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 15%, 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 Lissitsyn2, Khoung Le3, Mohammed Moghadasian1, 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 ω-3-polyunsaturated fatty acids (PUFAs)) 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 BM 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; and 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 ω-3-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 ω-3-PUFAs, aspirin, and aspirin-triggered lipoxins may offer novel ways to counteract aGVHD. Our interventions approximate acceptable human dietary intake for ω-3-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 Hassbullah3, Anne Horner1, 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