while related vs. unrelated donor, complete HLA match, ATG use, and recipient age are not. Multivariable analysis was challenging given the correlation among covariates. However, male donor is significantly associated with improved OS for pts with grade 3-4 aGVHD in all models, while time pd is not significant when adjusting for other factors.

**Conclusions:** While OS for pts with grade 3-4 aGVHD has improved, it continues to impact >13% of pts and has poor outcomes. The use of a male donor may predict improved OS for pts with grade 3-4 aGVHD independent of time pd. Additional study is warranted to validate these findings and improve therapies.

**Ethnic Variation in Chronic Graft-Versus-Host Disease (cGVHD) Manifestations**

Maria Elvira Correa ¹, Eliana Miranda ², Afonso Vigorito ², Luis Fernando S. Bousaz ³, Vanezuca Funke ⁴, Vergilio Antonio Colturato ⁵, Maria Claudia R. Moreira ⁶, Rita Tavares ⁷, Marcos A. Mauad ⁵, Mair Pedro De Souza ⁸, Sally Arai ⁹, Stephanie J. Lee ¹⁰, Barry Storer ¹¹, Mary E.D. Flowers ¹, ¹ Clinical Research, Fred Hutchinson Cancer Research Center, Seattle, WA; ² Hemocentro, University of Campinas, Campinas, Brazil; ³ National Institute of Cancer INCA, Rio de Janeiro, Brazil; ⁴ Universidade do Parana - UFPR, Curitiba, Brazil; ⁵ Hospital Amaral Carvalho - HAC, Jau, Brazil; ⁶ National Institute of Cancer INCA, Rio de Janeiro, Brazil; ⁷ Hospital Universidade de Sao Paulo - UNIFESP, Ribeirao Preto, Brazil; ⁸ Hemocentro, University of Campinas, Campinas, Brazil; ⁹ Stanford University, Stanford, CA; ¹⁰ Clinical Transplant Research, Fred Hutchinson Cancer Research Center, Seattle, WA; ¹¹ Division of Clinical Research, Fred Hutchinson Cancer Research Center, Seattle, WA

Risk of acute GVHD varies among different ethnic population. Thus, we evaluated potential differences in cGVHD manifestations in two ethnic distinct cohorts. The study included a Brazilian cohort diagnosed with cGVHD by 2005 NIH criteria who were enrolled in a prospective multicenter longitudinal study at 5 centers in Brazil and compared with a North American cohort reported by the cGVHD consortium (Arai S. et al. Blood 2011). Pts. were assessed using standardized clinical data forms every 3 months (124 visits). Any elevation of liver function tests was scored as cGVHD. The Brazilian study cohort included 36 pts. with a median age of 44 (13-64) years and 21 (58%) were male. At study enrollment, 24 (67%) had classic cGVHD, and 12 (33%) pts. had overlap subtype (with feature of both acute and chronic). Distribution of organ involvement attributed to cGVHD for the Brazilian and the North American cohorts at study enrollment is shown in the Figure. Liver severity scores at study enrollment was mild in 10 (34%), moderate in 12 (40%) and severe in 8 (26%) pts. among Brazilian cohort, and it was mild in 113 (76%), moderated in 36 (24%) and none severe in the North American cohort. Overall, cGVHD global severity at study enrollment was calculated from reported data as mild in 2 (5.5%), moderate in 17 (47%) and severe in 17 (47%) of Brazilian cohort compared to 32 (10%), 175 (59%) and 91 (31%) in the North American cohort, respectively. Similar to North American cohort, distribution of global severity was similar in the Brazilian cohort across 22 incident (enrollment < 3 months of cGVHD diagnosis) and 14 prevalent cases (enrollment 3 or 6 months after cGVHD diagnosis) and, between pts. with classic and overlap cGVHD. Prevalence of organs involvement at study enrollment was significant different between the two population. Compared to the North American cohort, the Brazilian cohort had higher rates of liver involvement (83% vs. 50%; p < .001) and lower rate of lung (8% vs. 50%; p < .001), respectively. The cause for the high incidence and severity scores in the liver among the Brazilian cohort is unknown, but we speculated potential contributors. For instance, 100% of Brazilian cohort was CMV positive and pre-emptive treatment for CMV reactivation is not used after day 100 posttransplant, thus reactivation of CMV may have contributed to the elevation of liver function tests. Moreover, it is not standard practice in Brazil to add ursodiol to treat elevation of liver tests attributed to GVHD, thus allowing for further potential increase in liver severity score. The lower rates of lung in the Brazilian cohort may reflect non-standardization of pulmonary function test in Brazil. In conclusion, prevalence of organ manifestations in cGVHD varied between the two ethnic distinct cohort studied. Attention should be taken into consideration when evaluating prognosis and outcomes in cGVHD in different ethnic population.

