Real-world demographics, clinical characteristics and treatment patterns in relapsing multiple sclerosis patients on disease-modifying therapy (encore from ACTRIMS-ECTRIMS; September 11–13 2020)

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Background

- Approximately 240,000 people in Germany are living with relapsing-remitting multiple sclerosis (RMS).[1]
- Real-world data are increasingly needed to inform healthcare professionals and payers in their multiple sclerosis treatment decision-making.
- Glatiramer acetate (GA) has been licensed as an injectable RMS treatment in Europe for over 20 years. Follow-on glatiramer acetate (FOGA) received approval in 2016.[2]
- Various oral disease-modifying therapies (DMTs) have become available in the European market for the treatment of RMS, including dimethyl fumarate (DMF) and teriflunomide (TER).[3]
- However, overall real-world data on treatment patterns and associated health outcomes in RMS patients using these DMTs are limited.

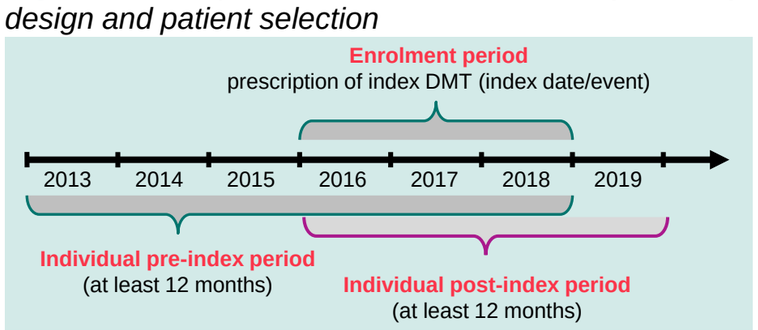
Objectives

- To descriptively compare:
  - Demographic and clinical characteristics of four RMS patient cohorts receiving GA, FOGA, DMF or TER
  - Treatment persistence, discontinuation and switching patterns of the four patient cohorts.

Methods

- This retrospective study analysed real-word data from the *Institute for Applied Health Research Berlin (InGef)* – a German health insurance claims database pool. **Figure 1** presents the study design
  - Retrospective claims data were the sole source for this analysis, no prospectively collected data were included.
- Overall, 16,283 patients were identified using the International Classification of Diseases 10th edition German modification (ICD-10-GM) codes for RMS in combination with Anatomical Therapeutic Chemical (ATC) classification codes for DMT treatment during the study enrolment period (1st January 2016 and 31st December 2018).
- Patient eligibility criteria included:
  - ≥1 inpatient or ≥2 outpatient ICD-10-GM codes for RMS diagnoses in the study enrolment period or;
  - ≥1 outpatient diagnosis and a DMT prescription in the study enrolment period.
- Overall, 1,577 patients met all inclusion criteria and were included in analysis (GA, n=575; FOGA, n=24; DMF, n=608; TER, n=370).

Figure 1 *Retrospective insurance claims analysis study design and patient selection*



Index date/event: First initiation of treatment with DMT in scope (GA, FOGA, DMF or TER)

DMF, dimethyl fumarate; DMT, disease-modifying therapy; FOGA, follow-on glatiramer acetate; GA, glatiramer acetate; TER, teriflunomide.

Results

Demographic characteristics of patient cohorts

- RMS patients prescribed GA and DMF were generally comparable in terms of demographics (**Table 1**)
- The FOGA group comprised too few patients to be included in the analyses (n=24)
- Average age distribution was similar in the GA and DMF cohorts; the TER cohort was slightly older
- Overall, interferons (IFNs) were the most frequently used DMTs in the pre-index period for all cohorts.

