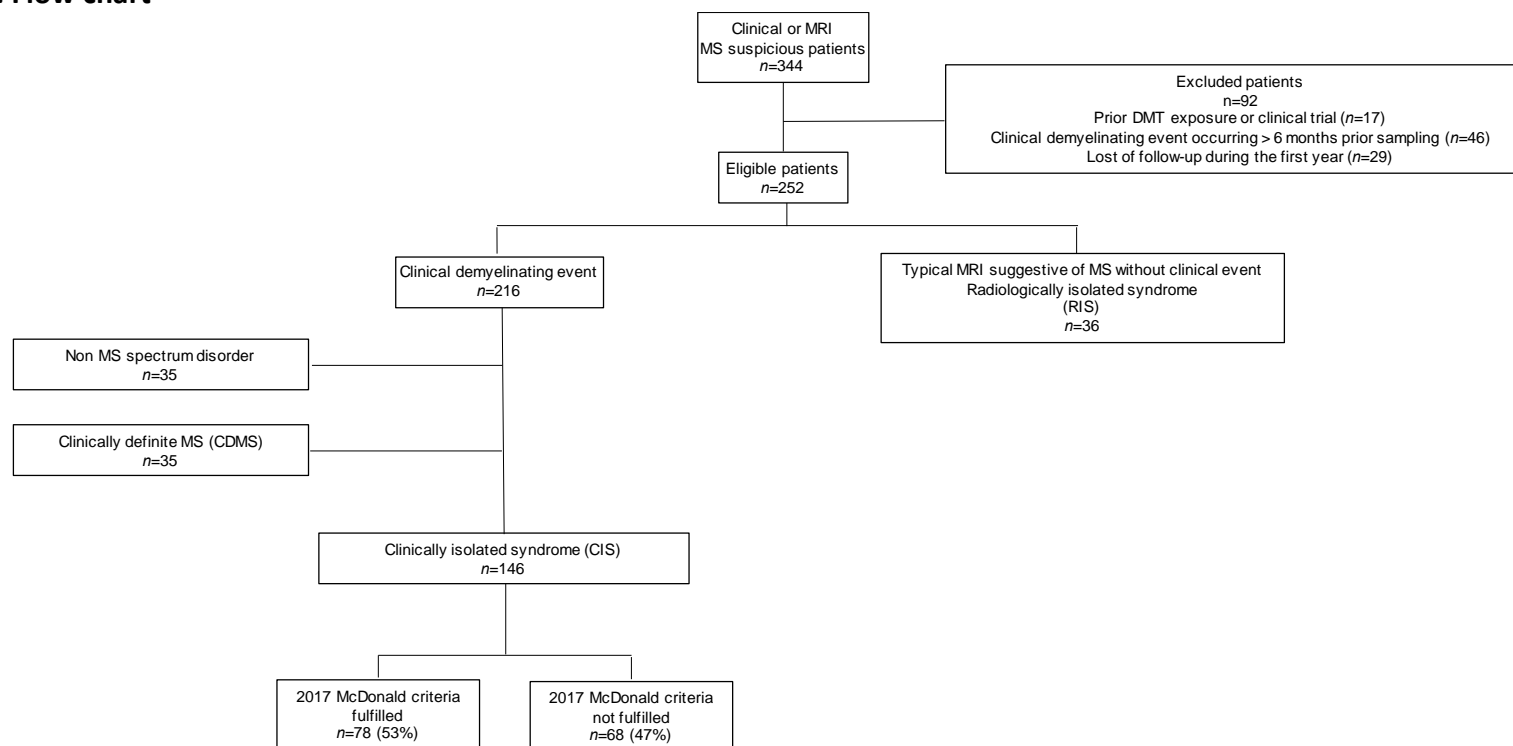
