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Abstract Title: Remibrutinib ameliorates CNS autoimmune disease - insights from EAE

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Preferred Presentation Type: Oral or poster presentation

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Introduction:

Bruton's tyrosine kinase (BTK) regulates the functions of B and myeloid cells, implicated in the pathogenesis of multiple sclerosis (MS). Remibrutinib (LOU064) is a covalent, oral BTK inhibitor exhibiting high selectivity and potency, with the potential to minimize off-target toxicity and is currently being investigated in phase 3 trials for the treatment of multiple sclerosis (NCT05147220, NCT05156281).

Objectives/Aims:

To assess the *in vivo* efficacy of remibrutinib and to better understand its impact on inflammation and tissue destruction in the central nervous system in an MS animal model.

Methods:

Experimental autoimmune encephalomyelitis (EAE) was induced by immunization with myelin oligodendrocyte glycoprotein (MOG). Target engagement was assessed in tissue and clinical disease activity was determined. Inflammation, tissue destruction, the degree of reactive gliosis and other measures were studied using immunohistochemistry.

Results:

Remibrutinib ameliorated the clinical course of MOG-induced EAE. In addition, several readouts for CNS inflammation and demyelination were reduced by remibrutinib. The assessment of selective B cell inhibition and BTK engagement confirmed the activity based on the role of BTK in B cells and macrophages/microglia.

Conclusion:

Remibrutinib demonstrated clinical efficacy in a BTK dependent EAE model, which was associated with CNS tissue protection. Our findings in an experimental MS model support the view that BTK might represent a promising target for treating patients with MS. The clinical outcomes of the ongoing phase 3 trials studying remibrutinib in MS are warranted to allow any translation from model systems to patients.

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Travel / Abstract Grant Application and Young Scientific Investigators' Session: I will not apply for Travel Grant or Young Scientific Investigators' Session

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