Trends in disease-modifying therapies´ (DMTs) use and efficacy between 2010 and 2017 in outpatients with relapsing-remitting-multiple-sclerosis (RRMS) in Germany

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Background: The impact of five new DMTs since 2010 on disease activity in RRMS is unknown. Three periods are analyzed: 2010-2012 (injectables, natalizumab & fingolimod), 2013-2015 (high disease activity (HDA) DMT: alemtuzumab, new oral DMTs: teriflunomid, dimethylfumarate), 2016-2017: (consolidation period with daclizumab temporary).

Population: The doctor´s owned NeuroTransData (NTD) MS-registry (www.neurotransdata.com) captured clinical data of 16.663 RRMS out-patients in Germany undergoing 13.588 DMT cycles between 2010 and 2017 with high data density (means): 3.36 visits/a (SD 2.42), 2.52 EDSS/a (SD 2.03), follow-up 5.21 years (SD 4.43).

Results: Results are given as percentages or means and standard deviation (SD) per period of time. Results in italic are preliminary due to shorter observation time.

Treatment pattern			2010-2012	2013-2015	2016-2017
Proportion of RRMS patients on DMT		%	68.4	75.1	76.8
Time-first-symptom-to-first-DMT		days SD	224 (365)	124 (349	108 (138)
Proportion of patients starting first-DMT within 6 months after diagnosis of RRMS		%	83	89	92
Time-to-discontinuation-of-DMT		months SD	19.9 (19.3)	14.11 (12.6)	*6.1* *(5.49)*
	due to adverse events	%	6.6	21.2	16.0
	due to lack of efficacy	%	8.2	4.5	13.9
Switches	to injectables	%	42.8	19.1	16.4
	to orals	%	42.3	70.3	65.2
	to infusions	%	14.9	10.6	18.4
	to HDA-label DMTs (incl. Fingolimod)	%	56.8	35.4	46.6

Treatment efficacy			2010-2012	2013-2015	2016-2017
Annualized relapse rate (ARR)	all DMTs		0.23	0.18	0.16
		SD	(0.49)	(0.44)	(0.45)
	injectable DMT		0.25	0.21	0.16
		SD	(0.52)	(0.52)	(0.46)
	oral DMT		0.20	0.16	0.16
		SD	(0.39)	(0.39)	(0.46)
	infusions		0.11	0.16	0.12
		SD	(0.30)	(0.40)	80.33)
Time-first-symptom-to-3m-confirmed EDSS ≥ 3-5		months SD	127.1 (70.6)	138.5 (89.4)	*166.5* *(102.8)*
3m-confirmed EDSS ≥ 5		months SD	175.8 (113.7)	182.8 (78.9)	*247.1* *(106.0)*
Proportion of RRMS patients switching to SPMS		%	6.2	2.2	*1.6*

Conclusions: Since 2010 more RRMS patients are treated at an earlier stage. DMTs are discontinued sooner increasingly due to adverse events or lack of efficacy, with the majority of reasons still related to other considerations. Horizontal switches within injectables were chosen less frequently in parallel with increasing decisions for oral DMTs. Over time ARRs decrease overall, but also for patients on injectable and oral DMTs and longer times are observed until patients reach EDSS stages ≥ 3-5 or ≥5. Proportions of patients switching from RRMS to SPMS decrease. In conclusion these results indicate a better allocation of individually efficient DMTs associated not only with the growing diversity of DMTs available but also based on a growing preparedness of patients and neurologist to switch DMTs.