

Andrew Kung<sup>4</sup>, Prakash Satwani<sup>7</sup>. <sup>1</sup> Pediatric Hematology/Oncology/Stem Cell Transplantation, New York Presbyterian Hospital-Columbia University Medical Center, New York, NY; <sup>2</sup> Pediatric Hematology/Oncology/Stem Cell Transplantation, New York Presbyterian Hospital-Columbia University Medical Center, New York, NY; <sup>3</sup> Biostatistics, Columbia University, New York, NY; <sup>4</sup> Pediatrics, Columbia University, New York, NY; <sup>5</sup> Division of Pediatric Hematology, Oncology, and Stem Cell Transplantation, Department of Pediatrics, Columbia University, New York, NY; <sup>6</sup> Columbia University Medical Center, New York, NY; <sup>7</sup> Division of Pediatric Hematology, Oncology, and Stem Cell Transplantation, Department of Pediatrics, Columbia University Medical Center, New York, NY

**Background:** Grade III-IV toxicities in the 30 days post allogeneic hematopoietic cell transplantation (alloHCT) is correlated with higher transplant-related mortality (TRM) at 1 year in adults. Despite extensive literature in the field there remains a paucity of data on the incidence of grade III-IV toxicities in children and adolescents undergoing alloHCT.

**Methods:** Retrospective cohort study of 166 patients (0.1-22y) who underwent alloHCT from January 2000 and December 2013 for malignant and non-malignant disease. Patients were conditioned on 1 of 3 Busulfan (Bu)-based conditioning regimens: reduced intensity (RIC): Bu(6.4-8mg/kg)+ Fludarabine (Flu) [150mg/m<sup>2</sup>], reduced toxicity (RTC): Bu(12.8-16mg/kg)+ Flu (180mg/m<sup>2</sup>) and myeloablative (MAC): Bu(12.8-16mg/kg)+ cyclophosphamide (120-200mg/kg) or melphalan (135mg/m<sup>2</sup>). Toxicities were scored using the CTCAE grading system in the 30 days post-alloHCT.

**Results:** Median age at alloHCT was 8.5y (0.1-22y), malignant n=102, non-malignant n=64. Median number of grade III-IV toxicities in all groups was 3 (0-17). On univariate analysis, age  $\geq$ 12 (p=0.002) was the single risk factor associated with an increased incidence of grade III-IV toxicities in the 30 days post-transplant. Incidence of toxicities was not significantly different in malignant v. non-malignant groups, RIC v. RTC v. MAC regimens, donor, HLA, primary disease or hematopoietic co-morbidity index. 1yr TRM in patients with number of grade III-IV toxicities below median (<3) was 2.6% and 1yr TRM in those with above median ( $\geq$ 3) toxicities was 15.6% (p=0.007). A total of 59 pediatric patients received MAC regimens, n=37 <12y and n=22  $\geq$ 12. Of this cohort, 43% of patients <12y and 72.7% of patients  $\geq$ 12 had above median number of grade III-IV toxicities (p=0.034). 1 year TRM was 10.8% for <12y and 22.7% for  $\geq$ 12y (p=0.272). RIC and RTC regimens were not associated with more than median toxicities in patients  $\geq$ 12 yrs. Detailed information provided below.

**Conclusion:** Despite recent advances in alloHCT, toxicity and organ impairment remain a significant cause of morbidity and mortality during the first year following alloHCT. Our preliminary results suggest that higher incidence of grade III-IV toxicities in the 30 days post-alloHCT correlates with

higher risk of TRM at 1yr. Age  $\geq$ 12y was significantly correlated with incidence of grade III-IV toxicities in the 30d post-transplant. Prospective studies to validate our finding and methods to decrease serious toxicities in adolescents are warranted.

