Table S1. Sample numbers, positivity rates, and differences in methodology and diagnostic criteria; data from 59 studies including 93 test series.

A. Tissue based assays	**Criteria (NMO/MS)**	**Tissue (species)**	**NMO (N, %)**	**LETM (N, %)**	**ON (N, %)**	**ON+NETM (N, %)**	**Other HRS (N, %)**	**NETM (N, %)**	**MS* (N, %)**	**OSMS (N, %)**	**OND (N, %)**	**ONND (N, %)**	**HC (N, %)**
Fluoroimmunohistochemistry (IHC-F)													
1. Original assay													
Lennon 2004 (91)	1999/1983	Mouse	33/45 (73.3)	14/27 (51.9)	2/8 (25)	-	-	-	2/41 (4.88)	-	0/56 (0)	-	-
Wingerchuk 2006 (158)	**	Mouse	67/88 (76.1)	-	-	-	-	-	2/32 (6.25)	-	-	-	-
Weinshenker 2006 (154)	N.a./n.a.	Mouse	-	11/29 (37.9)	-	-	-	-	-	-	-	-	-
Matiello 2008 (105)	N.a./n.a.	Mouse	-	-	5/25 (20)	-	-	-	-	-	-	-	-
Scott 2008 (137)	1999/1983	Mouse	3/4 (75)	-	-	-	-	1/22 (4.55)	0/6 (0)	0/6 (0)	-	-	-
Adoni 2008 (1)	1999/n.a.	Mouse	18/28 (64.3)	-	-	-	-	-	-	-	-	-	-
Smith 2009 (140)	N.a./2001	Mouse		-	-	-	-	-	0/130 (0)	-	-	-	-
McKeon 2009 (110)	2006/n.d.	Mouse	23/40 (57.5)	5/43 (11.6)	2/57 (3.5)	-	-	0/64 (0)	0/249 (0)	-	2/382 (0.52)	-	-
Kalluri 2010 (72)	N.d./n.d.	Mouse	7/11 (63.6)	-	-	-	-	-	1/3 (33.33)	1/3 (33.33)	-	-	-
Petzold 2010 (124)	2006/2005	Mouse	5/9 (55.6)	-	4/77 (5.2)	-	-	-	0/28 (0)	-	-	-	-
Waters 2012 (152)	1999 or 2006/ n.d.	Mouse	17/35 (48.6)	5/15 (33.3)	5/8 (62.5)		2/3 (66.7)	0/2 (0)	0/39 (0)		0/7 (0)	0/15 (0)	0/22 (0)
Sum			*173/260 (66.5)*	*35/114 (30.7)*	*18/175 (10.3)*	*0/0 (n.a.)*	*2/3 (66.7)*	*1/88 (1.14)*	*5/528 (0.95)*	*1/9 (11.11)*	*2/445 (0.45)*	*0/15 (0)*	*0/22 (0)*
Asian patients													
Lennon 2004 (91)	1999/1983	Mouse	-	1/1 (100)	-	-	-	-	6/16 (37.5)	6/11 (54.55)	0/5 (0)	-	-
Nakashima 2006 (116)	1999/2001	Mouse	12/19 (63.2)	-	-	-	-	0/3 (0)	2/13 (15.38)	-	-	-	-
Matsuoka 2007 (106)	Kira 1996	Mouse	-	1/3 (33.3)	-	-	2/22 (9.1)	0/1 (0)	14/91 (15.38)	13/48 (27.08)	0/26 (0)	-	0/35 (0)
Hayakawa 2008 (32)	2006/2001 or 2005	Mouse	13/21 (61.9)	-	-	-	-	-	2/46 (4.35)	-	-	-	-
Matsushita 2009 (107)	1999/2005	Mouse	9/24 (37.5)	-	-	-	-	-	9/74 (12.16)	-	-	-	-
Apiwattanakul 2012 (4)	2006/2005	Mouse	4/10 (40)	2/7 (28.6)	1/3 (33.3)	1/3 (33.3)	1/2 (50)	0/1 (0)	0/5 (0)	-	-	-	-
Sum			*38/74 (51.4)*	*4/11 (36.4)*	*1/3 (33.3)*	*1/3 (33.3)*	*3/24 (12.5)*	*0/5 (0)*	*33/245 (13.47)*	*19/59 (32.2)*	*0/31 (0)*	*0/0 (n.a.)*	*0/35 (0)*
Children													
