SSH SCT Data

- Total : 559
- Allogeneic : 380
- Autologous : 179
- Non Malignant : 255 / 559 (45%)

B Thal Major : 112
Aplastic Anemia : 92
MDS : 16
Immune Deficiency : 18
AID (AUTO) : 17
Indian Scenario

- Genetic diseases are common
- Many can afford only one therapy
- SCT can be Cheaper than long term drug therapy
PRINCIPLES OF HSC TRANSPLANT

- Myeloablation
- Immunosuppression
- Non-myeloablative
Stem Cell Source

- BM - Bone Marrow
- PBSC - Peripheral Blood Stem Cell
- P-UCB - Placental Umbilical cord Blood
Types of Allogeneic Donor

- Syngenic
- Sibling
- Close family member
- Unrelated
B Thal Major : 112

- Common
- Age : 10m - 13 yrs
- FU : 2m - 16 yrs
Ideal Mx of Beta Thal major

- Prevent Birth of Beta Thal major
- Hb > 10 gm%
- Use of leucocyte filter
- Proper chelation, Ferritin < 1000 ng/ml
- Avoid family blood Tx
- Monitoring of hemosiderosis
- Cost – Rs. 125000/ yr
Myeloablative Regimens

- Bu Cy
- ATG + Bu + Cy
- Flu + Treosulphan + Thiotipa
Risk Classification for Beta Thal

- **Risk Factors** – Hepatomegaly, Portal fibrosis, Inadequate chelation

- **Class I** – No risk factors
- **Class II** – Any one risk factor
- **Class III** - Inadequate chelation plus one
Problems of BMT in Beta Thal

- Hemosiderosis increases the risk of hepatic, cardiac and neuroendocrine complications

- Recurrent Tx – HLA sensitization, risk of BM rejection

- Platelet refractoriness

- Donor is usually a Child
Risk Stratification Data

- Class I: 22 / 112 (19%)
- Class II: 37 / 112 (33%)
- Class III: 53 / 112 (48%)
Survival Data

- Class I: $21 / 22 (95\%)$
- Class II: $29 / 37 (78\%)$
- Class III: $32 / 53 (61\%)$
- Early SCT in Class I: Excellent results, cheap
- Avoid Family Transfusions
- Haplo / Unrelated PUCB: Experimental
- Position of MUD SCT?
Aplastic Anemia: 92

- Very common in India,
- Young median Age
Rx algorithm for VSAA / SAA

Age <20y
- high-risk for IST failure
- low-risk for TRM
  → BMT

Age 20-50y
- high-risk for TRM
- low-risk for IST failure
  → IST
  → No response recurrence
  → BMT

Age >50y
- BMT

No response
recurrence

No response
recurrence

No response
recurrence

HLA identical sibling BMT

Initial treatment of choice if

- VSAA or SAA
- HLA identical sibling
- age <50 yr

Controversy over

- Children with non-severe AA may be considered
- Controversy over upper age limit
MUD / Haplo SCT - VSAA / SAA

- Not as first line
- As a FIRST LINE in children
- Failed Initial TRIPLE IST
- Feasible in India
- May be better than second ATG
AA Data, SSH, Pune (Aug 1997-Dec 2015)

- Total: 1012
- VSAA + SAA: 770 (76%)
- HLA matched SCT: 83
- Haplo SCT: 9
- Triple IST: 194 (hATG), 9 (rATG)
- Fludarabine: 86
- Fludara + CyA: 27
- Anabolic Steroids & Transfusion alone: 487 (58%)
Risk Stratification

- **High Risk** - > 6 months from diagnosis to Rx
  > 20 transfusions
  Failed Prior IST
  Active infections
Risk Factors at the time of SCT

- Time to Rx: 6-60 days
- Transfusions prior to Rx: PCV - 2-21, RDP - 4-132
- Infection at Rx: Documented Sepsis at Rx - 8, Pneumonia at Rx - 2, Fever at Rx - 11
- Clinical Risk Category: HR - 39, LR - 16
SSH SCT Data (1999 – 2015)

- MRD - 83
- Haplo - 9
SAA SCT - SSH data (1999 – 2015)

- Total: 83 + 9
- Cy 200 + hATG 90: 10
- Flu 180 + Cy 120: 73
- SAA Allo grafts: 92 / 543 (16%) of all SCT
  - 92 / 770 (12%) of VSAA + SAA
Risk factors & SAA SCT

- **High Risk** - > 6 months from diagnosis to HSCT
  
  > 20 transfusions

  Failed Prior IST

  Active infections
Cy + hATG - 10 cases (1999-2003)

