

Table 2: Group comparison of outcomes at 12 weeks and 6 months							
		Total	CR + EX	CR + EX-S	CR-S + EX	CR-S+EX-S	p value*
N	Baseline	311	77	79	80	75	-
	12-week	284	70	76	71	67	
	6 month	258	65	68	65	60	
Cognitive outcomes							
SDMT [†]	Baseline	33.4 (8.2)	32.2 (8.6)	33.0 (7.4)	35.1 (8.1)	33.3 (8.4)	0.85
	12-week	39.3 (11.5)	38.0 (11.9)	39.1 (10.3)	39.9 (11.1)	40.2 (12.8)	
	6 month	36.8 (11.6)	35.8 (11.1)	35.9 (12.5)	37.9 (10.3)	37.8 (12.4)	
Difference in SDMT [†]	Baseline to 12-week	5.9 (7.5)	5.7 (7.2)	6.3 (6.6)	4.5 (7.5)	7.1 (8.6)	0.23
	4 points or greater, n (%) [‡]	171 (60.2)	45 (64.3)	50 (65.8)	36 (50.7)	40 (59.7)	0.24
	8 points or greater, n (%) [§]	106 (37.3)	26 (37.1)	31 (40.8)	24 (33.8)	25 (37.3)	0.86
	Baseline to 6 month	3.5 (7.3)	3.5 (6.8)	3.1 (8.2)	2.8 (6.7)	4.4 (7.2)	0.63
	4 points or greater, n (%) [‡]	119 (46.1)	30 (46.2)	34 (50.0)	29 (44.6)	26 (43.3)	0.88
	8 points or greater, n (%) [§]	68 (26.4)	17 (26.2)	17 (25.0)	15 (23.1)	19 (31.7)	0.73
CVLT*	Baseline	45.1 (11.9)	44.9 (12.2)	44.2 (10.9)	46.3 (12.7)	45.1 (11.9)	0.95
	12-week	46.2 (11.4)	46.6 (11.7)	45.6 (10.8)	47.5 (11.8)	45.1 (11.3)	
	6 month	48.7 (12.5)	48.7 (12.3)	47.9 (12.6)	50.6 (12.7)	47.7 (12.4)	
BVMT-R*	Baseline	20.8 (7.5)	20.6 (7.2)	21.1 (7.4)	21.2 (7.2)	20.2 (8.1)	0.93
	12-week	20.1 (7.8)	19.7 (7.7)	19.6 (7.6)	20.9 (7.7)	20.4 (8.2)	
	6 month	19.5 (7.8)	19.3 (8.3)	18.8 (8.0)	19.8 (7.1)	20.1 (8.1)	
Physical outcomes							
IET - VO ₂ Peak*	Baseline	17.5 (6.3)	16.4 (5.3)	17.3 (5.8)	18.5 (6.7)	17.6 (7.2)	0.22
	12-week	18.2 (6.9)	17.9 (6.7)	17.2 (6.6)	20.0 (7.4)	17.6 (6.6)	
	6 month	17.6 (6.0)	17.8 (5.6)	17.4 (5.9)	18.4 (6.5)	16.6 (6.0)	
IET – Peak Watts*	Baseline	81.0 (33.6)	76.8 (32.3)	77.1 (28.8)	86.1 (35.6)	83.9 (36.9)	0.004
	12-week	87.7 (38.0)	89.7 (33.8)	78.2 (32.4)	100.4 (39.7)	83.0 (43.0)	
	6 month	81.2 (34.6)	81.3 (33.8)	78.3 (33.4)	83.3 (36.4)	82.2 (35.8)	
IET –Peak HR*	Baseline	132.8 (21.3)	130.9 (22.2)	132.0 (20.4)	137.0 (21.6)	131.0 (20.8)	0.04
	12-week	133.9 (22.5)	133.3 (21.3)	130.0 (23.4)	142.5 (21.7)	129.7 (21.2)	
	6 month	131.3 (20.9)	129.6 (20.1)	132.6 (19.3)	134.0 (23.0)	128.4 (21.1)	
CMI Dual Task Cost (DTC) Cognition*	Baseline	0.39 (43.6)	-7.9 (68.6)	0.73 (36.8)	3.8 (26.9)	5.0 (27.8)	0.92
	12-week	3.7 (29.9)	-4.4 (43.1)	2.2 (22.6)	9.0 (23.0)	8.4 (25.1)	
	6 month	4.1 (39.4)	-2.4 (48.6)	5.7 (39.2)	5.2 (29.7)	8.0 (38.1)	
CMI Dual Task Cost (DTC) Motor*	Baseline	15.9 (14.4)	14.4 (16.5)	17.5 (12.9)	15.6 (15.3)	16.1 (12.7)	0.92
	12-week	15.7 (15.0)	13.4 (13.4)	17.0 (14.3)	16.2 (15.9)	16.1 (16.4)	
	6 month	14.6 (16.0)	11.4(18.4)	15.7(16.0)	16.6(15.6)	14.7(13.5)	
6MWT, total distance*	Baseline	265.5 (141.0)	258.5 (143.1)	241.7 (136.2)	286.8 (142.7)	275.3 (140.4)	0.40
	12-week	281.0 (141.5)	273.6 (138.0)	259.5 (150.6)	299.8 (135.3)	293.2 (140.0)	
	6 month	273.3 (138.0)	277.2 (137.6)	258.2 (151.6)	272.0 (128.0)	287.6 (135.7)	
Accelerometer Average % MVPA*	Baseline	1.7 (2.3)	1.7 (2.4)	1.5 (2.7)	2.1 (2.5)	1.4 (1.6)	0.95
	12-week	1.7 (2.3)	1.8 (2.8)	1.5 (1.8)	1.8 (2.3)	1.5 (2.0)	

