derlying disease (Mb. Gaucher). Donor examination prior to donation was as follows: hemoglobin level 110 g/L, platelet 148 × $10^9$/L, WBC in normal range. Bone MR revealed typical changes for Gaucher disease. Beta glucosidase level was low ( 2.4 nmol/h/mg of protein) and chitotriosidase very high (60000 nmol/h/ml of plasma). There were no other signs of other diseases and we decided to proceed with HSCT. Patients were conditioned with a standard Bu + Cy regimen followed by graft versus host disease (GVHD) prevention with a combination of CSP + MTX. Marrow harvesting was complicated due to the lacking to collect sufficient number of cells and two leukaphereses were performed. After hematopoietic stem cell infusion recovery was successful and the patient was discharged form the hospital on day +35. There were no signs of acute or chronic GVHD. Complete chimerism was obtained from marrow and blood. There were no signs of Gaucher disease in bone marrow. Donor ERT was started immediately after hematopoietic stem cell donation. Recipient ERT was started 3 months after hematopoietic stem cell infusion. There were no signs of Gaucher disease in the recipient. Due to administrative reasons ERT was stopped after 2 years of treatment. Recent examinations showed that the recipient started to develop signs of Gaucher disease. ERT was introduced again in the recipient. **Conclusions:** This case report shows that hematopoietic stem cells of a donor with Gaucher disease can be successfully transplanted. Harvesting could be complicated due to the insufficient number of collected cells. Enzyme replacement therapy (ERT) can prevent the development of Gaucher disease in the recipient transplanted with Gaucher marrow.

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### DONOR SPECIFIC TRANSFUSION AND EITHER METHOTREXATE OR CD154-BLOCKADE BEFORE TRANSPLANT IMPROVES RATES OF SUSTAINED ENGRAFTMENT IN DOGS CONDITIONED WITH 100 CGY TOTAL BODY IRRADIATION

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**Introduction:** Stable mixed chimerism can be established in dogs given a sublethal dose of 200 cGy total body irradiation (TBI) before and immunosuppression with mycophenolate mofetil (MMF) or rapamycin combined with cyclosporine (CSP) after marrow transplantation. When the TBI dose is reduced to 100 cGy, only transient engraftment is observed (11 of 11 dogs rejected their grafts). Here we asked whether stable engraftment after 100 cGy TBI could be accomplished by reducing host immune responsiveness using either the antimetabolite methotrexate (MTX) or an anti-CD154 antibody, which blocks the CD40-CD154 T-cell costimulatory pathway in conjunction with infusions of donor peripheral blood mononuclear cells (PBMC). **Methods:** One group of recipients was given iv infusions of $5 \times 10^6$ PBMC/kg from their intended DLA-identical littermate marrow donors on days −5 and −3 followed by 0.4 mg/kg MTX on days −4 and −2 (group 1). A second group received a single iv injection of 5 mg/kg anti-CD154 antibody (day −5) followed one day later by donor PBMC (combined iv/sc injections of $10^7$ PBMC/kg) (group 2). Antibody dosing was based on studies of suppression of mixed leucocyte culture reactivity in vitro and in vivo pharmacokinetics. 100 cGy TBI (delivered at 7 cGy/min) was given to all dogs on day 0 followed by infusion of a median of $3.46 \times 10^8$ marrow cells/kg. Postgrafting immunosuppression consisted of MMF (10 mg/kg, BID, days 0 to 28) and CSP (15 mg/kg BID, days −1 to 35) in all dogs. **Results:** All six dogs in group 1 showed initial engraftment. Two of the six showed sustained engraftment while 4 dogs rejected their grafts at weeks 5, 8 and 10, respectively, and survived with autologous recovery. Five of six dogs in group 2 were evaluable, while one dog was too early to be evaluated. All five evaluable dogs had initial engraftment. Three of the five dogs continued to show stable mixed donor/host hematopoietic chimerism, one for >16 weeks and two for >26 weeks. Two dogs rejected their grafts, 9 and 12 weeks after transplantation, respectively, and recovered autologous hematopoiesis. **Conclusions:** Donor PBMC infusions and pretransplant host immunosuppression with either MTX or anti-CD154 antibody were partially effective in assuring sustained engraftment of DLA-identical marrow after non-myeloablative conditioning with 100 cGy TBI combined with MMF and CSP.

