



# EXTENDING ACCESS TO BONE MARROW TRANSPLANTATION IN LOWER INCOME COUNTRIES

## THE PRELIMINARY EXPERIENCE OF THE CURE2CHILDREN FOUNDATION IN PAKISTAN

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### Background

Thalassemia major is very prevalent in Pakistan with almost 70,000 known cases and 5,000 born yearly.

Since August 2008 the Cure2Children Foundation has supported, both financially and professionally, a network of centers in Pakistan performing bone marrow transplantation (BMT) for the cure of transfusion-dependent thalassemia as well as inductive screening and prevention.

### Patient characteristics

#### Selection criteria

- Transfusion-dependent thalassemia (>8 transfusions per year)
- Availability of an HLA-matched related donor.
- Clear understanding of the risks and benefits of BMT by parents or legal guardians
- Patients younger than 8 years, with no major infectious diseases (HIV, Hepatitis B) or other conditions affecting transplant outcome.
- No hepatomegaly (liver <2cm).
- Creatinine, bilirubin and transaminase less than twice normal values, normal chest x-ray and echocardiogram, normal age-appropriate performance scale.

<b>Total patients</b>	<b>28</b>	16M, 12F
Median age (y)	3.2	0.9-9.4
Small for age (Ht < 5%)	8	29%
Consanguinity	74%	

### Transplant regimen

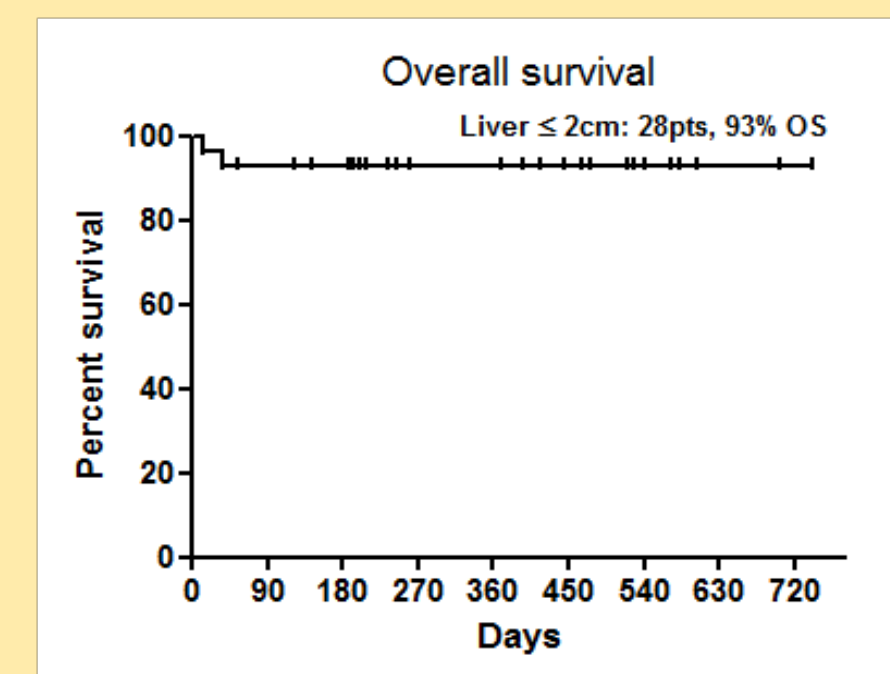
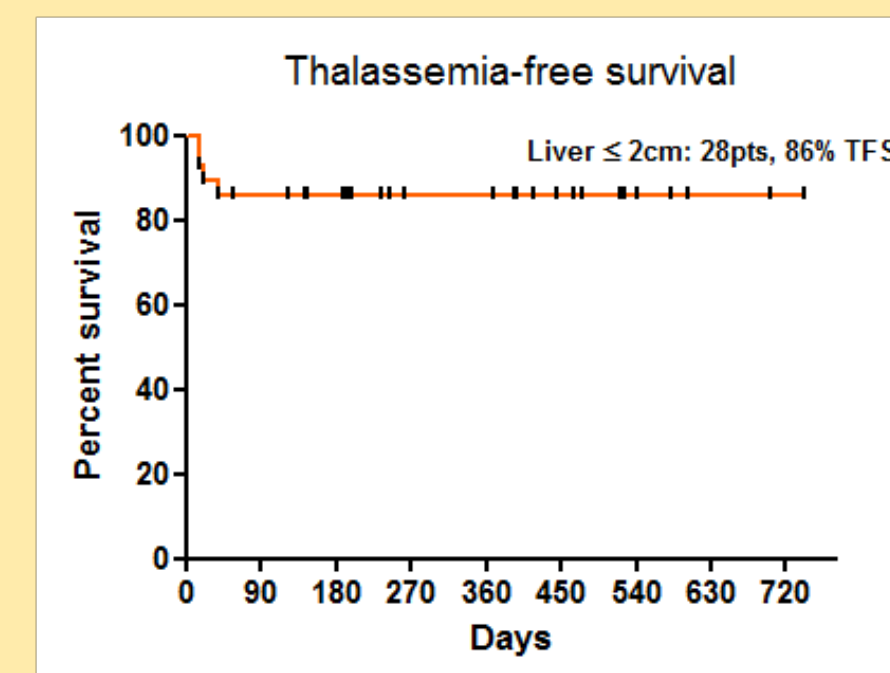
Matched-related bone marrow was administered after **conditioning** with busulfan 14 mg/kg, thiotepa 10 mg/kg, and cyclophosphamide 200 mg/kg total doses, followed by GVHD/rejection prophylaxis with prednisone, methotrexate, and cyclosporin (Lucarelli's protocol 6 for younger children).

