Neurol Ther
https://doi.org/10.1007/s40120-025-00762-6

BRIEF REPORT

Persistence to Ocrelizumab Compared with Other Disease-Modifying Therapies for Multiple Sclerosis: Results from the German NeuroTransData Registry

Stefan Braune · Petra Dirks · Seya Colloud · Qing Wang · Evan Davies · Yanic Heer · Mel Zürcher · Diana Sun · Arnfin Bergmann · the NeuroTransData Study Group

Received: December 17, 2024 / Accepted: May 1, 2025

ABSTRACT

Introduction: Treatment persistence is critical to obtaining full therapeutic benefit and can indicate favorable outcomes. This study examined real-world persistence with ocrelizumab (OCR) versus other disease-modifying therapies (DMTs) and its association with outcomes in relapsing–remitting multiple sclerosis (RRMS) using German NeuroTransData (NTD) registry data.

Methods: This retrospective cohort analysis included outpatients with RRMS who initiated a DMT between January 2014 and April 2022. DMT initiation date was defined as the index date. DMTs were grouped into OCR, injectable, oral, oral for highly active disease (oral HA), and other intravenous (IV) therapies. Persistence, based on having continuous records of a DMT for 2 years from index date, was evaluated within each group. Association between persistence and the risk of relapse, 3-months confirmed disability progression (3mCDP), and sick leave were assessed.

Results: Overall, 3907 patients with RRMS were included. OCR users had the highest persistence at 2 years (93%), then oral HA (78%), oral (67%), natalizumab (67%), and injectable therapies (55%). Compared with OCR users, patients initiating injectable (hazard ratio [HR] 8.51, 95% confidence interval [CI] 4.03–17.90), oral (HR 5.92, 95% CI 2.81–12.50), oral HA (HR 3.49, 95% CI 1.63–7.48) therapies, and natalizumab (HR 5.47, 95% CI 2.47–12.10) were more likely to discontinue. Adverse events (32.47%), lack of efficacy (21.17%), and patient-driven factors (19.73%) were the main reasons for discontinuation. Compared with persisters, non-persisters were associated with higher risks of relapse activity (rate ratio: 2.18, 95% CI 1.98–2.39), 3mCDP (rate ratio 1.52, 95% CI 1.28–1.77), and sick leave (rate ratio 1.71, 95% CI 1.49–1.98).

Conclusion: In a German real-world setting, patients initiating OCR achieved higher rates of persistence over 2 years compared with those on other DMTs. High persistence was associated

Prior Presentation: Braune S, et al. Poster P732: "Persistence to Ocrelizumab Compared with Other Disease-Modifying Therapies for Multiple Sclerosis in the German NeuroTransData Registry" presented at the 9th Joint ECTRIMS-ACTRIMS 2023 at Milan, Italy, 11–13 October 2023.

S. Braune (✉) · A. Bergmann
NeuroTransData, Neuburg an der Donau, Germany
e-mail: sbraune@neurotransdata.com

P. Dirks · S. Colloud · Q. Wang · E. Davies
F. Hoffmann-La Roche Ltd, Basel, Switzerland

Y. Heer · M. Zürcher
PricewaterhouseCoopers AG, Zurich, Switzerland

D. Sun
Genentech, Inc., South San Francisco, CA, USA

Published online: 02 June 2025

with lower risk of clinical disease activity, disease progression, and sick leave.

Keywords: Disease-modifying therapy; Multiple sclerosis; Ocrelizumab; Patient outcomes; Persistence; Real-world setting

Key Summary Points

Why carry out this study?

Previous research has shown that ocrelizumab (OCR) achieves higher persistence than other disease-modifying therapies (DMTs) in the USA; however, there is limited evidence on OCR persistence from other countries.

High persistence is important for controlling disease worsening in multiple sclerosis and can be an indicator of favorable outcomes.

What was learned from the study?

This study found that in a German real-world setting, outpatient OCR users achieved higher persistence over 2 years compared with those taking other DMTs.

High persistence was associated with a lower risk of clinical disease activity, disease progression, and sick leave.

Our findings indicate that high persistence is important for controlling disease progression and is a relevant indicator of favorable outcomes.

INTRODUCTION

Multiple sclerosis (MS) can significantly impact patients' physical, psychological, social, and economic well-being, leading to a reduced quality of life, decreased work participation, and increased use of healthcare resources [1, 2]. Over the past 2 decades, several disease-modifying therapies (DMTs) have become available for the treatment of MS [3]. The reciprocal association of persistence with DMTs and their effectiveness has been a key area of medical and scientific interest since the early days of DMT development [4–6].

