

On-line Table 1: Demographic, clinical, and MR imaging of patients with MS with characteristics of disability progressed, disability improved, and stable status^a

Demographic and Clinical Variables	Disability Progression at Follow-Up (n = 241)	Disability Improvement at Follow-Up (n = 101)	Stable at Follow-Up (n = 638)	P Value
Females (No.) (%)	188 (78.0)	78 (77.2)	476 (74.6)	.54
Age at onset of the first clinical event (mean) (SD) (yr)	33.3 (9.6)	31.3 (9.8)	33.2 (10.4)	.2
Age at baseline (mean) (SD) (yr)	47.1 (9.8)	44.7 (9.9)	45.4 (11.2)	.07
Race (No.) (%)				
White	203 (84.2)	93 (92.1)	576 (90.3)	.06
African American	33 (13.7)	8 (7.9)	57 (8.9)	
Other	5 (2.1)	0 (0.0)	4 (0.7)	
Time from baseline to follow-up (mean) (SD) (yr)	4.8 (2.4)	4.7 (2.4)	4.8 (2.4)	.89
Disease duration at baseline (mean) (SD) (yr)	13.3 (9.6)	12.8 (9.5)	11.8 (9.5)	.10
EDSS at baseline (median) (IQR)	3.0 (3.0)	3.5 (3.0)	2.5 (2.5)	<.001
EDSS at follow-up (median) (IQR)	6.0 (3.0)	2.5 (2.5)	2.5 (2.5)	<.001
Annualized relapse rate over the follow-up (mean) (SD)	0.25 (0.55)	0.28 (0.69)	0.18 (0.37)	.03
Disease subtype at baseline (No.) (%)				
RR	182 (75.5)	85 (84.2)	527 (82.6)	.29
SP	49 (20.3)	14 (13.9)	100 (15.7)	
PP	10 (4.1)	2 (2.0)	11 (1.7)	
Benign MS at baseline (No.) (%)	45 (18.7)	8 (7.9)	97 (15.2)	.04
T2-LV at baseline (mean) (SD)	21.9 (18.0)	17.2 (15.9)	16.8 (14.9)	<.001
DMT at baseline (No.) (%)				.15
Interferon- β -1a	67 (27.8)	20 (19.8)	209 (32.8)	
Glatiramer acetate	52 (21.7)	22 (21.8)	125 (19.6)	
Natalizumab	24 (9.9)	13 (12.9)	76 (11.9)	
Oral	41 (17)	16 (15.8)	101 (15.8)	
Immunosuppressive	17 (7.0)	5 (4.9)	15 (2.3)	
Intravenous immunoglobulin	1 (0.4)	16 (15.8)	1 (0.1)	
No DMT	37 (15.4)	22 (21.8)	95 (14.9)	
Missing data	2 (0.8)	3 (3.0)	16 (2.5)	
DMT at follow-up (No.) (%)				.03
Interferon- β	71 (29.4)	25 (24.8)	223 (35)	
Glatiramer acetate	54 (22.4)	22 (21.8)	127 (19.9)	
Natalizumab	24 (9.9)	13 (12.9)	86 (13.4)	
Oral	34 (14.1)	10 (15.8)	86 (13.4)	
Immunosuppressive	11 (4.6)	3 (2.9)	11 (1.7)	
Intravenous immunoglobulin	11 (4.6)	4 (3.9)	10 (1.6)	
No DMT	37 (15.4)	24 (21.8)	95 (14.9)	
Missing data	0 (0)	0 (0)	0 (0)	
DMT status during follow-up (No.) (%)				.2
Started DMT	39 (16.2)	10 (9.9)	62 (9.7)	
Stopped DMT	16 (10.1)	13 (12.9)	45 (7.1)	
Remained on the same DMT	85 (35.3)	38 (37.6)	296 (46.4)	
Switched to a different DMT	78 (32.4)	28 (27.7)	169 (26.5)	
No DMT	21 (8.7)	9 (8.9)	50 (7.8)	
Missing data	2 (0.8)	3 (3.0)	16 (2.5)	

Note:—IQR indicates interquartile range.

^a The data are presented as mean (SD) and median (IQR). The absolute values are expressed in milliliters. Immunosuppressive therapies included mycophenolate mofetil, methotrexate, cyclophosphamide, mitoxantrone, and azathioprine. Oral DMT included dimethyl fumarate, fingolimod, and teriflunomide. Differences among disability progression, disability improvement, and stable status were calculated using 1-way ANOVA, the Kruskal–Wallis test, and χ^2 as appropriate.

