Adherence, Cognition and Behavioral Outcomes in Multiple Sclerosis (MS) Patients on Dimethyl Fumarate – 12-Month Results of a Longitudinal Registry Study in German MS Practice Centers (TREAT)

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Conclusions

- DMF is effective in stabilizing clinical, cognitive and behavioral parameters in early RRMS-patients.
- Behavioral factors, gender and pre-treatment issues emerged as putative predictors for non-adherence. Multiple regression analyses considering collinearity will be performed in the forthcoming final analysis.
- DMF is well tolerated with 73.2% patients remaining on constant treatment during the first year. Discontinuations (of treatment or study) primarily occured during the first months of treatment.

Introduction

- NeuroTransData is a German network of currently 72 neurology practice centers using its MS database (n=22,000 MS patients) to collect “real world” data about longitudinal evolution and treatment in MS.

Objectives

(1) Assessment of adherence, disability, cognition and patient-reported outcomes (PRO) in relapsing-remitting MS (RRMS) patients on dimethyl fumarate DMF as first-line treatment or switching from other disease-modifying therapies.

(2) Identification of relevant factors for non-adherence (discontinuation of study or DMF intake)

Methods

- 12 months interim analysis (T12) of a 2-year prospective, multicenter, open-label registry study with assessments at baseline (T0) and at T3, T6, T9, T12, T18 and T24 months.
- Demographic baseline charactaristics of the study population (12 months analysis set) are shown in Table 1.

- At T12, 721 RRMS patients treated with DMF (mean age 40.9 years, 72.4% female, 27.6% male, median EDSS 2.0) entered analysis.
- Outcomes: adherence (yes/no) and time to non-adherence, disability, cognition and PROs representing treatment/life satisfaction, depression, anxiety, fatigue, QoL, disease coping and personality.
- Descriptive analysis and univariate regression models (logistic and Cox) were used to assess the factors associated with adherence.

Results

- All clinical, behavioral and cognitive parameters remained stable during the first 12 months of DMF treatment (Table 2)
- By T12, 26.8 % (193/721) of patients reported to be non-adherent. Women were more likely to be non-adherent (OR 1.9, HR 1.8). Among the non-adherents at T12, 41.5% (80/193) discontinued by T3. The primary reason for non-adherence by T12 was physical complaints (13.0%; 95/721), mainly of gastrointestinal origin (7.9%; 57/721). (Figures 2 and 3)
- Univariate (logistic/Cox) regression analyses ($p<0.15$) identified gender, premedication pause, pre-treatments (≥2), depression, QoL, life/treatment satisfaction, fatigue, anxiety and nonverbal memory as putative predictors of non-adherence. (Table 3)

Table 1. Demographic baseline characteristics (12 months analysis set)

Variable (SD = standard deviation; min = minimum; max = maximum)		Patient number
Sex	male: 27.6%	199
	female: 72.4%	522
Age (years), mean (SD)	40.9 (10.7)	721
BMI, mean (SD)	25.0 (5,2)	648
Professional achievement	none: 4.0%	29
	apprenticeship: 72.4%	522
	university degree: 23.6%	170
EDSS, median (min, max)	2.0 (0.0, 7.5)	704
Number of relapses (last 12 months), median (min, max)	0.0 (0.0, 5.0)	721
Time since diagnosis (years), median (min, max)	5.7 (0.0, 33.0)	721

Table 2. Development of clinical, behavioral and cognitive parameters during 12 months of DMF treatment

Variable (N = number of patients; SD = standard deviation; min = minimum; max = maximum)	T0	T12
EDSS, N, median (min, max)	704, 2.0 (0.0, 7.5)	399, 2.0 (0.0, 6.5)
AI (Walking), N, median (min, max)	580, 0.0 (0.0, 8.0)	332, 0.0 (0.0, 8.0)
BDI, N, median (min, max)	668, 2.0 (0.0, 15.0)	388, 1.0 (0.0, 15.0)
EQ5D-VAS, N, mean (SD)	675, 73.7 (18.7)	376, 76.7 (18.0)
FSMC, N, mean (SD)	610, 53.7 (21.8)	373, 54.2 (22.7)
STAI-G-X1, N, mean (SD)	609, 39.7 (11.1)	362, 38.2 (11.3)
STAI-G-X2, N, mean (SD)	604, 40.1 (11.3)	348, 38.8 (11.4)
TSQM-9, N, mean (SD)	363, 45.9 (9.5)	373, 49.5 (7.8)
SDMT, N, mean (SD)	663, 49.0 (14.4)	349, 49.5 (13.7)
CVLT, N, mean (SD)	665, 57.4 (11.7)	356, 58.4 (12.0)
BVMT-R, N, mean (SD)	665, 25.2 (7.8)	353, 26.8 (7.2)
FLZ health, N, mean (SD)	605, 32.8 (8.9)	316, 35.1 (8.7)
FLZ work and career, N, mean (SD)	571, 36.2 (8.3)	313, 36.5 (8.6)
FLZ own self, N, mean (SD)	605, 37.7 (6.9)	324, 37.9 (7.0)
FLZ marriage and partnership, N, mean (SD)	512, 41.5 (7.7)	278, 41.1 (7.6)

