2 in RIC groups had successful pregnancy. Premature ovarian failure is less common among patients given RIC regimens than among those given HDC regimens for HST. Future prospective study is justified to determine the overall incidence of POF and the role of RIC regimens in lowering the treatment-related toxicity.

LEUKEMIA

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TREATMENT OF PATIENTS (PTS) WITH CHEMOTHERAPY-REFRACTORY CHRONIC LYMPHOCYTIC LEUKEMIA (CLL) WITH NONMYELOABLATIVE (NM) CONDITIONING AND HEMATOPOIETIC CELL TRANSPLANTATION (HCT) FROM HLA-MATCHED RELATED (MRD) OR UNRELATED DONORS (URD)

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Pts with CLL refractory to fludarabine (FLU)-based chemotherapy have poor prognosis with a median survival of less than 1 year. We examined the safety and efficacy of NM-HCT for pts with CLL refractory to at least 1 cytotoxic regimen and ineligible for conventional allogeneic HCT due to age and/or comorbidities. Forty-seven pts with diagnoses of CLL (n = 42), small lymphocytic lymphoma (n = 2), or prolymphocytic leukemia (n = 3) were treated with NM-HCT from MRD (n = 33) and URD (n = 14). Median pt age was 58 (range 47-68) years (62% of pts >55 years). Median number of prior regimens was 4 (range 1-12) with 94% of pts refractory to at least 1 regimen. Thirty-six pts (77%) were refractory to FLU, 19 to alkylating agents and 6 to rituxumab. Two pts had prior autologous HCT. Nineteen pts (40%) had responsive disease to salvage chemotherapy given prior to HCT [partial (PR) (30%) or complete remission (CR) (10%)] while remaining pts were either nonresponsive (51%) or in relapse (9%). Median interval from diagnosis to HCT was 5 (0.6–25) years. Conditioning consisted of 2 Gy TBI alone (n = 19) or combined with FLU (n = 28), 90mg/m^2 followed by mycophenolate mofetil and cyclosporine immunosuppression. All pts received G-CSF mobilized peripheral blood mononuclear cells as source of stem cells. After HCT, all pts became neutropenic (median ANC nadir=30 cells/ul) for a median of 11 days. Eighteen pts never had platelet counts below 20,000 cells/ul. Three pts had graft rejection; 1 died with aplasia and 2 had autologous recovery and are alive, 1 after multiple treatments and 1 relapsed at 2 years. Incidences of grades II, III, and IV acute GVHD were 38%, 15%, and 2% respectively and chronic extensive GVHD was estimated to be 48% at 4 years. With median follow up of 32 (range 6-69) months, overall response rate was 57% (CR = 43%). Overall, 26 patients are alive; 14 in CR, 4 in PR, 4 with stable disease, and 4 with progressive disease (PD). Seven patients died from PD, 9 from infections ± GVHD, 2 from cardiac problems, 1 from multiorgan failure, 1 from metastatic lung cancer, and 1 from rejection and aplasia. Estimated 2-year rates of non-relapse mortality, relapse-related mortality, progression free survival, and overall survival (OS) were 29%, 15%, 49%, and 56% respectively (Table 1). Projected 4-year OS was 47%. **Conclusion:** NM-HCT provides powerful graft–versus–leukemia activity in CLL and should be explored in phase II trials for treatment of pts with FLU-refractory disease.

Table. *CLL Patients Treated with NM Conditioning and HCT with MRD and URD*

	MRD (n = 33)	URD (n = 14)
Acute GVHD grades II, III, and IV	36%, 15%, and 3%	43%, 14%, and 0%
Two-year Chronic extensive GVHD	44%	61%
Median follow-up (range)	37 (7-69) months	19 (5-39) months
Overall response rate (CR)	55% (40%)	64% (50%)
Alive patients	7 CR, 2 PR, 4 stable, 3PD	7 CR, 2 PR, 1 PD
Two-year NRM	31%	23%
Two-year relapse-related mortality	16%	8%
Two-year PFS	45%	62%
Two-year OS	53%	70%

NRM, non-relapse mortality; PFS, progression-free survival.

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ALLOGENEIC BONE MARROW TRANSPLANTATION (BMT) FOR THE TREATMENT OF CHILDREN WITH VERY HIGH RISK ACUTE LYMPHOBLASTIC LEUKEMIA (ALL) IN FIRST REMISSION (CR1)

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Children with very high risk ALL treated with chemotherapy only have an expected disease-free survival of 20-40%, and are therefore candidates for allogeneic BMT. Between August 1988 and January 2002, eighteen patients received an allogeneic BMT for the treatment of very high risk ALL in CR1. They were 10 males and 8 females, aged 1.5–19.2 years (median 11.6). The very high risk features of the patients were as follows: Unfavorable cytogenetics with t(9;22) N = 2, or infant with t(4;11) N = 1; very high white count at diagnosis (>200,000/mm3) N = 5; poor initial response to induction chemotherapy [>25% blasts on day +7 or >5% blasts on day +14 and/or day +28] N = 10; hypodiploidy N = 2. Three patients had more than one very high-risk feature.

Patients received bone marrow from HLA-matched siblings (N = 9) or unrelated donors (N = 9). Cytoreductive regimens included: hyperfractionated total body irradiation (HF-TBI) 1,375 or 1,500 cGy and cyclophosphamide (CY) 60 mg/Kg/day × 2 [N = 6], or HF-TBI 1,375 or 1,500 cGy, Thiotepa (Thio) 5 mg/Kg/day × 2 and CY 60 mg/Kg/day × 2 [N = 10]. In addition two patients received other regimens: busulfan and melphalan (N = 1), or HFTBI, Thio and etoposide (N = 1). Graft-versus-host disease (GvHD) prophylaxis included T-cell depleted grafts (N = 10) or unmodified grafts with cyclosporin + methotrexate or steroids (N = 8).

With a median follow-up of 4.7 years (range 1.5-14.7), the overall survival and disease-free survival of the entire cohort were respectively 84% and 83% respectively. Two patients relapsed 4.9 and 18 months post BMT and one patient died of an accidental death (head trauma) 11.3 months post BMT. Two patients, both recipients of unmodified grafts developed grade 2 GvHD that resolved.

In summary, the outcome of allogeneic BMT for children with very high risk ALL in CR1 appears to be superior to that with chemotherapy (reported as 20-40%). The use of hyperfractionated TBI, Thio and CY followed by T-cell depleted grafts from related or unrelated donors was associated with a very good outcome (10/10 pts alive, disease-free) and no GvHD.