was 51 (range, 18–67) y., with 46 (54%) female donors, 33 (39%) myeloid malignancies, 49 (58%) lymphoid malignancies, and 3 cases of SAA. The stem cell source was PBSC in 66 (78%) patients, while BM was used in 19 (22%) patients. 37 (43.5%) were transplanted from a matched related donor, and 48 (56.5%) from a matched unrelated donor. A myeloablative conditioning regimen was used in 24 (28%) patients, and 61 (72%) received a reduced intensity regimen. The median concentrations of CsA in the blood at 1, 2, 3 and 4 weeks after allo-SCT were 348 (range, 172–733), 284 (range, 137–535), 274 (range, 107–649), and 247 (37–695) ng/mL, respectively. All patients engrafted at a median of 17 (range, 0–42) days after allo-SCT. With a median follow-up of 16 (range, 5–29) months, grade 2–4 acute GVHD occurred in 36 patients (42%) at a median of 29 (range, 6–100) days after allo-SCT. The incidence of severe grade 3–4 acute GVHD was 23% (95%CI, 14–32%). In multivariate analysis, we found that higher whole-blood CsA concentration in the first week following graft infusion, and before onset of acute GVHD was the strongest parameter significantly associated with a reduced risk of severe grade 3–4 acute GVHD (P = 0.01; RR = 0.24; 95%CI, 0.08–0.73). This data indicates a close relationship between CsA trough blood concentration during the early post-allo-SCT period and the severity of acute GVHD. Inadequate or insufficient early exposures to CsA could be a serious risk for developing severe acute GVHD. Therefore, precise monitoring of CsA concentrations and achievement of a high CsA target concentration may be an effective tool to prevent the onset of severe acute GVHD.

### Table 1. Patient Characteristics and Treatment Results

<table>
<thead>
<tr>
<th>Etoposide/</th>
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</tr>
</thead>
<tbody>
<tr>
<td>TBI</td>
<td>TBI/Rituximab</td>
</tr>
<tr>
<td>No. pts</td>
<td>No. pts</td>
</tr>
<tr>
<td>Total Treated</td>
<td>11</td>
</tr>
<tr>
<td>Median Recipient</td>
<td>33 (20–47)</td>
</tr>
</tbody>
</table>

**Age in Years (range)**
- Gender (%): 0.999
  - Female: 3 (27) / 3 (30)
  - Male: 8 (73) / 7 (70)
- Diagnosis Status (%): 0.158
  - CR1: 7 (64) / 3 (30)
  - CR2: 4 (36) / 3 (30)
- Beyond CR2: 0 (0) / 1 (10)
- Relapse: 0 (0) / 3 (30)
- Histology (%): 0.035
- T-cell: 0 (0) / 4 (40)
- B-cell: 11 (100) / 6 (68)
- Ph+ (%): 0.311
- No: 7 (64) / 9 (90)
- Yes: 4 (36) / 1 (10)
- Donor Type (%): 0.387
  - Matched related: 6 (55) / 3 (30)
  - Matched unrelated: 5 (45) / 7 (70)
- Stem Cell Source (%)*: 0.008
  - Bone marrow: 3 (27) / 9 (90)
- Peripheral blood: 8 (73) / 1 (10)
- Acute GVHD (%): 0.999
  - Grades II-IV: 3 (27) / 9 (90)
  - Grades III-IV: 0 / 0
  - Chronic Extensive GVHD (%): 0 / 0
- Overall Survival: 100% / 30% / 0.005
- Progression-Free Survival: 90% / 60% / 0.009

### 326 INFERIOR OUTCOME WITH ADDITION OF RITUXIMAB FOR ALLOGENIC HEMATOPOIETIC STEM CELL TRANSPLANTATION (HSCT) IN ACUTE LYMPHOBLASTIC LEUKEMIA (ALL)

Kebraei, P.1, Mussell, M.2, Gutierrez, K.1, de Lima, M.1, Giralt, S.1, Hosing, C.1, Papat, U.1, Qazilbash, M.H.1, Thomas, D.1, Kantarjian, H.2, Khouri, I.F.1, Champlin, R.E.1 1 University of Texas M.D. Anderson Cancer Center, Houston, TX; 2 University of Texas M.D. Anderson Cancer Center, Houston, TX

We previously reported that rituximab was associated with a reduced incidence of acute graft versus host disease (GVHD) when incorporated into a standard transplant preparative regimen for ALL. To confirm our findings, we conducted a randomized, prospective study.