On-line Table 2: Lateral ventricular volume and brain volume measures in patients with MS with disability progressed, disability improved, and stable status^a

LVV Measures	Disability Progression (Mean) (SD)	Disability Improvement (Mean) (SD)	Stable (Mean) (SD)	Cohen D (Disability Progression, Disability Improvement)	Cohen D (Disability Progression, Stable)	P Value (Disability Progression, Improvement) ^b		P Value (Disability Progression, Stable) ^b	
						Disability Progression, Improvement	Disability Progression, Stable	Disability Progression, Improvement	Disability Progression, Stable
LVV at baseline	24.0 (13.4) (n = 241)	24.1 (14.5) (n = 101)	23.1 (13.5) (n = 638)	0.007	0.067	.67 ^c	1.0 ^c	1.0 ^c	1.0 ^c
Whole-brain volume at baseline PLVVC during follow-up	1518.3 (106.3) (n = 209)	1541.9 (99.7) (n = 94)	1537.2 (99.9) (n = 570)	0.229	0.183	.37 ^d	.55 ^d	.89 ^d	.71 ^e
						.74 ^e	1.0 ^e	.98 ^c	.44 ^c
						.33 ^c	1.0 ^d	1.0 ^d	1.0 ^d
Annualized PLVVC during follow-up	20.9 (22.0) (n = 241)	6.5 (13.5) (n = 101)	9.1 (13.5) (n = 638)	0.789	0.647	.84 ^d	1.0 ^e	1.0 ^e	1.0 ^e
						.71 ^e	<.001 ^c	<.001 ^c	<.001 ^c
						<.001 ^d	<.001 ^d	<.001 ^d	<.001 ^d
PBVC during follow-up	4.1 (5.5) (n = 241)	1.6 (2.7) (n = 100)	2.1 (3.7) (n = 638)	0.577	0.427	<.001 ^e	<.001 ^e	<.001 ^e	<.001 ^e
						<.001 ^c	<.001 ^c	<.001 ^c	<.001 ^c
						<.001 ^d	<.001 ^d	<.001 ^d	<.001 ^d
Annualized PBVC during follow-up	-4.6 (3.3) (n = 149)	-3.3 (2.6) (n = 72)	-3.3 (2.6) (n = 391)	0.438	0.438	<.001 ^e	.004 ^c	.004 ^c	.004 ^c
						<.001 ^d	.015 ^d	.015 ^d	.015 ^d
						<.001 ^e	.011 ^e	.011 ^e	.011 ^e
Annualized PBVC during follow-up	-1.1 (1.1) (n = 149)	-0.7 (0.7) (n = 72)	-0.8 (0.7) (n = 391)	0.434	0.325	<.001 ^e	.009 ^e	.009 ^e	.009 ^e
						.001 ^d	.03 ^d	.03 ^d	.03 ^d
						.001 ^e	.02 ^e	.02 ^e	.02 ^e

^a The data are presented as mean (SD). The absolute values are expressed in milliliters.

^b Bonferroni adjusted pair-wise comparison.

^{c-e} The differences between the groups were calculated using ANCOVA adjusted for:

^c Age at first MR imaging and race.

^d Age at first MR imaging, race, T2-LV, and corresponding baseline structural volume.

^e Age at first MR imaging, race, T2-LV, corresponding baseline structural volume, and EDSS.

On line Table 3: Estimated means for lateral ventricular volume and brain volume measures in patients with MS in disability progressed, disability improved, and stable status groups (based on On-line Table)^a

