induction chemotherapy (cyclophosphamide, daunorubicin, vincristine and MTX i.t.). After induction all patients had to receive a HAM consolidation course (HD-AraC 3 g/m^2 every 12 hours, days 1-4; mitoxantrone 10 mg/m^2, days 5-7 and MTX i.t.). Patients in CR received two courses of MA consolidation (MTX 1.5 g/m^2 day 1 and L-asparaginase 10^4 IU/m^2 day 2), and then underwent allo-SCT or patients without a donor were randomized either to receive autologous stem cells from peripheral blood or high maintenance therapy. The median follow-up was 4.9 years. Between 1998 and 2003, a total of 325 pts entered the study. The median age was 32 yrs range 15-72 yrs. In 248 (76%) patients CR1 was reached and 227 of them were HLA typed; 100 had an identical sibling donor and 127 had no sibling donor. Allo-SCT was performed in 69 (69%) pts and auto-SCT or high maintenance therapy in 58 (46%). The 5-year DFS of pts with a donor vs pts without a donor was 41.8% vs. 35.5% , $P = .40$, hazard ratio 0.86, 95% CI 0.61-1.22). The relapse incidence was significantly lower (37.3% vs. 58.8% $P = .004$) and treatment related mortality (TRM) was significantly higher (20.9% vs. 5.7%, $P = .0005$) in the donor group compared to the no donor group. Five-year survival in pts with and without the donor was 43.0% and 36.9% respectively. For pts ≤50 years of age 199 of them were HLA-typed; 91 had a donor and 108 had no sibling donor. The 5-yr DFS rate in the donor vs no donor group was 42.2% vs. 36.2%, $P = .36$, hazard ratio 0.84 95% CI 0.58-1.22). Relapse rate was significantly lower and TRM was significantly higher in the donor versus no donor group. Five-year survival for patients with and without a donor was 43.9% and 37.4% respectively ($P = .58$), hazard ratio 0.90 (95% CI 0.61-1.32). In conclusion, in the EORTC ALL-4 trial, the intention to treat analysis shows that DFS and survival rate for allografted pts younger than 50 years of age were not significantly different compared to those receiving auto-SCT or high maintenance. High TRM (~20%) remains the main problem of allografting.

13

THE FEASIBILITY OF CONDITIONING REGIMEN OF FLUDARABINE, ATG, AND REDUCED DOSE OF CYCLOPHOSPHAMIDE IN PATIENTS WITH SEVERE APLASTIC ANEMIA WHO RECEIVED HLA-MATCHED SIBLING TRANSPLANTATION

Lee, J.W.[1], Kim, S.Y.[1], Eom, K.S.[1], Kim, Y.J.[1], Kim, H.J.[1], Min, C.K.[1], Lee, S.[1], Cho, S.G.[1], Min, W.S.[1], Kim, C.C.[1] [1]Catholic Hematopoietic Stem Cell Transplantation Center, The Catholic University of Korea, Seoul, Korea.

Background: High dose (HD) cyclophosphamide (CY, 200 mg/kg) plus ATG seems to be accepted as standard conditioning regimen in HLA-matched sibling stem cell transplantation (SCT) for severe aplastic anemia (SAA). However, HD CY causes serious cardiac toxicity in some cases which may lead to death within a few weeks. To avoid HD CY-associated cardiac toxicity we underwent HLA-matched sibling SCT using ATG, reduced CY to half dose with incorporation of fludarabine. **Methods:** Between March 2002 and August 2005, consecutive twenty-six patients with adult SAA (six patients were AA/PNH syndrome) received matched sibling SCT. The median age of patients was 41 (21-52) and median interval between Dx and SCT was 30 months (1-352). The median number of transfusions prior to SCT was 34 units (4-680). Ten patients (38%) had a history of IST before SCT. The conditioning regimen consisted of fludarabine (30 mg/m^2/day, 6 days), cyclophosphamide (50 mg/kg/day, 2 days) and ATG (2.5 mg/kg/day, 4 days, IMTIX-SangStat). Stem cell sources were BM plus CD34$^+$-selected PBSC (n = 9), BM (n = 14), or PBSC (n = 3). All patients received of cyclosporine and methotrexate as GVHD prophylaxis. **Results:** The median dose of CD34$^+$ cells infused was 3.6 × 10^6/kg (1.2-11.9). All patients achieved successful sustained engraftment, and the median time for ANC and platelet to reach 0.5 × 10^9/L and 20 × 10^9/L was 12 (6-16) and 18 (10-23) days, respectively. None of the patients developed cardiac toxicity or regimen-related toxicities. One patient developed delayed graft failure, but achieved successful engraftment after second SCT using TNI + ATG. The incidence of acute GVHD (more than grade II) was 8% (n = 2) and none developed chronic GVHD. The incidence of CMV infection requiring preemptive treatment was 38% (n = 10). Only one patient died of hepatic failure due to reactivation of chronic hepatitis C with hepatic GVHD posttransplant 3 months. PNH clone measured by flow cytometry disappeared posttransplant in 6 PNH patients. With median follow up of 12 months (2-41), the estimated probability of survival at 2 years was 96%. **Conclusions:** These data demonstrate that the conditioning regimen used in this study is feasible for patients with SAA who receive matched sibling SCT. Of note, the observations of successful engraftment as well as lesser acute GVHD and no chronic GVHD suggest that a fludarabine-based regimen has more potent immunomodulatory activity.