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### Health-Related Quality of Life and Perception of Care of Mucopolysaccharidosis Type I - Hurler Syndrome Patients after Successful Hematopoietic Cell Transplantation: A Parents' Perspective

Mieke Aldenhoven<sup>1</sup>, Robert F. Wynn<sup>2</sup>, Anne O'Meara<sup>3</sup>, Paul Veys<sup>4</sup>, Attilio Rovelli<sup>5</sup>, Simon A. Jones<sup>6</sup>, Rossella Parini<sup>7</sup>, Marleen Renard<sup>8</sup>, Victoria Bordon<sup>9</sup>, Tom J. de Koning<sup>10</sup>, Jaap Boelens<sup>1</sup>. <sup>1</sup> Pediatric Blood and Marrow Transplantation Program, University Medical Center Utrecht, Utrecht, Netherlands; <sup>2</sup> Royal Manchester Children's Hospital, Manchester, United Kingdom; <sup>3</sup> Department of Hematology and Bone Marrow Transplantation, Our Lady's Children's Hospital, Dublin, Ireland; <sup>4</sup> Great Ormond Street Hospital for Children, London, United Kingdom; <sup>5</sup> Pediatric Bone Marrow Transplant Unit, Department of Pediatrics, San Gerardo University Hospital, Monza, Italy; <sup>6</sup> Willink Unit, Manchester Centre for Genomic Medicine, CMFT, University of Manchester, Manchester, United Kingdom; <sup>7</sup> Rare Metabolic Disorders Unit, Department of Pediatrics, San Gerardo University Hospital, Monza, Italy; <sup>8</sup> Pediatric Hematology and Oncology, University Hospital Leuven, Leuven, Belgium; <sup>9</sup> Pediatric Hematology and Oncology, Ghent University Hospital, Ghent, Belgium; <sup>10</sup> Department of Genetics, University Groningen, University Medical Center Groningen, Groningen, Netherlands

**Background:** Mucopolysaccharidosis type I-Hurler syndrome (MPS IH) is a lysosomal storage disease characterized by multi-system morbidity and death in early childhood. Hematopoietic cell transplantation (HCT) results in long-term survival, although with significant residual disease burden. The effect of this disease burden on the health-related quality of life of MPS IH patients after HCT is however still unknown. Furthermore, little is known about the perception of care of transplanted MPS IH patients.

**Methods:** 63 alive and engrafted MPS IH patients, transplanted at one of the seven participating centers within Europe were included in the study. The functional and psychosocial health were evaluated using two validated questionnaires: the Child Health Questionnaire (CHQ) and Pediatric Outcomes Data Collection Instrument (PODCI). Subscale and summary scores were compared to normative samples to derive z-scores and standard deviations (SD). The influence of various patient, donor, transplantation as well as disease-specific predictors was evaluated using univariate and multivariate linear regression analysis. Correlation analysis between the functional and psychosocial scores of the CHQ and PODCI was performed using Spearman's rank correlation. The perception of care was evaluated by a third validated questionnaire: the Measure of Processes of Care (MPOC) questionnaire.

**Results:** The functional health of transplanted MPS IH patients was significantly diminished compared with normative data; mean physical summary z-score -2.5 (SD 1.5), mean global functioning z-score -3.6 (SD 2.5) (figure 1 and 2). The psychosocial health appeared to be comparable or only slightly reduced compared to normative data; mean psychosocial summary z-score -0.1 (SD 1.3) (figure 1). A higher obtained IDUA enzyme level after HCT predicted for superior functional health, supporting the use of only

Grade III-V toxicities	Regimen			
	MAC (n/%)	RTC (n/%)	RIC (n/%)	Total (n/%)
	59/36	62/37	45/27	166/100
Hepatic	18/30	13/20.97	16/35	47/28
Renal	4/6.78	0/0	4/8.9	8/4.8
Gastrointestinal	20/34	28/45.1	7/15	55/33
Hemorrhagic cystitis	5/8.5	6/9.7	0/0	11/6.6
Cardiac	3/5	1/1.6	1/2.2	5/3
Lungs	9/15	6/9.68	1/2.2	16/9.6
Sepsis	9/15	4/6.45	2/4.4	15/9
VOD	12/20	3/4.8	2/4.4	17/10.2
Total # toxicities	79	61	35	175

