1. **Introduction**
   a. Minutes from February, 2010 meeting (Attachment 1)

2. **Accrual summary** (Attachment 2)

3. **Published or submitted papers**

4. **Studies in progress** (Attachment 3)
   a. **ID98-05** HCT for infantile osteopetrosis (A Fasth / P Orchard) **Data File Preparation**
   b. **ID99-02** The role of HCT in Langerhans cell histiocytosis (P Veys) **Data File Preparation**
   c. **ID06-03** HCT for Hurler syndrome: analysis by donor/graft source (JJ Boelens) **Manuscript Preparation**
d. **ID10-01** HSCT for meta-chromatic leukodystrophy (J Kurztberg / V Prasad / P Shaw)  
Protocol Development

e. **ID10-02** Outcome of HSCT for DNA repair disorders (A Gennery)  
Protocol Development

5. **Future/proposed studies**
   a. **PROP0310-01** ALD (P Orchard) (Attachment 4)
   b. **PROP1210-46** I-cell Disease (T Lund) (Attachment 5)

6. **Other business**
   Hurler long term follow-up outcomes (M Aldenhoven)
1. **Introduction**

The meeting was called to order; the minutes from the 2009 Tandem meeting were approved. Mitch introduced the new committee co-chair, Harry Malech from NIH. Mitch’s term is up; Ed thanked him and presented him with a gift.

LAD paper was acknowledged. This study was a collaboration between CIBMTR and EBMT and can serve as an example for future studies.

2. **Studies in Progress**

   a. **ID98-02** *Allo transplant for SCID (A Filipovich)*. *Data collection.*

      Mitch discussed the PIDD consortium, which will overlap efforts of this committee. The SCID study will be merged into the PIDD effort. There are no updates on the study as is but it will be merged into the PIDD effort. The PIDD will initiate studies and the CIBMTR will assist in data collection and statistical analysis.

   b. **ID98-05** *HCT for infantile osteopetrosis (A Fasth / P Orchard)*. *Data file preparation.*

      The study file for this study will be updated and analyzed.

   c. **ID99-02** *The role of HCT in Langerhans cell histiocytosis (M Egeler / A Filipovich)*. *Data file preparation.*

      This study dataset will also be updated with more current data. The committee discussed an existing prospective study on LCH. Scott Baker commented that the clinical trial will be folded into another CH4 clinical trial, which should start accruing patients towards the end of the year. The current retrieval show ~50 patients, both myeloablative and non-myeloablative.
The current retrospective study may help with accrual for that trial. ME asked if the committee supports moving forward with the current study. The committee is OK with moving forward.

d. **ID00-01** Cancer after allo HCT for immunodeficiencies (N Kamani). *Manuscript preparation.*

Naynesh updated the committee. Anna and Mary are working on the data file. The numbers have been updated with recent reports of secondary malignancies, therefore the number of reported malignancies has increased. The control population has been limited to those patients with at least 3 months follow-up. The additional data should not substantially change the message of the paper, which is that the vast majority of malignancies seen in patients with immune deficiencies are lymphoproliferative disorders and the risk factors in those patients is T-cell depletion. Mary will be contacting some centers that indicated patients had a 2nd malignancy but do not have a diagnosis and asked that the centers look out for the request and respond promptly. The datafile will be completed upon hearing back from these centers and the manuscript circulated thereafter.

e. **ID04-02** Unrelated cord blood vs. bone marrow for Wiskott-Aldrich syndrome (L Filipovich). *Data collection.*

This study will also be encompassed in the PIDD consortium efforts.


Jaap updated the committee on the final analysis, which V. Rocha completed a few weeks prior to the meeting. The results indicate that unrelated CB appear to be a good alternative cell source and enzyme levels appear to be a preferred cell source (?). The aim of this study was to look at transplant outcomes using various graft sources in children after myeloablative regimen. Non-myeloablative transplants were excluded because in previous studies, it was shown that these patients had higher rates of graft failure. The endpoints of interest were Event Free Survival (EFS) and Overall Survival (OS); other term endpoints are neutrophil recovery, GVHD and full donor chimerism. Patients registered to EBMT, Eurocord, Duke and UMN were included between 1995-2007 with at least 6 months of follow-up. The total n = 258 patients. Jaap reviewed the patient characteristics. OS = 63% in all patients. The primary causes of death were viral infection, GVHD, multi-organ failure. Jaap reviewed the variables that affected EFS. EVS improved after 2004. Those transplanted before 1999 had the worst EFS. Analysis indicates that Enzyme Replacement Therapy (ERT) is influencing the EFS but most patients received ERT after 2004. Other variables affecting EFS included age at transplant, time from diagnosis to transplant, donor type and cell count for unrelated cord blood. For unrelated BM group, HLA-matching, T-cell depletion both affect EFS. HLA sibs and unrelated matched CB do better than HLA-matched BM. The rest perform worse. In multivariate Cox analysis, adjusted for year of tx and previous use of ERT, median age remains significant and HLA sibs and Unrelated Matched CB do better than the other two groups. Engraftment and cGVHD were not affected by graft source. aGVHD was affected, with 4,5/6 matched CB had a higher aGVHD II-IV but not III-IV. Full donor chimerism was reached in almost all unrelated CB and was associated with normal enzymes. In the MUD, T-depl and sibling setting, enzyme levels are only normal in 55-65%. EFS was affected by graft source, the highest was seen in HLA-identical sibs and uidentical unrelated CB, followed by identical BM and 4, 5/-6 CB and unmatched BM. Question: Were center effects considered in this analysis? Answer: Not looked at-CIBMTR can provide code so that it can be considered. Comment: Adjusted for year of transplant. Were the unrelated CB vs. unrelated donors-were they over the same time periods? Comment: 20% had a 6/6 matched CB. For < 6/6 and high
cell dose, outcomes are comparable to matched unrelated donors. Q: is it possible to compare those patients who were carriers (70% of HLA-id sibs had at least one affected sibling) with those who were not carriers? It’s possible centers lean towards doing a transplant using HLA-id sibs but perhaps they should use an unrelated CB if the sibling is a carrier. The numbers are small in these two groups so analysis is not possible, but the events can be described in the manuscript. The carrier issue will be more important in the long-term outcomes study. Take-home message is that HLA-id sibs are doing as well as 6/6 unrelated matched CB. Enzyme levels are important in outcomes. Comment: This dataset gives a great opportunity to study mixed chimerism and GVHD.