Banwell 2008 (6)	1999/1983 or 2001	Mouse	8/17 (47.1)	1/10 (10)	1/13 (7.7)	-	0/3 (0)	0/3 (0)	0/41 (0)	-	-	-	-
Lotze 2008 (97)	2007/n.d.	Mouse	7/9 (77.8)	1/1 (100)	-	-	-	-	-	-	-	-	-
Sum			*15/26 (57.7)*	*2/11 (18.2)*	*1/13 (7.7)*	*0/0 (n.a.)*	*0/3 (0)*	*0/3 (0)*	*0/41 (0)*	*0/0 (n.a.)*	*0/0 (n.a.)*	*0/0 (n.a.)*	*0/0 (n.a.)*
Total, original assay			*226/360 (62.8)*	*41/136 (30.1)*	*20/191 (10.5)*	*1/3 (33.3)*	*5/30 (16.7)*	*1/96 (1.04)*	*38/814 (4.67)*	*20/68 (29.41)*	*2/476 (0.42)*	*0/15 (0)*	*0/57 (0)*
2. Independent assays													
Jarius 2007 (46)	1999/2005	Mouse	22/36 (61.1)	4/5 (80)	-	-	-	0/11 (0)	1/80 (1.25)	-	0/21 (0)	-	0/25 (0)
Waters 2008 (151)	2006/2001	Mouse	14/24 (58.3)	5/10 (50)	-	-	-	-	0/38 (0)	-	1/26 (3.85)	-	0/14 (0)
Marignier 2008 (102)	1999/2001	Rat	14/26 (53.8)	7/13 (53.8)	4/21 (19)	-	-	0/8 (0)	5/52 (9.62)	-	0/43 (0)	-	-

Bizzoco 2009 (10)	2006/1983	Rat	4/7 (57.1)	3/10 (30)	0/66 (0)	2/28 (7.1)	-	0/137 (0)	1/556 (0.18)	-	0/874 (0)	0/105 (0)	-
Fazio 2009 (26)	2006/2001	Mouse	13/33 (39.4)	-	-	-	-	0/6 (0)	0/20 (0)	-	-	-	3/67 (4.48)
Fazio 2009 (26)	2006/2001	Monkey	14/30 (46.7)	-	-	-	-	0/6 (0)	1/20 (5)	-	-	-	3/67 (4.48)
Jarius 2010 (59)	2006/2001	Mouse	21/32 (65.6)	8/12 (66.7)	0/5 (0)	1/2 (50)	-	-	1/66 (1.52)	-	0/23 (0)	-	0/11 (0)
De Vidi 2010 (19)	2006/2001	Monkey	18/48 (37.5)	3/4 (75)	0/3 (0)	-	-	-	0/28 (0)	-	-	-	0/8 (0)
Jarius 2012 (47)	2006/2001	Mouse	38/58 (65.5)	7/14 (50)	2/14 (14.3)	1/3 (33.3)	-	-	2/87 (2.3)	-	0/26 (0)	-	0/5 (0)
Granieri 2012 (31)	2006/2005	Monkey	19/20 (95)	-	-	-	-	-	1/41 (2.44)	-	-	-	2/30 (6.67)
Delavance 2012 (21)	2006/n.d.	Rat	40/47 (85.1)	10/17 (58.8)	3/5 (60)	-	-	-	1/13 (7.69)	-	0/46 (0)	0/545 (0)	-
Alvarenga 2012 (2)	N.a./n.a.	Rat	-	7/17 (41.2)	-	-	-	0/9 (0)	-	-	-	-	-
Sum			*217/361 (60.1)*	*54/102 (52.9)*	*9/114 (7.9)*	*4/33 (12.1)*	*0/0 (n.a.)*	*0/177 (0)*	*13/1001 (1.3)*	*0/0 (n.a.)*	*1/1059 (0.09)*	*0/650 (0)*	*8/227 (3.52)*
Asian patients													
Chan 2010 (12)	2006/2005	Monkey	11/18 (61.1)	6/14 (42.9)	3/23 (13)	-	-	0/26 (0)	0/40 (0)	-	0/42 (0)	-	0/10 (0)
Kim 2012 (83)	2006/2005	Mouse	4/9 (44.4)		2/32 (6.3)	-	-	-	3/10 (30)	2/2 (100)	1/60 (1.67)	-	-
Long 2012 (92)	2006/2005	Mouse	35/50 (70)	10/18 (55.6)	3/10 (30)	-	-	0/3 (0)	7/57 (12.28)	-	0/10 (0)	-	0/20 (0)
Long 2012 (92)	2006/2005	Monkey	31/50 (62)	7/18 (38.9)	5/10 (50)	-	-	0/3 (0)	6/57 (10.53)	-	0/10 (0)	-	0/20 (0)
