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# Preliminary results of RETRO PPMS: A retrospective study investigating best supportive and medical care in clinical practice in patients with primary progressive multiple sclerosis (PPMS) in Germany

**Herbert Schreiber[1], Iris-Katharina Penner[2,3], Cornelia Cooper[4], Stefanie Hieke-Schulz[4], Tjalf Ziemssen[5]**

*[1]Neurologische Gemeinschaftspraxis, NTD & Neuropoint Akademie, Ulm, Deutschland; [2]Medizinische Fakultät, Neurologische Klinik, Heinrich Heine Universität Düsseldorf, Deutschland; [3]COGITO Zentrum für Angewandte Neurokognition und Neuropsychologische Forschung, Düsseldorf, Deutschland; [4]Roche Pharma AG, Grenzach-Wyhlen, Deutschland; [5]Klinik und Poliklinik für Neurologie, Universitätsklinikum Carl Gustav Carus, Dresden, Deutschland*

## BACKGROUND

- Primary progressive multiple sclerosis (PPMS) is part of the spectrum of progressive MS phenotypes characterized by the absence of relapses prior to progression of clinical disability
- PPMS affects approximately 6–16% of the estimated 252,000 patients diagnosed with MS in Germany[1,2]
- Common symptoms associated with PPMS include impaired mobility, progressive weakness, spasticity, pain, depression, cognitive difficulties, bladder and bowel dysfunction, and dysphagia[3]
- Before the European Medicines Agency approved ocrelizumab, a CD20+ B-cell targeting antibody, as the first disease-modifying treatment (DMT) for PPMS in January 2018, PPMS management focused on symptomatic treatment and non-evidence-based use of DMTs
- Little is known about qualitative and quantitative patterns of individual best supportive care (BSC) adopted in relation to patient disease status and history, or the off-label use of DMT in PPMS when no approved DMT was yet available.
- We present results from the interim analysis of RETRO PPMS (ML39631), an ongoing retrospective study to investigate the best supportive and medical care in clinical practice in patients with PPMS in Germany

## OBJECTIVES

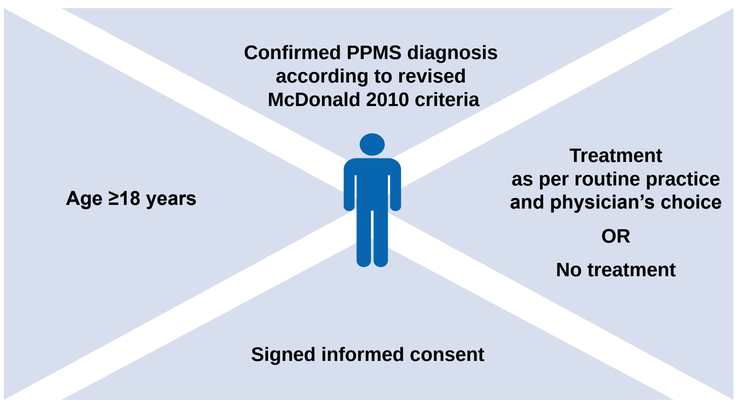
- The primary objective is to generate representative BSC data from patients with PPMS in Germany by retrospective chart analysis
- Secondary objectives include the collection of data from health records regarding off-label treatment with DMTs or cortisone, as well as data on disease course, such as disease activity with respect to disability, mobility, and clinical global impression (CGI) as reported by the physician. In addition, diagnostic issues, such as first PPMS symptoms and time of diagnosis are recorded. Furthermore, chronic comorbidities including psychiatric disorders and adverse events (AEs) are described.