LVV Measures	Disability Progression Estimated (Mean) (95% CI)	Disability Improvement Estimated (Mean) (95% CI)	Stable Estimated (Mean) (95% CI)	P Value (Disability Progression, Disability Improvement, Stable)	P Value (Disability Progression, Disability Improvement) ^b	P Value (Disability Progression, Stable) ^b
LVV at baseline	23.6 (21.9–25.3) 22.7 (21.2–24.2) 22.7 (21.2–24.2)	24.4 (21.9–26.9) 24.6 (22.3–26.9) 23.8 (21.4–26.2)	23.0.2 (22.2–24.2) 23.6 (22.7–24.6) 23.8 (22.9–24.7)	.67 ^c .37 ^d .738 ^e	1.0 ^c .55 ^d 1.0 ^e	1.0 ^c .89 ^d .71 ^e
Whole-brain volume at baseline	1525.2 (1512.9–1537.4) 1530.8 (1519.3–1542.4) 1531.2 (1519.9–1542.6)	1536.1 (1518.0–1554.2) 1529.3 (1512.6–1546.1) 1531.2 (1519.9–1542.6)	1535.7 (1528.3–1543.1) 1533.7 (1526.9–1540.5) 1531.9 (1525.2–1538.7)	.33 ^c .84 ^d .71 ^e	.98 ^c 1.0 ^d 1.0 ^e	.44 ^c 1.0 ^d 1.0 ^e
PLVVC during follow-up	21.1 (19.1–23.2) 20.9 (18.9–23.1) 20.9 (18.7–23.1)	6.4 (3.2–9.5) 6.4 (3.2–9.6) 6.7 (3.4–9.9)	9.0 (7.8–10.3) 9.0 (7.8–10.3) 8.9 (7.7–10.3)	<.001 ^c <.001 ^d <.001 ^e	<.001 ^c <.001 ^d <.001 ^e	<.001 ^c <.001 ^d <.001 ^e
Annualized PLVVC during follow-up	4.1 (3.6–4.6) 4.0 (3.5–4.6) 4.0 (3.5–4.6)	1.6 (0.8–2.4) 1.6 (0.8–2.5) 1.6 (0.7–2.4)	2.1 (1.7–2.4) 2.1 (1.7–2.4) 2.1 (1.7–2.4)	<.001 ^c <.001 ^d <.001 ^e	<.001 ^c <.001 ^d <.001 ^e	<.001 ^c <.001 ^d <.001 ^e
PBVC during follow-up	–4.6 (–5.1 to –5.2) –4.6 (–5.0 to –4.1) –4.6 (–5.0 to –4.1)	–3.3 (–3.9 to –2.7) –3.4 (–4.1 to –2.7) –3.3 (–4.0 to –2.6)	–3.3 (–3.5 to –2.9) –3.3 (–3.5 to –2.9) –3.3 (–3.6 to –2.9)	<.001 ^c <.001 ^d <.001 ^e	.004 ^c .015 ^d .011 ^e	<.001 ^c <.001 ^d <.001 ^e
Annualized PBVC during follow-up	–1.1 (–1.2 to –0.9) –1.1 (–1.2 to –0.9) –1.1 (–1.2 to –0.9)	–0.7 (–0.9 to –0.6) –0.8 (–0.9 to –0.6) –0.7 (–0.9 to –0.5)	–0.8 (–0.9 to –0.7) –0.8 (–0.9 to –0.7) –0.8 (–0.9 to –0.7)	<.001 ^c .001 ^d .001 ^e	.009 ^c .03 ^d .02 ^e	<.001 ^c .001 ^d .01 ^e

^a The data are presented as estimated mean (95% confidence intervals). The absolute values are expressed in milliliters.

^b Bonferroni adjusted pair-wise comparison.

^{c–e} The differences between the groups were calculated using ANCOVA adjusted for:

^c Age at first MR imaging and race.

^d Age at first MR imaging, race, T2–LV, and corresponding baseline structural volume.

^e Age at first MR imaging, race, T2–LV, corresponding baseline structural volume, and EDSS.

On-line Table 4 : Lateral ventricular volume and brain volume measures in patients with MS in disability progressed, disability improved, and stable status with follow-up ≤ 2 years^a

