Evaluation of specific unmet medical needs in the care of relapsing MS: Interim analysis of the PROFILE RMS study

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Multiple sclerosis is a diverse disease with heterogeneity in activity, symptoms and response to treatment; outcomes show clear differentiation for various profiles of patients with unmet medical needs

Background and methods

- The prospective, non-interventional study **PROFILE RMS** (ML39348) aims to characterize the real-world treatment of patients with RMS (relapsing multiple sclerosis) in five pre-defined profiles with unmet medical needs
- The planned enrollment is ≤1215 patients at ~100 centers in Germany (max 243 patients per profile)
- **Patients:** ≥18 years old with RRMS (relapsing-remitting MS) or rSPMS (relapsing secondary progressive MS) according to McDonald 2010 criteria
- **Primary outcome** is 48-week treatment failure rate (defined as confirmed relapse, EDSS progression, MRI activity or treatment change, patients with <48 weeks of observation were censored; n numbers are in figures 1 & 2 of the sup. material provided via QR code)
- **Secondary outcomes** (measured during the entire observation period) include the proportion of patients with treatment change, patient-reported outcomes, and MS signs and symptoms

Medical need profiles

1 Disease activity
on current DMT in the past 12 months (occurrence of confirmed relapse, new/enlarged MRI lesions, or disease progression)

2 Significant adverse drug reaction
(e.g. infections, injection problems) or findings of theoretical safety concerns as assessed by the treating physician

3 Low treatment satisfaction
Treatment Satisfaction Questionnaire for Medication version 1.4 Global (score <75)

4 Treatment-naïve

5 No current treatment
but previously treated with DMT

If patients fit in more than one profile, profile 1 was given the highest priority followed by profile 2. Profile 3 was given the lowest priority and therefore had neither disease activity nor safety issues.

Current and prior medications include: glatiramer acetate, beta-interferons, dimethyl fumarate, teriflunomide, fingolimod, alemtuzumab, natalizumab, peginterferon, cladribine, mitoxantrone, ocrelizumab, daclizumab (retrospectively up to 2 March 2018).

Baseline characteristics

- As of 4 November 2020, 691 patients were enrolled and had at least one post-baseline assessment

	1	2	3	4	5
Patients with RMS, n	234	112	59	120	166
Median age, years	41.5	42.0	46.0	44.5	44.0
Male sex, n (%)	50 (21.4)	22 (19.6)	16 (27.1)	23 (19.2)	29 (17.5)
Median time since first MS symptoms, years	7.1	11.9	10.8	5.0	13.2
Median time since MS diagnosis, years	6.0	10.8	9.3	0.7	10.7
EDSS, median	2.0	2.0	2.0	1.5	2.0
Completed 1 year in the study, %	88.0	73.2	88.1	60.8	67.5

- 4 patients had rSPMS (all female, 3/4 patients in profile 4, and 1 patient in profile 5; with the median age of 66.0 years and 25.8 years median time since MS diagnosis)

Interim data for medical need profiles

1 Ongoing disease activity was observed despite treatment

48-week treatment failure rate (41.3%)
- Relapse (20.3%)
- MRI activity (21.2%)

- Most **T1 lesions**
- Second most **Gd lesions**
- Highest **relapse** probability (19.5%)*

Therapy switches
- **Only 4.3% of patients**

2 No striking side effects and safety concerns, lowest subjective impairment

Second lowest 48-week failure rate (33.0%)
- Most commonly due to **treatment change** (21.6%)

Reasons for treatment change:
- Low treatment satisfaction (3.6%)
- Ongoing disease activity (3.6%)
- Side effects (1.8%)
- **Highest across all profiles**

3 Least impacted by side effects and disease activity, but highest impairment in cognition & PROs

- **Lowest 48-week treatment failure rate (25.9%)**
- **Low disease activity (17.8%)**
- **Lowest AE rates (11.9%)**

- **2x higher proportion of depression**
- **5x higher proportion of anxiety disorders**

Worst results for:
2MWT (120m), SDMT (50.0), MSIS, HR-QoL (16) & **high** fatigue (FSMC, 58.5)

4 Majority with new MS diagnosis and some with longest disease course

Median time since diagnosis
- <1 year (**range of 0.0−49.2 years**)
- 3 of 4 rSPMS patients (all 3 treatment-naïve)

Highest 48-week treatment failure rate (46.6%)
- Main reason was **starting a therapy** (51.7%)
- MRI activity (17.2%) & relapse (10.3%)

Most common first-line therapies:
- DMF (15.0%), GA (10.0%) and Terifl (8.3%)

5 High level of impairment & highest risk of progression with similar baseline EDSS

Long median time
- **Since diagnosis (10.7 years)**

48-week treatment failure rate (36.2%)
- 25% due to re-starting a new treatment

Highest risk of EDSS progression
- **At 48 weeks (5.8%)***

*Data relative to entire study duration **According to KKNMS guidelines (fingolimod, natalizumab, ocrelizumab, alemtuzumab, cladribine, mitoxantrone).
AE, adverse event; DMT, disease-modifying therapy; DMF, dimethyl fumarate; EDSS, Expanded Disability Status Scale; FSMC, Fatigue Scale for Motor and Cognitive Functions; GA, glatiramer acetate; HR-QoL, health-related quality of life; KKNMS, Krankheitsbezogenes Kompetenz-netz Multiple Sklerose; MRI, magnetic resonance imaging; MS, multiple sclerosis, MSIS-29, Multiple Sclerosis Impact Scale 29; 2MWT, 2-Minute Walk Test; PRO, patient-reported outcome; RMS, relapsing MS; RRMS, relapsing-remitting MS; rSPMS, relapsing secondary progressive MS; SDMT, Symbol Digit Modalities Test; Terifl, teriflunomide; TSQM, Treatment Satisfaction Questionnaire for Medication; SAE, serious AE.