14

RESPIRATORY VIRUS INFECTION AMONG HEMATOPOIETIC CELL TRANSPLANTATION (HCT) RECIPIENTS: QUANTITATIVE VIRAL LOAD IN SYMPTOMATIC AND ASYMPTOMATIC INFECTIONS

Peck, A.J.[1,2,3], Englund, J.A.[1,2], Kuypers, J.[1,2,3], Corey, L.[2,3], Morrow, R.[1,2,3], Cent, A.[1,2,3], Boeckh, M.[2,3] [1]Children's Hospital & Regional Medical Center, Seattle, WA; [2]University of Washington, Seattle, WA; [3]Fred Hutchinson Cancer Research Center, Seattle, WA.

Background: Influenza (flu), respiratory syncytial virus (RSV), and parainfluenza virus (PIV) may cause serious respiratory disease following HCT, with infection rates of 2-10%. The extent of infection and disease due to human metapneumovirus (MPV) is largely unknown. We assessed viral infectious episodes after HCT using conventional and quantitative molecular detection. **Methods:** Weekly symptom surveys, nasal washes and throat swabs were collected from HCT recipients for 100 days post-HCT between Jan. 2001-June 2004. Samples were tested by culture and DFA for RSV, PIV and Flu, and by RT-PCR for RSV, PIV, MPV, and flu (detection limit 1100 copies/ml). Longitudinal analysis was performed for patients with ≥5 serial samples or a positive test or death. **Results:** Of 119 patients, 29 had 31 (26%) separate infectious episodes due to RSV (5), PIV (16), MPV (6), flu (3), RSV and flu (1). Median time to viral detection was 48 (range 3-96) days after HCT; median duration of viral shedding was 14 (range 5-42) days in 19 evaluable episodes. Six patients with PIV remained asymptomatic at the time of positivity, conventional testing was negative in 5. No asymptomatic shedding of RSV, MPV or flu was found. PCR testing nearly doubled first identification of RSV and PIV infectious episodes: 11 were detected by PCR plus conventional methods (in 2 patients, PCR detection preceded conventional methods) and 9 were detected by PCR alone. Median virus copy number in samples from asymptomatic weeks (2.3 × 10^4 copies/ml) differed from samples from symptomatic weeks (8.6 × 10^5 copies/ml; P value .004). Similarly, viral load in samples from patients with 0 or 1 symptoms (2.4 × 10^4 copies/ml) was significantly lower compared with patients that reported >1 symptom (1.8 × 10^6; P value .001). PIV was the only virus that showed a lower viral load in patients with 0 or 1 symptoms compared with >1 (P value .04). **Conclusion:** Both symptomatic and asymptomatic viral shedding among allogeneic HCT recipients were detectable using virus-specific molecular testing. Utilization of PCR viral detection methods increased yield of detectable episodes. PIV infections were more likely to be transiently asymptomatic than RSV, MPV, or flu. Asymptomatic shedding of PIV provides a possible explanation of why infection control programs emphasizing symptoms are highly effective against RSV but often not versus other viruses such as PIV. These data may guide implementation of more effective diagnosis and infection control strategies.

15

ALLOGENEIC STEM CELL TRANSPLANTATION FOR ADULT ACUTE LEUKAEMIA IN CR1 AND CR2 WITH A NOVEL MYELOABLATIVE CONDITIONING REGIMEN INCORPORATING DAILY INTRAVENOUS BUSULFAN, FLUDARABINE, 400 cGy TOTAL BODY IRRADIATION AND LOW-DOSE ANTITHYMOCYTE GLOBULIN

Russell, J.[1], Savoie, L.[1], Chaudhry, A.[1], Brown, C.[1], Bahlis, N.[1], Larratt, L.[1], Turner, R.[1], Storek, J.[1], Quinlan, D.[1], Geddes, M.[1], Balogh, A.[1], Stewart, D.[1] [1]Alberta Blood & Marrow Transplant Program, Calgary and Edmonton, Alberta, Canada.