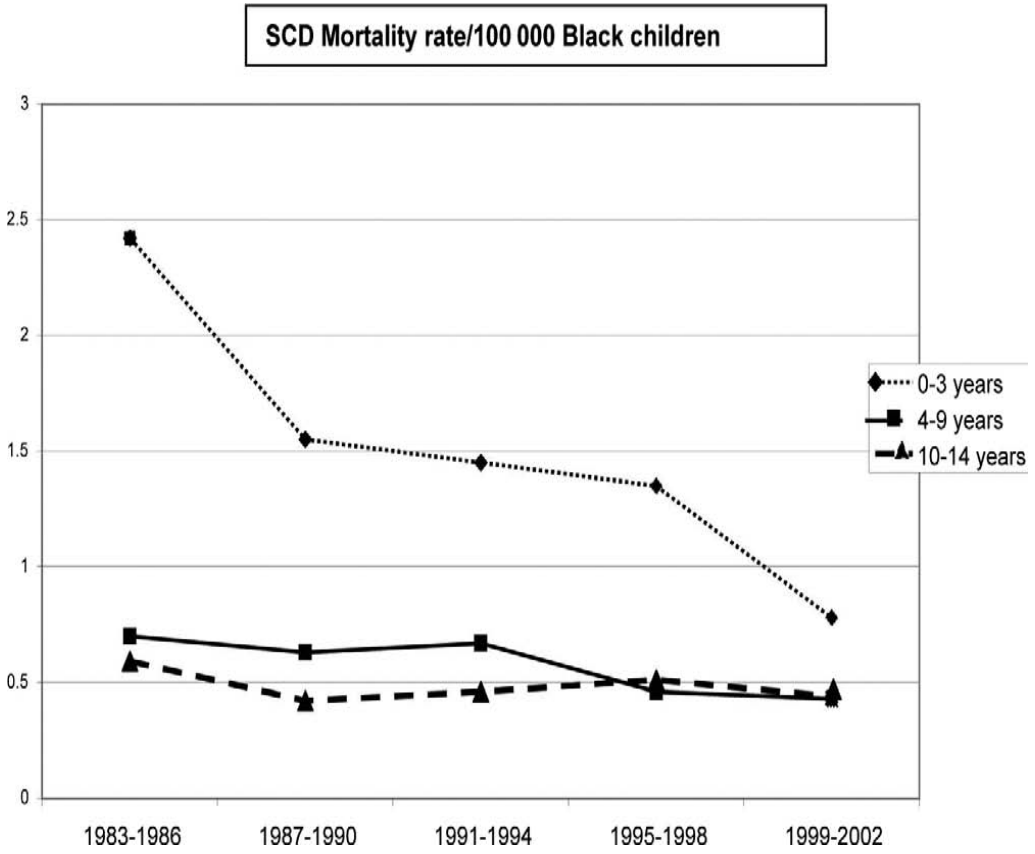
Global burden of SCD



Piel FB, Hay SI, Gupta S, Weatherall DJ, Williams TN (2013). PLoS Med 10(7):

Advances in therapies in treatment of SCD

- Penicillin and immunisations- 70's
- Hydroxycarbamide- 80'S
- Stem cell transplant-90's



Yanni et al J of Pediatrics 2008

Organ damage in sickle cell disease

- Spleen
- Brain
- Lungs
- Kidneys
- Eyes
- Joints

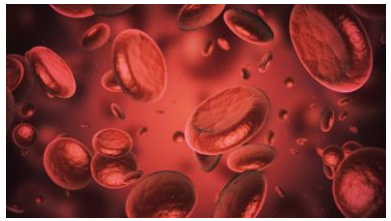
BMT in SCD

- First reported in 1984 for a patient with acute leukaemia and SCD-transplantation causing cure of both haematological conditions

- Since then, hundreds (mostly children) have undergone curative treatment with BMT

- Large studies have indicated reported overall survival (OS) of 92–94% and event-free survival (EFS) of 82–86%, the cumulative incidence of transplantation-related mortality (TRM) being in the order of 2–8%.

