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Building predictive testing for multiple myeloma

By combining genomic testing and next generation sequencing technology, a new partnership aims to advance predictive tests for multiple myeloma (MM).

Dr Siobhan Glavey, RSCI

Multiple myeloma is a cancer of plasma cells in the bone marrow that normally produce antibodies to help fight infection. Approximately 250 patients are diagnosed with this condition in Ireland every year. Globally the incidence of this disease is rising, due to population growth, an ageing world population and a rise in age-specific incidence rates. Due to the complex nature of the disease, patients often require multidisciplinary medical input and myeloma drugs are amongst the highest cost therapies worldwide.

The study will be carried out at Beaumont Hospital Dublin and run through the Blood Cancer Network Ireland with several other cancer hospitals in Ireland participating. It represents a collaboration between Royal College of Surgeons Ireland (RCSI) University of Medicine and Health Sciences and SkylineDx with funding support from Amgen; Celgene, a Bristol Myers Squibb company; and Janssen.

Due to improvements in new treatments for multiple myeloma, the outlook for patients has greatly improved with survival times and treatment free intervals increasing. However, in 2020 multiple myeloma is still considered an incurable disease, with the majority of patients following a relapsing course and requiring further treatment to keep the disease at bay. According to the National Cancer Registry, Ireland the five-year survival of multiple myeloma patients is approximately 50%, in keeping with international best standards, but greater advances in therapy and knowledge of the disease is required to improve this figure.

Predicting the course of the disease and guiding treatment choice in newly diagnosed patients, is one of the major challenges in this cancer and currently available tests at diagnosis fall short of providing this information to patients and haematologists. Newly developed tests over the last number of years are helping to do this and one such example is minimal residual disease (MRD). This is a test performed on the patients DNA at diagnosis by Next Generation Sequencing (NGS), which can detect if there are trace amounts of the cancer remaining in a patient after treatment, and has been shown to be highly predictive of long-term outcomes in several studies. Another test that can help to predict patients outcomes has been developed by SkylineDx, which uses a novel gene expression based test to guide prognosis called the “MMprofiler”.

Genetic risk

At Beaumont and RCSI, in collaboration with SkylineDx, scientists have implemented these novel gene based tests SkylineDx for the testing of MM patients in order to guide prognosis. This test called MMprofiler with SKY92 establishes if patients have a high risk of relapsing and has been increasingly adopted in global clinical trials as a more predictive and robuster marker than older tests like fluorescence in-situ hybridisation (FISH). This study at RCSI and Beaumont aims to combine these two highly predictive modalities to provide a personalized medicine approach for patients.

This in-depth analysis of genetic risk could enable doctors to identify which patients are at high-risk of relapse after a stem cell transplant. With this knowledge, it may in the future be possible to refine treatment for individual patients based on their specific disease molecular signature.

“If our study can definitively determine which patients will benefit from certain treatments, and when, it will provide clinicians with invaluable information that will lead to better outcomes for patients with multiple myeloma.” said Dr Siobhan Glavey, honorary senior lecturer at RCSI, consultant haematologist at Beaumont Hospital and the project’s principal investigator.

“As we move toward personalised medicine, studies like ours will hopefully become more and more common and will help to target high cost effective therapies with greater precision. The study will initially enroll a small number of patients and follow them over time to test this theory.”

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