g. **ID09-01 Late mortality post-allo HCT for PID / metabolic diseases (M Eapen). Manuscript preparation.**

ME reviewed this study, which is in the manuscript preparation stage. The study included patients who were transplanted for primary immune deficiency and inborn errors of metabolism (IEM) and were still surviving two years post-transplant. The goals of the study were to look at the probability of long term survival in these patients, to identify risk factors for late mortality after transplantation, and to determine the excess mortality relative to rates in an age-, sex-, and nationality-matched general population. 954 patients were included. In order to be included, non-SCID and IEM patients must have had > 95% donor chimerism at study entry; SCID patients had to have normal T-cell function. Pts were transplanted btw 1980-2003. Mary reviewed the patient-, disease- and transplant-related characteristics. The risk factor analysis was done separately for SCID, non-SCID and IEM patients, except for active cGVHD. In any of the three disease groups, if a patient had active cGVHD at 2 years, they were more likely to experience a fatal event after 2 years. There were no other risk factors identified for SCID patients; for non-SCID immune deficiency patients, T-cell depletion patients were more likely to die; for IEM patients, donor source was a significant risk factor. There were not many CB grafts due to the years of transplant being cut at 2003. All disease groups had excess deaths during 2-6 years post-transplant when compared to an age-, sex-, and nationality-matched general population. After 6 years, however, the excess deaths decrease considerably and for SCID and non-SCID patients, the mortality rates are similar to the matched population. The mortality rate remains high for the IEM patients however. CGVHD, infection without cGVHD and organ failure were the highest causes of death in this population. The rate of 2nd malignancy for these patients was higher than that of the matched population. Q. Were all the AML 2nd malignancy in donor cells? A: not all were tested; would have to review the charts. Q. What is the definition of T-cell function for SCID patients? Were some patients excluded who had cGVHD? A. To ensure that these patients were “cured”, these patients must be excluded, so there is a possibility that some patients with cGVHD were excluded. A: >80% functional assays = T-cell function. Q: What were the SCID phenotypes? Look at T-B- vs T-B+ to see if there’s a difference. A. There are probably not enough numbers for that but we could look at T-B- vs other or B- vs B+. Q: Did organ failure receive high-dose Bu? A. Most organ failures were cardiac. Would have to check about the Bu question. Q. For those with organ failure > 2 years-do we know if they were on the way down hill at 2 years? A. Our forms don’t collect that kind of data. Q. Can neurologic death be categorized as persistent disease? Q. What type of infection was seen in those patients with and without cGVHD? A. Infections were primarily bacterial.

Ed reviewed the Immune Deficiency forms to get the committee’s opinion on what is being collected-the molecular typing of the disease instead of phenotype as it used to be collected. It was the consensus of the committee that many centers, especially international centers, will have problems collecting the data as is now. The group recommended adding the disease phenotypes back to the forms. It was also recommended that a question on whether there is...
whole blood stored or whether there is an established cell line. The molecular typing would not be known at the time that the core form is completed, so the teams would have to send an error correction later. It was suggested to add the question to the 1-year follow-up form so that it could be completed without an error form.

3. **Future / Proposed Studies**
   a. **PROP1209-04** *Outcome of HSCT for DNA repair disorders-DNA ligase 4, Cernunnos-XLF, Nijegen breakage syndrome, Artemis, RAG. (A Gennery).*
   
   We know that increasingly, immunodeficient patients are being diagnosed who have defects in the DNA-components. These patients are sensitive to DNA-damaging agents. We know that many of the conditioning regimens used are particularly DNA damaging. These patients, if exposed to these agents are much more likely to suffer severe side effects, both morbidity and mortality, particularly very early post-transplant. Therefore, less toxic conditioning regimens should be used to treat these patients. Artemis patients are not as radiosensitive as other DNA-repair disorders and should probably be considered separately. There are very few data available on patients with these DNA-disorders, published or unpublished. Different regimens and donors used at different centers makes it difficult to put all the DNA-repair disorders together. This proposal is to capture as much data on the conditioning, the complications and outcomes as possible. This would be a joint EBMT, CIBMTR study and possibly include other registries such as Japan. This study would not need to send out additional forms. Mary asked the committee which centers have done transplants for these diseases. Several committee members indicated that they have done these transplants at their centers. Q. Should Artemis patients be included? A. Can include in the study but look at separately for the manuscript. Q. Can we examine whether myeloablative or NST have different outcomes? A. There will probably not be enough patients to look at this. This study will have to be descriptive only. There is a current retrospective study currently looking at Artemis and RAG deficient patients being done.

   b. **PROP1209-03** *Follow-up of patients undergoing HSCT for meta-chromatic leukodystrophy.* *(P Shaw).*
   
