

Safe and effective reduced-cost bone marrow transplantation for thalassemia: The preliminary experience in Pakistan

Saqib Ansari¹, Tahir Shamsi¹, Sadaf Khalid, Naila Yaqub²,
Tasneem Farzana¹, Kamran Rashid³, Yasir Iqbal³, Kousar
Parveeni^{1&4}, Pietro Sodani⁴, Cristiano Gallucci⁴, Buket Erer⁴, and
Lawrence Faulkner.

Cure2Children Foundation, Florence, Italy; ¹National Institute of Blood Diseases (NIBD), Karachi, Pakistan, ²Pakistan Institute of Medical Sciences (PIMS), Islamabad, Pakistan; ³Shifa International Hospital (SIH), Islamabad, Pakistan; ⁴Mediterranean Institute of Hematology, Rome, Italy.

Beta-Thalassaemia Major

- ◆ With allografts from HLA identical siblings, up to 90% DFS is obtained in children between 2 - 5 years of age
- ◆ Success of Transplant in β -thalassaemia depends:
 - ◆ Normal liver size
 - ◆ Absence of hepatic fibrosis
 - ◆ Adequacy of iron chelation

(Lucarelli G et al, Blood 1996, NEJM 1993,)

Patients & Methods - Allografts

- *From 2001-july 2008*
- *Total Patients: 44*
- *Median Age 6 Years (Range 1.5 – 14)*
- *24 male and 20 females*
- Since August 2008
- A total of 15 BMTs have been performed in low-risk patients
- Median age : 3.3 years (range 0.9 to 6.2)
- 6 males and 9 females
- liver <2cm

Methods

- Nine BMTs were performed at an established center **National Institute of Blood diseases, Karachi**
- 6 at newly developed services:
 - 4 at **Pakistan Institute of Medical Sciences**
 - 2 at **Shifa International Hospital, Islamabad**

Patients, Methods: Patients' Characteristics

- Class I 31
 - Class II 13
 - Serum Ferritin 1405
– 3890 (Median 2310)
 - HCV antibody positive 2
- Class I 15
 - Serum Ferritin <1000
 - HCV antibody positive Nil

Patients & Methods

- HLA identical donors
 - Filgrastim was used for stem cell priming
 - 1.5 to 2.0 times the blood volume of the donors were processed
 - Haemonetics MCS+ cell separator was used for harvesting
 - MNC dose of $>4.0 \times 10^8/\text{kg}$ body weight
- HLA identical donors
 - Filgrastim was not used for stem cell priming
 - Under general anesthesia Bone Marrow was harvested from iliac crest
 - MNC dose of $>4.0 \times 10^8/\text{kg}$ body weight

Patients & Methods

• Conditioning therapy

- Busulphan 14mg / kg over 4 days
- Cyclophosphamide 160mg / kg over 4 days

• Conditioning therapy

- Busulphan 14mg / kg over 4 days
- Thiotepa 10mg/kg for one day
- Cyclophosphamide 160mg / kg over 4 days

Patients & Methods

- Anti-GvHD prophylaxis
 - Cyclosporin PO 5-10 mg/kg started on day -5
 - Cyclosporin C2 level
 - Mycophenolate Mofetil 1.0 – 1.5 gm/day
 - Oral Methotrexate 10mg/m²
 - Prednisone
- Post transplant follow up

