Assessing the impact of persistency for disease-modifying therapies in a German registry for multiple sclerosis

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Introduction

- Multiple sclerosis (MS) is a chronic, progressive inflammatory disease of the central nervous system characterized by reversible episodes of neurological dysfunction that can eventually lead to irreversible neurological disability.[1,2]
- Several disease-modifying therapies (DMTs) have demonstrated effectiveness in reducing disease activity and progression in people with relapsing–remitting MS (RRMS).[2]
- A key element for successful treatment with DMTs in people with MS is the degree of patient treatment persistence and adherence. Previous studies have demonstrated an association between high treatment persistence and adherence and improved outcomes, including a reduction in relapses[3] and reduced healthcare resource utilization.[3,4]

Objective

- To identify and characterize patients with RRMS based on treatment persistence, and to compare real-world clinical outcomes in patients with high versus low treatment persistence.

Methods

- Data including demographic information, clinical history and clinical variables during outpatient visits were obtained from the MS disease registry of the German NeuroTransData network of neurologists and psychiatrists.
- Included patients had RRMS, had received a maximum of one prior DMT, and had at least one clinical visit after the date of therapy initiation (the index date). Only patients with an index date after 1 January 2009 were included.
- High treatment persistence (HP) was defined as continuous exposure to the same DMT for at least 2 years. Low treatment persistence (LP) was defined as continuous exposure to the same treatment for less than 2 years.
- To ensure similar baseline characteristics, HP and LP patients were compared after 1:1 propensity score matching by age, sex, number of relapses in the previous 12 months, baseline Expanded Disability Status Scale (EDSS) score and time since disease onset.
- A sensitivity analysis was performed, including HP and LP patients who were matched by including the mode of administration of DMTs to the matching factors.
- The main outcomes were the time to first relapse, time to 12-week confirmed disability progression (CDP) and annualized relapse rates (ARRs). Treatment outcomes (relapses and 12-week CDP) were censored after the index DMT was discontinued, or after 2 years or the end of follow-up (whichever occurred first). Hazard ratios for HP versus LP cohorts were calculated using a Cox proportional hazards regression model. ARRs were compared using a Poisson regression (for each DMT or group of DMTs) with a binary cohort coefficient to encode HP and LP patients. A log offset was used to account for varying exposure times.

Results

- Patient baseline demographic and disease characteristics for all included patients before propensity score matching are shown in **Table 1**.
- In total, 2367 patients were matched into each of the HP and LP cohorts (**Table 2**).
- Patient baseline demographic and disease characteristics were similar between the matched HP and LP cohorts; a higher proportion of patients in the HP cohort received oral DMTs than the LP cohort. Overall mean (standard deviation) duration of exposure to DMTs was 4.7 (2.2) years for the HP cohort and 0.8 (0.6) years for the LP cohort.
- In matched patients, the time to first relapse was longer for HP patients than LP patients (**Figure 1**). The hazard ratio (HR) (95% confidence interval [CI]) for time to first relapse for HP versus LP was 2.0 (95% CI, 1.7–2.2; Wald $p < 0.001$).

Table 1. Baseline demographic and disease characteristics in HP and LP patients with RRMS

Demographic or characteristic	HP patients n = 3590	LP patients n = 2373
Age at index date, years, mean (SD)	39.9 (10.7)	38.3 (10.8)
Sex, female, n (%)	2481 (69.1)	1812 (76.4)
Time since disease onset, years, mean (SD)	7.4 (7.7)	6.7 (7.3)
EDSS score, mean (SD)	1.9 (1.5)	2.0 (1.5)
ARR in the 12 months before index date, mean (SD)	0.7 (0.8)	0.7 (0.8)
Type of DMT, n (%)		
Injection	1603 (44.7)	1285 (54.2)
Oral	1651 (46.0)	843 (35.5)
Infusion	15 (0.4)	97 (4.1)
Monoclonal	321 (8.9)	148 (6.2)

ARR, annualized relapse rate; DMT, disease-modifying therapy; EDSS, Expanded Disability Status Scale; HP, high treatment persistence; LP, low treatment persistence; RRMS, relapsing–remitting multiple sclerosis; SD, standard deviation.

