component of the innate immune system specialized to kill host cells that have become transformed or virally infected [1]. KIR are diverse in terms of the number, type, and combination of genes present in individuals, and display extensive polymorphism at the nucleotide level. The ligands for NK receptors include the polymorphic human leukocyte antigen (HLA) class I cell surface molecules. Recent evidence suggests that interactions between an individual's KIR molecular profile and HLA class I ligands may play an important role in stem cell transplant outcome; NK activation may be of benefit in hematopoietic transplants as donor NK cells in a KIR/HLA mismatched transplant have shown the ability to attack host leukemias and reduce graft versus host disease and graft rejection [2,3,5]. Thus assessment of KIR genotypes may become part of the donor selection process. As part of a larger study to analyze the role of donor and recipient KIR and HLA ligand profiles in stem cell transplantation, we are developing a novel, high-throughput single nucleotide polymorphism (SNP)-based KIR genotyping methodology. In this assay, the masses generated in a SNP-based primer extension reaction are analyzed on a matrix-assisted laser desorption/ionization time-of-flight mass spectrometer (MALDI-TOF). The method uses 384-well microarray chips, and is both highly accurate and rapid [4]. We present data using this novel typing method to demonstrate that the method is capable of accurately defining KIR genotypes in a panel of 100 donor recipient pairs from the NMDP. We are collaborating with the NMDP on an analysis of the KIR/HLA profiles of this panel and their relationship to hematopoietic transplant outcomes.

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EVALUATION OF UNRELATED DONOR SEARCH STRATEGY PROFICIENCIES

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A study completed by the National Marrow Donor Program (NMDP) evaluated search strategy proficiencies of U.S. transplant centers in selecting matched unrelated donors (MUD). The three objectives were: 1) to assess the quality of transplant center search practices, 2) to evaluate effectiveness of NMDP services and 3) to identify areas where further education is needed. Within the one year study, the first 5 new MUD searches were evaluated for each transplant center. For centers with lower transplant activity, all MUD searches were evaluated (15% had ≤4 searches). Search indicators scored were: 1) patient HLA typing—loci and level of resolution, 2) search strategy and 3) number of donors selected. Scores were averaged and centers were placed into prospectively determined groups. Center specific factors in the statistical evaluation were: 1) use of NMDP HLA expert consultations, 2) receipt of preliminary search reviews, 3) having Certified Hematopoietic Transplant Coordinator (CHTC) staff, and 4) volume of unrelated donor transplants per year. The study included 484 MUD searches for 106 transplant centers. The cumulative scores separated centers into three proficiency categories of high (56% of the centers), medium (29%) and low (15%). Multivariate logistic regression was performed to control for bias. Since the response variable "proficiency category" is ordinal, a proportional odds model was used, with the probability of having higher ranking being modeled. After adjusting for other factors, expert HLA consultations (P = .007) and CHTC (P = .03) significantly affected the proficiency ranking (Table 1). Centers with at least one CHTC staff or centers using HLA expert consultations tended to have higher rankings. Unrelated transplant volume and receipt of NMDP preliminary search reviews did not significantly affect the performance ratings (Table 1). The majority of the transplant centers scored in the highest category demonstrating optimal practices. The transplant centers in the lowest category tended to select too few donors and use less than optimal resolution for recipient HLA typing, indicating a need for targeted education in these areas. Two NMDP programs, Certified Hematopoietic Transplant Coordinator and HLA search consultation, were significantly associated with optimal search practices.

Table 1. *Logistic Regression Result for TC Proficiency Rankings*

Factor	Odds Ratio	95% CI	P Value	Favorable Characteristic
Center volume				**Not significant**
Low	1	***	***	
Medium and high	1.85	(0.82, 4.15)	.10	
HLA consultant used?				**Used HLA consultant**
No	1	***	***	
Yes	3.96	(1.45, 10.86)	.007	
CHTC staff				**Had CHTC staff**
No	1	***	***	
Yes	2.46	(1.08, 5.57)	.03	
Preliminary reviews				**Not significant**
No	1	***	***	
Yes	1.47	(0.67, 3.26)	.30	

