Abstract: PB3121

Title: GUT MICROBIOTA EFFECT ON IMMUNOSUPPRESSIVE THERAPY IN PATIENTS AFTER ALLO-HSCT

Abstract Type: Publication Only

Topic: Stem cell transplantation - Experimental

Background:

Immunosuppressive therapy (IT) is a necessary condition for effective prevention of graft-versus-host disease in patients after allo-HSCT. Taking into account the possible influence of gut microbiota on bioavailability of immunosuppressive drugs, such studys may allow for safer and better prevention of GVHD.

Aims:

The aim of this study in real clinical practice was studying the influence of the gut microbiota composition on the necessity to adjust the dose of immunosuppressive drugs.

Methods:

The prospective study included 36 patients after allo-HSCT: 28 patients with acute leukemia (AML, ALL, MPAL), 4 patients with aplastic anemia, 1 patient with myelodysplastic syndrome, 1 patient with non-Hodgkin's lymphoma and 2 patients with chronic myeloid leukemia. Pre-engraftment stool samples were collected from 21 patients and post-engraftment samples from 29 patients. In agranulocytosis, IT was prescribed as i.v. infusion and per os after engraftment. Bacterial diversity were assessed by sequencing the V3-V4 regions of the 16S rRNA gene on the Miseq platform (Illumina, USA). In 24 patients, the basic drug was tacrolimus, in 12 patients - cyclosporine A. The following statistical methods were used in the study: multivariate models DESeq2 and ANCOMBC. An alpha-value of 0.05 was chosen as our significance cutoff and FDR adjusted p-values (using Benjamini-Hochberg adjustment) were used for methods that output p-values. The effect of taxon on changes in drug dose was considered significant if confirmed by 2 or more methods.

Results:

Before engraftment, 62% (n=13) of patients required adjustment immunosuppression dose within a week after stool sample collection, in 38% (n=8) patients within a week from the day of stool sample collection the dose remained stable. Dose increasing was required in 3 patients, decreasing in 10. The median time for sample collection was 6 (3-15) days after HSCT. After engraftment, dose adjustment of immunosuppressive drugs was required in 76% (n=22) of patients. Both dose reductions and increases were required in 11 patients. The median time for collecting stool samples was 25 (12-34). High abundance of Family Akkermansiaceae, Order Verrucomicrobiales, Class Verrucomicrobiae, Phylum Verrucomicrobia and Genus Akkermansia (Figure1) before engraftment were independent factors for reducing the dose of immunosuppressive therapy in patients after allo-HSCT ($p<0.005$). Genus Paeniclostridium was the only taxa shows a significant effect on IT dose changes ($p<0.0005$) after engrafment.

Summary/Conclusion:

Gut microbiome is an independent risk factor for changes in IT dose in patients after allo-HSCT. Further studies are needed to determine the mechanism of the influence of the gut microbiota on the dosage and concentration of immunosuppressive drugs under different dosage regimens.

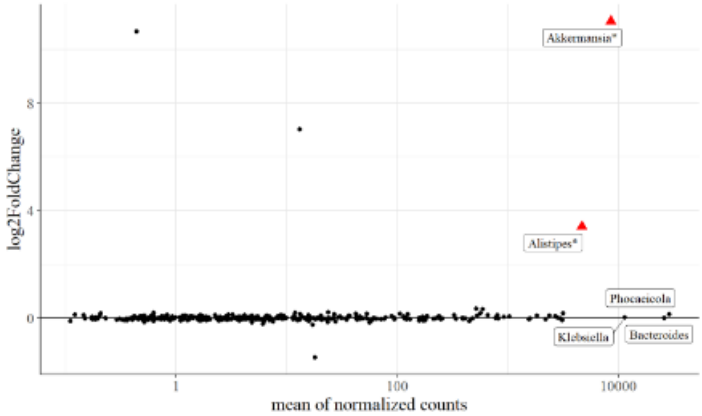

Figure 1 - Analysis of differential distribution of taxa before engraftment, depending on the necessity to reduce the dose of immunosuppressive drugs

Keywords: Immunosuppression, Allogeneic hematopoietic stem cell transplant, Allogeneic stem cell transplant