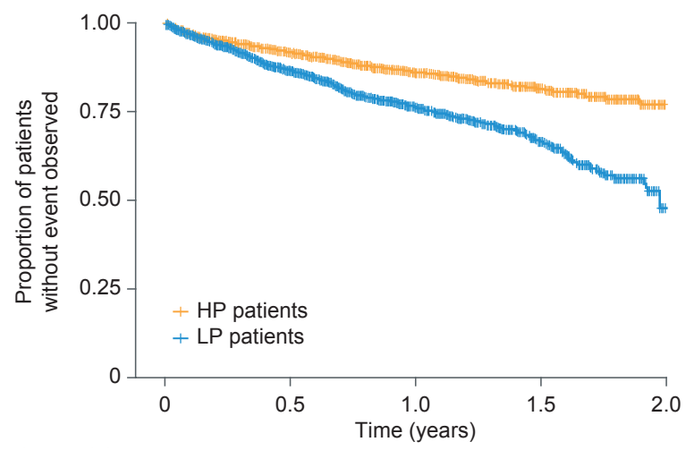
Table 2. Baseline demographic and disease characteristics were similar in propensity score-matched HP and LP patients with RRMS (excluding DMT type as a matching factor)

Characteristic	HP patients n = 2367	LP patients n = 2367
Age at index date, mean (SD)	38.4 (10.6)	38.3 (10.8)
Sex, female, n (%)	1800 (76.0)	1808 (76.4)
Time since disease onset, years, mean (SD)	6.6 (7.2)	6.7 (7.3)
EDSS score, mean (SD)	2.0 (1.5)	2.0 (1.5)
ARR in the 12 months before index date, mean (SD)	0.7 (0.8)	0.7 (0.8)
Type of DMT, n (%)		
Injection	1041 (44.0)	1285 (54.3)
Oral	1080 (45.6)	838 (35.4)
Infusion	8 (0.3)	96 (4.1)
Monoclonal	238 (10.1)	148 (6.3)

ARR, annualized relapse rate; DMT, disease-modifying therapy; EDSS, Expanded Disability Status Scale; HP, high treatment persistence; LP, low treatment persistence; RRMS, relapsing–remitting multiple sclerosis; SD, standard deviation.

- The time to 12-week CDP was also longer for HP patients than LP patients (**Figure 2**). The HR was 1.5 (95% CI, 1.2–2.0; Wald $p < 0.001$).
- The sensitivity analysis, accounting for mode of administration, produced similar results for both time to first relapse (HR, 2.0 [95% CI, 1.7–2.3]; Wald $p < 0.001$) and time to 12-week CDP (HR, 1.7 [95% CI, 1.4–2.2]; Wald $p < 0.001$).

Figure 1. Time to first relapse was longer for HP patients than LP patients

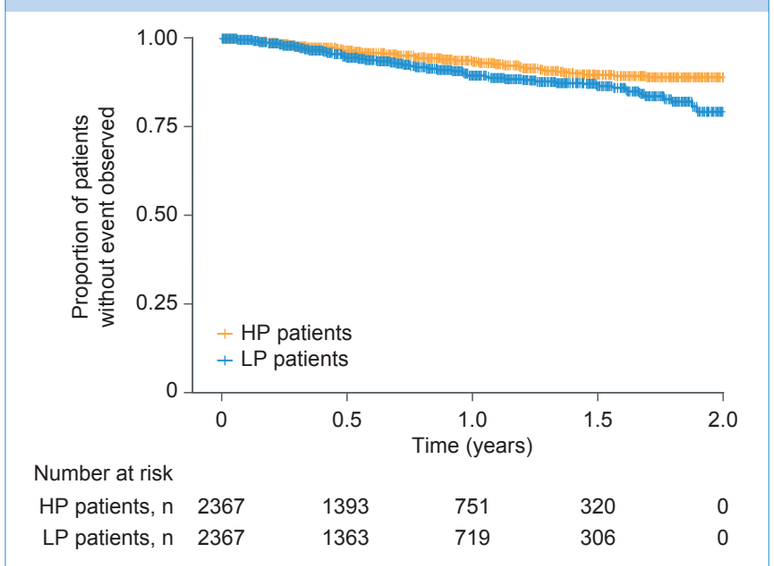


HP, high treatment persistence; LP, low treatment persistence.

