Efficacy of Early Ofatumumab versus Late-Switch from Teriflunomide: Subgroup Analysis of the ALITHIOS Open-Label Extension Study by Prior Disease Modifying Therapy Exposure and Age

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Topic: 31: Immunomodulation/Immunosuppression
Abstract text: **Introduction**
Ofatumumab (OMB), a fully human anti-CD20 monoclonal antibody, reduced annualized relapse rate (ARR) and MRI lesion activity, and delayed disability worsening vs teriflunomide (TER) in relapsing multiple sclerosis patients who were treatment-naive or previously treated with disease-modifying therapies (DMTs) in the Phase 3 ASCLEPIOS I/II trials. Patients entering the ALITHIOS open-label extension study continued OMB or switched from TER to OMB.

Objective
To compare clinical and MRI outcomes in patients initiating OMB in ASCLEPIOS (core) vs switching from TER to OMB in ALITHIOS (extension), according to the number of prior DMTs and age.

Methods
Cumulative clinical and MRI outcomes from ASCLEPIOS and ALITHIOS (ARR, time to 3- or 6-month-confirmed disability worsening [3/6mCDW],number of gadolinium enhancing [Gd+] T1 lesions, and annualized T2 lesion rate) were analysed in patients who received OMB during the core and extension (OMB-OMB) and patients who switched from TER to OMB in the extension (TER-OMB) according to number of DMTs prior to enrolment in ASCLEPIOS I/II (0,1, 2, >2, any) and age at baseline (≤40, >40).

Results
Of the 1882 patients randomized in the core, 946/936 received OMB/TER and 690/677 continued/were switched to OMB in the extension. Switching from TER to OMB in the extension significantly reduced the ARR by 68.3–76.6%; continuing OMB in the extension further reduced ARR by 39.9–65.1%. Within the prior DMT subgroups, the lowest mean ARR was achieved in patients in the OMB-OMB group with ≤1 DMT (0.046–0.049). Switching to, or continuing OMB was associated with a consistent numerical reduction in the risk of 3/6mCDW with the greatest benefit observed in patients on continuous OMB with ≤1 DMT or ≤40 years old. The almost complete suppression of T1 Gd+ activity seen in those randomised to OMB in the core was mirrored in the TER-OMB groups in the extension (90.00–100% across all prior DMT and age subgroups) and sustained in the OMB-OMB group. New/enlarging T2 lesions showed a similar, though delayed, suppression in the TER-OMB group. Incidence of adverse events was consistent with the ASCLEPIOS I/II studies across all subgroups.

Conclusions
Switching from TER to OMB in ALITHIOS reduced clinical and MRI disease activity across all prior DMT and age subgroups. However, younger patients and those treated with ≤1 DMT at baseline appear to experience the greatest benefit, emphasizing the importance of earlier treatment initiation.
Disclosure: **Funding:** This study was funded by Novartis Pharma AG (Basel, Switzerland).

Jeffrey A. Cohen received personal compensation for consulting for Biogen, Bristol-Myers Squibb, Convelo, Genentech, Janssen, NervGen, Novartis, and PSI; speaking for H3 Communications; and serving as an Editor of Multiple Sclerosis Journal.

Ralf Gold has received compensation for serving as a consultant or speaker from Bayer HealthCare, Biogen Idec, Merck Serono, Novartis and Teva Neuroscience. He, or the institution he works for, has received research support from Bayer HealthCare, Biogen Idec, Merck Serono, Novartis and Teva Neuroscience. He has also received honoraria as a Journal Editor from SAGE and Thieme Verlag.

Jérôme de Seze received personal compensation from Alexion, Allergan, Almirall, Bayer, Biogen, Chugai, CSL Behring, F. Hoffmann-La Roche Ltd., Genzyme, LFB, Merck, Novartis and Teva.

Derrick Robertson has received fees for consulting, contracted research and speaker's bureau from Biogen, Celgene, EMD Serono, Genentech, Sanofi Genzyme, Janssen, TG therapeutics, Mallinckrodt; consulting fees and speakers bureau for Bristol Myers Squibb, Horizon, and Alexion; consulting fees and contracted research for Novartis; consulting fees for Greenwich biosciences; contracted research for GW Pharmaceuticals, PCORI, Atara Biotherapeutics, CorEvitas, MedDay Pharmaceuticals, PRIME CME, and Actelion.

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.

Sibyl Wray received consulting fees from and advisory boards for Biogen, Celgene, and EMO Serano; speaker bureaus for Biogen, Celgene, EMO Serano, Genentech-Roche, and Sanofi-Genzyme; research support from Biogen, Celgene, EMO Sereno, Genentech-Roche, Novartis, Receptos, Sanofi- Genzyme, and TG Therapeutics.

Francesco Saccà served on advisory boards for Almirall, Argenx, Avexis, Biogen, Forward Pharma, Merck, Novartis, Pomona, Roche, Sanofi, Alexion, and Takeda. He received public speaking or travel honoraria from Biogen, Mylan, Novartis, Roche, Sanofi, and Teva. He received honoraria from Almirall, Novartis, and Sanofi for educational editorial work. He received consultancy fees from Argenx, Forward Pharma, Novartis, and Novatek.

Amin Azmon, Miriam King, Simone Fantaccini, Ronald Zeilman are employees of Novartis.

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).

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