Jian-Jian Luan Award

CMV-replication after allogeneic stem cell transplantation is associated with a GvHD-independent reduced relapse risk in lymphoma: evidence for a putative virus-versus-lymphoma effect
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We have previously showed that a CMV-reactivation after HSCT is associated with a reduced risk for leukemic relapse in pts with AML. Further, Erlach et al showed in a lymphoma mice transplant model that coinfection with mCMV induced a strong anti-lymphoma effect by induction of apoptosis in lymphoma cells, which consecutively improved OS in mice.

This prompted us to investigate the influence of replicative CMV infection in 94 (median age 45, 18 – 70) pts with lymphoma, who received transplants from unrelated (n=67, 71%) or related (n=27, 29%) donors. Pts were transplanted from HLA-ident. (n=74), HLA-MM (n=16) or HLA-haploident. SIB (n=4). 13 pts (14%) were transplanted for indolent lymphoma (FL n=11, CLL n=2), 67 pts (79%) for aggressive lymphoma (B-lineage n=35, T-lineage n=27, transformed n=5), 11 pts (12%) for MCL and 3 pts (3%) for HD. The disease status of pts at HSCT was CR in 20 pts, PR in 40 pts, refractory in 30 pts and untested in 2 pts. 55 pts (59%) received previous autograft and 82 pts (87%) were treated prior to transplant with at least 3 chemotherapy lines. The HCT-CI were 0-2 in 76 pts (81%) and 3+ in 18 pts (19%). Myeloablative conditioning was applied in 60 pts (64%) while 34 pts (36%) received RIC. 68% of pts (n=48) were at risk for CMV reactivation. CMV replication as detected by pp65 antigenemia assay occurred in 34 pts (36%).

Taking all competitive risks into account, the cumulative incidence of PFS at 5 yrs after HSCT was 62 % (95 % CL: 31 – 45) in pts without as compared to 80 % (95 % CL: 9 – 31) in pts with pp65 antigenemia (p<0.018). In multivariate analysis including all effecting factors, CMV replicative status was confirmed as a strong independent predictor of PFS (HR: 0.29, 95 % CL: 0.08 – 1.00, p<0.049) together with chronic GvHD (HR: 0.32, 95 % CL: 0.13 - 0.80, p<0.016), and chemorefractory (HR: 3.3, 95 % CL: 1.28 - 8.4, p<0.015). The anti-lymphoma effect was detectable across all lymphoma subsets and was most pronounced in pts with CMV-R. vs 51% without, n.s., and 39% vs 35%, n.s, respectively), whereas 5-yr NRM was higher in group with CMV-repl. (42% vs 23%,p=0.05).

This is the first report which demonstrates a strong and GVHD-independent effect of CMV replication on the PFS in pts with lymphoma, which deserves further prospective studies.