## METHODS

### Study design

- RETRO PPMS is a multicenter, cross-sectional, secondary data use, retrospective, non-interventional study in patients with PPMS
- It is planned to recruit a maximum of 1070 patients with PPMS at 80 centers in Germany
- Inclusion criteria are age ≥18 years, PPMS according to revised McDonald 2010 criteria and written informed consent (**Figure 1**)
- To avoid selection bias, all eligible patients are planned to be consecutively included beginning with the first patient visiting the physician after study onset
- Interim analysis was conducted on the core analysis population, based on the first 100 patients with complete BSC documentation available

**Figure 1. Study population**




PPMS, primary progressive multiple sclerosis

- Interim data were collected between Q3/2018 and Q1/2020 by patient chart review. Data were recorded until the first infusion of ocrelizumab
  - Data regarding medical history, disease status, disease activity, AEs, and treatments from 12 months prior to PPMS diagnosis to study start
  - Data regarding acute measures (non-medicinal and medicinal BSC parameters and rehabilitation) from the last 27 months prior to study onset
  - Pharmacoeconomic data from the last 3 months prior to study start will be shown in the final analysis
- Data were analyzed using descriptive statistics

## RESULTS

### Study population

- The core analysis population comprised 99 patients from 18 centers
  - Of the first 100 patients with complete BSC documentation available, one patient did not fulfill inclusion criteria
- Baseline demographics and comorbidities are shown in **Table 1**
  - Time from PPMS diagnosis to study start ranged from 0.1 to 30.4 years, with time from first MS symptoms to study start ranging from 0.7 to 35.4 years
  - Comorbidities were present in 59.6% of the patients
  - The most common comorbidities were hypertension (16.2%) and vitamin D deficiency (11.1%)

### PPMS symptoms

- The most frequent first PPMS symptoms were gait disturbance (36.4%), hypoesthesia (26.3%), and muscle spasticity (22.2%) (**Figure 2A**)
- The most frequent PPMS symptoms, including first PPMS symptoms, were muscle spasticity (55.6%), gait disturbance (51.5%), bladder dysfunction (43.4%), ataxia (36.4%), hypoesthesia (33.3%), and fatigue (31.3%) (**Figure 2B**)

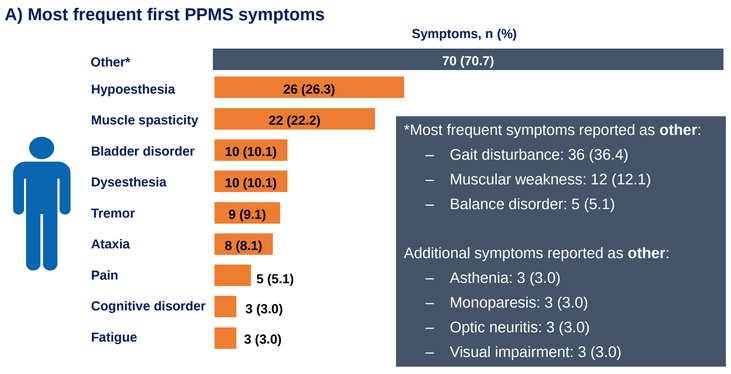
**Table 1. Patient demographics and comorbidities**

| Variable | CAP (N=99) |
|---|---|
| Age at study start (years), mean (SD) | 57.1 (11.2) |
| Sex, n (%) | |
| Male | 55 (55.6) |
| Female | 44 (44.4) |
| Years from first MS symptoms to study start, mean (SD) | 11.83 (7.9) |
| Years from PPMS diagnosis to study start, mean (SD) | 7.87 (6.8) |
| Comorbidity,* n (%) | |
| Total | 59 (59.6) |
| Hypertension | 16 (16.2) |
| Vitamin D deficiency | 11 (11.1) |
| Depression | 10 (10.1) |
| Restless leg syndrome | 5 (5.1) |

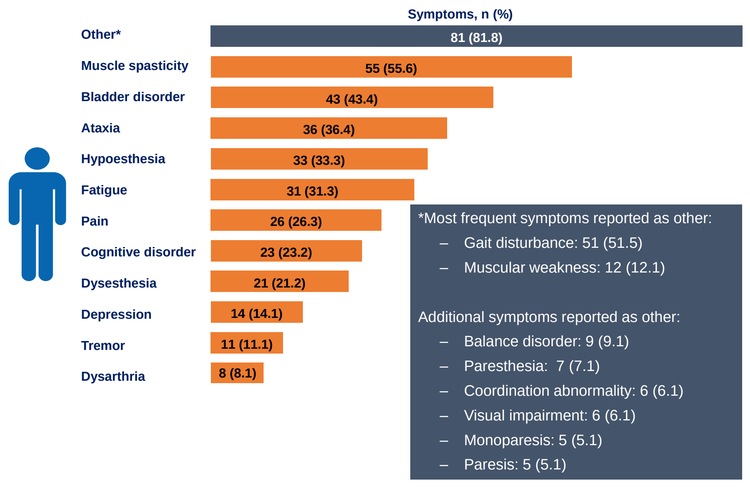
* Comorbidities observed in ≥5% of the patients are presented.
CAP, core analysis population; MS, multiple sclerosis; PPMS, primary progressive multiple sclerosis; SD, standard deviation

