Indicators of disease activity in people with MS after escalation from DMT of mild/moderate efficacy to DMT of high efficacy

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Background

To reduce disease activity (DA) in people with MS (PwMS), switching from disease-modifying therapies (DMTs) of mild/moderate efficacy (ME) to those of high(er) efficacy (HE) is a common clinical strategy.

Objective

To analyse onset of DA after DMT escalation from ME- to HE-DMTs.

Methods

- Inclusion criteria:
  - Relapsing-remitting disease course (RRMS)
  - MS diagnosis ≥2017
  - DA under initial ME-DMT (dimethyl/diroximel fumarate [FUM], glatiramer acetate [GLAT], [peg-] interferon beta [IFN-β], teriflunomide [TER])
  - ≥1 follow-up after escalation to HE-DMT (anti-CD20 monoclonal antibodies [Anti-CD20]: ocrelizumab, ofatumumab; sphingosine-1-phosphate receptor modulators [S1P-RM]: fingolimod, ozanimod, siponimod; natalizumab [NTZ]; others: alemtuzumab, cladribine)
- Data as of 01-03-2023 from the German MS Registry
- Definition DA criteria:
  - Relapse activity (≥1 relapse)
  - MRI activity (≥1 gd+/new T2 lesion)
  - 3-month confirmed disability progression (CDP; ≥0.5-point EDSS increase if EDSS≥5.5; ≥1 if EDSS≤5.0; ≥1.5 if EDSS=0)

Results

A total of 90 PwMS were analysed (Table 1). 22 PwMS (24.4%) showed DA after escalation (relapse activity only: N=4; MRI activity only: N=10; CDP only: N=2; relapse + MRI activity: N=3; relapse activity + CDP: N=3) (Figure 1).

Table 1. Characteristics of PwMS

Variables	PwMS (N=90)	No DA (N=68)	DA (N=22)	p-value
Sex, N (%)				0.728
Male	28 (31.1)	20 (29.4)	8 (36.4)	
Female	62 (68.9)	48 (70.6)	14 (63.6)	
Age at MS onset [years], mean (± SD)	32.7 (8.8)	32.5 (8.9)	33.2 (8.8)	0.754
Time to diagnosis [years], mean (± SD)	1.3 (3.0)	0.8 (2.5)	2.8 (3.6)	0.033
Age at DMT initiation [years], mean (± SD)	34.6 (9.3)	34.0 (9.4)	36.5 (9.1)	0.285
Duration from onset to escalation [median (25%; 75%-quantiles]	2.8 [1.7;5.0]	2.8 [1.7;4.5]	2.9 [2.3;6.9]	0.162
Observation period from escalation to last Follow-Up [median (25%; 75%-quantiles]	1.4 [0.6;2.7]	1.2 [0.3;2.08]	2.8 [1.6;3.2]	<0.001
EDSS at escalation, median (25%; 75%-quantiles)	2.0 [1.0;3.5]	1.5 [1.0;2.0]	2.8 [1.9;3.5]	0.013

DMT - Disease modifying therapy; EDSS - Expanded Disability Status Scale ; MS – Multiple sclerosis; SD - Standard deviation

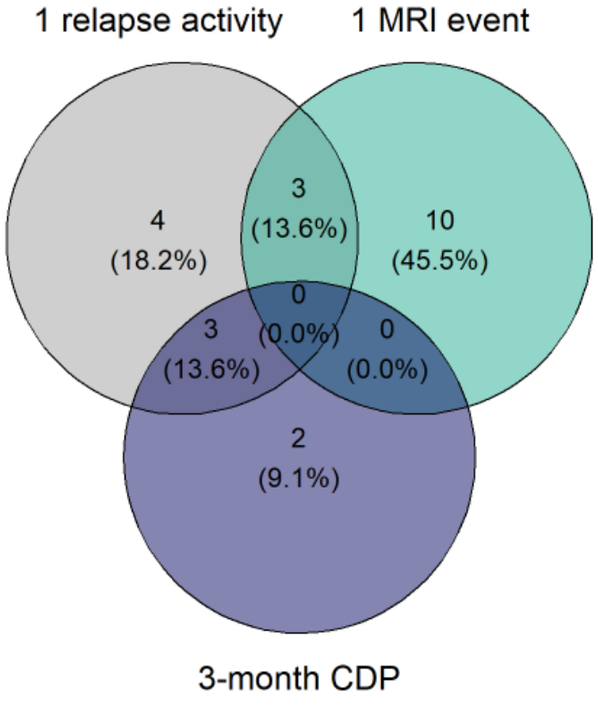

Figure 1. Venn diagram with overlapping proportions of different criteria of disease activity. CDP - confirmed disability progression; MRI - Magnetic resonance imaging

The most prevalent initial ME-DMT was GLAT (34.4%), followed by DMF (26.7%), IFN-β (21.1%) and TER (17.8%). PwMS were most often escalated to anti-CD20 MAB (41.1%), followed by S1P-RM (31.1%), NTZ (24.4%) and others (3.3%), with median EDSS score at escalation of 2.0 (1.0, 3.5).

