Indicators of disease activity in people with MS treated with DMTs for mild/moderate MS: time to escalation

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Background

Reported rates of disease activity (DA) are higher in people with MS (PwMS) treated with disease modifying therapy (DMT) for mild/moderate disease courses (ME-DMT). Thus, DMT escalation from ME- to high-efficacy- (HE-) DMT is suggested by guidelines to reduce the risk of further DA.

Objective

To determine the proportion of PwMS escalating DMT after DA, considering different (sub)clinical DA criteria.

Methods

- Data as of 01-03-2023 from the German MS Registry
- Inclusion criteria:
  - relapsing-remitting disease course
  - MS diagnosis ≥2017
  - DA under initial ME-DMT(dimethyl/diroximel fumarate [FUM], glatiramer acetate [GLAT], [peg-] interferon beta [IFN-β], teriflunomide [TER])
- ≥1 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≤1.5)
- ≥1 post-DA follow-up
- Time to Escalation was estimated using Kaplan-Meier estimators (delay was censored on the last neurological consultation)

Results

Of the total 359 patients included, PwMS suffering from a relapse activity, MRI event and 3-month CDP were 26.3%, 32.6% and 18.1% respectively. Two or more DA criteria were fulfilled by 24.0% of PwMS.

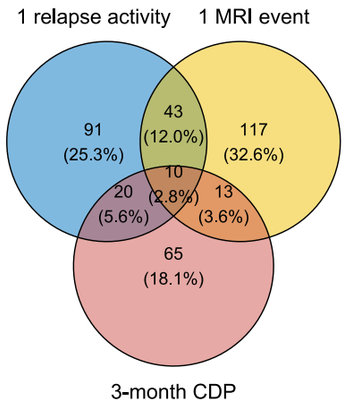

Figure 1. Venn diagram with overlapping proportions of different criteria of disease activity. CDP - confirmed disability progression; MRI - Magnetic resonance imaging

Variables	PwMS (N=359)
Sex, N (%)	
Male	103 (28.7)
Female	256 (71.3)
Age at MS onset [years], mean (± SD)	33.6 (10.3)
Disease Duration at DA [years], mean (± SD)	2.1 [1.2;3.9]
EDSS at DA, median (25%; 75%-quantiles)	1.5 [1.0;2.5]
Initial DMT, N (%)	
dimethyl/diroximel fumarate	100 (27.9)
glatiramer acetate	128 (35.7)
[peg-]interferon beta	79 (22.0)
teriflunomide	52 (14.5)

Table 1. Characteristics of PwMS
DA – Diasease activity; DMT - Disease modifying therapy; EDSS - Expanded Disability Status Scale ; MS – Multiple sclerosis; PwMS - people with MS; SD - Standard deviation

Within 2 years after DA, 39.3% of PwMS were estimated to have escalated to HE-DMT (Figure 1).

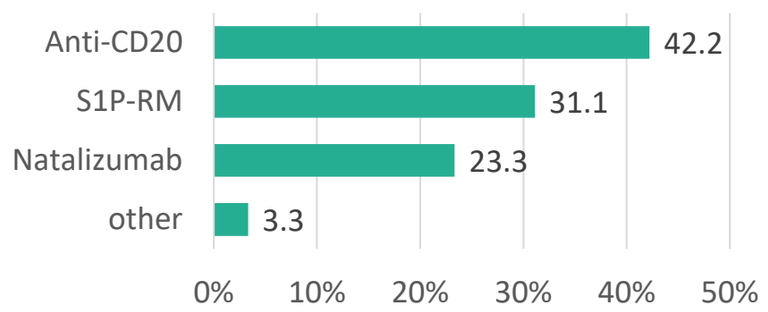

Figure 1. Kaplan-Meier estimates of the proportion of high-efficacy-DMT two years after disease activity. Anti-CD20 - Anti-CD20 monoclonal antibodies; DMT - Disease modifying therapy; S1P-RM - sphingosine-1-phosphate receptor modulators

Comparing the different clinical criteria, the proportions of PwMS who escalated within 2 years after DA were higher in the group with 1 relapse (43.4%) than in the groups with 1 MRI event (31.2%) or 3-month CDP (20.2%) (Figure 2).

