

Table S1: Evidence of studies on κ -FLC index in patients with clinically isolated syndrome and multiple sclerosis

Reference	No. of patients	No. of controls	MS diagnostic criteria	Type of controls	No. of κ -FLC positive patients	No. of κ -FLC negative controls	κ -FLC cut-off	κ -FLC assay	Method	Analyzer	No. of OCB positive patients	No. of OCB negative controls	OCB cut-off	Prior corticosteroids	Prior DMT	Sensitivity κ -FLC	Specificity κ -FLC	Sensitivity OCB	Specificity OCB
Multiple Sclerosis																			
Desplat-Jego 2005	33	33	2001	NIND, IND	23	27	20,00	Freelite	Ne	Behring	31	33				70	82	94	100
Presslauer 2008	41	368	2001 / 2005	NIND	40	318	5,90	Freelite	Ne	Behring	39	338				98	86	95	92
Duranti 2013	23	57	2010	NIND, IND	22	52	12,00	N Latex	Ne	Behring	18	52	2	no	no	96	91	78	91
Menendez-Valladares 2015	29	70		NIND, IND	27	67	10,62	Freelite	Ne	Behring	28	69				93	96	97	99
Presslauer 2016	60	60	2005	NIND, PIND	56	57	5,90	Freelite	Ne	Behring	56	59		yes	yes	93	95	93	98
Crespi 2017	48	102	2010	NIND, IND, PIND, NND	48	88	5,00	N Latex	Ne	Behring	47	87		no	no	100	86	98	85
Pieri 2017	71	105		NIND, IND	66	105	12,30	N Latex	Ne	Behring	65	99				93	100	92	94
Bayart 2018	59	83		NIND, IND	46	64	12,45	Freelite	Tu	SPAPLUS	46	66	2	no	no	78	77	78	80
Christiansen 2018	96	97	2010	SC, OND	87	88	7,50	Freelite	Tu	SPAPLUS	79	91				91	91	82	94
Valencia-Vera 2018	37	85		OND	28	77	5,90	Freelite	Ne	Behring	33	69		no	no	76	91	89	81
Crespi 2019	127	258	2017	NIND, IND	122	208	5,00	N Latex	Ne	Behring	123	214				96	81	97	83
Emersic 2019	80	50	2010	NIND	77	48	5,30	N Latex	Ne	Behring	73	49	2			96	96	91	98
Schwenkenbecher 2019	100		2017		96		5,90	N Latex	Ne	Behring	99					96		99	
Senel 2019	75	1149	2010	NIND, IND, PIND	69	1115	9,58	N Latex	Ne	Behring	71	1072	2			92	97	95	93
Duell 2020	62	60	2010	SC, HC	56	60	7,15	N Latex	Ne	Behring	54	60	2			90	100	87	100
Gudowska-Sawczuk 2020	34	42	2017	OND	32	29	9,42	Freelite	Tu	Optilite	34	38		no	no	94	68	100	90
Ferraro 2020a	146	299	2010 / 2017	NIND, IND, PIND	76	282	5,80	Freelite	Tu	Optilite	54	299	2			52	94	37	100
Ferraro 2020b	84	456	2017	NIND, IND	75	385	6,20	Freelite	Tu	Optilite	71	405				89	84	85	89
Leurs 2020	284	219	2005 / 2010	NIND, IND, SC, HC	264	182	6,60	Freelite	Tu	Optilite	245	202		yes	yes	93	83	86	92
Vecchio 2020	133	240	2017	NIND, IND	124	205	5,00	N Latex	Ne	Behring	127	204				93	85	95	85

