Confirmed Disability Improvement and Progression in Nonactive Progressive Multiple Sclerosis Patients in a Real-World Registry

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*At the time of study

BACKGROUND

- There is limited information on the natural history of disability improvement and/or progression in patients with nonactive PMS
  - Although there are real-world data available for patients with PMS, these data are difficult to analyze and differentiate between RRMS, as the International Classification of Diseases-10 Clinical Modification (ICD-10) contains a single code for MS (G35–MS), despite differences in outcomes for patients with RRMS and PMS
- The natural history of disability changes in nonactive PMS can be described using real-world data from the German NeuroTransData (NTD) MS registry
- Utility of the NTD registry:
  - Contains standardized, repeated EDSS assessments from a large sample of individuals with PMS
  - Broader MS diagnosis documentation allows selection of patients with PPMS or SPMS
  - Longitudinal patient documentation with a multi-year historical patient record at the individual level

OBJECTIVE AND STUDY DESIGN

Objective: Characterize CDI and CDP over time in patients with nonactive PMS using the German NTD MS registry

Study design:

- In this retrospective study, eligible patients were identified to mimic inclusion and exclusion criteria from EMBOLD, a Phase 2 clinical trial in nonactive PMS using ATA188, an allogeneic EBV-targeted immunotherapy
- Patients met the following criteria:
  - Nonactive PMS (PPMS [ICD-10 G35.2] or SPMS [ICD-10 G35.3]), defined as ≥2 years without relapses and no gadolinium-enhancing lesions prior to index for those who had MRI available
  - Age at least 18 and <61 years of age
  - Baseline EDSS score between 3 and 6.5, inclusive
- The index date was the earliest visit with an EDSS score after patient identification starting in 2008
  - Patients needed ≥2 post-index EDSS scores during the ~2-year follow-up
  - Patients were considered treated if they received DMT at index or untreated if they received no DMT at index and had sufficient washout period

METHODS

- Outcomes of interest were percentages of patients with CDI or CDP at 12, 18, or 24 months
- CDI and CDP were defined by change from index EDSS score at 6 months confirmed at 12 months, at 12 months confirmed at 18 months, and at 18 months confirmed at 24 months
- For disability improvement, a minimal clinically significant change was defined as a decrease of:
  - ≥1.0 from an EDSS baseline score of ≤5.0
  - ≥0.5 from an EDSS baseline score of ≥5.5
- For disability progression, a minimal clinically significant change was defined as an increase of:
  - ≥1.0 from an EDSS baseline score of ≤5.0
  - ≥0.5 from an EDSS baseline score of ≥5.5

METHODS (continued)

- Analyses were also stratified by PPMS and SPMS when numbers were large enough to report

Propensity score-based approach:

- For clinical relevance, key variables were identified from the literature search
- Inverse probability weighting was used to balance the distributions of the NTD demographics at index of the untreated population to the EMBOLD population using:
  - Gradient-boosting algorithm
  - Weight stabilization
  - Trimming the extreme 5% of weights

RESULTS

In total, 719 untreated (206 PPMS, 513 SPMS; **Table 1**) and 555 treated (**Table 2**) patients with nonactive PMS were identified

Table 1. Patient Characteristics—Untreated Patients

Characteristics	Untreated (N=719)		
	PPMS (n=206)	SPMS (n=513)	Total (N=719)
Age, years			
Mean (SD)	52 (7)	51 (7)	51 (7)
Gender, n (%)			
Male	90 (43.7)	153 (29.8)	450 (62.6)
Female	116 (56.3)	360 (70.2)	269 (37.4)
EDSS score, n (%)			
3–5	140 (68.0)	278 (54.2)	418 (58.1)
5.5–6.5	66 (32.0)	235 (45.8)	301 (41.9)

Table 2. Patient Characteristics—Treated Patients

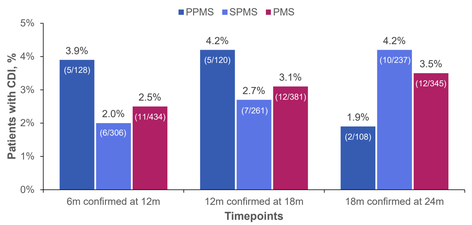
Characteristics	Treated* (N=555)
Age, years	
Mean (SD)	49 (7)
Gender, n (%)	
Male	182 (32.8)
Female	373 (67.2)
EDSS score, n (%)	
3–5	340 (61.3)
5.5–6.5	215 (38.7)

*There were not enough data available on treated patients to separate into PPMS and SPMS populations

RESULTS (continued)

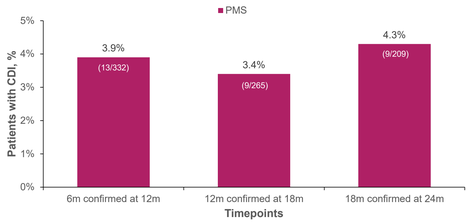
CDI was 2.5–3.5% of patients with nonactive PMS at 6-month time intervals up to 24 months for the untreated group (**Figure 1**)

