Mage-related differences in switching highly effective disease-modifying therapies in MS patients         David Ellenberger <sup>1*</sup> , Niklas Frahm <sup>1*</sup> , Alexander Stahmann <sup>1</sup> , Clemens Warnke <sup>2</sup> , Kerstin Hellwig <sup>3</sup> , Christoph Kleins Flachenecker <sup>5</sup> , Michaela Mai <sup>6</sup> , Matthias Grothe <sup>7†</sup> , Uwe K. Zettl <sup>8†</sup> <sup>1</sup> German MS Register, MS Forschungs- und Projektentwicklungs- gGmbH (MS Research and Project Development gGmbH [MSFP]), Hannover, Germany <sup>2</sup> University Hospital of Cologne Medical Eaculty Department of Neurology Cologne Germany									
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<ul> <li>Disease-modify</li> <li>Decision to sw</li> <li>Age-related in factor for cease</li> <li>→ systematic of</li> <li>At higher age (likely when cease</li> </ul>	ying thera itch DMTs creased r ng/switch data on di ≥50 years asing HET	pies (DMTs) ar is is influenced b isk of comorbic ing highly effect sease activity th s vs. <50), any n	e essential in manage y various individual f dities and side effect tive DMTs (HET) hereafter are rare return of disease activ	ing MS actors is may be a relev vity may become I	vant ess (H-D) ess (H-D)	tigation of arios: HET to HE rately effective discontinuation f s on age-related ctors of switching	three switching ET (H-H), HET to DMTs (H-M) and or at ≥12 months d differences and patterns		
			Me	ethods					
<ul> <li>Retrospective</li> <li>Relapse rates</li> <li>index (washout</li> <li>Predictors for</li> <li>recent disease</li> </ul>	cohort stu were asse ) and up DMT swit activity, c	idy on patients f essed for each s to subsequent s ch pattern were demographics a	rom the German MS subgroup over a 12-n months under the n investigated with b nd MS history	Register who had nonths period befo ew therapy oosted regressior	ended HET sir bre HET stop da models and ir	nce 2018 ate (index), a 3-m ncluded reasons	onths period after for discontinuing,		
			R	esults					
<ul> <li>1091 MS patie</li> <li>Each subgroup (H-H [n=228], I</li> <li>Before HET sto (0.13) or H-D g</li> <li>H-H ≤50: overa decreased to 0</li> <li>H-M: ARR incr in older age gro</li> <li>H-D: higher AF</li> </ul>	nts catego stratified H-M [n=19 op date, h roup (0.0 all ARR ir .12 under eased on oup	orized into: H-H I by age: <50 ye 9], H-D [n=70]) ( igher annualize 8) ncreased tempo the new HET ly in younger (0 ents >50 ys. \$5	(n=786), H-M (n=86) ears (H-H [n=558], H- Table 1) d relapse rate (ARR) rarily during washout, ( 36 during washout, (	and H-D (n=219) M [n=67], H-D [n= in H-H group (0.1 t period (0.27) bu 0.63 during new th vs. 0.05) before i	(Figure 1) =149]) and ≥50 8) than in H-M t subsequently herapy) but not	Age Disease duration EDSS at index Lack of efficacy Adverse events JCV Patient's choice			
increase after (	3 months	after index was	only observed in you	inger age group (C	0.11 vs. 0.13)	■ H-D (vs. H-H) 0	10 20 30 40 Relative information		
H-H ≤50 (N=558) 0.12	0.19 0.27	<ul> <li>■ ARR 12m before index</li> <li>■ ARR ≤3m after index</li> </ul>	<ul> <li>Main factors de-escalation adverse e</li> </ul>	associated with (H-M vs. H-H): events, age,	, 15,867 patients tha complete documentati in GMSR and had 3,064 started and ende	t are part of the cohort for ion of DMD treatment history a relapsing onset of MS V d a HET with either Rituximab.	▲ <b>Figure 3.</b> Factors distinguishing H-M (green) and H-D (blue) from H-H by		



**Figure 2.** Estimated annualized relapse rates (ARR) in the last 12 months on discontinued HE-DMT (green), 3 months afterwards (grey), and from therapy start (restricted to >3 months) until 12 months after discontinuation / under new therapy (blue).

<ul> <li>disability (me Expanded Dis Scale [EDSS]) (</li> <li>EDSS, age, duration were for discontinua H-H)</li> </ul>	ability (Figure and <b>d</b> main tion (H	I via Status 3) <b>isease</b> factors -D vs.	Oz 1,101	Ozanimod, Siponimod, Ponesimod, Ofatumumab at any point in time 7 1,905 ended HET episode after 1.1.2018 7 1,495 on HET for at least 12 months 1,101 had a follow-up of >12 months after HET enddate 86 switched to non-HET DMTs 219				the boosted regression models.		
moderate efficacy HET) within a months of HET discontinuation				12 (including inmunoglobuline) within 12 months of HET discontinuation				discontinuation		
<b>Table 1.</b> Patient characteristics	H-H			H-M			H-D			
		<b>≤50y</b>	>50y		≤50y	>50y	total	<b>≤50y</b>	>50y	
Tamalaa	/V=/00	740/	IN=220	/v=00	/V=0/	N=19	IN=2 19	700/	N=70	
	12%	74%		76%		74%	74%	78%	67%	
Age [years], mean (sd)	42.5 (11.3)	30.8 (7.6)	56.4 (4.7)	41.6 (10.4)	37.6 (7.5)	56.0 (4.8)	44.1 (11.7)	31.1 (1.4)	57.7 (6.1)	
vis duration [years], mean (sd)	13.9 (8.4)	11.7 (6.7)	19.3 (9.7)	13.1 (7.3)	12.1 (7.0)	16.6 (7.4)	13.9 (8.1)	11.7 (6.9)	18.6 (8.4)	
EDSS at index, mean (sd)	3.1 (1.9)	2.6 (1.7)	4.1 (1.7)	3.0 (1.8)	2.6 (1.6)	4.2 (2.0)	3.7 (2.2)	3.2 (2.2)	4.6 (1.8)	
OMT discontinuation reasons:										
Lack of efficacy	30%	30%	30%	12%	12%	14%	18%	13%	26%	
Adverse events	12%	10%	14%	38%	33%	57%	12%	10%	17%	
Positive JCV status	17%	18%	14%	14%	17%	0%	5%	8%	0%	
Patient's choice	11%	10%	13%	14%	15%	7%	23%	24%	21%	

relative information in

## Conclusions

Age does not strongly impact ARR following a switch between HET, but it does in the de-escalation groups

- ► ARR increases after de-escalation (H-M and H-D) in patients <50 years, and remain unchanged in patients ≥50 years
- Beside age, the difference in relapse rates in older compared to younger patients might also be related to the different reasons for DMT discontinuation (i.e. adverse events and lack of efficacy) for H-M and H-D
- Effects stratified by DMT will be investigated in greater detail

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