“This reprint might contain references to “Merck” or “Merck KGaA”, which refer to (1) Merck KGaA, Darmstadt, Germany; (2) an affiliate of Merck KGaA, Darmstadt, Germany; or (3) one of the businesses of Merck KGaA, Darmstadt, Germany, which operate as EMD Serono in the healthcare, MilliporeSigma in the life science and EMD Electronics in the electronics business in the U.S. and Canada.
There are two different, unaffiliated companies that use the name “Merck”. Merck KGaA, Darmstadt, Germany, which is providing this content, uses the firm name “Merck KGaA, Darmstadt, Germany” and the business names EMD Serono in the healthcare, MilliporeSigma in the life science and EMD Electronics in the electronics business in the U.S. and Canada. The other company, Merck & Co., Inc. holds the rights in the trademark “Merck” in the U.S. and Canada. Merck & Co., Inc. is not affiliated with or related to Merck KGaA, Darmstadt, Germany, which owns the “Merck” trademark in all other countries of the world.”

NIB01

The effect of evobrutinib, a BTK inhibitor, on blood neurofilament light chain levels in relapsing multiple sclerosis

Jens Kuhle,[1] Ludwig Kappos,[2] Xavier Montalban,[3] Ying Li,[4] Karthinathan Thangavelu,[4] Yann Hyvert,[5] Davorka Tomic[5]

[1]Neurologic Clinic and Policlinic, MS Center and Research Center for Clinical Neuroimmunology and Neuroscience Basel (RC2NB), University Hospital Basel, and University of Basel, Basel, Switzerland; [2]Research Center for Clinical Neuroimmunology and Neuroscience Basel (RC2NB), Departments of Medicine, Clinical Research and Biomedical Engineering, University Hospital Basel, and University of Basel, Basel, Switzerland; [3]Department of Neurology-Neuroimmunology, Centre d'Esclerosi Múltiple de Catalunya (Cemcat), Hospital Universitario Vall d'Hebron, Barcelona, Spain; [4]EMD Serono Research and Development Institute, Inc., Billerica, MA, USA; [5]Merck KGaA, Darmstadt, Germany

GET POSTER PDF

Copies of this poster obtained through QR (Quick Response) code are for personal use only and may not be reproduced without written permission of the authors

CONCLUSION

- **These data on NfL dynamics are the first to be reported for any BTK inhibitor investigated for MS**
- **Evobrutinib 75 mg BID significantly lowers blood NfL levels as early as Week 12, with reduced levels maintained until 24 weeks (last analysis timepoint)**
- **These results indicate evobrutinib 75 mg BID has a beneficial effect on reducing neuro-axonal damage in MS**

BID, twice daily; **BTK**, Bruton's tyrosine kinase; **NfL**, neurofilament light chain

INTRODUCTION

- Evobrutinib is a highly selective BTK inhibitor that targets B cells and myeloid cells, including macrophages and microglia[1-3]
- A Phase II, placebo-controlled, randomized trial (NCT02975349) in patients with relapsing MS showed evobrutinib reduced total T1 Gd+ lesions over 24 weeks versus placebo[4]
- A low annualized relapse rate with evobrutinib 75 mg BID at Week 48 (0.11; 95% CI 0.04–0.25) was maintained in a long-term extension through 108 weeks[a] (0.12; 95% CI 0.06–0.22)[5]
- Blood NfL levels are a biomarker of neuro-axonal damage in MS, with proposed prognostic value for monitoring disease progression[6,7]

[a]Evobrutinib dosing in the open-label extension was 75 mg QD for ~48 weeks, then 75 mg BID
CI, confidence interval; **Gd+**, gadolinium-enhancing; **QD**, once daily

OBJECTIVE

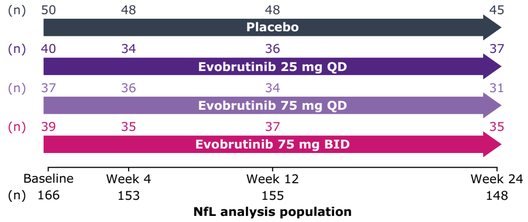
- In a *post hoc* analysis of a Phase II placebo-controlled, randomized trial in relapsing MS, we evaluated the effect of evobrutinib on blood NfL levels

METHODS

Study design

- All patients from the double-blind arms (ITT, n=213[b]) with NfL values at baseline and ⩾1 post-baseline were included (n=166) (**Figure 1**)
- Baseline demographics were similar between the double-blind arms in the ITT and NfL populations
- NfL was measured blinded to treatment allocation (Simoa NF-light™)

Figure 1. Study design



[b]Samples were not available from the open-label dimethyl fumarate arm (n=54)
BID, twice daily; **ITT**, intention-to-treat; **NfL**, neurofilament light chain; **QD**, once daily

Identification of baseline covariates

- An MMRM model identified key baseline variables that significantly affected NfL levels over time (**Table 1**)

Table 1. Baseline variables and their effects on NfL levels over time

Tested baseline covariates	Significance
Age dichotomized by 42 years	**p=0.023**
Sex	NS
T1 Gd+ lesions	NS
T2 lesion volume	**p=0.008**
EDSS score dichotomized by 3	**p=0.022**
Number of relapses in prior 2 years	NS
Time since MS onset	NS
High disease activity	NS
Type of MS	NS

