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CD206-Targeted Liposomal Myelin Basic Protein Peptides in Patients with Multiple Sclerosis Resistant to First-Line Disease-Modifying Therapies: A First-in-Human, Proof-o--Concept Dose-Escalation Study

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Abstract

© 2016, The Author(s).Previously, we showed that CD206-targeted liposomal delivery of co-encapsulated immunodominant myelin basic protein (MBP) sequences MBP46–62, MBP124–139 and MBP147–170 (Xemys) suppressed experimental autoimmune encephalomyelitis in dark Agouti rats. The objective of this study was to assess the safety of Xemys in the treatment of patients with relapsing-remitting multiple sclerosis (MS) and secondary progressive MS, who failed to achieve a sustained response to first-line disease-modifying therapies. In this phase I, open-label, dose-escalating, proof-of-concept study, 20 patients with relapsing-remitting or secondary progressive MS received weekly subcutaneously injections with ascending doses of Xemys up to a total dose of 2.675 mg. Clinical examinations, including Expanded Disability Status Scale score, magnetic resonance imaging results, and serum cytokine concentrations, were assessed before the first injection and for up to 17 weeks after the final injection. Xemys was safe and well tolerated when administered for 6 weeks to a maximum single dose of 900 µg. Expanded Disability Status Scale scores and numbers of T2-weighted and new gadolinium-enhancing lesions on magnetic resonance imaging were statistically unchanged at study exit compared with baseline; nonetheless, the increase of number of active gadolinium-enhancing lesions on weeks 7 and 10 in comparison with baseline was statistically significant. During treatment, the serum concentrations of the cytokines monocyte chemoattractant protein-1, macrophage inflammatory protein-1β, and interleukin-7 decreased, whereas the level of tumor necrosis factor-α increased. These results provide evidence for the further development of Xemys as an antigen-specific, disease-modifying therapy for patients with MS.

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Keywords

Clinical trial, Liposomes, Mannose, MRI, Myelin basic protein, Xemys