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Reasons for switching initial disease-modifying therapies in early relapsing multiple sclerosis: lateral vs. escalation strategies

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BACKGROUND

The number of treatment options for relapsing multiple sclerosis (MS) has increased considerably in recent years. Switches from one disease-modifying therapy (DMT) to another are common clinical practice. This study analyses reasons for switching from DMT of mild to moderate efficacy (MME-DMTs) either lateral (within the same efficacy category) or through escalation (to highly effective therapies, HE-DMTs).

METHODS

Data from the German MS Register (as of 1-Sep-2024) included patients with relapsing-remitting MS (RRMS) with a documented switch from the initial MME-DMT to another MME-/HE-DMT. Inclusion criteria were MS diagnosis ≥2016, initial DMT ≥2018 and discontinuation of the initial DMT. In the absence of a reported reason for DMT discontinuation, a surrogate for lack of therapy efficacy was used to evaluate switch reasons.
The time to switch was analyzed with Kaplan-Meier estimates and groups were compared with the log-rank test.

RESULTS

- Study population included 622 MS patients (73.6% female)
- Of these, 389 switched laterally to another MME-DMT and 233 escalated to HE-DMTs
- Median age at start of the first DMT was 32.7 years [25% quantile: 25.8; 75% quantile: 40.2]
- Median time to switch was 0.75 years for lateral and 1.25 years for escalation switch, with most switches occurring within the first 2 years of DMT initiation

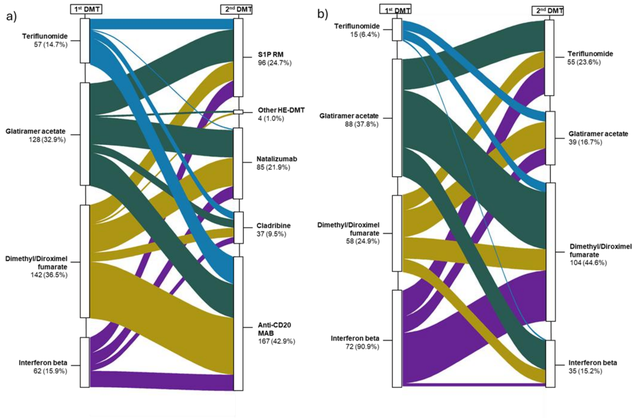

Figure 1: Characterisation of switches from initial DMT to immediate subsequent DMTs. Alluvial (a) represents the escalation switch to HE-DMTs, while alluvial (b) shows the lateral switch to MME-DMTs. The boxes on the left side represent the proportion of patients stratified by the initial MME-DMT usage, while the boxes on the right-hand side show the immediate subsequent DMTs. The thickness of the coloured connecting lines between the boxes indicate the proportions of patients switching between the respective DMTs. Anti-CD20 MAB - anti-CD 20 monoclonal antibodies (ocrelizumab/ ofatumumab/ rituximab/ ublituximab); DMF - dimethyl fumarate; DMT - disease-modifying therapy; S1P RM - sphingosine-1-phosphate receptor modulators (fingolimod/ ozanimod/ ponesimod/ siponimod).

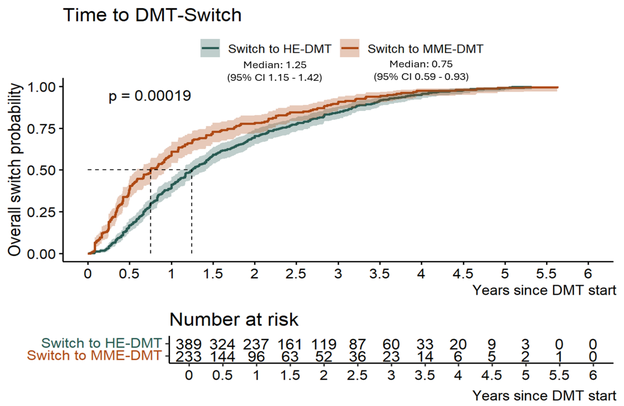

Figure 2: Time to switch from the initial DMT. The Kaplan-Meier curves show the probability of switching from the initial DMT over time. Patients switching to HE-DMT (green) had a median switch time of 1.25 years (95% CI: 1.15–1.42), while those switching to MME-DMT (orange) had a median switch time of 0.75 years (95% CI: 0.59–0.93). The p-value of <0.001 indicates a significant difference between the two groups. The shaded areas represent 95% CIs, and the table below shows the number of patients at risk over time.
CI - confidence interval; DMT - disease-modifying therapy; HE - high efficacy; MME - mild to moderate efficacy; MS - multiple sclerosis; N - number of patients; p - log-rank test p-value.