Ocrelizumab (OCR), approved in Germany in 2018, is given twice yearly as intravenous (IV) infusions. Past studies have shown that patients starting treatment with OCR achieved higher persistence at 12, 18, and 24 months compared with those initiating other DMTs [6, 7]. Although there is evidence to suggest that higher persistence is linked to better outcomes [8–10], most of these studies are based on claims data from the USA, which carry several limitations related to indirect measures of treatment persistence (i.e., gaps in continuous supply of drug) and lack of clinical information (e.g., MS disease course) to adjust for major confounders. Further research is needed to understand the relationship between treatment persistence and outcomes in other countries, as differences in healthcare systems and access conditions to DMTs, or differences in treatment guidelines may influence treatment patterns and use.

We conducted a retrospective cohort analysis of outpatients with relapsing–remitting multiple sclerosis (RRMS) who initiated an approved DMT between January 2014 and April 2022, as captured by the NeuroTransData (NTD) registry. The aim of this study was to examine the persistence with OCR compared with other DMTs and its association with outcomes in outpatients with RRMS in a German real-world setting.

METHODS

Data Source

NTD is a Germany-wide network of neurologists and psychiatrists founded in 2008 (www.neurotransdata.com). Currently, the NTD network includes 135 specialists in 50 practices throughout Germany, serving approximately 600,000 outpatients per year. Each practice is certified according to network-specific and International Organization for Standardization

9001 criteria. Compliance with these criteria is audited annually by an external certified organization.

The NTD MS registry is a disease-specific database run by the NTD network. The NTD registry includes approximately 25,000 patients with MS and captures demographic, clinical history, and clinical variables as defined in a minimal dataset in real time during clinical visits, employing the NTD web-based registry data entry system DESTINY® [11]. Patient inclusion with informed consent is completed in the respective NTD practice as part of routine clinical care. Patients included in this analysis provided their informed consent (via tablets in NTD practices, electronic questionnaires, or via a patient portal) to the NTD registry and agreed to secondary use of their data. Standardized clinical assessments of functional system scores and Expanded Disability Status Scale (EDSS) were performed by certified raters (www.neurostatus.net). All personnel undergo regular training to ensure quality of data in the registry. Both automatic and manually executed queries are implemented to further ensure data quality [12]. All data are pseudonymized and pooled to form the NTD registry [12]. The data acquisition protocol was approved by the ethical committee of the Bavarian Medical Board (Bayerische Landesärztekammer, June 14, 2012, No. 11144) and reapproved by the ethical committee of the Medical Board North-Rhine (Ärztekammer Nordrhein, April 25, 2017, ID 2017071). The study conforms to the World Medical Association Declaration of Helsinki as published on the website of the *Journal of American Medical Association*, the Guidelines for Good Pharmacoepidemiology Practices (GPP) published by the International Society of Pharmacoepidemiology (ISPE), and the laws and regulations of Germany.

Study Population

Patients were required to be ≥ 18 years of age at the date of DMT initiation (index date), with at least 2 years of follow-up after the index date and minimal data available at the index date (EDSS score and date of diagnosis). DMTs were grouped into five groups (with orals split into two groups according to German MS DMT guidelines [13, 14]): (1) OCR, (2) injectable (interferon β-1a/b, glatiramer acetate), (3) oral (teriflunomide, dimethyl fumarate), (4) oral for highly active (HA) disease (oral HA; cladribine, fingolimod), and (5) natalizumab. Ozanimod, ponesimod, ofatumumab, diroximel fumarate, rituximab, alemtuzumab, and subcutaneously administered natalizumab were not included because of insufficient follow-up or being off-label.

Study Outcomes

Persistence was defined as having no discontinuation of the index DMT group, no treatment pauses/interruptions of more than 3 months, or switch to a new group of DMT during follow-up. Persistence was evaluated within each index DMT group, and in-group switches of DMT were allowed. The reasons for discontinuation were classified as follows: *Adverse events*: flu-like symptoms, side effects; *Patient driven*: fear of side effects, being compliant is difficult, lack of compliance, patient wish, no confidence in treatment, fear of needles; *Lack of efficacy*: lack of efficacy; *Pregnancy or child wish*: pregnancy, child wish; *Other*: maximal dosage reached (includes John Cunningham virus (JCV)-related discontinuations), antibodies, COVID-19, depression fatigue, freedom of disease activity, patient feels too healthy, other; *Unknown*: unknown. Risk of relapse was assessed using the annualized relapse rate (total number of relapses divided by the total person-years at risk). Risk of 3-months confirmed disability progression (3mCDP) during follow-up was assessed using the presence of a 3mCDP (an increase in EDSS score of at least 1.0 if baseline EDSS score was 0.0–5.0, or of at least 0.5 if baseline score was 5.5–6.5, confirmed after at least 3 months). Risk of sick leave was assessed using the presence of a sick leave day during follow-up.