Table 1 *Patient characteristics per treatment cohort*

	GA (n=575)	DMF (n=608)	TER (n=370)
Gender, female, n (%)	398 (69.2)	434 (71.4)	229 (61.9)
Mean age, years (SD)	38.6 (11.5)	39.6 (11.4)	45.3 (10.7)
DMT treatment use in pre-index period*, n (%)			
IFNβ 1a/1b	59 (10.3)	142 (23.4)	84 (22.7)
Peg-IFNβ 1a	18 (3.1)	27 (4.4)	29 (7.8)
Fingolimod	14 (2.4)	21 (3.5)	12 (3.2)
Natalizumab	6 (1.0)	15 (2.5)	<5 (0.0)
Treatment sequencing pre-index period*, n (%)			
0 DMT agents	469 (81.6)	399 (65.6)	234 (63.2)
1 DMT agent	103 (17.9)	200 (32.9)	129 (34.9)
2 DMT agents	<5 (0.5)	8 (1.3)	7 (1.9)
3+ DMT agents	0 (0.0)	<5 (0.3)	0 (0.0)

DMF, dimethyl fumarate; DMT, disease-modifying therapy; GA, glatiramer acetate; IFNβ 1a/1b, interferon beta 1a/1b; Peg-IFNβ 1a, peginterferon beta 1a; SD, standard deviation; TER, teriflunomide.
*In the 12 months before being initiated with the DMT in scope.
Note: Due to data protection regulations patient counts <5 and corresponding percentages cannot be reported.

Clinical characteristics of patient cohorts

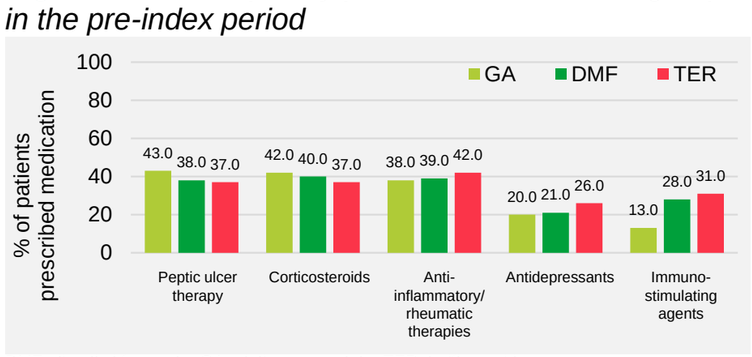
- No substantial clinical differences were observed between cohorts in the pre-index period
  - Patients in the TER cohort had a higher proportion of comorbid hypertension, depression and antidepressant use than the other groups in the 12-month pre-index period (**Table 2; Figure 2**).

Table 2 *Patient comorbidities per treatment cohort*

Comorbidities, n (%)	GA (n=575)	DMF (n=608)	TER (n=370)
Affective disorders	175 (30.4)	184 (30.3)	141 (38.1)
Anxiety	71 (12.4)	68 (11.2)	52 (14.1)
Chronic lung disease	100 (17.4)	90 (14.8)	53 (14.3)
Depression	168 (29.2)	175 (28.8)	132 (35.7)
GI disorders	202 (35.1)	179 (29.4)	136 (36.8)
Hyperlipidemia	68 (11.8)	84 (13.8)	71 (19.2)
Hypertension	106 (18.4)	106 (17.4)	92 (24.9)
Neurotic, stress and somatoform disorders	228 (39.7)	220 (36.2)	155 (41.9)
Thyroid disease	131 (22.8)	126 (20.7)	88 (23.8)

DMF, dimethyl fumarate; GA, glatiramer acetate; GI, gastrointestinal; TER, teriflunomide.
Note: Due to data protection regulations patient counts <5 and corresponding percentages cannot be reported.

