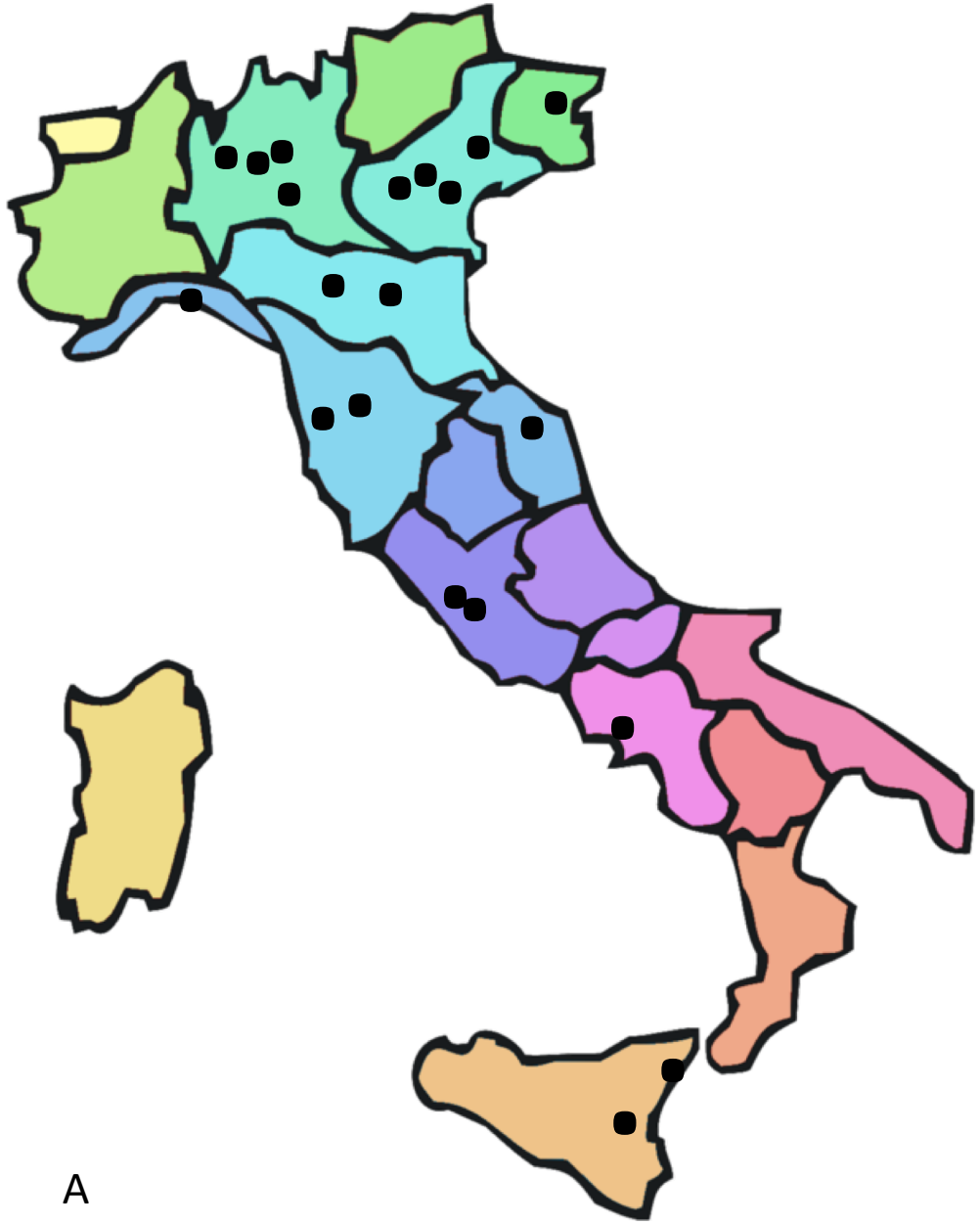
