ORAL LAQUINIMOD FOR RELAPSING-REMITTING MULTIPLE SCLEROSIS: INSIGHTS INTO MECHANISM OF ACTION AND RECENT CLINICAL DATA

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Laquinimod is a novel oral, once-daily immunomodulator with CNS protective properties, currently in advanced stages of clinical development for the treatment of relapsing-remitting multiple sclerosis (RRMS). It is a small molecule that was found to reduce inflammatory processes that originate in the periphery and also to penetrate the CNS, having direct effect on resident inflammatory cells, thereby reducing demyelination and axonal damage. The Phase III ALLEGRO trial was a multi-center, randomized, double-blind, placebo-controlled study of patients with RRMS. Patients were equally randomized to receive a once daily oral dose of 0.6 mg laquinimod or placebo for 24 months.

Eighty percent of laquinimod and 77% of placebo patients completed the two-year study. The study met the primary endpoint, with laquinimod achieving a decrease in relapse rate (23% reduction, $p = 0.0024$). The risk for EDSS disability progression was significantly reduced (36%; $p=0.0122$), as compared to placebo. In addition, rate of brain atrophy progression was reduced by 32.8% ($p<0.0001$) at month 24. Both mean cumulative number of GdE and of new T2 lesions were significantly lower for laquinimod (37% reduction, $p=0.0003$ and 30% reduction, $p=0.0002$, respectively).

Laquinimod was well-tolerated. The adverse events and serious adverse events in the laquinimod group were similar to those of the placebo group with the exception of transient, reversible elevations of liver enzymes without concomitant signs of liver dysfunction. There were no signals of impaired immune surveillance or an increased rate of infections or malignancies.

In conclusion, preclinical and clinical data suggest that laquinimod is a promising oral immunomodulator that is active in the CNS, with clear effects on clinical disease activity and on the accumulation of irreversible brain tissue loss.