Key message

- In propensity score-matched patients with MS, reduced relapse activity and slower disease progression is associated with higher persistence across all DMTs.
- Within the HP and LP groups, ARRs were similar across DMTs. However, for each DMT, the proportions of HP and LP patients varied.

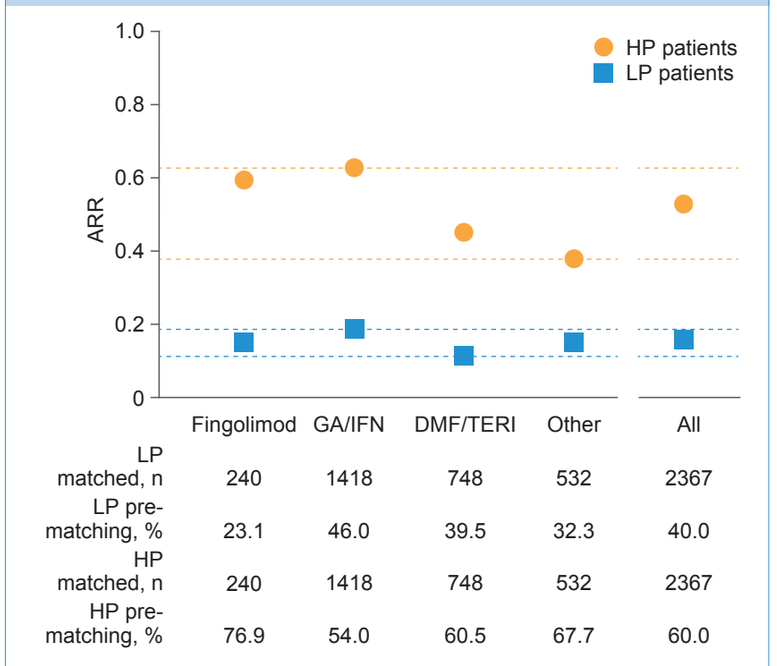
Figure 2. Time to 12-week CDP was longer for HP patients than LP patients



CDP, confirmed disability progression; HP, high treatment persistence; LP, low treatment persistence.

- ARRs were consistently lower for matched HP patients than LP patients across a range of DMTs (**Figure 3**).
- Within LP patients and HP patients, the pairwise ratios of ARR across DMTs were narrow.

Figure 3. ARRs for matched HP patients were lower than for LP patients across a range of DMTs



Dashed lines show the minimum and maximum ARRs across all DMT types for HP and LP patients. ARR, annualized relapse rate; DMF, dimethyl fumarate; DMT, disease-modifying therapy; GA, glatiramer acetate; HP, high treatment persistence; IFN, interferon; LP, low treatment persistence; TERI, teriflunomide.

Conclusions

- **Longer time to first relapse and 12-week CDP are associated with higher treatment persistence.**
- **The high proportion of patients with LP suggests that neurologists and patients with RRMS are responding to poor disease control.**
- **While ARRs were similar across DMTs within HP and LP groups, we did observe higher oral DMT use in HP patients. Future studies may further characterize HP patients on oral DMTs.**
- **The ARRs across DMT types within LP and HP groups remained in a narrow range suggesting that availability of various DMTs is a valuable tool in individualizing treatments.**
- **These data highlight the importance of clinicians and patients making personalized treatment decisions based on the individual's clinical situation to identify the optimal DMT.**
- **As the analysis was limited to a maximum of 2 years follow up, future studies may investigate the impact of persistency on even longer-term clinical outcomes.**

Disclosures

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