0820

DACLIZUMAB HAS POOR EFFICACY IN STEROID-REFRACTORY ACUTE GRAFT VERSUS HOST DISEASE: A SINGLE CENTRE EXPERIENCE WITH 12 ALLOGRAFT PATIENTS

H. Sia, C.H. Hui, H. Mangos, N. Horvath, H.K. Lee, I. Lewis, T. Hughes, B. To, P. Bardy

Royal Adelaide Hospital, Adelaide, Australia

Backgrounds. Daclizumab, a humanised monoclonal antibody against interleukin-2 receptor, has been used in steroid-refractory acute graft-versus-host disease (aGVHD). Reported results were conflicting. Aims and Methods. We performed a retrospective audit of the outcome data of 12 consecutive allograft patients who had been treated with Daclizumab for steroid-refractory (to > 2mg/kg/d of iv Methylprednisolone) grade III-IV aGVHD from year 2000-2004 in our unit. All patients received standard anti-microbial prophylaxis, and Cyclosporin and Methotrexate GVHD prophylaxis, except for three reduced-intensity allografts who received cyclosporine alone. Clinical grading of aGVHD was performed according to standard criteria. 1mg/kg of iv Daclizumab was given on days 1, 4, 8, 15 and 22 and definition of treatment response as previously described (*Przepiorka 2000*). *Results.* Twelve patients developed grade III-IV aGVHD after HLA-matched blood stem-cell allogeneic transplants, who consisted of 9 sibling (7 ablative, 2 reduced-intensity) and 3 unrelated (1 ablative, 2 reduced-intensity) allografts. Daclizumab was commenced after failure of iv Methylprednisolone at a median of 81/2 days (range: 3-28). These patients also received numerous (range: 3-7) concomitant GVHD therapies, including Steroids, Cyclosporin/Tacrolimus, Mycophenolate, and Etanercept (for gut aGvHD). Anti-thymocyte globulin (ATG) was additionally given for poor responders to Daclizumab in 6/12 patients. The only complete responder to Daclizumab (patient 7) died of subsequent exacerbation of gut GVHD, haemorrhagic cystitis and CMV viraemia. The single partial responder (patient 6) eventually died of progressive gut GVHD and bacterial sepsis. There was no long-term survivor with infections as terminal events in 10/12 patients. *Conclusions.* In contrast to initial published reports, allograft patients with severe steroid-refractory aGVHD had poor response and dismal outcome when treated with Daclizumab in our institution. It was our major concern that the poor survival may be contributed by the delay of more appropriate GVHD therapy and the aggravation of infective complications. As a result, we have moved away from Daclizumab back to ATG since 2005. Novel GvHD therapies such as photopheresis, mesenchymal stem cells should be explored.

Table 1. Pre- and post-Daclizumab responses and outcome.

	Skin GVHD		Gut GVHD		Liver GVHD		
Score	Pre-	Day 43	Pre-	Day 43	Pre-	Day 43	Outcome
1	0	0	1	2	3	4	Death, d60
2	3	3	2	2	1	3	Death, d57
3	3	2	2	3	0	4	Death, d124
4	3	3	3	4	0	1	Death, d180
5	0	0	0	0	4	4	Death, d31
6	1	0	3	1	2	1	Death, d345
7	0	0	2	0	2	0	Death, d323
8	0	0	0	0	4	4	Death, d240
9	1	1	3	4	2	4	Death, d247
10	0	0	3	4	0	0	Death, d72
11	1	0	3	4	2	4	Death, d53
12	2	1	3	1	3	4	Death, d166

0821

ALLOGENEIC STEM CELL TRANSPLANTATIONS AFTER REDUCED INTENSITY CONDITIONING REGIMEN FLUDARABIN, BUSULFAN AND ATG (FRESENIUS)

Y. Brychtova,[1] M. Doubek,[1] J. Muk,[2] J. Mayer,[1] J Vorlcek[1]

[1]*University Hospital Brno, Brno, Czech Republic;* [2]*Centre Biostatistics Masaryk University, Brno, Czech Republic*

