Evobrutinib acts on microglia: therapeutic implication in progression of MS?

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Introduction
In multiple sclerosis (MS) persisting disability can derive from acute relapses or alternatively, from slow and steady deterioration, termed chronic progression. Emerging data suggest that the later process occurs largely independent from relapse activity or development of new central nervous system (CNS) inflammatory lesions. To control MS progression, agents are necessary that exert effects on novel targets within the CNS. In this regard, one promising strategy may be the inhibition of the enzyme Bruton's tyrosine kinase (BTK), which is centrally involved in the activation of both B cells as well as myeloid cells, such as macrophages and microglia.
In the present study, we analysed the potential of the BTK inhibitor evobrutinib as a therapeutic strategy in halting progression in MS by targeting microglial cells.

Methods
We cultured activated primary microglia in the presence of evobrutinib and assessed the phenotype and function of microglial cells by ELISA and flow cytometry. Further we treated C57BL/6 mice with evobrutinib (10m/kg) or vehicle control preventive to induction of passive EAE by adoptive transfer of activated T cells. We examined microglial cells by ELISA and flow cytometry.

Results
In vitro, treatment with evobrutinib reduced the inflammatory microglial phenotype while enhancing the phagocytosis capacity in primary murine microglial cells. Furthermore, microglial cells isolated from mice treated with evobrutinib in the passive EAE model of MS, showed a reduced microglial expression of CD68, CD69, markers involved in activation and CD86 and MHCII, markers involved in antigen presentation in the spinal cord and brain.

Conclusion
We showed that BTK inhibition by evobrutinib can shape microglial cells in an anti-inflammatory manner, diminishing inflammatory responses of microglial cells. These data highlight the therapeutic potential of the BTK inhibitor evobrutinib in ameliorating pro-inflammatory activity of microglia, an assumed key process in chronic progression of MS.