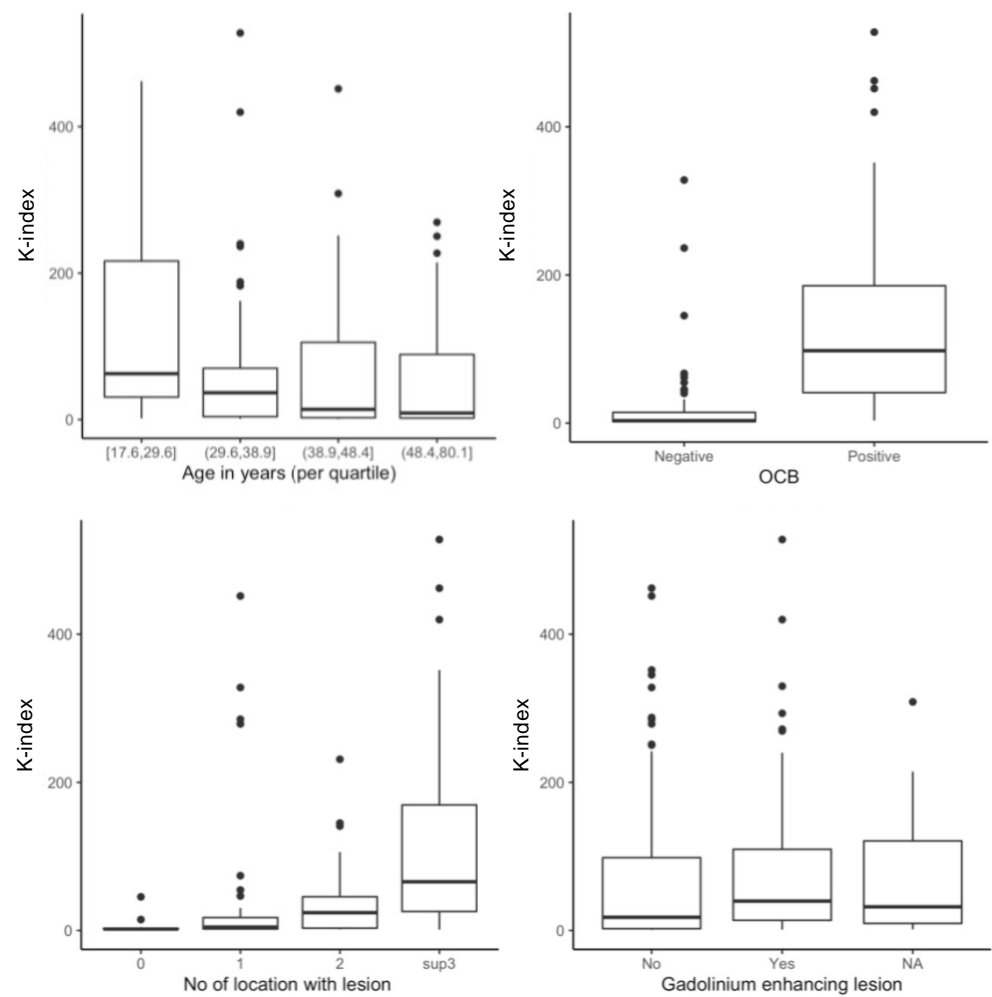