   There is not a lot of evidence on when and even whether transplant is the correct procedure to do on patients with MLD. Currently there are 125 patients from 39 different centers. However, only 70 patients have more detailed information, most of which come from 2 different centers. In order to improve the dataset, we could nominate a contact at the other 37 centers to try to get detailed data. This would include no additional forms, rather would just be a concentrated effort in getting centers to complete the current CIBMTR forms. Q. If we can not do this for MLD, which has relatively large numbers, can we do it for any other diseases with even fewer cases? Q. Are centers paid for filling out forms? A. Yes. Q. Does the committee think it’s reasonable to ask for this information or is it not feasible? Comments: the transplant community needs this data so we should try to get it. Q. Are the current follow-up forms collecting the functional outcomes needed to do this study? It has been discussed previously that the forms should be reviewed/revised. A. Olle, Kurt (?), Joanne, Ed are interested in revising the MLD/ALD forms. Mary will download the forms and forward to those interested to begin the revision process. Comment: The Lansky score is not relevant for these diseases. Q. Can registration teams be contacted to fill out report forms? A. Teams can’t just complete forms for these patients, they would have to complete forms for all their patients who are randomly selected to complete forms, so it is unlikely to happen. Reporting only one patient will introduce bias, so they need to complete all patients.
c. **PROP1209-46 Morbidity and mortality following HSCT for the treatment of mucopolysaccharidosis VI. (S Turbeville).**

This analysis is about morbidity and mortality following transplant for patients with Mucopolysaccharidosis VI. There is very little data published for patients with this disease. This is a retrospective analysis used to look at morbidity and overall survival at 100-days and 1- and 3-years after transplantation. The analysis does not provide information on enzyme replacement therapy because that therapy is so recent. Q. Can we look at Karnofsky score? A: This is on the registration forms but is < 80 vs. 80-100. Q. Can we go back to teams and ask for more detailed data on these patients? A. If the committee thinks it is worth-while, we can do that. Q. Are these US patients? A. They are from both US and non-US centers. Comment: what is really needed is quality of life data. We need to be careful because BioMarin is going to want to say that the ERT is better than transplantation but we may not have the data to support that. It would also be interesting to know how much the ERT costs.

4. Other Business

The meeting was adjourned at 2:15 pm.
### Accrual Summary for Immune Deficiencies and Inborn Errors of Metabolism

Working Committee

Allogeneic transplants for immune deficiencies reported to the CIBMTR through December 2010

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>TED N (%)</th>
<th>CRF N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of patients</td>
<td>4862</td>
<td>2613</td>
</tr>
<tr>
<td>Number of centers</td>
<td>278</td>
<td>209</td>
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#### Severe Combined Immunodeficiency (SCID)

<table>
<thead>
<tr>
<th>Condition</th>
<th>TED N (%)</th>
<th>CRF N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ADA deficiency</td>
<td>183 (4)</td>
<td>90 (3)</td>
</tr>
<tr>
<td>SCID absence of T and B cells</td>
<td>379 (8)</td>
<td>269 (10)</td>
</tr>
<tr>
<td>SCID absence of T, normal B cell SCID</td>
<td>471 (10)</td>
<td>288 (11)</td>
</tr>
<tr>
<td>Omenn syndrome</td>
<td>157 (3)</td>
<td>74 (3)</td>
</tr>
<tr>
<td>Reticular dysgenesis</td>
<td>20 (&lt;1)</td>
<td>12 (&lt;1)</td>
</tr>
<tr>
<td>SCID, NOS</td>
<td>556 (12)</td>
<td>260 (10)</td>
</tr>
<tr>
<td>Wiskott Aldrich syndrome</td>
<td>626 (13)</td>
<td>369 (14)</td>
</tr>
<tr>
<td>Chediak-Higashi syndrome</td>
<td>102 (2)</td>
<td>62 (2)</td>
</tr>
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</table>

#### Combined immune deficiencies (CID)

<table>
<thead>
<tr>
<th>Condition</th>
<th>TED N (%)</th>
<th>CRF N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Common variable immunodeficiency</td>
<td>73 (2)</td>
<td>41 (2)</td>
</tr>
<tr>
<td>Combined immunodef dis (CID), NOS</td>
<td>140 (3)</td>
<td>86 (3)</td>
</tr>
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#### Other immune deficiency disorders

<table>
<thead>
<tr>
<th>Condition</th>
<th>TED N (%)</th>
<th>CRF N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bare lymphocyte syndrome</td>
<td>73 (2)</td>
<td>47 (2)</td>
</tr>
<tr>
<td>Ataxia telangiectasia</td>
<td>9 (&lt;1)</td>
<td>8 (&lt;1)</td>
</tr>
<tr>
<td>HIV infection</td>
<td>6 (&lt;1)</td>
<td>6 (&lt;1)</td>
</tr>
<tr>
<td>DiGeorge anomaly</td>
<td>32 (1)</td>
<td>24 (1)</td>
</tr>
<tr>
<td>Chronic granulomatous disease</td>
<td>205 (4)</td>
<td>86 (3)</td>
</tr>
<tr>
<td>X-linked lymphoproliferative syndrome</td>
<td>103 (2)</td>
<td>59 (2)</td>
</tr>
<tr>
<td>Leukocyte adhesion deficiencies</td>
<td>101 (2)</td>
<td>50 (2)</td>
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<tr>
<td>Kostmann agranulocytosis</td>
<td>111 (2)</td>
<td>50 (2)</td>
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<tr>
<td>Neutrophil actin deficiency</td>
<td>1 (&lt;1)</td>
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</tr>
<tr>
<td>Cartilage hair hypoplasia</td>
<td>21 (&lt;1)</td>
<td>9 (&lt;1)</td>
</tr>
<tr>
<td>CD40 ligand deficiency</td>
<td>43 (1)</td>
<td>18 (1)</td>
</tr>
<tr>
<td>Other immunodeficiencies</td>
<td>515 (10)</td>
<td>170 (7)</td>
</tr>
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</table>

#### Histiocytic disorders

<table>
<thead>
<tr>
<th>Condition</th>
<th>TED N (%)</th>
<th>CRF N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Familial erythrophagocytic lymphohistiocytosis (FELH)</td>
<td>597 (12)</td>
<td>326 (12)</td>
</tr>
<tr>
<td>Hemophagocytosis</td>
<td>149 (3)</td>
<td>86 (3)</td>
</tr>
<tr>
<td>Langerhans Cell Histiocytosis</td>
<td>71 (1)</td>
<td>44 (2)</td>
</tr>
<tr>
<td>Malignant histiocytosis</td>
<td>12 (&lt;1)</td>
<td>7 (&lt;1)</td>
</tr>
<tr>
<td>Other histiocytic disorders</td>
<td>106 (2)</td>
<td>72 (3)</td>
</tr>
</tbody>
</table>

Abbreviations: ADA = adenosine deaminase; HIV = Human immunodeficiency virus.