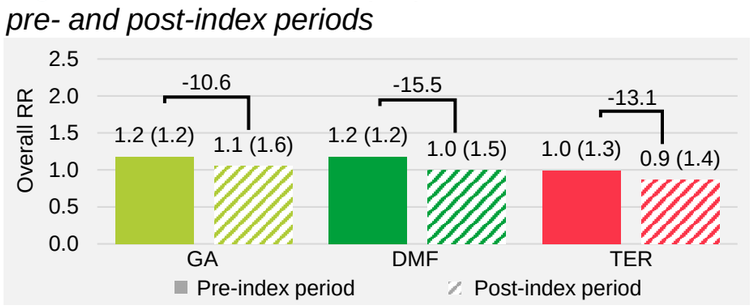
Figure 2 *Most frequently prescribed medication groups in the pre-index period*



DMF, dimethyl fumarate; GA, glatiramer acetate; TER, teriflunomide
Note: Due to data protection regulations patient counts <5 and corresponding percentages cannot be reported. Reported are agents that are among the top 10 most prescribed agents in all of the assessed groups.

- RMS patients prescribed GA and DMF were generally comparable in risk of relapse (**Figure 3**)
  - Relative change of overall relapses from pre- to post-index period was similar for GA and DMF cohorts and lowest for TER.

Figure 3 *Mean overall RR (SD) in the 12-month pre- and post-index periods*

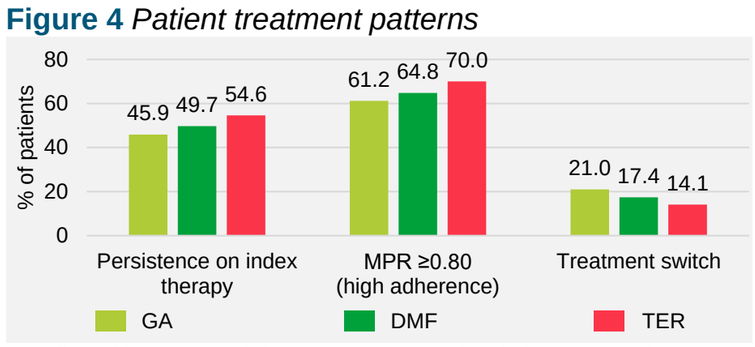


DMF, dimethyl fumarate; GA, glatiramer acetate; RR, relapse rate; SD, standard deviation; TER, teriflunomide.
Note: Overall RR includes both inpatient and outpatient relapses.

Treatment patterns of patient cohorts

- Despite different administration methods, similar treatment persistence was observed for GA and DMF cohorts (**Figure 4**)
  - Overall, approximately half (45.9–54.6%) of all patients were persistent with taking their DMT
  - A large proportion of patients (61.2–70%) had high treatment adherence in all cohorts.

Figure 4 *Patient treatment patterns*



DMF, dimethyl fumarate; GA, glatiramer acetate; GI, gastrointestinal; MPR, medication process ratio; TER, teriflunomide.
Note: Persistence on index DMT defined as continuously on treatment, without a gap of more than 30 days within the 12-month follow-up. MPR calculation = total number of days treatment is supplied / (number of patients in the cohort * number of days observable); MPR for every patient is capped at 1, ≥0.8 = high adherence.

- The majority of patients remained on their index-DMT treatment (**Figure 4**).
- A small proportion of patients across the treatment groups switched therapy (14.1–21%; **Table 3**).

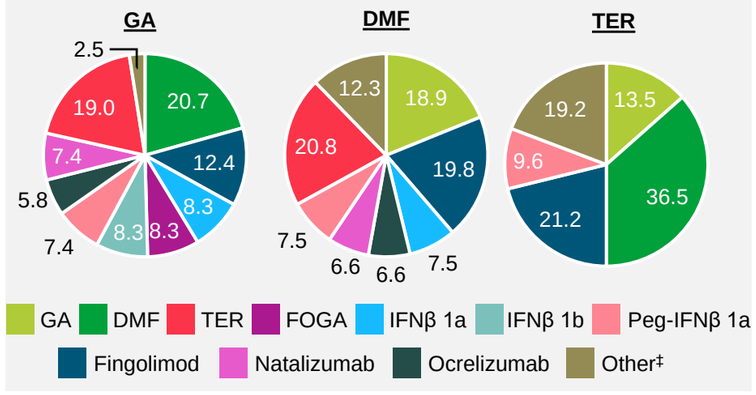
Table 3 *Patient switching patterns per treatment cohort*