Sanz Diaz 2021	45	197	2017	NIND, IND, PIND	42	172	6,60	Freelite	Tu	Optilite	40	179	2			93	87	89	91
Bernardi 2022	171	235	2017	NIND, IND, PIND	143	208	6,40	Freelite	Tu	Optilite	144	213	2			84	89	84	91
Clinically isolated syndrome																			
Presslauer 2008	29	368	2001 / 2005	NIND	27	318	5,90	Freelite	Ne	Behring	25	338				93	86	86	92
Menendez-Valladares 2015	77			NIND, IND	49		10,62	Freelite	Ne	Behring	48					64		62	
Presslauer 2016	60	60	2005	NIND, PIND	47	57	5,90	Freelite	Ne	Behring	43	59		yes	no	78	95	72	98
Christiansen 2018	37	97	2010	SC, OND	26	88	7,50	Freelite	Tu	SPAPLUS	21	91		no	no	70	91	57	94
Vasilij 2018	101	50	2017	OND	91	37	9,09	N Latex	Ne	Behring	101	50				90	73	100	100
Reiber 2019	95	256		OND	86	241	5,00				89	256	2			90	94	94	100
Schwenkenbecher 2019	68		2017		26		5,90	N Latex	Ne	Behring	32					38		47	
Leurs 2020	242	219	2005 / 2010	NIND, IND, SC, HC	196	182	6,60	Freelite	Tu	Optilite	186	202		yes	yes	81	83	77	92
Mixed cohorts comprising patients with clinically isolated syndrome and multiple sclerosis																			
Passerini 2016	56	44	2010	NIND, IND	50	34	2,40	N Latex	Ne	Behring	40	38				89	77	71	86
Gurtner 2018	67	253	2010	NIND, IND	58	193	10,46	Freelite	Ne	Behring	63	187	2			87	76	94	74
Agnello 2020	39	17	2017	NIND, IND	33	14	7,30	Freelite	Tu	Optilite	37	14	2	no	no	85	82	95	82
Cavalla 2020	140	233	2017	NMOSD, IND, OND	127	207	6,15	N Latex	Ne	Behring	121	208				90	89	86	89
Gaetani 2020	64	106	2010	NIND, IND	57	86	7,83	Freelite	Ne	Behring	53	97	2			89	81	83	92
Suesse 2020	98	302	2005 / 2010 / 2017	NIND, PIND, SC	97	299	6,60	N Latex	Ne	Behring	91	302	2			99	99	93	100
Berek 2021	88		2017		76		6,60	N Latex	Ne	Behring	79		2	yes	no	86		90	
Rosenstein 2021	223	104	2017	IND, SC	207	90	4,60	N Latex	Ne	Behring	196	93				93	87	88	89

Table S2: Evidence of studies on intrathecal κ -FLC fraction in patients with clinically isolated syndrome and multiple sclerosis

Reference	No. of patients	No. of controls	MS diagnostic criteria	Type of controls	No. of κ -FLC positive patients	No. of κ -FLC negative controls	κ -FLC cut-off	κ -FLC assay	Method	Analyzer	No. of OCB positive patients	No. of OCB negative controls	OCB cut-off	Prior cortico-steroids	Prior DMT	Sensitivity κ -FLC	Specificity κ -FLC	Sensitivity OCB	Specificity OCB
Multiple Sclerosis																			
Presslauer 2016	60	60	2005	NIND, PIND	57	57	0,00	Freelite	Ne	Behring	56	59		yes	yes	95	95	93	98
Puthenparampil 2018	70	37	2017	HC	46	37	0,00	Freelite	Ne	Behring	40	37				66	100	57	100
Crespi 2019	127	258	2017	NIND, IND	122	208	0,00	N Latex	Ne	Behring	123	214				96	81	97	83
Emersic 2019	80	50	2010	NIND	76	48	10,00	N Latex	Ne	Behring	73	49	2			95	96	91	98
Schwenkenbecher 2019	100		2017		98		0,00	N Latex	Ne	Behring	99					98		99	
Senel 2019	75	1149	2010	NIND, IND, PIND	70	1077	0,00	N Latex	Ne	Behring	71	1072	2			93	94	95	93
Duell 2020	62	60	2010	HC, SC	59	58	0,00	N Latex	Ne	Behring	54	60	2			95	97	87	100
Ferraro 2020b	84	456	2017	NIND, IND	77	324	0,00	Freelite	Tu	Optilite	71	405				92	71	85	89
Vecchio 2020	133	240	2017	NIND, IND	130	128	0,00	N Latex	Ne	Behring	127	204				98	53	95	85
Clinically isolated syndrome																			
Presslauer 2016	60	60	2005	NIND, PIND	49	57	0,00	Freelite	Ne	Behring	43	59		yes	no	82	95	72	98
Reiber 2019	95	256		OND	88	236	0,00				89	256	2			93	92	94	100
Schwenkenbecher 2019	68		2017		30		0,00	N Latex	Ne	Behring	32					44		47	
Mixed cohorts comprising patients with clinically isolated syndrome and multiple sclerosis																			
Gurtner 2018	67	253	2010	NIND, IND	64	172	0,00	Freelite	Ne	Behring	63	187	2			96	68	94	74
Suesse 2020	26	14	2017	NIND	25	12	0,00	N Latex	Ne	Behring	23	14			no	96	86	88	100
Suesse 2020	98	302	2005 / 2010 / 2017	NIND, PIND, SC	98	282	0,00	N Latex	Ne	Behring	91	302	2			100	93	93	100
Rosenstein 2021	223	104	2017	IND, SC	214	85	0,00	N Latex	Ne	Behring	197	93				96	82	88	89

