Prognostic factors of future disability accrual and improvement in multiple sclerosis

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ECTRIMS 2023 Abstract: 2359/2556 characters (including spaces)

INTRODUCTION

The individual disease course of multiple sclerosis (MS) is extremely variable. Today, evidence from clinical trials and real-world data demonstrates that the long-term disease trajectory for people living with MS can be improved by initiating efficacious treatment early. However, one of the greatest challenges encountered to optimize individual treatment decisions early in the disease course is a more precise assessment of future disease, including the risk of disability accrual and the probability of disability improvement.

OBJECTIVE

To inform clinical decision making early in the disease course through the identification of factors robustly associated with an increased risk of disability accrual and/or a reduced potential for improvement in people living with MS.

METHODS

We analyzed expanded disability status scale (EDSS) data from the Novartis-Oxford MS database (NO.MS), containing ~130,000 EDSS assessments and ~45,000 MRI scans from ~8000 patients diagnosed with MS (spanning all phenotypes). We developed a Bayesian continuous time Markov model to quantify the influence of various factors (demographic, clinical, imaging) on both disability worsening and improvement as a function of baseline disability.

This study was funded by Novartis Pharma AG, Basel, Switzerland

RESULTS

As a novelty, we identified a high T2 lesion load and/or a reduced normalized brain volume as significant factors limiting the patient's capacity for disability improvement. Higher versus lower disease burden as measured by these MRI markers was highly significantly associated with lower chances of disability improvement. In addition, older age, time since first symptoms, and the number of relapses in the past year were confirmed as consistent drivers of future disability accrual.

CONCLUSIONS

Based on a very large clinical dataset, we identified markers of focal and diffuse damage to the brain as key factors that limit disability improvement in MS patients. Damage to the brain accumulates gradually as the disease evolves. Increasing exhaustion of the patients reserve capacity could be an important contributing factor to the gradual disability accumulation typically seen in the progressive phase of the disease. The importance of protecting the integrity of the central nervous system early in the disease may still be underestimated and should be considered when making clinical decisions.

DISCLOSURES:

The study was supported by Novartis Pharma AG, Switzerland.

Alex Ocampo, **Jelena Cuklina, Gordon Graham, Wendy Su, Piet Aarden, Bernd Kieseier and Dieter Häring** are employees of Novartis.

Farhad Hatami is currently employee of Exact Sciences, which was not involved in the study.

Douglas Arnold has received personal compensation for serving as a Consultant for Alexion, Biogen, Celgene, Eli Lilly, EMD Serono, Frequency Therapeutics, Genentech, Merck, Novartis, Roche, Sanofi, and Shionogi, and holds an equity interest in NeuroRx

Robert Bermel has served as a consultant for Astra Zeneca, Biogen, EMD Serono, Genzyme, Genentech, Novartis and VielaBio. He receives research support from Biogen, Genentech and Novartis.

Heinz Wiendl has received honoraria for acting as a member of scientific advisory boards for Biogen, Evgen, Genzyme, MedDay Pharmaceuticals, Merck Serono, Novartis, Roche Pharma AG, and Sanofi-Aventis, as well as speaker honoraria and travel support from Alexion, Biogen, Cognomed, F. Hoffmann-La Roche Ltd., Gemeinnützige Hertie-Stiftung, Merck Serono, Novartis, Roche Pharma AG, Genzyme, Teva, and WebMD Global. Heinz Wiendl is acting as a paid consultant for AbbVie, Actelion, Biogen, IGES, Johnson & Johnson, Novartis, Roche, Sanofi-Aventis, and the Swiss Multiple Sclerosis Society. His research is funded by the German Ministry for Education and Research (BMBF), Deutsche Forschungsgemeinschaft (DFG), Else Kröner Fresenius Foundation, Fresenius Foundation, the European Union, Hertie Foundation, NRW Ministry of Education and Research, Interdisciplinary Center for Clinical Studies (IZKF) Muenster and RE Children's Foundation, Biogen, GlaxoSmithKline GmbH, Roche Pharma AG, and Sanofi-Genzyme.

This study was funded by Novartis Pharma AG, Basel, Switzerland

Habib Ganjgahi, Yang Sun, Stephen Gardiner, Samantha Pendleton and Thomas Nichols report no competing interests.

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This study was funded by Novartis Pharma AG, Basel, Switzerland