	No IFD	Proven or Probable IFD
MBL>1000	79 (84.9%)	14 (15.1%)
MBL<1000	52 (88.1%)	7 (11.9%)

Methods: We conducted an analysis of MBL levels among patients enrolled in a previous prospective cohort study. Serum samples from 152 patients with hematologic malignancies who received chemotherapy and/or HSCT between December 2001 and November 2006 were collected before or early after treatment initiation and stored at -70°C. Quantification of MBL levels was performed by a sandwich-ELISA assay (Viracor-IBT laboratories, Mo). Patients were followed for 6 months and scored as developing proven or probable IFD or not. The relationship between MBL level and developing proven or probable IFD was assessed using chi-square and Mann-Whitney tests. Survival analyses including logistic regression and Cox Proportional Hazards models were used to test the effect of MBL level and IFD status on overall survival and whether MBL level has an effect on IFD-free survival time.

Results: Forty-five of 152 patients (29.6%) developed IFD during the 6 months follow-up period of which 21 (46.7% of IFD cases and 13.8% of patients) were proven or probable IFD. Fifty-nine of 152 patients (38.8%) had MBL levels below 1,000 ng/ml. The rates of proven or probable IFD in patients with MBL levels below and above 1,000 ng/mL were 11.9% and 15.1 % respectively (P=.579). Mean MBL levels were lower in the IFD-free group (2085 vs 2398, p=.429). MBL levels below 1,000 ng/ml were not a predictor of death (P=.233). Mean IFD- free survival times in patients with MBL levels below and above 1,000 ng/ml were 20 weeks and 21 weeks respectively (P=.423). As expected, proven or probable IFD was associated with death (P<.0001).

Conclusions: Our findings indicate that low MBL levels were not associated with an increased risk of developing proven or probable IFD or overall survival in patients with hematologic malignancy.

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Clofarabine-Based Salvage Therapy and Conditioning Regimen in Patients with Relapsed or Refractory AML

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Background: In relapsed or refractory AML allogeneic transplantation (HCT) is considered to be the only chance to achieve long-term survival but still only about 40% of younger patients receive allogeneic HCT. Moderate activity of salvage regimens and accumulating toxicity of chemotherapy are reasons that may prevent from transplantation. Our goal was to study the safety and efficacy of a clofarabine salvage therapy prior to allogeneic HCT. Here, we report data from patients of stage I of a two-stage phase II study.

Patients and Methods: Patients above the age of 40 with relapsed or refractory AML who were fit for allogeneic HCT were eligible to participate in this multicenter, single-arm study. All patients received at least one cycle of clofarabine 40 mg/m^2 followed by intermediate dose cytarabine 1 g/m^2 days 1-5 (CLARA). Patients with a donor who exposed at least a reduction of leukemic blasts were scheduled for allogeneic HCT in aplasia after CLARA. The conditioning regimen consisted of clofarabine 30 mg/m^2 on days -6 to -3 and melphalan 140 mg/m^2 on day -2. Cyclosporine in combination with MMF was used for GvHD prophylaxis. In patients with partially matched unrelated donors the administration of ATG was recommended. Primary endpoint was treatment success defined as a complete remission (CR, CR(i)) six weeks after completion of therapy.

Results: Twenty-six patients were enrolled into stage I of this trial. Median age was 60 years. Fifty percent of the patients each had refractory or relapsed AML. At early response assessment on day 15 after CLARA-1 13 patients (50%) had less than 10% marrow blasts. Ten patients (38%) showed a reduction in marrow cellularity or blast percentage. Two patients did not have a significant marrow blast reduction. One patient died after the first cycle CLARA from septic multi-organ failure. Twenty-two patients (85%) received allogeneic HCT within this trial. Donors were HLA-identical siblings in 5 patients (23%), HLA-compatible unrelated donors in 11 patients (50%) and unrelated donors with one mismatch in 6 patients (27%). Liver toxicity was the most frequent adverse event. Seventeen patients (65%) developed grade III liver enzyme elevation while Grade IV was observed in 1 patient. Grad III/IV GvHD occurred in 6 patients (27%). All 26 patients have been evaluated for the primary endpoint. Sixteen patients had a CR (62%) and 6 patients a CRi (23%) at final response evaluation.

With a maximum follow up of 19 months 16 patients have died (7 patients died after relapse). At present 10 patients are alive, 6 of them had refractory disease.

Conclusion: Salvage therapy with CLARA and subsequent conditioning with clofarabine and melphalan prior to allogeneic HCT provides good anti-leukemic activity in patients with relapsed or refractory AML. The CR rate of the first 26 patients was evaluated favorably and the trial is currently recruiting into stage 2.

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Autologous Stem Cell Transplant (ASCT) As an Effective Post-Remission Consolidation Strategy for Good Risk Acute Myeloid Leukemia (AML) Patients

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Background: Good risk AML patients (core binding factor AML; diploid cytogenetics AML without Flt-3 ITD) are frequently consolidated with 3-4 cycles of high dose cytarabine (HIDAC) after induction of remission. About 50% of these patients relapse resulting in long term survival of 40-60% (Marcucci et al. JCO vol. 23 :5705-5717; 2005).