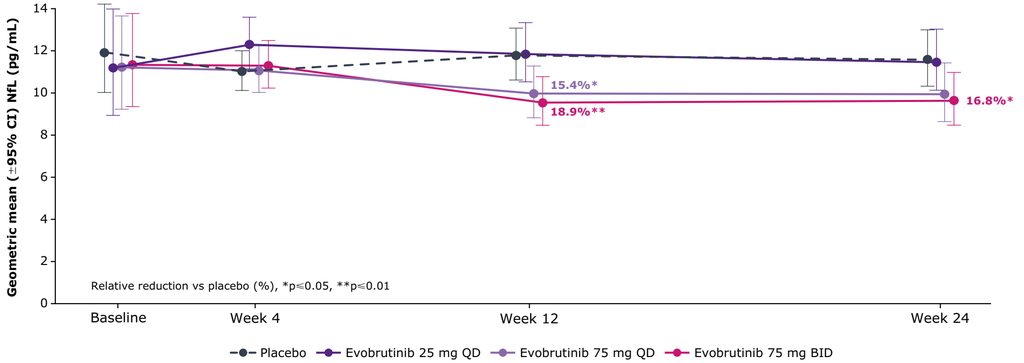
EDSS, Expanded Disability Status Scale; **Gd+**, gadolinium-enhancing; **MMRM**, mixed model repeated measures; **NfL**, neurofilament light chain; **NS**, non-significant

RESULTS

Evobrutinib significantly reduces blood NfL levels

- The effect of evobrutinib versus placebo on NfL over time was evaluated using an MMRM model, controlling for significant baseline covariates: age, T2 lesion volume, and EDSS score (**Figure 2**)

Figure 2. Effect of evobrutinib versus placebo on NfL over time



BID, twice daily; **CI**, confidence interval; **NfL**, neurofilament light chain; **QD**, once daily

REFERENCES

1. Haselmayer P et al. *J Immunol* 2019;202:2888–906
2. Caldwell RD et al. *J Med Chem* 2019;62:7643–55
3. Martin E et al. *Brain Plast* 2020;5:123–33
4. Montalban X et al. *N Engl J Med* 2019;380:2406–17
5. Montalban X et al. *Mult Scler* 2020;26(Suppl. 3):213(Abstract 0197)
6. Kuhle J et al. *Neurology* 2019;92:e1007–15
7. Varhaug KN et al. *Front Neurol* 2019;10:338

ACKNOWLEDGMENTS

The authors thank the patients and their families, as well as the investigators and study teams, for their participation in this study.
This study was sponsored by EMD Serono Research & Development Institute, Inc, Billerica, MA, USA.
These data were previously presented at the American Academy of Neurology (AAN) 2021 Virtual Congress; April 17–22, 2021.

DISCLOSURES

JK has received speaker fees, research support, or travel support from, and/or has served on advisory boards for Bayer, Biogen, Celgene, Merck KGaA, Darmstadt, Germany, Novartis, Octave Bioscience, Progressive MS Alliance, Roche, Sanofi, Swiss MS Society, Swiss National Science Foundation (320030_189140/1), and University of Basel. LK has received research support from AbbVie, Bayer, Biogen, Celgene, Eisai, EMD Serono, Inc., Rockland, MA, USA, European Union, Genentech, Innosuisse, Janssen, Merck KGaA, Darmstadt, Germany, Minoryx, Novartis, Roche, Roche Research Foundation, Sanofi, Sanofi Genzyme, Santhera, Swiss MS Society, Swiss National Science Foundation, and TG Therapeutics. XM has received consultancy fees from Biogen, EMD Serono, Inc., Rockland, MA, USA, F. Hoffmann-La Roche, MedDay, Merck KGaA, Darmstadt, Germany, and Novartis; has received research support from AbbVie, Biogen, F. Hoffmann-La Roche, MedDay, Merck KGaA, Darmstadt, Germany, Novartis, Sanofi, and Teva; and has served on scientific advisory or data safety monitoring boards for Alexion, Biogen, Celgene/Receptos, EMD Serono, Inc., Rockland, MA, USA, F. Hoffmann-La Roche, MedDay, Merck KGaA, Darmstadt, Germany, NervGen, Novartis, Sanofi Genzyme, and TG Therapeutics. YL is an employee of EMD Serono Research & Development Institute, Inc., Billerica, MA, USA. KT is an employee of Sanofi Genzyme and EMD Serono Research & Development Institute, Inc., Billerica, MA, USA. YH is an employee of Merck KGaA, Darmstadt, Germany, and was previously an employee of EMD Serono Research & Development Institute, Inc., Billerica, MA, USA; an immediate family member is an employee of EMD Serono Research & Development Institute, Inc., Billerica, MA, USA, and Merck KGaA, Darmstadt, Germany. DT is an employee of Merck KGaA, Darmstadt, Germany, and has stock or an ownership interest in Novartis.

Presented at the Consortium of Multiple Sclerosis Centers Annual Meeting | October 25–28, 2021 | Orlando, FL, USA and virtual

FOR REACTIVE MEDICAL USE ONLY

This study was sponsored by EMD Serono Research and Development Institute, Inc., Billerica, MA, USA. Copyright © 2021 remains with the authors.