LVV Measures	Cohen D			P Value (Disability Progression, Disability Improvement, Stable) ^b			P Value (Disability Progression, Disability Improvement, Stable) ^b		
	Disability Progression (Mean) (SD)	Disability Improvement (Mean) (SD)	Stable (Mean) (SD)	(Disability Progression, Disability Improvement)	(Disability Progression, Stable)	(Disability Improvement, Stable)	Disability Progression	Disability Improvement	Stable ^b
LVV at baseline	21.8 (11.7) (n = 35)	26.3 (15.1) (n = 16)	22.8 (11.2) (n = 104)	0.333	0.087		.81 ^c	.21 ^d	1.0 ^c
Whole-brain volume at baseline	1525.9 (99.1) (n = 32)	1495.4 (112.3) (n = 13)	1513.8 (104.7) (n = 96)	0.288	0.119		.32 ^e	.17 ^e	.17 ^e
PLVVC during follow-up	4.4 (10.9) (n = 35)	2.9 (6.9) (n = 16)	4.5 (9.5) (n = 104)	0.164	0.009		1.0 ^c	.66 ^d	.25 ^e
Annualized PLVVC during follow-up	4.3 (10.7) (n = 35)	2.2 (4.4) (n = 16)	2.9 (6.4) (n = 104)	0.258	0.159		.79 ^c	.73 ^d	.98 ^c
PBVC during follow-up	−1.9 (2.1) (n = 24)	−1.1 (1.8) (n = 12)	−1.5 (1.6) (n = 79)	0.429	0.214		.26 ^e	.72 ^e	.77 ^e
Annualized PBVC during follow-up	−1.8 (2.5) (n = 24)	−0.7 (1.3) (n = 12)	−1.1 (1.1) (n = 79)	0.552	0.362		.6 ^c	.22 ^c	1.0 ^c
							.4 ^d	.55 ^d	1.0 ^d
							.38 ^e	.49 ^e	1.0 ^e
							.07 ^c	.1 ^c	.12 ^c
							.12 ^d	.28 ^d	.18 ^d
							.13 ^e	.27 ^e	.24 ^e

^a The data are presented as mean (SD). The absolute values are expressed in milliliters.^b Bonferroni adjusted pair-wise comparison.^{c–e} The differences between the groups were calculated using ANCOVA adjusted for:^c Age at first MR imaging and race.^d Age at first MR imaging, race, T2–LV, and corresponding baseline structural volume.^e Age at first MR imaging, race, T2–LV, corresponding baseline structural volume, and EDSS.

On-line Table 5: Estimated means for lateral ventricular volume and brain volume measures in patients with MS in disability progressed, disability improved, and stable status with follow-up of ≤2 years (based on On-line Table 4)^a

LVV Measures	Disability Progression Estimated (95% CI)	Disability Improvement Estimated (Mean) (95% CI)	Stable Estimated (Mean) (95% CI)	P Value (Disability Progression, Disability Improvement, Stable)	P Value (Disability Progression, Disability Improvement) ^b	P Value (Disability Progression, Stable) ^b
LVV at baseline	21.9 (18.1–25.6) 20.1 (16.9–23.3) 19.8 (16.6–22.9)	25.6 (20.1–31.2) 25.4 (20.6–30.2) 24.5 (19.7–29.3)	22.8 (20.7–25.0) 25.4 (20.6–30.2) 23.4 (21.5–25.3)	.54 ^c .14 ^d .11 ^e	.81 ^c .21 ^d .32 ^e	1.0 ^c .31 ^d .17 ^e
Whole-brain volume at baseline	1525.2 (1492.9–1556.5) 1535.1 (1504.0–1567.3) 1540.1 (1509.9–1570.2)	1497.9 (1447.2–1548.6) 1494.3 (1444.8–1540.8) 1505.5 (1458.7–1442.3)	1413.7 (1495.2–1532.3) 1512.6 (1494.5–1530.6) 1409.1 (1491.6–1526.6)	.66 ^c .29 ^d .2 ^e	1.0 ^c .44 ^d .66 ^e	1.0 ^c .66 ^d .25 ^e
PLVVC during follow-up	4.5 (1.3–7.7) 4.8 (1.5–8.2) 4.8 (1.4–8.1)	2.6 (–2.1–7.4) 2.4 (–2.6–7.4) 2.2 (–2.9–7.3)	4.5 (2.6–6.3) 4.3 (2.4–6.2) 4.4 (2.4–6.3)	.79 ^c .79 ^d .7 ^e	1.0 ^c 1.0 ^d 1.0 ^e	1.0 ^c 1.0 ^d 1.0 ^e
Annualized PLVVC during follow-up	4.3 (1.9–6.8) 4.6 (1.9–7.2) 4.6 (1.9–7.2)	1.9 (–1.7–5.7) 1.8 (–2.1–5.7) 1.7 (–2.3–5.7)	2.9 (1.4–4.3) 2.8 (1.3–4.3) 2.8 (1.3–4.3)	.5 ^c .4 ^d .26 ^e	.9 ^c .73 ^d .72 ^e	.98 ^c .71 ^d .77 ^e
PBVC during follow-up	–1.9 (–2.6 to –1.2) –1.9 (–2.6 to –1.2) –1.9 (–2.6 to –1.2)	–0.8 (–1.8–0.2) –1.0 (–2.1–0.1) –0.9 (–2.0–0.2)	–1.6 (–1.9 to –1.2) –1.6 (–1.9 to –1.2) –1.6 (–1.9 to –1.2)	.2 ^c .4 ^d .38 ^e	.22 ^c .55 ^d .49 ^e	1.0 ^c 1.0 ^d 1.0 ^e
Annualized PBVC during follow-up	–1.8 (–2.4 to –1.1) –1.8 (–2.4 to –1.2) –1.8 (–2.4 to –1.1)	–0.6 (–1.5–0.3) –0.8 (–1.8–0.2) –0.7 (–1.7–0.3)	–1.1 (–1.4 to –0.8) –1.1 (–1.5 to –0.7) –1.1 (–1.5 to –0.8)	.07 ^c .12 ^d .13 ^e	.1 ^c .28 ^d .27 ^e	.2 ^c .18 ^d .24 ^e

