



ISBMT

Indian Society for Blood & Marrow Transplantation

BMT MASTER CLASS

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Graft manipulation: Haploidentical HSCT in Mucopolysaccharidosis type I

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Case history

- Ms. A

- Only c

- LSCS/

- Ingu

- Corr

- Hep

- Diag

- Alph

- Star

- HSCT effective in MPS I, II, IVA, VI, VII

- <2.5 years preferred

- ERT upto 12 weeks before and 15 weeks after HSCT: reduce respiratory and cardiac complications, buy time

- Bone marrow source, non carrier- HLA donor

- Myeloablative conditioning

- Cannot alter pre-existing CNS , valvular, musculoskeletal damage, corneal clouding

No MSD/ MUD donors available

DSA negative with parents

HAPLOIDENTICAL HSCT WITH TCR AB DEPLETION AND CD45RA DEPLETION

Transplant details

Apheresis
STEM CELL PRODUCT (Ex vivo manipulation)

TCR alpha/beta
depletion

CD45RA
depletion

Efficient TCR α/β +
cell depletion

Maintenance of
stem cells , NK
Cells, TCR $\gamma\delta$ Cells

Infusion

Efficient CD45RA
depletion

CD45 RO DLI

Reduced GvHD

Facilitate Engraftment
Exert GVL effect
Decreased Infection
Support Immune
Reconstitution

Reduced GvHD

Decreased infection
Decreased relapse

Transplant details

- **Haploidentical HSCT with TCR AB depletion and CD45RA depletion**
- Conditioning: ATLG (20mg/kg) + Thiotepa + Treosulfan + Fludarabine
- Rituximab on D-1
- **Cell dose:** CD34 = 15.2×10^6 cells/kg,
TCR AB cells/kg = 0, TCR gamma/delta dose = 41.8×10^6 cells/kg

Post transplant complications:

- **D+7 : Severe veno-occlusive disease**

Rx with defibrotide, fluid restriction, diuretics

- **Engraftment details:** Neutrophil engraftment D + 11
Platelet engraftment D+12
- **D+15 :**Non neutropenic fever x 3days
- Discharged on D+23

Post transplant events

- **Discharged on D+23**
 - GVHD prophylaxis: MMF (stopped by D +30)
 - Voriconazole, Aciclovir/ Letermovir, PCP prophylaxis: TMP/SMX
- **Chimerism** on D + 27, D + 86 : 100% donor chimerism
- **T, B and NK subset**
 - D+ 28 : ALC:1527/uL, CD3:725/uL, CD4:18/uL, CD8: 66/uL , CD19: 0/uL , CD16+56: 730/uL
 - D + 86 : ALC:1426/uL , CD3:814/uL , CD4 : 94/uL ; CD8:204/uL; CD19:0, CD16+56: 587/uL
- **DLI with CD45RO cells on D+33:** 1×10^5 cells/kg₅
 - D + 52 : 2×10^5 cells/kg
 - D+69 : 5×10^5 cells/kg
- **D + 90:** improvement in coarse facial features, organomegaly
- Enzyme levels 3 months post transplant: 23 nmol/hr/mg (ref: 20 -108)

DISCUSSION POINTS

- Ex-vivo T cell depletion: comments and concerns
- Choice of various depletions platforms: TCR AB/CD19; TCRAB/CD45RA; CD45RA
- How to time the CD45RO cell addbacks? Considerations and concerns