Because of that, it is important that the early-administration of steroid is considerable due to the clinical finding.

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ALLOGENEIC IMMUNOTHERAPY: AN EFFECTIVE TREATMENT FOR LUNG CANCER

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Therapeutic strategies for non-small cell lung carcinoma (NSCLC) include surgery, chemotherapy and radiation. Many NSCLC patients present with advanced disease that is not treatable by surgery or does not respond to chemotherapy or radiation treatment. An alternative therapeutic approach is the use of allogeneic hematopoietic stem cell transplantation (HSCT) that utilizes the responsiveness of a donor T lymphocyte graft to respond against histocompatibility antigens present on lung cancer cells. It has been shown that a beneficial graft-versus-tumor (GVT) response is associated with a major complication of HSCT, graft-versus-host disease (GVHD). Allogeneic HSCT has been utilized to treat a number of hematologic malignancies and recently selected epithelial solid tumors. The use of this procedure resulted in regression of renal cell carcinoma lung metastases and a case report demonstrated the elimination of NSCLC following HSCT. Given these findings, we utilized major histocompatibility antigen mismatched murine bone marrow transplantation (BMT) models and bioluminescence imaging to test the hypothesis that the allogeneic immune response that develops following allogeneic HSCT will be effective in controlling growth of lung cancer. Our results demonstrated that while GVHD did not develop following reduced intensity (RIC) conditioning and allogeneic donor lymphocyte infusion (DLI) 28 days after BMT, DLI failed to limit the growth of lung tumors. In contrast, when DLI was given after lethal myeloablative conditioning and BMT, a significant reduction in lung tumor growth was observed in the absence of GVHD. In line with a reduction in tumor growth, trafficking studies demonstrated that allogeneic donor cells migrated at an increased frequency to the lungs of myeloablated recipients compared to those conditioned with the RIC regimen. These studies demonstrate the potential efficacy of allogeneic immunotherapy and provide a model system to study alternative therapeutic options in the treatment of malignancies of the lung.

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GVHD FOLLOWED BY FULL MYELOID AND LYMPHOID DONOR CHIMERISM AFTER CADAVERIC LIVER TRANSPLANTATION

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Introduction: Using hematopoietic donor engraftment as a way to establish immune tolerance in solid organ transplantation remains an attractive but elusive goal. We report a case of orthotopic liver transplantation (OLT)-related aGVHD followed by full chimerism of highly HLA-mismatched myeloid and lymphoid donor cells.

Case report: A 58-year old male with HCV cirrhosis underwent OLT from a sex and blood type matched (O+) deceased donor. HLA typing of the donor and recipient demonstrated only one shared antigen on DRB1. On post-op day (POD) 42, profound pancytopenia developed. BM Bx showed aplastic anemia. On POD 62, the patient developed grade III skin aGVHD. Methylprednisolone (1 mg/kg) was added to tacrolimus. Infliximab (10 mg/kg) was given on POD 81 and 88. The rash and blood counts gradually improved. Immunosuppression and hematopoietic growth factors were tapered and blood and transfusion requirements decreased substantially. Molecular-based HLA typing of PB nucleated cells on POD 71 showed a major population of donor cells. VNTR/STR chimerism analysis at the D1S80 locus showed 100% donor type in BM (POD 98) and PB $CD3^+$ and $CD33^+$ compartments (POD 103). Skin GVHD resolved and counts remained stable with modest growth factor support and periodic transfusion of red cells and platelets.

Discussion: GHVD occurs in approximately 1% of OLT's and is a life-threatening complication. It is mediated by passenger lymphocytes across major HLA barriers and facilitated by permissive antigen sharing between donor and recipient. While donor chimerism of lymphoid cells is often seen in these cases, full hematopoietic engraftment has only been documented once. Our patient and donor shared a single class II HLA antigen. After complete suppression of host hematopoiesis, sustained donor lymphoid and myeloid engraftment occurred with minimal immunosuppression. This observation suggests the emergence of immune tolerance in the graft-versus-host direction across HLA barriers beyond a full haplotype. It also demonstrates the existence of hematopoietic progenitors in a liver graft capable of reconstituting in an adult patient.

PHARMACY

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EFFECT OF NEBULIZED DORNASE ALFA ON PULMONARY GAS EXCHANGE IN CRITICALLY ILL STEM CELL TRANSPLANT RECIPIENTS

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Introduction: Dornase alfa (DA), a recombinant human deoxyribonuclease, is used in non-cystic fibrosis patients primarily for its mucolytic properties. The objective of this study was to examine the effect of DA on gas exchange in critically ill adult cancer patients with tenacious pulmonary secretions or atelectasis.

Methods: Following IRB approval, medical records of ICU patients who received nebulized DA for > 72 hrs between 1/1/05 and 10/1/08 were retrospectively studied, including a subset analysis of stem cell transplant (SCT) patients. The PaO_2, FiO_2, and PaO_2/FiO_2 (PF) ratio at baseline, 24 hrs, and 48 hrs post-DA administration were analyzed using the paired t-test and the Wilcoxon sign rank test. P-values < 0.05 were considered statistically significant, while an improvement in PF ratio by 50% or to a value of 100 above baseline were considered clinically significant.

Results: During the six-month study period, 109 critically-ill adult patients underwent treatment with DA, of which 9 (8%) were SCT recipients. Six patients received allogeneic transplants and 3 received autologous transplants. Sixty-seven percent of SCT recipients had radiographic evidence of pulmonary infiltrates and 33% had pulmonary collapse. All nine patients were mechanically ventilated. No statistically significant results were observed in SCT recipients with regards to change in PF ratio or FiO_2 from baseline to 24 or 48 hrs (see Table). The PF ratio increased by 50% above baseline in 22.2% and 33.3% of SCT recipients at 24 hrs and 48 hrs, respectively. The PF ratio increased to a value of 100 above baseline in one SCT recipient (11.1%) at 24 hrs and 48 hrs.

Conclusion: No statistically or clinically significant pulmonary gas exchange benefits were seen in SCT recipients who were treated with DA when used as a mucolytic agent. Further research is needed to establish if DA may be a viable treatment option in critically ill adult SCT patients.

Gas Exchange Outcomes in Criticall Ill Stem Cell Transplant Recipients who Received Nebulized Dornase Alfa

	Mean PF ratio	95% CI (p-value vs baseline)	Mean FiO2	95% CI (p-value vs baseline)
Baseline	235.8	147.5 - 324.0	0.54	0.33 - 0.76
24 hour	252.8	166.5 - 339.1 (p = 0.6461)	0.53	0.36 - 0.71 (p = 0.9060)
48 hour	251.9	165.9 - 338.9 (p = 0.6725)	0.45	0.34 - 0.56 (p = 0.2610)