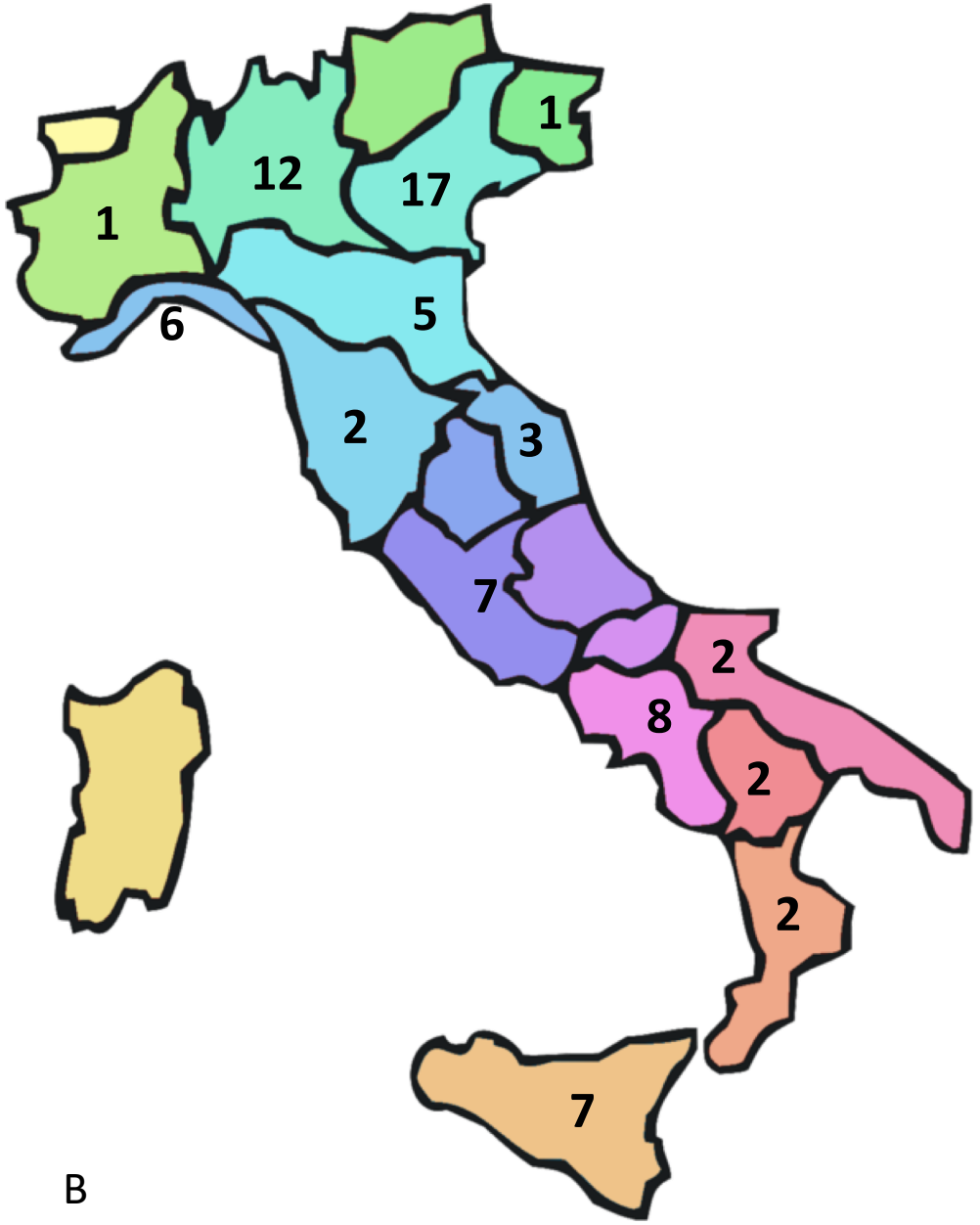
eFigure 1