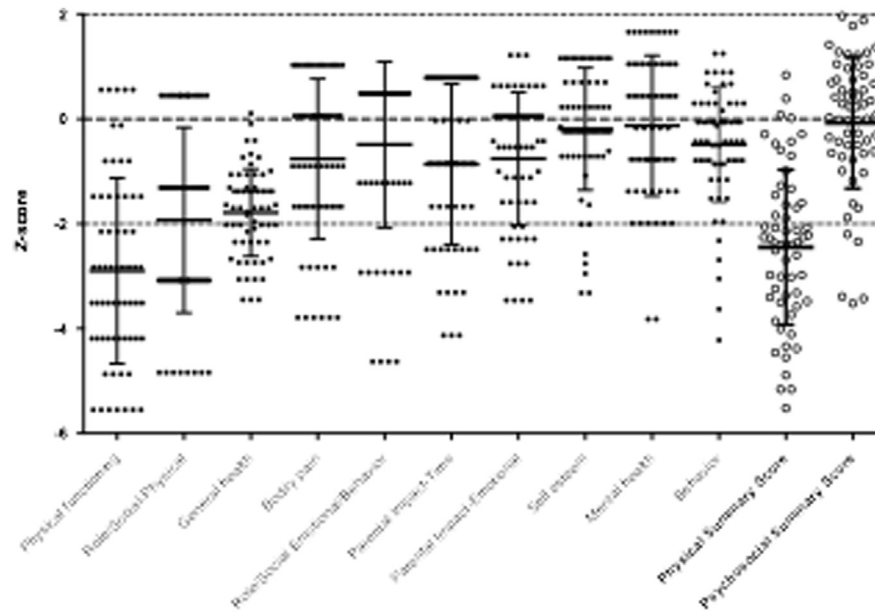


Figure 1. Results of the Child Health Questionnaire (CHQ)

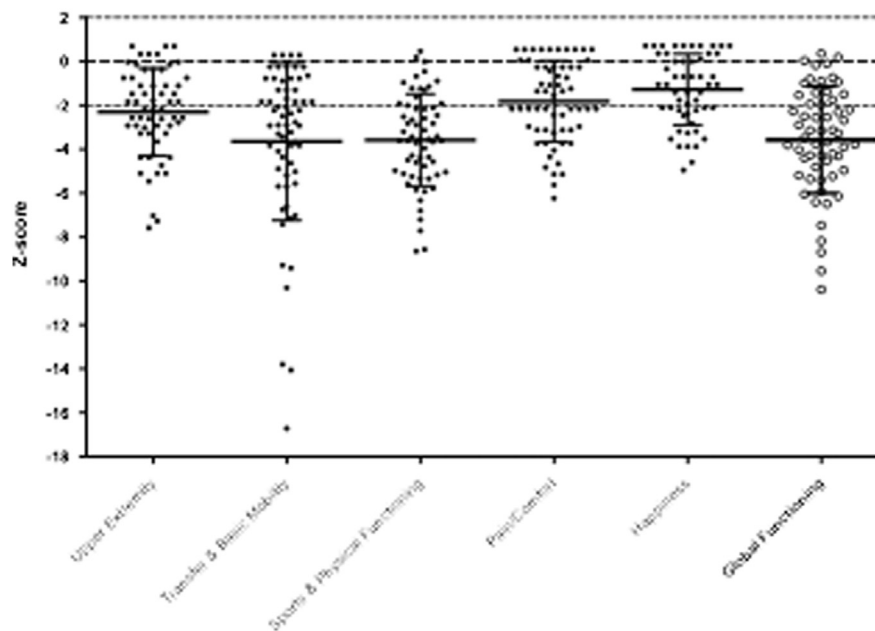


Figure 2. Results of the Pediatric Outcomes Data Collection Instrument (PODCI)

non-carrier donors and approaches to achieve full-donor chimerism. There was a modest to strong correlation between the functional and psychosocial domain scores of the CHQ and PODCI. Furthermore, the parents were overall satisfied with the care received. The multidisciplinary follow-up setting with experienced specialists in all participating centers might have positively contributed to this high level of satisfaction.

**Conclusion:** The functional health of transplanted MPS IH patients was significantly more affected than the psychosocial health compared to their healthy peers. Assessing the functional as well as the psychosocial health can play an important role in the evaluation of outcomes in MPS IH patients receiving HCT as well as new therapeutic approaches.

### Emergent Substitution of Fludarabine for Cyclophosphamide Due to Acute Cardiac Toxicity during Conditioning with Successful Engraftment

Hawazen Saleh Alsaedi<sup>1</sup>, Andrew Savage<sup>2</sup>, Michelle Hudspeth<sup>1</sup>. <sup>1</sup> Pediatric Hematology/Oncology, Medical University of South Carolina, Charleston, SC; <sup>2</sup> Pediatric Cardiology, Medical University Of South Carolina, Charleston, SC

Cyclophosphamide (CY) is an alkylating agent with potent antineoplastic, immunosuppressive, and immunomodulatory properties. CY induced cardiac toxicity has been documented with higher doses, including cardiomyopathy and