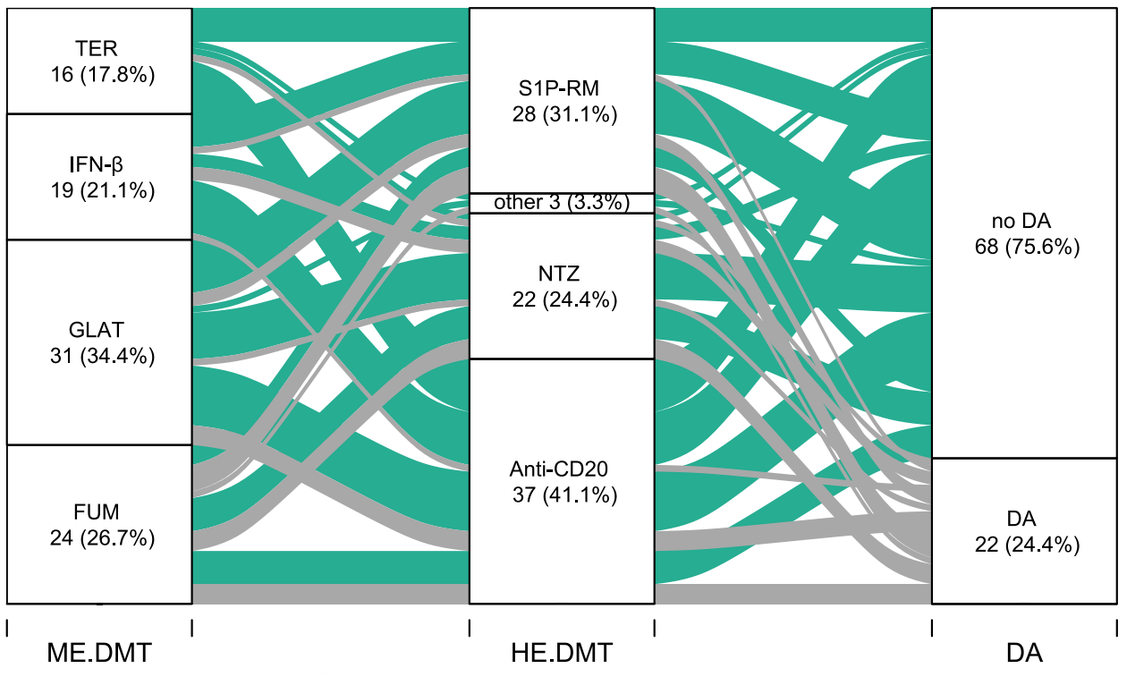

Figure 2. Alluvial plot of occurrence of disease activity by DMT

1P-RM - sphingosine-1-phosphate receptor modulators ; anti-CD20: anti-CD20 monoclonal antibodies; FUM - dimethyl/diroximel fumarate; GLAT - glatiramer acetate; HE-DMT - high efficacy; IFN-β - [peg-] interferon beta; ME - mild/moderate efficacy; NTZ - natalizumab; TER - teriflunomide

PwMS with post-escalation-DA were longer under observation (from DMT escalation onwards: 2.8 [1.6, 3.2] vs. 1.2 [0.3, 2.1] years) and showed a higher median EDSS score at escalation (2.8 [1.9, 3.5] vs. 1.5 [1.0, 2.0]) than stable PwMS (N=68). Further DMT switches after escalation were observed in 15.6% of PwMS in total.

Conclusions

For most analysed PwMS, the escalation from ME- to HE-DMTs represented an effective method to control DA. However, treatment strategies are changing in Germany, e.g. HE-DMTs as first choice for DMT initiation is becoming more popular.

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Declaration of interest: Niklas Frahm 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. None resulted in a conflict of interest. David Ellenberger, Firas Fneish and Melanie Peters had no personal financial interests to disclose other than being employees of the German MS Registry. Alexander Stahmann has no personal financial interests to disclose, other than being the leader of the German MS Registry, which receives (project) funding from a range of public and corporate sponsors, recently including G-BA, The German Retirement Insurance, The German MS Trust, German MS Society, Biogen, Bristol Myers Squibb, Merck, Novartis and Roche. None resulted in a conflict of interest. Tim Friede has received personal fees for consultancies (including data monitoring committees) in the past three years from Bayer, BiosenseWebster, Boehringer Ingelheim, Cardialysis, CSL Behring, DaiichiSankyo, Enanta, Feldmann Patent Attorneys, Fresenius Kabi, Galapagos, IQVIA, Janssen, Mediconomics, Novartis, Penumbra, Roche, SGS, Vifor; all outside the submitted work. Klaus Berger received a grant from the German Ministry of Education and Research (within the German Competence Net Multiple Sclerosis) plus additional funds from Biogen, all to the University of Muenster for an investigator initiated adverse events register for patients with multiple sclerosis. None resulted in a conflict of interest. Peter Flachenecker 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. None resulted in a conflict of interest. Judith Haas serves as president of the German MS Society, federal association, which receives funding from a range of public and corporate sponsors, recently including BMG, G-BA, The German MS Trust, Biogen, BMS, Merck Serono, Novartis, Roche, Sanofi, and Viatris. None resulted in a conflict of interest. None resulted in a conflict of interest. Clemens Warnke has received institutional support from Novartis, Alexion, Sanofi Genzyme, Biogen, Merck and Roche. None resulted in a conflict of interest. Friedemann Paul 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. None resulted in a conflict of interest. Uwe K. Zettl has received speaking fees, travel support and /or financial support for research activities from Alexion, Almirall, Bayer, Biogen, Bristol Myers Squibb, Janssen, Merck Serono, Novartis, Octapharma, Roche, Sanofi Genzyme, Teva as well as EU, BMBF, BMWi and DFG. None resulted in a conflict of interest.