Table S3: Evidence of studies on CSF κ -FLC concentration in patients with clinically isolated syndrome and multiple sclerosis

Reference	No. of patients	No. of controls	MS diagnostic criteria	Type of controls	No. of κ -FLC positive patients	No. of κ -FLC negative controls	κ -FLC cut-off	κ -FLC assay	Method	Analyzer	No. of OCB positive patients	No. of OCB negative controls	OCB cut-off	Prior corticosteroids	Prior DMT	Sensitivity κ -FLC	Specificity κ -FLC	Sensitivity OCB	Specificity OCB
Multiple Sclerosis																			
Christiansen 2018	96	97	2010	SC, OND	84	86	0,82	Freelite	Tu	SPAPLUS	79	91		no	no	88	89	82	94
Emersic 2019	80	50	2010	NIND	76	45	0,30	N Latex	Ne	Behring	73	49	2			95	90	91	98
Saez 2019	41	42	2010 / 2017	NIND	39	41	7,10	Freelite	Tu	SPAPLUS	38	38		no	no	95	97	93	90
Duell 2020	62	60	2010	HC, SC	55	59	0,47	N Latex	Ne	Behring	54	60	2			89	98	87	100
Vecchio 2020	133	240	2017	NIND, IND	105	234		N Latex	Ne	Behring	127	204				79	98	95	85
Saadeh 2021	84	602	2010	OND	57	518	1,00	Freelite	Ne	Behring	63	527				68	86	75	88
Saadeh 2021	70	583	2010	OND	55	508	1,00	Freelite	Ne	Behring	55	521				79	87	79	89
Clinically isolated syndrome																			
Hassan-Smith 2014	21	21	2010	OND, IND	20	21	0,99	Freelite	Ne	Behring	18	20		yes	no	95	100	86	95
Christiansen 2018	37	97	2010	SC, OND	25	86	0,82	Freelite	Tu	SPAPLUS	21	91		no	no	68	89	57	94
Vasilj 2018	101	50	2017	OND	95	35	0,38	N Latex	Ne	Behring	101	50				94	70	100	100
Mixed cohorts comprising patients with clinically isolated syndrome and multiple sclerosis																			
Hassan-Smith 2014	53	107	2010	OND, IND	51	105	0,87	Freelite	Ne	Behring	47	106		yes	yes	96	98	89	99
Passerini 2016	56	44	2010	NIND, IND	37	34	4,10	N Latex	Ne	Behring	40	38				66	77	71	86
Gurtner 2018	67	258	2010	NIND, IND	62	185	0,53	Freelite	Ne	Behring	63	187	2			93	72	94	72

Table S4: Evidence of studies on CSF/ serum κ -FLC quotient in patients with clinically isolated syndrome and multiple sclerosis

Reference	No. of patients	No. of controls	MS diagnostic criteria	Type of controls	No. of κ -FLC positive patients	No. of κ -FLC negative controls	κ -FLC cut-off	κ -FLC assay	Method	Analyzer	No. of OCB positive patients	No. of OCB negative controls	OCB cut-off	Prior cortico-steroids	Prior DMT	Sensitivity κ -FLC	Specificity κ -FLC	Sensitivity OCB	Specificity OCB
Multiple Sclerosis																			
Emersic 2019	80	50	2010	NIND	75	48	30,00	N Latex	Ne	Behring	73	49	2			94	96	91	98
Senel 2019	75	1149	2010	NIND, IND, PIND	69	1102	60,00	N Latex	Ne	Behring	71	1072	2			92	96	95	93
Clinically isolated syndrome																			
Vasilij 2018	101	50	2017	OND	93	37	49,00	N Latex	Ne	Behring	101	50				92	73	100	100

Legend:

All studies used CSF and serum samples, apart from Duell et al. 2020 and Senel et al. 2020 that used CSF and plasma samples; Menendez-Valladares did not specify the type of blood sample. *Abbreviations:* DMT, disease-modifying treatment; FLC, free light chain; HC, healthy control; IND, inflammatory neurological disease; MS, multiple sclerosis; Ne, nephelometry; NIND, non-inflammatory neurological disease; NND, non-neurological disease; No., number; PIND, peripheral inflammatory neurological disease; OCB, oligoclonal bands; OND, other neurological disease; SC, symptomatic control; Tu, turbidimetry