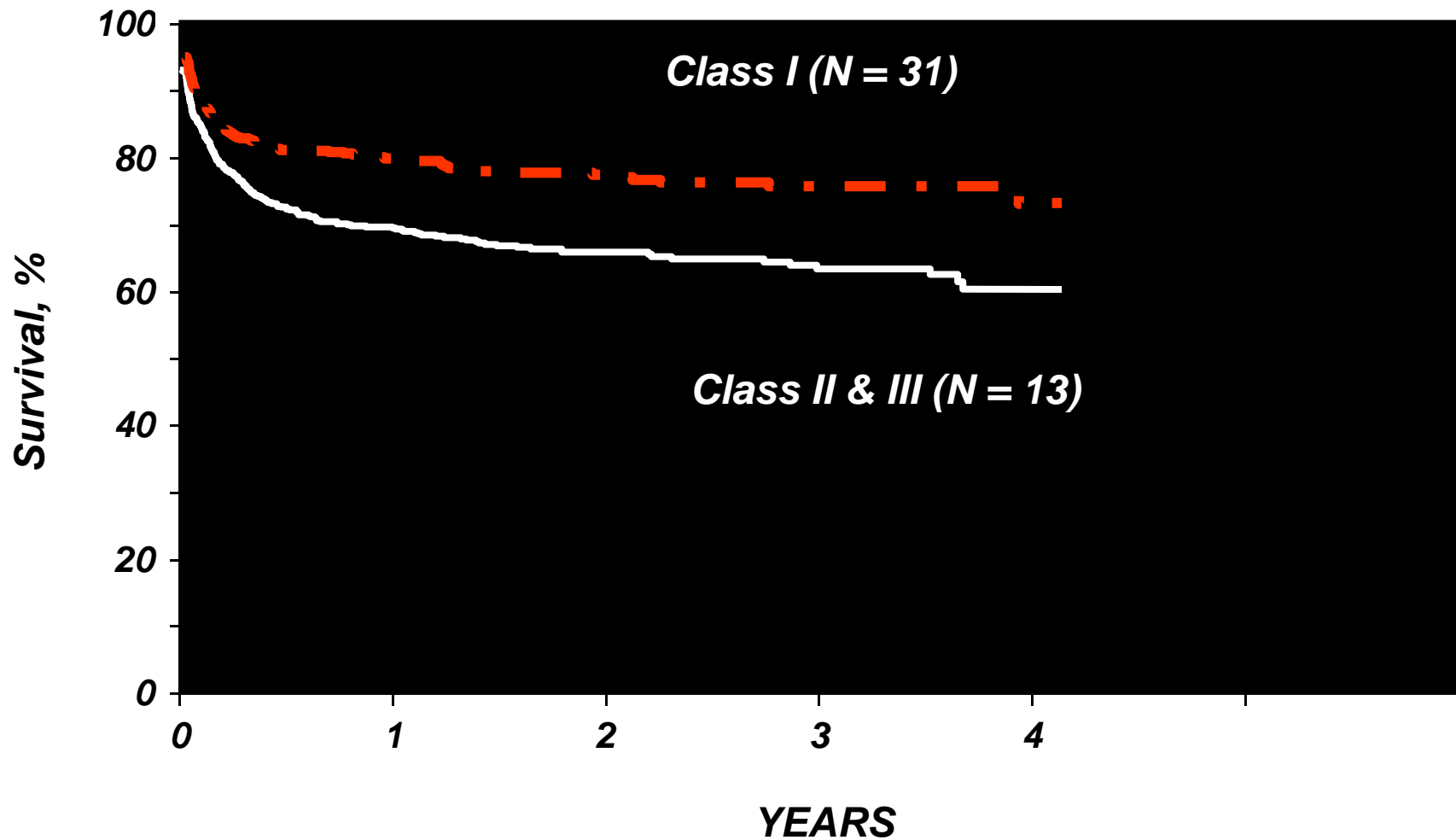
Results – β -Thalassaemia major

- Neutrophil engraftment 8-15 days (Median 11)
 - Platelet engraftment 11 – 20 days (Median 14)
 - Acute GvHD
 - Grade III 4
 - Grade II 2
 - Grade I 1
 - Neutrophil engraftment 18-28 days (Median 22)
 - Platelets engraftment 25-30 days (Median 26)
 - Acute GvHD
 - Grade III 1
 - Grade II 1
 - 5 had subclinical CMV activation by RT-PCR
 - One developed pulmonary tuberculosis.
- Other complications hypertension and hemorrhagic cystitis.
No case of VOD or chronic GVHD has been observed.