Introduction: Allogeneic stem cell transplantation with reduced intensity conditioning (RIC) is effective therapy for hematologiccl diseases. Methods. This is a retrospective report about 63 patients [21 women, 42 men, median age 51 years (15-65)] who underwent hematopoietic stem cell transplantation (HSCT) after reduced intensity conditioning regimen (RIC) with Fludarabin (30mg/m2, 5 days), Busulfan (8-12 mg/kg p.o.) and ATG Fresenius (10mg/kg/d, 4 days for hematological disease in our transplant center between March 1998 and December 2005. The diagnosis were 17 AML [15 in 1st.CR, 1 in 2nd CR, 1 in relaps (R)], 3 MDS, 1 AA, 22 CML (21 in chronic phase, 1 in acceleration), 1 myelofibrosis, 3 HD (1R, 1 CR, 1 PR), 8 B-NHL (2 DLBCL, 1 FL, 3 MCL, 2 SCLL) (1R, 4 PR, 3 CR), 6 CLL (4 R, 2 PR), 2 MM (1R, 1 PR). Peripherial blood stem cells (PBSC) were used in 60 patients, bone marrow in 3 patients. Median of infused CD 34+cells was $6{,}76\times10^6$/kg. Donors were 57 related and 6 unrelated respectively. As GVHD prophylaxis, 58 patients received CsA, 2 received CsA+MTX and 3 CsA+ mycophenolat mophetil. *Results.* Median time of follow up was 25 months. After transplantation, any toxicity was observed in 25% (16) patients, 66% (42) patients developed a toxicity grade I-II, 7% (4) patients a toxicity grade III, 2% (1) patient a toxicity grade IV.

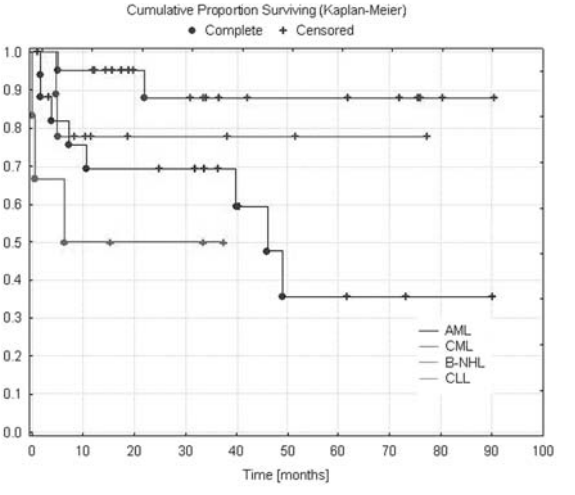

Figure. Overall survival of patients AML, CML, NHL, CLL.

Without any parenteral nutrition were 68% (43) patients, and 32% (20) patients have parenteral nutrition in median 11 days (3-22 days). Recovery of neutrofils($>1.0\times10^9$/L) was in median time 18 days, trombocytes ($>20\times10^9$/L) in median 13 days. Complete chimerism (CC) was reached in median time 73 days in 49 (78%) patients, 2 (3%) patient still didn't reach CC, 2 (3%) patients didn´t reach CC for short time after transplantation, the others didn´t reach CC because of rejection of graft (1), giving his autologous back up of stem cells for severe GVHD (1), relaps of disease (4pts=7%), death from other reason (3 infections, 1 bleeding). Twenty-two (35%) patients developed an acute GVHD: 9 patients maximal grade I, 8 patients maximal grade II, 3 patients maximal grade III, 2 patients grade IV. A chronic GVHD was presented in 28 (44%) patients (23 limited,5 extensive). Secondary rejection of graft occured in 2 patients with unrelated donor. Fourteen patients had preemptive therapy of CMV. Any infection since day +100 had 28 (44%) pts, after day +100 31 (49%) patients. Twenty patients (31%) died, the causes of death: 10 (15%) relapses of disease, 3 (5%) infections, 4 (6%) GVHD,1(2%) toxicity, 2 (3%)from other reason. Early transplant related mortality (TRM) was 10% (6 patients:2 relaps, 1 GVHD, 1 bleeding, 2 infections), late TRM 5% (3 patients GVHD). Median time of overall survival for all patients (Kaplan-Meier) wasn´t reached, AML patients had 46 months, CLL patients 6.4 months and CML patients and B-NHL patients wasn´t reached it. Conclusions. RIC is associated with favorable outcome and low toxicity in patients in remission at the time of transplantation.

0822

LOW-DOSE METHOTREXATE AS SALVAGE THERAPY FOR REFRACTORY GRAFT-VERSUS-HOST DISEASE AFTER REDUCED-INTENSITY CONDITIONING ALLOGENEIC STEM CELL TRANSPLANTATION

H. de Lavallade, M. Mohty, C. Faucher, S. Furst, J. El Cheikh, D. Blaise

Institut Paoli-Calmettes, Marseille, France

Corticosteroid (CS)-resistant GVHD is associated with high morbidity and mortality, and therapeutic options are limited for those patients. Also, elderly patients undergoing RIC allo-SCT are more exposed to the