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### SUCCESSFUL USE OF AN ANTI-TUMOR NECROSIS FACTOR-ALPHA (TNF-α) MONOCLONAL ANTIBODY (INFLIXIMAB) FOR THE TREATMENT OF CYTOMEGALOVIRUS (CMV)–INDUCED PNEUMONITIS AFTER ALLOGENEIC HAEMOPOIETIC STEM CELL TRANSPLANTATION (Allo-HSCT)

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Several pro-inflammatory cytokines have been shown to play a fundamental role in the genesis and perpetuation of adaptive immune responses. Recent investigations into the biological relevance of such cytokines in systemic inflammatory responses have demonstrated a protective role for them during the early phase of infection. However, the activity of inflammatory cytokines after the pathogenic challenge has been resolved has also been shown to represent a deleterious, often lethal, role in which unspecific inflammatory reactions (but not the infectious agent) overwhelm the body. Recently, a monoclonal antibody capable of blocking the effects of TNF-α (infliximab) has been proven capable of modulating systemic inflammatory responses. Here we describe the successful treatment of adult respiratory distress syndrome caused by CMV with infliximab in a recipient of allo-HSCT. The patient involved was a 35 year old male that received an HLA-compatible unrelated peripheral blood HSCT for chronic myelogenous leukemia in June 2001. The patient was subjected to myeloablative conditioning (fractionated total body irradiation + cyclophosphamide) and received cyclosporin A and methotrexate for GvHD prophylaxis. On day +34 the patient complained of chest pain and developed dyspnea, fever and chills; CT scan revealed the presence of bilateral diffuse micronodular interstitial infiltrates. Lung biopsy and culture demonstrated the presence of inclusion bodies suggestive of CMV infection while the presence of other bacterial, viral and fungal agents was ruled out. Qualitative CMV-specific PCR subsequently confirmed the diagnosis at titers of 313.8 pg/mL. The patient received IV immunoglobulins + ganciclovir therapy and supportive care. By day +45 the patient continued with fever and showed worsening lung edema (became polypneic, attained less than 75% blood-oxygen saturations in spite of non-invasive mechanical ventilatory support and developed hypoxic encephalopathy). On day +48 the patient received the first of two 200 mg doses of infliximab. By day +50 the patient was feverless, had less dyspnea and achieved blood oxygen saturations above 90% at ambient air and without mechanical ventilatory support. Both physical examination and chest x-rays revealed a dramatic clinical improvement by day +53. Here we discuss a therapeutical role for TNF-α blocking monoclonal antibody (infliximab) in the management of post-infectious pathogen-induced systemic inflammatory responses.

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### ALLOTRANSPLANTATION WITH REDUCED INTENSITY CONDITIONING THAT INCLUDES ALEMTUZUMAB LESSENS TRANSPLANT-RELATED MORTALITY AND INCIDENCE OF RELAPSE IN PATIENTS WITH HIGH-RISK MYELOID DISEASES

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Patients with high risk myeloid disease can be transplanted with reduced intensity conditioning regimens that maximize remission duration while minimizing transplant-related mortality. Incidence of survival, relapse, tempo of engraftment and incidence of grades I-II and III-IV acute GVHD were evaluated. Three conditioning regimens have been utilized: fludarabine 30 mg/m$^2$ × 5 days, melphalan 140 mg/m$^2$ × 1 day in all groups and alemtuzumab 20 mg/d × 5 days (group 1), × 3 days (group 2) and × 2 days (group 3). Fifteen patients (median age 48, range 24-58 years) were in the study. Twelve patients had AML, two had CML and one had MDS. Six patients were in CR at time of transplant and nine had relapsed or refractory disease. Patients were consecutively assigned to group 1 (seven patients), group 2 (five patients) and group 3