Materials and Methods: We retrospectively analyzed the outcomes of patients with good risk AML who underwent ASCT since 2009.

Results: 17 patients (10 males; 7 females) were identified in the database. Their median age was 60 years (range 29-80). All patients had received HIDAC based induction followed by at least one cycle of HIDAC based consolidation. Mobilizing

chemotherapy was HIDAC (1-3 grams/m2 for 6-8 doses)/ Etoposide(15-40mg/kg) in 16 patients and growth factor alone in one patient. Median time from diagnosis to ASCT was 4.2 (range 3.6-7) months. Preparative regimen for ASCT was Busulfan (3.2mg/kg x 4)/Etoposide (60 mg/kg) in 12 patients and high dose melphalan in 5 patients. The median CD34 cells infused was 4.9 x 10e6/kg (range 2.8 to 15.9).All patients engrafted with a median time to neutrophil engraftment of 11 (range10-12) days. The median time to platelet engraftment was 20 (range15-40) days. The median length of inpatient stay during the ASCT admission was 14 (range 10-25) days. One patient died of progressive disease 14 months post ASCT. Two patients died in remission on day 53 (sepsis) and day 836 (unknown cause) post ASCT. Fourteen patients (82%) are currently alive in complete remission. at a median follow-up of 20 (range 1- 40) months post ASCT. **Conclusion:** Consolidation of good risk AML patients with ASCT following induction of complete remission is safe and effective in preventing relapse in good risk AML patients.

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Anti-CD45 Pretargeted Radioimmunotherapy Prior to Bone Marrow Transplantation without Total Body Irradiation Facilitates Engraftment From Haploidentical Donors and Prolongs Survival in a Disseminated Murine Leukemia Model

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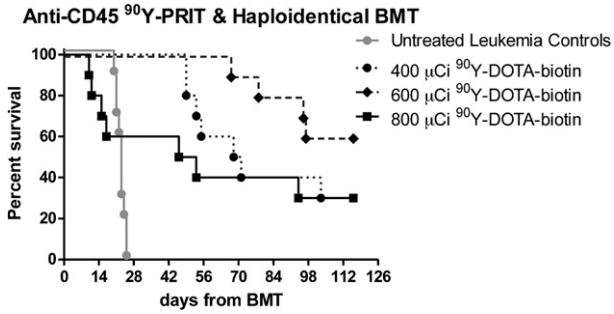
In many cases the only curative treatment option for patients with advanced leukemias may be hematopoietic cell transplantation (HCT), which is often associated with toxicities. Despite HCT, patients still relapse while others will not have the option of HCT due to the unavailability of an HLA-matched donor. We aim to overcome these hurdles using anti-CD45 pretargeted radioimmunotherapy (PRIT) in lieu of total body irradiation (TBI) for haploidentical bone marrow transplantation (BMT). B6SJLF1/J mice were given 10^5 syngeneic myeloid leukemia cells followed by injection of anti-CD45 antibody (30F11; 140 μg) conjugated to streptavidin (SAv). Eight hours later a biotinylated synthetic clearing agent (CA) (50 μg) was injected, followed by ^{90}Y-labeled DOTA- (2 μg) 2 hours later. This strategy resulted in excellent localization of radioactivity in spleen [38.1 ± 7.3 percent of the injected dose of radioactivity per gram of organ (% ID/g)] and bone marrow (BM; 3.4 ± 1.1% ID/g), with minimal uptake in non-target organs (kidneys, 0.70 ± 0.13% ID/g; lungs, 0.3 ± 0.1% ID/g) 24 hours after radiobiotin injection. In separate BMT studies, mice were treated with and without fludarabine (FLU) (100 mg/kg/day) on days -8 to -4, and/or cyclophosphamide (CY; 200 mg/kg/day) on days -2 and +2, and 30F11-SAv (140 μg) followed by CA (50 μg) and 400-800 μCi of ^{90}Y-DOTA-biotin three days prior to infusion of 15x10^6 BM cells from haploidentical donor mice (CB6F1/J, H-2D^d). In mice transplanted without TBI but using 800 μCi of ^{90}Y-DOTA-biotin, day 28 flow cytometry analysis detected up to 12% donor CD8+ cells, with no reduction in levels of chimerism in the absence of FLU or CY. Subsequently, mice with disseminated syngeneic leukemia treated with the PRIT approach in the absence of FLU and TBI showed an improvement in median survival (OS) compared to untreated leukemic mice (see FIGURE). Mice treated with 400-800 μCi of ^{90}Y-DOTA-biotin had a median OS of at least 50 days compared to a median OS of 23 days in untreated control mice. Forty percent of mice given 800 μCi of ^{90}Y-DOTA-biotin died early from complications from BM aplasia. These results suggest that anti-CD45 PRIT can localize radiation effectively to BM and spleen, and when used in conjunction with haploidentical BMT without TBI or FLU, can facilitate engraftment and lead to improvements in OS in a disseminated murine leukemia model.



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Allogeneic HSCT from Unrelated and Sibling Donors are Equal for Children with Acute Lymphoblastic Leukemia

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Allogeneic hematopoietic stem-cell transplantation (HSCT) from HLA identical sibling donors is standard of care for children with high-risk acute lymphoblastic leukemia