- Better outcome when performed in children transplanted from HLA-identical sibling donors



Case 1

- A 6yr old girl with sickle cell anaemia
- First sickle crisis at age 4yrs
- In addition hospitalisations every four months for chest infections.
- Age 5- abnormal transcranial doppler. MRI/MRA head normal.

Case 1

- Fever
- Viral infection - severe anaemia
- Found fitting on the bathroom floor
- Urgent MRI scan – stroke, MRA scan- damage to blood vessels
- Blood exchanges
- Brother was a match

Options?

- Continue regular transfusion and iron chelation therapy
- Continue transfusions through to age 18y and then change to hydroxycarbamide
- Work up for BMT

Case 1

- Underwent sibling BMT
- Successful transplant
- Yearly follow up
- Needed hormones to have menstrual periods for a few months

Assessment of clinical and pulmonary function after BMT

- 59 patients from 27 centres, 3.3–15.9 (median 9.9) years of age, received HLA-ID sibling marrow allografts between September 1991 and April 2000
- Indications
  - stroke (N = 30)
  - other CNS disease (N = 1)
  - recurrent ACS/pulmonary disease (N = 20)
  - recurrent pain (N = 8)

ACS, acute chest syndrome; CNS, central nervous system.
ATG, anti-thymocyte globulin; BU, busulfan;
CsA, ciclosporin; Cy, cyclophosphamide;
GVHD, graft-versus-host disease; MTX, methotrexate.

Walters MC, et al. Blood. 2000;95:1918-24.
Walters MC, et al. Biol Blood Marrow Transplant. 2010;16:263-72.

Post BMT Clinical outcomes

- No painful crises
- No episodes of ACS
- No episodes of splenic or hepatic sequestration
- No RBC transfusions
- No stroke, transient ischaemic attack, or haemorrhagic CNS events

Walters MC, et al. Biol Blood Marrow Transplant. 2010;16:263-72.

Case 2

- HbSS diagnosed at birth
- First crisis age 4 months
- Recurrent crisis- hydroxycarbamide (HC) therapy
- Some improvement but not fully improved
- Also had hip joint damage
- Unable to tolerate transfusions

Options

- Improve compliance of hydroxycarbamide
- Commence on automated red cell exchange transfusion programme
- Refer for a bone marrow transplant

