Information Sheet

MSIreland
THE MULTIPLE SCLEROSIS SOCIETY OF IRELAND

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Lemtrada (Alemtuzumab)

What is Lemtrada?

Lemtrada is a treatment for active and very active relapsing remitting MS.

How does Lemtrada work?

The drug works by targeting a protein called CD52 which is found on the surface of certain immune cells. It acts by binding to the surface of these cells ultimately killing them. For that reason, it is called a cell depleting antibody. By killing immune cells (certain B lymphocytes), it prevents these cells during inflammation from crossing into the brain and attacking the myelin sheath which protects our nerves.

How is Lemtrada given?

In clinical trials, Lemtrada has been given by intravenous (iv.) infusion once per year. In year one, as an infusion administered over 5 consecutive days and in following years as an infusion administered over 3 consecutive days. Exact dosage will not be known until licensing.

How does it compare to current therapies?

Lemtrada was more successful at reducing the relapse rate and accumulation of disability compared with beta-interferon and appeared to be a more effective treatment. Despite this, Lemtrada was associated with a number of side effects that beta-interferon was not associated with.

What side effects are associated with Lemtrada?

In clinical trials, both adverse events and side effects were noted. Common adverse events were infusion-associated reactions, the symptoms of which most commonly included headache, rash, nausea, fever, itching, insomnia, and fatigue.
Lemtrada causes immunosuppression, therefore infections were common. The most common infections included upper respiratory and urinary tract infections, sinusitis and herpes simplex infections. Infections were predominantly mild to moderate in severity.

Two significant side effects have occurred during Lemtrada treatment: • idiopathic thrombocytopenic purpura (ITP), a disorder that prevents blood from clotting, was fatal in one case, has affected 1-3% of participants • overactive thyroid gland (Grave's disease) or abnormal thyroid function, affecting 20-30% of participants Additional safety measures are being taken to allow early diagnosis and treatment of these side effects.

What are the results of Lemtrada in Clinical Trials?

In MS, Lemtrada has been studied for almost 20 years (then called Campath), it is also licensed for use in B-cell chronic lymphocytic leukaemia, a type of cancer. The early clinical trials of Lemtrada were run in both relapsing and progressive types of MS. In people with relapsing remitting MS, Lemtrada reduced the numbers of relapses that people experienced and improved their disability levels immediately. More mixed results were seen in a study with secondary progressive MS.

Further research – The CAMMS 223 trial

Results from a Phase II trial (CAMMS 223) were published in the New England Journal of Medicine in October 2008. This study enrolled 334 people with active, early relapsing remitting MS, and compared two doses of Lemtrada with a high dose of beta interferon 1a.The results showed that people receiving both doses of Lemtrada performed significantly better comparing the number of relapses at the end of the trial. At three years, 77% of low-dose Lemtrada and 84% of high-dose Lemtrada recipients had experienced no relapses, compared with 52% of people receiving beta interferon 1a. The results also show that compared with beta interferon 1a, Lemtrada reduced the risk of sustained disability by 71%. At four years, the data indicated that around 71% of people treated with Lemtrada remained free of disease activity up to three years after their last course of treatment. Furthermore, around 91% of people receiving Lemtrada showed no worsening of their disability compared to 68% of people taking Rebiferon.

CAMMS 223 trial's 5 year follow up was published in March 2012 edition of Neurology. At five years, data showed that 65% of those receiving Lemtrada remained free of clinically active disease (defined as both relapse-free and with no sustained increase in disability) up to four years after their last course of treatment, compared to 27% of patients receiving beta interferon 1a. However, participants on either drug in whom their MS had worsened in the first few years were excluded from the follow-up studies

Further Research – The CAMMS 323 and 324 trials

Results of two larger phase III studies were announced in 2011. CAMMS 323 (also called CARE-MS I), a phase III trial compared Lemtrada with interferon beta 1a (Rebif) in 581 people with relapsing remitting MS who had received no prior MS therapy. Lemtrada reduced relapses by 55% compared to interferon beta 1a over the two years of the trial. The effect on disease progression was similar, with 8% of the Lemtrada group and 11% of interferon beta group showing a sustained worsening in their disability. CAMMS 324 (also called CARE-MS II), also a phase III trial, compared Lemtrada with beta interferon 1a (Rebif) in 840 people who had experienced at least one relapse whilst taking a disease modifying therapy. Over the course of the two year study, Lemtrada reduced relapse rates by 49% compared to beta interferon 1a. There was also a 42% reduction in risk of worsening disability. Using a subset of participants of the CAMMS 324 trial, a comparison study of Lemtrada and beta interferon 1a (Rebif) on Cognition in MS, is being undertaken. The study is designed to investigate how well Lemtrada and Rebif work in treating MS-related cognitive problems (e.g., attention, memory, speed of thinking). Extension studies of the CAMMS 223,

323, 324 trials will examine long-term safety and efficacy of Lemtrada and determine if and when further Lemtrada treatment is needed, and the safety and efficacy of this treatment.

How is Lemtrada funded?

Lemtrada is funded through individual hospital budgets.

For more information please see our *'Access to Medicines Campaign Handbook'* which is available on the publications section of our website -

http://www.ms-society.ie/pages/living-with-ms/information-centre/our-publications

Further Information Links to further information on Lemtrada

Genzyme Lemtrada Press Releases:

April 24th 2012 http://en.sanofi.com/Images/30261_20120424_GENZYMECARE-MS-II_en.pdf

and

http://en.sanofi.com/Images/30230_20120420_GENZYME_en.pdf

April 20th 2012 http://en.sanofi.com/Images/30230_20120420_GENZYME_en.pdf

November 14th 2011 http://en.sanofi.com/Images/29137_20111114_CARE_en.pdf

October 22nd http://en.sanofi.com/Images/28988_20111022_Alemtuzumab_en.pdf Multiple Sclerosis Resource Centre Alemtuzumab (Lemtrada)
http://www.msrc.co.uk/index.cfm/fuseaction/show/pageid/1307 MS Trust Alemtuzumab
http://www.mstrust.co.uk/research/drugsindevelopment/alemtuzumab.jsp
http://www.mstrust.co.uk/information/publications/factsheets/campath.jsp MS Society UK Alemtuzumab http://www.mssociety.org.uk/ms-research/new-and-potentialtreatments/alemtuzumab-campath Neurology Alemtuzumab more effective than interferon β-1a at 5-year follow-up of CAMMS223 Clinical Trial
http://www.neurology.org/content/78/14/1069 For more information on the trials CAMS 223
http://clinicaltrials.gov/show/NCT00050778 Care MS 1
http://clinicaltrials.gov/show/NCT00530348 Care MS 2
http://clinicaltrials.gov/show/NCT00548405 Extension
http://clinicaltrials.gov/show/NCT00930553 Cognition
http://clinicaltrials.gov/show/NCT00914758

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