

LAQUINIMOD: A NEW ORAL IMMUNOMODULATOR FOR THE TREATMENT OF RELAPSING-REMITTING MULTIPLE SCLEROSIS

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Laquinimod is a novel oral, once-daily immunomodulator which is currently in advanced stages of clinical development for the treatment of relapsing-remitting multiple sclerosis (RRMS). Laquinimod was demonstrated to be effective in various experimental autoimmune encephalomyelitis models. The ameliorating activity of laquinimod is mediated by various effects, modulating the immune system away from its typical disease properties. These include effects seen on cytokine profile, leukocytes infiltration to inflamed tissues and antigen presentation. Neuroprotective effects were demonstrated by reduced spinal cord demyelination and axonal loss in MS animal models.

The effects of oral daily 0.6 mg laquinimod on MRI-monitored disease activity were assessed in a 36-week, double-blind, Phase II placebo-controlled study. The 0.6mg dose showed a robust effect on MRI parameters [50% reduction of mean cumulative number (weeks 12-36) of new-T2 lesions ($p=0.0001$) (55% effect on median number) as well as a 50% reduction in the mean cumulative number (weeks 24-36) of new T1-hypointense lesions ($p=0.0064$)]. The 0.6mg dose also showed a 33% reduction of annualized relapse rate ($p=0.0978$). The rate of adverse events was similar in all treatment groups. Liver enzymes were elevated in a dose-dependent manner, reversible in all cases, without accompanying bilirubinemia. The efficacy profile was reproduced and sustained in an additional 36-weeks double-blind active extension study and there were no new safety signals. This Phase II study was further extended in an open label manner for additional 24 months, with patients demonstrating no safety signals suggestive of immunosuppression and sustained effect on MRI activity.

Based on these encouraging results, two global phase III studies with 0.6mg laquinimod in RRMS patients were launched, enrolling more than 2200 patients worldwide, and are about to be completed during 2011.