**Clinical Features of Acute Cutaneous Graft-Versus-Host Disease Following Allogeneic Hematopoietic Stem Cell Transplantation**

Daniel Bach ¹, Elizabeth Damstetter ¹, Dennis West ², Jayesh Mehta ³, Jonathan Cotliar ⁴, ¹ Northwestern University Feinberg School of Medicine, Chicago, IL; ² Northwestern University Feinberg School of Medicine, IL; ³ Northwestern Memorial Hospital, Chicago, IL; ⁴ Dermatology, Northwestern University Feinberg School of Medicine, Chicago, IL

**Background:** Acute graft-versus-host disease (aGVHD) is a frequent complication of allogeneic hematopoietic stem cell transplantation (HSCT). Although the presence of a skin eruption is a cornerstone in the diagnosis of aGVHD according to the Glucksberg criteria and the 2005 NIH Consensus Conference, specific cutaneous features such as morphology and anatomic distribution have not been studied in a systematic manner. Subsequently, the relative incidences of specific skin lesions remain unclear and contribute to the ongoing challenge of delineating aGVHD from other commonly seen skin eruptions early after HSCT.

**Methods:** A retrospective review of all patients receiving an allogeneic HSCT from 2010 to 2011 at Northwestern Memorial Hospital identified those individuals with cutaneous aGVHD. Each case of aGVHD was confirmed by both skin
biopsy and evaluation by the dermatology consult service. Cutaneous features with respect to lesion morphology, location, and time of onset following transplantation were collected for each patient and further stratified by aGVHD clinical grade.

**Results:** For all cutaneous aGVHD patients (n = 37), the onset of rash was on average, day +45 (range +4 to +153). The most common skin lesion morphology was morbilliform (55%) followed by patchy erythema (38%). Follicular accentuation was seen in 29% of rashes. The cutaneous eruptions most commonly occurred on the trunk (69%), arms/legs (67%), face (62%), ears (38%) and palms (38%).

Comparing grade I and II skin aGVHD patients, grade I patients (n = 11) had more patchy erythema (73% vs 23%, P = .008), purpuric/violaceous lesions (55% vs 13%, P = .038) or a reticular pattern (36% vs 0%, P = .005) than grade II patients (n = 26). Grade II aGVHD patients were found to have cutaneous eruptions located more often on the trunk (85% vs 36%, P = .006) and arms/legs (77% vs 36%, P = .028) when compared to grade I aGVHD patients. Comparison to grade III (n = 3) and IV (n = 2) aGVHD patients was not performed given the paucity of cases.

**Conclusion:** We profiled the salient cutaneous features associated with aGVHD and their relative incidences based on clinical grade, skin lesion morphology and anatomic site of involvement. Application of this analysis will allow for improvements in the diagnosis of aGVHD and differentiation from other clinical mimickers. Differences in lesional morphology and location may differentiate grade I and II cutaneous aGVHD and serve to guide appropriate treatment.

---

**427**

Survival Improvements Following Omega-3 Polyunsaturated Fatty Acid Dietary Enrichment, Acetylsalicylic Acid, and Aspirin-Triggered Lipoxin Administration in a Lethal Mouse Model of Acute Graft-versus-Host Disease

Geoff Cuvelier1, Yuri Lisitsyn2, Khoung Le3,
Mohammed Moghadasian3, Cindy Ellison2,4, 1 Pediatric Oncology-Hematology, CancerCare Manitoba, Winnipeg, MB, Canada; 2 Department of Pathology, University of Manitoba, Winnipeg, MB, Canada; 3 Human Nutritional Sciences, University of Manitoba; 4 CancerCare Manitoba, Winnipeg, MB, Canada

**Background:** Lipoxins (derived from arachidonic acid) and the resolvins and protectins (derived from ω3-polyunsaturated fatty acids [n-3PUFAs]) are endogenously produced lipid mediators with potent anti-inflammatory and tissue healing properties. Acetylsalicylic acid (ASA, aspirin) results in the synthesis of aspirin-triggered lipoxins, isomers for these lipid mediators with identical anti-inflammatory actions. In part, these lipid mediators act through down-regulation of Th1 cytokines known to be important in aGVHD pathogenesis. The C56BL/6 → (C57BL/6 x DBA/2)F1-hybrid is a major histocompatibility mismatched mouse model of lethal aGVHD (similar to a non T-cell depleted HLA haploidentical BMT without GVHD prophylaxis) that allows isolation of the aGVHD effect. We wanted to test whether these novel lipid mediators could attenuate aGVHD in this highly inflammatory allogeneic transplant mouse model.

