Blood-based highly sensitive diagnostics of multiple myeloma

Development status

Phase 2

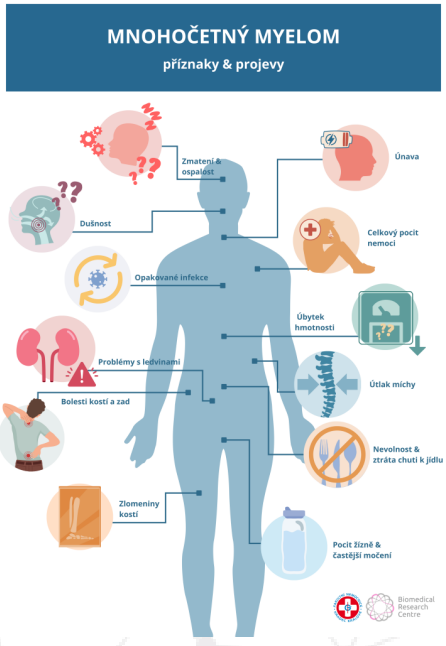
Feasibility study. There is a realistic design of the technology and the initial tests in the laboratory are leading to the specification of the technology requirements and its capabilities.

IP protection status

Know-how

Partnering strategy

Collaboration, licensing



Challenge

MM is a malignant disease of the bone marrow that results from uncontrolled proliferation of myeloma cells. Disease is very creeping and can only be detected at early stage by random examination. Symptoms usually bring the patient to the doctor at advanced stage. The disease has a profound effect on the bones, blood formation, antibody production or the kidneys. MM occurs in 3-4 people/100,000 population/year and is a relatively aggressive. In most cases, it cannot be cured. Currently, early detection of clones of these cells from blood, resp. pathological antibodies produced by these cells, is limited due to the low sensitivity of current diagnostic methods from serum. More sensitive methods require invasive bone marrow biopsy. The main goal is to develop a simple and widely applicable method for the sensitive detection of malignant clones that will allow the detection of disease progression before it causes severe and irreparable damage to the skeleton or even to neural structures.

Description

MM is characterised by minimal residual disease (MRD), where residual tumor cells remain in the body even after the end of treatment but are not detectable by conventional diagnostic procedures. These cells are responsible for the relapse of the disease. Achieving MRD negativity is prognostically important. Currently, MRD assessment in MM patients is performed by direct methods (from bone marrow samples aimed at detecting tumor plasma cells) and indirect methods that focus on detecting M-protein released by the tumor into the blood and/or urine. Although indirect methods effectively monitor patients with active MM disease and are reliable, rapid and inexpensive, they lack the sensitivity to detect MRD. Modern and highly sensitive diagnostic methods for MRD rely on bone marrow testing to detect tumor cells. A new method, UV-HPLC analysis of plasma samples, capable of reliably detecting M-protein in MRD and, in addition, distinguishing their oligoclonal profile, represents an elegant and gentle tool for assessing response to MM treatment and for prognostic prediction of MM. It is

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also an indirect method. Our method is suitable even for more complex samples with multiple clones and allows individual clones to be matched or distinguished from each other. Our method is based on the principle of HPLC with UV detection, which distinguishes it from other protocols. The new method is particularly beneficial for the patient, as the MRD check will be less invasive and only a blood draw will be sufficient instead of a bone marrow collection. This less invasive monitoring is also associated with a possible increase in the interval of follow-ups, which could catch a relapse earlier than is currently the case, when patient follow-up is limited to a maximum number of bone marrow collections (approximately 1 per year). According to the tests performed, the new method is about 6 times more sensitive than immunofixation electrophoresis, which will allow better estimation of the depth of treatment response and earlier detection of relapse. It can distinguish pathological antibodies from therapeutic antibodies administered to the patient, which in some tested samples after treatment meant an incorrectly determined therapeutic response. It can also better handle oligoclonal profiles in samples and typify the M-proteins contained in them. It can identify original clones present before treatment or distinguish them from clones that appeared after treatment. All this from about 60 µl of serum. The method uses a common analytical instrument, which makes it easy to use and thus has the potential to replace standard immunofixation electrophoresis, avoiding invasive and problematic bone marrow aspiration and thus facilitating early detection of disease relapse due to the possibility of close patient monitoring at short intervals.

Commercial opportunity

MM represents about 10 % of all blood cancers. Its incidence in the Czech Republic is increasing from 6.3 to 18.8 living MM patients per 100,000 population in the period 1990-2014. The incidence of MM is higher in the Afro-Caribbean population. The global prevalence of MM is currently set at 0.7 %, which represents approximately 1 case in 132 individuals. The majority of MM patients are not cured (almost 50 %) and 100 % of patients relapse after treatment. Monitoring of patients is therefore very important. The method is now being prepared to complete full analytical and clinical validation according to Act No. 375/2022 Coll. on medical devices and in vitro diagnostic medical devices, which introduces the IVDR Regulation into Czech legislation. The validation will take place in the laboratory of the Department of Clinical Biochemistry and Diagnostics of the University Hospital Hradec Králové, as a laboratory of a healthcare facility compliant with EN ISO 15189. A minimum of 760 samples will be involved. This will increase

the commercialization potential of the methodology and reduce the risks for a potential investor who would finance the commercialization of the technology as an IVDR certified kit or as a SW for a chromatograph.