* Only first transplants are included in this accrual.
Accrual Summary for Immune Deficiencies and Inborn Errors of Metabolism
Working Committee

Allogeneic transplants for inborn errors of metabolism reported to the CIBMTR through December 2010

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>TED N (%)</th>
<th>CRF N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of Patients</td>
<td>1950</td>
<td>1211</td>
</tr>
<tr>
<td>Number of Centers</td>
<td>200</td>
<td>137</td>
</tr>
<tr>
<td>Osteopetrosis</td>
<td>363 (19)</td>
<td>225 (19)</td>
</tr>
<tr>
<td>Lesch-Nyhan(HGPTR deficiency)</td>
<td>6 (&lt;1)</td>
<td>5 (&lt;1)</td>
</tr>
<tr>
<td>Neuronal ceroid lipofuscinosis</td>
<td>3 (&lt;1)</td>
<td></td>
</tr>
<tr>
<td>Mucopolysaccharidosis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>IH Hurler syndrome</td>
<td>500 (26)</td>
<td>338 (28)</td>
</tr>
<tr>
<td>II Hunter syndrome</td>
<td>64 (3)</td>
<td>44 (4)</td>
</tr>
<tr>
<td>III Sanfillippo</td>
<td>49 (3)</td>
<td>39 (3)</td>
</tr>
<tr>
<td>IV Morquio</td>
<td>11 (1)</td>
<td>8 (1)</td>
</tr>
<tr>
<td>VI Maroteaux-Lamy</td>
<td>55 (3)</td>
<td>38 (3)</td>
</tr>
<tr>
<td>VII B-glucuronidase deficiency</td>
<td>4 (&lt;1)</td>
<td>4 (&lt;1)</td>
</tr>
<tr>
<td>V Mucopolysaccharidosis</td>
<td>1 (&lt;1)</td>
<td></td>
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<tr>
<td>Other mucopolysaccharidos</td>
<td>22 (1)</td>
<td>17 (1)</td>
</tr>
<tr>
<td>Mucolipidosi</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gaucher disease</td>
<td>50 (3)</td>
<td>34 (3)</td>
</tr>
<tr>
<td>Metachromatic leukodystrophy (MLD)</td>
<td>173 (9)</td>
<td>114 (9)</td>
</tr>
<tr>
<td>Adrenoleukodystrophy (ALD)</td>
<td>316 (16)</td>
<td>170 (14)</td>
</tr>
<tr>
<td>Globoid leukodystrophy/Krabbe disease</td>
<td>89 (5)</td>
<td>61 (5)</td>
</tr>
<tr>
<td>Neiman-Pick disease</td>
<td>37 (2)</td>
<td>22 (2)</td>
</tr>
<tr>
<td>I-cell disease</td>
<td>27 (1)</td>
<td>16 (1)</td>
</tr>
<tr>
<td>Wolman disease</td>
<td>20 (1)</td>
<td>13 (1)</td>
</tr>
<tr>
<td>Lysosomal storage disease</td>
<td>7 (&lt;1)</td>
<td>5 (&lt;1)</td>
</tr>
<tr>
<td>Other mucolipidoses</td>
<td>10 (&lt;1)</td>
<td>6 (&lt;1)</td>
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<tr>
<td>Polysaccharide hydrolas abnormalities</td>
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<tr>
<td>Aspartyl glucosaminuria</td>
<td>5 (&lt;1)</td>
<td>2 (&lt;1)</td>
</tr>
<tr>
<td>Fucosidosis</td>
<td>3 (&lt;1)</td>
<td>3 (&lt;1)</td>
</tr>
<tr>
<td>Mannosidosis</td>
<td>20 (1)</td>
<td>8 (1)</td>
</tr>
<tr>
<td>Other inherited metabolic disorders</td>
<td>115 (5)</td>
<td>39 (3)</td>
</tr>
</tbody>
</table>

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TO: Immune Deficiencies and Inborn Errors of Metabolism Working Committee Members

FROM: Mary Eapen, MD, MS; Scientific Director for the Immune Deficiencies WC

RE: Studies in Progress Summary

**ID98-05:** Hematopoietic cell transplantation (HCT) for infantile osteopetrosis (A Fasth / P Orchard): This study will assess the effectiveness of reconstituting osteodast function in patients receiving transplant for infantile osteopetrosis. The data file is currently being prepared for this study.

**ID99-02:** The role of hematopoietic cell transplantation (HCT) in Langerhans cell histiocytosis (RM Egeler / A Filipovich): The goal of this study is to assess the feasibility of transplant in patients with Langerhans cell histiocytosis. The data file is currently being prepared for a descriptive study.

**ID00-01:** Malignancies after hematopoietic cell transplantation (HCT) for primary immune deficiency disorders (PIDD) (N Kamani): This study is describing the incidence of malignancies in children with primary immune deficiencies following allogeneic HCT. The manuscript was submitted to Blood in November 2010.

**ID06-03:** Outcomes of transplantation using various cell sources for Hurler’s Syndrome: A Eurocord-EBMT-CIBMTR collaborative study (JJ Boelens / V Rocha / J Kurtzberg / P Orchard): This objective of this study is to analyze the impact of various cell sources (matched sibling, unrelated and unrelated cord blood donors) on outcomes after allogeneic HCT. A draft manuscript is being prepared.

