logistic regression analysis was used to predict cluster membership by demographic and clinical characteristics. The association of SA/DP net days with the trajectories was assessed using generalized estimating equations.
Results: Four trajectories of treatment use were identified: *long-term non-high-efficacy DMTs* (38.6%), *escalation to high-efficacy DMTs* (31.2%), *discontinued/no DMTs* (15.3%), and *delayed start and escalation to high-efficacy DMTs* (14.9%). Age, MS type, expanded disability status scale score, and the number of DMT switches were associated with cluster membership. In the final years of follow-up, PwMS using non-high-efficacy DMTs showed lower mean SA/DP net days, whereas the *escalation to high-efficacy* and *discontinued/no DMT* clusters showed higher mean SA/DP net days. PwMS in the*delayed start and escalation to high-efficacy DMTs* cluster showed increasing mean SA/DP net days over time.
Conclusions: This study adds a description of the long-term trajectories of DMTs among PwMS in Sweden and their association with SA/DP net days, sociodemographic and clinical characteristics.

Disclosure
The project was supported by unrestricted research grants from Biogen. We utilised data from the REWHARD consortium, supported by the Swedish Research Council (VR grant number: 2017-00624). The design of the study, data collection, analyses, interpretations of data, and manuscript drafting were performed without the involvement of the funding bodies. Biogen was given the opportunity to comment on the manuscript before submission.
FST: funded partly by unrestricted research grant from Biogen; **AM**: funded partly by unrestricted research grant from Biogen; **CM**: funded partly by unrestricted research grant from Biogen; **AH**: declares no conflicting interests; **KF**: received honoraria for serving on advisory boards for Biogen, Merck, Roche and speaker's fees from Merck; **HG**: currently employed part-time by IQVIA; a contract research organization that perform commissioned pharmacoepidemiological studies, and therefore are collaborating with several pharmaceutical companies; **AG**: has received research support from Novartis; **KA**: had unrestricted research grants from Biogen; **JH**: received honoraria for serving on advisory boards for Biogen and Novartis and speaker's fees from Biogen, Merck-Serono, Bayer-Schering, Teva, and Sanofi-Aventis. He has served as PI for projects sponsored by, or received unrestricted research support from, Biogen, Merck-Serono, TEVA, Novartis, and Bayer-Schering. JH's MS research is also funded by the Swedish Research Council; **EF**: funded partly by unrestricted research grant from Biogen, and has received unrestricted research grants from Celgene.

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Ocrelizumab in patients with early-stage RRMS – results from the phase IIIb ENSEMBLE trial and the matched real-world NTD MS registry cohort

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Background: Early treatment of multiple sclerosis (MS) with high efficacy disease-modifying therapies (DMTs) can provide long-term benefits on disease outcomes. Our understanding of ocrelizumab (OCR) effectiveness in early-stage MS is still limited.
Aims: To assess treatment effectiveness of OCR in patients with early-stage relapsing-remitting MS (RRMS) from ENSEMBLE (NCT03085810) compared with commonly used first-line DMTs in a real-world setting, using the German NeuroTransData (NTD) MS registry as an external control arm.
Methods: Treatment-naive patients with early-stage RRMS (age 18–55 years; disease duration ⩽3 years; Expanded Disability Status Scale [EDSS] ⩽3.5; with ⩾1 signs of MRI activity or ⩾1 relapses in the prior 12 months) from the multicentre, open-label, single-arm Phase IIIb ENSEMBLE study, received OCR 600 mg every 24 weeks for 192 weeks. The matched NTD cohort was selected using ENSEMBLE inclusion criteria, with interferon β-1a/1b, glatiramer acetate, dimethyl fumarate and teriflunomide as comparators. NTD patients were matched to ENSEMBLE using 1:1 propensity score matching adjusted for age, EDSS score, prior relapses, baseline (BL) T1-weighted contrast-enhancing lesions (T1w-CELs) and time since first MS symptom. NTD patients had sufficient on-therapy data to assess no evidence of disease activity (NEDA)-2 (no relapses and no 24-week confirmed disability progression [CDP]) up to Week 48 and Week 72. Sensitivity analyses with varying matching factors were performed.
Results: BL characteristics for ENSEMBLE (N=1,050 with sufficient data [BL MRI, Week 48 MRI, Week 72 EDSS]) and NTD (N=601) were similar (ENSEMBLE/NTD: Median age, 32.0/33.9; female, 63.4/66.7%; median duration since first MS symptom, 0.75/0.43 years; median duration since RRMS diagnosis, 0.22/0.16 years; BL EDSS score, 1.79/1.06). The odds ratio (95% CI) for ENSEMBLE vs NTD (462 vs 278 patients) for NEDA-2 was 1.68 (1.04–2.72; p=0.047) at Week 48, and 1.99 (1.29–3.07; p<0.001) at Week 72. Week 72 NEDA-2 did not change substantially when duration since first MS symptom or (T1w-CELs) were excluded from matching. NEDA-3 results (including no MRI activity) up to 48 weeks will also be presented.
Conclusions: Treatment with ocrelizumab in patients with early RRMS was associated with significantly lower risk of relapses or CDP compared with first-line treatment with other DMTs in the

real-world. Sensitivity analyses of NEDA-2 and NEDA-3 and its components support robustness of results.

