between 2001-2009, with a secondary analysis limited to AML and ALL patients receiving myeloablative conditioning extending from 1995 to 2009, prior to availability of novel antifungal agents, and the emergence of PBSC allografts. Patients with pre-transplant IFI were older, have lower performance status, have advanced disease, carry the diagnosis of AML, receive a cord blood transplant, receive RT, receive mold-active fungal prophylaxis and be transplanted more recently. Aspergillus and Candida infections were the most commonly identified pre-transplant IFI and 68% of patients presented with pulmonary involvement. Univariable outcomes analysis reveals lower 1-year, 3-year, and 5-year DFS and OS for patients with pre-transplant IFI (Table 1). Relapses were higher in this cohort and there was a trend to increased TRM. The probability of post-transplant fungal infection was 24% for the study group and 17% for the control group (p < 0.001). Interestingly, cause of death was associated with a greater likelihood of having recurrent/persistent disease. Infectious mortality causes were only slightly increased (13 vs 9%) between the study group and the control group. With regard to the 2nd analysis comparing patients with pre-transplant IFI diagnosed between 1995-2000 vs 2001-2009, TRM @ 1, 3, 5 yrs was significantly higher with associated reduction in OS and DFS for the early cohort. However, there were no observable differences in IFI post-transplant and in relapse rates.

**Conclusions:** Documentation of pre-HSCT IFI is associated with lower DFS and OS after allogeneic HSCT. However, mortality is most influenced by patients with more advanced disease status than infectious etiologies. Treated pre-transplant IFI does not appear to be a contraindication to allogeneic HSCT.

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**Human Herpesvirus-6 (HHV-6) Viremia Is Frequent but the Incidence of Encephalitis Is Low in Double-Unit Cord Blood Transplantation (CBT) Recipients Transplanted without ATG**

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**Background:** While CBT is a known risk factor for HHV-6 reactivation, the level of viremia associated with a high risk of HHV-6 encephalitis is not established and the association with CBT outcomes is controversial.

**Methods:** We analyzed the nature of HHV-6 reactivation in 125 double-unit CB recipients who were transplanted for hematologic malignancies from 2006-3/2012. Viremia was measured by quantitative PCR of plasma HHV-6 DNA (lower detection limit 100 DNA copies/ml).

**Results:** Of 125 patients (median age 42 years, range 1-69), 93 (74%) received myeloablative and 32 (26%) received non-myeloablative conditioning followed by 4/6 HLA-A,B,H antigens, -DRB1 allele matched CBT for the treatment of AML (n = 43, 34%), ALL (n = 24, 19%), MDS/ CML/ other leukemia (n = 12, 10%), or lymphoma/ CLL (n = 46, 37%). No patient received anti-thymocyte globulin (ATG). One-hundred and seventeen (94%) patients reactivated HHV-6 (median peak 7,600 copies/ml, range 100-160,000) at a median of 20 days (range 10-59). The median time to peak viremia was 23 days (range 12-62) and the median viremia duration was 8 days (range 1-60 days). Fifty-one patients (41% of total, 44% of viremic patients) developed HHV-6 > 10,000 copies/ml (median peak 31,200 copies/ml at 20 days, range 12-57). Only 6 patients (5% of total, 5% of viremic patients) had HHV-6 > 100,000 copies/ml (median peak 130,000 copies/ml at 19 days, range 14-29). HHV-6 encephalitis occurred in 2 patients (1.6%, peak viremias 13,000, 118,000, respectively); 1 died from encephalitis and the other recovered with therapy. Four other viremic patients had HHV-6 isolated from bronchoalveolar lavage but did not meet criteria for HHV-6 pneumonia. Defining high level viremia as > 10,000 copies/ml in days 14-60, viremia was not associated with diagnosis or conditioning, engrafting unit-recipient HLA-match or TNC, CD34+ cell doses. Treating viremia as a time-dependent covariate in Cox regression analysis, no association was found between viremia and neutrophil or platelet engraftment. There was also no association between viremia and CMV reactivation, day 100 grade II-IV aGVHD, day 100 TRM, relapse, or overall survival. If high level viremia was defined as > 25,000 copies/ml (n = 31, the highest peak viremia quartile days 14-60), no associations with CBT outcomes were detected. Finally, 24 patients had a second viremia (median onset day 49, range 100-2730) without obvious sequelae.

**Conclusions:** Nearly all our CBT recipients reactivate HHV-6. While the incidence of end-organ disease is low, possibly due to our exclusion of ATG from the conditioning, our understanding of the significance of HHV-6 viremia is incomplete. We are currently evaluating anti-viral treatment responses, and ultimately a prospective trial is needed to better define the causality between HHV-6 viremia and transplantation outcomes, and to investigate the risk-benefits of pre-emptive therapy.

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**High Dose Therapy Improves Survival in Systemic Light Chain Amyloidosis**

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**Background:** Treatment remains a challenge for systemic light chain amyloidosis (AL). Autologous stem cell transplant (AutoSCT) has been associated with long term survival. However, a recent multicenter randomized study failed to show survival benefit for AutoSCT perhaps due to high non-relapse mortality (NRM). Here we present a comparison of AutoSCT to other conventional therapies in AL patients treated at our institution with a 14-year follow up.