Statistical Analysis

Descriptive statistics were used to summarize patient characteristics at baseline. Mann–Whitney (for all continuous variables)

and chi-squared tests (for all dichotomous variables) were used to compare baseline characteristics and discontinuation reasons of each cohort to the overall cohort (removing patients from the overall cohort occurring otherwise twice). Kaplan–Meier analysis was used to estimate the time to discontinuation of the index DMT group (persistence). An unadjusted Cox regression model was performed to compare the risk of discontinuation across index DMT groups. Marginal structural models (MSMs) were used to estimate the time-dependent effects of persistence while adjusting for time-dependent confounders (relapse and MRI activity). MSM weights were fitted using logistic regression. A marginal structural Poisson model, adjusted for time-dependent confounders, was used to estimate the effect of persistence on annualized relapse rate (accounting for the exposure time with a log offset). A marginal structural logistic model adjusted for time-dependent confounders was used to estimate the effect of persistence on the proportion of patients with 3mCDP (accounting for the exposure time with a complementary log–log offset) and on the proportion of patients with sick leave (accounting for the exposure time with a complementary log–log offset).

RESULTS

A total of 3907 patients with RRMS were included in the study. Their characteristics are summarized in Table 1. The majority of patients received oral DMTs (54%, $n=2095$), followed by injectable (25%, $n=984$), oral HA (15%, $n=581$), natalizumab (4%, $n=144$), and OCR (3%, $n=103$). At the index date, the mean age of the study population was 40.7 years, with a mean EDSS score of 1.95 and a female predominance of 72.1%. The mean number of relapses in the year prior to the index date ranged from 0.45 (oral) to 0.88 (natalizumab). The mean time from the date of diagnosis to the index date ranged from 3.9 (injectable) to 10.6 (OCR) years.

OCR users demonstrated the highest persistence (93%), followed by oral HA (78%), oral (67%), natalizumab (67%), and injectable therapies (55%) over a 2-year follow-up period (Fig. 1). When discontinuation rates were compared, patients initiating injectable (hazard ratio [HR] 8.51, 95% confidence interval [CI] 4.03–17.90), oral (HR 5.92, 95% CI 2.81–12.50), oral HA (HR 3.49, 95% CI 1.63–7.48), and natalizumab therapies (HR 5.47, 95% CI 2.47–12.10) were more likely to discontinue treatment within 2 years compared with OCR users. Patients receiving injectable DMTs had the highest rates of discontinuation (442/984, 44.92%), whereas OCR users had the lowest (7/103, 6.80%) (Table 2). Overall, the main reasons for discontinuation were adverse events (32.47%), lack of efficacy (21.17%), and patient-driven factors (19.73%). The primary reasons for discontinuation were reported as adverse events in the injectable (28.51%) and oral (37.59%) DMT groups; lack of efficacy in the OCR (42.86%) and oral HA (31.20%) DMT groups; and "other" (38.30%) in the natalizumab group. Further analysis revealed that non-persisters at 2 years had a higher risk of relapse (rate ratio 2.18, 95% CI 1.98–2.39), 3mCDP (rate ratio 1.52, 95% CI 1.28–1.77), and sick leave (rate ratio 1.71, 95% CI 1.49–1.98) than persisters across index DMT groups.

DISCUSSION

In this retrospective real-world analysis of outpatients in Germany, outpatients with RRMS who initiated OCR demonstrated higher persistence rates during the first 2 years compared with those on other DMTs. High persistence was also linked to a reduced risk of clinical disease activity, disease progression, and sick leave. Nonetheless, it is important to note that these results reflect associations rather than causal relationships.

Although there are differences in methodology, our findings are generally in line with those from previous studies [6–10]. Engmann et al. [7] analyzed US claims data from 4587 patients with MS and found that those initiating OCR had higher persistence and adherence rates at 12 and 18 months compared with other DMTs. Similarly, Nicholas et al. [8] conducted a