Referral centres (A) and region of residency (B) of the patients

Patients were referred by 20 different Italian centres (A) and were residents of 14 different Italian regions (B)



A



B

eTable 1. Demographics, investigations, overall disease course and outcome in children ≤8 years old versus >8 years old at onset (A) and in females versus males (B).

	A. Age ≤8 years at onset (n=42)	Age >8 years at onset (n=33)	B. Females (n=40)	Males (n=35)
Demographics				
Females	23/42 (54.8%)	17/33 (51.5%)	40/40 (100.0%)	35/35 (100.0%)
White race^	37/40 (92.5%)	27/32 (84.4%)	34/39 (87.2%)	30/33 (90.9%)
Age at onset (years)	Median 4.5, mean 4.8, range 1.8-8 (d.a. 42/42)	Median 10.8, mean 11.4, range 8.2-18.6 (d.a. 33/33)	Median 7.3, mean 7.8, range 2.5-18.6 (d.a. 40/40)	Median 7, mean 7.5, range 1.8-15 (d.a. 35/35)
≤4 years	16/42 (38.1%)	0/33 (0.0%)	7/40 (17.5%)	9/35 (25.7%)
Type of first MOGAD event				
ADEM	28/42 (66.7%)	10/33 (30.3%)	17/40 (42.5%)	21/35 (60.0%)
ON (+/- CNS lesions)	9/42 (21.4%)	19/33 (57.6%)	19/40 (47.5%)	9/35 (25.7%)
NMOSD	1/42 (2.4%)	1/33 (3.0%)	2/40 (5.0%)	0/35 (0.0%)
CIS	2/42 (4.8%)	2/33 (6.1%)	1/40 (2.5%)	3/35 (8.6%)
Encephalitis (+/- ON)	2/42 (4.8%)	0/33 (0.0%)	1/40 (2.5%)	1/35 (2.9%)
Isolated LETM	0/42 (0.0%)	1/33 (3.0%)	0/40 (0.0%)	1/35 (2.9%)
Severity at first MOGAD event				
Worst EDSS at first event	Median 4, mean 4.6, range 1-8.5 (d.a. 37/42)	Median 3, mean 3.8, range 1-8 (d.a. 31/33)	Median 3, mean 3.8, range 1-8.5 (d.a. 35/40)	Median 4, mean 4.7, range 1-8 (d.a. 33/35)
EDSS ≥4	19/37 (51.4%)	15/31 (48.4%)	15/35 (53.1%)	19/33 (57.6%)
EDSS ≥5	16/27 (43.2%)	9/31 (29.0%)	9/35 (25.7%)	16/33 (48.5%)
EDSS ≥6	13/37 (35.1%)	6/31 (19.4%)	6/35 (17.1%)	13/33 (39.4%)
Investigations at first MOGAD event				
Abnormal brain MRI	37/41 (90.2%)	16/31 (51.6%)	26/39 (66.7%)	27/33 (81.8%)
Abnormal optic nerves on MRI	17/41 (41.5%)	16/31 (51.6%)	23/39 (59.0%)	12/33 (36.4%)
Abnormal spine MRI	13/36 (36.1%)	10/19 (52.6%)	8/27 (29.6%)	15/28 (53.6%)
Abnormal CSF	23/34 (67.6%)	13/26 (50.0%)	20/31 (64.5%)	16/29 (55.2%)
CSF white blood cells >4/uL	22/33 (66.7%)	13/25 (52.0%)	19/30 (63.3%)	16/28 (57.1%)
CSF-restricted oligoclonal bands (OCBs)^^	7/31 (22.6%)	2/25 (8.0%)	4/30 (13.3%)	5/26 (19.2%)
CSF proteins >45 mg/dL	2/34 (5.9%)	5/24 (20.8%)	3/31 (9.7%)	4/27 (14.8%)
Abnormal EEG	21/28 (75.0%)	9/14 (64.3%)	12/20 (60.0%)	18/22 (81.8%)
Slow or disorganised activity	20/28 (71.4%)	7/14 (50.0%)	11/20 (55.0%)	16/22 (72.7%)
Epileptic activity	4/28 (14.3%)	3/14 (21.4%)	3/20 (15.0%)	4/22 (18.2%)
IT at MOGAD onset				
≥2 different ITs (= CS + other)	10/42 (23.8%)	6/33 (18.2%)	4/40 (10.0%)	12/35 (34.3%)
Days from onset to first IT (any)	Median 5, mean 10.1, range 0-75 (d.a. 39/42)	Median 6, mean 8.4, range 1-40 (d.a. 27/33)	Median 6, mean 9.5, range 0-75 (d.a. 35/40)	Median 5, mean 9.3, range 0-75 (d.a. 31/35)
Any IT <7 days from onset	23/40 (57.5%)	14/29 (48.3%)	19/38 (50.0%)	18/31 (58.1%)
Outcome				
Length of follow-up (months)	Median 34.5, mean 46.9, range 4-130 (d.a. 42/42)	Median 27, mean 33.2, range 1-96 (d.a. 33/33)	Median 36, mean 44.3, range 2.2-130 (d.a. 40/40)	Median 30, mean 37.0, range 1-122 (d.a. 35/35)
Relapsing course (≥2 total events)°	15/39 (38.5%)	11/26 (42.3%)	15/35 (42.9%)	11/30 (36.7%)
Relapsing course (≥3 total events)°	10/39 (25.6%)	6/26 (23.1%)	11/35 (31.4%)	5/30 (16.7%)
Time to first relapse (months)	Median 18, mean 25.3, range 1-84 (d.a. 15/15)	Median 4, mean 10.6, range 1.3-80 (d.a. 11/11)	Median 9, mean 25.9, range 1-84 (d.a. 15/15)	Median 6, mean 9.8, range 1.3-32 (d.a. 11/11)
≤6 months	3/15 (20.0%)	9/11 (81.8%)	6/15 (40.0%)	6/11 (54.5%)
≤12 months	6/15 (40.0%)	10/11 (90.0%)	8/15 (53.3%)	8/11 (72.7%)
EDSS at last follow-up°°	Median 0, mean 0.3, range 0-3 (d.a. 41/42)	Median 0, mean 0.5, range 0-4 (d.a. 30/33)	Median 0, mean 0.3, range 0-3 (d.a. 37/40)	Median 0, mean 0.5, range 0-4 (d.a. 34/35)
EDSS ≥1°°	6/41 (14.6%)	9/30 (30.0%)	6/37 (16.2%)	9/34 (26.5%)
EDSS ≥2°°	4/41 (9.8%)	3/30 (10.0%)	2/37 (5.4%)	5/34 (14.7%)