**ID09-01:** Long-term survival and late deaths after hematopoietic cell transplantation (HCT) for primary immunodeficiency diseases and inborn errors of metabolism (M Eapen): This analysis looked at late mortality after transplant for SCID, non-SCID immune diseases and inborn errors of mortality. The manuscript is complete and being submitted.

**ID10-01:** Follow-up of patients undergoing HSCT for meta-chromatic leukodystrophy (J Kurtzberg / P Shaw): The aims of this study are to report disease- and transplant-specific outcomes of patients undergoing HCT for metachromatic leukodystrophy. A subcommittee has been formed to review the CIBMTR forms and make suggestions on how to improve the forms for this and future studies.

**ID10-02:** Outcome of HSCT for DNA repair disorders (A Gennery): This is a descriptive study that will describe the complications, immunoreconstitution and outcomes of patients with rare DNR-repair disorders. The protocol is being developed.

**ID10-03:** Morbidity and mortality following HSCT for the treatment of mucopolysaccharidosis VI (S Turbeville): This analysis assessed patient demographics, morbidity and overall survival of patients who had MPS VI and undergone HCT. The manuscript has been accepted for publication in Molecular Genetics and Metabolism.
Study Proposal 0310-01

Study Title:
Outcomes of patients undergoing allogeneic transplantation for adrenoleukodystrophy (ALD).
Paul J. Orchard, MD, University of Minnesota, Minneapolis, MN

Scientific Justification:
We propose to initiate a study through the CIBMTR of the outcomes of patients undergoing allogeneic transplantation for adrenoleukodystrophy (ALD). This is an X-linked disorder, and a proportion of these patients (> 40%), have an acute inflammatory process affecting the white matter of the brain, termed cerebral-ALD.

Variables to be Analyzed:
The specifics to be studied and incorporated into a manuscript will include:
- Distribution of the age of patients at diagnosis and at transplant
- Proportion of patients with frontal disease, occipital disease and those with other locations
- Scoring of the MRI severity (Loes score) prior to transplantation and at 1 year post transplant
- Prevalence of adrenal insufficiency at the time of transplant
- Proportion of patients identified by:
  - family history
  - adrenal insufficiency
  - neurologic symptoms
- Type of preparative regimen used

Outcomes:
The outcome analysis to include:
- Survival
- Progression of Loes score at 1 yr (change from pre-transplant to 1 year post)

Subgroup analysis will look at survival and increase in MRI score severity as events, with the analysis of the effects of the following:
- The effect of age
- Loes score pre-transplantation
- Location of disease
- Type of preparative regimen
- Graft source, including carrier sisters as donors,
- Presence/absence of adrenal function pre-transplantation
- Development of GVHD
- Use of steroids during transplantation, either for GVHD prophylaxis or therapy
### Characteristics of patients transplanted for adrenoleukodystrophy (ALD)

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of patients</td>
<td>170</td>
</tr>
<tr>
<td>Number of centers</td>
<td>51</td>
</tr>
<tr>
<td>Age at transplant, years</td>
<td></td>
</tr>
<tr>
<td>Median (range)</td>
<td>8 (&lt;1-48)</td>
</tr>
<tr>
<td>≤ 5</td>
<td>26 (15)</td>
</tr>
<tr>
<td>6-9</td>
<td>91 (54)</td>
</tr>
<tr>
<td>≥ 10</td>
<td>53 (31)</td>
</tr>
<tr>
<td>Karnofsky status pre-tx</td>
<td></td>
</tr>
<tr>
<td>&lt; 90</td>
<td>45 (26)</td>
</tr>
<tr>
<td>90-100</td>
<td>119 (70)</td>
</tr>
<tr>
<td>Missing</td>
<td>6 ( 4)</td>
</tr>
<tr>
<td>Graft type</td>
<td></td>
</tr>
<tr>
<td>BM</td>
<td>99 (58)</td>
</tr>
<tr>
<td>PBSC</td>
<td>13 ( 8)</td>
</tr>
<tr>
<td>Cord blood</td>
<td>58 (34)</td>
</tr>
<tr>
<td>Donor type</td>
<td></td>
</tr>
<tr>
<td>HLA-id sibling</td>
<td>26 (15)</td>
</tr>
<tr>
<td>Other relative</td>
<td>7 ( 4)</td>
</tr>
<tr>
<td>Unrelated</td>
<td>133 (78)</td>
</tr>
<tr>
<td>Missing</td>
<td>4 ( 2)</td>
</tr>
<tr>
<td>Survival status</td>
<td></td>
</tr>
<tr>
<td>Alive</td>
<td>93 (55)</td>
</tr>
<tr>
<td>Dead</td>
<td>77 (45)</td>
</tr>
</tbody>
</table>

* 41 patients have complete report forms
Study Proposal 1210-46

Study Title:
Outcomes after HSC transplant in patients with I-cell disease.
T. Lund, University of Minnesota, Minneapolis, MN

Introduction:
I-cell disease, or mucolipidosis-II, is an autosomal recessive storage disease with skeletal, pulmonary and neurological manifestations from infancy. There is no cure or medical management for this disease, and severely affected patients with ML-II die of their disease at an early age. Hematopoietic cell transplant (HSCT) has been performed in some patients in hopes that a cross-correction effect could be utilized to ameliorate disease as in Hurler patients. However, the gene product in ML-II is a phosphotransferase that is important in establishing the mannose-6-phosphate signal necessary for localization of lysosomal enzymes to the lysosome. Due to this, high levels of many lysosomal enzymes are observed in the blood, as they are secreted instead of transported to the lysosome. In this, the biology of ML-II is different than the isolated lysosomal enzyme deficiencies. Outcomes after transplant for I-cell disease have not been reported.

Specific Aims:
- To determine the overall survival after HSCT.
- To describe complications associated with transplantation in this population (incidence of intubation, veno-occlusive disease, renal dysfunction, etc.)
- To determine a genotype/outcome correlation.
- To determine if the natural history of I cell disease is altered by HSCT.