Table 1 Characteristics of study population

Characteristic	Total ($N = 3907$)	OCR ($n = 103$)	Injectable ($n = 984$)	Oral ($n = 2095$)	Oral HA ($n = 581$)	NTZ ($n = 144$)
Age at index date[a], mean (SD), years	40.7 (10.9)	42.8 (11.6)^{NS}	37.6 (11.1)***	42.3 (10.7)***	40.6 (10.3)^{NS}	37.4 (9.0)***
Female, *n* (%)	2816 (72.1)	64 (62.1)*	740 (75.2)*	1489 (71.1)^{NS}	411 (70.7)^{NS}	112 (77.8)^{NS}
EDSS score at index date[a], mean (SD)	1.95 (1.55)	2.62 (1.81)***	1.49 (1.34)***	1.94 (1.54)^{NS}	2.48 (1.56)***	2.64 (1.82)***
Number of relapses in 1 year before index date[a], mean (SD)	0.56 (0.70)	0.57 (0.72)^{NS}	0.59 (0.67)**	0.45 (0.64)***	0.79 (0.82)***	0.88 (0.85)***
Time from date of diagnosis to index date[a], mean (SD), years	6.90 (7.09)	10.60 (8.49)***	3.89 (5.75)***	7.52 (7.22)***	8.79 (6.92)***	8.23 (6.47)***
DMT naïve at index date[a], *n* (%)	1716 (43.9)	41 (39.8)^{NS}	704 (71.5)***	830 (39.6)***	100 (17.2)***	41 (28.5)***

DMTs were grouped into the following categories: (1) OCR, (2) injectable (interferon β-1a/b, glatiramer acetate), (3) oral (teriflunomide, dimethyl fumarate), (4) oral for highly active disease (oral HA; cladribine, fingolimod), and (5) natalizumab. Ozanimod, ponesimod, ofatumumab, diroximel fumarate, rituximab, alemtuzumab, and subcutaneously administered natalizumab were excluded because of insufficient follow-up or being off-label

DMT disease-modifying therapy, *EDSS* Expanded Disability Status Scale, *HA* highly active disease, *IV* intravenous, *NS*, not significant, *NTZ* natalizumab, *OCR* ocrelizumab, *SD* standard deviation

[a]Index date: date of DMT initiation during the identification period (January 2014 to April 2020)

NS, *$p < 0.05$, **$p < 0.01$, ***$p < 0.001$ vs overall cohort

retrospective chart review of 300 patients with RRMS initiating injectable DMTs and observed that non-persistent patients experienced a higher relapse rate, greater MRI-detected disease progression, and an increase in symptom incidence compared with persistent patients.

Persistence is challenging to achieve in MS and can be influenced by various factors, such as mode of administration, efficacy, tolerability, cost, and treatment satisfaction [15]. In our study, the main reasons for discontinuation in the overall population were adverse events, lack of efficacy, and patient-driven factors. These findings are consistent with previous research [9, 16]. Nicholas et al. [8] reported that the most commonly identified reasons for non-persistence were perceived lack of efficacy (22.2%), adverse events (18.8%), and fear of needles or self-injecting (9.4%). Likewise, Patti et al. [16] indicated that lack of efficacy was the most common reason for treatment switching.

One potential approach is to simplify dosing regimens by reducing both their complexity and frequency [17]. A real-world study by Tallantyre et al. [18] found that DMTs administered monthly (natalizumab) or annually (alemtuzumab and cladribine) had moderate or high (77.3%, 96.5%, and 95.5%, respectively) persistence rates over 2 years. However, the increased risk of progressive multifocal leukoencephalopathy associated with natalizumab limits its use and long-term persistence [19]. The high efficacy profile of OCR and its biannual dosing schedule (based on fixed dates jointly agreed upon by patients and their treating neurologists) may explain the higher persistence observed with OCR in our study; this is suggested by the low number of discontinuations due to lack of efficacy

