325

SECOND TRANSPLANT FOR ACUTE MYELOGENOUS LEUKEMIA RELAPSING AFTER FIRST TRANSPLANT

Kim, H.-J., Min, W.-S., Eom, K.-S., Cho, B.-S., Lee, S., Min, C.-K., Cho, S.-G., Kim, D.-W., Lee, J.-W., Kim, C.-C. Catholic HSCT Center, St. Mary's Hospital, Seoul, Republic of Korea.

Second hematopoietic stem cell transplantation (HSCT) may be an effective salvage therapy in some patients with acute myelogenous leukemia (AML) who relapse after an initial transplant. To investigate the availability of second HSCT, we reviewed our medical records of 10 recipients of second allogeneic transplants for leukemia recurring after initial autologous or allogeneic transplantation. Since year 2002, ten relapsed patients after first HSCT who received second HSCT from the available HLA-matched (N = 7) or –mismatched (N = 3) sibling or unrelated donors were retrospectively reviewed. The median patient age was 35 (range, 18~51) and there were 6 males and 4 females. The median follow-up duration after second transplant was 14 months (range, 4–59). The majority of patients had intermediate or unfavourable cytogenetic features. Seven patients were relapsed after autologous HSCT, as a first transplant. Others received from HLA-matched sibling donors. The main conditioning regimen for second transplant consisted in cyclophosphamide plus busulfan. For graft-versus-host-disease (GVHD) prophylaxis, we used combinations of cyclosporine A or tacrolimus in addition to short-term methotrexate. In all, 6 patients received peripheral blood stem cells. All transplanted patients were successfully engrafted. The overall incidence of acute and chronic GvHD was 60% and 43%, respectively. Two (20%) patients were relapsed so far. The estimated probability of disease-free survival rate at 4-year was 50%. The overall 5-year survival rate was 55%. When we considered the incidence of non-relapse transplant-related mortality (TRM), two recipients (20%) died due to one from severe acute GvHD and the other from fatal infectious cause. These results demonstrate that second HSCT for relapsed AML patients performed with appropriate clinical schedule is feasible, and is associated with a favourable outcome.

Characteristics of patients

Diagnosis	Age/Sex	Cytogenetics	1st transplant	2nd transplant	Stem cell source	Conditioning	Status
AML, M1	33/F	46 XX	Sib allo	Sib allo	PBSC	Busulfex/ Cy	Alive, 50 m
AML, M1	36/M	t(8;21),21q,+4	Auto	Unrelated	PBSC	Busulfex/Cy/ ATG	Died, 4 m
AML, M2	35/M	inv(16)	Auto	Sib allo	PBSC	Busulfex/ Cy	Alive, 11 m
AML, M4	46/M	46 XY	Sib allo	Sib allo	PBSC	Busulfex/ Cy	Alive, 53 m
AML, M2	49/F	45 X,-9	Auto	Unrelated	BM	Busulfex/Cy/ ATG	Alive, 19 m
AML, M2	44/F	t(1;1)	Auto	Unrelated	BM	Busulfex/Cy	Alive, 59 m
AML, M2	35/M	del(16)	Auto	Unrelated	BM	Busulfex/Cy/ ATG	Died, 12 m
AML, M1	21/F	inv(16)	Auto	Sib allo	BM	Busulfex/Cy	Died, 6 m
AML, M5	34/M	47 XX,+21, add(3), add(15), t(4;18)	Sib allo	Sib allo	PBSC	Busulfex/ Fludarabine/ Ara-C	Alive, 6 m
AML, M1	18/F	47 XX,+21	Auto	Sib allo	PBSC	Busulfex/Cy	Died, 24 m

IDA/BHAC, idarubicin/N4-behenoyl-1-b-Darabinofuranosylcytosine; FLANG, fludarabine, Ara-C, mitoxantrone, and G-CSF combination chemotherapy in a sequence manner; Topo, topotecan; M, mitoxantrone; Vp, etoposide; Cy, cyclophosphamide; ATG, anti-thymocyte globulin; TRM, transplant-related mortality; CR2, second complete remission; CTx, chemotherapy; F/U, follow-up.