Case 2

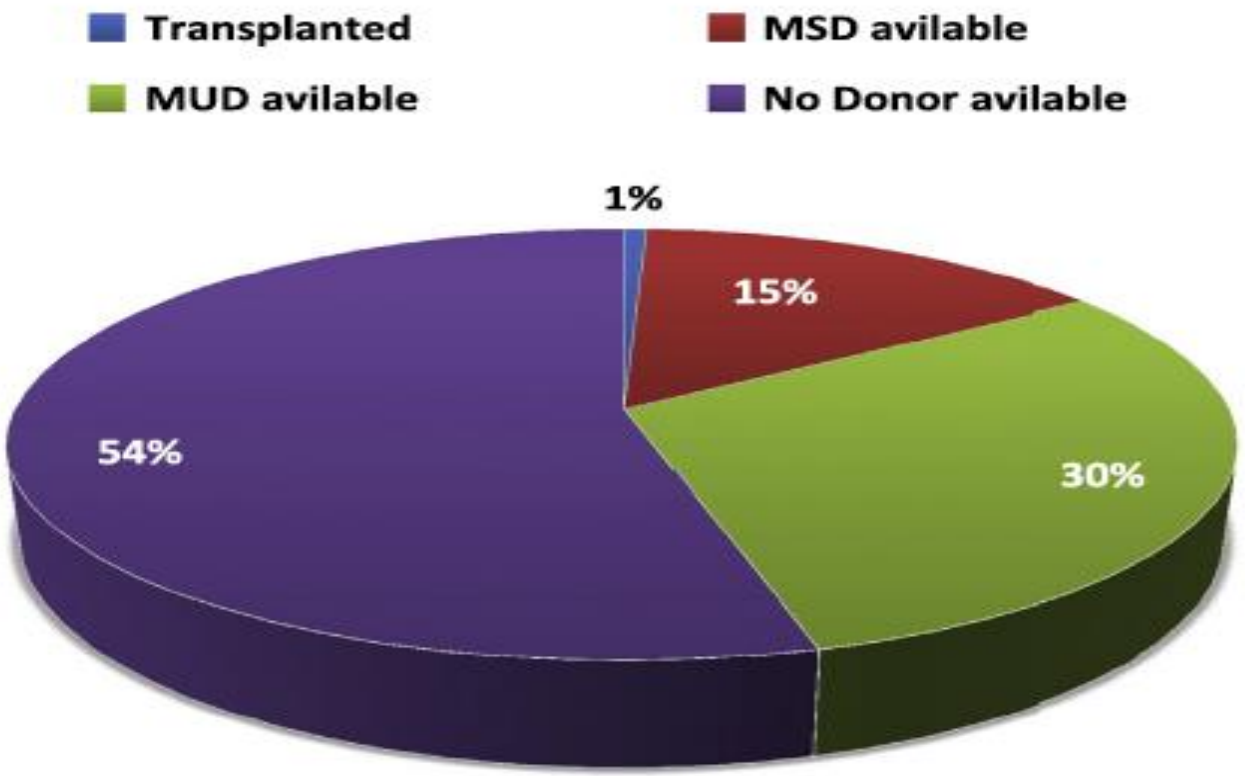
- Sibling BMT

- Remains cured of SCD on 4 years follow up

Barriers to BMT in SCD

- Vast majority of children (85%) who qualify for transplants do not have a suitable matched related donor
- This has led to consideration of other stem cell sources:
  - Unrelated bone marrow (BM) or peripheral blood stem cells (PBSC)
  - Unrelated cord blood
  - Mismatched related bone marrow
  - Haploidentical (parent or sibling) PBSC or BM

Searching for a donor in SCD BMT

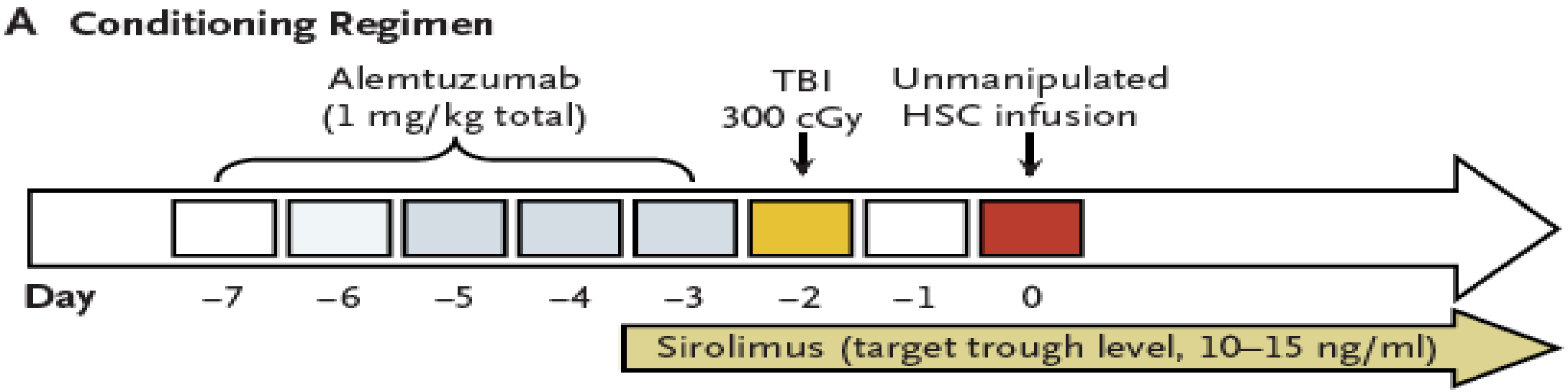


. The frequency of donors and transplants in patients with SCD.

Case3

- 20 year old female
- Long history of recurrent painful crises
- Poor response to hydroxycarbamide- compliance issue
- Red cell top up transfusion programme- complicated by very difficult venous access
- Three chest crises within 6 months of stopping red cell transfusions
- Chronic sickle lung disease and nephropathy
- Sibling is HLA matched

Reduced intensity conditioning-HSCT in adults



HSCT- Haemopoietic stem cell transplant

Hsieh MM, et al. N Engl J Med. 2009;361:2309-17.

