Remibrutinib Ameliorates CNS Autoimmune Disease - Insights From EAE

Short title: Efficacy of Remibrutinib in EAE Model of MS

Presenter: Virginia DeLasHeras

Bruno Cenni[1], Barbara Nuesslein-Hildesheim[1], Antje Marcantonio[1], Grazyna Wieczorek[1], Frederique Lafossas[1], Meike Lang[1], Pamela Ramseier[1], Sarah Tisserand[1], Giuseppe Locatelli[1], Virginia DeLasHeras[2], Bernd C. Kieseier[2]

[1]Novartis Institutes for Biomedical Research, Basel, Switzerland; [2]Novartis Pharma AG, Basel, Switzerland

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 MS (NCT05147220, NCT05156281).

OBJECTIVES

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.

CONCLUSIONS

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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