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TREATMENT FOR ACUTE MYELOGENOUS LEUKEMIA BY LOW DOSE TOTAL BODY IRRADIATION (TBI) BASED CONDITIONING AND HEMATOPOIETIC CELL TRANSPLANTATION FROM RELATED AND UNRELATED DONORS

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Conventional allogeneic hematopoietic cell transplantation (HCT) is an effective treatment for patients with acute myelogenous leukemia (AML), but its use is restricted to younger individuals in good medical condition. The use of low-dose irradiation based preparative regimens has allowed the extension of allografting to older and medically infirm patients. The present study included 122 patients, 117 of whom were ineligible for conventional HCT. Their disease stages ranged from complete remission (CR1) to resistant AML. Patients were conditioned with 200 cGy TBI on day 0 with or without preceding fludarabine (30 mg/m^2/day from days −4 to −2), and given postgrafting cyclosporine at 6.25 mg/kg twice daily from day −3 and mycophenolate mofetil at 15 mg/kg twice daily from day 0. Human leukocyte antigen (HLA) matched related donors were used in 58 and HLA matched/partially mismatched unrelated donors in 64 patients. Among the 121 evaluable patients, 117 (96.7%) had durable hematopoietic engraftment. Cumulative incidences of acute graft-versus-host disease (GvHD) grades II-IV at 6 months were 33% after related and 42% after unrelated HCT, respectively. With a median follow up of 17 months (range 4-57), 58 patients were alive, 53 of whom were in complete remission. Cumulative non-relapse mortalities were 12% and 27%, and cumulative mortalities from disease progression were 46% and 34% at 2

years for related and unrelated recipients, respectively. Two year overall survival was 42% and disease-free survival was 36%, with disease stages and cytogenetic risks being major determinants for outcome. Patients transplanted in CR1 had 2-year overall survivals of 40% after related and 57% after unrelated HCT. We conclude that HCT from related and unrelated donors after low-dose TBI is a promising treatment for elderly patients and medically infirm younger patients with AML not eligible for conventional HCT.

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FEWER EARLY BACTERIAL AND VIRAL INFECTIONS FOLLOWING NON-MYELOABLATIVE VS. MYELOABLATIVE CONDITIONING FOR ALLO-TRANSPLANTATION

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To examine the incidence and timing of infectious complications, we reviewed 141 consecutive lymphoma patients receiving allogeneic hematopoietic stem cell transplantation using either myeloablative (MA) (n = 65) or non-myeloablative (NMA) (n = 76) conditioning. The NMA cohort was older (48.4 vs 41.4 years, $P < .01$), more often given unrelated umbilical cord blood as a stem cell source (43% vs 9%, $P < .01$), had comparable CMV seropositivity (39% vs 49%) and 39% had received a prior autologous transplant. All patients received antimicrobial prophylaxis including an extended spectrum fluoroquinolone, fluconazole, and acyclovir in addition to weekly CMV surveillance. The time to initial infection was determined for each patient to analyze potential differences in types and time to onset of infection between the cohorts. For this, patients were evaluated once in each of three microbial categories bacterial, viral, and fungal (Table 1). Fatal infections were uncommon and the incidence was similar in the MA and NMA cohorts [MA: 12 (18%); NMA: 12 (16%)]. In the peri-transplant period (day 0-30), the MA cohort had 2.2-fold greater primary bacterial infections, but the risks of initial bacterial infection were similar in the early (day 31-100) and late (day 101-365) post transplant periods. Viral infections were twice as frequent in the MA cohort during the peritransplant period though similar from day 30-100. Beyond day 100, the MA cohort again had 2-fold greater primary viral infections. Fungal infections developed in approximately 10% of patients in both cohorts and the risks were similar during all three time periods. These data demonstrate a significantly greater incidence of bacterial and viral peri-transplant infections using MA conditioning though infectious mortality was similar using either conditioning. Quicker engraftment and shorter periods of neutropenia may explain in part the reduced incidence of initial peri-transplant bacterial infections in the NMA cohort, but the pathophysiology underlying the later infectious risks is uncertain. Immune reconstitution is delayed after both MA and NMA conditioning but protection against infection appears similar using either treatment approach. Future studies to correlate immune reconstitution with infections are required to identify patients at greatest risk of later infections and to design new strategies for their prevention.

