

Retrospective longitudinal analysis of cognition and clinical-behavioral parameters (PRO) in relapsing-remitting multiple sclerosis (RRMS) patients treated with Teriflunomide – results from a 12 month registry study in German practice centers.



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Background:

There is limited experience about the longitudinal effects of oral first-line MS treatments on cognition, behavioral and clinical outcomes under real-life conditions, although cognition, fatigue and depression are important indicators and predictive factors for disease progression.

Objectives:

- (1) To longitudinally assess clinical, cognitive and behavioral profiles in RRMS patients being orally treated with teriflunomide (TFL, Aubagio®) as first-line therapy (de novo/DNG) or changing from other MS therapies (switchers/SWG)
- (2) To evaluate differences in therapeutic outcomes between de novos and switchers
- (3) To check for differences in test/re-test effects between RRMS and normative controls.

Methods:

Retrospective, multicenter, open-label registry data analysis from 35 German MS practices (NTD network). Data was available at baseline (T0) and after 12 months (T12) identifying 293 TFL-treated patients (McDonald; mean age: 48.4 yr, 67.2% female, mean EDSS 2.3) that had completed a 12-month treatment period. Among them were 96 (32,7%) de-novos (DNG) and 197 (67,3%) switchers (SWG) coming from various medications (ref. Fig.1+2). **Outcomes:** Clinical status (EDSS), IQ (MWT-B), cognition indexed by (1) information processing speed and capacity (SDMT), (2) verbal (CVLT) and visuo-spatial memory (BVRT-R) from BICAMS battery, (2) interference control (Stroop), (3) fluency (RWT), and PROs represented by motor and cognitive fatigue (FSMC), depression (BDI-FS, fast screen) and QoL (EQ-5D).

change). Interference processing significantly improved over time ($p < 0.01$). Depression distinctly increased (2.3 vs. 2.8, $p < 0.04$), without reaching clinically relevant threshold (5.0). Motor FSMC subscore persisted at a medium level (29.3), whereas cognitive fatigue, despite significantly augmenting (26.0 vs 27.4, $p < 0.04$), remained on a low level.

When comparing de novos and switchers, baseline and longitudinal outcomes were generally better in DNG than SWG. EDSS worsened significantly more in SWG than NCG ($p < .000$; ref. Fig. 3), and significant cognitive improvement was found in DNG vs. SWG for non-verbal memory (BVRT: $p < 0.03$; ref. Fig.4) and lexical fluency (RWT-FLW, RWT-FLK: $p < 0.004$; ref. Fig.5), while SWG only improved in interference processing time ($p < 0.002$), however starting from a significantly lower base level than DNG. Positive test/re-test effects of cognitive variables were present in RRMS patients but less dynamic than in normative control groups.

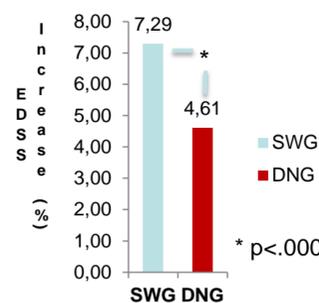


Fig.3: Evolution of disability (%) in Switchers (SWG) vs. de novos (DNG)

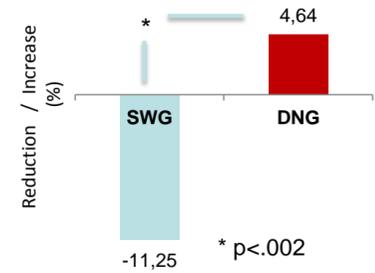


Fig. 6: Improvement of interference processing time (Stroop) in SWG vs. DNG

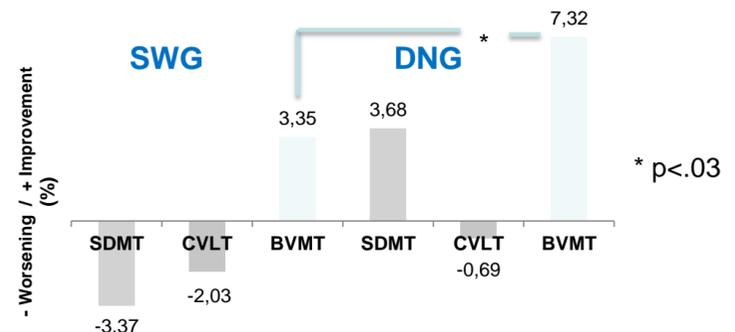


Fig. 4: BICAMS outcomes in Switchers (SWG) vs. De novos (DNG) SDMT, Symbol Digit Modality Test; CVLT, California Verbal Learning Test; BVRT, Brief Visual Memory Test

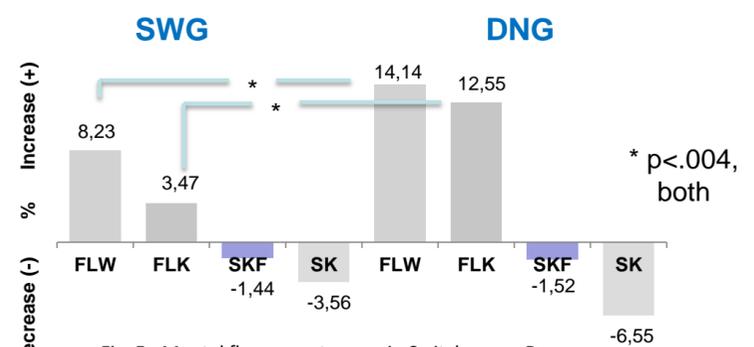


Fig. 5: Mental fluency outcomes in Switchers vs. De novos FLW, formal-lexical, FLK, lexical, category change, SK, semantic, SKF, semantic category change

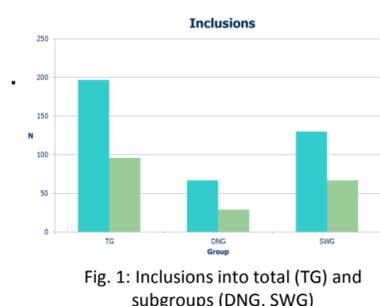


Fig. 1: Inclusions into total (TG) and subgroups (DNG, SWG)

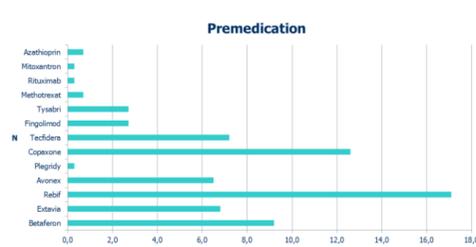


Fig. 2: Premedications of switchers (SWG) prior to TFL treatment

Results:

At baseline (T0), RRMS patients performed insignificantly below the arithmetic mean of normative controls in cognitive testing. Motor fatigue scored at a medium, cognitive fatigue at a low level, depression in the normal range.

Across 12 months (T12:T0), **86,4%** of all RRMS patients remained relapse-free and EDSS stable (2.3 vs. 2.4), as did BICAMS parameters (SDMT, CVLT, BVRT-R) and all 4 dimensions of fluency (RWT), i.e.. formal-lexical, semantic fluency, formal-lexical and semantic category

Conclusion:

- (1) Teriflunomide has the potential to stabilize/improve clinical course and cognition, but not behavioral outcomes in RRMS.
- (2) Switchers take less benefit from TFL therapy than de novo patients highlighting the importance of early treatment onset
- (3) Positive test/re-test effects are expressed to a lower degree in RRMS patients than normative controls.

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