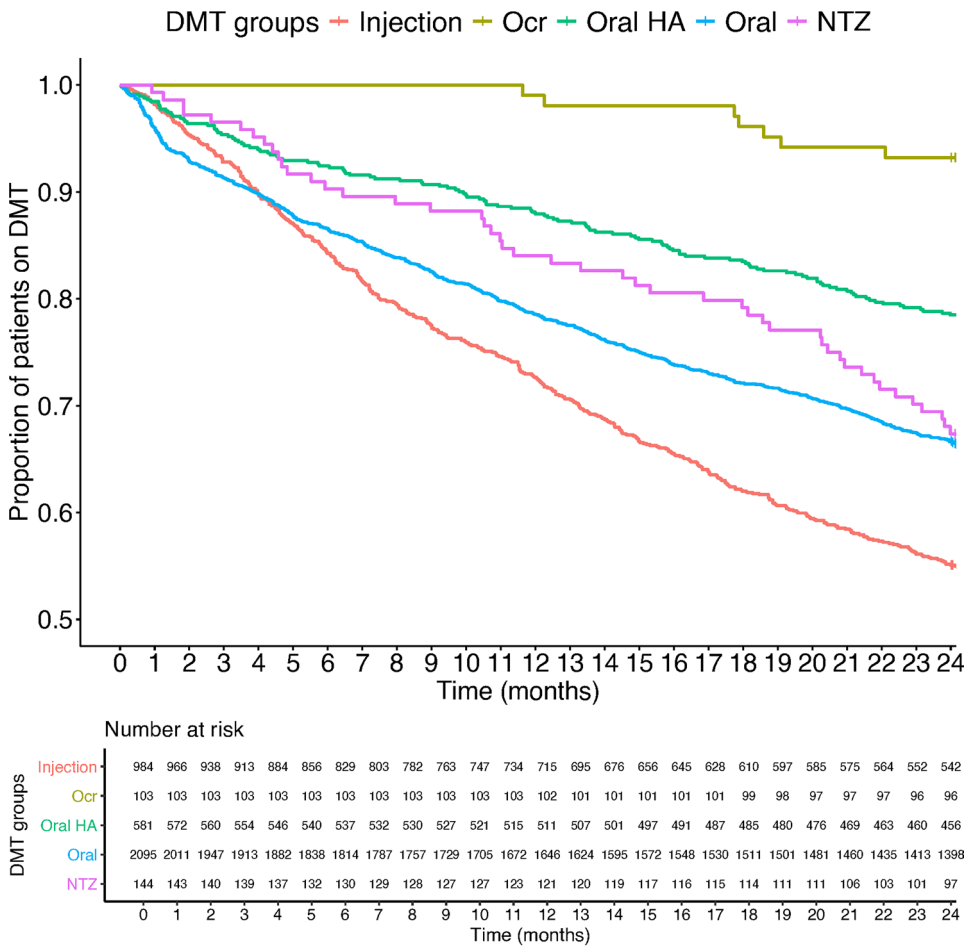

Fig. 1 Persistence with index DMT group in patients with RRMS over 2 years of follow-up. DMTs were grouped into the following categories: (1) OCR, (2) injectable (interferon β-1a/b, glatiramer acetate), (3) oral (teriflunomide, dimethyl fumarate), (4) oral for highly active disease (oral HA; cladribine, fingolimod), and (5) natalizumab. Ozanimod, ponesimod, ofatumumab, diroximel fumarate, rituximab, alemtuzumab, and subcutaneously administered natalizumab were excluded because of insufficient follow-up or being off-label. *DMT* disease-modifying therapy, *HA* highly active disease, *IV* intravenous, *NTZ* natalizumab, *OCR* ocrelizumab, *RRMS* relapsing–remitting multiple sclerosis

and patient preference in the OCR group. Additionally, continuous OCR administration for up to 11 years showed effective control of long-term disease activity and prevention of disability accumulation in RMS and PPMS populations [20]. OCR also continued to exhibit a favorable and manageable safety profile, with no new safety concerns in RMS and PMS populations [21]. However, long-term assessment of the safety of OCR in the treatment of MS in real-world setting is ongoing through several post-marketing safety studies [22–24].

A major strength of our study was the access to a large cohort of patients with MS in Germany, with high data density throughout the observation period. This allowed us to measure and adjust for clinical characteristics, such as MS subtype and EDSS score—factors often unaccounted for in previous studies comparing treatment groups. However, several limitations should be noted. First, this study did not

Table 2 Reasons for discontinuation of index DMT group

Reason for discontinuation[a]	Total ($N = 3907$)	OCR ($n = 103$)	Injectable ($n = 984$)	Oral ($n = 2095$)	Oral HA ($n = 581$)	NTZ ($n = 144$)
Number of patients who discontinued, *n* (%)[b]	1318 (33.73)	7 (6.80)***	442 (44.92)***	697 (33.27)^{NS}	125 (21.51)***	47 (32.64)^{NS}
Adverse events, *n* (%)[c]	428 (32.47)	0 (0.00)***	126 (28.51)*	262 (37.59)**	37 (29.60)***	3 (6.38)***
Patient driven, *n* (%)[c]	260 (19.73)	0 (0.00)*	86 (19.46)**	143 (20.52)^{NS}	17 (13.60)***	14 (29.79)^{NS}
Lack of efficacy, *n* (%)[c]	279 (21.17)	3 (42.86)^{NS}	101 (22.85)***	131 (18.79)*	39 (31.20)^{NS}	5 (10.64)^{NS}
Pregnancy or child wish, *n* (%)[c]	132 (10.02)	2 (28.57)^{NS}	64 (14.48)***	48 (6.89)***	13 (10.40)^{NS}	5 (10.64)^{NS}
Other, *n* (%)[c]	220 (16.69)	1 (14.29)^{NS}	82 (18.55)***	102 (14.63)*	17 (13.60)**	18 (38.30)***
Unknown, *n* (%)[c]	23 (1.75)	1 (14.29)^{NS}	7 (1.58)^{NS}	11 (1.58)^{NS}	2 (1.60)^{NS}	2 (4.26)^{NS}