**Management standards** for therapy administration, central venous lines, pancytopenia, immunosuppression, and hospital infection control were addressed by local training, daily web-based data management and videoconferencing. Individualized treatment plans were also provided. All patients were cared for in single rooms with private bathrooms.

### Results

Cell dose (nucleated cells/kg x 10 <sup>8</sup> )	5.7	1.4-23
Major ABO mismatch	3%	
Donor thalassemia minor	61%	
Median day ANC > 500/μL	16	9-35
Median day Plt > 20,000/μL	17	10-49
Median n. Plt transfusions	5	1-33
Median n. RBC transfusions	2	0-9
Last RBC transfusion day	15	-10-152
Median discharge day	26	12-109
Rejection	14%	

At a median follow up of 381 days (range 14-741), actuarial **thalassemia-free survival is 86% and overall survival 93%**.



### Toxicity

Fever & neutropenia	85%	
Hypertension	45%	
CMV activation	20%	
Central venous line infection	20%	
Hemorrhagic cystitis	14%	
Acute GVHD > grade 2	11%	
Chronic GVHD	7%	mild
Mucositis > grade 2 ECOG	7%	
Tuberculosis	7%	
Aspergillosis	3%	
Neurotoxicity	3%	
Renal failure	3%	
VOD	3%	mild
<b>Death</b>	<b>7%</b>	Sepsis

### Cost details

#### Transplant procedures

Pre-BMT evaluations	\$500
Diagnostics throughout BMT	\$2,600
Blood Products	\$200
Hospitalization Charges	\$800
Surgical (CVC)	\$400
Drug costs	\$2,000
Professional Cost	\$6,500
Follow up cost	\$1,300
Family Support	\$2,000
<b>Total</b>	<b>\$16,300</b>

Costs obtained from the mean of three patients with at least 6 months of follow up post-BMT.

#### BMT unit set up

The cost of setting up a two-bed BMT unit (at PIMS), only including renovation and basic equipment, was \$ 40,000

### Conclusions

In low- to middle-income settings bone marrow transplantation can be performed in selected cases with cure rates comparable to those obtained in more affluent countries but with a fraction of the costs.