HCT-CI Comorbidities and their corresponding HCT-CI and CCI scores

Comorbidity	Prevalence: No. of pts (%)	HCT-CI score	CCI score
Hepatic (mild)	11 (13.8)	1	1
Cardiac	12 (15)	1	1
Cerebrovascular disease	3 (3.8)	1	1
Arrhythmia	7 (8.8)	1	0
Pulmonary (moderate)	9 (11.3)	2	1
Pulmonary (severe)	6 (7.5)	3	1
Rheumatologic	4 (5)	2	1
Diabetes	18 (22.5)	1	1
Inflammatory bowel disease	2 (2.5)	1	0
Renal dysfunction (moderate/severe)	1 (1.3)	2	2
Psychiatric disturbance	9 (11.3)	1	Not included
Infection	5 (6.3)	1	Not included
Obesity	9(11.3)	1	Not included
Peptic ulcer disease	0(0)	2	1
Hepatic (moderate/severe)	0(0)	3	3
Heart valve disease	0(0)	3	0

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ALLOANATIGENIC REACTIONS AFTER HEMATOPOIETIC CELL TRANSPLANTATION (HCT) INDUCE GENOMIC ALTERATIONS IN EPITHELIAL CELLS AS SHOWN IN HUMAN STUDIES AND IN AN IN VITRO MODEL

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We previously demonstrated frequent genomic alterations measured by microsatellite instability (MSI) in non-neoplastic epithelial tissues of pts who underwent allogeneic HCT (Blood 2006; 107:3389-3396). These genomic alterations were found only after allogeneic but not after autologous HCT, and therefore we hypothesized that an allogeneic effect is substantially involved in the mutation process. We extended our previous analyses by examining 210 bucall swabs obtained from 70 pts between day (d+) 26 and d+3514 after allogeneic HCT for the presence of MSI. MSI was found in the buccal smears of 38% allografted patients. In a prospective trial, in which pts were followed from time before HCT until d+365, 5 out of 14 (35%) pts exhibited MSI post-HCT although all showed stable microsatellites before transplantation. Statistical analyses in order to identify which clinical factors influence the presence of MS are in progress. To test the hypothesis that an alloantigenic effect is responsible for th induction of MSI, we developed a model system in which keratinocyte (HaCaT) cells were transfected with a plasmid vector which carries a G418 selectable marker and a microsatellite repeat (CA) that places the sequence for Hygromycin Resistance (HygR) out of frame for protein translation. DNA slippage mutations can restore the HygR reading frame and become detectable as HygR+ colonies. Pools of stably transfected HaCaT cells were treated with supernatant (SN) of major histocompatibility complex nonmatched mixed lymphocyte cultures (MLC) and assayed for HygR+ colonies 48h later. We found that HaCaT cells aquire hygromycin resistance after treatment with supernatatant from MLC. Treatment of cells with hydrogen hyperoxid which has been shown in a E. Coli system to induce MSI generated HygR+ colonies at a >80% lower frequency than the SN-MLC treatment. Control cells transfected with an in-frame hygromycin B gene construct (p12) were grown with high efficiency in the presence of hygromycin B. In summary, our in vivo data confirm our previous results and provide evidence of genomic alterations after allogeneic HCT and our in vitro data are compatible with the hypothesis that an alloantigenic factor is the driving force in producing detectable MSI in the allografted patients. Elucidating the ultimate mechanisms underlying the genomic instability following allogeneic HCT may prove to be of major therapeutic value.

LEUKEMIA

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QUANTIFYING THE SURVIVAL BENEFIT OF ALLOGENEIC STEM CELL TRANSPLANT IN THE MANAGEMENT OF RELAPSED ACUTE MYELOID LEUKEMIA

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Outcomes data comparing patients with relapsed acute myeloid leukemia (AML) who undergo transplant versus traditional chemotherapy alone are limited, due primarily to difficulty obtaining adequate patient sample sizes. To address these issues, a retrospective chart review was performed on all AML patients (n=600) treated at first relapse at MD Anderson Cancer Center from 1995 through 2004. Median age was 58 (range 15-85, 66% of patients >50), and poor risk cytogenetics (-5 or -7 deletions) were present in 23%. 139 (23%) patients achieved a second complete remission (CR2), 64 (11%) patients died during salvage chemotherapy, and 397 (66%) patients were resistant to therapy. Remission duration and overall survival were compared between patients in second remission who underwent allogeneic transplant and *only* those patients who did not undergo transplant because of patient preference or lack of a suitable donor.

Of the 102 patients who achieved a CR2 and were evaluated for tranplant, 72 (71%) underwent transplant and 30 (29%) did not. Twenty-one of the 30 patients not undergoing transplant declined the procedure or did not have a suitable donor. There was a statistically significant difference in remission duration favoring the transplant cohort (2-year actuarial relapse-free survival of 46% vs. 13%, p=0.007), and a trend toward overall survival benefit (2-year actuarial survival 44% vs. 23%, p=0.105). Differences is relapse-free and overall survival for patients >50 years old (n=24 patients transplanted vs. 14 patients not transplanted) were not statistically significant (2 year relapse-free survival 50% vs. 15%, p=0.373; 2-year overall survival 43% vs. 23%, p=0.832).

Of the 239 patients resistant to their first salvage regimen who underwent a transplant evaluation, 105 (44%) patients underwent allogeneic transplant while 71 (30%) patients did not because of lack of an available donor. A significant survival advantage was noted in the cohort of patients undergoing transplant (2-year actuarial survival 13% vs. 0%, p<0.001). This benefit was also observed in patients in the cohort who were >50 years old (2-year actuarial survival 12% vs. 0%, p<0.001).

Allogeneic transplant at the time of second remission or failed first salvage is a feasible strategy in many patients (30% of patients in this cohort). Given the large number of AML patients who will need salvage therapy, greater efforts should be made in identifying donors prior to the patient's first relapse.

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OUTCOMES FOR ALLOGENEIC TRANSPLANTATION IN IMATINIB-REFRACTORY CHRONIC MYELOID LEUKAEMIA (CML) ARE EQUIVALENT TO OUTCOMES IN IMATINIB-RESPONSIVE/IMATINIB-NAIVE CML AND CAN BE PREDICTED BY THE EBMT RISK SCORE

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Aims: To review the outcome of allogeneic stem cell transplantation (SCT) in imatinib refractory chronic myeloid leukaemia (CML).

Methods: Outcomes of all allogeneic transplants performed after