Alemtuzumab (Campath)
We hope you find the information in this factsheet helpful. If you would like to speak with someone about any aspect of MS, contact the MS Trust information team and they will help find answers to your questions.

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Freephone 0800 032 3839 (Lines are open Monday - Friday 9am-5pm)

email infoteam@mstrust.org.uk

write MS Trust
Spirella Building
Letchworth Garden City
SG6 4ET
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This factsheet is written for anyone affected by MS who needs basic information about alemtuzumab (Campath). It is not intended as a full guide, and should be used only to support discussion with a neurologist or MS nurse.

1. What is alemtuzumab?
Alemtuzumab is an experimental drug treatment that is currently being tested in clinical trials for people with relapsing remitting MS. Although alemtuzumab is not currently licensed for use in MS, it is licensed for use in B-cell chronic lymphocytic leukaemia, a type of cancer.

2. How does alemtuzumab work?
Alemtuzumab is a humanised monoclonal antibody. Antibodies are proteins produced by the immune system to fight foreign substances, such as infections. Monoclonal antibodies can be produced in large quantities in cell culture in a laboratory and can be designed to bind to proteins on the body’s normal cells, altering the immune response.

Alemtuzumab acts by killing T-cells which form part of the immune system. In multiple sclerosis T-cells mistakenly attack myelin and cause the inflammation seen on MRI scans. It is thought that the T-cells that regenerate following treatment with alemtuzumab do not include the subset which destroys myelin.
3. Trials of alemtuzumab in MS

The first clinical trials of alemtuzumab tested the treatment in both relapsing remitting and secondary progressive MS. In people with relapsing remitting MS alemtuzumab was shown to reduce the numbers of relapses experienced and improved disability levels immediately. Improvement in disability continued to be seen for up to three years after treatment. However, more mixed results were seen in the 25 people with secondary progressive MS. Although MRI scans over a seven year period showed no new lesions had formed in the brain and spinal cords of those participants who were treated with alemtuzumab, they still continued to accrue disability. This led researchers to hypothesise that something other than effect of inflammation is at work in progressive MS\(^1\). Subsequent trials have focused on whether alemtuzumab works best if used in the early stages of relapsing remitting MS.

Results from a phase II trial* of alemtuzumab (known as CAMMS-223) were published in October 2008\(^2\). The study enrolled 334 people with active, early relapsing remitting MS, and compared two different doses of alemtuzumab to a high dose of beta interferon 1a (one of the treatments currently licensed for relapsing remitting MS). Participants were randomised to receive either high-dose alemtuzumab, low-dose alemtuzumab, or beta interferon 1a.

Alemtuzumab was administered via a course of annual infusions: at the first treatment it was given daily for five consecutive days, then 12 months later it was given daily for three days. A third course of three infusions were planned after a further 12 months, but not all participants received their third course due to safety concerns (see section 4). Beta interferon 1a was self-administered three times a week by subcutaneous (under the skin) injection. Everyone on the trial received intravenous steroids (methylprednisolone) for three days every 12 months.

The results showed that people receiving alemtuzumab experienced significantly fewer relapses than those receiving beta interferon 1a over the course of the trial. At three years, 77% of those on low-dose and 84% on high-dose alemtuzumab had experienced no relapses compared with 52% of those on beta interferon 1a\(^2\).
The results also showed that compared with beta interferon 1a, alemtuzumab reduced the risk of sustained disability by 71%. Although some people on the trial only received two courses of the drug rather than the three originally planned, results from the full trial could still be collated as enough patients had received the full three courses of alemtuzumab.

Five-year follow up data from this study was presented at the Annual Meeting of the American Academy of Neurology in April 2011. It showed that nearly two-thirds of those receiving alemtuzumab remained free of clinically active disease (defined as both relapse-free and with no sustained increase in disability as measured by the Expanded Disability Status Scale) up to four years after their last course of treatment, compared to 27% of patients receiving beta interferon 1a\(^3\). However, people on either drug whose MS had worsened in the first few years were excluded from the follow-up studies.