- **Age**: 9 – 47 yrs
- **HR**: 5, **LR**: 5
- **SC source**: BM
- **Cell dose**: 3.9 – 10.2 x 10^8 / kg
- **Rejection**: 3 / 10 (All HR)
- **Gr. III / IV GVHD**: 1 (LR)
- **Majority of the cases are HR**
- **Rejection was a major problem**
Flu Cy data- 2003 – till date

- Total - 73
- Age - 3 – 56 yrs, M: F = 55 : 18
- Time to SCT - 12 days - 3 years
- Conditioning - Flu 150 mg /m2 + Cy 120 mg /kg + hATG 40mg / kg (6 pts)
- Graft Source - PBSC, G mobilised
Risk Factors

- **Risk Category**
  - HR: 49 / 83 (59%)
  - LR: 34 / 62 (41%)

- **Prior therapy**
  - NIL
  - Triple IST: 14
  - CyA: 10
  - Dan + Wys: 15

- **Time to SCT**
  - Less than 3 months: 63
  - More than 3 months: 20

- **Transfusions**
  - More than 20: 27

- **Infection before SCT**
  - 12
GVH prophylaxis - CyA + MTx - 66
Endoxan D3 / D4 - 17

Engraftment - ANC > 500 - D 12 (9 – 14)
Plat > 20000 - D 14 (12 - 21)

100 % Donor Chimerism on D 28 - 92 / 92

aGVH (III /IV) - 22 / 92 (24 %) HR -21 , LR-1
survival - 6 / 22

cGVH (extensive) - 15 / 92 (16 %) HR – 10 , LR- 4
survival - 7 / 15
Cont …

- **Sepsis** - Bacterial - 24%  HR 13 , LR 3
  Fungal - 17 %  HR 11
  B + F - 22 %  HR 14
  CMV - 6 %  HR 3 , LR 1

- **D 100 mortality** - 10 / 92 (11 %)  HR 9 LR 1

- **OS** - 2m – 12 years
  Entire cohort - 74 %
  HR - 58 %
  LR - 92 %

- **Rejection** - NIL
Post SCT Cy alone as GVH prophylaxis

- Total - 17
- HR - nil
- LR - 17

- Period - 1 - 32 months

- Rejection - Nil

- Gr 3/4 aGVHD - 3/17 (18%)

- Extensive cGVHD – 3/17 (18%)

- Death - 1/17
### Allo SCT in AA – Indian Perspective

**Dr. Biju George et al, ASH 2009**

- **Period**: 1999 to 2009

- **Total Numbers**: 127

- **Centers**:
  - CMC Vellore: 79
  - SSH Pune: 27
  - Army Hosp R & R New Delhi: 21

- **Conditioning**:
  - Flu 150 mg/m² + Cy 120 mg/kg +/- ATG

- **Graft Source**: PBSC

- **Age**: 7 yrs to 54 yrs

- **Risk Category**:
  - HR: 75 / 127
  - LR: 52 / 127
SCT Data - cont

- **High Risk** - > 6 months from diagnosis to HSCT
  > 20 transfusions
  Failed Prior IST
  Active infections

- **OS** - Entire Cohort - 73 %
  HR - 60 %
  LR - 92 %

- Rejection < 5 %

- aGVHD - 31 %
Causes of Morbidity & Mortality

- Infections - fungus / CMV
- Bleeding
- Increased incidence of Platelet Refractory state
Cost Equations for Average Patient - SSH

- Allo Sibling SCT - Rs. 600,000 (Uncomplicated)
- TRIPLE IST - Rs. 800,000
- CyA based - Rs. 150,000
- Fludarabine - Rs. 100,000
- Androgen - Rs. 10,000
- MUD SCT - Rs. 30,00,000
- HAPLO SCT - Rs. 20,00,000
Impressions

- Sibling Allo SCT may be cheaper and better Rx option in India if done early

- HR AA is primarily DELAY in definitive Rx

- Extremely important to avoid unnecessary Tx

- Mortality will definitely come down with early SCT

- Better documentation

- More than 50% patients do not receive definitive Rx
Immune Deficiency SCT : 18

- **Period**: March 2005 - Dec 2015
- **Pt ‘s Age**: 7 wks - 4 years
- **Donor**: 20 months - 32 yrs

- **Indications** ---
  - Osteopetrosis - 3
  - HLH - 3
  - LAD - 2
  - CGD - 2
  - Hyper IgM - 1
  - Wiscott Aldrich - 1
  - SCID - 6
Types of SCT

