aGVHD, it was 6.5 infections/1000 person-days (p-value=0.022). These data support the hypothesis that gut aGVHD predisposes patients to development of EB-BSI, given the asymmetric distribution of EB-BSI after onset of aGVHD. We plan to analyze the infection densities in several other groups and risk factors associated with higher infection density in patients with gut aGVHD specifically.

To our knowledge, this is the first study to demonstrate that the development of gut aGVHD increases the risk for EB-BSI. Strategies to reduce the elevated risk of EB-BSI in patients who develop gut aGVHD, such as prophylactic use of probiotics, should be considered based on these findings.

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Complement Component C3 Mediates Th1/Th17 Polarization in Human T Cell Activation and Cutaneous Graft-Versus-Host Disease

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Graft-verses-host disease (GVHD) is a major complication in allogeneic bone marrow transplantation (allo-HSCT), and characterized by epithelial cell injury in skin, intestine and liver. The development of GVHD involves donor T cell activation including proliferation, differentiation and inflammatory cytokine production, which lead to specific tissue damage. The interactions between the complement system and lymphocytes have been shown to regulate alloreactive T cell and APC function in the setting of allograft rejection. There are three pathways that activate the complement system: the alternative, lectin and classical pathways; all of which converge on the formation of the C3 convertase to propagate the complement cascade. Recently, we reported that mice deficient in the central component of complement system C3 had significantly lower GVHD-related mortality/morbidity and C3 modulated Th1/Th17 polarization in mouse GVHD. Given the emerging role of complement in alloimmune responses and T cell activation in animal models, it is important to address whether C3 modulates human T cell activation, polarization, expansion and differentiation. Compstatin is a 13-residue cyclic peptide that specifically binds to human C3 and inhibits complement activation, thus a favorable precursor peptide for the development of an anti-complement drug for oral use. Herein, we investigate the functional consequences of blocking C3 activation on human T cell activation. The production of IFN-γ (Th1), IL-4 (Th2), IL-17 (Th17), IL-2 and TNF-α was determined simultaneously in normal donor samples to examine whether Compstatin affects T cell activation and polarization in vitro. We found that blocking C3 activation with Compstatin significantly inhibits Th1/Th17 polarization in activated human CD4$^+$ T cells. The production of IL-2 and TNF-α are reduced in CD4$^+$ but not in CD8$^+$ T cells. Moreover, Compstatin treatment significantly decreases the proliferation of both CD4$^+$ and CD8 $^+$T cells stimulated with OKT3 plus CD28 or allogeneic DCs in MLR. It has been reported that patients with sclerotic-type chronic GVHD (ScGVHD) have significantly elevated C3 in the serum. We examined the degree of C3 deposition in the skin and lip samples retrieved from our GVHD tissue repository of human allo-HSCT recipients. In the skin GVHD tissues, C3 depositions are found in the squamous epithelium and dermis, blood vessels and damaged sweat glands. In the lip biopsy of GVHD patients, C3 depositions are found in the lesions associated with gland damage and regeneration, and damaged blood vessels. In summary, we conclude that C3 mediates Th1/Th17 polarization in human T cell activation and skin GVHD in patients. Studies on complement system and GVHD will not only significantly advance our knowledge of GVHD but also provide a rationale for using complement inhibitors as novel therapeutic interventions for GVHD.

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Early T-Cell Chimerism Is Valuable in Predicting Early Mortality from Steroid-Resistant Acute Graft Versus Host Disease after Myeloablative Allogeneic Haematopoietic Cell Transplantation

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The aim of this study was to evaluate the impact of early chimerism status on incidence and clinical course of acute GVHD in allogeneic transplant recipients. From March 2008 to February 2013, 106 eligible patients were included in the study. Median patient age was 40 (16-58) years with 66 (62%) males and 40 (38%) females. Pre-transplant diagnoses were AML (44 patients, 42%), ALL (29 patients, 27%), MDS (17 patients, 16%), CML (8 patients, 8%), NHL (2 patients, 2%) and other (6 patients, 6%). Donors were HLA-identical siblings in 33 (31%) patients and matched unrelated donors in 73 (69%) patients. Stem cell sources were bone marrow (61 patients, 58%) and peripheral blood (45 patients, 42 %). Patients were conditioned with Cyclophosphamide and TBI 12 Gy (63 patients, 59%), VP16 and TBI 12 Gy (31 patients, 29%), Cyclophosphamide and Busulfan (10 patients, 9%), moreover 1 patients received Busulfan and Melphalan and another patient Busulfan and VP16.