**Figure 2. First and overall PPMS symptoms (CAP, N=99)**

**A) Most frequent first PPMS symptoms**




**B) Most frequent PPMS symptoms (including first PPMS symptoms)**




Some multiple sclerosis symptoms were reported as chronic comorbidities rather than as PPMS symptoms, which might lead to an underrepresentation in this category.
CAP, core analysis population; PPMS, primary progressive multiple sclerosis

### AEs

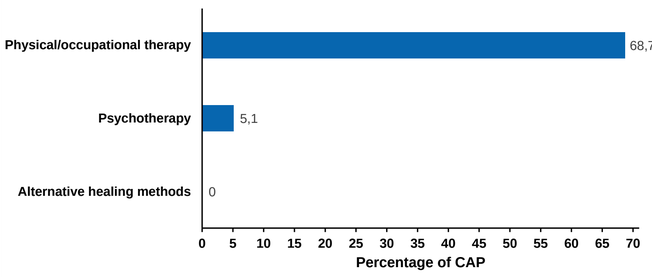
- AEs were reported for only 8 patients (8.1%), of which 2 (2.0%) were reported as serious AEs
  - 6 patients had an infection, one patient epilepsy, and one patient breast cancer

### BSC treatment

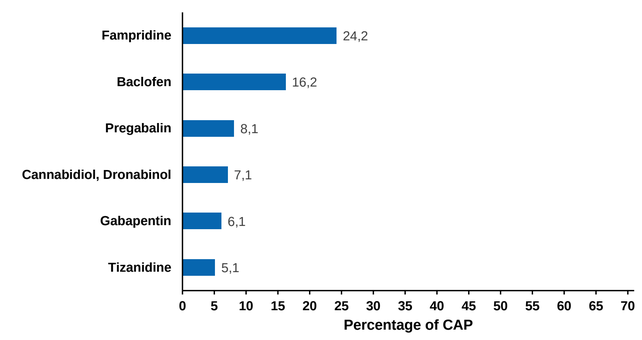
- About two thirds of patients (68.7%) received physical/occupational therapy in the last 27 months before study start (**Figure 3**)
- The three most common medications used by patients were fampridine (24.2%), baclofen (16.2%) and pregabalin (8.1%) (**Figure 3**)

**Figure 3. Most common (≥5%) non-medicinal and medicinal BSC**

**A) Non-medicinal therapies**




**B) Medicinal therapies**

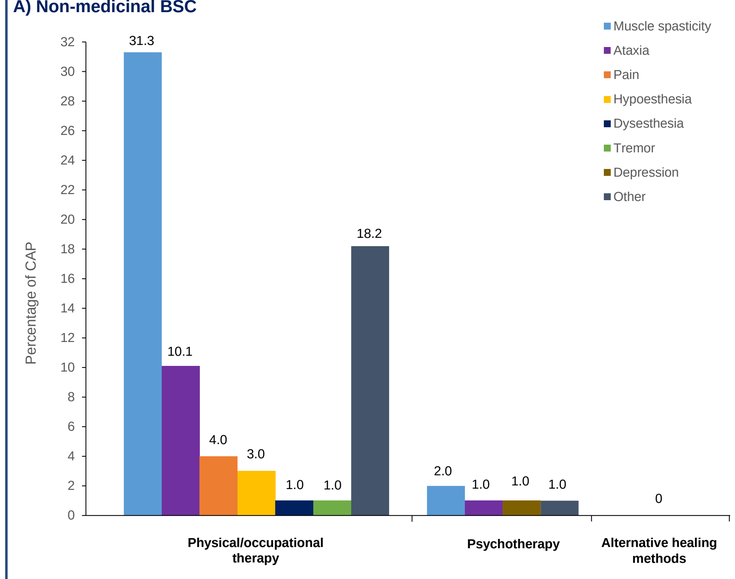



Some BSC measures were reported as concomitant medication, which might lead to an underrepresentation in this category. BSC measures received within 27 months prior to the start of study are included. BSC, best supportive care; CAP, core analysis population; PPMS, primary progressive multiple sclerosis

