LATE EFFECTS/QUALITY OF LIFE

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THE PREVALENCE AND SEVERITY OF FATIGUE IN LONG-TERM SURVIVORS OF ALLOGENEIC STEM CELL TRANSPLANTATION: A PRELIMINARY ANALYSIS

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In allogeneic stem cell transplantation (alloSCT) populations, long-term fatigue is an important determinant of QOL that needs to be addressed. The contribution of anemia to patients self-reported fatigue levels was examined. A questionnaire package was mailed to 290 recipients of blood or marrow allografts transplanted at our institution 1 to 7 years ago. The package included: 1) a 100 mm Linear Analogue Self-Assessment (LASA) measure of energy, ability to perform daily activities, and overall QOL, 2) the anemia subscale of the FACT (FACT-An), which also includes 13 items relating to fatigue (FACT-An fatigue subscale), and 3) a request for their most recent hemoglobin (Hb) level. An interim analysis was performed after 123 completed surveys (42%) had been returned. A total of 64% of the sample reported at least a mild level of fatigue, with 35% reporting moderate to severe levels of fatigue on the FACT-An fatigue subscale. The FACT-An fatigue subscale scores were also standardized on a 1-100 scale (100 = no fatigue) and then compared to scores reported in studies of anemic cancer patients and healthy US individuals (1, 2). The mean score observed in our sample (63.3) was higher than the mean score observed in anemic cancer patients (56.7), but lower than the mean score observed in healthy people (85.0). A total of 26% of the sample met the criterion for anemia (Hb < 130 g/L for men and < 120 g/L for women). No significant correlations were found between Hb level and any of the fatigue measures. Other potential factors contributing to fatigue were also examined. Subjects who were > 44 years old (median age) reported a higher level of fatigue than younger subjects on the LASA (energy level and daily activities) and the FACT-An fatigue subscale ($p \leq 0.022$). Level of fatigue was not related to the following potential risk factors: gender, diagnosis, related vs. unrelated donor, GVHD, and time after SCT. Our findings suggest that fatigue is a significant symptom for the majority of long-term survivors of alloSCT that appears to persist for years. However, anemia may not be a primary contributor to patients experience of fatigue. 1. Littlewood TJ et al. J Clin Oncol 2001; 19:2865-2874. 2. Nortier JWR et al.(abstract) Eur J Cancer 2001; 37:S351 (Supported by an unrestricted grant from Ortho Biotech Canada).

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POST-TRAUMATIC GROWTH: A LATE EFFECT OF STEM CELL TRANSPLANTATION

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Stem cell transplantation (SCT) prolongs life for many people and offers a cure for some. However, its late effects can significantly negatively impact the quality of life (QOL) of survivors. Often overlooked, positive quality of life outcomes are possible, as well, particularly in the area of psychological growth. A large, multi-center, cross-sectional study was conducted to characterize the QOL and quality of close relationships of long-term survivors of autologous and allogeneic SCT diagnosed with acute leukemia, chronic myelogenous leukemia, lymphoma, and breast cancer. Four hundred seventy seven survivors, 159 spouses, and 123 healthy controls (matched on gender, age, marital status, and education) were assessed as of June 2002. As part of this study, post-traumatic growth was measured using the Post-Traumatic Growth Inventory (PTGI). Survivors were mostly Caucasian (92%), married (70%), of mean age 49 years (range = 21 - 77), and employed fulltime (51%). Mean years since transplant at assessment was 6.9 (range = 1.8 - 22.6). Compared to spouses (M = 59.0) and controls (M = 57.8), survivors reported more psychological growth (M = 66.4, $p < .0001$). In univariate analyses greater post-traumatic growth was associated with lower levels of education, and higher support group participation, as well as being female, having had an autologous transplant, having had less intensive prior therapy, and being diagnosed with breast cancer (all relationships significant at $p < .05$) . Post-traumatic growth in survivors was associated with greater use of certain coping strategies including positive reframing (r = .33), emotional support (r = .35), instrumental support (r = .27), emotional processing (r = .27), and emotional expression (r = .21) (all values significant at $p<.0001$). In addition, psychological growth was associated with greater levels of spiritual well-being (r = .29, $p < .0001$). We conclude that psychological growth is possible post-transplant and further study of this positive late effect is warranted.

LYMPHOMA/MULTIPLE MYELOMA

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IN VIVO PURGING AND POST TRANSPLANT IMMUNOTHERAPY WITH RITUXIMAB PRODUCES DURABLE REMISSIONS IN PATIENTS WITH LOW GRADE AND MANTLE CELL LYMPHOMA

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The efficacy of autologous stem cell transplantation for patients with lymphoma is complicated by residual disease remaining in the patient despite the high dose therapy and the re-introduction of neoplastic cells with the autologous graft. We are conducting trials of rituximab used during stem cell mobilization and as a post transplant adjuvant in an attempt to overcome both of these obstacles. Patients with NHL received 375 mg/m^2 of rituximab day 1 of mobilization, followed by cyclophosphamide 2.5 gm/m^2 day 4, and either G-CSF or G-CSF and GM-CSF starting day 6 through subsequent stem cell collection. Later patients were CD34 selected if at least 5 X 10^6 CD 34 + cells/kg were collected. The preparative regimen consisted of either Cy/TBI or Bu/Cy. The first 25 patients received a single dose of rituximab 375 mg/m^2 given post-transplant 7 days after plts reach 20,000. Subsequent patient received GM-CSF post-transplant with four weekly doses of rituximab. One hundred and twelve patients (75M:37F), median age 52.5 (range 32-69)and 2 (range 1-7) prior therapies have started therapy. Diagnoses include 60 FCC, 24 mantle cell, and 18 SLL/CLL. At time of transplant, 37 patients were in CR, 72 in PR. Mobilization was successful in 89% of pts with a median 14.0 x 10^6 CD+ 34 cells/kg. The median day ANC > 1000 was 12 (7-24) and unsupported platelet > 20, 000 was 9 (3-663). The purging results measured by lymphoma colony forming units and PCR before and after CD34 selection are displayed in the table. The median follow-up is 2 years. Kaplan-Meier estimates of the three year overall and relapse free survival are 91.4% [82.8%, 95.8%] and 84% [70.4%, 91.7%]respectively. Notable toxicities include increased incidence of cytopenias (predominantly neutropenia) after engraftment and several late infections (aspergillus, atypical mycobacterium, pseudomonas). We conclude that rituximab used as an *in vivo* purging agent and post-transplant adjuvant is well tolerated and produces durable remissions in patients with low grade and mantle cell NHL. Evaluation of immune reconstitution and late infections is ongoing. This approach will be tested in a randomized phase III intergroup trial in patients with diffuse large cell lymphoma.