eFigure 1. Flow chart



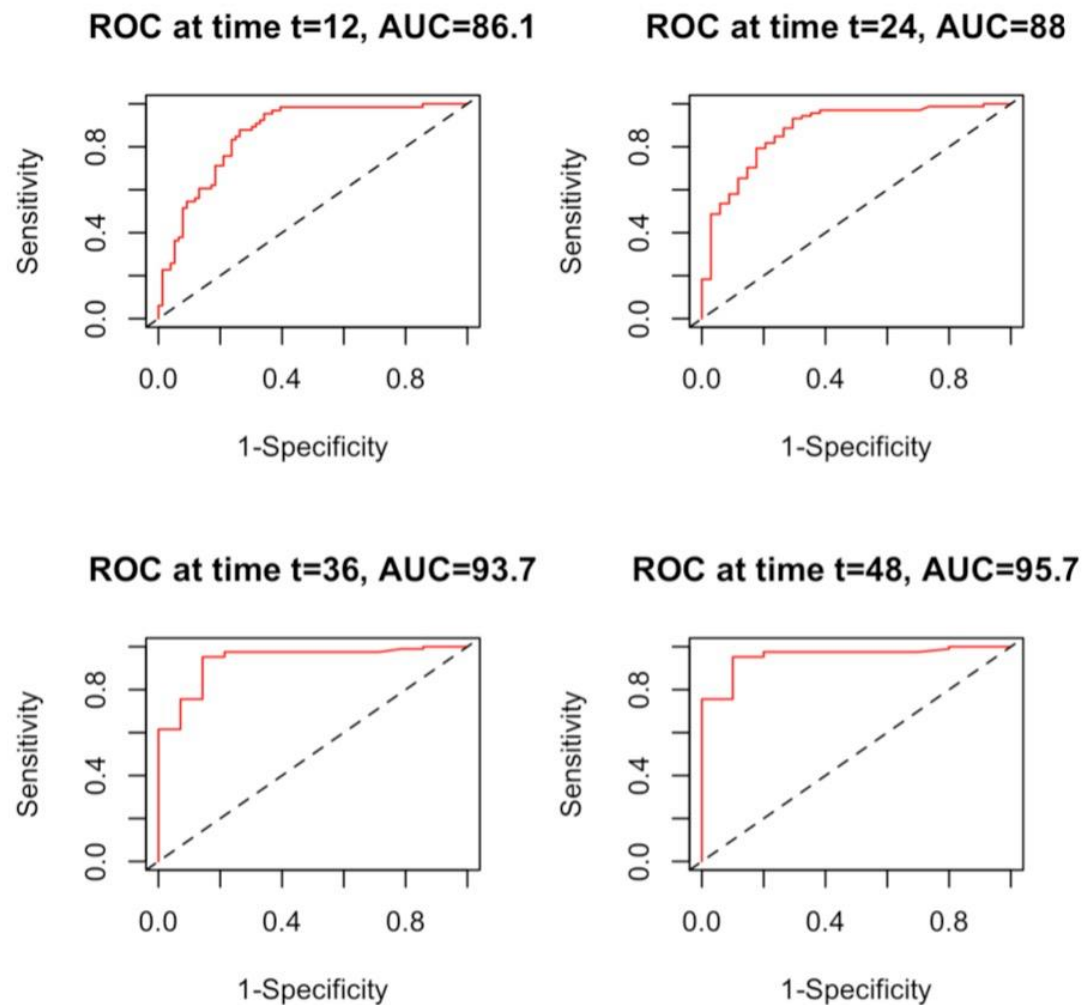
Abbreviations: CDMS: clinically definite multiple sclerosis, CIS: clinically isolated syndrome, DMT: disease modifying treatment, MRI: magnetic resonance imaging, MS: multiple sclerosis, RIS: radiologically isolated syndrome.

eFigure 2. Evaluation of the association between the K-index and other predictive variables at baseline



Abbreviations: NA: Not applicable, No: number, OCB: oligoclonal bands

eFigure 3. Diagnostic performance of the K-index to predict new T2L in CIS patients according to individual ROC analyses at different time points (months)

