Screening for mobilization failure during stem cell transplant through non-coding RNA profiling.

Transplantation of bone marrow hematopoietic stem cells is a recognized method of treating hematooncological, metabolic and autoimmune diseases. More than 40,000 bone marrow transplants are performed annually in Europe, most of them are autologous hematopoietic stem-cell transplants (AHSCT). Most candidates for this procedure are newly diagnosed patients with multiple myeloma and patients with relapsed and refractory lymphomas.

The AHSCT procedure consists of three steps. In the mobilization process, after administering granulocyte colony-stimulating factor (G-CSF) with or without chemotherapy, hematopoietic stem cells (HSCs) with CD34 + antigen are transferred from the marrow into the circulation. They are collected from peripheral blood by apheresis. Then, high-dose chemotherapy is administered to eradicate the tumor. Transplantation of the collected HSCs during mobilization allows the restoration of the hematopoietic function of the bone marrow after high-dose chemotherapy.

The greater number of CD34 + cells transplanted is associated with a faster recovery time of hematopoiesis, shorter hospitalization time, fewer complications, and longer survival of patients undergoing AHSCT. Unfortunately, some patients are unable to mobilize a sufficient number of HSCs for transplantation. An insufficient number of collected HSCs is associated with repeated moblization procedures, hospitalizations, delayed transplantation, and even, in some cases, AHSCT is impossible. According to various estimates, the percentage of "bad mobilizers" is 5-30% of patients qualified for AHSCT.

Some predisposing factors for mobilization failure were identified - multiple lines of prior treatment, bone marrow involvement, and age> 65 years. However, the models predicting the occurrence of this complication are characterized by insufficient diagnostic parameters. Thus, there are no tools available to correctly identify patients at risk of mobilization failure prior to this procedure.

We present a study proposal in which we want to assess the profile of small, non-coding RNA-microRNA (miRNA) molecules in patients undergoing HSCs mobilization. These molecules are involved in gene expression, regulating the processes of differentiation, apoptosis, and migration of HSC cells after transplantation. Therefore, we believe that miRNA expression may also be essential in mobilization failure.

The proposed study will enable the discovery and understanding of the role of miRNAs in the mobilization of HSCs and the determination of their clinical role as potential biomarkers. The following stages of the study include:

1.miRNA sequencing in a group of 18 patients in order to determine the most differentiated miRNA molecules between the group of "bad mobilizers" and "good mobilizers" and changes in their expression occurring after treatment,

2. testing the expression of the most promising miRNAs in a larger group of patients by quantitative Polymerase Chain Reaction (qPCR) and creating diagnostic models using them using data mining and machine learning techniques,

3. assessment of the quality of the developed diagnostic tools on a new, independent group of patients and selection of the best predictor of mobilization failure.

The project will enable the identification of the signature of miRNAs experiencing mobilization failure, the identification of new predisposing factors, and the development and validation of a tool that can stratify patients into risk groups, which will allow for the personalization of the treatment process.