New hope for multiple sclerosis sufferers

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A drug which was developed in Cambridge and initially designed to treat a form of leukaemia has also proven effective against combating the debilitating neurological disease multiple sclerosis (MS).

The study, led by researchers from the University of Cambridge, has found that alemtuzumab not only stops MS from advancing in patients with early stage active relapsing-remitting multiple sclerosis (RRMS) but may also restore lost function caused by the disease. The findings were published today in the *New England Journal of Medicine*.

Alemtuzumab has a long connection with Cambridge, England. In 1984, Cambridge scientist Cesar Milstein was awarded the Nobel Prize for Physiology or Medicine, jointly with George Kohler, for inventing the technology to make large quantities of a desired type of monoclonal antibody. Further work in Cambridge, by Herman Waldmann and Greg Winter, led to the production of the first humanised monoclonal antibody for use as a medicine, Campath-1H, now known as alemtuzumab. It has been licensed for the treatment of chronic lymphocytic leukaemia, and has also been tested in several diseases where the immune system is overactive, such as multiple sclerosis.

The new study, which was funded by Genzyme and Bayer Schering Pharma AG, Germany , found that alemtuzumab reduces the number of attacks experienced by people with relapsing-remitting multiple sclerosis by 74 per cent over and above that achieved with interferon beta-1a, one of the most effective licensed therapies for similar cases of MS. More importantly, alemtuzumab also reduced the risk of sustained

accumulation of disability by 71 per cent compared to interferon beta-1a.

Additionally, the investigators showed that many individuals in the trial who received alemtuzumab recovered some of their lost functions and so were less disabled after three years than at the beginning of the study, in contrast to worsening disability in the interferon beta-1a treated patients. These findings suggest that alemtuzumab may allow damaged brain tissue to repair, enabling the recovery of neurologic functions lost following poor recovery from previous MS attacks.

The new research shows that alemtuzumab is a much more effective treatment for early-stage RRMS than the currently approved drug interferon beta-1a. However, as the study was a Phase 2 clinical trial, additional research will need to be conducted before the drug is considered for approval in the treatment of MS.

"Alemtuzumab is the most promising experimental drug for the treatment of multiple sclerosis, and we are hopeful that the Phase 3 trials will confirm that it can both stabilize and allow some recovery of what had previously been assumed to be irreversible disabilities," says the principal investigator Alastair Compston, Professor of Neurology and the Head of the Department of Clinical Neurosciences at the University of Cambridge.

Multiple sclerosis is an autoimmune disease which is caused by the body's immune system attacking nerve fibres and their protective insulation, the myelin sheath, in the central nervous system. This damage prevents the nerves from 'firing' properly, and then leads to their destruction, resulting in physical and intellectual disabilities. Alemtuzumab works by destroying one population of white blood cell (lymphocytes) and, by shutting down the immune system, inhibits the damage to brain tissue that occurs in MS.

"The ability of an MS drug to promote brain repair is unprecedented. We are witnessing a drug which, if given early enough, might effectively stop the advancement of the disease and also restore lost function by promoting repair of the damaged brain tissue," says Dr Alasdair Coles, University Lecturer at the Department of Clinical Neurosciences, University of Cambridge who coordinated many aspects of the study.

The main side effect of treatment is, paradoxically, that people can develop other autoimmune diseases as the immune system gradually recovers following exposure to alemtuzumab. During the trial, 20% of people treated with alemtuzumab developed an over- or under-active thyroid gland. Rarely (3%) people developed a low platelet count and were vulnerable to bleeding. This complication led to one fatality during the trial. Although potentially very serious, this complication can be easily treated if recognised early.

The Phase 2 clinical study involved 334 patients who had been diagnosed with early-stage RRMS but had not previously been treated. Patients either received alemtuzumab (one of two dose levels intravenously for five days initially and three days of re-treatment 12 months later) or interferon beta-1a (given by injection three times per week). The patients were followed for three years to determine the efficacy of the treatments as well as the effect on the patients' disabilities.

MS affects almost 100,000 people in the United Kingdom, 400,000 in the United States and several million worldwide. Symptoms of the disease can include loss of physical skills, sensation, vision, bladder control, and intellectual abilities.

Source: University of Cambridge