Serum Neurofilament Light Chain Levels and NEDA-3 Status With Ofatumumab Treatment in RMS Patients: Longer-term Analysis from ASCLEPIOS I/II and ALITHIOS

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Topic: 29: Fluid Biomarkers

Abstract text: **INTRODUCTION**

Ofatumumab (OMB), a fully human anti-CD20 monoclonal antibody (20 mg s.c.), is approved for treating relapsing MS (RMS) in adults. The ASCLEPIOS I/II trials were the first pivotal trials in MS, where serum NfL (sNfL) was a predefined secondary endpoint. OMB lowered sNfL levels vs teriflunomide (TER) over 96 weeks. Also, OMB increased the chances of achieving NEDA-3 in both the first and second year of treatment.

OBJECTIVE

To assess the longer-term efficacy of OMB on sNfL levels and odds of maintaining NEDA-3 status in RMS patients receiving continuous OMB and those switched from TER in the core ASCLEPIOS I/II and ALITHIOS open label extension trials.

METHODS

These analyses included cumulative data from patients randomized to OMB/TER (946/936) in the pooled ASCLEPIOS I/II trials, and then continued OMB (OMB-OMB; 690) or switched from TER to OMB (TER-OMB; 677) in the ALITHIOS trial. Between group comparisons of geometric mean sNfL levels over time and the proportion of patients achieving NEDA-3 cumulatively up to 4 years, and by core and extension periods were assessed.

RESULTS

In ASCLEPIOS I/II, sNfL levels were reduced with OMB vs TER (M12: 8.03 vs 10.25; M24: 7.96 vs 9.97; p<0.001, both timepoints). In ALITHIOS, low sNfL levels were maintained with continuous OMB treatment [M24: 8.50]. Switching from TER to OMB resulted in a decline in sNfL levels; the difference vs OMB-OMB remained significant up to M6 after switch (9.07 vs 8.31; p<0.001), while from M12 onwards low sNfL levels were observed in both groups (M24: 8.23 vs 8.50). In ASCLEPIOS I/II, the odds of achieving NEDA-3 were ~3-fold higher for OMB vs TER during Year 1 (48% vs 25.2%; OR [95% CI], 3.39 [2.71-4.25]; p<0.001) and 10-fold higher during Year 2 (85% vs 38.4%; 10.09 [7.82-13.02]; p<0.001). In ALITHIOS nearly 8 of 10 patients in OMB-OMB and 6 of 10 patients in TER-OMB achieved NEDA-3 during Year 1 (85.8% vs 59.5%; 4.50 [3.40-5.94]; p<0.001). During Year 2, a similarly high percentage of patients with NEDA-3 status were observed in the OMB-OMB and TER-OMB groups (86.4% vs 90.4%; 1.55 [1.07-2.22]; p=0.019).

CONCLUSION

Early use of OMB resulted in sustained reduction of neuroaxonal injury and increased the odds of maintaining NEDA-3 status. A near complete and sustained suppression of disease activity was observed in patients initiating OMB early, and a rapid reduction of disease activity followed switching from TER to OMB.

Disclosure: **Jens Kuhle** received speaker fees, research support, travel support, and/or served on advisory boards by Swiss MS Society, Swiss National Research Foundation (320030_189140/1), University of Basel, Progressive MS Alliance, Bayer, Biogen, Bristol Myers Squibb, Celgene, Merck, Novartis, Octave Bioscience, Roche, Sanofi.

Ludwig Kappos institution (University Hospital Basel) has received research support: steering committee, advisory board, consultancy fees: Abbvie, Actelion, AurigaVision AG, Biogen, Celgene, Desitin, Eli Lilly, EMD Serono, Genentech, Genzyme, GlaxoSmithKline, Janssen, Japan Tobacco, Merck, Minoryx, Novartis, Roche, Sanofi, Santhera, Senda, Shionogi, Teva, and Wellmera; speaker fees (Celgene, Janssen, Merck, Novartis, and Roche); support for educational activities (Biogen, Desitin, Novartis, Sanofi, and Teva); license fees for Neurostatus products; and grants (European Union, Innosuisse, Novartis, Roche Research Foundation, Swiss MS Society, and Swiss National Research Foundation)

Tjalf Ziemssen has received research support, consulting fee, and honoraria for lectures from Alexion, Biogen, Celgene, Merck, Novartis, Roche, Sanofi, Teva.

Douglas Arnold has received personal fees from Acorda, Albert Charitable Trust, Biogen, Celgene, Frequency Therapeutics, GeNeuro, MedDay, Merck Serono, Novartis, Roche, Sanofi-Aventis, and Wave Life Sciences; grants from Biogen, Immunotec, and Novartis; and has equity interest in NeuroRx, outside the submitted work.

Enrique Alvarez received compensation for consulting from Actelion/Janssen, Alexion, Bayer, Biogen, Celgene/BMS, EMD Serono/Merck, Genentech/Roche, Genzyme, Novartis, Sanofi, and TG Therapeutics and for research from Biogen, Genentech/Roche, Novartis, TG Therapeutics, Patient-Centered Outcomes Research Initiative, National Multiple Sclerosis Society, National Institutes of Health, and Rocky Mountain MS Center

Anne H. Cross has received consulting fees, support, and honoraria from Biogen, Celgene, Bristol Myers Squibb, EMD Serono, Merck, Genentech, Roche, Greenwich Biosciences (Jazz Pharmaceuticals), Horizon Therapeutics, Janssen (subsidiary of Johnson & Johnson), Novartis, TG Therapeutics, Academic CME, Projects In Knowledge, CME Outfitters, WebMD, Conrad N. Hilton Foundation, Potomac Center for Medical Education, The Consortium of Multiple Sclerosis Centers, and ACTRIMS; has received a grant from the Department of Defense, USA; has been the secretary (elected) of The Consortium of Multiple Sclerosis Centers, member of the scientific advisory board of Race to Erase MS, program committee (chair) of ACTRIMS, member of the COVID-19 advisory committee of the National Multiple Sclerosis Society and National Multiple Sclerosis Society representative on the Progressive MS Alliance; has participated on the data safety monitoring board or advisory board for National Multiple Sclerosis Society, Novartis and EMD Serono, and holds a patent for “Yablonskiy DA, Sukstansky AL, Wen J, Cross AH. Methods for simultaneous multi-angular relaxometry of tissue using magnetic resonance imaging. Patent 15060-630 (015875).

Ibolya Boer, Ayan Das Gupta, Xixi Hu, Petra Kukkaro, Bernd Kieseier, Ronald Zielman are employees of Novartis.

Stephen L. Hauser has received personal compensation from Annexon, Alector, Accure, and Neurona; he has also received travel reimbursement from F. Hoffmann-La Roche Ltd and Novartis for CD20-related meetings and presentations.

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