Supplemental Material

Table S1. BL demographic and disease characteristics in patients with abnormal vs normal baseline 9HPT for both hands.

	Both hands			
	9HPT >25 seconds		9HPT ≤25 seconds	
	Placebo	Ocrelizumab	Placebo	Ocrelizumab
N	137	297	107	191
Age, mean (SD), years	44·2 (7·8)	44·5 (7·7)	44·6 (8·8)	45·0 (8·2)
Female sex, n (%)	60 (43·8)	129 (43·4)	64 (59·8)	108 (56·5)
Time since onset of MS symptoms, years				
Mean (SD)	6·84 (3·92)	6·97 (4·02)	5·25 (2·91)	6·16 (3·96)
Median	6·16	6·40	4·72	5·56
Range	1·1–23·8	1·1–32·9	0·9–15·9	1·2–31·3
Interquartile range	3·84–9·77	3·86–9·39	2·97–7·09	3·49–7·76
Time since PPMS diagnosis, years				
Mean (SD)	3·34 (3·86)	3·20 (3·33)	1·99 (2·27)	2·31 (2·81)
Median	1·68	1·89	0·96	1·13
Range	0·1–23·8	0·1–14·1	0·1–11·9	0·1–16·8
Interquartile range	0·5–5·09	0·67–4·65	0·47–2·75	0·43–3·53
No previous DMT use, n (%)	116 (84·7)	258 (86·9)	98 (91·6)	175 (91·6)
EDSS				
Mean (SD)	5·12 (1·14)	4·98 (1·17)	4·23 (1·02)	4·38 (1·08)
Median	5·50	5·00	4·00	4·00
Range	3·0–6·5	2·5–7·0	2·5–6·5	3·0–6·5
Patients with Gd-enhancing T1 lesions, n (%)	40 (29·4)	88 (29·6)	20 (18·7)	45 (23·6)
Number of Gd-enhancing T1 lesions				
Mean (SD)	0·81 (1·90)	1·43 (6·17)	0·33 (0·87)	0·87 (2·90)
Median	0	0	0	0
Range	0–10	0–77	0–6	0–24
Total volume of T2 lesions, cm^3				
Mean (SD)	14·4 (15·32)	16·1 (17·0)	6·4 (6·92)	7·4 (9·47)
Median	9·46	10·13	3·81	3·61
Range	0·1–81·1	0–90·3	0–36·5	0–62·9
Normalized brain volume, cm^3				
Median	1,451·3	1,443·5	1,485·7	1,491·4
Range	1,216·3–1,701·7	1,214·3–1,630·6	1,323·9–1,667·6	1,291·0–1,711·1

Table S2. BL demographic and disease characteristics in patients with BL EDSS ≥6 or <6.

	EDSS ≥6		EDSS <6	
	Placebo	**Ocrelizumab**	**Placebo**	**Ocrelizumab**
N	81	139	163	349
Age, years, mean (SD)	45·7 (7·2)	45·0 (7·8)	43·8 (8·7)	44·6 (7·9)
Female sex, n (%)	40 (49·4)	76 (54·7)	84 (51·5)	161 (46·1)
Time since onset of MS symptoms, years				
Mean (SD)	8·01 (4·25)	8·83 (4·61)	5·23 (2·83)	5·79 (3·39)
Median	7·09	8·39	4·80	5·31
Range	1·3–23·8	1·2–32·9	0·9–13·1	1·1–31·3
Interquartile range	5·24–10·64	5·84–11·87	2·89–7·23	3·31–7·49
Time since PPMS diagnosis, years				
Mean (SD)	4·20 (4·40)	4·61 (4·11)	2·04 (2·34)	2·15 (2·37)
Median	2·57	3·48	0·96	1·16
Range	0·1–23·8	0·1–16·8	0·1–11·3	0·1–12·3
Interquartile range	0·83–6·30	1·20–7·12	0·47–3·02	0·44–3·46
No previous DMT use, n (%)	66 (81·5)	115 (82·7)	148 (90·8)	318 (91·1)
EDSS				
Mean (SD)	6·15 (0·23)	6·23 (0·26)	4·03 (0·72)	4·15 (0·81)
Median	6·0	6·0	4·0	4·0
Range	6·0–6·5	6·0–7·0	2·5–5·5	2·5–5·5
Patients with Gd-enhancing T1 lesions, n (%)	23 (28·4)	42 (30·2)	37 (22·7)	91 (26·3)
Number of Gd-enhancing T1 lesions				
Mean (SD)	0·71 (1·58)	1·96 (8·66)	0·54 (1·54)	0·91 (2·63)
Median	0	0	0	0
Range	0–10	0–77	0–10·0	0–24·0
Total volume of T2 lesions, cm^3				
Mean (SD)	11·5 (11·94)	16·7 (18·90)	10·6 (13·44)	11·1 (12·98)
Median	7·16	9·08	5·42	7·08
Range	0·1–58·9	0–90·3	0–81·1	0–82·4
Normalized brain volume, cm^3				
Median	1,456·8	1,443·5	1,468·0	1,465·6
Range	1,216·3–1,701·7	1,221·5–1,676·6	1,222·5–1,690·9	1,214·3–1,711·1

BL, baseline; DMT, disease-modifying treatment, EDSS, Expanded Disability Status Scale; Gd, gadolinium; MS, multiple sclerosis, PPMS, primary progressive multiple sclerosis.

