Alemtuzumab (Lemtrada®)

Lemtrada is a monoclonal antibody that binds to cells expressing CD52, which results in depletion of most of the body's adaptive immune cells in the blood (white blood cells). These cells slowly recover over many months to years. Alemtuzumab is given by an IV infusion over several hours, once daily for 5 days in a row. The next infusions occur 52 weeks later and are given for 3 days in a row. After this, the drug is only re-dosed if the patient has new MS attacks and/or new MRI lesions.

Clinical Research: At 8 years, 44% of CARE MS II patients had only received the first 2 courses. 29% received a 3rd course, 16% received a 4th course, and 6% received a 5th course. Efficacy: CARE MS II studied Alemtuzumab vs. Interferon Beta 1a (Rebif) in RRMS patients with breakthrough disease despite prior disease modifying therapy. These patients most closely match the US label. Relapses: Compared to Rebif, Alemtuzumab patients had 49% relative risk reduction attacks (annualized relapse rate/ARR). Disability: Compared to Rebif patients, Alemtuzumab treated patients had a 42% relative risk reduction (p=0.0084) for 6 month sustained disability progression at two years (p=0.0084). NEDA: At two years, 32% of Alemtuzumab patients achieved no evidence of disease activity (NEDA). At the 6-year follow up, 56% of patients required another course of therapy or other DMT and 70% of patients had unchanged or improved neurological examinations. CDI (Confirmed disability Improvements): At 8 years 47% of Alemtuzumab patients experienced 6-month CDI. 8 year Long Term Efficacy: We now have 8 year long-term follow up data on MS patients who participated in the CARE MS II trial and continued in the extension arm (TOPAZ). At 8 years, annualized relapse rate was 0.18, 70% of patients had stable or improved EDSS, 53%-60% had experienced NEDA, 70% had no new or enlarged T2 MRI lesions, 89% had no new gad enhancing lesions, 86%-93% had no new T1 black holes. The median annual brain volume loss was -0.19. All of this occurred despite the fact that 44% of cohort never had additional treatment after the initial 2 courses of Alemtuzumab.

What to expect during the infusions: Patients will first receive IV steroids, IV fluids and several pre-treatment pills (Benadryl, Claritin, Tylenol) the hour before starting Alemtuzumab. Then alemtuzumab is infused over a minimum of 4 hours. Halfway through the infusion more medications (Benadryl, Claritin and Tylenol) are given again. After the Alemtuzumab infusions, the patient may receive more IV fluids for the post infusion observation period.

Infusion Reactions: Infusion reactions are very common (up to 92% of patients) during Alemtuzumab administration. This can include chills, rigor, headaches, nausea, chest tightness, shortness of breath, slow or fast heart rate, and even transient neurological symptoms. There have been two cases of anaphylaxis with Alemtuzumab infusions. We will give you medications to minimize these reactions. Cases of pulmonary alveolar hemorrhage have been reported within 48 hours of Alemtuzumab infusion. Cases of severe, including fatal, neutropenia have been reported within 2 months of Alemtuzumab infusion. Some cases resolved with treatment. Serious and life-threatening strokes have been reported within 3 days of infusion, most occurring within 1 day. Cases of cervico-cephalic arterial dissection have been reported within 3 days of Alemtuzumab infusion.

Medications taken after the infusions: After the course of Alemtuzumab (either 5 or 3 days in a row) the patient takes an oral prednisone taper for a few days, as well as a single pill of Diflucan. Starting on the 1st day of the 1st infusion, patients take Acyclovir 400mg twice daily. Acyclovir must be continued for a full year after their last infusion of Alemtuzumab.

Monthly lab testing: After receiving Alemtuzumab, patients are required to have monthly blood and urine tests to screen for immune thrombocytopenia (ITP), thyroid dysfunction, and/or liver and kidney dysfunction.

Yearly examinations: In addition to seeing the MS neurologists, patients treated with Alemtuzumab will need an annual skin examination and neck examination (thyroid) performed by their dermatologist or PCP. Women will also require an annual pap smear.

