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cells on day 14 after allo-BMT, revealed that these cells displayed substantial levels of cell-surface P-selectin ligands as defined by positive staining with recombinant P-selectin-IgG-Fc fusion protein at levels similar to those found on WT T cells, suggesting that although absence of P-selectin on host tissues may ameliorate GVHD, multiple donor leukocyte P-selectin ligands interact meaningfully with P-selectin.

Our studies suggest that P-selectin may be required for trafficking into inflamed tissues but not SLO, and that donor T cells may utilize multiple P-selectin ligands apart from PSGL1 to interact with P-selectin and traffic into inflamed tissues during GVHD.

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PATTERNS OF CHRONIC GRAFT-VS-HOST DISEASE AND ASSOCIATED MORTALITY AFTER MYELOABLATIVE CONDITIONING INCORPORATING FLUDARABINE, BUSULFAN AND ATG

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Preparative regimens incorporating antithymocyte globulin (ATG) have been shown to decrease the incidence of both acute and chronic graft-versus-host disease (aGVHD and cGVHD). It is less clear whether prior ATG influences the pattern of onset, duration of treatment and graft-versus-malignancy(GVM) effect of cGVHD. Between 1999 and 2008, 538 patients (pts) with hematologic malignancy aged 18–66 years (median 46) received blood cell (n = 440, 82%) or marrow transplants after conditioning with Flu 50 mg/m2 daily × 5 and IV Bu 3.2 mg/kg daily × 4. Two hundred and thirty-four (43%) had additional total body irradiation (TBI) 200 cGy × 2. GVHD prophylaxis was cyclosporin A, methotrexate and Thymoglobulin (Genzyme) 4.5 mg/kg total dose. Donors were matched siblings in 299 (56%), mismatched related in 27(5%), 10/10 matched unrelated in 146 (27%) and mismatched unrelated in 66(12%). Two hundred and fifty-six pts (48%) had low-risk (LR, acute leukemia CR1/CR2, CML CP1) disease. Incidence of aGVHD grade II-IV, aGVHD grade III-IV and cGVHD (at 2 years) was 24%, 10% and 56% respectively. Of 474 pts surviving >100days, 371 (78%) had no or grade I aGVHD, 167 (45%) of whom developed cGVHD. Of the 103 pts with prior grade II-IV aGVHD, 4 died before d126 of late effects of aGVHD (and are excluded from the analysis of the no cGVHD group), 17 survived without cGVHD, 21 developed cGVHD after discontinuing treatment for aGVHD ("quiescent" cGVHD) of whom 2 (10%) died without relapse. Sixty-one developed cGVHD before completing treatment for aGVHD grade II-IV, defined as "progressive" cGVHD (pcGVHD) for the purpose of this study. There were therefore 188 pts with "non-progressive" cGVHD (npcGVHD) (167 de novo plus 21 "quiescent") and 221 with no cGVHD. At follow-up of survivors of 14–124 months (median 60) 5 year outcomes (%) were as follows:(see table).

All pcGVHD pts and 143 npcGVHD pts (76%) required systemic therapy. Median time on treatment was 495 days compared with 286 days (p = 0.07), with 79% and 83% respectively being off immunosuppression by 3 years from onset of cGVHD. Despite a relatively low incidence of aGVHD with this regimen about 60% of those who do develop grade II-IV aGVHD and live100 days develop pcGVHD with a significantly higher risk of NRM than other pts. Because of less relapse and equivalent NRM, OS and DFS are better in pts with npcGVHD than those with no cGVHD. The challenge remains to prevent aGVHD without sacrificing the GVM effect of cGVHD.

5 years outcomes in relation to cGVHD

	npcGVHD(%)	No cGVHD(%)	pcGVHD(%)	p value
OS	68*†	61*	50†	*0.02, † 0.006
DFS	66*†	55*	42†	*0.003,† 0.004
NRM	8*	12†	42*†	*†<0.0001
Relapse	28*	39*†	28†	*0.006, †0.02

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FLUTICASONE, AZITHROMYCIN, AND MONTELUKAST (FAM) THERAPY IN REDUCING STEROID EXPOSURE IN BRONCHIOLITIS OBLITERANS SYNDROME AFTER ALLOGENEIC HEMATOPOETIC STEM CELL TRANSPLANT (HCT)– A CASE SERIES OF 8 PATIENTS

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Background: Bronchiolitis obliterans syndrome (BOS) is a rare and serious complication of allogeneic HCT, requiring long courses of systemic corticosteroids that are often associated with adverse consequences. Thus, novel therapies to reduce corticosteroid exposure may be beneficial.

Hypothesis: Combined treatment with fluticasone, azithromycin and montelukast (FAM), three agents with anti-inflammatory and antifibrotic properties, all with low toxicity, will reduce the overall six-month exposure to corticosteroids in BOS patients.

Methods: Between June 2008 and the present, we reviewed 8 patients who met NIH criteria for newly diagnosed BOS and were treated with FAM therapy indefinitely and a 2-week pulse of high dose (1 mg/kg/day) prednisone followed by a rapid taper. These patients were compared with 14 historical controls identified from a pre-existing database, who also met NIH criteria, and received high dose prednisone therapy followed by a standard taper. The total prednisone exposure (median values and interquartile ranges) six months after diagnosis and interval change in FEV_1 at three, and/or six months after BOS diagnosis were compared. FEV_1 was reported as percent predicted with preference given to post-bronchodilator values. FEV_1 change was defined as change in FEV_1 from diagnosis to three or six months, depending on pulmonary function test availability. Treatment failure was defined as a decline in $FEV_1 \geq 10\%$ and clinical worsening of symptoms resulting in increase in prednisone dose within six months of diagnosis.

Results: The median six month prednisone exposure for the FAM-treated patients was 1819 mg [25^{th} percentile = 0 mg; 75^{th} percentile = 4036 mg] compared to 7163 mg [25^{th} percentile = 6551 mg; 75^{th} percentile = 7829 mg] in the control group. The median FEV_1 change in the FAM group was 2% [25^{th} percentile = -7%; 75^{th} percentile = 4%] compared to 1% [25^{th} percentile = -4%; 75^{th} percentile = 5%] in the control group. There was one treatment failure in the FAM group (12%) compared to one in the control group (7%).

Conclusions: The total six month prednisone exposure in a group of eight patients treated with FAM therapy was one quarter that of a retrospective group of BOS patients who were treated with standard prednisone therapy, with minimal change in median FEV_1 in both groups. FAM therapy may allow for less total exposure to corticosteroids and may avert some complications associated with steroid therapy.

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PATIENTS WITH CUTANEOUS GRAFT VERSUS HOST DISEASE EXHIBIT REDUCED PRODUCTION OF IL-17

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It is well recognized that T cells are the principal orchestrators of graft versus host disease (GVHD). Historically, IFN-γ producing Th1 cells have been implicated in the pathogenesis of acute GVHD (aGVHD) whereas Th2 cells have been thought to be involved in the pathogenesis of chronic GVHD (cGVHD). The recent discovery of a distinct lineage of IL-17 producing Th17 cells, thought to be the major perpetrators in a number of inflammatory and autoimmune disorders, has prompted re-evaluation of the Th1/Th2 paradigm of GVHD. Studies in IL-17 deficient mice have shown conflicting results with IL-17 having both a protective or deleterious effect, whereas transplantation of purified Th17 cells causes GVHD-related tissue damage with a predilection for the skin and lungs. In this study we aimed to determine whether Th17 cells play a role in the pathogenesis of human GVHD. 37