^a The data are presented as estimated mean (95% confidence intervals). The absolute values are expressed in milliliters.

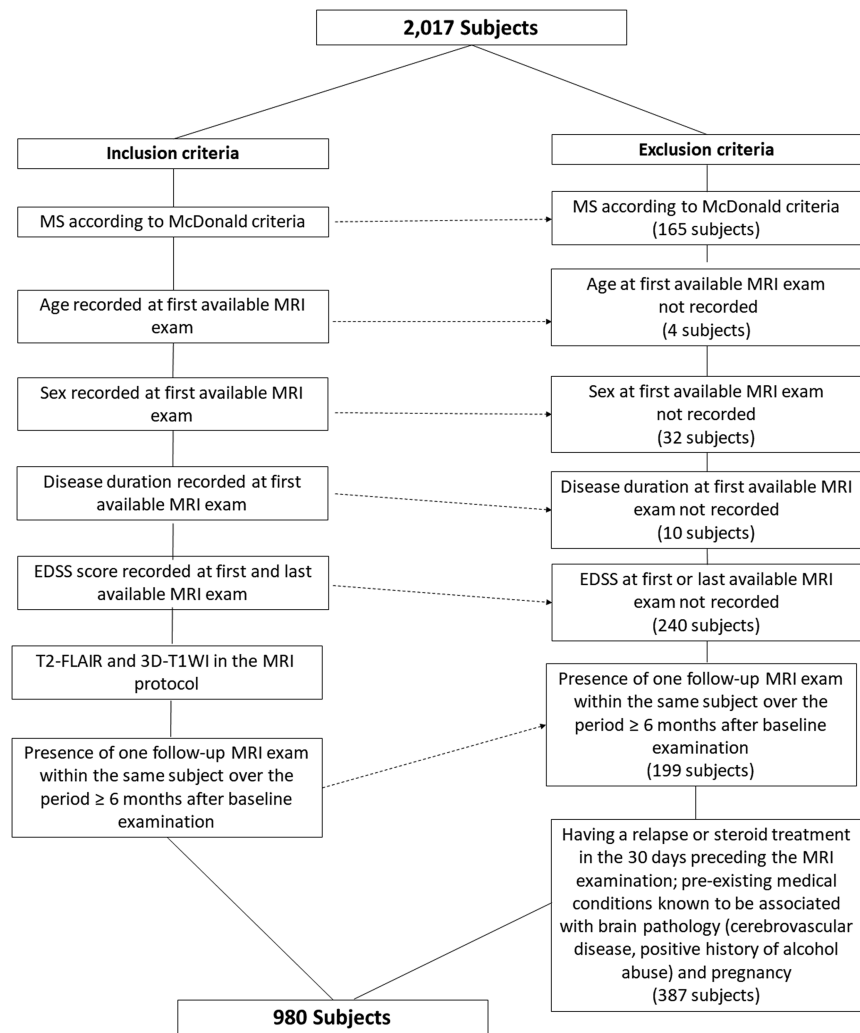
^b Bonferroni adjusted pair-wise comparison.

^{c–e} The differences between the groups were calculated using ANCOVA adjusted for:

^c Age at first MR imaging and race.

^d Age at first MR imaging, race, T2–LV, and corresponding baseline structural volume.

^e Age at first MR imaging, race, T2–LV, corresponding baseline structural volume, and EDSS.



ON-LINE FIGURE. Flow chart of inclusion and exclusion criteria.