P732

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

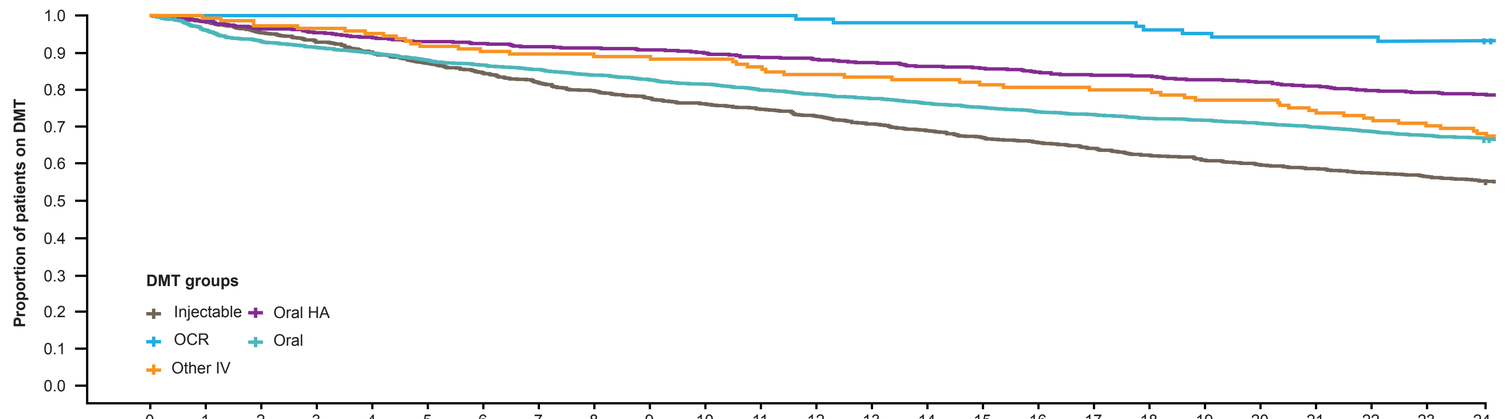
- A total of 3,907 patients with RRMS with 2 years of follow-up (OCR: 103; injectable: 984; oral HA: 581; oral: 2,095; other IV: 144) were included (**Table 1**)
- OCR users had the highest persistence at 2 years (93%), followed by oral HA (78%), oral (67%), other IV (67%) and injectable (55%) therapies (**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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DISCLOSURES
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Supplementary materials

Results

- A total of 3,216 patients with RRMS with 3 years of follow-up (OCR: 47; injectable: 806; oral: 1,771; oral HA: 477; other IV: 115) were included (**Table 1b**)
- OCR users had the highest persistence at 3 years (79%), followed by oral HA (73%), oral (59%), other IV (57%) and injectable (45%) (**Figure 1b**)
  - Compared with OCR users, patients initiating injectable (HR: 3.5, 95% CI: 1.9–6.5), oral (HR: 2.3, 95% CI: 1.3–4.4), oral HA (HR: 1.4, 95% CI: 0.7–2.6) and other IV (HR: 2.3, 95% CI: 1.2–4.5) were more likely to discontinue at 3 years
- Overall, adverse events (29.4%), lack of efficacy (23.4%) and patient driven (20.4%) were the main reasons for discontinuation (**Table 2b**)
- Compared with persisters, non-persisters at 3 years were associated with higher risk of relapse (risk ratio: 2.0, 95% CI: 1.8–2.2), 3mCDP (risk ratio: 1.5, 95% CI: 1.3–1.6) and sick leave (risk ratio: 1.8, 95% CI: 1.5–2.0) across index DMT groups

3mCDP, 3-month confirmed disability progression; CI, confidence interval; DMT, disease-modifying therapy; HA, highly active disease; HR, hazard ratio; IV, intravenous; OCR, ocrelizumab; RRMS, relapsing-remitting multiple sclerosis.

