compared to 19% (CI95 11.8, 26.1%) (P < .0001) for those who did not have LI at 1 month post-AlloHSCT. On multivariate analysis, only bloodstream bacterial infections (P = .0059) and invasive fungal infections (P = .0020) were significant risk factors for developing LI at 1 month. On multivariate analysis for risk factors for TRM, only LI at 1 month post-AlloHSCT (P = .0001), primary graft failure (P = .0096) and bloodstream bacterial infections (P = .0328) were significant. However, LI prior to AlloHSCT conditioning was not associated with higher TRM.

Conclusions: TRM among pediatric patients with LI at 1 month post-AlloHSCT is extremely high, with infections being the primary risk factor for LI.

### The Safety and Tolerability of the Novel Therakos Cellex Machine for Extracorporeal Photopheresis in the Treatment of GVHD in Children

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Extracorporeal photopheresis (ECP) is an established second line treatment option for graft versus host disease post hematopoietic progenitor cell transplant. At our center the Therakos Cellex has replaced the UVAR-XTS machine for ECP since 2009. We reviewed the records of 385 procedures using the Therakos Cellex. Nine patients underwent ECP for GVHD. The median age was 13.5 years (range 3.7 to 24) and weight was 49.2 kg (range 18.5-86.3). ECP was initiated at a median of 7.5 months (range 0.3-34.8) from the onset of GVHD. The mean duration per procedure was 106 minutes (range 60-205). Fifteen (3.9%) procedures were cancelled and 10 (2.6%) were delayed with central venous line (CVL) issues being the most frequent problem. Instillation of prophylactic tissue plasminogen activator (tPA) in the CVL lumens prior to a procedure was instituted 6 months before the end of study period, to reduce the incidence of CVL related occlusions and sluggish returns. With change in practice, fewer CVL related occlusions were observed (4.7% vs. 2.3%). There was one episode of CVL-associated thrombosis and one episode of delayed bleeding (mild and spontaneously resolved). There were four episodes of viral reactivation, 4 CVL-associated infections (1142 catheter days) and 1 episode of systemic inflammatory response syndrome. No patient experienced hypotension that required medical intervention. Although no additional adverse events were noted, there was considerable blood exposure in the smallest patients because of the need for machine blood prime. The Therakos Cellex appears to be safe and well-tolerated in 385 procedures performed in our institution. This is the first report regarding the safety and tolerability of this device for ECP in children and young adults.

### Table 1

<table>
<thead>
<tr>
<th>Disease</th>
<th>MRD ≤ 0.01%</th>
<th>Total (n)</th>
<th>Relapse (n)</th>
<th>Relapse Rates</th>
</tr>
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<tbody>
<tr>
<td>Acute lymphoblastic leukemia</td>
<td>No</td>
<td>20</td>
<td>7</td>
<td>35%</td>
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<td>20%</td>
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<td>11</td>
<td>4</td>
<td>36%</td>
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<td>3</td>
<td>38%</td>
</tr>
<tr>
<td>Acute leukemia</td>
<td>Yes</td>
<td>1</td>
<td>0</td>
<td>0%</td>
</tr>
</tbody>
</table>

Branch, National Cancer Institute/National Institutes of Health, Bethesda, MD; 2 Pediatric Oncology, Johns Hopkins Hospital, Baltimore, MD; 3 Department of Pathology, Johns Hopkins Hospital; 4 Biostatistics and Data Management Section, Center for Cancer Research, National Cancer Institute, National Institutes of Health

### Background:
Relapse is the primary cause of treatment failure post alloHCT. We sought to identify risk factors that predict relapse of hematologic malignancies after allogeneic hematopoietic cell transplantation (alloHCT) to identify those at highest risk of relapse who may benefit from novel therapies.

### Design:
This was a single institution, retrospective cohort study of children with acute lymphoblastic leukemia (ALL), acute myelogenous leukemia (AML), mixed phenotypic acute leukemia (MPAL) and myelodysplastic syndrome (MDS) who had undergone alloHCT between 1/1/2003 and 12/31/2010. Relapse was defined as any evidence of increasing disease post-alloHCT, including minimal residual disease (MRD). Relapse-free survival (RFS) was estimated by the Kaplan-Meier method and the log-rank test used to assess univariate associations with various characteristics. A Cox proportional hazards model was used to identify factors jointly associated with RFS.