DMTs were grouped into the following categories: (1) OCR, (2) injectable (interferon β-1a/b, glatiramer acetate), (3) oral (teriflunomide, dimethyl fumarate), (4) oral for highly active disease (oral HA; cladribine, fingolimod), and (5) natalizumab. Ozanimod, ponesimod, ofatumumab, diroximel fumarate, rituximab, alemtuzumab, and subcutaneously administered natalizumab were excluded because of insufficient follow-up or being off-label

Discontinuation was defined as a ≥ 90-day treatment gap in index DMT or a switch to another DMT. "Date of DMT initiation", "Date of DMT discontinuation", and "Reason for DMT discontinuation" were recorded on a standardized form completed by the treating neurologist at each clinic visit

DMT disease-modifying therapy, *HA* highly active disease, *IV* intravenous, *NS*, not significant; *NTZ*, natalizumab, *OCR* ocrelizumab

[a]The reasons for discontinuation were classified as follows: *Adverse events*: flu-like symptoms, side effects; *Patient driven*: fear of side effects, being compliant is difficult, lack of compliance, patient wish, no confidence in treatment, fear of needles; *Lack of efficacy*: lack of efficacy; *Pregnancy or child wish*: pregnancy, child wish; *Other*: maximal dosage reached (includes JCV-related discontinuations), antibodies, COVID-19, depression fatigue, freedom of disease activity, patient feels too healthy, other; *Unknown*: unknown

[b]Percentage was calculated among all patients

[c]Percentage was calculated among patients who discontinued

NS, *$p < 0.05$, **$p < 0.01$, ***$p < 0.001$ vs overall cohort

distinguish between tolerability issues and side effects leading to patient-driven discontinuation, versus adverse events resulting in healthcare professional-driven discontinuation [25, 26]. Second, the limited sample size of patients on OCR prevented us from comparing persisters and non-persisters within the OCR group. Third, the uneven distribution of DMT usage, with a high number of patients on oral medications ($n > 2000$) compared with OCR users ($n < 110$), may have introduced some bias into our findings. Fourth, ofatumumab was approved in March 2021; however, our study inclusion criteria required at least 2 years of follow-up post treatment initiation by April 2022. Finally, there may be unmeasured confounders not accounted for in the study limiting our findings.

CONCLUSION

Consistent with previous US claims data studies, this real-world study confirms that patients initiating OCR are more likely to persist with treatment compared with those on other DMTs

within a 2-year follow-up period in a German real-world setting. High persistence was associated with a lower risk of relapse activity, disease progression, and sick leave. Nonetheless, further research is needed to understand the complexity, multidirectional interactions between persistence and other influencing factors.

ACKNOWLEDGEMENTS

We would like to thank all patients, their families, and the investigators who participated in this study.

Medical Writing, Editorial, and Other Assistance. Editorial support (including assistance with revisions to the manuscript for non-intellectual content, figure redraws, and copy-editing) was provided by Thato Motlhalamme, PhD, of Nucleus Global, an Inizio company, UK, and funded by F. Hoffmann-La Roche Ltd, Basel, Switzerland. The authors had full editorial control of the manuscript and provided their final approval of all content.

Authorship. All authors whose names appear on the submission have: Made substantial contributions to the conception or design of the work; or the acquisition, analysis, or interpretation of data; or the creation of new software used in the work. Drafted the work or revised it critically for important intellectual content. Approved the version to be published. Agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy of integrity of any part of the work are appropriately investigated and resolved.

Author Contributions. Stefan Braune, Petra Dirks, Seya Colloud, Qing Wang, Evan Davies, Yanic Heer and Diana Sun contributed to the study conception and design. Material preparation, data collection and analysis were performed by Yanic Heer, Mel Zürcher and Arnfin Bergmann. The first draft of the manuscript was written by Stefan Braune, Yanic Heer and Diana Sun. Stefan Braune, Petra Dirks, Seya Colloud, Qing Wang, Evan Davies, Yanic Heer, Diana Sun and Arnfin Bergmann commented on previous versions of the manuscript and read and approved the final manuscript.

Funding. This study was sponsored by F. Hoffmann-La Roche Ltd, Basel, Switzerland. F. Hoffmann-La Roche Ltd, Basel, Switzerland was involved in the design and conduct of the study; the collection, management, analysis, and interpretation of the data; the preparation, review, or approval of the manuscript; and the decision to submit the manuscript for publication. Funding for the journal's rapid service fee was provided by F. Hoffmann-La Roche Ltd, Basel, Switzerland.

