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Immune cell composition in patients with and without steroid-refractory acute graft-versus-host disease after allogeneic hematopoietic cell transplantation

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Background One of the most life-threatening complications of allogeneic hematopoietic stem cell transplantation (allo-HCT) is acute Graft versus host disease (GVHD). It occurs almost exclusively in skin, liver, and gastrointestinal (GI) tract within the first 100 days after HCT. The first-line therapy is methylprednisolone, but only half of all patients respond and steroid-refractory is associated with a poor prognosis. Prognostic marker that predicts response to glucocorticoid therapy are still needed. In this retrospective study, we analysed the composition of T cells, innate lymphoid cells (ILCs) and tissue-resident memory T cells (TRMs) in acute GI GVHD samples and relate them to the response to glucocorticoid therapy.

Methods We searched for clinical data of allo-HCT patients with suitable stored samples of GI GVHD biopsies. We were able to obtain samples from 27 patients who have responded to glucocorticoid therapy (CR group) and 28 patients who developed glucocorticoid resistance (SR group). GVHD free GI biopsies taken from patients with bowel adenomas were included as control cohort. For Immunofluorescence staining, cells were labeled with the T cell markers, CD3, CD4 and CD8, and the TRM marker CD103. ILC3 were defined as CD3- RORgt+. Stained slides were imaged on a TissueFAXS imaging system and analyzed using TissueQuest software.

Results Our analysis showed that the percentage of ILC3s in the acute GI GVHD tends to be, but not significantly, higher than the SR group, but a significantly higher than the control group (p=0,008). In contrast, TRMs in the CR group were significantly reduced compared to the SR group (p=0,0261) and the control cohort (p=0,0014). In particular the TRMs with CD4 signature were lower in the CR cohort than in the SR cohort (p=0,0395).

Conclusion We have shown that TRMs and ILC3 are expressed differently in acute GI GVHD and might serve therefore as a useful clinical prognostic marker for response to glucocorticoid therapy.