Off of index DMT	On to escalation DMT**	On to 1st line DMT†
GA, 121 (21.0)	24 (19.8)	87 (71.9)
DMF, 106 (17.4)	28 (26.4)	58 (54.7)
TER, 52 (14.1)	11 (21.2)	31 (59.6)

DMF, dimethyl fumarate; GA, glatiramer acetate; IFNβ 1a/1b, interferon beta 1a/1b; Peg-IFNβ 1a, peginterferon beta 1a; TER, teriflunomide.
**Escalation therapy included natalizumab, fingolimod, alemtuzumab, cladribine, mitoxantrone.
†First-line therapy included FOGA, DMF, TER, Peg-IFNβ 1a, IFNβ 1a, IFNβ 1b.
Note: Due to data protection regulations patients counts <5 and corresponding percentages cannot be reported; escalation therapy is reported as >, as values <5 were present.

- **Figure 5** shows that of the patients who switched:
  - Most GA patients switched to DMF (20.7%), followed by TER (19%), then fingolimod (12.4%)
  - Most DMF patients switched to TER (20.8%), followed by fingolimod (19.8%) then GA (18.9%)
  - Most TER patients switched to DMF (36.5%), followed by fingolimod (21.2%) then GA (13.5%).

Figure 5 *Most common first therapy switched to per cohort*



DMF, dimethyl fumarate; FOGA, follow-on glatiramer acetate; GA, glatiramer acetate; IFNβ 1a/1b, interferon beta 1a/1b; Peg-IFNβ 1a, peginterferon beta 1a; TER, teriflunomide.
‡ For GA cohort 'other' therapies were alemtuzumab and cladribine; for DMF cohort 'other' therapies were alemtuzumab, cladribine, FOGA and IFNβ 1b; for TER cohort 'other' therapies were alemtuzumab, cladribine, FOGA, IFNβ 1a, natalizumab and ocrelizumab.

Conclusions

- While IFNs were the most frequently used DMTs in the pre-index period for all groups, patients in the GA cohort had the lowest proportion of IFN use.
- RMS patients prescribed GA and DMF were generally comparable in terms of demographics, overall RR, and treatment persistence.
- Patients prescribed TER were older and had more comorbidities and lower pre- and post-treatment overall RR than other cohorts.
- Despite different administration methods and mechanisms of action, similar overall RR and treatment persistence were observed across all three treatment groups.
- Further research is needed to confirm these trends.

Initial presentation at 8th *Joint Americas Committee for Treatment and Research in Multiple Sclerosis/European Committee for Treatment and Research in Multiple Sclerosis (ACTRIMS/ECTRIMS)* meeting, MSVirtual2020; September 11–13, 2020

Encore presentation at 28th Annual *European Charcot Foundation (ECF)* meeting, digital edition; November 15–19, 2020

Disclosures
TZ declares advisory boards fees from Bayer, Biogen, Celgene, Merck, Novartis, Roche, Sanofi-Genzyme and Teva; speaker fees from Almirall, Bayer, Biogen, Celgene, Novartis, Roche, Sanofi-Genzyme and Teva; research support from Biogen, Novartis, Sanofi-Genzyme and Teva. AK, JA and MD are employees of Teva Pharmaceuticals. JSH is an employee of Xcenda GmbH, Xcenda received funding and consulting fees for the conduct of the study from Teva Pharmaceuticals

Acknowledgements
Medical writing support was provided by Katie Holmes and funded by Teva Pharmaceuticals Europe. The data analysis was performed in cooperation with Prof. Dr. Wolfgang Greiner and the Institut für angewandte Gesundheitsforschung Berlin (InGef).

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