Disclosure

Sponsored by F. Hoffmann-La Roche Ltd; writing and editorial assistance was provided by Articulate Science, UK.

HP Hartung has received honoraria for consulting, serving on steering committees and speaking at scientific symposia with approval by the Rector of Heinrich-Heine University Düsseldorf from Bayer, Biogen, BMS Celgene, F. Hoffmann-La Roche Ltd, GeNeuro SA, Genzyme, MedImmune, Merck Serono, Novartis, Octapharma, Sanofi Genzyme, Teva, TG Therapeutics and Viela Bio.

T Holmøy has received honoraria/consultation fees from Biogen Idec., Merck, F. Hoffmann-La Roche Ltd, Bristol Myers Squibb, Santen and Sanofi Genzyme.

J Wuerfel is an employee of MIAC AG. He has received grants from EU (Horizon2020), Else Kröner-Fresenius Foundation and Novartis Foundation; and has been serving on advisory boards for Biogen, F. Hoffmann-La Roche Ltd, Genzyme/Sanofi, Idorsia, Novartis and Teva.

Y Heer is an employee of PricewaterhouseCoopers AG.

S Braune receives honoraria for patient care from public and private health insurances in Germany; for clinical studies from Biogen, Bristol Myers Squibb, Novartis and F. Hoffmann-La Roche Ltd; for lectures from Biogen, CSL Behring and Novartis; for consultancy from Celgene, NTD, F. Hoffmann-La Roche Ltd, Teva and TG Therapeutics; and as a board member of NTD.

A Bergman has received consulting fees from advisory board, speaker and other activities for NeuroTransData; project management and clinical studies for and travel expenses from Novartis and Servier.

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C Liu is an employee of F. Hoffmann-La Roche Ltd.

T Kuenzel is an employee of F. Hoffmann-La Roche Ltd.

S Moore is an employee of F. Hoffmann-La Roche Ltd.

T Vollmer has received compensation for activities such as advisory boards, lectures and consultancy from the following companies and organisations: Biogen, Genentech/F. Hoffmann-La Roche Ltd, and Novartis and has received research support from Rocky Mountain Multiple Sclerosis Center, Celgene, Biogen, Anokion, Genentech, F. Hoffmann-La Roche Ltd, GW Pharma and TG Therapeutics, Inc.

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Treatment emergent adverse events experienced early and transiently in the treatment course with cladribine tablets: data from the CLEVER real-world study

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Background: Cladribine tablets are a short-term treatment approach for patients with highly active relapsing multiple sclerosis (RMS) administered in 2 treatment courses in 2 consecutive years (with a maximum of 20 days of oral treatment).

Little is known about the occurrence of treatment-emergent adverse events (TEAEs) over time reported in patients treated with the oral pulsed therapy regime of cladribine tablets and the associated short periods of drug exposure.

Objective: To investigate the dynamics of safety reporting in a real-world setting and identify TEAE patterns that occur early in the course of treatment.

Method: The analysis of the adverse event (AE) occurrence pattern over the observation time of 6 months revealed an accumulation of AE reports early after treatment initiation. To further stratify the background of AEs, the number of TEAEs was assessed and subgroups based on the last previous MS medication were formed: naïve, platform (Interferon beta, Dimethylfumarate, Teriflunomide) and high efficacy (Alemtuzumab, Fingolimod, Natalizumab).

Results: In the CLEVER study 185 (37,7%) patients reported 310 AEs in total. For most of the patients (62,1%) AEs were reported within 45 days after first cladribine tablet intake.

To better understand the relevance of this early time period after treatment initiation, the AE analysis was extended to include TEAE and last previous therapy of the affected patients.

74 (52,5%) of 141 patients reported 97 AEs out of which 32 (22,6%) patients had 38 TEAEs. No treatment related serious adverse events (SAE) have been reported. The most frequent TEAEs were headache (9 patients), skin and subcutaneous tissue disorders (5), gastrointestinal disorders (5), fatigue (4), lymphopenia (3).

The analysis by last previous MS medication within the 45 days' time interval suggested that lymphopenia occurred more frequently in the high efficacy treatment group, gastrointestinal symptoms in treatment naïve patients, nervous system related symptoms (e.g. headache, dizziness) in platform therapy treated patients.

Conclusion: Cladribine tablets were well tolerated during the first 45 days of treatment as suggested by a relatively low incidence of TEAEs. Following this 45-day time period the rest of the AEs were distributed over the remaining observation time with proportionally less AEs and affected patients. This is in line with the post hoc analysis of CLARITY and ORACLE-MS safety.

Disclosure

Tjalf Ziemssen has received personal compensation for participating on advisory boards, trial steering committees, and data and safety monitoring committees as well as for scientific talks and project support from Bayer HealthCare, Biogen, Celgene, Genzyme, Merck, Novartis, Roche, Sanofi, and Teva.

Iris-Katharina Penner has received honoraria for speaking at scientific meetings, serving on scientific advisory boards and consulting activities from Adamas Pharma, Almirall, Bayer Pharma, Biogen, Celgene, Desitin, Sanofi-Genzyme, Janssen, Merck Serono GmbH, an affiliate of Merck KGaA, Darmstadt, Germany,