

Supplemental table 1. Sequences obtained as part of study imaging protocol (all sequences comprised a 3D sagittal acquisition of entire brain).

Sequence	Isotropic Resolution (mm)	TR/TE	Acquisition time	Other Parameters
Precontrast T2-weighted FLAIR	1.0	4800/352	7 min 9s	Inversion time (TI) = 1800 ms
Pre- and postcontrast T2*-weighted segmented echo-planar imaging (EPI)	0.65	64/35	5 min 48 s	Flip angle = 10°, EPI factor = 15
Pre- and postcontrast T1-weighted imaging	1.0	7.8/3.0	3 min 16 s	Flip angle= 18°

Supplemental table 2. Demographics and main characteristics of the entire CAVS-MS Pilot based on the availability of cerebrospinal fluid results.

Variable	n		p-value
	Lumbar puncture performed	Lumbar puncture not performed	
Participants	53	39	
Age (median years, Q1, Q3)	43 [33, 52]	49 [38, 57]	0.167 ^a
Sex (female)	37 (69.8%)	30 (76.9%)	0.603 ^b
Race			0.480 ^b
White	43 (81.1%)	34 (87.2%)	
African American or Black	3 (5.7%)	4 (10.3%)	
American Indian or Alaska Native	1 (1.9%)	0 (0.0%)	
Asian	2 (3.8%)	1 (2.6%)	
Unknown	3 (5.7%)	0 (0.0%)	
Latinx ethnicity	6 (11.3%)	2 (5.1%)	0.505 ^b
Weeks since first symptom onset (median, Q1, Q3)	66.14 [21.57, 275.00]	106.71 [14.11, 282.93]	0.461 ^a
Neurologic symptoms at the time of initial assessment	49 (92.5%)	36 (92.3%)	1.000 ^b
Typical syndrome at presentation	11 (20.8%)	5 (12.8%)	0.475 ^b
EDSS (median, Q1, Q3)	1.50 [1.00, 2.00]	1.00 [0.00, 2.00]	0.786 ^a
Dissemination in space by MRI	41 (77.4)	26 (66.7%)	0.367 ^b
Dissemination in time by MRI	20 (37.7%)	12 (30.8%)	0.637 ^b
Dissemination in space and time by MRI	18 (34.0%)	11 (28.2%)	0.719 ^b

a – bootstrap median difference

b – chi-square or Fisher's exact test

Abbreviations: EDSS – Expanded Disability Status Scale; MRI – magnetic resonance imaging; Q1/3 – first/third quartile

Supplemental table 3. Presentations and final diagnoses of participants (n=53).

Presentation	Number of participants
First-time neurologic symptoms evaluated for a clinical attack	38 (10 with typical syndrome presentation)
Two or more episodes of neurologic symptoms evaluated for a clinical attack	11 (1 with typical syndrome presentation)
White matter lesions on MRI brain	4
Final diagnosis	
Multiple sclerosis	27
Clinically isolated syndrome	5
Small vessel ischemic disease	4
Radiologically isolated syndrome	3
Vitamin B12 deficiency	2
Migraine and post-concussive syndrome	2
Migraine	1
Fibromyalgia	1
Sleep apnea	1
Paresthesia	1
Small fiber neuropathy	1
Traumatic cervical myelopathy	1
Systemic lupus erythematosus	1
Cranial neuropathy	1
Thoracic myelitis	1
Non-specific white matter changes	1

Abbreviations: MRI – magnetic resonance imaging.

Supplemental table 4. Proportions of participants presenting after first-time neurologic symptoms evaluated for a clinical attack diagnosed with multiple sclerosis at initial assessment and at 12-month follow-up.

	n/total per variable	
	MS diagnosis at initial visit (19/38)	MS diagnosis at 12 months (22/38)
OCB positive	14/20 (70%)	17/20 (85%)
Select-3 positive	16/27 (59%)	18/27 (67%)
Select-6 positive	13/16 (81%)	16/16 (100%)
OCB positive and Select-3 positive	12/16 (75%)	14/16 (88%)
OCB positive and Select-3 negative	2/4 (50%)	3/4 (75%)
OCB positive and Select-6 positive	11/13 (85%)	13/13 (100%)
OCB positive and Select-6 negative	3/7 (43%)	4/7 (57%)
Select-6 positive and MRI DIS	13/15 (87%)	15/15 (100%)
OCB positive and MRI DIS	13/18 (72%)	16/18 (89%)

Abbreviations: MRI DIS – dissemination in space on magnetic resonance imaging (according to McDonald 2017 criteria); MS – multiple sclerosis; OCB – serum-unmatched oligoclonal bands in the cerebrospinal fluid

Supplemental table 5. Sensitivity, specificity, positive and negative predictive values of Select-3, Select-6, oligoclonal bands, or combinations for diagnosis of MS in participants presenting after first-time neurologic symptoms evaluated for a clinical attack..

