Mocravimod, a S1P receptor agonist, increases both T cell counts in bone marrow biopsies from patients undergoing allogeneic HCT and acute GvHD-freedom probability

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Abstract 59

Background and Objective

A polyclonal donor T cell response called graft-versus-leukemia (GvL) is critical to prevent relapses after allo-HCT. GvL occurs in hematolymphoid tissues, where respective malignant cells usually reside. However, graft-versus-host disease (GvHD) can be triggered by the same alloreactive donor T cells in peripheral organs. The sphingosine-1-phosphate receptor (S1PR) signaling plays a crucial role in lymphocyte trafficking. Mocravimod is a S1PR modulator and its administration blocks lymphocyte egress from lymphoid organs, thus resulting in reduced peripheral lymphocyte counts and decreased T-cell infiltration in GvHD target organs. We therefore hypothesized that higher T cell counts will be detected in the bone marrow (BM) from mocravimod-treated compared to non-mocravimod treated patients.

Methods

BM biopsies were collected pre-transplant and one- and three-months post-transplant. The subjects were diagnosed with hematological malignancies, underwent allo-HCT and given 3 mg mocravimod for 111 days in combination with cyclosporine A or tacrolimus as GvHD prophylaxis (Table 1). In total, biopsies from 9 patients, who had received mocravimod were analyzed. 10 patients, who have been allo-HC transplanated but had not been given mocravimod, served as controls. To measure T cell counts and composition in the BM, the biopsy material was analyzed by immunohistochemistry for CD3, CD4, CD8, TIA1, FoxP3, PD1, T-Bet, GATA3, ROR-γt.

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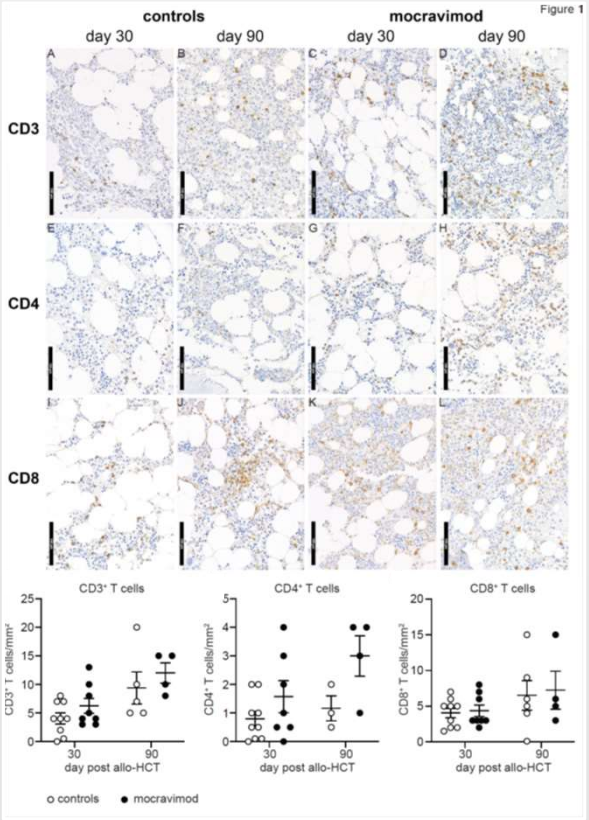
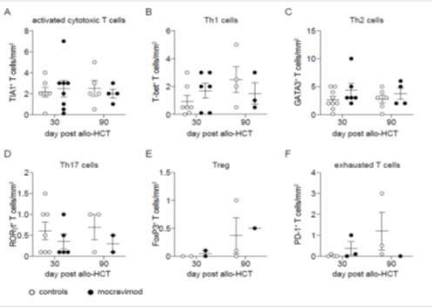
Figure 1: Immunohistochemical staining for CD3, CD4 and CD8 of bone marrow biopsies and quantitative data

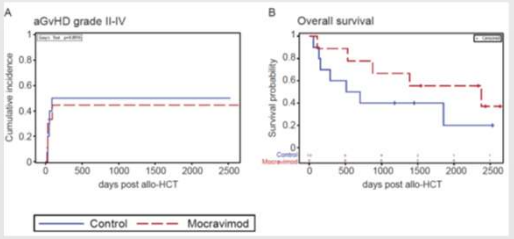


Results: Patients, quantitative data on T-Bet (Th1), GATA3 (Th2), ROR-γt (Th17), FoxP3 (Treg) and PD1 (exhausted T cells), and survival

Table 1. Patient characteristics

	Mocravimod group (n=9)	Control group (n=10)
Age median (range), yr	50 (23-60)	49 (23-65)
Male sex, no. (%)	4 (44.4)	3 (30
Diagnosis, no. (%)		
AML	1 (11.1)	9 (90)
MDS	2 (22.2)	1 (10)
ALL	3 (33.3)	0 (0)
Multiple myeloma	1 (11.1)	0 (0)
Follicular lymphoma	1 (11.1)	0 (0)
CML	1 (11.1)	0 (0)
Ressmission state pre-HSCT, no. (%)		
CR	5 (55.5)	4 (40)
Persistence	3 (33.3)	5 (50)
Relapse	0 (0)	1 (10)
PR	1 (11.1)	0 (0)
Conditioning, no. (%)		
BuCy	3 (33.3)	9 (90)
FluBu	1 (11.1)	1 (10)
CyTBI (12 Gy)	3 (33.3)	0 (0)
FluTBI (2 Gy)	1 (11.1)	0 (0)
BEAM	1 (11.1)	0 (0)





Conclusion

This is the first study to investigate *in situ* BM lymphocyte retention by the S1PR modulator, mocravimod, in samples from patients undergoing allo-HCT. Collected data support the hypothesis that mocravimod not only sequesters T cells within lymph nodes but also results in retention in the BM. Though limited by numbers, study observations indicate favorable overall survival, fewer relapses and slightly lower GvHD severity for allo-HCT patients treated with mocravimod.