Efficacy of Cenerimod, a Selective S1P1 receptor modulator, in the MRL/lpr mouse model of systemic lupus erythematosus


Background Systemic lupus erythematosus (SLE) is a complex autoimmune disease driven by pathological autoreactive T and B lymphocytes. Sphingosine 1-phosphate (S1P) regulates the egress of T and B lymphocytes from peripheral lymphoid organs. Cenerimod, a potent, selective, and orally active S1P1 receptor modulator that induces receptor internalization, targets this mechanism and prevents lymphocyte exit from lymphoid organs. Based on this rationale, we tested the potential of cenerimod to reduce the pathological manifestations of SLE in the MRL/lpr lupus mouse model.

Methods 7-week-old MRL/lpr mice (n=20/group) were assigned to either a vehicle (control) or a cenerimod group and received their respective treatments as food admix at libitum (around 20–40 mg cenerimod/kg body weight). The study was predefined to end when 20% mortality or morbidity was reached in one group. Mice were weighed twice a week and blood and urine samples were collected before treatment (week 0), at week 6, and at the end of treatment (week 11). At sacrifice, organs were collected, weighed, and evaluated by flow cytometry or histology. All in vivo readouts and histological data analyses were performed in a blinded fashion.

Results More than 20% mortality was observed in the control group after 10 weeks of treatment, whereas all mice in the cenerimod group remained alive during this period. Cenerimod-treated mice had significantly fewer circulating immune cells and immune cell infiltrates in the kidney and brain. This translated in preserved organ function as demonstrated by the significantly reduced urine albumin concentrations and kidney and brain histopathological scores. Furthermore, anti-dsDNA antibody, and both plasma BAFF and IFN- levels, two proteins currently targeted clinically, were significantly lower in the cenerimod group.

Conclusions Cenerimod treatment led to increased survival and significantly improved organ pathology in MRL/lpr mice by targeting the S1P1 axis. These results support clinical evaluation of cenerimod for the treatment of SLE.

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