Data Availability. The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

Declarations

Conflict of Interest. Stefan Braune received honoraria from Kassenärztliche Vereinigung Bayerns and health maintenance organizations for patient care; and from, Merck, NeuroTransData, Novartis, Sanofi and Roche for consulting, project management, clinical studies, and lectures; he also received honoraria and expense compensation as a board member of NeuroTransData. Petra Dirks was an employee of F. Hoffmann-La Roche Ltd during completion of this work and is a shareholder in F. Hoffmann-La Roche Ltd; her current affiliation is Carl-von-Ossietzky University, Oldenburg, Germany. Seya Colloud is an employee of and a shareholder in F. Hoffmann-La Roche Ltd. Evan Davies is an employee of and a shareholder in F. Hoffmann-La Roche Ltd. Qing Wang is an employee of and a shareholder in F. Hoffmann-La Roche Ltd. Yanic Heer was contracted to perform statistical projects for NeuroTransData and was an employee of PricewaterhouseCoopers AG during completion of this work. Mel Zürcher was contracted to perform statistical projects for NeuroTransData and was an employee of PricewaterhouseCoopers AG during completion of this work. Diana Sun is an

employee of Genentech, Inc., and a shareholder in F. Hoffmann-La Roche Ltd. Arnfin Bergmann received consultancy fees from advisory board, speaker, and other activities for NeuroTransData; project management and clinical studies from Novartis and Servier.

Ethical Approval. The data acquisition protocol was approved by the ethical committee of the Bavarian Medical Board (Bayerische Landesärztekammer, June 14, 2012, No. 11144) and reapproved by the ethical committee of the Medical Board North-Rhine (Ärztekammer Nordrhein, April 25, 2017, ID 2017071). The study conforms to the World Medical Association Declaration of Helsinki as published on the website of the *Journal of American Medical Association*, the Guidelines for Good Pharmacoepidemiology Practices (GPP) published by the International Society of Pharmacoepidemiology (ISPE), and the laws and regulations of Germany. Patient inclusion with informed consent is completed in the respective NTD practice as part of routine clinical care. Patients included in this analysis provided their informed consent (via tablets in NTD practices, electronic questionnaires, or via a patient portal) to the NTD registry. Patients explicitly agreed to secondary use of their data. All personnel undergo regular training to ensure quality of data in the registry. Both automatic and manually executed queries are implemented to further ensure data quality [13]. All data are pseudonymized and pooled to form the NTD registry.

REFERENCES

1. Kobelt G, Berg J, Lindgren P, et al. Costs and quality of life of multiple sclerosis in Germany. Eur J Health Econ. 2006;7(Suppl 2):S34-44.

2. Flachenecker P, Kobelt G, Berg J, Capsa D, Gannedahl M. New insights into the burden and costs of multiple sclerosis in Europe: results for Germany. Mult Scler. 2017;23(2_suppl):78–90.

3. Lee CY, Chan KH. Personalized use of disease-modifying therapies in multiple sclerosis. Pharmaceutics. 2024;16(1):120.

4. Tan H, Cai Q, Agarwal S, Stephenson JJ, Kamat S. Impact of adherence to disease-modifying therapies on clinical and economic outcomes among patients with multiple sclerosis. Adv Ther. 2011;28(1):51–61.

5. Freeman L, Kee A, Tian M, Mehta R. Retrospective claims analysis of treatment patterns, relapse, utilization, and cost among patients with multiple sclerosis initiating second-line disease-modifying therapy. Drugs Real World Outcomes. 2021;8:497–508.

6. Pardo G, Pineda ED, Ng CD, Bawa KK, Sheinson D, Bonine NG. Adherence to and persistence with disease-modifying therapies for multiple sclerosis over 24 months: a retrospective claims analysis. Neurol Ther. 2022;11:337–51.

7. Engmann NJ, Sheinson D, Bawa K, Ng CD, Pardo G. Persistence and adherence to ocrelizumab compared with other disease-modifying therapies for multiple sclerosis in US commercial claims data. J Manag Care Spec Pharm. 2021;27:639–49.

8. Nicholas J, Ko JJ, Park Y, et al. Assessment of treatment patterns associated with injectable disease-modifying therapy among relapsing-remitting multiple sclerosis patients. Mult Scler J Exp Transl Clin. 2017;3:1–9.

9. Thomas NP, Curkendall S, Farr AM, Yu E, Hurley D. The impact of persistence with therapy on inpatient admissions and emergency room visits in the U.S. among patients with multiple sclerosis. J Med Econ. 2016;19(5):497–505.