Figure 1. CDI in Untreated Patients with Nonactive PMS



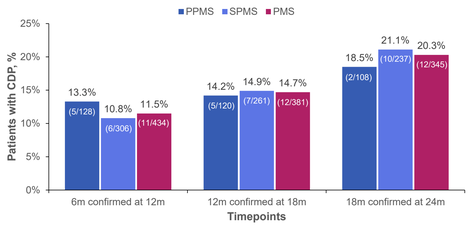
CDI was 3.4–4.3% of patients with nonactive PMS at 6-month time intervals up to 24 months for the DMT-treated group (**Figure 2**)

Figure 2. CDI in Treated Patients with Nonactive PMS



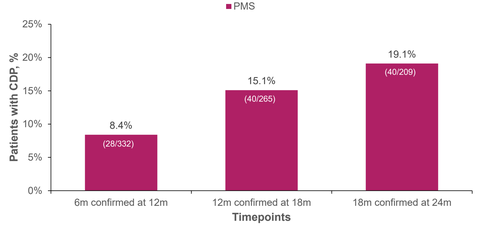
CDP occurred in 11.5–20.3% of patients with nonactive PMS at 6-month time intervals up to 24 months for the untreated group (**Figure 3**)

Figure 3. CDP in Untreated Patients with Nonactive PMS



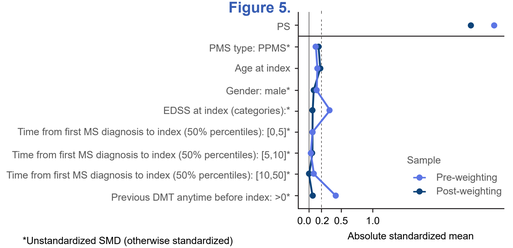
CDP occurred in 8.4–19.1% of patients with nonactive PMS at 6-month time intervals up to 24 months for the DMT-treated group (**Figure 4**)

Figure 4. CDP in Treated Patients with Nonactive PMS



The real-world (NTD) and clinical trial (EMBOLD) cohorts' baseline demographics are balanced after weighting based on key covariates (**Figure 5**)

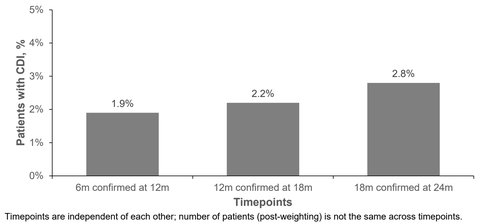
Figure 5.



*Unstandardized SMD (otherwise standardized)

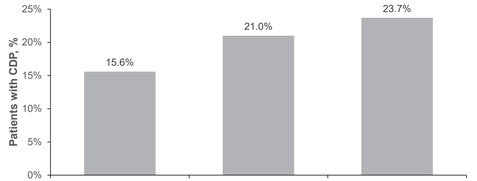
After balancing the population, CDI was <5.0% (**Figure 6**) and CDP was between 15.6–23.7% (**Figure 7**) for untreated nonactive PMS

Figure 6. CDI in Untreated Patients with Nonactive PMS



Timepoints are independent of each other; number of patients (post-weighting) is not the same across timepoints.

Figure 7. CDP in Untreated Patients with Nonactive PMS



Timepoints are independent of each other; number of patients (post-weighting) is not the same across timepoints.

CONCLUSIONS

- **Results from this real-world study in a nonactive PMS population from the NTD MS registry revealed rates of CDI below 5.0% and rates of CDP around 16.0–24.0% among treated and untreated patients over a 2-year time period**
  - **The percentages of patients with a CDI were 1.9–4.3% at 6-month time intervals from 12 to 24 months for DMT-treated and untreated groups**
  - **The percentages of patients with a CDP were 8.4–21.1% at 6-month time intervals from 12 to 24 months for DMT-treated and untreated groups**
  - **After propensity score weighting, the percentages of patients with untreated nonactive PMS with a CDI remained <5.0%; CDP increased over time from 15.6% at year 1 to 23.7% at year 2**
- **More transformative therapies are needed to improve disability in patients with PMS, especially in nonactive disease, where there are limited approved treatment options to slow disability and none that improve it**

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ABBREVIATIONS

CDI = confirmed disability improvement; CDP = confirmed disability progression; DMT = disease-modifying therapy; EBV = Epstein–Barr virus; EDSS = Expanded Disability Status Scale; MS = multiple sclerosis; PMS = progressive multiple sclerosis; PPMS = primary progressive multiple sclerosis; PS = propensity score; RRMS = relapsing-remitting multiple sclerosis; SD = standard deviation; SPMS = secondary progressive multiple sclerosis

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