4. Side effects and contraindications

A low blood platelet count was seen in 3% of the trial participants. Although potentially serious, this is treatable if caught early enough. However, the use of alemtuzumab in the phase II trial was temporarily suspended in September 2004 following the death of one of the participants from idiopathic thrombocytopenic purpura (ITP). ITP is a blood clotting disorder caused by low numbers of platelets in the blood, symptoms include purple bruises on the skin and in the mouth, but it can also cause internal bleeding. Following the fatality, strategies were put in place to ensure that all future cases of ITP were recognised early. However, ITP remains a significant risk.

22.6% of the trial participants developed thyroid-related side effects, some more serious than others. These are treatable but can mean lifelong thyroid medication is required.

Flu-like symptoms after infusion were also reported. As alemtuzumab works by suppressing the immune system, anyone on treatment will be more vulnerable to infections such as colds and viruses for some time after the infusion.
The published results of the phase II research discussed the issues associated with treating people in the early stages of MS: "Although our study suggests that alemtuzumab is more effective than interferon beta 1a when given at the earliest stages of relapsing remitting multiple sclerosis, our findings raise the difficult issue of exposing young adults who have little disability to a drug having potentially serious adverse effects. Our trial was not powered to assess the long-term safety of alemtuzumab, nor was it powered to detect uncommon adverse events."²

5. Current trials in MS
A phase III trial known as CARE-MS1 (Comparison of alemtuzumab and Rebif efficacy in MS, Study I) comparing the lower dose of alemtuzumab used in the phase II study with beta interferon 1a over a two year period began in the UK and the USA in 2007. This trial is also known as CAMMS-323. This trial is fully recruited and is expected to be completed in mid-2011⁴.

A second study, CARE-MS2, is comparing two doses of alemtuzumab with beta interferon 1a in 200 people who have continued to experience relapses whilst on one of the licensed disease modifying therapies (Avonex, Betaferon, Copaxone or Rebif). This trial is also known as CAMMS-324. This trial is also fully recruited and is expected to be completed in late-2011⁵.

A subset of the patients in the CAMMS-324 study will receive further testing in a study, known as Comparison of Campath and Rebif treatment on cognition in multiple sclerosis⁶, designed to investigate how well alemtuzumab and interferon beta 1a work in treating MS-related cognitive problems (eg attention, memory, speed of thinking). This study is expected to be completed in late-2011. Results of the above three trials are expected in late-2011 to mid-2012.

There are also a series of three year extension studies of the following trials: CAMMS-223, CAMMS-323 and CAMMS-324, which will examine the long-term safety and efficacy of alemtuzumab and to determine if and when further treatment with alemtuzumab is needed⁷.
6. References

3. Author unknown. [P06-003] More alemtuzumab relapsing-remitting Multiple sclerosis patients are free of clinical disease activity at five years. AAN 63rd Annual Meeting; 2011 April 9-16; Hawaii, USA.
4. CARE-MS1 ClinicalTrials.gov website: http://clinicaltrials.gov/show/NCT00530348
5. CARE-MS2 ClinicalTrials.gov website: http://clinicaltrials.gov/show/NCT00548405
7. An extension protocol for MS patients who participated in Genzyme-sponsored studies of alemtuzumab ClinicalTrials.gov website: http://clinicaltrials.gov/show/NCT00930553

* Note - Drug trials
Phase I studies primarily assess the safety of a drug or procedure. They usually involve a small number of healthy volunteers (10-100) all of whom are given the same treatment.

Once a medical intervention has been proven safe, phase II trials test its effectiveness and whether it has the potential to be of benefit. These trials are larger, typically involving 100-300 people with the condition for which the intervention has been developed - in this case MS.

If the phase II study shows the treatment to be beneficial, phase III studies are conducted to gain a definitive understanding of the effectiveness, benefits and potential side effects in a large group of people (300-3,000) with the condition to be treated. Interventions have to successfully complete a phase III trial before they can be considered for a licence by regulatory authorities.

Please contact the MS Trust Information Team if you would like any further information about reference sources used in the production of this publication.