Patient reported outcomes							
HADS-D*	Baseline	6.2 (4.0)	6.2 (4.0)	6.7 (4.5)	5.6 (3.7)	6.2 (3.7)	0.51
	12-week	5.7 (3.6)	6.4 (3.9)	5.5 (3.8)	5.0 (3.3)	5.9 (3.3)	
	6 month	6.3 (4.1)	6.5 (4.0)	6.4 (4.4)	6.2 (4.4)	6.3 (3.8)	
HADS-A*	Baseline	6.5 (4.5)	6.8 (5.0)	6.5 (4.6)	6.2 (3.9)	6.7 (4.5)	0.87
	12-week	6.0 (4.1)	6.7 (4.7)	5.7 (3.9)	5.4 (3.8)	6.1 (4.0)	
	6 month	6.4 (4.2)	7.1 (4.7)	5.8 (3.9)	6.3 (4.2)	6.4 (3.8)	
FAMS Total*	Baseline	103.4 (28.7)	100.6 (29.4)	98.9 (29.5)	110.3 (25.5)	103.6 (29.5)	0.88
	12-week	106.2 (29.5)	100.5 (30.7)	105.6 (30.0)	111.0 (28.3)	107.9 (28.6)	
	6 month	100.9 (29.5)	98.7 (29.3)	100.3 (29.2)	104.4 (30.0)	99.9 (29.9)	
EQ-5D-5L VAS*	Baseline	59.7 (20.7)	59.3 (23.3)	56.8 (20.9)	61.9 (20.4)	60.7 (18.1)	0.93
	12-week	64.5 (18.8)	63.5 (20.9)	64.1 (20.0)	65.5 (17.7)	64.9 (16.4)	
	6 month	62.3 (19.5)	63.1 (19.3)	62.8 (21.2)	62.1 (18.8)	61.1 (18.9)	
MSIS-29, Physical*	Baseline	47.0 (22.9)	51.3 (22.7)	49.2 (23.4)	43.6 (22.2)	43.7 (22.7)	0.85
	12-week	42.8 (23.1)	49.3 (24.3)	42.7 (23.1)	37.6 (21.6)	41.7 (22.0)	
	6 month	48.5 (23.0)	53.2 (22.6)	47.4 (23.6)	44.8 (21.8)	48.7 (23.6)	
MSIS-29, Mental*	Baseline	37.2 (24.1)	40.5 (24.5)	37.3 (24.6)	34.4 (22.5)	36.8 (24.9)	0.07
	12-week	34.4 (23.6)	41.5 (25.5)	34.1 (23.7)	30.6 (22.0)	31.4 (22.0)	
	6 month	39.4 (24.9)	40.9 (25.6)	38.3 (23.3)	37.8 (24.0)	40.8 (27.1)	
MSWS-12*	Baseline	63.3 (26.6)	67.1 (26.5)	64.6 (25.5)	60.0 (28.0)	61.7 (26.0)	0.74
	12-week	59.3 (26.6)	61.7(25.5)	60.7(27.6)	57.3(27.1)	57.5 (26.4)	
	6 month	63.9 (26.9)	65.4 (25.4)	62.4 (28.9)	63.3 (28.3)	64.9 (24.9)	
PDQ Total*	Baseline	28.5 (17.2)	30.7 (18.9)	28.9 (16.2)	26.6 (17.5)	27.8 (16.1)	0.80
	12-week	26.4 (16.6)	29.9 (17.3)	25.1 (15.0)	23.2 (17.1)	27.4 (16.7)	
	6 month	29.4 (16.6)	31.6(16.7)	27.7(14.7)	27.4(17.8)	31.3(17.2)	
MFIS*	Baseline	44.1 (17.1)	46.4 (17.9)	45.8 (16.3)	40.9 (16.8)	43.6 (17.1)	0.84
	12-week	40.1 (17.3)	43.1 (17.7)	40.7 (18.0)	36.2 (16.3)	40.2 (16.7)	
	6 month	44.7 (16.7)	46.7 (16.3)	44.7 (17.5)	42.9 (16.6)	44.5 (16.5)	

SDMT=Symbol Digit Modalities Test; CVLT=California Verbal Learning Test; BVMT=Brief Visual Memory Test – revised
IET=incremental exercise test; VO₂=V stands for volume and O₂ stands for oxygen; HR=Heart Rate; CMI=Cognitive-motor interference; 6MWT=6 minute walk test; MVPA=Moderate to vigorous physical activities *p-value is based on the longitudinal model adjusting for baseline and site; HADS-D=Hospital Anxiety and Depression Scale-Depression; HADS-A=Hospital Anxiety and Depression Scale-Anxiety; FAMS=Functional Assessment of Multiple Sclerosis; EQ-5D-5L=European Quality of Life 5 Dimensions 5 Level; VAS=Visual Analog Scale; MSIS-29=Multiple Sclerosis Impact Scale-29; MSWS-12=12-Item MS Walking Scale; MFIS=Modified Fatigue Impact Scale.
*[†]p-value is based on the longitudinal model adjusting for baseline and site. *[‡]=Difference in raw SDMT score between baseline and 12-week follow-up; [§] 4 points or greater change on the SDMT at 12-weeks; [§] 8 points or greater change on the SDMT at 12-weeks.
[‡]Primary analysis *Secondary analysis [†]Sensitivity analysis

No multiple comparison correction was performed for secondary outcomes.