Table 1. *Incidence of Infections*

	Myeloablative	Non-myeloablative	*P*-Value
Bacterial			
Day 0–30	**49% (36–62)**	**22% (13–32)**	**<.01**
Day 31–100	**47% (28–66)**	**48% (35–62)**	**NS**
Day 101–365	**23% (0–45)**	**11% (0–22)**	**NS**
Viral			
Day 0–30	**18% (9–28)**	**9% (3–16)**	**.08**
Day 31–100	**31% (17–45)**	**44% (32–56)**	**NS**
Day 101–365	**44% (25–64)**	**21% (7–35)**	**.05**
Fungal			
Day 0–30	**12% (4–21)**	**9% (3–16)**	**NS**
Day 31–100	**12% (3–21)**	**13% (5–22)**	**NS**
Day 101–365	**10% (1–20)**	**17% (7–28)**	**NS**

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ALLOGENEIC HEMATOPOIETIC CELL TRANSPLANTATION (ALLO HCT) FOR METASTATIC BREAST CANCER (MBC)

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We reviewed data on women who received allogeneic hematopoietic cell transplantation (HCT) for metastatic breast cancer at 16 centers participating in the CIBMTR and the EBMT between 1992 and 2000. Probabilities of transplant-related mortality (TRM), graft-vs-host disease (GVHD), disease relapse or progression, progression-free survival (PFS), and overall survival were determined. Seventy-five patients were identified; median age at transplantation was 41 years (range, 25-60). Median follow-up time for survivors was 25 months (range, 3-64). Thirty-nine patients (52%) received myeloablative conditioning regimens and 36 (48%) received reduced-intensity conditioning (RIC) regimens. Nine of the RIC patients were treated with a planned tandem autologous-allogeneic approach. Patient characteristics were similar between the two groups except that more patients in the RIC group (72%) had poor pretransplant performance status than in the myeloablative group (28%). More patients in the myeloablative group developed acute GVHD (44% vs 34% at 100 days), chronic GVHD (36% vs. 8% at one year) and TRM (29% vs 7% at 100 days) compared to RIC. Overall response rates (complete or partial response) were 31% in the myeloablative group and 29% in the RIC group. Eleven of 42 patients (26%) who underwent immune manipulation (withdrawal of immunosuppression and/or donor lymphocyte infusion) after transplantation had disease control (complete, partial, minor, or stable response), providing evidence of a graft-vs-tumor (GVT) effect. Overall survival at 2 yrs was 24% (15-35%) for all patients. PFS at 1 year was 23% for myeloablative patients and 8% for RIC (excludes planned tandem) patients. Development of acute GVHD after an RIC regimen compared to no GVHD reduced the risk of relapse or progression (RR 3.05, $P = .03$) in multivariate analysis, consistent with a GVT effect, but this did not affect PFS. These findings support development of innovative allotransplantation approaches to exploit GVT effects for disease control while minimizing TRM. Planned tandem autologous-allogeneic RIC HCT, where probabilities of TRM and PFS at 2 years were 11% and 44% respectively for a small number of patients in these data, may represent such an alternative approach.

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HAEMOPOIETIC STEM CELL TRANSPLANTS FOR CHRONIC MYELOFIBROSIS—A REVIEW FROM THE ABMTRR

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The Australasian Bone Marrow Transplant Recipient Registry (ABMTRR) has been recording activity and outcome data for haemopoietic stem cell transplants in Australia since 1992 and New Zealand since 1998. Between 1992 and 2004 there were 50 haemopoietic stem cell transplants for chronic myelofibrosis in Australia and 1 in New Zealand. Of these, 46 were allogeneic, 3 syngeneic and 2 autologous; 35 were male and 16 were female. The median age at transplant was 48 with a range of 16 to 71. The annual number of transplants for this indication is small but increasing. In the five years 2000 to 2004, there were 33 transplants for this indication compared to 14 in 1995-1999. Of the donors for allogeneic transplants, 33 were HLA-identical siblings, 3 were siblings or other relatives with 1 HLA mismatch and 10 were unrelated volunteers. Within the allogeneic transplants performed