achieved in 81.2% (13/16) of responders, and occurred a median 10 (2-34.7) months after ECP. Nine cases (56.2%) had recurrent cGvHD at 8.4 (3-19.3) months after achieving response and 1 (6.25%) had late primary disease relapse (>6 months after ECP initiation). Another non-responder had a late relapse. Factors associated with OR were younger age at cGvHD diagnosis and at ECP initiation (<50 years, P=0.046), while that with CR was early initiation of ECP within 18 months of cGvHD diagnosis (P=0.018). The 1-year, 2-year and 3-year post ECP initiation survival rates were 66.7%, 38.1% and 23.8%. Types of cGvHD onset and donor were associated with survival post ECP initiation (P=0.028 and P=0.05). The patients with non-progressive onset cGvHD and with HLA-MRD survived longer (1-year post ECP initiation survival rates of 88.9% and 78.6%) than those with progressive onset cGvHD and with HLA-MUD (50% and 33.3%). However, OR and CR to ECP were not associated with prolonged post ECP initiation survival. In summary, our results suggest that ECP is an effective second-line treatment option for cGvHD especially with early initiation. Progressive onset cGvHD and HLA-MUD were associated with poor survival rates in patients receiving ECP for cGvHD. Whether response to ECP would be translated to higher survival requires a larger study.

Table

Characteristics	Details
Sex: male/female (n/n)	**9/12**
Median age (median, range)	
-- At day 0	**42.6 (26.5-60.1) years**
-- At cGvHD diagnosis	**42.8 (26.8-60.4) years**
-- At ECP initiation	**43.4 (28-60.4) years**
Type: HLA-MRD/-MUD/-mismatched unrelated CBD (n)	**14/6/1**
GvHD Prophylaxis (n)	
-- Calcineurin inhibitor and methotrexate	**18**
-- Calcineurin inhibitor and methylprednisolone	**2**
-- Triple regimen	**1**
Acute GvHD (n)	**19**
-- Clinical Grade: I/II/III/IV	**5/12/1/1**
-- ECP for aGvHD	**1**
Chronic GvHD (n)	**21**
-- Onset: *De novo*/Progressive/Recurrent (n)	**1/13/7**
-- CIBMTR Overall Severity at ECP initiation (n)	
.....Mild	**2**
.....Moderate	**11**
.....Severe	**8**
-- Maximum Grade (n)	
.....Limited	**3**
.....Extensive	**18**
-- Median duration of ECP (median, range)	**10.8 (1.3-58.8) months**
-- Median follow-up time after ECP initiation (median,range)	**15.5 (1.3-62.4) months**
-- Overall and complete response to ECP by CIBMTR Severity	
.....Mild (n (%))	**1 (50%), 1 (50%)**
.....Moderate (n (%))	**5 (45.4%), 4 (36.4%)**
.....Severe (n (%))	**5 (62.5%), 3 (37.5%)**

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INTERACTION BETWEEN HOST NATURAL KILLER T CELLS AND DONOR $CD4^+CD25^+$ T_{REG} CELLS PROTECTS AGAINST GVHD AFTER TLI/ATS HOST CONDITIONING AND ALLOGENEIC BONE MARROW TRANSPLANTATION

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The murine non-myeloablative regimen of total lymphoid irradiation (TLI) and anti-thymocyte serum (ATS) prevents acute graft-versus host disease (aGVHD) and was recently successfully applied for human hematolymphoid malignancies (Lowsky et al, NEJM, 2005). To investigate GVHD protection, we transplanted (BMT) 50×10^6 bone marrow cells and 60×10^6 splenocytes from wild-type (WT), $CD4^{-/-}$, IL-$4^{-/-}$, or IL-$10^{-/-}$ C57BL/6 (H-2^b) donor mice into wild-type (WT) or natural killer (NK) T cell deficient J$\alpha18^{-/-}$ BALB/c (H-2^d) hosts following TLI/ATS. Controls were WT BALB/c mice given 800cGy total body irradiation (TBI) and ATS with BMT from WT C57BL/6 donors. TBI/ATS-conditioned WT hosts given BMT from WT donors and TLI/ATS conditioned WT hosts given BMT from $CD4^{-/-}$, IL-$4^{-/-}$, or IL-$10^{-/-}$ donors developed aGVHD, with marked donor $CD8^+$ T cell accumulation in liver, mesenteric lymph nodes (MLN), and colon at day 6. Since GVHD protection depends on donor $CD4^+$ cells, IL-4, and IL-10, we investigated the role of donor $CD4^+$ T_{regs} in GVHD protection. TLI/ATS-conditioned WT hosts given BMT from WT donors survived without aGVHD and demonstrated a dramatic ($p< 0.01$) ten-fold increase in the absolute number of donor $CD4^+CD25^+Foxp3^+$ T_{regs} in the spleen at day 6 after BMT relative to TBI/ATS-conditioned WT hosts or TLI/ATS-conditioned J$\alpha18^{-/-}$ hosts that succumbed to aGVHD. These $CD4^+CD25^+Foxp3^+$ T_{regs} secreted IL-4 and IL-10 and had the GVHD suppression capacity of conventional $CD4^+CD25^+$ T_{regs}. Pre-transplant adoptive transfer of sorted WT host invariant NK T cells protected TLI/ATS-conditioned J$\alpha18^{-/-}$ hosts from day 6 donor $CD8^+$ T cell accumulation and caused a significant ($p < 0.01$) increase in the absolute number of donor $CD4^+CD25^+Foxp3^+$ T_{regs}. Using congenic markers (CD45.1/CD45.2), we found that these $CD4^+$ T_{regs} arise from donor splenic (peripheral) T cells after BMT. CD25 depletion of WT donor cells before BMT into TLI/ATS-conditioned WT hosts or into TLI/ATS-conditioned J$\alpha18^{-/-}$ hosts given adoptive transfer of WT host NK T cells resulted in loss of the donor $CD4^+CD25^+Foxp3^+$ T_{regs} subsets in the spleen, and significantly increased day 6 donor $CD8^+$ T cell accumulation in the host liver, MLN, and colon, accompanied by lethal aGVHD. These studies show that host invariant NK T cells are critical for GVHD protection and that they can facilitate the expansion of donor $CD4^+CD25^+Foxp3^+$ T_{regs}, which protect TLI/ATS treated hosts from lethal GVHD after allogeneic BMT.

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IN VIVO ACTIVATION OF APCS WITH TLR LIGANDS AND TISSUE DAMAGE RATHER THAN AMOUNT OF HOST APCS ARE CRITICAL FACTORS THAT DETERMINE DLI-MEDIATED GVL REACTIVITY AND GVHD IN MHC-MATCHED MINOR HISTOCOMPATIBILITY ANTIGEN (MHAG)-MISMATCHED CHIMERAS

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We recently found that residual host $CD11c^+$ DCs persist in the skin of MHC-matched chimeras after myeloablative conditioning and transplantation of T cell-repleted BM, and that those residual host APCs are insufficient for the induction of optimal DLI-mediated alloreactivity (J Immunol.,2006). Since the latter observation in established C3H.SW→B6 chimeras differs from the current paradigm in freshly irradiated MHC-matched chimeras, we hypothesized that in established chimeras, beside host APCs and donor T cells, the induction of DLI-mediated GVL reactivity and GVHD requires two additional factors: (a) TLR-mediated activation of APCs and (b) tissue damage. *In vivo* coadministration