**Methods:** Adult ALL pts received a standard myeloablative conditioning regimen of total body irradiation (TBI, 12 Gy in four daily fractions) followed by etoposide 60 mg/kg × 1 dose with allogeneic HSCT. Rituximab was administered at 375 mg/m² on days 1, 2, and 3 following stem cell infusion in pts randomized to receive the drug. GVHD prophylaxis consisted of tacrolimus and mini-dose methotrexate for all pts, and anti-thymocyte-globulin was added to matched unrelated pts. Palifermin to reduce the incidence of mucositis was administered to all pts. Palifermin to reduce the incidence of mucositis was administered to all pts. Palifermin to reduce the incidence of mucositis was administered to all pts.

**Results:** Twenty-one pts have been entered onto study. Patient characteristics and treatment outcomes are detailed in Table 1. Of note, there were greater numbers of pts with disease beyond CR1 in the rituximab group. There was no significant difference between the 2 treatment groups with respect to the incidence of acute GVHD; 3 pts in the rituximab group developed chronic extensive GVHD. Seven of 10 (70%) pts on the standard treatment arm have died with a median time to death of 6.9 months; relapse n = 4, infection n = 2, organ failure n = 1; no pts on the standard treatment arm have died with a median follow-up of 14 months (range 3–32 months). Overall survival for the rituximab group was significantly worse at 30% versus 100% for the standard treatment arm, p = 0.005. Four of 10 (40%) pts on the rituximab treatment arm have had progressive disease, and all 4 of these pts died. Only 1 of 11 (9%) pts on the standard treatment arm had progressive disease at 14.5 months after HSCT and remains alive at 17.6 months after HSCT. In conclusion, our results demonstrate that the addition of rituximab to the standard etoposide and TBI conditioning regimen for allogeneic HSCT in ALL does not impact GVHD. Furthermore, rituximab appears to negatively impact survival, with increased risk of disease relapse. However, the small sample size and greater numbers of pts with advanced disease in the rituximab arm limit these conclusions.

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  - Grades II-IV: 3 (27) / 9 (90)
  - Grades III-IV: 0 / 0
  - Chronic Extensive GVHD (%): 0 / 0
- Overall Survival: 100% / 30% / 0.005
- Progression-Free Survival: 90% / 60% / 0.009

### 327 DEFECTIVE IMMUNE SYNAPSE FORMATION OF UMBILICAL CORD BLOOD-DERIVED NATURAL KILLER CELL S IS ABROGATED BY EX VIVO EXPANSION

Xing, D.1, Ramnay, A.G.2, Gräbhen, J.G.2, Decker, W.K.1, Li, S.1, Robinson, S.N.1, Yang, H.1, Davig, S.1, Huang, C.M.1, Elizabeth, S.J.1, Zeedele-Kay, P.A.1, Bolland, C.M.1, 1 University of Texas MD Anderson Cancer Center, Houston, TX; 2 Institute of Cancer Barts and the London School of Medicine, London, United Kingdom; 3 Baylor College of Medicine, Houston, TX

Activated natural killer (NK) cells derived from cord blood (CB) have been reported to mediate a significant graft versus leukemia effect (GVL). However, unmanipulated CB NK cells exhibit poor cytolytic activity against tumor cells in vitro, thus limiting their clinical application. We investigated the mechanism for the poor cytolytic activity of CB NK cells and whether the defect can be overcome with ex vivo expansion. NK cell killing of the tumor target cells is achieved by the formation of a mature immune synapse, followed by secretion of lytic granules containing perforin and granzymes. We hypothesized that CB NK cells exhibit low cytotoxicity against leukemia blasts due to a defect in the formation of the immune synapse. We have found reduced ability of CB NK cells to form immune synapses with leukemia target cells contributing to the decreased cytotoxicity of unmanipulated CB NK cells compared to adult peripheral blood (APB) NK cells. F-actin polarization was observed in a mean of 12% (range 9–21%) of the CB NK cell/tumor cell conjugates versus a mean of 85% (range 68–87) of APB NK/tumor conjugates (p < 0.001). This impairment could then be reversed by ex vivo expansion of CB NK cells with...