**Methods:** Mice were transplanted according to standard protocols. Four diets were created, including a control diet containing 2% ω-6-PUFAs; three experimental diets, enriched for (1) 2% ω-3-PUFAs (2) 2% ω-6-PUFAs plus ASA (0.02 mg/g of feed) (3) 2% ω-3-PUFAs plus ASA. Mice were randomly fed one diet (n = 10-12 per group) for 8-weeks before transplant and the same diet after transplant. A separate experiment confirmed that feeding the different diets for 8-weeks before transplant resulted in differential tissue (liver) stores of ω-6 and ω-3-PUFAs. A fifth group (n = 10) was fed the control diet but injected with the aspirin-triggered lipoxin 15-epi-LxA4 IV on day 0 and IP on day 7 (200 mcg/kg/dose). The primary outcome was days before the onset of aGVHD-associated morbidity (humane end point) post-transplant.

**Results:** Control GVH mice met the humane end-point for euthanasia as result of aGVHD at a median of 14 days post-transplant (range: 9-16 days). Kaplan-Meier survival curves showed modest but statistically significant improvements in survival for mice fed a diet enriched for ω3-PUFAs plus ASA (P = .0117) and mice receiving the aspirin-triggered lipoxin (P = .034) compared to the control group. Survival improvements and the onset of lethal aGVHD were delayed by a matter of days for the mice receiving the interventions.

**Conclusion:** We provide proof-of-principle that dietary ω3-PUFAs, aspirin, and aspirin-triggered lipoxins may offer novel ways to counteract aGVHD. Our interventions approximate acceptable human dietary intake for ω3-PUFAs and taking a baby-aspirin once per day. Further experiments using different aGVHD mouse models are planned.

---

**428**

An Immunological Assessment of Cytokine Profile of CD4+ Cells in Patients with Chronic Graft vs Host Disease (cGVHD) Undergoing Extracorporeal Photopheresis (ECP)

Jignesh Dalal1, Thomas Yankee2, Ashraf Hassbullah1, Anne Hirner3, Robin Ryan4, Siddhartha Ganguly5,
Joseph P. McGuirk6, Sunil Abhyankar7. 1 BMT, Children’s Mercy Hospital, Kansas City, MO; 2 Microbiology and Immunology, University of Kansas Medical Center, KS; 3 University of Kansas Medical Center, KS; 4 Apheresis, University of Kansas Hospital, Kansas City, MO; 5 Children’s Mercy Hospital; 6 BMT Program/Division of Hematology-Oncology, University of Kansas Medical Center, Westwood, KS; 7 Kansas University Med Ctr MS 5003, Westwood, KS; 8 Blood and Marrow Transplant, University of Kansas Medical Center, Westwood, KS

CGVHD develops in more than 50% of survivors of allogeneic stem cell transplantation and is responsible for mortality in one third of patients. Long term immunosuppressive therapy with steroids is the standard treatment. ECP has shown activity in acute and cGVHD and is successful in about 50% of the patients after 3–6 months of therapy. We studied the cytokine profiles in 6 patients with cGVHD undergoing ECP. A comprehensive assessment of organ system involvement using NIH Consensus response assessment tools was done at study entry and at six months. Patients underwent ECP treatments twice on two consecutive days every two weeks for 3 to 6 months. All patients underwent baseline, two-months, four months and six-month assessments. 10 ml of leukopheresed blood was obtained from the ECP machine prior to the initiation of ECP at baseline, and at 2, 4 and 6 months post treatment to assess peripheral blood B and T cells and the cytokine analysis. CD4+ T cells were purified from PBMCs and stimulated with anti-CD3 and anti-CD28 for five days. Tissue culture supernatants were collected and analyzed for the production of 42 cytokines using LumineX® technology. Three patients responded to treatment with ECP and three did not and later received other therapies. We have previously reported that responding patients had higher CD4+CD25+FoxP3+ cells. Of the cytokines analyzed, soluble CD25 and TNFβ were secreted at significantly higher levels in responding patients prior to ECP initiating therapy (Figure). In responders, sCD25 and TNFβ levels remained high