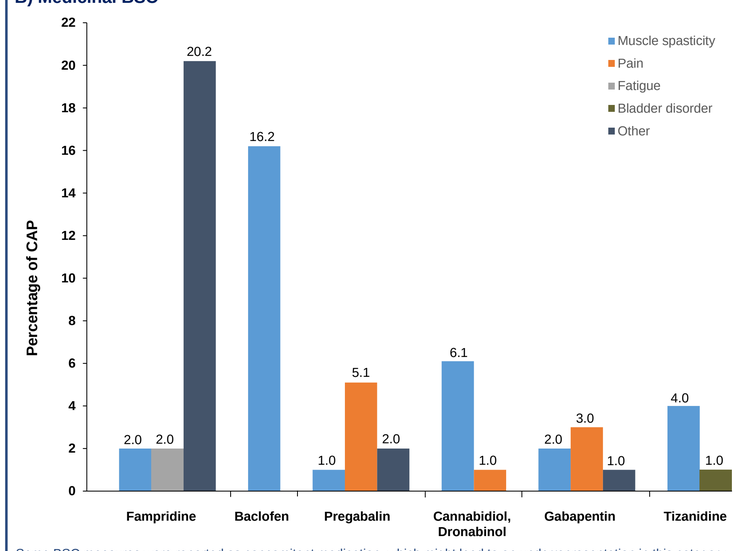
- The prevalence of symptoms in patients receiving BSC treatments is shown in **Figure 4**
  - In 20 of 24 (83.3%) patients the symptoms treated with fampridine were reported under "other" symptoms. Of all patients with "other" symptoms, 51.5% had gait disturbances
  - The most common non-medicinal therapy was physical/occupational therapy. 31 of 68 (45.6%) patients who received this treatment had muscle spasticity

**Figure 4. Most common non-medicinal and medicinal BSC by PPMS symptoms**

**A) Non-medicinal BSC**




**B) Medicinal BSC**




Some BSC measures were reported as concomitant medication, which might lead to an underrepresentation in this category.
BSC, best supportive care; CAP, core analysis population

### Off-label treatments

- Overall, 60.6% of patients received ≥1 off-label treatment (**Table 2**)
  - 45.5% had received corticosteroids and 8.1% interferon-beta-1α

**Table 2. Off-label treatments**

| Off-label treatment use | CAP (N=99), n (%) |
|---|---|
| Number of medications per patient | |
| None | 39 (39.4) |
| 1 | 46 (46.5) |
| 2 | 12 (12.1) |
| 3 | 1 (1.0) |
| >3 | 1 (1.0) |
| Medication (≥4.0% of patients) | |
| Cortisone | 45 (45.5) |
| Interferon beta-1α | 8 (8.1) |
| Glatiramer acetate | 4 (4.0) |

CAP, core analysis population

## CONCLUSIONS

- **The interim results from RETRO PPMS reflect the urgent medical need prior to the availability of the first DMT for PPMS**
  - **The most frequent PPMS symptoms were muscle spasticity (55.6%), gait disturbance (51.5%), bladder disorder (43.4%), ataxia (36.4%), hypoesthesia (33.3%), and fatigue (31.3%)**
  - **The most common non-medicinal treatment for patients with PPMS was physical/occupational therapy (68.7%)**
  - **The three most common medications were fampridine (24.2%), baclofen (16.2%) and pregabalin (8.1%)**
  - **60.6% of patients received an off-label treatment, most commonly cortisone (45.5%)**
- **RETRO PPMS provides valuable real-world data about the epidemiology and individual patterns of care of patients with PPMS in Germany prior to the era of B-cell targeted therapy**
- **Final results are expected in 2022 and will include pre-specified subgroup analyses, and data on pharmacoeconomics and disease activity**

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## DISCLOSURES

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