Scientific Justification:
HSCT is performed for I cell disease, but outcomes are not reported. Due to the rarity of this disease, the use of registry data is critical to generate sufficient numbers of patients to determine the utility of transplantation.

It is unknown if HSCT should be offered to I cell patients, this study may be able to determine that.

Variables to be Analyzed:

Patients:
- All those with I cell diagnosis
- Parameters
  - Age
- Genotype (Dr. Sara Cathey, Greenwood Genetic Center, has agreed to assist with this, she is a geneticist who has done most of the I cell genotyping in the USA).

Disease-related:
- Enzyme levels prior to transplantation
- Premorbid conditions

Transplant-related:
- Survival
- Type of preparative regimen
- GVHD status
- Type of HSCT
- Lanksy pre/post HSCT
- Post-HSCT complications (intubation, VOD, renal failure requiring dialysis, etc.)
- Cause of death
Characteristics of patients with I-cell disease who received an allogeneic transplant and reported to the CIBMTR

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of patients</td>
<td>27</td>
</tr>
<tr>
<td>Number of centers</td>
<td>16</td>
</tr>
<tr>
<td>Age at transplant, years</td>
<td></td>
</tr>
<tr>
<td>Median (range)</td>
<td>1 (&lt;1-8)</td>
</tr>
<tr>
<td>&lt; 1</td>
<td>13 (48)</td>
</tr>
<tr>
<td>1-2</td>
<td>12 (44)</td>
</tr>
<tr>
<td>&gt; 2</td>
<td>1 (4)</td>
</tr>
<tr>
<td>Missing</td>
<td>1 (4)</td>
</tr>
<tr>
<td>Male</td>
<td>13 (48)</td>
</tr>
<tr>
<td>Lansky status pre-transplant</td>
<td></td>
</tr>
<tr>
<td>&lt; 80</td>
<td>3 (11)</td>
</tr>
<tr>
<td>80-100</td>
<td>14 (52)</td>
</tr>
<tr>
<td>Missing</td>
<td>10 (37)</td>
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<tr>
<td>Graft type</td>
<td></td>
</tr>
<tr>
<td>BM</td>
<td>10 (37)</td>
</tr>
<tr>
<td>PBSC</td>
<td>1 (4)</td>
</tr>
<tr>
<td>Cord blood</td>
<td>15 (56)</td>
</tr>
<tr>
<td>Missing</td>
<td>1 (4)</td>
</tr>
<tr>
<td>Donor type</td>
<td></td>
</tr>
<tr>
<td>HLA-id sibling</td>
<td>3 (11)</td>
</tr>
<tr>
<td>Other relative</td>
<td>4 (15)</td>
</tr>
<tr>
<td>Unrelated</td>
<td>20 (74)</td>
</tr>
<tr>
<td>Survival status</td>
<td></td>
</tr>
<tr>
<td>Alive</td>
<td>18 (67)</td>
</tr>
<tr>
<td>Dead</td>
<td>8 (30)</td>
</tr>
<tr>
<td>Missing</td>
<td>1 (3)</td>
</tr>
</tbody>
</table>
1. Was diagnosis Sanfilippo?
   1  Yes
   0  No
   8  Unknown

   2. Specify (check only one):
      552  Heparan N-sulfatase (Sanfilippo A – MPS IIIA)
      553  α-N-acetylgalactosaminidase (Sanfilippo B – MPS IIIB)
      554  Acetyl CoA: α-glucosaminide acetyltransferase (Sanfilippo C – MPS IIIC)
      555  N-acetylgalactosamine 6-sulfatase (Sanfilippo D – MPS IIID)

3. Was diagnosis Morquio?
   1  Yes
   0  No
   8  Unknown

   4. Specify (check only one):
      556  Galactose 6-sulfatase (Morquio A – MPS IVA)
      557  β-galactosidase (Morquio B – MPS IVB)

Record the leukocyte enzyme activity levels at diagnosis:

5. Date tested: 
   Month   Day   Year

6. Patient enzyme activity level: 1 1 nmol/hr/mg protein 2 pmol/hr/mg protein

7. Donor enzyme activity level: 1 1 nmol/hr/mg protein 2 pmol/hr/mg protein 8 Unknown

8. Was treatment given for the disease between diagnosis and anytime prior to conditioning?
   1  Yes
   0  No
   8  Unknown

   9. 1  0  8  Enzyme replacement
   10. 1  0  8  Substrate deprivation/inhibitor
   11. 1  0  8  Gene transfer/Gene therapy
   12. 1  Other, specify: ___________________________________________________
Clinical status pretransplant

13. Was cerebrospinal fluid (CSF) testing done anytime prior to conditioning?
   1 □ Yes
   0 □ No
   8 □ Unknown

14. Date of most recent test prior to conditioning: ______/_____/______

   Results of most recent tests:
   Yes □ No □ Unknown
   15. □ Opening pressure ______ cm H₂O
   16. □ Closing pressure ______ cm H₂O
   17. □ Total protein ______ mg/dL 2 □ g/L

18. Was Magnetic Resonance Imaging (MRI) of the brain/spine done anytime prior to conditioning?
   1 □ Yes
   0 □ No
   8 □ Unknown

19. Date of most recent test prior to conditioning: ______/_____/______

   Location of abnormalities:
   Yes □ No □ Unknown
   20. □ Hydrocephalus
   21. □ Odontoid hypoplasia

   If MRI Report is available, check here □, attach copy and reference Q.18

22. Was a Mental Development test done anytime prior to conditioning?
   1 □ Yes
   0 □ No
   8 □ Unknown

23. Date of most recent test prior to conditioning: ______/_____/______

24. Indicate test instrument and standard score of test done closest to conditioning

   (check only one):
   1 □ Bayley Scales of Infant Development
   2 □ Stanford Binet Intelligence Scale 4th Edition
   3 □ Wechsler Preschool and Primary Scale of Intelligence (WPPSI – Revised)
   4 □ Wechsler Intelligence Scale for Children – III (WISC – III)
   7 □ Other, specify:

