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# Persistence to Ocrelizumab Compared with Other Disease-Modifying Therapies for Multiple Sclerosis in the German NeuroTransData Registry

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## STUDY AIMS

We aimed to examine the persistence to OCR compared with other DMTs and its association with outcomes in patients with relapsing-remitting MS (RRMS) from the NeuroTransData (NTD) MS registry

## CONCLUSIONS

**In a real-world setting, ocrelizumab users showed higher persistence compared with those taking other DMTs within 2 and 3 years of follow-up, and persistence was found to be associated with lower risk of clinical disease activity, disease progression and sick leave**

Our findings indicate that high persistence reflects better disease control

## BACKGROUND

**Ocrelizumab (OCR) is given twice a year as intravenous (IV) infusions for the treatment of multiple sclerosis (MS) and has shown higher persistence than other disease-modifying therapies (DMTs) in US claims data[1,2]**

High persistence is important for controlling disease worsening and can be an indicator of a favourable outcome[3]

## METHODS

### Data Source

- NTD is a Germany-wide network of neurologists and psychiatrists, founded in 2008. Currently, the NTD network includes 164 specialists in 56 practices serving ~600,000 outpatients per year
- The NTD MS registry is a disease-specific database run by the NTD network. Currently, the NTD MS registry includes ~25,000 patients with MS

### Study Design and Population

- This was a retrospective cohort analysis of German outpatients diagnosed with RRMS enrolled in the NTD MS registry who initiated an approved DMT between January 2014 and April 2022
- Patients had to be ≥18 years of age at index; had a minimum of 2 years (or 3 years) of follow-up after their index date; and had minimal data availability at index (Expanded Disability Status Scale [EDSS] score, date of diagnosis, date of manifestation). Index date was defined as the date of DMT initiation during the study period
- DMTs were grouped into: 1) OCR, 2) injectable (interferon β-1a/1b, glatiramer acetate), 3) oral (teriflunomide, dimethyl fumarate), 4) oral for highly active disease (HA) (oral HA; cladribine, fingolimod) and 5) other IV (natalizumab). Ozanimod, ponesimod, ofatumumab, diroximel fumarate and subcutaneous natalizumab were excluded due to insufficient follow-up
- Persistence was defined as no discontinuation of the index DMT group 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

### Study Outcomes and Analyses

- Descriptive statistics were used to summarise patient characteristics at baseline
- Kaplan–Meier analysis was used to estimate the time to discontinuation of the index DMT group (i.e. persistence). An unadjusted Cox regression model was performed to compare the risk of discontinuation across index DMT groups
- Marginal structural models were performed to estimate the effect of persistence on study outcomes while accounting for time-dependent confounders
  - Risk of relapse was defined as the annualised relapse rate (total number of relapses divided by the total person-years at risk). A marginal structural Poisson model, adjusted for time-dependent confounders, was used to estimate the effect of persistence on annualised relapse rate
  - Risk of 3-months confirmed disability progression (3mCDP) was defined as the presence of a 3mCDP (an increase in EDSS score of at least 1.0 if baseline EDSS score was 3.0–5.0, or of at least 0.5 if baseline EDSS score was 5.5–6.5, confirmed after at least 3 months). 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
  - Risk of sick leave was defined as the presence of a sick leave day. A marginal structural logistic model, adjusted for time-dependent confounders, was used to estimate the effect of persistence on the proportion of patients with sick leave

