SCIENTIFIC PROGRAMME

A03.b Theme A: β-Amyloid Diseases
A03.b. Drug Development, Clinical Trials: Immunomodulators

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Abstract: 100

REPURPOSING OF THE ANTI-ASTHMATIC DRUG MONTELUKAST FOR THE TREATMENT OF ALZHEIMER’S DISEASE.

Aims

Alzheimer’s disease (AD) is the most prevalent neurodegenerative disease in the Western world characterized by a progressive loss of cognitive functions leading to dementia. Leukotrienes, small lipid mediators of inflammation, have been implicated in the pathogenesis of brain aging and of neurodegenerative diseases, therefore, defining leukotriene signalling as a target for therapeutic intervention. Recently, we demonstrated that a 6 weeks treatment of aged rats, a model of brain aging and mild cognitive impairment, with the leukotriene receptor antagonist and anti-asthmatic drug Montelukast elevated hippocampal neurogenesis, reduced neuroinflammation, and improved learning and memory. As Montelukast is known to have a low bioavailability, we were now aiming to optimize the pharmacology of Montelukast by improving its formulation.

Method

Clinical Phase 1 Study

Results

In a Phase I study, we demonstrated that an oral film formulation of Montelukast (Montelukast VersaFilm) is safe and tolerable in healthy subjects, reduces the first-pass-effect and has a 52% higher bioavailability compared to the regular Montelukast tablet. Of importance for any CNS-active drugs, we detected Montelukast in the cerebrospinal fluid of the Montelukast VersaFilm treated healthy volunteers clearly indicating blood brain barrier penetrance. Of note, Montelukast, in contrast to many other CNS penetrating drugs, has an excellent safety and tolerability profile. We are at this stage preparing a Phase II trial to demonstrate efficacy of the Montelukast VersaFilm to improve cognitive function in AD.

Conclusion

In summary, Montelukast VersaFilm is a novel product, which will be developed for the treatment of AD.

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<< Back to session