

Table S1. Pretreatment, on-treatment, and posttreatment discontinuation sample characteristics from the 12 DMT discontinuation studies

Study Ref. No. ^b	First-line DMTs (IFNβ-1a and/or IFNβ-1b and/or glatiramer acetate)				Second-line DMTs (NTZ)								Mixed first- and second-line DMTs ^a		DMTs not specified			
	6	7	8	9	10		11	12	13		14		15	16		17		
Study design (n)	PCS (43)	PCS (221)	RCS (100)	PCS (1278)		RCT (50)		RCS (54)	RCS (132)	PCS (32)		PCS (84)		PCS (110)	PCS+RCS (70)		PCS (94)	
Disease course	RRMS	RRMS	SPMS	Not specified		RRMS		RRMS	RRMS	Mixed RRMS and SPMS		Mixed RRMS, SPMS, and PRMS		Not specified	Mixed RRMS, SPMS, and PRMS		Mixed RRMS and SPMS	
Study group (n)	NA	NA	NA	Stoppers (426)	Stayers (852)	Tapered (23)	Immediate discontinue (27)	NA	NA	With relapse (18)	Relapse free (14)	Rx interruption (68)	No Rx interruption (16)	NA	NTZ group (15)	First-line (55)	Advised to stop (77)	Chose to stop (17)
Pretreatment characteristics																		
Dx dur before Rx, y	NR	NR	NR	NR	NR	12.8	13.4	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR
MRI; Gd+; T2; any new activity	NR	NR	NR	NR	NR	NR	NR	n=54; 58% Gd+; 73.9% T2	NR	n=18; Gd+=2.2±3.7	n=14; Gd+ = 2.4 ± 3.0	NR	NR	n=110; Gd+=2.24	NR	NR	NR	NR
On-treatment characteristics																		
Rx dur, y	2	4.2	5	NR	NR	≥2	≥2	1.8	NR	[2.2]	[2.6]	NR	NR	NR	5.6	5.6	[11]	[7]
ARR	0.22±0.1	NR	0.12	NR	NR	NR	NR	0.21	NR	NR	NR	NR	NR	0.06	NR	NR	NR	NR
% with relapse	41.8	48.9	27	NR	NR	26.1	33.3	NR	NR	NR	NR	NR	NR	11	NR	NR	NR	NR
Age at Rx start, y	NR	NR	NR	NR	NR	NR	NR	NR	34.5	NR	NR	NR	NR	NR	[42]	[37]	NR	NR
EDSS score	NR	NR	4.7	NR	NR	≤7.0	≤7.0	[2.25]	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR
MRI; Gd+; T2; any new activity	NR	NR	n=78; 14% MRI activity	NR	NR	NR	NR	n=54; 2% Gd+; 11% new L	NR	NR	NR	NR	NR	n=110; Gd+=2.24±4.5	NR	NR	NR	NR
Main finding(s) of posttreatment discontinuation																		
F/U dur, y	2.8	[3.8]	5.2	[4.9]	[5]	1	1	1	1	NR	NR	NR	NR	1.9	[1.6]	[4.6]	NR	NR
Dx dur at stop, y	8.5	9	≥2	[13.7]	[13.1]	16.9	16.5	NR	NR	NR	NR	NR	NR	10.6±6.0	16	11	NR	NR
EDSS score at Rx stop	1.27±0.85	[1.5]	5.7±1.4	[3.5]	[3.5]	[3.5]±2.1	[4.1]±1.9	NR	NR	NR	NR	[3.0]	NR	[2.0]	NR	NR	NR	NR
EDSS score at last F/U	NR	[2.0]	6.3±1.2	NR	NR	[3.8]±2.4	[4.6] ± 1.8	[2.75]	[4.0]	4.7±1.9	5.7±2.2	NR	NR	[3.0]	NR	NR	[6.0]	[2.0]
ARR	0.48±0.2	NR	0.07	0.27±0.57	0.25±0.51	NR	NR	0.94	1	1.8±0.8	NA	NR	NR	0.84	NR	NR	NR	NR
% with relapse	65.1	44.3	16	36.4	37.8	30.5	59.3	57.4	54.5	9	NA	27.9	None	50	67	35	11.7	58.8
Age at Rx stop, y	NR	37.9	47.2±8.4	NR	NR	52.6	45.7	NR	NR	NR	NR	NR	NR	NR	[50]	[42]	[61]	[49]

