Treating Clinically Isolated Syndrome – the long game

Jeremy Chataway Queen Square Multiple Sclerosis Centre, Department of Neuroinflammation, UCL Institute of Neurology, University College London, London, WC1B 5EH, UK.

j.chataway@ucl.ac.uk

Summary/abstract

This study demonstrates the durability of beta-interferon in reducing the conversion rate of a first clinical demyelinating event to clinical definite multiple sclerosis, with both 3 and 5 year data.

One of the fundamental tasks in the inflammatory arena is to prevent the conversion of a Whilst there are many theories, over many years, the exact cause of multiple sclerosis (MS) is unknown. Despite having to peer through this mist, unparalled advances have been made over the last 2 decades with transformative treatments, usually with an anti-inflammatory basis. Yet if treatment could begin at the earliest of manifestations, then logic would dictate a better outcome. The clinically isolated syndrome (CIS) is this first point in the graph. Studies stretching over 20 years have given indicative conversion rates to clinically definite MS (CDMS) of the order of 60%, but ranging from 20-80% depending on the original MRI appearance.[1]

A suite of studies, commencing with the original injectable agents, before moving onto more recent oral drugs, have convincing shown a significant reduction in that conversion to clinically definite MS (CDMS). Of course, they were the therapeutic first pass and had relatively short follow-up. MS lasts for many decades and to have information about a longer time period would be of immense value.

In this edition of the JNNP more data is in, in the form of the REFLEXION study, the child of the original 2 year REFLEX study.[2] Those CIS patients, who had not converted to CDMS over the course of the REFLEX study (placebo or active arms), as well as those who had developed CDMS, were dosed with subcutaneous beta-interferon 1a, 44mcg once or three times per week and followed for 5 years. The primary endpoint was the proportion with CDMS at 3 years, then secondarily 5 years, as well as much other clinical, safety and MRI information.

Overall 80% of the original REFLEX cohort took part (402/517) and 90% lasted to 5 years. They seem a typical population: mean age of 30 years, majority female, a low disability score and 40% with some enhancing MRI activity. Figure 3 gives the top-line information, with 27% reaching CDMS (cumulative probability) at year 3 if actively treated from start versus 40% if delayed (ie, the original placebo arm), with some coalescing of figures at 5 years (increasing to 40% versus 45%). Paired with this, was reduction in MRI activity and an advantage with the three over once/week dosing schedule.

The authors should be congratulated on their fortitude in holding on to such a large portion of the original cohort, a very difficult task, but one which is immensely valuable. We look forward to 10 year data, and to further advances which can reduce further the long-term conversion rate to CDMS.

References

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Conflicts of interest

JC declares none relevant to this article

Jeremy Chataway Queen Square Multiple Sclerosis Centre, Department of Neuroinflammation, UCL Institute of Neurology, University College London, London, WC1B 5EH, UK.