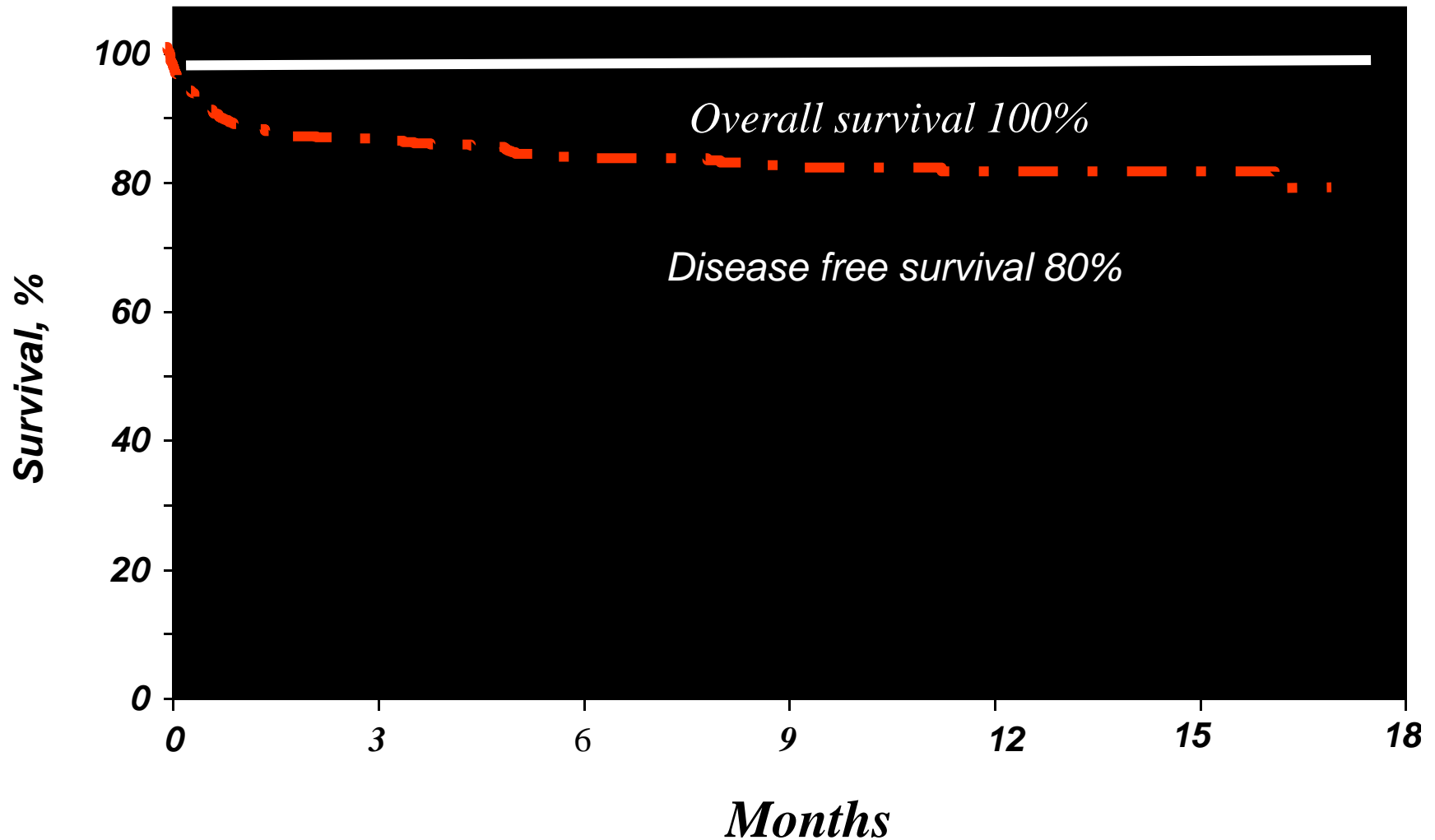
Results

- At a median follow up of 60 months
- Actuarial thalassemia-free survival is 65%
- Overall survival 70%
- So far 2 patients had a graft failure and are alive and well
- At a median follow up of 242 days (range 90-463)
- Actuarial thalassemia-free survival is 80%
- Overall survival 100%
- So far 3 patients had a graft failure and are alive and well after autologous reconstitution.

Probability Of Survival After Allogeneic Transplant For β -Thalassaemia Major in Pakistan



Survival After Allogeneic Transplant For low risk β -Thalassaemia Major using protocol 6i



Results

- NIBD Results:
- 13 transplanted (as of today)
- All alive and disease free
- One child had grade one GVHD
- One child had TB, (Responded to ATT)
- 10/13 had cyclosporine associated hypertension

Costs

- The cost of setting up a two-bedded BMT unit (at PIMS) including civil works and basic equipment was 30,000€
- Each BMT was in the range of 12,000€, including full family support for a minimum of 8 months.

Conclusions

- BMT is the only curative treatment
- Overall and disease free survival can be improved with better selection of patients (pessaro class 1)
- In low resource settings safe and effective bone marrow transplantation can be performed with a fraction of the costs compared to western centers.