**Methods:** A total of 2018 cases were identified upon pathology review from 1998-2012. AL was confirmed in 264 patients; primary amyloidosis (PA) in 147 pts and multiple myeloma with amyloidosis (AM) in 110 patients; solitary
amyloidoma in 7 patients. AutoSCT was performed in 126 patients (PA=79 and AM=47).

Results: The day 100 NRM was 5% and 1-year NRM was 8%. With a follow up of 14 years in surviving patients, the 10-year overall survival (OS) of AL patients was significantly better in those undergoing AutoSCT (41% vs. 17%; p<0.0001; Figure 1). Involvement of more than one organ (6-yr OS 36% vs. 55%; p=0.04) and cardiac involvement (2-yr OS of 57% vs. 78%; p=0.01) were associated with poor outcome. In the patients undergoing AutoSCT: PA vs. AM, Mayo staging, Boston University (BU) staging or bone marrow plasma cells >10% at the time of autoSCT did not have an impact on OS. Cardiac biomarkers including NT-ProBNP and Troponin-I and T levels were available in a limited number of patients and were not analyzed for survival outcomes. In multivariate analysis, superior OS was associated with: age <60yrs (HR 2.1, p=0.022); and induction treatment before AutoSCT (HR 2.7, p=0.02). Involvement of kidney as the only end organ showed a trend toward improved survival (HR 1.6, p=0.06). Specifically for PA patients (n=79); treatment before autoSCT was associated with improved 3-yr OS: 85% vs. 66%; p=0.02.

Figure 1. OS: AutoSCT vs. Conventional Therapy in AL Amyloidosis patients.

Conclusions: AL patients should be evaluated for AutoSCT and selected patients should undergo induction therapy to decrease amyloid burden prior to AutoSCT.

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Are Outcomes After Myeloablative Conditioning Regimen in Double Cord Blood Transplantation (UCBT) Better Than Single UCBT for Adults with Acute Leukemia in Remission?

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Allogeneic hematopoietic stem cell transplantation (HSCT) is indicated for patients (pts) with acute leukemia (AL). For adults requiring HSCT urgently, such as pts in first complete remission (CR1), UCBT is a valid stem cells source. With the aim to compare single vs double UCBT after MAC we analyzed 239 adults with AL in CR1. Pts were transplanted with sUCBT (n=156) or dUCBT (n=83) from 2005-2011 in EBMT centers for ALL (n=101) and AML (n=138). Type of MAC was statistically associated with outcomes therefore pts were analyzed in 3 different groups: Group 1: pts receiving sUCBT with TBI-based-Cy (+Flu) (n=68) (performed in 42 transplant centers (TC)), Group 2: pts receiving sUCBT with Bu+Flu+Thiotepa (n=88) (performed in 23 TC) and Group 3: pts receiving dUCBT with Cy+TBI+Flu (n=83) (performed in 47 TC). Median follow-up: 24 months. No statistical differences were found among the 3 groups for pts and disease characteristics however pts in group2 were older than in group1 and 3 (p=0.03).

Median infused TNC was 2.9x10^8/kg for group1, 3x10^7/kg for group2, and 3.7x10^7/kg for group3 (p=0.01). ATG was part of conditioning regimen in 73% of pts. The use of ATG was different in the 3 groups (70%, 90% and 40% for group1, 2 and 3, respectively p<0.001).

For group1, group2 and group3, cumulative incidence (CI) of 60 days neutrophil recovery was 82%, 89% and 87% (p=0.15), with median time of 27, 21 and 24 days, respectively (p<0.001).

CI of acute GVHD (grade II-IV) was 30% vs 20% vs 45% for group1, group2 and group3, respectively (p=0.001). CI of chronic GVHD at 1 year was 29%, no differences in CI among the groups.

At 1 year, CI of TRM was 44% for group1, 33% for group2 and 36% for group3 (p=0.46). In multivariate analysis, two factors were associated with higher TRM: diagnosis of ALL (p=0.048) and age>35 years (p=0.049). One-Hundred-six six pts died and causes of death were infection (n=38), GVHD (n=18), other transplant-related-events (n=31) or relapse (n=18).

CI of 2y relapse was 25% for group1, 18% for group2 and 16% for group3 (p=0.22). No factors were found associated with increase relapse incidence in multivariate analysis. The 2y probability of leukemia-free-survival (LFS) was 31% for group1 (sUCBT-TBI based), 48% for group2 (sUCBT-BuFluTT), and 47% for group3 (dUCBT) (p=0.03). No center effect was found. In multivariate analysis, use of sUCBT using TBI based MAC (HR=0.9, p=0.003), diagnosis of ALL (HR=0.69, p=0.04) and age>35years (HR=1.4, p=0.04) were independently associated with decreased LFS.

In this registry based analysis, in the myeloablative setting for adults with AL in CR1, outcomes (TRM, RI and LFS) after dUCBT were not statistically different from sUCBT using iv-BuFluTT. However, compared to sUCBT using TBI-based MAC, dUCBT was associated with lower RI and better LFS rates.

In the MAC setting, the combination of conditioning regimens and type of graft (single vs. double) may have different impact UCBT outcomes.