### Results:
Of 70 children who underwent a myeloablative HCT for MDS or acute leukemia in complete remission at the time of HCT, 24 (34%) relapsed at a median of 214 days (range 1 month–57 months) post-HCT. Relapse rates by disease were 14/31 (45%) for ALL; 7/26 (27%) for AML; 3/9 (33%) for MPAL; 0/4 (0%) for MDS. Univariate analysis demonstrated that black race, central nervous system (CNS) disease at diagnosis (Figure 1), greater number of regimens given to induce remission and MRD pre-HCT were associated with higher relapse probability. In a Cox model, either two or more regimens needed to achieve remission or the presence of both pre-HCT MRD and CNS disease were approximately equally predictive of increased relapse risk. In patients with ALL, CNS disease was more highly associated with relapse risk than MRD. For those who were MRD negative, based on 19 total patients, the presence of CNS disease at diagnosis (n=2) was significantly associated with higher relapse risk (P < .0001).

### Conclusion:
We identified CNS involvement at diagnosis as a novel risk factor associated with relapse risk after alloHCT. This may be due to inherent biologic differences leading to higher risk disease, or as a sanctuary site, the CNS may be less amenable to an allogeneic effect. These patients may benefit from earlier or more intensive CNS-directed therapy to reduce relapse risk. Validation of these risk factors in a larger population and development of a prognostic score to identify those at highest risk of relapse in addition to a biology study to evaluate for MRD in the CNS using flow cytometry is planned. The goal is for prospective use of this prognostic tool in the development of relapse prevention trials.
bacteremia and for patient 2 included transaminitis, mild SOS, and CMV reactivation. Both patients are alive and well at 830 (patient 1) and 53 days (patient 2) post-HCT.

**Conclusions:** These two patients illustrate the successes and challenges of NBS for SCID. For example, rapid radiosensitive assays are needed along with widely available and standardized protocols for assessing B cell function in infants. Large, multicenter, prospective trials are needed to define criteria for HCT, optimal conditioning regimen, and age for HCT in clinically well newborns lacking a genetic diagnosis.

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**Figure 1.** RFS by CNS Disease at Diagnosis

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**Recovery of Lymphocyte Function May Predict Risk of Leukemic Relapse in Pediatric Patients Undergoing Allogeneic Stem Cell Transplant**

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Delayed immune reconstitution after allogeneic transplant for pediatric acute leukemia has been implicated by some studies as a risk for leukemic relapse. However, results regarding the specific laboratory parameters of interest have been conflicting. We initiated a retrospective review of 97 pediatric patients who underwent allogeneic stem cell transplantation for ALL, AML or JMML between the years of 2000 and 2010. We collected available clinical outcomes data which included lymphocyte subset (CD3, CD4, CD8, CD19, CD16/56) recovery at 90 and 180 days, proliferative response of CD3 T cells to phytohemagglutinin (PHA) at 90 and 180 days, and donor CD3 chimerism at 30 days post-transplant. Median cutoffs associated with immune reconstitution that were used for data analysis included a CD4 count >200, CD8 count >200, and PHA >30% of lower limit of normal control. Full donor CD3 chimerism was defined as no evidence of host DNA down to a sensitivity of 1%. Data for immunophenotype was unavailable for 71 patients; CD3 chimerism was available for 50 patients, and PHA responses were available for 47 patients.

No significant difference in CD4 or CD8 T cell recovery was detected between relapse and non-relapse patients. However, a higher rate of relapse was observed in patients with a PHA response <30% within the first 180 days (4/7, 5-year RFS 42.8%), compared to those with PHA >30% (5/40, 5-year RFS 84.8%, P = .02). In the subset of patients for whom both PHA and chimerism data were available, a higher rate of relapse was observed in patients with either mixed CD3 chimerism or poor PHA response (8/27), compared to those who recovered both full donor CD3 chimerism and CD3 PHA response >30% (0/7, P = .1).

Historically, tailoring of immunotherapy post-transplant has focused on the treatment of graft-versus-host disease. With the availability of clinical tools to better predict leukemic relapse post-transplant, further intervention (such as withdrawal of immunosuppression and/or DLI) may be implemented safely and effectively for those who require it. This preliminary data indicates that PHA response is a clinically accessible indicator of immune reconstitution that may be an important variable to consider when predicting a patient’s risk for relapse. Further study is needed to determine the degree to which PHA response might affect specific groups of patients.