## RESULTS

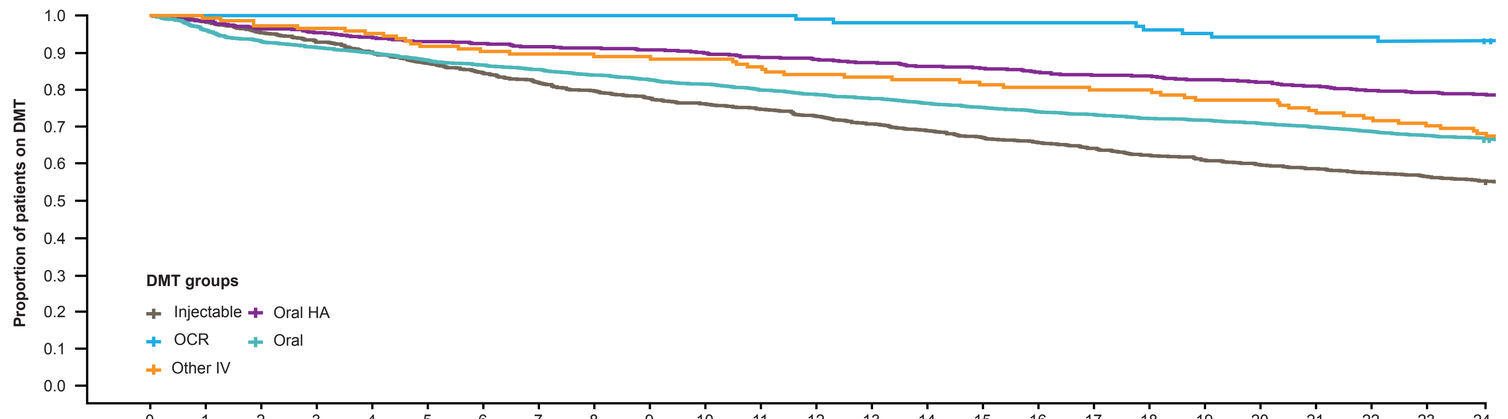
- A total of 3,907 patients with RRMS with 2 years of follow-up (OCR: 103; injectable: 984; oral HA: 581; oral: 2,095; other IV: 144) were included (**Table 1**)
- OCR users had the highest persistence at 2 years (93%), followed by oral HA (78%), oral (67%), other IV (67%) and injectable (55%) therapies (**Figure 1**)
  - 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) and other IV (HR: 5.47, 95% CI: 2.47–12.10) therapies were more likely to discontinue within 2 years
- Overall, adverse events (32.5%), lack of efficacy (21.2%) and patient driven (19.7%) were the main reasons for discontinuation (**Table 2**)
- Compared with persisters, non-persisters at 2 years were associated with higher risk for relapse (rate ratio: 2.18, 95% CI: 1.98–2.39), 3mCDP (risk ratio: 1.52, 95% CI: 1.28–1.77) and sick leave (risk ratio: 1.71, 95% CI: 1.49–1.98) across index DMT groups
- Similar results were observed over 3 years of follow-up (**Supplementary Materials**)

### Table 1. Baseline Characteristics of Patients with RRMS with 2 Years of Follow-Up

| Characteristic | Overall (N=3,907) | OCR (n=103) | Injectable (n=984) | Oral (n=2,095) | Oral HA (n=581) | Other IV (n=144) |
|---|---|---|---|---|---|---|
| **Age at index date**,[a] mean (SD), years | **40.7** (10.9) | **42.8** (11.6) | **37.6** (11.1) | **42.3** (10.7) | **40.6** (10.3) | **37.4** (9.0) |
| **Females**, n (%) | **2,816** (72.1) | **64** (62.1) | **740** (75.2) | **1,489** (71.1) | **411** (70.7) | **112** (77.8) |
| **EDSS score at index date**,[a] mean (SD) | **1.95** (1.6) | **2.62** (1.8) | **1.49** (1.3) | **1.94** (1.5) | **2.48** (1.6) | **2.64** (1.8) |
| **Number of relapses in 1 year before index date**,[a] mean (SD) | **0.56** (0.7) | **0.57** (0.7) | **0.59** (0.7) | **0.45** (0.6) | **0.79** (0.8) | **0.88** (0.8) |
| **Time from date of diagnosis to index date[a] (years)**, mean (SD) | **6.9** (7.1) | **10.6** (8.5) | **3.9** (5.8) | **7.5** (7.2) | **8.8** (6.9) | **8.2** (6.5) |

[a]Index date: Date of DMT initiation during the study period.
DMTs were grouped into the following categories: 1) OCR, 2) injectable (interferon β-1a/1b, glatiramer acetate), 3) oral (teriflunomide, dimethyl fumarate), 4) oral for highly active disease (oral HA; cladribine, fingolimod) and 5) other intravenous (other IV; natalizumab). Ozanimod, ponesimod, ofatumumab, diroximel fumarate and subcutaneous natalizumab were excluded due to insufficient follow-up.
DMT, disease-modifying therapy; EDSS, Expanded Disability Status Scale; HA, highly active disease; IV, intravenous; OCR, ocrelizumab; RRMS, relapsing-remitting multiple sclerosis; SD, standard deviation.