T-cell line specific chimerism was analysed by PCR-VNTR and chimerism samples were measured on day 35. Donor chimerism (DC) was defined as 95% or more cells of donor origin within CD4 and CD8 T-cells and mixed chimerism (MC) as less than 95% donor CD4 and CD8 T-cells. At a follow-up time of 767 (140-1940) days 71 (67%) patients were still alive. Among deceased patients, cause of death was TRM in 23 (66%) patients and relapse in 12 (34%) patients. Acute GVHD occurred in 68 (64%) patients with 49 (46%) patients diagnosed with grade II-IV aGVHD. The incidence and grade of aGVHD was not different in DC versus MC patients. Early survival probability at day 180 estimated by Kaplan-Meier showed significantly better outcome for patients with MC compared to DC (p=0.04). Death from TRM with relapse as competing risk analysed with cumulative incidence emphasized poorer outcome for MC patients compared to DC patients (p=0.03).We then analysed the clinical course in MC and DC patients diagnosed with aGVHD grade II-IV who later on died from TRM. Of these 21 patients, 12/14 DC patients compared to 1/7 MC were under treatment with either high dose Prednisolone ($\geq$ 1.5 mg/kg body weight) or Infliximab by their time of death (p=0.007, figure 1), associating early T-cell DC with steroid-resistant aGVHD. This suggest, that even though the incidence and grade of aGVHD were not different between patients with DC versus MC, the clinical course of aGVHD seem to differ significantly in the two groups with higher mortality from steroid-resistant aGVHD in DC
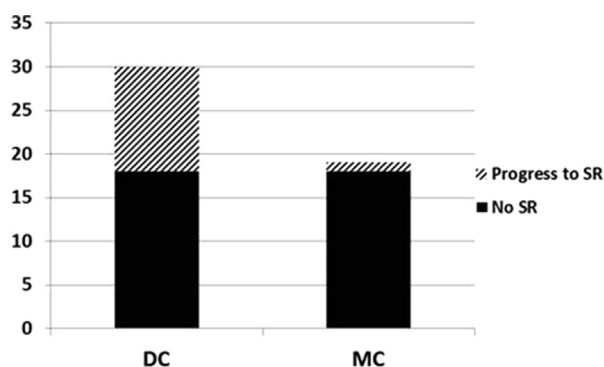
Fig 1. Patients with grade II-IV acute GVHD, DC: Donor T-cell Chimerism, MC: Mixed T-cell Chimerism. Diagonal pattern in bar indicates patients progressing to steroid resistant (SR) GVHD. P=0.007.

patients compared to MC patients. Early T-cell DC may be an early predictor of development of steroid-resistant GVHD.

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Diagnostic Criteria for Myositis As a Facet of Chronic Gvhd

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Background: There is paucity of data on diagnostic criteria of Myositis/Muscle chronic Graft-versus-Host disease [cGVHD] due to rarity of the condition (<0.7% of all Allogeneic-Hematopoietic-Stem-Cell-Transplants [HSCT]. Myalgias are common after HSCT and confounding factors such as drugs (statins, steroids etc.), infections (muscle abscess) and tumor infiltration make diagnosis elusive. A diagnostic algorithm is lacking.

Methods: We retrospectively analyzed all allogeneic-HSCTs through the Mayo Clinic Database from Jan 1994-July 2013 to search for cases of myositis in association with cGVHD using terms "GVH", "Muscle biopsy" and "Myositis". Diagnostic criteria utilized were 1) Muscle Biopsy; 2) Elevated Enzymes: CK or Aldolase; 3) Serum Antibodies: ANA, anti-striated-muscle, Anti Ro/Jo/La, Sm, Scl-70, RNP 4) EMG and 5) Imaging: MRI or PET scan.

Results: Of 1058 screened allogeneic-HSCT, 68 were suspected clinically of having myositis, mostly presenting as focal or diffuse myalgias. 14 had muscle biopsies. 7 had confirmed myositis (Age 43-66 yrs., median 47). Median time to diagnosis was 19 months post-HSCT. All had cGVHD involving at least one other organ. 5/7 had AML and 6/7 received a fludarabine based conditioning. All biopsy positive and 2 biopsy indeterminate patients met at least 2 additional criteria besides biopsy (total criteria met ≥3). Of the 61 patients that were biopsy negative or not biopsied, none met 3 criteria (except 2 who could not be biopsied). 17 were tested but met none of the criteria (excluded). Remaining met ≤2 criteria not deemed sufficient for diagnosis. All biopsy proven patients received prednisone treatment. 5 received additional therapies including IVIG, ECP, Rituximab and Sirolimus.

Conclusions: Muscle biopsy, while confirmative, is invasive and is rarely pursued (20%). Only half of the biopsies were positive for myositis, likely due to patchy nature of the

Conflicts of Interest: None

Table 1
Workup panel results of suspected Myositis.* 10 excluded due to lack of testing from n=68.

No. of patients	Muscle Biopsy	Enzymes+	Antibodies+	EMG+	MRI/PET+
7	**Positive**	**6/7**	**4/7**	**7/7**	**2/2**
2	Equivocal	2/2	0/2	1/1	1/1
5	Negative	1/5	0/3	4/4	0/3
44	Not Done	30/40	7/23	8/16	11/19
58*	**TOTAL**	**39/54**	**11/35**	**20/28**	**14/25**

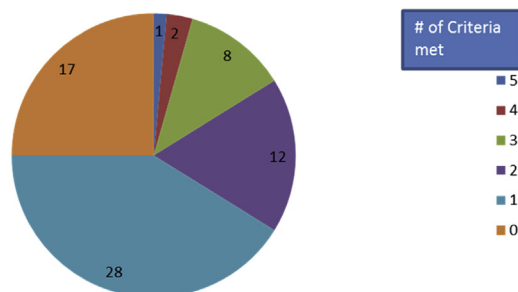## No. of patients meeting Myositis criteria

Fig-1. Number of patients meeting Myositis criteria.

disease. All biopsy proven myositis patients met ≥3 criteria. Myositis as a component of cGVHD can be diagnosed using a composite of autoantibodies, muscle enzymes, EMG and imaging. This new criteria could be used to establish an algorithm in delineating the need for muscle biopsy for suspected myositis. (Fig 1 & Table 1).

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Impact of Conditioning Intensity with or without Total Body Irradiation on Acute Graft-Versus-Host Disease and Clinical Outcomes

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