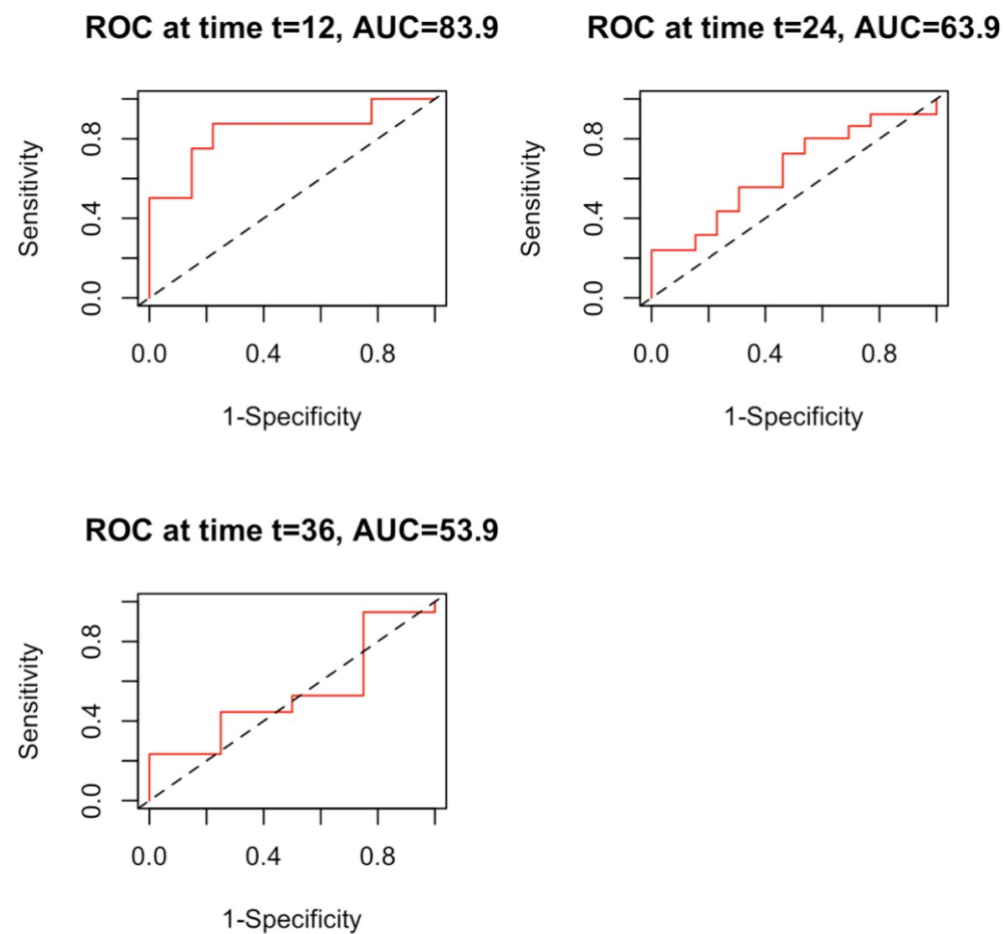


eTable 1. Diagnosis performance of the binary K-index and OCB to predict new T2L in CIS patients over time.

	K-index (8.9 cutoff)			OCB status		
Time point (months)	12	24	36	12	24	36
Sensitivity	0.98 [0.96; 1.00]	0.97 [0.93; 1.00]	0.98 [0.94; 1.00]	0.82 [0.72; 0.91]	0.77 [0.68; 0.87]	0.70 [0.59; 0.81]
Specificity	0.55 [0.44; 0.66]	0.59 [0.42; 0.75]	0.79 [0.57; 1.00]	0.67 [0.57; 0.78]	0.74 [0.59; 0.88]	0.79 [0.57; 1.00]
PPV	0.65 [0.55; 0.74]	0.75 [0.65; 0.85]	0.90 [0.80; 1.00]	0.67 [0.57; 0.78]	0.79 [0.68; 0.90]	0.87 [0.74; 0.99]
NPV	0.98 [0.93; 1.00]	0.94 [0.86; 1.00]	0.94 [0.86; 1.00]	0.82 [0.72; 0.91]	0.72 [0.60; 0.84]	0.57 [0.41; 0.74]

Abbreviations: NPV: negative predictive value, PPV: positive predictive value, OCB: oligoclonal bands

eFigure 4. Diagnostic performance of the K-index to predict new T2L in people with RIS according to individual ROC analyses at different time points (months)



eTable 2. Diagnosis performance of the binary K-index and OCB to predict new T2L in people with RIS over time.

	K-index (8.9 cutoff)			OCB status		
Time point (months)	12	24	36	12	24	36
Sensitivity	0.88 [0.64; 1.00]	0.80 [0.60; 1.00]	0.87 [0.72; 1.00]	0.75 [0.45; 1.00]	0.58 [0.33; 0.84]	0.55 [0.31; 0.78]
Specificity	0.48 [0.29; 0.67]	0.38 [0.12; 0.65]	0.25 [0.01; 0.68]	0.67 [0.49; 0.85]	0.62 [0.35; 0.88]	0.25 [0.01; 0.68]
PPV	0.33 [0.12; 0.74]	0.53 [0.31; 0.76]	0.72 [0.49; 0.94]	0.39 [0.14; 0.64]	0.57 [0.30; 0.84]	0.61 [0.34; 0.89]
NPV	0.93 [0.80; 1.00]	0.69 [0.38; 1.00]	0.46 [0.01; 1.00]	0.90 [0.77; 1.00]	0.63 [0.38; 0.88]	0.20 [0.01; 0.53]

Abbreviations: NPV: negative predictive value, PPV: positive predictive value, OCB: oligoclonal bands

eFigure 5: Survival analysis showing the probability of new T2L over time in people with RIS according to the K-index and the OCB status.