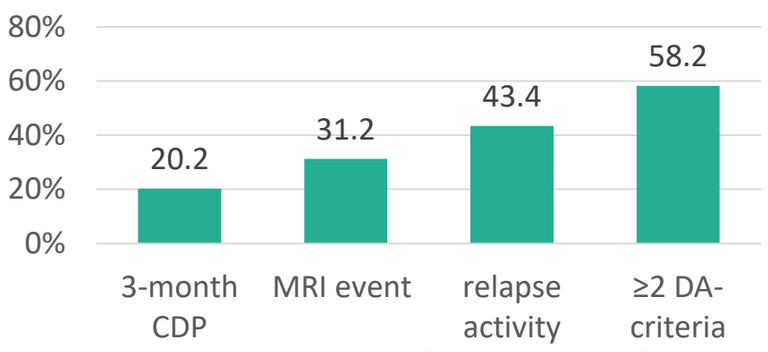

Figure 2. Kaplan-Meier estimates of the proportion of switching to high-efficacy-DMT. CDP - confirmed disability progression; DMT - Disease modifying therapy ; MRI - Magnetic resonance imaging

The time to switch to HE-DMT is estimated to be earlier and more often if the respective criterion occurred more than once. However, the confirmation time at CDP does not reflect this (Figure 3).

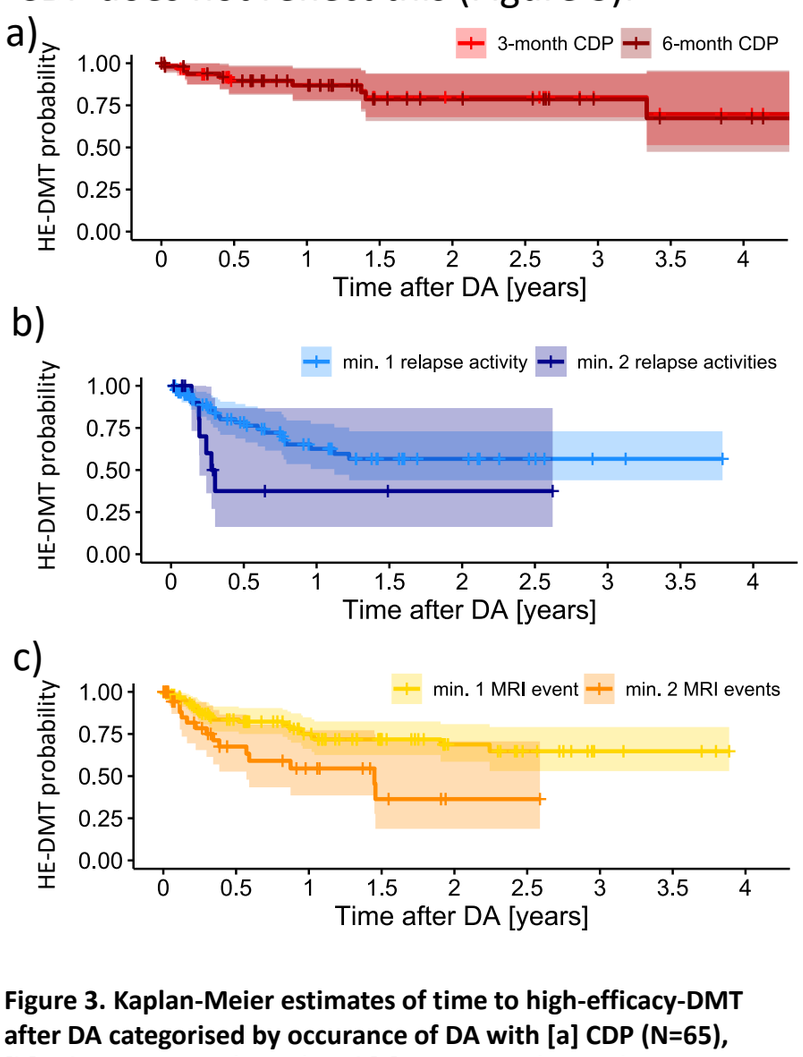

Figure 3. Kaplan-Meier estimates of time to high-efficacy-DMT after DA categorised by occurance of DA with [a] CDP (N=65), [b] relapse activity (N=91) and [c] MRI event (N=117).
CDP - confirmed disability progression; DA – Disease activity; DMT - diseasemodifying therapy; MRI - Magnetic resonance imaging; MS – Multiple sclerosis

Conclusions

- Relapses seem to have the larger impact on the decision to switch to more effective DMTs after signals of DA
- All current guidelines agree on relapses and MRI activity as signals of DA; however, CDP is not considered in all guidelines
- CDP could be considered as an additional measure to (re-) assess treatment options
- Careful, continuous monitoring is required to assess adequate response to DMT

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