- MRD: 8 (7/8)
- MUD: 2 (2/2)
- Unrelated PUCB: 1 (0/1)
- Haplo: 7 (5/7)
Uniqueness

- Very small patients
- Low weight
- Infected
- Hickman by real expert Pead Surgeon

- Very low immunity at the outset
- Less rejections
- Excellent results with Haplo
  - T–ve, B–ve, NK–ve: persistence of Maternal T cells

- Early Diagnosis and Early SCT
More than 2000 procedures were reported to the Registries for AID

Most of available data are derived from small series and registry analysis

Comparative trials in major diseases are ongoing

Still lot of skepticism / lack of interest among referring specialists
## Table 1a. Activity

<table>
<thead>
<tr>
<th>Condition</th>
<th>Number</th>
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<tr>
<td><strong>Multiple Sclerosis</strong></td>
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<tr>
<td>Connective tissue</td>
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<tr>
<td>SSc</td>
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<td>SLE</td>
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<td>PM-DM</td>
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<td>Sjogren</td>
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<td>Antiphosph. Syndrome</td>
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<tr>
<td><strong>Other</strong></td>
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</tbody>
</table>
Concept of Auto PBSCT in AID

- **To kill auto reactive T cells**, various drugs kill but remission lasts for few months / years
- Mobilize PBSC
- Chemotherapy **To kill auto reactive T cells**
- To replace stem cells after chemotherapy
- **Hope that new T cells will not have Auto Reactivity**
Conditioning Chemotherapy

- hATG + BEAM
- Cy + hATG
- Cy + Campath
End Point Definitions

- Relapse free status

- MRI event free status, decrease in T2 volume

- Optical Coherence Tomography Measure

- EDSS

- DFS at 5 years - No relapse / No new MRI lesion
  Decrease in T2 volume
  No worsening of EDSS/ MSFS/NRS

- Transplant Related Mortality at Day +100 : 1-2%
Figure 2: Kaplan-Meier curves of progression-free survival (PFS) according to age and years from diagnosis. Analysis of 443 patients with neurological outcome data reported in the EBMT database registry. According to a bivariate Cox regression analysis, patients above the age of 40 years had a significantly higher progression rate compared with patients younger than 40 years of age (hazard ratio [HR] = 1.9, 95% CI = 1.1–3.3, p = 0.02), whereas disease duration was not significantly correlated with PFS (HR = 1.2, 95% CI = 0.6–2.2, p = 0.6). Adapted from Saccardi et al. with permission from Sage publications.
SSH Data on AID Auto PBSCT
2009 - 2015

- MS - 7
- JRA – 3
- SLE – 3
- SSc – 3
- CML + Ulc Colitis (Allo SCT) - 1
MS Data – 7 MS

- **Age**: 27 – 44 yrs, All Females
- **Time to SCT from Diagnosis**: 14 m – 66 m
- **Types of MS**
  - Relapsing Remitting: 4
  - Secondary Progressive: 2
  - Rapidly Progressing: 1
- **EDSS score at SCT**: 1 – 6
- **MRI +ve lesions at SCT**: 7
Prior Therapies:

- < 3 Rx : 3
- 3-5 Rx : 3
- 5 Rx : 1
- IFN Rx : 3
- Exp Rx : 3

- CD 34 +ve Cell - 3.9 – 14.5 x 10^6 /kg
- Engraftment data:
  - ANC > 500 /cmm : Day + 9 – Day + 18
  - Platelet > 20000/cmm : Day + 10 – Day + 22

IFN exposure had Less CD 34 +ve cells and Delayed Engraftment

FU period : 3m – 74 m

Completed 5 year FU : 3/7

MRI improvement : 5/7 (Complete)

Improved EDSS Score : 6/7
Cont.

- CD 4+ve / CD 8+ve /CD 25-ve : 6/7
- Normal Th 1/ Th 2 ratio : 6/7

- Duration To achieve T-Cell Recovery : 8m-17m

- IgG Recovery : 12m – 18m

- CMV Reactivation : 2/7
- HZV / HSV Infection : 4/7
- Fungal Infection : 1/7
- Blood Culture +ve Septicemia : 2/7
- Re – Vaccination completed : 5/7

- 2 patients Delivered FTND after 5 years Fu
Summary

- SCT has a significant role to play in Genetic and Non malignant conditions
- Imm Deficiency Haplo SCT is reasonable, cost effective Rx
- Rapid intervention improves outcome
- AID is emerging as strong indication for Auto SCT
- MUD, Haplo & Unrelated Cord SCT for B Thal Major ??
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- Blood Bank & Pathology teams, SSH
- Administrative staff and SSH
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