10. Reynolds MW, Stephen R, Seaman C, Rajagopalan K. Healthcare resource utilization following switch or discontinuation in multiple sclerosis patients on disease modifying drugs. J Med Econ. 2010;13(1):90–8.

11. Bergmann A, Stangel M, Weih M, et al. Development of registry data to create interactive doctor-patient platforms for personalized patient care, taking the example of the DESTINY System. Front Digit Health. 2021;3:633427.

12. Wehrle K, Tozzi V, Braune S, et al. Implementation of a data control framework to ensure confidentiality, integrity, and availability of high-quality real-world data (RWD) in the NeuroTransData (NTD) registry. JAMIA Open. 2022;5(1):ooac017.

13. Wiendl H, Gold R, Berger T, et al. Multiple Sclerosis Therapy Consensus Group (MSTCG): position statement on disease-modifying therapies for multiple sclerosis (white paper). Ther Adv Neurol Disord. 2021;14:17562864211039648.

14. Hemmer B, et al. Diagnose und Therapie der Multiplen Sklerose, Neuromyelitis-optica-Spektrum-Erkrankungen und MOG-IgG-assoziierten Erkrankungen, S2k-Leitlinie, 2024, In: Deutsche Gesellschaft für Neurologie (Hrsg.), Leitlinien für Diagnostik und Therapie in der Neurologie. www.dgn.org/leitlinien). Accessed 7 Apr 2025.

15. Araujo L, Geertsen SS, Amedume A, Higuchi K, van Wingerden J. Persistence, adherence, and switching to higher-cost therapy in patients with multiple sclerosis initiating oral disease-modifying therapies: a retrospective real-world study. Neurol Ther. 2022;11(4):1735–48.

16. Patti F, Chisari CG, D'Amico E, et al. Clinical and patient determinants of changing therapy in relapsing-remitting multiple sclerosis (SWITCH study). Mult Scler Relat Disord. 2020;42:102124.

17. Menzin J, Caon C, Nichols C, White LA, Friedman M, Pill MW. Narrative review of the literature on adherence to disease-modifying therapies among patients with multiple sclerosis. J Manag Care Pharm. 2013;19(1 Suppl A):24-S40.

18. Tallantyre EC, Dobson R, Froud JLJ, et al. Real-world persistence of multiple sclerosis disease-modifying therapies. Eur J Neurol. 2024;31(7):e16289.

19. Amin M, Hersh CM. Updates and advances in multiple sclerosis neurotherapeutics. Neurodegener Dis Manag. 2023;13(1):47–70.

20. Hauser SL, Giovannoni G, Filippi M, et al. The patient impact of 11 years of ocrelizumab treatment in multiple sclerosis: long-term data from the Phase III OPERA and ORATORIO studies. Poster presented at the European Committee for Treatment and Research in Multiple Sclerosis (ECTRIMS); 18–20 September 2024; Copenhagen, Denmark.2024 (P1664).

21. Hauser SL, Kappos L, Montalban X, et al. Safety of ocrelizumab in multiple sclerosis: up to 11 years of updated analysis in patients with relapsing and progressive multiple sclerosis. Poster presented at the European Committee for Treatment and Research in Multiple Sclerosis (ECTRIMS); 18–20 September 2024; Copenhagen, Denmark.2024 (P300).

22. EMA RWD Catalogues. An observational study of ocrelizumab treated patients with multiple sclerosis to determine the incidence and mortality rates of breast cancer and all malignancies (VERISMO Study). EU PAS number: EUPAS30752. https://catalogues.ema.europa.eu/node/2960/administrative-details. Accessed Dec 10 2024.

23. EMA RWD Catalogues. Long-term surveillance of ocrelizumab treated patients with multiple sclerosis (MANUSCRIPT Study). EU PAS number: EUPAS28619. https://catalogues.ema.europa.eu/node/2050/administrative-details. Accessed Dec 10 2024.

24. EMA RWD Catalogues. Safety and effectiveness of ocrelizumab under real world conditions: a non-interventional post authorization safety study in patients diagnosed with relapsing or primary progressive multiple sclerosis (CONFIDENCE). EU PAS number: EUPAS22951. https://catalogues.ema.europa.eu/node/3142/administrative-details. Accessed Dec 10 2024.

25. Wicks P, Rasouliyan L, Katic B, et al. The real-world patient experience of fingolimod and dimethyl fumarate for multiple sclerosis. BMC Res Notes. 2016;9:434.

26. Saccà F, Lanzillo R, Signori A, et al. Determinants of therapy switch in multiple sclerosis treatment-naïve patients: a real-life study. Mult Scler. 2019;25(9):1263–72.