25. Full scale score (not percentile): □ □ □ □ □ □ □ Unknown

26. Verbal score (not percentile): □ □ □ □ Unknown

27. Performance score (not percentile): □ □ □ □ Unknown

28. Were the Vineland Adaptive Behavior Scales done anytime prior to conditioning?
   1 □ Yes
   0 □ No
   8 □ Unknown

   Results of test done closest to conditioning, report score:
   29. Date of most recent test prior to conditioning: ______/_____/______

   30. Communication skills:

   31. Daily living skills:

   32. Socialization skills:
33. Was an eye exam done anytime prior to conditioning?
   1 ☐ Yes
   0 ☐ No
   8 ☐ Unknown

34. Date of most recent test prior to conditioning: [Month] [Day] [Year] ☐ Unknown
   Visual acuity (uncorrected only):
   35. Right eye (OD): [Month] [Day] ☐ Unknown
   36. Left eye (OS): [Month] [Day] ☐ Unknown
   37. Binocular/both eyes (OU): [Month] [Day] ☐ Unknown

38. Was corneal clouding present? 1 ☐ Yes 0 ☐ No 8 ☐ Unknown

39. Did the patient undergo an ophthalmologic exam under anesthesia anytime prior to conditioning?
   1 ☐ Yes
   0 ☐ No
   8 ☐ Unknown

40. Date of most recent test prior to conditioning: [Month] [Day] [Year] ☐ Unknown

41. Results of test (check only one):
   0 ☐ Normal
   1 ☐ Abnormal/Impaired
   8 ☐ Unknown

   If the report is available, check here ☐, attach copy and reference Q.39

42. Was the patient's hearing tested anytime prior to conditioning?
   1 ☐ Yes
   0 ☐ No
   8 ☐ Unknown

43. Date of most recent test prior to conditioning: [Month] [Day] [Year] ☐ Unknown

44. Results of hearing test (check only one):
   0 ☐ Normal
   1 ☐ Abnormal/Impaired
   8 ☐ Unknown

   If the report is available, check here ☐, attach copy and reference Q.42

45. Was a pulmonary evaluation done anytime prior to conditioning?
   1 ☐ Yes
   0 ☐ No
   8 ☐ Unknown

46. Date of most recent test prior to conditioning: [Month] [Day] [Year] ☐ Unknown

47. Oxygen saturation on room air: [Month] [Day] ☐ Unknown

48. Results of pulmonary evaluation (check only one):
   0 ☐ Normal
   1 ☐ Abnormal/Impaired
   8 ☐ Unknown

   If Pulmonary Function Report is available, check here ☐, attach copy and reference Q.45
49. Was an echocardiogram done anytime prior to conditioning?

1 ☐ Yes  
0 ☐ No  
8 ☐ Unknown

Table:

50. Date of most recent test prior to conditioning: [ ] [ ] [ ] [ ] ☐ Unknown

Valvular insufficiency:

51. Tricuspid (check only one):

0 ☐ None  
1 ☐ Mild or trivial  
2 ☐ Moderate or severe  
3 ☐ Valve replacement  
8 ☐ Unknown

52. Mitral (check only one):

0 ☐ None  
1 ☐ Mild or trivial  
2 ☐ Moderate or severe  
3 ☐ Valve replacement  
8 ☐ Unknown

53. Aortic (check only one):

0 ☐ None  
1 ☐ Mild or trivial  
2 ☐ Moderate or severe  
3 ☐ Valve replacement  
8 ☐ Unknown

54. Pulmonary (check only one):

0 ☐ None  
1 ☐ Mild or trivial  
2 ☐ Moderate or severe  
3 ☐ Valve replacement  
8 ☐ Unknown

55. Was the cardiac contractility tested anytime prior to conditioning?

1 ☐ Yes  
0 ☐ No  
8 ☐ Unknown

Table:

56. Date of most recent test prior to conditioning: [ ] [ ] [ ] ☐ Unknown

57. Ejection fraction (EF): [ ] % ☐ Unknown

58. Shortening fraction (SF): [ ] % ☐ Unknown

Posttransplant Information*

*To be completed 100 days posttransplant, or at time of death if death occurred <100 days posttransplant, or immediately prior to start of high-dose therapy (conditioning) for second transplant if second transplant done <100 days after first transplant.

Record the leukocyte enzyme levels at current evaluation:

59. Date of test: [ ] [ ] [ ] [ ]

60. Patient enzyme activity level: [ ] [ ] [ ] [ ] 1  nmol/hr/mg protein  
2  pmol/hr/mg protein  
8  Unknown
Follow-up Information*

* Report data for date of last contact as reported in Q.3 of Follow-up Core Form or immediately prior to death

Record the leukocyte enzyme activity level at current evaluation:

1. Date tested:
   Month       Day       Year

2. Patient enzyme activity level:
   1. nmol/hr/mg protein
   2. pmol/hr/mg protein
   3. Unknown

3. Was treatment given for the disease since last report?
   1. Yes
   2. No
   3. Unknown

4. Enzyme replacement
5. Substrate deprivation/inhibitor
6. Gene transfer/Gene therapy
7. Other, specify: ________________________________________________

Clinical status posttransplant

8. Was cerebrospinal fluid (CSF) testing done since last report?
   1. Yes
   2. No
   3. Unknown

9. Date of most recent test:
   Month       Day       Year

   Results of most recent tests:
   10. Opening pressure
       cm H₂O
   11. Closing pressure
       cm H₂O
   12. Total protein
       1. mg/dL
       2. g/L