Table 1: Reasons for discontinuation of the initial DMT by switch type. If the reason for the first DMT discontinuation was not available or previously unknown, it was excluded from this table

Reasons for first DMT discontinuation, N (%)	Escalation Switch (N = 330)	Lateral Switch (N = 199)
Lack of therapy efficacy (reported + surrogate):	236 (71.5)	43 (21.7)
Lack of therapy efficacy (reported)	194 (58.8)	19 (9.6)
*Lack of therapy efficacy (surrogate)**	42 (12.7)	24 (12.1)
Adverse events	41 (12.4)	107 (53.8)
Patient request	20 (6.1)	25 (12.6)
Physician's decision	19 (5.8)	0 (0.0)
Pregnancy / wish to have children	5 (1.5)	17 (8.5)
Other	9 (2.7)	7 (3.5)

* Lack of therapy efficacy indicated by fulfilling ≥1 of the following criteria: any relapse, increases in EDSS, MRI activity, increase in symptom load, or conversion to SPMS within half a year before the end of therapy (surrogate was only used in patients who discontinued the first DMT without providing a reason).
DMT - disease-modifying therapy; EDSS - Expanded Disability Status Scale; MRI - magnetic resonance imaging; MS - multiple sclerosis; n - number of patients; SPMS - secondary progressive multiple sclerosis

CONCLUSION

- Reasons for escalation switches were primarily disease activity and progression (lack of efficacy) vs. switches due to adverse events in lateral switches
- Escalation switches occured later compared to lateral switches
- The findings highlight the differing clinical contexts and patient priorities influencing therapy decisions

Declaration of interest: MP, DE, and FF had no personal financial interests to disclose other than being employees of the German MS Registry. NF is an employee of the MSFP. Moreover, he is an employee of Rostock's University Medical Center and received travel funds for research meetings from Novartis. PF has received speaker's fees and honoraria for advisory boards from Almirall, Bayer, Biogen Idec, BMS-Celgene, Coloplast, Genzyme, GW Pharma, Hexal, Janssen-Cilag, Novartis, Merck, Roche, Sanofi, Stadapharm and Teva. FP has received speaking fees, travel support, honoraria from advisory boards and/or financial support for research activities from Bayer, Novartis, Biogen, Bristol Myers Squibb, Teva, Sanofi-Aventis/Genzyme, Merck Serono, Alexion, Chugai, MedImmune, Shire, German Research Council, Werth Stiftung of the City of Cologne, German Ministry of Education and Research, EU FP7 Framework Program, Arthur Arnstein Foundation Berlin, Guthy Jackson Charitable Foundation and National Multiple Sclerosis of the USA. He serves as academic editor for PLoS ONE and associate editor for Neurology, Neuroimmunology and Neuroinflammation. HT has no personal pecuniary interests to disclose, other than being the Secretary General of the German MS Society, federal association, which receives funding from a range of public and corporate sponsors, recently including Bundesgesundheitsministerium (BMG), The German Innovation Fund (G-BA), The German MS Trust, Biogen, (Bristol Myers Squibb, Merck Serono, Novartis, Roche, Sanofi, Viatris (former Mylan). KH has received speaking fees and/or institutional grant support from Bayer, Biogen, BMS, Merck Serono, Novartis, Roche, Sanofi-Genzyme, and Teva. AS has no personal pecuniary interests to disclose, other than being the lead of the German MS Registry, which receives (project) funding from a range of public and corporate sponsors, recently including The German Innovation Fund (G-BA), The German Retirement Insurance, The German MS Trust, The German MS Society, Bristol Myers Squibb, Merck Healthcare Germany GmbH, Novartis Pharma GmbH, Roche Pharma AG and TG Therapeutics/Neuraxpharm. None resulted in a conflict of interest.