Case 5

- A 6yr old boy
- Never been admitted for vaso-occlusive crises
- Stroke age 5
- Sibling not match

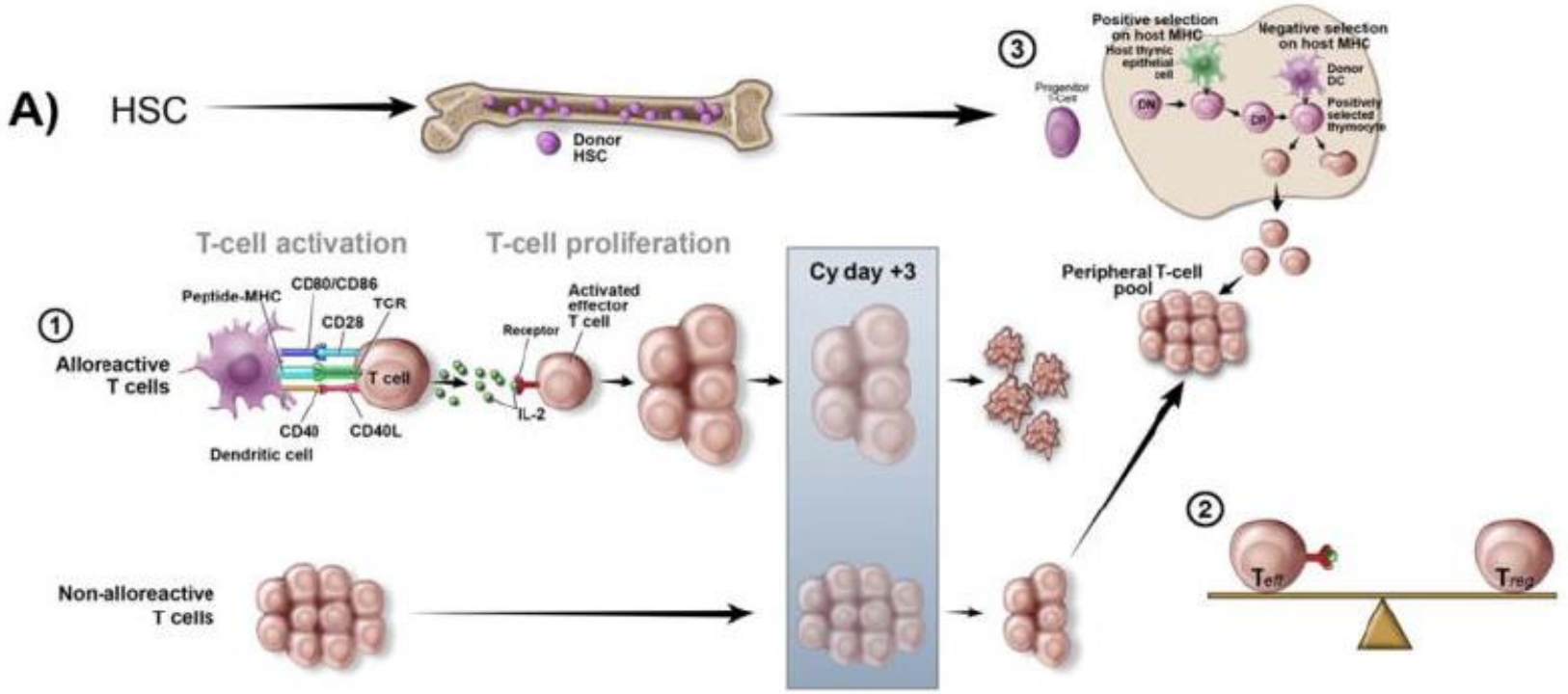
Case 5- therapeutic options

- Continue red cell transfusions but add hydroxycarbamide
- Refer for consideration of neuro-surgical procedure for bypass of stenosis
- Proceed with unrelated donor BMT

Case 6

- 8 year old boy
- Multiple vaso-occlusive crises from very early age
- Right peri-rolandic cortical stroke with left hemiplegia age 2.5- transfusion programme
- Progression of vasculopathy on MRA despite transfusions
- Only child, no UD available on search

Post-transplant cyclophosphamide for induction of tolerance in haplo-identical transplant



Luznik et al Semin Onc 2012

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