326

ONCE DAILY BUSULFAN AND FLUDARABINE IS WELL TOLERATED AND EFFECTIVE IN OLDER HEAVILY TREATED PATIENTS PRIOR TO UNRELATED DONOR ALLOGENEIC PERIPHERAL BLOOD STEM CELL TRANSPLANT

Potter, G.W., Bachier, C., Smith, B., Houghman, M., LeMaistre, C.F., Shaughnessy, P.J. Texas Transplant Institute, San Antonio, TX.

We report the results of a prospective phase II study using a reduced intensity (RI) regimen and unrelated donor hematopoietic stem cell transplant (HCT) consisting of intravenous busulfan (Bu) 3.2 mg/kg daily for 2 doses, fludarabine 30 mg/m^2 daily for 5 doses, and ATG 15 mg/kg daily for 4 doses. GVHD prophylaxis was tacrolimus and methotrexate 15 mg/m^2 on day 1, and 10 mg/m^2 on days 3 and 6. Twenty-one patients (median age 60, range 39–67) were treated; 19 were HLA matched with unrelated donors at A, B, C, DR, and DQ, and 2 pts had unrelated donors mismatched at one HLA class I allele, and 9 pts had one or more autologous HCTs prior to beginning the study. Follow up data is available on 20 pts. Grade II or higher regimen related toxicity (RRT) was reported in seventeen (85%) pts; gastrointestinal (n = 14), mucositis (n = 7), hepatic function (n = 4), fever and infection (n = 3), pulmonary function (n = 2), and renal function (n = 1). Veno-occlusive disease did not manifest in any pts. Six pts did not receive the full dosage of ATG because of ATG toxicities, including fever and chills, hypotension, capillary leak syndrome, and elevated bilirubin levels. The median day of engraftment was 15 days and 19 (95%) of twenty pts achieved 100% donor chimerism by day 80. Three pts subsequently lost donor chimerism and one never achieved higher than 90% donor chimerism; all 4 pts relapsed. Thirteen pts (65%) developed grade II or higher overall acute GHVD and chronic GVHD developed in five pts. Treatment related mortality (TRM) was 15% (95% confidence interval [CI], 5%-40%) at 3 months, and 35% (95% CI, 17%-63%) at 12 months. The most common cause of TRM was GVHD and infection. Actuarial overall survival at 3 years was 52% (95% CI, 27%-71%). All six pts who received reduced ATG dosages developed acute GVHD and one had relapse of disease, while of the remaining fourteen pts who received full ATG dosages 7 developed acute GVHD and 5 had relapse of disease. In conclusion, once daily Bu and fludarabine and unrelated donor HCT demonstrated good long term survival and disease control, however, TRM still exists with this regimen in this heavily treated, older pt population. Future use of a co-morbidity scoring tool may help select pts more suitable for this regimen. ATG significantly contributed to RRT, while GVHD and its treatment and complications primarily resulted in the TRM. Removing ATG and using other measures for GVHD prophylaxis and treatment may improve this RI regimen.

327

SAFETY AND TOXICITY OF REDUCED INTENSITY ALLOGENEIC TRANSPLANTATION WITH FLUDARABINE/MELPHALAN IN PATIENTS WITH ADVANCED HAEMATOLOGICAL DISEASES. A SINGLE CENTRE EXPERIENCE

Khoo, L., Johnston, A.-M., Larsen, S., Joshua, D., Gibson, J. Royal Prince Alfred Hospital, Sydney, New South Wales, Australia.

Aim: The safety and toxicity outcomes in a group of patients with advanced haematological diseases undergoing reduced intensity allogeneic stem cell transplantation using Fludarabine (30 mg/m^2) and Melphalan (140 mg/m^2) conditioning was examined. The majority (62%) of these heavily pre-treated patients had failed previous transplantation (22 autologous, and 1 allogeneic). **Method:** Thirty-seven patients underwent Sibling (Full Match) - 19; Mismatch Sibling/Other Family – 4, Matched Unrelated Donor – 13 or Umbilical Cord Blood – 1 transplantation. The median patient age was 50 years (range, 29 – 64 years). Disease at time of transplant was: 6 primary acute leukaemia, 3 secondary acute leukaemia, 3 secondary MDS, 1 primary MDS, 11 multiple myeloma, 12 NHL and 1 myelofibrosis. **Results:** The median follow-up period was 21 months (range, 0.2 – 84 months. Median survival was 9 months