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THE ROLE OF LOW DOSE BUSULFAN (BU) (4MG/KG) WITH CYCLOPHOSPHAMIDE (CY) AS A CONDITIONING REGIMEN FOR SEVERE APLASTIC ANAEMIA (SAA)

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Bu is an agent currently used in BMT.Bu have minor toxicity to the lymphoid system and cause little immunosuppression. However, successful allogeneic engraftment after the Tutschka regimen suggests that Bu can enhance the immunosupressive properties of Cy. Graft rejection has been a problem in SAA who were conditioned with Cy alone.Aiming to reduce graft rejection and to improve the immunosuppressive activity of Cy, we used Bu/Cy 4mg/Kg and 200mg/Kg, respectively, as a conditioning in 81 pts with SAA.Pts were 3-53 years of age (mean, 24). The previous transfusions number was 1-276 (mean, 39), and 48% had therapy immunossupressive before transplant. MTX/CSA were used in order to prevent GVHD.12/81 (15%) pts rejected their transplants in a mean time of 317 days (28-1001), 2 primarily (3%) and 10 (12%) as a late rejection. aGVHD grades 2 or 3 occurred in 20/67 (31%) pts and cGVHD in 24/61 (39%). The actuarial survival rate at 2850 days was 56% (CI 46-68%). In the univariate analysis age, previous treatment, number of previous transfusions, time of CSA use and aGVHD were statistically significant for survival. The OS for patients who received less and more than 15 transfusions was 78% and 50%, respectively (P=0, 001); less and more than 50 transfusions was 67% and 28%, respectively (P=0, 002). The cumulative incidence of rejection was 22% (CI 10-33%). In the univariate analysis number of previous transfusions and time of CSA were statistically significant for rejection. The cumulative incidence of rejection for patients who received less and more than 50 transfusions was 15% and 43%, respectively (P=0, 06). The following risk factors were statistically significant for survival in the multivariate analysis: number of previous transfusions, time of CSA, and aGVHD; for rejection: number of previous transfusions, and time of CSA.Low dose Bu/Cy showed to be effective and safe as conditioning regimen for SAA with acceptable rejection and survival rates. Moreover, higher number of transfusions showed to be associated with poor survival and more frequent rejections.

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QUANTITATIVE DETECTION OF CHIMERISM AFTER ALLOGENEIC PERIPHERAL BLOOD STEM CELL TRANSPLANTATION

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For peripheral blood stem cell transplantation (PSCT), several methods for engraftment analysis, including detection of restriction fragment length polymorphisms and amplification of polymorphic genetic loci, have been described previously. We report here a quantitative, non-isotopic method using short tandem repeat (STR) marker to facilitate the monitoring of engraftment. The DNA from the donors and the pre-transplant recipients were amplified with the AmpFlSTR Profiler Plus kit that contained 9 STR markers. The fluorescent polymerase chain reaction products were then fractionated on the polyacrylamide gels in the ABI PRISM 377 DNA Sequencer and were analyzed by the GeneScan 2.1 software. The best markers were selected as the informative alleles to distinguish donor from recipient. For quantitative analysis of engraftment, the chimeric samples were prepared by mixing pretransplant recipient and donor DNAs in different ratio to generate a standard curve. After amplifying the post-transplant recipient DNA, the extent of engraftment was determined by interpolating the percent peak area of the informative alleles according to the standard curve. This method was evaluated by the samples from 30 patients who received allogeneic PSCT during 1999 to 2002. Four of them were informative for some degree of mixed chimerism indicating leukemic relapse. Of these 4 cases, 35%, 6.5%, 15.5%, and 2.7% recipient DNA were first detected in the third, tenth, fourth, and fourth month after PSCT, respectively. These four mixed chimeric patients were soon treated with a rapid taper of immunosuppression. Three of them were then allowed a second PBST. In summary, this method provided an accurate, quantitative, and early assessment of mixed chimerism in post-transplant patients. Such information may be useful to guide implementation of additional treatment to circumvent graft failure or relapse in the future.

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STEM CELL TRANSPLANTATION IN AUSTRALIA AND NEW ZEALAND: AN UPDATE FROM THE AUSTRALASIAN BONE MARROW TRANSPLANT RECIPIENT REGISTRY (ABMTRR)

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The ABMTRR has captured data for an estimated 99.5% of transplants performed in the region from 1992-2001. In 2001, 1042 transplants were performed, fewer than the peak of 1094 in 1998. This change is due to a reduction in staged, autologous transplants (mainly for breast cancer) and allografts for CML, despite an increase in unrelated donor and reduced-intensity allografts. For adult patients, the most common indications for single autografts (total 578) were NHL (42%), myeloma (35%) and Hodgkin lymphoma (9%). There were 17 transplants performed for solid tumours (3%) and 4 for autoimmune disease, while 34 staged autografts were done for myeloma (6), germ cell tumours (6), breast cancer (4) and others (18). Of 232 related donor allografts, AML (31%), CML (16%), ALL (11%) and NHL (10%) were the most common indications. In 1996, 97 patients were transplanted for breast cancer while in 2001 there were only 6. In 1999, there were 81 allografts for CML, 73 in 2000, but only 38 in 2001 coinciding with the initiation of trials with imatinib mesylate. For CML in 1st chronic phase, the numbers dropped from 63 in 1999 to 29 in 2001. Outcome data were available with a minimum of 12 months follow-up. For allografts, the major cause of death in the first and second year was relapse (26%, 68%) with GVHD responsible for 15% and 5% respectively. For autografts disease-related deaths were 78% and 86% in the first and second years. Of 1673 adult recipients of related donor allografts, the estimated probability of survival at 9 years was 42% and was 32% for 406 VUDS. We conclude that the ABMTRR is a valuable resource in identifying trends in transplantation.

	2001 Australia	2001 New Zealand
Total transplants	937	105
Male:Female	582:355	61:44
%male	62.1	58.1
Number of autografts	611	67
Allo related	234	29
Allo unrelated	92	9
1st transplants (allo&auto)	871	104
2nd or 3rd transplants	66	1
staged autografts	57	3
mismatched allografts	24	4
age range (yr)	.3-75	1-64
Aged 0-15 yr	109	22
Aged 16-49 yr	391	45
Aged 50+ yr	437	38
% aged 50+ yr	46.6	36.2
Number of contributing centres	31	6

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EFFECT OF ALLOGENEIC STEM CELL TRANSPLANTATION ON BONE MARROW (BM) ANGIOGENESIS IN CHRONIC MYELOGENOUS LEUKEMIA

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Aim: Angiogenesis or new vessel formation is integral to the biology of many malignancies. Increased BM angiogenesis has