Alemtuzumab Side Effects: *Immune Thrombocytopenia*: There is a 2% chance of developing immune thrombocytopenia (ITP), a disorder that causes platelets to be destroyed and can lead to easy bruising, petechiae (a red rash) or bleeding from mucus membranes. If you develop any of these symptoms contact your MS neurologist immediately. There was one death from ITP before the current monitoring program was put into place. All Alemtuzumab treated patients must have a monthly blood test to check their platelet count for four years after their last dose. Other Autoimmune Cytopenias: Autoimmune cytopenias including neutropenia (0.1%), hemolytic anemia (0.3%), and pancytopenia (0.2%) have occurred in Alemtuzumab-treated patients. Blood cell counts are monitored monthly for cytopenias. Prompt medical intervention is indicated if a cytopenia is confirmed. Immune System Disorders: Rare cases of vasculitis, Guillain-Barre syndrome, and hemophagocytic lympho- histiocytosis have been reported. Kidney disorders (Goodpasture's syndrome, nephrotic syndrome): 0.3% risk of developing a kidney problem. If you develop swollen legs or stop making urine, contact your MS neurologist immediately. Patients must have a monthly blood test and a monthly urine test to assess kidney function for 4 years after their last dose. Thyroid Disorder: There is a 36.8% risk of developing a thyroid problem (grave's disease, hyper functional multinodular goiter, hyper-functional adenoma of thyroid, thyroiditis). The highest risk of thyroid disorders are 3 years after your 1st dose. Patients must have a yearly neck (thyroid) examination and a blood test will be monitored for 4 years after their last dose.

Infections: Lemtrada likely increases the risk for a more severe COVID19 infection for several years following each infusion. Patients are at slightly increased risk for infections (nasopharyngitis, URI, pharyngitis sinusitis, bronchitis, pneumonitis, oral herpes, influenza, herpes Zoster, gastroenteritis, UTI, candidiasis). There was one death from sepsis. Because of the increased risk of herpes zoster ("shingles") patients must take acyclovir 400mg twice daily for up to a year after their last dose. Serious, sometimes fatal, opportunistic infections have been reported in patients taking Alemtuzumab including aspergillosis, coccidioidomycosis, histoplasmosis, Pneumocystis jirovecii pneumonia, nocardiosis and cytomegalovirus infections. Listeria: Listeria infections including fatal cases of Listeria meningoencephalitis have occurred in Alemtuzumab treated patients. These cases have occurred as early as 3 days after treatment and up to 8 months after the last dose. Alemtuzumab treated patients should avoid or adequately heat foods that are potential sources of Listeria (deli meat, dairy products made with unpasteurized milk, soft cheeses, or undercooked meat, seafood, or poultry). Patients should avoid these potential sources prior to starting Alemtuzumab. Listeria can incubate in the body between 3 to 70 days. Symptoms include fever, chills, diarrhea, nausea, vomiting, headache, joint and muscle pain, neck stiffness, difficulty walking, mental status changes, coma, and other neurologic changes.

Thyroid Cancer: To date there have been 6 cases of stage I papillary thyroid cancer. If you feel a new lump or swelling in your neck, pain in the front of your neck, change in your voice, trouble swallowing, cough or trouble breathing you must contact your MS neurologist immediately.

Melanoma: To date there have been 5 cases of melanoma or melanoma in situ. If you notice a change in your moles contact your MS neurologist immediately. Patients must have an annual skin examination by their PCP or dermatologist once annually for 4 years after their last dose.

Lymphoproliferative disorders (lymphoma, Castleman's syndrome): To date there have been 4 cases of lymphoproliferative disorders.

Autoimmune hepatitis: Autoimmune hepatitis causing significant liver injury, including acute liver failure requiring transplant, has been reported in patients treated with Alemtuzumab. Alemtuzumab treated patients should have liver function tests performed prior to starting treatment and then periodically after for 4 years.

Acute Acalculous Cholecystitis: There is a 0.2% chance of developing acute acalculous cholecystitis with Alemtuzumab treatment. Onset of symptoms ranged from less than 24 hours to 2 months after infusion. Symptoms include abdominal pain, abdominal tenderness, fever, nausea, and vomiting.

Pneumonitis: There is a 0.5% chance of developing pneumonitis with alemtuzumab treatment. Symptoms include shortness of breath, cough wheezing, chest pain or tightness, and hemoptysis.

Immunizations and Vaccinations: Alemtuzumab treated patients should NOT receive live attenuated vaccinations. Any such vaccination must be administered 6 weeks before their next infusion and only after checking with your MS neurologist first.

Pregnancy: Women of childbearing potential must agree to use contraception and avoid pregnancy for at least 4 months after their last dose, and only after clearance from their MS neurologist