eTable 1.
Legend: ADEM: acute disseminated encephalomyelitis; ADEM-ON: ADEM followed by optic neuritis; CIS: clinically isolated syndrome; CNS: central nervous system; CS: corticosteroid; CSF: cerebrospinal fluid; d.a.: data available; EDSS: Expanded disability status scale; EEG: electroencephalography; IgG: immunoglobulin G; LETM: longitudinally extensive transverse myelitis; Mono: monophasic; Mono/Rel: monophasic or relapsing; MRI: magnetic resonance imaging; NMOSD: neuromyelitis optica spectrum disorder; OCB: oligoclonal bands; ON: optic neuritis; Rel: relapsing.
°For the study of monophasic versus relapsing disease, only patients with follow-up duration ≥12 months from onset (or with relapse at any time) were included in the analysis (65/75).
°°For the study of patients with final EDSS 0 versus ≥1, only patients with available follow-up of >3 months after last event (or with EDSS 0 at any time) were included in the analysis (71/75).
^Other races were: Asian (5/72), and Black or African American (3/72); data not available in 3/72.
^^The presence of CSF-restricted oligoclonal bands (OCBs) was recorded (Franciotta 2008). Among the 9/56 patients with CSF-restricted OCBs, 2/9 had one single band. Additional 7/56 patients had identical serum and CSF OCBs in CSF (‘mirror pattern’).

eTable 2. Comparative features in patients with abnormal and normal optic nerve(s) at first MRI