MRI; Gd+; T2; any new activity	NR	n=168; 23.2% Gd+; 57.6 % T2 L	n=87; 19% Gd+	NR	NR	n=23; 4.3% Gd+; 17.3% T2	n=27; 11.1% Gd+; 44.4% T2	n=54; 47.1% Gd+; 52.9% new L	n=125; 48% new MRI activity	n=18; Gd+ L= 17.2±18.2	n=14; Gd+=0.3±0.6	n=19; 36.8% Gd+	n=16; 6.25% new T2 L	n=26; Gd+=1.70	n=15; 20%, new T2 L	NR	n=77; 11.7% Gd+; 14 new MRI L	NR
--------------------------------	----	-------------------------------	---------------	----	----	--------------------------	---------------------------	------------------------------	-----------------------------	------------------------	-------------------	-----------------	----------------------	----------------	---------------------	----	-------------------------------	----

Note: Unless otherwise noted, values are given as mean or [median].

Abbreviations and definitions: any new activity, T2 or Gd lesion increase reported; ARR, annualized relapse rate; DMT, disease-modifying therapy; Dx, disease; dur, duration; EDSS, Expanded Disability Status Scale; F/U, follow-up since stop date; Gd+, gadolinium-enhancing lesions on MRI; IFN, interferon; L, lesion (mean number of lesions reported if specified); MRI, magnetic resonance imaging; MS, multiple sclerosis; NR, not reported; NTZ, natalizumab; PCS, prospective cohort study; PRMS, primary progressive MS; RCS, retrospective cohort study; RCT, randomized control trial; Ref, reference; RRMS, relapsing-remitting MS; Rx, treatment; SPMS, secondary progressive MS; stayer, person who kept taking Rx; stopper, person who stopped taking Rx; T2, T2 lesions on MRI.

^aInterferons, glatiramer acetate, intravenous immunoglobulins, and natalizumab

^b **References (numbered as in article):**

6. Siger M, Durko A, Nicpan A, Konarska M, Grudziecka M, Selmaj K. Discontinuation of interferon beta therapy in multiple sclerosis patients with high pre-treatment disease activity leads to prompt return to previous disease activity. *J Neurol Sci*. 2011;303:50-52. \
7. Bsteh G, Feige J, Ehling R, et al. Discontinuation of disease-modifying therapies in multiple sclerosis: clinical outcome and prognostic factors. *Mult Scler*. 2016;23:1241-1248.
8. Bonenfant J, Bajoux E, Deburghgraeve V, Le Page E, Edan G, Kerbrat A. Can we stop immunomodulatory treatments in secondary progressive multiple sclerosis? *Eur J Neurol*. 2016;24:237-244. \
9. Kister I, Spelman T, Alroughani R, et al. Discontinuing disease-modifying therapy in MS after a prolonged relapse-free period: a propensity score-matched study. *J Neurol Neurosurg Psychiatry*. 2016;87:1133-1137.
10. Weinstock-Guttman B, Hagemeyer J, Kavak K, et al. Randomised natalizumab discontinuation study: taper protocol may prevent disease reactivation. *J Neurol Neurosurg Psychiatry*. 2016;87:937-943.
11. Melis M, Cocco E, Frau J, et al. Post-natalizumab clinical and radiological findings in a cohort of multiple sclerosis patients: 12-month follow-up. *Neurol Sci*. 2014;35:401-408.
12. Lo Re M, Capobianco M, Ragonese P, et al. Natalizumab discontinuation and treatment strategies in patients with multiple sclerosis (MS): a retrospective study from two Italian MS centers. *Neurol Ther*. 2015;4:147-157.
13. Gueguen A, Roux P, Deschamps R, et al. Abnormal inflammatory activity returns after natalizumab cessation in multiple sclerosis. *J Neurol Neurosurg Psychiatry*. 2014;85:1038-1040.
14. West TW, Cree BAC. Natalizumab dosage suspension: are we helping or hurting? *Ann Neurol*. 2010;68:395-399.
15. Sangalli F, Moiola L, Ferre L, et al. Long-term management of natalizumab discontinuation in a large monocentric cohort of multiple sclerosis patients. *Mult Scler Relat Disord*. 2014;3:520-526.
16. Fagius J, Feresiadou A, Larsson E, Burman J. Discontinuation of disease modifying treatments in middle aged multiple sclerosis patients: first line drugs vs natalizumab. *Mult Scler Relat Disord*. 2017;12:82-87.
17. Birnbaum G. Stopping disease-modifying therapy in nonrelapsing multiple sclerosis. *Int J MS Care*. 2017;19:11-14.