### Figure 1. Persistence with Index DMT Group in Patients with RRMS Over 2 Years of Follow-Up




| Number at risk: | | | | | | | | | | | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| DMT groups | Injectable | 984 | 966 | 938 | 913 | 884 | 856 | 829 | 803 | 782 | 763 | 747 | 734 | 715 | 695 | 676 | 656 | 645 | 628 | 610 | 597 | 585 | 575 | 564 | 552 | 542 |
| | OCR | 103 | 103 | 103 | 103 | 103 | 103 | 103 | 103 | 103 | 103 | 103 | 103 | 102 | 101 | 101 | 101 | 101 | 101 | 99 | 98 | 97 | 97 | 97 | 96 | 96 |
| | Oral HA | 581 | 572 | 560 | 554 | 546 | 540 | 537 | 532 | 530 | 527 | 521 | 515 | 511 | 507 | 501 | 497 | 491 | 487 | 485 | 480 | 476 | 469 | 463 | 460 | 456 |
| | Oral | 2,095 | 2,011 | 1,947 | 1,913 | 1,882 | 1,838 | 1,814 | 1,787 | 1,757 | 1,729 | 1,705 | 1,672 | 1,646 | 1,624 | 1,595 | 1,572 | 1,548 | 1,530 | 1,511 | 1,501 | 1,481 | 1,460 | 1,435 | 1,413 | 1,398 |
| | Other IV | 144 | 143 | 140 | 139 | 137 | 132 | 130 | 129 | 128 | 127 | 127 | 123 | 121 | 120 | 119 | 117 | 116 | 115 | 114 | 111 | 111 | 106 | 103 | 101 | 97 |

DMTs were grouped into the following categories: 1) OCR, 2) injectable (interferon β-1a/1b, glatiramer acetate), 3) oral (teriflunomide, dimethyl fumarate), 4) oral for highly active disease (oral HA; cladribine, fingolimod) and 5) other intravenous (other IV; natalizumab). Ozanimod, ponesimod, ofatumumab, diroximel fumarate and subcutaneous natalizumab were excluded due to insufficient follow-up.
DMT, disease-modifying therapy; HA, highly active disease; IV, intravenous; OCR, ocrelizumab; RRMS, relapsing-remitting multiple sclerosis.

### Table 2. Reasons for Discontinuation of Index DMT Group in Patients with RRMS During the 2-Year Follow-Up

| Reason for discontinuation | Overall (N=3,907) | OCR (n=103) | Injectable (n=984) | Oral (n=2,095) | Oral HA (n=581) | Other IV (n=144) |
|---|---|---|---|---|---|---|
| **Number of patients who discontinued, n (%)[a]** | **1,318** (33.7) | **7** (6.8) | **442** (44.9) | **697** (33.3) | **125** (21.5) | **47** (32.6) |
| Adverse events, n (%)[b] | **428** (32.5) | **0** (0.0) | **126** (28.5) | **262** (37.6) | **37** (29.6) | **3** (6.4) |
| Patient driven, n (%)[b] | **260** (19.7) | **0** (0.0) | **86** (19.5) | **143** (20.5) | **17** (13.6) | **14** (29.8) |
| Lack of efficacy, n (%)[b] | **279** (21.2) | **3** (42.9) | **101** (22.9) | **131** (18.8) | **39** (31.2) | **5** (10.6) |
| Pregnancy or child wish, n (%)[b] | **132** (10.0) | **2** (28.6) | **64** (14.5) | **48** (6.9) | **13** (10.4) | **5** (10.6) |
| Other, n (%)[b] | **220** (16.7) | **1** (14.3) | **82** (18.6) | **102** (14.6) | **17** (13.6) | **18** (38.3) |
| Unknown, n (%)[b] | **23** (1.8) | **1** (14.3) | **7** (1.6) | **11** (1.6) | **2** (1.6) | **2** (4.3) |

[a]Percentage was calculated among all patients; [b]Percentage was calculated among patients who discontinued.
DMTs were grouped into the following categories: 1) OCR, 2) injectable (interferon β-1a/1b, glatiramer acetate), 3) oral (teriflunomide, dimethyl fumarate), 4) oral for highly active disease (oral HA; cladribine, fingolimod) and 5) other intravenous (other IV; natalizumab). Ozanimod, ponesimod, ofatumumab, diroximel fumarate and subcutaneous natalizumab were excluded due to insufficient follow-up.
DMT, disease-modifying therapy; HA, highly active disease; IV, intravenous; OCR, ocrelizumab; RRMS, relapsing-remitting multiple sclerosis.

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