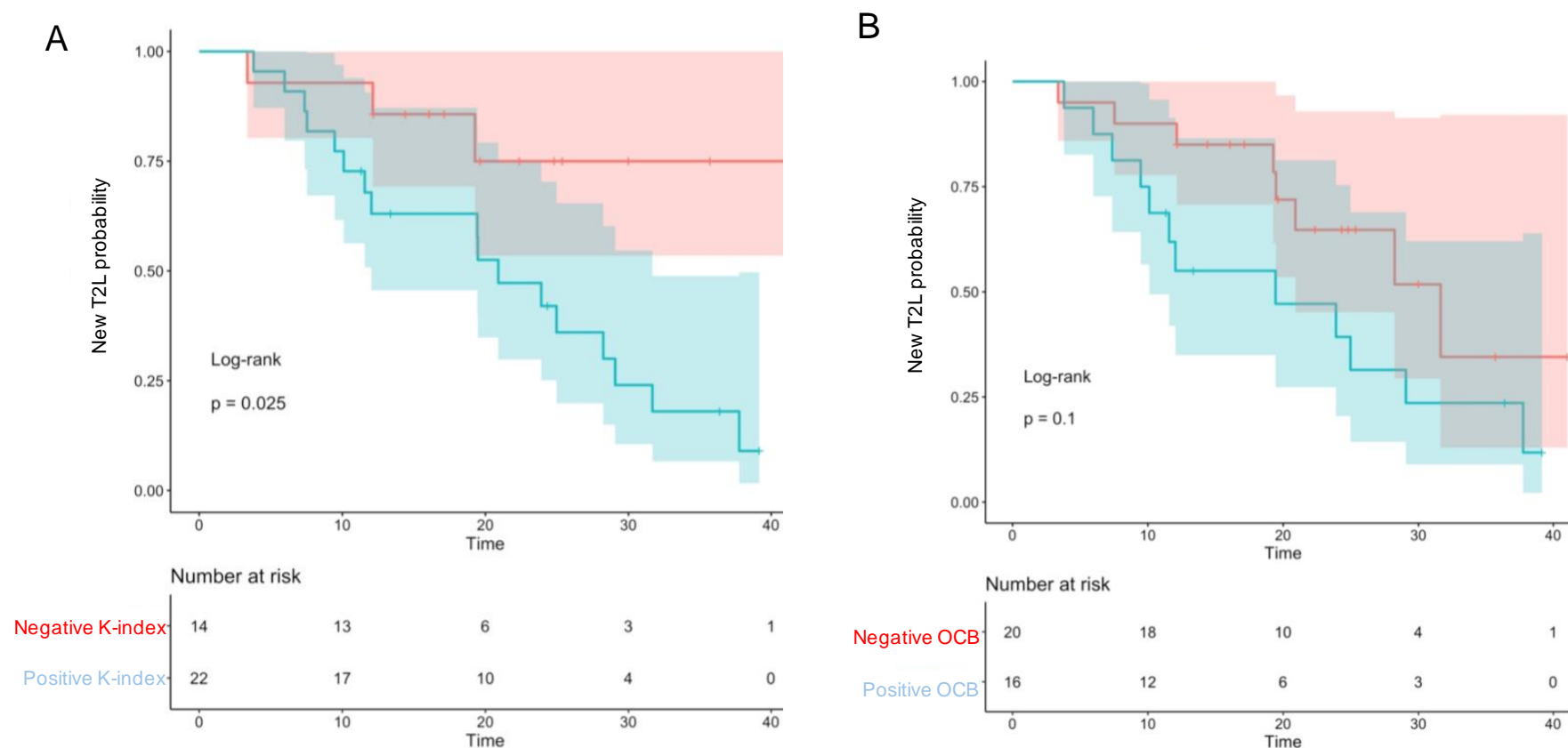
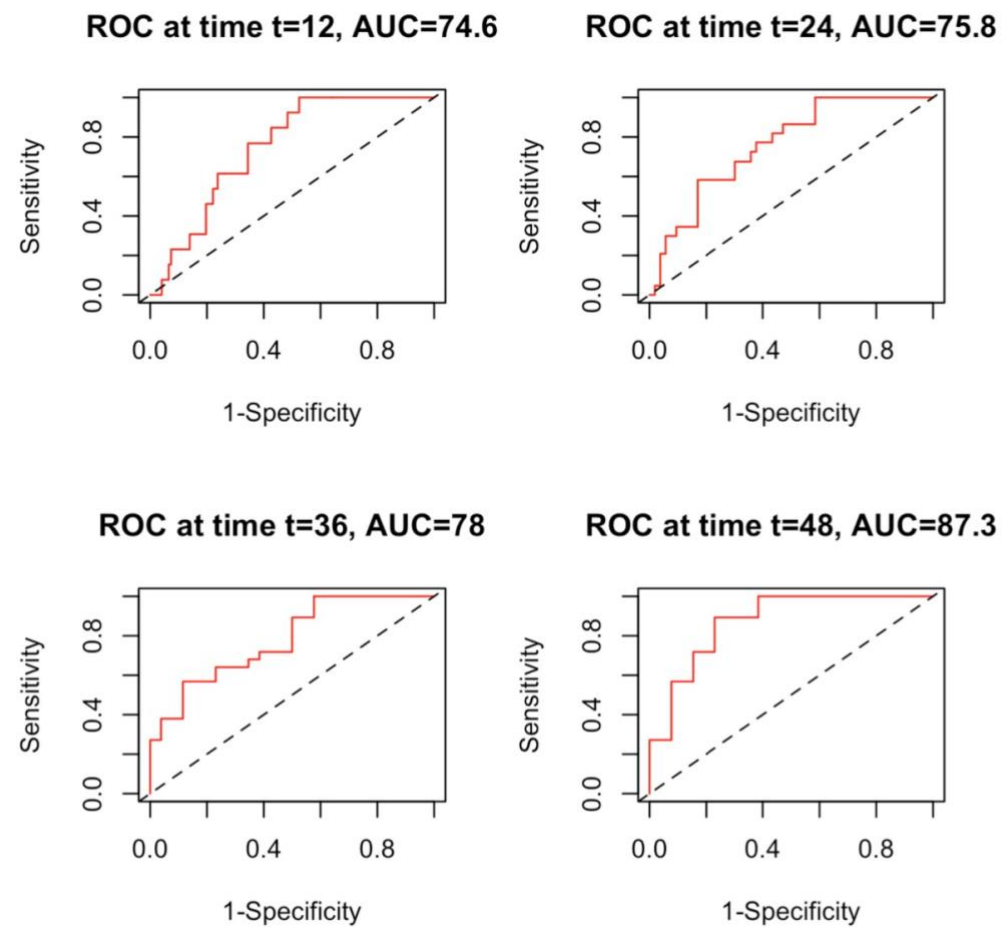