Results

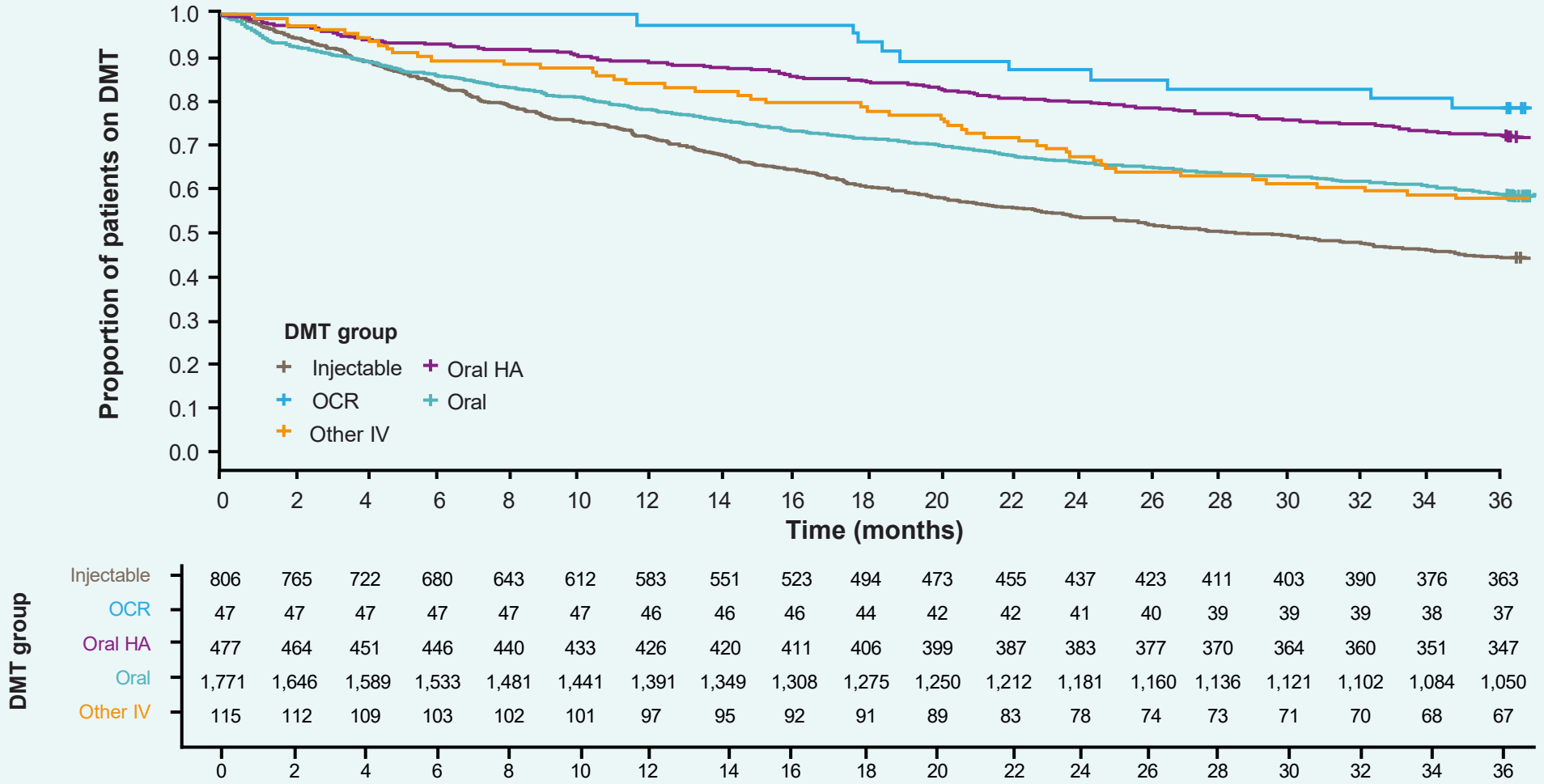
Table 1b. Baseline characteristics of patients with RRMS with 3 years of follow-up