	Sensitivity	Specificity	PPV	NPV
Diagnosis of multiple sclerosis at initial assessment				
OCB	0.74 (0.49, 0.91)	0.68 (0.43, 0.87)	0.70 (0.46, 0.88)	0.72 (0.47, 0.90)
Select-3	0.84 (0.60, 0.97)	0.42 (0.20, 0.67)	0.59 (0.39, 0.78)	0.73 (0.39, 0.94)
Select-6	0.68 (0.43, 0.87)	0.84 (0.60, 0.97)	0.81 (0.54, 0.96)	0.73 (0.50, 0.89)
Select-3 + OCB	0.63 (0.38, 0.84)	0.79 (0.54, 0.94)	0.75 (0.48, 0.93)	0.68 (0.45, 0.86)
Select-6 + OCB	0.58 (0.33, 0.80)	0.89 (0.67, 0.99)	0.85 (0.55, 0.98)	0.68 (0.46, 0.85)
Select-6 + MRI DIS	0.68 (0.43, 0.87)	0.89 (0.67, 0.99)	0.87 (0.60, 0.98)	0.74 (0.52, 0.90)
OCB + MRI DIS	0.68 (0.43, 0.87)	0.74 (0.49, 0.91)	0.72 (0.47, 0.90)	0.70 (0.46, 0.88)
p-values				
OCB vs Select-3	0.157	0.025	0.086	0.952
OCB vs Select-6	0.317	0.083	0.117	0.910
Select-3 vs Select-6	0.083	0.005	0.014	1.000
Select-3 + OCB vs Select-3	0.046	0.008	0.055	0.639
Select-6 + OCB vs Select-6	0.157	0.317	0.556	0.275
Select-3 + OCB vs Select-6 + OCB	0.317	0.157	0.207	0.958
Select-6 + MRI DIS vs OCB + MRI DIS	-	0.083	0.062	0.116
Diagnosis of multiple sclerosis at 12-month follow-up				
OCB	0.77 (0.55, 0.92)	0.81 (0.54, 0.96)	0.85 (0.62, 0.97)	0.72 (0.47, 0.90)
Select-3	0.82 (0.60, 0.95)	0.44 (0.20, 0.70)	0.67 (0.46, 0.83)	0.64 (0.31, 0.89)
Select-6	0.73 (0.50, 0.89)	1.00 (0.79, 1.00)	1.00 (0.79, 1.00)	0.73 (0.50, 0.89)
Select-3 + OCB	0.64 (0.41, 0.83)	0.88 (0.62, 0.98)	0.88 (0.62, 0.98)	0.64 (0.41, 0.83)
Select-6 + OCB	0.59 (0.36, 0.79)	1.00 (0.79, 1.00)	1.00 (0.75, 1.00)	0.64 (0.43, 0.82)
Select-6 + MRI DIS	0.68 (0.45, 0.86)	1.00 (0.79, 1.00)	1.00 (0.78, 1.00)	0.70 (0.47, 0.87)
OCB + MRI DIS	0.73 (0.50, 0.89)	0.88 (0.62, 0.98)	0.89 (0.65, 0.99)	0.70 (0.46, 0.88)
p-values				
OCB vs Select-3	0.317	0.014	0.019	0.337
OCB vs Select-6	0.317	0.083	0.084	0.910
Select-3 vs Select-6	0.157	0.003	0.003	0.384
Select-3 + OCB vs Select-3	0.046	0.008	0.020	1.000
Select-6 + OCB vs Select-6	0.083	1.000	1.000	0.083
Select-3 + OCB vs Select-6 + OCB	0.317	0.157	0.158	0.917
Select-6 + MRI DIS vs OCB + MRI DIS	0.317	0.157	0.133	0.909

Abbreviations: MRI DIS – dissemination in space on magnetic resonance imaging (according to McDonald 2017 criteria); NPV – negative predictive value; OCB – serum-unmatched oligoclonal bands in cerebrospinal fluid; PPV – positive predictive value. Estimates provided as proportions with 95% confidence intervals.