13. Was Magnetic Resonance Imaging (MRI) of the brain/spine done since last report?
   1. Yes
   2. No
   3. Unknown

   Location of abnormalities:
   14. Date of most recent test:
       Month       Day       Year

   If MRI Report is available, check here ☐, attach copy and reference Q.13

   15. Hydrocephalus
   16. Odontoid hypoplasia
17. Was a Mental Development test done since last report?

- [ ] Yes
- [ ] No
- [ ] Unknown

18. Date of most recent test:

- [ ] Unknown

19. Indicate test instrument and standard score (check only one):

- [ ] Bayley Scales of Infant Development
- [ ] Stanford Binet Intelligence Scale 4th Edition
- [ ] Wechsler Preschool and Primary Scale of Intelligence (WPPSI – Revised)
- [ ] Wechsler Intelligence Scale for Children – III (WISC – III)
- [ ] Other, specify: _______________________________________

20. Full scale score (not percentile):

- [ ] Unknown

21. Verbal score (not percentile):

- [ ] Unknown

22. Performance score (not percentile):

- [ ] Unknown

23. Were the Vineland Adaptive Behavior Scales done since last report?

- [ ] Yes
- [ ] No
- [ ] Unknown

24. Date of most recent test:

- [ ] Unknown

25. Communication skills:

- [ ] Unknown

26. Daily living skills:

- [ ] Unknown

27. Socialization skills:

- [ ] Unknown

28. Was an eye exam done since last report?

- [ ] Yes
- [ ] No
- [ ] Unknown

29. Date of most recent test:

- [ ] Unknown

30. Right eye (OD):

- [ ] Unknown

31. Left eye (OS):

- [ ] Unknown

32. Binocular/both eyes (OU):

- [ ] Unknown

33. Was corneal clouding present?

- [ ] Yes
- [ ] No
- [ ] Unknown

34. Did the patient undergo an ophthalmologic exam under anesthesia since last report?

- [ ] Yes
- [ ] No
- [ ] Unknown

35. Date of most recent test:

- [ ] Unknown

36. Results of test (check only one):

- [ ] Normal
- [ ] Abnormal/Impaired
- [ ] Unknown

If the report is available, check here ☐, attach copy and reference Q.34
### 37. Was the patient's hearing tested since last report?

| 1 | Yes |
| 0 | No  |
| 8 | Unknown |

### 38. Date of most recent test:

- Month
- Day
- Year

### 39. Results of hearing test (check only one):

- Normal
- Abnormal/Impaired
- Unknown

*If the report is available, check here [ ] attach copy and reference Q.37*

### 40. Did neurologic status change since precondition evaluation?

| 1 | Yes |
| 0 | Stable/Unchanged |
| 8 | Unknown |

### 41. Date of most recent test:

- Month
- Day
- Year

### 42. Status:

- 1. Improved
- 2. Worsened

*If Physical Examination or Neurologic Examination Reports are available, check here [ ] attach copy and reference Q.40*

### 43. Was a pulmonary evaluation done since last report?

| 1 | Yes |
| 0 | No  |
| 8 | Unknown |

### 44. Date of most recent test:

- Month
- Day
- Year

### 45. Oxygen saturation on room air:

- %

### 46. Results of pulmonary evaluation (check only one):

- Normal
- Abnormal/Impaired
- Unknown

*If Pulmonary Function Report is available, check here [ ] attach copy and reference Q.43*

### 47. Was an echocardiogram done since last report?

| 1 | Yes |
| 0 | No  |
| 8 | Unknown |

### 48. Date of most recent test:

- Month
- Day
- Year

### 49. Tricuspid (check only one):

- None
- Mild or trivial
- Moderate or severe
- Valve replacement
- Unknown

### 50. Mitral (check only one):

- None
- Mild or trivial
- Moderate or severe
- Valve replacement
- Unknown

### 51. Aortic (check only one):

- None
- Mild or trivial
- Moderate or severe
- Valve replacement
- Unknown

### 52. Pulmonary (check only one):

- None
- Mild or trivial
- Moderate or severe
- Valve replacement
- Unknown

### 53. Was the cardiac contractility tested since last report?

| 1 | Yes |
| 0 | No  |
| 8 | Unknown |

### 54. Date of most recent test:

- Month
- Day
- Year

### 55. Ejection fraction (EF):

- %

### 56. Shortening fraction (SF):

- %
57. Was orthopedic surgery performed since last report?

<table>
<thead>
<tr>
<th></th>
<th>Yes</th>
<th>No</th>
<th>Unknown</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td></td>
<td>0</td>
<td>8</td>
</tr>
</tbody>
</table>

Specify site(s) (check all that apply):

58. Date of most recent orthopedic surgery:

<table>
<thead>
<tr>
<th>Month</th>
<th>Day</th>
<th>Year</th>
</tr>
</thead>
</table>

59. Knees

60. Hips

61. Spine

62. Fingers

63. Wrist (carpal tunnel syndrome)

64. Other, specify: ________________________________________________

59. Date of most recent test:

<table>
<thead>
<tr>
<th>Month</th>
<th>Day</th>
<th>Year</th>
</tr>
</thead>
</table>

66. Results of test (check only one):

<table>
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<th>Unknown</th>
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</thead>
<tbody>
<tr>
<td>1</td>
<td></td>
<td>0</td>
<td>8</td>
</tr>
</tbody>
</table>

If Report is available, check here ☐, attach copy and reference Q.65

67. Results of test (check only one):

<table>
<thead>
<tr>
<th></th>
<th>Normal</th>
<th>Abnormal/Impaired</th>
<th>Unknown</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td></td>
<td>0</td>
<td>8</td>
</tr>
</tbody>
</table>

If Report is available, check here ☐, attach copy and reference Q.65

68. Date of most recent test:

<table>
<thead>
<tr>
<th>Month</th>
<th>Day</th>
<th>Year</th>
</tr>
</thead>
</table>