MULTIPLE SCLEROSIS

Benefits of alemtuzumab in MS

The anti-CD52 monoclonal antibody alemtuzumab consistently outperforms interferon β 1a (IFN- β 1a) across a range of multiple sclerosis (MS) patient subgroups in terms of freedom from clinical disease activity and reduction of disability, a post-hoc analysis of the CAMMS223 study has revealed.

CAMMS223, the results of which were first published in 2008, was a randomized, controlled, rater-blinded phase II clinical trial conducted over a 3-year period in 334 patients with early, active relapsing–remitting MS (RRMS). The lead author of the new study, Alasdair Coles from the Department of Clinical Neurosciences, University of Cambridge, UK, was one of the original investigators on CAMMS223. “Alemtuzumab reduced the relapse rate by 71% and the risk of accumulation of disability by 74% compared to IFN- β 1a,” he explains. “An unprecedented result was that the mean disability of alemtuzumab-treated patients was improved at 3 years compared with baseline, with continued worsening of disability in the IFN- β 1a-treated patients.”

For their new analysis, published in *The Lancet Neurology*, Coles and colleagues revisited their data from the CAMMS223 study and asked whether any subgroups of patients in particular benefitted from alemtuzumab. They examined the influence of several factors, including age, disease duration, relapse history, and fixed disability or brain atrophy, on the efficacy of alemtuzumab.

The researchers employed a composite end point, ‘freedom from clinical disease activity’. It combines reduction in relapse rate with risk of sustained accumulation of disability, which were the two end points used in CAMMS223. They also introduced a new outcome measure, ‘sustained reduction of disability’ (SRD), which Coles defines as “an improvement in an individual patient’s change in disability from baseline of one or more Expanded Disability Status Scale (EDSS) points that is sustained for 6 months.”

In terms of halting clinical disease activity, alemtuzumab was found to be more effective than IFN- β 1a across all patient subgroups. In addition, SRD was almost twice as likely to be achieved in patients treated with alemtuzumab than in those treated with IFN- β 1a. “We hope that acceptance of SRD will raise expectations for what can be achieved with an effective MS therapy,” says Coles.

The mechanisms through which alemtuzumab treatment reduces disability in patients with MS remain to be clarified. Coles and his colleagues hypothesize that the observed improvements in EDSS scores could go beyond suppression of disease activity into the realms of brain tissue repair, and they are currently using imaging techniques to explore this possibility.

The efficacy and safety of alemtuzumab in patients with RRMS is now being explored further in two phase III studies, CARE-MS I and CARE-MS II. CARE-MS I is being conducted in treatment-naïve patients, whereas CARE-MS II has recruited patients who have previously experienced MS relapse on disease-modifying therapy. “The results of these studies will provide the basis for seeking approval for alemtuzumab as a therapy for MS,” says Coles. “The identification of markers of greater risk for safety concerns will be an important area for additional research.”

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Original article Coles, A. J. *et al.* Alemtuzumab versus interferon beta-1a in early relapsing–remitting multiple sclerosis: post-hoc and subset analyses of clinical efficacy outcomes. *Lancet Neurol.* **10**, 338–348 (2011)