Characteristic	Overall (N=3,216)	OCR (n=47)	Injectable (n=806)	Oral (n=1,771)	Oral HA (n=477)	Other IV (n=115)
Age at index date,[a] mean (SD), years	**40.9** (10.9)	**43.4** (11.6)	**37.9** (11.4)	**42.4** (10.5)	**40.8** (10.4)	**37.6** (8.7)
Females, n (%)	**2,311** (71.9)	**33** (70.2)	**611** (75.8)	**1,252** (70.7)	**330** (69.2)	**85** (73.9)
EDSS score at index date,[a] mean (SD)	**1.98** (1.6)	**2.43** (1.9)	**1.53** (1.3)	**1.99** (1.5)	**2.52** (1.6)	**2.69** (1.9)
Number of relapses in 1 year before index date,[a] mean (SD)	**0.57** (0.71)	**0.60** (0.68)	**0.60** (0.68)	**0.46** (0.65)	**0.83** (0.82)	**0.92** (0.86)
Time from date of diagnosis to index date,[a] mean (SD), years	**7.0** (7.1)	**9.9** (9.1)	**4.0** (5.9)	**7.8** (7.3)	**8.6** (6.9)	**8.4** (6.4)

DMTs were grouped into the following categories: 1) OCR; 2) injectable (interferon β-1a/1b, glatiramer acetate); 3) oral (teriflunomide, dimethyl fumarate); 4) oral HA (cladribine, fingolimod) and 5) other IV (natalizumab). Ozanimod, ponesimod, ofatumumab, diroximel fumarate and subcutaneous natalizumab were excluded due to insufficient follow-up.
[a]Index date: Date of DMT initiation during the study period.
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.

Results

Figure 1b. Persistence to index DMT group in patients with RRMS over 3 years of follow-up



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DMT, disease-modifying therapy; HA, highly active disease; IV, intravenous; OCR, ocrelizumab; RRMS, relapsing-remitting multiple sclerosis.

Results

Table 2b. Patients with RRMS who discontinued their index DMT group during the 3-year follow-up

Reason for discontinuation	Overall (N=3,216)	OCR (n=47)	Injectable (n=806)	Oral (n=1,771)	Oral HA (n=477)	Other IV (n=115)
Number of patients who discontinued, n (%)[a]	**1,352** (42.0)	**10** (21.3)	**443** (55.0)	**721** (40.7)	**130** (27.3)	**48** (41.7)
Adverse events, n (%)[b]	**398** (29.4)	**0** (0)	**120** (27.1)	**249** (34.5)	**25** (19.2)	**4** (8.3)
Patient driven, n (%)[b]	**276** (20.4)	**1** (10.0)	**88** (19.9)	**153** (21.2)	**19** (14.6)	**15** (31.2)
Lack of efficacy, n (%)[b]	**317** (23.4)	**3** (30.0)	**106** (23.9)	**149** (20.7)	**53** (40.8)	**6** (12.5)
Pregnancy or child wish, n (%)[b]	**141** (10.4)	**1** (10.0)	**65** (14.7)	**52** (7.2)	**16** (12.3)	**7** (14.6)
Other, n (%)[b]	**220** (16.3)	**3** (30.0)	**81** (18.3)	**107** (14.8)	**16** (12.3)	**13** (27.1)
Unknown, n (%)[b]	**23** (1.7)	**2** (20.0)	**6** (1.4)	**11** (1.5)	**1** (0.8)	**3** (6.3)

DMTs were grouped into the following categories: 1) OCR; 2) injectable (interferon β-1a/1b, glatiramer acetate); 3) oral (teriflunomide, dimethyl fumarate); 4) oral HA (cladribine, fingolimod) and 5) other IV (natalizumab). Ozanimod, ponesimod, ofatumumab, diroximel fumarate and subcutaneous natalizumab were excluded due to insufficient follow-up.
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