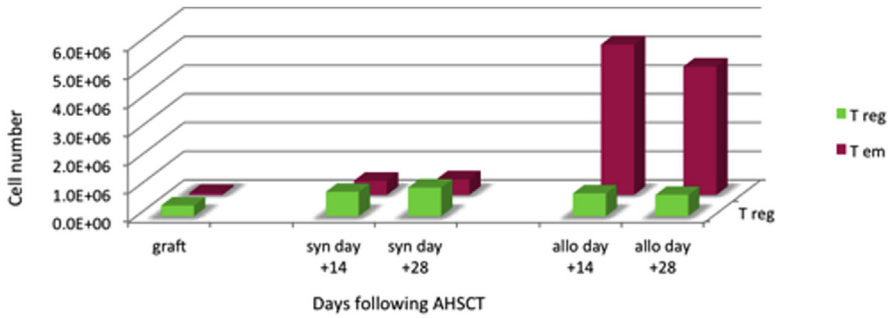

Figure 1. Total number of CD4+ Treg and Tem cells in the syngeneic vs. allogeneic recipients. Shown are total number of CD4+ Treg and Tem cells in the graft (day 0), and at subsequent time points following AHSCT for syngeneic (syn) recipients, identical host recipient pairs; and allogeneic (allo) recipients, with minor antigen mismatch between host and donor with resultant cGVHD induction. Day+14 is a time point early post AHSCT, while day +28 represents well-established cGVHD.

higher than the number present in the graft, but distributed to target rather than non-target tissues. Target sites of cGVHD (skin, gut and liver) had several fold greater number of Tem cells compared to controls both early and late in disease. The number of Tem cells in target sites was maintained as cGVHD progressed, and the Treg to Tem ratio in target tissues was significantly lower than that of the controls at all times. Cell division of Tem and Treg cells was high in the liver, and remained high for the Treg cells as disease progressed. Meanwhile, Treg cells underwent faster loss from the liver, likely due to cell death given that the total number of Treg cells did not change. Our findings shed light on *in vivo* behavior of Treg and Tem cells, T cell subtypes critical to the biology of cGVHD. Furthermore, our methodology will be translated to investigate *in vivo* T cell kinetics in patients undergoing AHSCT as deuterated water labeling is safe, not toxic and non-radioactive.

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Predictive Models Using NIH Criteria and Clinical Characteristics Define Diagnosis, Disease Activity and Risk Factors for Chronic Ocular Graft-Versus Host Disease

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Ocular chronic GVHD (cGVHD) is one of the most bothersome and common long-term complications after allogeneic HCT. The 2005 NIH cGVHD Consensus Project provided expert recommendations for diagnosis: dry, gritty, or painful eyes, cicatricial conjunctivitis, keratoconjunctivitis sicca or confluent areas of punctate keratopathy in conjunction with abnormally low Schirmer's tear test. However these have not been prospectively validated in patients. The goal of this analysis was to identify predictive models for ocular cGVHD diagnosis, disease activity and clinical correlates that could be feasibly employed by transplant clinicians to assess outcomes in clinical practice and therapeutic trials. Between 2004 and 2013, 210 patients with moderate (n=57) or severe (n=151) cGVHD were enrolled on the NIH/NCI cGVHD cross-sectional observational study (NCT00092235). Median time from cGVHD diagnosis to enrollment was 765 (20-6670) days. Patient-reported outcomes (PROs) and transplant-clinician-reported outcomes (ClinROs) were gathered: Schirmer's, NIH eye score (0-3), Lee cGVHD symptom scale (dry eye, needs eye drops frequently, and difficulty seeing clearly) (each 0-4) and chief eye symptom intensity scale (0-10). Participants were examined by ophthalmologists experienced in diagnosing and treating ocular cGVHD (MBD, RJB), who confirmed the diagnosis and classified patients as active vs. inactive. Univariate analyses and logistic models were developed to examine the associations among ophthalmologist assessment, PRO and ClinRO measures. Based on ophthalmology evaluation, 157 (75%) patients were diagnosed with ocular cGVHD; a majority (133/157; 85%) had active disease. In a multivariable model, the NIH eye score (3 vs. 2 vs. 1) ($p<0.0001$) and lower Schirmer's ($p<0.0001$) were significant independent predictors of ocular cGVHD (sensitivity 93.0%, specificity 92.2%). The Lee dry eye was the strongest predictor of active ocular cGVHD ($p<0.0001$) (sensitivity 68.5%, specificity 82.6%). The following risk factors for ocular cGVHD were identified: related donor ($p=0.0029$) and HLA matched ($p=0.0095$) HCT. Oral cGVHD was strongly associated with the diagnosis of ocular cGVHD ($p<0.0001$). NIH eye score and Schirmer's test are ClinRO measures that are strongly predictive for diagnosis of ocular cGVHD, while a single PRO item assessing dry eye symptom bother had 82.6% specificity for ocular cGVHD activity. Results support the use of these items for routine screening and ocular triage when providing long-term care to allogeneic HCT survivors. Prospective studies are needed to determine if a single PRO item assessing dry eye is sufficient for use as a trial outcome and to guide therapeutic decision-making in clinical practice. We confirm observations of others that HLA-matched and related donor transplants are associated with an increased risk of ocular cGVHD.

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Leukapheresis Safely and Effectively Yields Lymphocyte Populations Sufficient for Chronic Gvhd Research

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