	Abnormal optic nerve(s) at first MRI (n=35)	Normal optic nerves at first MRI (n=37)
Demographics		
Females	23/35 (65.7%)	16/37 (43.2%)
White race^	29/35 (82.9%)	34/36 (94.4%)
Age at onset (years)	Median 8.3, mean 8.8, range 2.8-16.1 (d.a. 35/35)	Median 5.5, mean 6.5, range 1.8-18.6 (d.a. 37/37)
≥12 years	8/35 (22.9%)	3/37 (8.1%)
Type of first MOGAD event		
ADEM	7/35 (20.0%)	29/37 (78.4%)
ON (+/- CNS lesions)	24/35 (68.6%)	3/37 (8.1%)
NMOSD	2/35 (5.7%)	0/37 (0.0%)
CIS	1/35 (2.6%)	3/37 (8.1%)
Encephalitis (+/- ON)	1/35 (2.6%)	1/37 (2.7%)
Isolated LETM	0/35 (0.0%)	1/37 (2.7%)
Severity at first MOGAD event		
Worst EDSS at first event	Median 3, mean 3.3, range 1-7 (d.a. 34/35)	Median 6, mean 5.3, range 1-8.5 (d.a. 33/37)
EDSS ≥4	12/34 (35.3%)	22/33 (67.7%)
EDSS ≥5	4/34 (11.8%)	21/33 (63.6%)
EDSS ≥6	2/34 (5.6%)	17/33 (51.5%)
Investigations at MOGAD onset		
Abnormal brain MRI	20/35 (57.1%)	33/37 (89.2%)
Abnormal optic nerves on MRI	35/35 (100.0%)	0/37 (0.0%)
Abnormal spine MRI	10/28 (35.7%)	13/27 (48.1%)
Abnormal CSF	13/29 (44.8%)	23/31 (74.2%)
CSF white blood cells >4/uL	12/28 (42.9%)	23/30 (76.7%)
CSF-restricted oligoclonal bands (OCBs)^^	6/29 (20.7%)	3/27 (11.1%)
CSF proteins >45 mg/dL	4/28 (14.3%)	3/30 (10.0%)
Abnormal EEG	6/12 (50.0%)	24/29 (82.8%)
Slow or disorganised activity	4/12 (33.3%)	23/29 79.3%)
Epileptic activity	3/12 (25.0%)	4/29 (13.8%)
IT at MOGAD onset		
Any immunotherapy (IT)	35/35 (100.0%)	34/37 (91.9%)
IV corticosteroids (CS)	35/35 (100.0%)	34/37 (91.9%)
Oral corticosteroids (CS)	26/35 (74.3%)	28/37 (75.7%)
Intravenous immunoglobulin	2/35 (5.7%)	11/37 (29.7%)
Therapeutic plasma exchange	1/35 (2.6%)	1/37 (2.7%)
Rituximab	2/35 (5.7%)	0/37 (0.0%)
Mycophenolate mofetil	2/35 (5.7%)	0/37 (0.0%)
≥2 different ITs (= CS + other)	4/35 (11.4%)	12/37 (32.4%)
Days from onset to first IT (any)	Median 5, mean 8.6, range 0-75 (d.a. 34/35)	Median 6, mean 10.1, range 0-75 (d.a. 31/37)
Any IT <7 days from onset	20/34 (58.8%)	17/34 (50.0%)
Duration of CS (weeks)	Median 5, mean 9.0, range 1-48 (d.a. 35/35)	Median 5, mean 6.7, range 0-27 (d.a. 37/37)
≥4 weeks	25/35 (71.4%)	26/37 (70.3%)
≥6 weeks	15/35 (42.6%)	17/37 (45.9%)
≥8 weeks	13/35 (37.1%)	11/37 (29.7%)
≥10 weeks	9/35 (25.7%)	6/37 (16.2%)
Duration of IT (any) (weeks)	Median 5, mean 17.9, range 1-248 (d.a. 35/35)	Median 6, mean 6.9, range 0-27 (d.a. 37/37)
≥4 weeks	25/35 (71.4%)	26/37 (70.3%)
≥6 weeks	15/35 (42.6%)	19/37 (51.4%)
≥8 weeks	13/35 (37.1%)	11/37 (29.7%)

≥10 weeks	10/35 (28.6%)	6/37 (16.2%)
Final diagnosis		
ADEM (Mono/Rel)	6/35 (17.1%)	24/37 (64.9%)
ON (+/- CNS lesions) (Mono/Rel)	24/35 (68.6%)	3/37 (8.1%)
CNS demyelination (Rel)	1/35 (2.6%)	4/37 (10.1%)
ADEM-ON (Rel)	0/35 (0.0%)	3/37 (8.1%)
NMOSD (Mono/Rel)	2/35 (5.7%)	0/37 (0.0%)
CIS (Mono)	1/35 (2.6%)	1/37 (2.7%)
Encephalitis (Mono)	1/35 (2.6%)	1/37 (2.7%)
Isolated LETM (Mono)	0/35 (0.0%)	1/37 (2.7%)
Outcome		
Length of follow-up (months)	Median 35, mean 42.4, range 2.2-130 (d.a. 35/35)	Median 30, mean 38.0, range 1-126 (d.a. 37/37)
Relapsing course (≥2 total events)°	7/32 (21.9%)	16/30 (53.3%)
Relapsing course (≥3 total events)°	7/32 (21.9%)	7/30 (23.3%)
Total number of disease events°	Median 1, mean 1.8, range 1-8 (d.a. 32/32)	Median 1.5, mean 2.0, range 1-5 (d.a. 30/30)
Time to first relapse (months)	Median 3, mean 12.2, range 1-60 (d.a. 7/7)	Median 8.5, mean 21.8, range 1.3-84 (d.a. 16/16)
≤6 months	5/7 (71.4%)	5/16 (31.3%)
EDSS at last follow-up°°	Median 0, mean 0.4, range 0-4 (d.a. 33/33)	Median 0, mean 0.3, range 0-2 (d.a. 35/35)
EDSS ≥1°°	7/33 (21.2%)	6/35 (17.1%)
EDSS ≥2°°	3/33 (9.1%)	3/35 (8.6%)

eTable 2.
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°For the study of monophasic versus relapsing disease, only patients with follow-up duration ≥12 months from onset (or with relapse at any time) were included in the analysis (65/75).
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