Table S3. Kaplan-Meier estimates of the proportion of patients with CP of ≥20% in 9HPT time at Week 120.

	12-Week CP		24-Week CP	
	Placebo	**Ocrelizumab**	**Placebo**	**Ocrelizumab**
ITT population				
Both hands	23·6	14·7	21·7	12·4
Better hand	25·1	17·4	22·3	14·1
Worse hand	23·7	16·7	22·0	14·3
Patients with abnormal BL 9HPT time for:				
Both hands	33·2	18·3	30·5	16·1
Better hand	32·1	23·1	29·1	19·9
Worse hand	28·4	19·7	26·5	18·3
Patients with normal BL 9HPT time for:				
Both hands	12·1	9·1	11·0	6·9
Better hand	19·6	12·2	17·0	8·8
Worse hand	14·0	9·2	12·6	4·7
Patients with BL EDSS <6:				
Both hands	15·1	10·2	14·4	8·4
Better hand	19·7	13·8	16·2	10·8
Worse hand	15·6	12·9	15·0	10·5
Patients with BL EDSS ≥6:				
Both hands	40·8	26·2	36·4	23·1
Better hand	36·3	26·8	35·0	22·8
Worse hand	40·4	26·5	36·3	24·3

9HPT, Nine-Hole Peg Test; BL, baseline; CP, confirmed progression; EDSS, Expanded Disability Status Scale; ITT, intention-to-treat.

Table S4. Time to first event of 12-week (A) and 24-week (B) CI of ≥15% and ≥20% (both hands) in 9HPT time

A

	ITT				Patients with BL UE impairment (9HPT>25s)			
	12-week confirmed improvement ≥15%		12-week confirmed improvement ≥20%		12-week confirmed improvement ≥15%		12-week confirmed improvement ≥20%	
	Placebo N = 244	OCR N = 488	Placebo N = 244	OCR N = 488	Placebo N = 137	OCR N = 297	Placebo N = 137	OCR N = 297
Hazard ratio* ocrelizumab vs placebo (95% CI), *p* value								
	1.36 (0.85-2.19) *p* = 0.205		1.63 (0.83-3.20) *p* = 0.152		1.46 (0.83-2.55) *p* = 0.184		1.59 (0.76-3.31) *p* = 0.218	
Event rate (%) up to the specified time point (95% CI)								
48 weeks	5.12 (2.30-7.94)	7.09 (4.75-9.42)	2.98 (0.80-5.15)	2.78 (1.29-4.27)	7.71 (3.12-12.30)	10.26 (6.72-13.80)	4.60 (1.01-8.20)	4.57 (2.14-7.00)
96 weeks	7.04 (3.71-10.38)	10.93 (8.07-13.80)	3.44 (1.10-5.78)	5.50 (3.40-7.60)	9.50 (4.37-14.63)	15.51 (11.24-19.78)	5.46 (1.52-9.40)	8.32 (5.06-11.58)
120 weeks	9.18 (5.32-13.05)	12.36 (9.32-15.40)	3.96 (1.42-6.50)	6.45 (4.18-8.73)	11.53 (5.79-17.27)	17.09 (12.63-21.55)	5.46 (1.52-9.40)	9.89 (6.34-13.44)

Stratified by Geographical Region (US vs. ROW) and Age (≤45, >45 years).

* Hazard ratios were derived from a stratified Cox proportional hazards model.

B

	ITT				Patients with BL UE impairment (9HPT>25s)			
	24-week confirmed improvement ≥15%		24-week confirmed improvement ≥20%		24-week confirmed improvement ≥15%		24-week confirmed improvement ≥20%	
	Placebo N = 244	OCR N = 488	Placebo N = 244	OCR N = 488	Placebo N = 137	OCR N = 297	Placebo N = 137	OCR N = 297
Hazard ratio* ocrelizumab vs placebo (95% CI), *p* value								
	1.46 (0.81-2.61) *p* = 0.207		1.61 (0.73-3.54) *p* = 0.238		1.72 (0.86-3.44) *p* = 0.126		1.55 (0.67-3.58) *p* = 0.303	
Event rate (%) up to the specified time point (95% CI)								
48 weeks	3.83 (1.38-6.29)	4.72 (2.80-6.65)	1.70 (0.05-3.35)	2.14 (0.83-3.44)	6.17 (2.03-10.31)	7.43 (4.37-10.48)	3.07 (0.11-6.04)	3.51 (1.37-5.64)
96 weeks	5.28 (2.36-8.19)	7.68 (5.23-10.12)	3.08 (0.83-5.33)	4.18 (2.34-6.02)	6.17 (2.03-10.31)	11.19 (7.47-14.91)	5.64 (1.57-9.72)	6.51 (3.60-9.42)
120 weeks	5.80 (2.73-8.87)	9.11 (6.45-11.78)	3.60 (1.14-6.05)	5.13 (3.09-7.18)	7.19 (2.64-11.75)	13.17 (9.15-17.19)	5.64 (1.57-9.72)	8.08 (4.84-11.32)

Stratified by Geographical Region (US vs. ROW) and Age (≤45, >45 years).

* Hazard ratios were derived from a stratified Cox proportional hazards model.