Figure legend: The figure shows the time to new T2L in people with RIS according to their positive (red line) or negative (blue line) K-index status (panel A) and their positive (red line) or negative (blue line) OCB status (panel B). People with RIS with positive K-index had a higher probability to present with new T2L during follow-up than those with negative K-index ($p=0.025$). No difference was found according to positive or negative OCB status ($p=0.100$).

eFigure 6. Diagnostic performance of the K-index to predict new T2L in people with RIS according to individual ROC analyses at different time points (months)



eTable 3. Diagnosis performance of the binary K-index and OCB to predict clinical attack in CIS patients over time.

	K-index (8.9 cutoff)			OCB status		
Time point (months)	12	24	36	12	24	36
Sensitivity	1.00 [-; -]	1.00 [-; -]	1.00 [-; -]	0.77 [0.54; 1.00]	0.72 [0.51; 0.93]	0.68 [0.45; 0.91]
Specificity	0.35 [0.27; 0.44]	0.40 [0.26; 0.53]	0.42 [0.23; 0.61]	0.49 [0.40; 0.58]	0.58 [0.45; 0.72]	0.65 [0.47; 0.84]
PPV	0.13 [0.06; 0.20]	0.23 [0.13; 0.32]	0.29 [0.16; 0.42]	0.13 [0.05; 0.21]	0.23 [0.12; 0.35]	0.31 [0.14; 0.49]
NPV	1.00 [-; -]	1.00 [-; -]	1.00 [-; -]	0.96 [0.91; 1.00]	0.92 [0.86; 0.99]	0.90 [0.81; 0.99]

Abbreviations: NPV: negative predictive value, PPV: positive predictive value, OCB: oligoclonal bands