GVHD grading but were included for the other analyses. Initial treatment included beginning or increasing systemic steroids (69%), continuing calcineurin inhibitors (64%) or beginning topical treatment (52%). Additional treatment was added within the first 28 days for 31% patients. Median lines of treatment for the total duration of follow-up were 1 (range 0–4).

Of the evaluable patients, 63/85 and 56/66 had a clinical response (CR/PK) at 28 days and at 180 days respectively. 36% developed recurrence of LA GVHD after a documented CR. 26% developed chronic GVHD after LA GVHD at a median of 169 (range 25–383) days after diagnosis of LA GVHD. Median number of hospital days in the first 6 months after the diagnosis of LA GVHD was 15 (range 1–120) days. 25% had discontinued immunosuppressive therapy (IST) at the time of last follow-up with the median duration of IST being 12.8 (range 6.1–24.7) months after HCT. 9% relapsed and 22% died with the main causes of death being GVHD, infection or multi organ failure. Median failure free survival (FFS) as defined by absence of relapse, death, addition of new IST or development of chronic GVHD was 3.6 months (95% CI: 1.7–6.8) (Figure). Median overall survival (OS) was 25.3 months. No patient/transplant or GVHD related factors emerged as significant predictors for FFS or OS in univariate analysis.

Conclusions: The overall incidence of LA GVHD is low, but it is associated with prolonged immunosuppression, poor failure free and overall survival.

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Phase II Clinical Trial of Etanercept Plus Extracorporeal Photopheresis GVHD Prophylaxis Following Unrelated Donor Reduced Intensity Transplant
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Introduction: Reduced intensity conditioning (RIC) regimens decrease early toxicity after allogeneic hematopoietic cell transplant (HCT), but their ultimate success depends on establishing a graft-versus-tumor effect (GVT). Because graft-versus-host disease (GVHD) and GVT are tightly linked, complete elimination of GVHD may lead to an unintended increased relapse risk in a RIC setting. Therefore, we tested a novel GVHD prophylaxis regimen intended to preserve GVT but minimize GVHD mortality.

Methods: 48 patients undergoing RIC unrelated donor transplant (URD HCT) enrolled from 2009-2012 on a phase II trial that added etanercept and extracorporeal photopheresis (ECP) to a standard GVHD prophylaxis of tacrolimus and mycophenolate mofetil (MMF). The preferred RIC was fludarabine 160 mg/m2 + busulfan 6.4–12.8 mg/kg +/- TBI 200 cGy. GVHD prophylaxis consisted of overlapping agents as follows: Tacrolimus from d-3 to d56 (then tapered over 4 months in the absence of acute GVHD), MMF d0-28, etanercept 25 mg subcutaneously 2x weekly from d0-56 (16 doses), and ECP beginning on d28. ECP was given once weekly from d28-70, then every other week until d100, then monthly until d180 for a total of 12 treatments. Donors were required to match to recipients for 7–8/8 HLA loci.

Results: The median age of the study patients was 60 yr (18–71). Donors were 7/8 (n=14, 29%) or 8/8 (n=34, 71%) matched. Patients engrafted at a median of 12d (8–26d). The 12mo post-HCT end points for the entire study cohort were as follows: overall survival 73% (95% CI 61–87) (Figure 1A), non-relapse mortality (NRM) 21% (9–32), and relapse of 19% (8–30). The cumulative incidence of grade II-IV acute GVHD at d100 and 6mo was 46% (32–60) and 57% (42–71) respectively, and for grade III-IV acute GVHD was 17% (6–27) and 19% (8–30). In an exploratory analysis (Figure 1B), GVHD that developed after 8 doses of etanercept and at least one ECP treatment (d28) was significantly less lethal than GVHD that developed before ECP began (6mo NRM 11% vs 40%, 12 mo 21% vs 50%; p=0.04), which suggests that ECP prophylaxis may ameliorate GVHD lethality. The possible benefit of prophylactic ECP on GVHD outcomes does not appear to be related to delayed GVHD onset as NRM did not differ in control patients diagnosed before or after d28. In 69 contemporaneous control patients with grade 2-4 GVHD, 6mo and 12 mo NRM was 32% and 39% respectively, and there was no difference between patients that developed GVHD after or before d28 (6mo 27% vs 36%, 12mo 33% vs 44%; p=0.57).

Conclusions: Six month (83%) and 1yr survival (73%) was excellent in older, frequently mismatched URD HCT patients, even though GVHD incidence was not lowered. An exploratory analysis suggested that if prophylactic ECP has benefit, the effect is confined to patients who start ECP before GVHD develops. Strategies focusing on earlier delivery of ECP to URD HCT patients could be explored in future studies.

Figure 1.