Toward personalised treatment for multiple sclerosis – Biomarkers for better diagnosis, prognosis and response-to-treatment evaluation

Experts at the Joint Congress of European Neurology reported that timely, accurate diagnosis of multiple sclerosis and early treatment with modern drugs can have a significant impact on the progression of the disease. Much work is being done to develop individualised therapy approaches, to use drugs in a more targeted way, and to avoid side effects more effectively. Biomarkers play an ever-increasing role in the management of the disease.

Istanbul, 2 June 2014 – “Multiple sclerosis is currently still incurable. Timely, accurate diagnosis and targeted early treatment using a growing number of modern drugs have been crucial factors behind the progress made recently in improving patients’ quality of life,” MS-expert Prof Aksel Siva from Istanbul University reported during the Joint Congress of European Neurology in Istanbul. “Important trends in our field include the constant expansion of therapeutic options, minimising the side effects of highly active substances or the use of biomarkers for diagnosis, prognosis and monitoring of treatment progress.”

According to epidemiological studies, about 600,000 Europeans and 2.8 million persons worldwide suffer from MS, an inflammatory, degenerative, progressive autoimmune disease. The increasing prevalence may result to a large extent from improved diagnostic capabilities. In young adults, MS is one of the most common neurological diseases leading to disability.

In addition to the development of new drugs, other key challenges in MS research are improved risk management of available substances and improved methods of early disease detection, according to Prof Siva: “Despite all the progress, we still lack important answers in MS therapy.” But a great number of research groups around the world are on track to meet those challenges. Indicative of this were the 10 scientific sessions and more than 200 new research papers at the European Joint Congress of Neurology that were devoted to MS. A much discussed topic was the increasing importance of biomarkers.

Growing role for biomarkers in diagnosis and prognosis

“With the increasing identification and use of biomarkers, a new and very promising chapter is opening in the management of MS,” Prof Siva said. “They help us greatly to quickly and non-invasively confirm or reject a diagnosis, to anticipate the outcome and to check whether or not the chosen therapy is effective in a particular patient.”

As far as diagnosis is concerned, although that recent data on of vitamin D serum levels, anti-myelin antibodies, or L-selectin are promising, more evidence is needed for understanding their role and potential contribution in MS. Cerebrospinal fluid inflammatory markers offer another example. According to a new study from the Czech Republic presented at the Congress, levels of beta-2-microglobulin and interleukin-8 in CSF were found to be significantly higher in MS patients as compared to controls. The results of another study discussed in Istanbul suggest that sIFNAR2 could also be a potential diagnostic biomarker of MS. The detection of iron in the brain by means of magnetic resonance imaging could further prove to be a new MS marker, as was demonstrated by an Austrian study presented at the Congress. It showed that iron accumulation increases rapidly in the brain of MS patients, especially in the early phases of the disease. “Research on the role of inflammatory and neurodegenerative markers in MS should certainly continue,” Prof Siva added.
Evaluating treatment response and minimising risks

Biomarkers are also increasingly used to monitor the individual response to therapy or to reduce the risk of side effects. “These are big steps towards personalised therapies that can be customised to a specific patient’s situation,” Prof Siva commented. There are many examples of the potential of biomarkers in this field. One such is the amount of natalizumab binding to mononuclear cells found in peripheral blood which can assess whether or not a patient responds to the monoclonal antibody natalizumab. A marker for the chances that cladribine will actually reduce disease activity is the activity measured before treatment. A large international study funded by the European Union was presented at the Istanbul Congress which showed that a number of serum markers such as CD40L, Eotaxin or IL-8 can predict the response to intaferon beta treatment.

MS-treatments now available can have significantly wide adverse effects ranging from bradycardia (reduced heart rate) or immune mediated thyroid disease to progressive multifocal leukoencephalopathy (PML), a dangerous viral infection. “This is why these drugs should be used in a targeted way, in patients for whom they can really bring benefits,” said Prof Siva. “A lot of work therefore is being done to identify biomarkers that can reliably predict not only the efficacy of treatment, but also the side effects that can be expected, so that the risks and benefits can be weighed up for each case.”

With the discovery of antibodies to the JC virus, for example, the number of PML cases in MS-patients under natalizumab therapy could be reduced. A new study presented at the Istanbul Congress further demonstrated the complementary value of a CSF JCV antibody index in the diagnosis of natalizumab-associated PML.

Currently the expanding research in the field of molecular biology and genetics including omics technologies such as genomics and proteomics, and the intensive research with microRNAs are likely to provide new answers and a much better understanding of MS pathophysiology and its management.

Data on new and established substances

The many innovations in improving diagnosis and monitoring of the disease as well as in personalising its treatment become even more important with the constant expansion of the therapeutic range, Prof Siva pointed out. “Many new treatment options are emerging, and there is justified optimism that we will be able to help people with MS more quickly and more effectively in the future.”

A broad range of study results were presented at the Joint Congress of European Neurology on the safety or efficacy of newly approved substances such as teriflunomid, dimethyl fumerate or alemtuzumab. Other papers centred on established therapies and their individualised application. Results on new monoclonal antibodies such as ofatumumab, ocrelizumab or daclizumab were also on the agenda of the Istanbul Congress.

Sources:
Congress-Abstracts Giovannoni, Biomarkers (including predictors/MRI); Comi, Future therapeutic strategies, Støersen, Therapeutic antibodies in the treatment of MS; Hegen et al, Serum biomarkers predict IFNb treatment response in patients with multiple sclerosis; Khalil et al, Dynamics of brain iron accumulation differ between clinically isolated syndrome and multiple sclerosis: a longitudinal 3T MRI study; Pichler et al, Longitudinal changes of global and compartmental brain atrophy in patients with clinically isolated syndrome and clinically definite multiple sclerosis using 3-Tesla magnetic resonance imaging; Warnke et al, The CSF JCV antibody index for diagnosis of natalizumab-associated PML;
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