BMI = Body Mass Index; BDI-FS = Beck Depression Inventory – Fast Screen; EQ5D-VAS = European Quality of Life Index, 5 dimensions – visual analogue scale; FLZ = Fragebogen zur Lebenszufriedenheit (Questions on Life Satisfaction); FSMC = Fatigue Scale for Motor and Cognitive Functions; STAI = State-Trait Anxiety Inventory; BVMT = Brief Visuospatial Memory Test; TSQM = Treatment Satisfaction Questionnaire for Medication; EDSS = Expanded Disability Status Scale; AI = Ambulation Index; SDMT = Symbol Digit Modalities Test; CVLT = California Verbal Learning Test

Table 3. Analysis of parameters probably affecting time to non-adherence ($p<0.15$) in RRMS-patients treated with DMF (T12 results)

Variable	Hazard Ratio (Confidence Interval, 85% Wald conf. limits)”	Odds Ratio (Confidence Interval, 85% Wald conf. limits)
Sex (female vs. male)	1.76 (1.35; 2.29)	1.95 (1.45; 2.63)
Number of pretreatments (≥2 vs. none)	1.37 (1.06; 1.78)	1.47 (1.08; 2.00)
BDI-FS	1.08 (1.04; 1.11)	1.08 (1.04; 1.13)
BVMT Learning	1.06 (1.01; 1.11)	1.07 (1.01; 1.13)
BMI	1.04 (1.02; 1.06)	1.04 (1.02; 1.07)
STAI-G-X1	1.02 (1.01; 1.03)	1.02 (1.01; 1.03)
STAI-G-X2	1.02 (1.01; 1.03)	1.02 (1.01; 1.03)
Premedpause	1.01 (1.00; 1.01)	1.01 (1.00; 1.02)
FSMC	1.01 (1.00; 1.02)	1.01 (1.01; 1.02)
EQ5D-VAS	0.99 (0.99; 1.00)	0.99 (0.99; 1.00)
FLZ Work & Career	0.98 (0.97; 1.00)	0.98 (0.97; 1.00)
FLZ Own self	0.98 (0.96; 0.99)	0.97 (0.96; 0.99)
BVMT Total Recall	0.98 (0.97; 1.00)	0.98 (0.96; 1.00)
FLZ Health	0.97 (0.96; 0.99)	0.97 (0.96; 0.99)
TSQM-9	0.96 (0.94; 0.97)	0.95 (0.93; 0.97)
BVMT Trial 1	0.94 (0.90; 0.97)	0.92 (0.88; 0.96)
Number of pretreatments (1 vs. none)	0.91 (0.71;1.18)	0.88 (0.66;1.19)

Figure 1. German NTD centers collaborating in the study

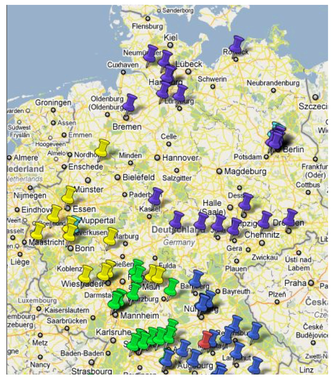


Figure 2. Kaplan-Meier curve depicting gender-related non-adherence (male/female) in RRMS-patients treated with DMF (721 patients)

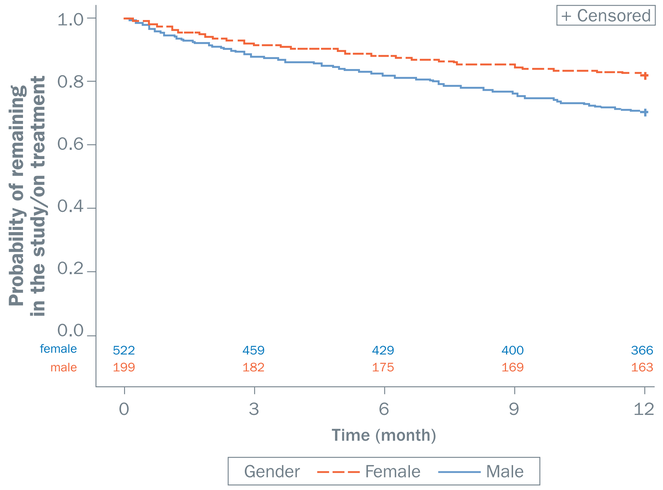
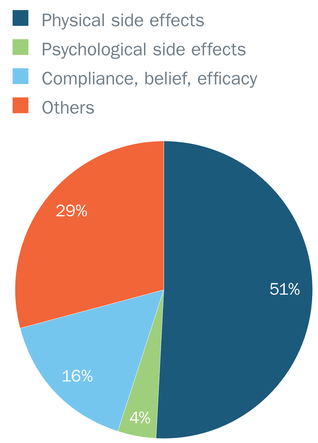


Figure 3. Reasons for study discontinuation in RRMS-patients treated with DMF (T12 results; 187 patients)



Disclosures 1. H. Schreiber: Adboards, speaker's honoraria and travel grants from Almirall, Bayer, Biogen, Genzyme, Novartis, Roche & Teva. Research grants from Bayer, Biogen, Novartis & Teva; 2. F. Roßnagel: Adboard from Pfizer; 3. A. Bergmann: Resarchgrants from Novartis, Biogen&Genzyme
Acknowledgements This Study was sponsored by Biogen (Ismaning, Germany). Support for medical writing and editorial work was funded by Biogen.