Sum			*81/127 (63.8)*	*23/50 (46)*	*13/75 (17.3)*	*0/0 (n.a.)*	*0/0 (n.a.)*	*0/32 (0)*	*16/164 (9.76)*	*2/2 (100)*	*1/122 (0.82)*	*0/0 (n.a.)*	*0/50 (0)*
Total, independent assays			*298/488 (61.1)*	*77/152 (50.7)*	*22/189 (11.6)*	*4/33 (12.1)*	*0/0 (n.a.)*	*0/209 (0)*	*29/1165 (2.49)*	*2/2 (100)*	*2/1181 (0.17)*	*0/650 (0)*	*8/277 (2.89)*
Total, all IHC-F			*524/848 (61.8)*	*118/288 (41)*	*42/380 (11.1)*	*5/36 (13.9)*	*5/30 (16.7)*	*1/305 (0.33)*	*67/1979 (3.39)*	*22/70 (31.43)*	*4/1657 (0.24)*	*0/665 (0)*	*8/334 (2.4)*
Conventional immunohistochemistry (IHC-C)													
Saiz 2007 (135)	1999 or 2006/ 1983	Rat	10/16 (62.5)	2/4 (50)	1/7 (14.3)	-	-	0/3 (0)	0/127 (0)	-	-	-	-

B. Cell-based assays	**Criteria (NMO/MS)**	**AQP4 (species, isoform, fluorophor)**	**NMO (N, %)**	**LETM (N, %)**	**ON (N, %)**	**ON+NETM (N, %)**	**Other HRS (N, %)**	**NETM (N, %)**	**MS* (N, %)**	**OSMS (N, %)**	**OND (N, %)**	**ONND (N, %)**	**HC (N, %)**
Fluoroimmunocytochemistry (ICC-F)													
a. In-house													
Lennon 2005 (90)	N.a./1999	Hu,M1,GFP	3/3 (100)	-	-	-	-	-	-	-	0/3 (0)	-	-
Waters 2008 (151)	2006/2001	Hu,M1+M23 EGFP	20/25 (80)	6/11 (54.5)	-	-	-	-	0/38 (0)	-	0/26 (0)	-	0/14 (0)
Mader 2011 (100)	1999/2005	Hu,M23, EmGFP	29/30 (96.7)	16/24 (66.7)	1/2 (50)	-	-	-	1/128 (0.78)	-	0/29 (0)	1/30 (3.33)	0/47 (0)
Mader 2011 (100)	1999/2005	Hu,M1, EmGFP	21/30 (70)	9/24 (37.5)	1/2 (50)	-	-	-	1/128 (0.78)	-	0/29 (0)	0/30 (0)	0/47 (0)
Waters 2012 (152)	1999,2006/ McDonald	Hu,M23	24/35 (68.6)	12/15 (80)	5/8 (62.5)	-	3/3 (100)	0/2 (0)	0/39 (0)	-	0/7 (0)	0/15 (0)	0/22 (0)
Sum			*97/123 (78.9)*	*43/74 (58.1)*	*7/12 (58.3)*	*0/0 (n.a.)*	*3/3 (100)*	*0/2 (0)*	*2/333 (0.6)*	*0/0 (n.a.)*	*0/94 (0)*	*1/75 (1.33)*	*0/130 (0)*

Asian patients													
Takahashi 2007 (142)	2006/1983	Hu,M1?	20/22 (90.9)	-	-	1/1 (100)	11/13 (84.6)	-	0/63 (0)	-	0/50 (0)	-	-
Matsuoka 2007 (106)	N.a./1983 +Kira1996	Hu,M1,GFP	-	1/3 (33.3)	-	-	2/22 (9.1)	0/1 (0)	14/91 (15.38)	13/48 (27.08)	0/26 (0)	-	0/35 (0)
Tanaka 2007 (144)	N.a.	Hu,M23	-	-	-	-	-	-	16/53 (30.19)	16/32 (50)	0/28 (0)	-	0/10 (0)
Tanaka 2009 (145)	2006/2001	Hu,M1	19/35 (54.3)	-	-	-	-	-		-	-	-	-
Matsushita 2009 (107)	1999/2005	Hu,M1,GFP	12/29 (41.4)	-	7/26 (26.9)	-	-	-	27/148 (18.24)	21/58 (36.21)	0/52 (0)	-	0/35 (0)
Kim 2013 (81)	2006/2010	Hu,n.d.	13/14 (92.9)	9/50 (18)	2/10 (20)	-	3/4 (75)	-	0/22 (0)	-	-	-	-
Isobe 2012 (38)	2005/1999	Hu,M1,GFP	12/29 (41.4)	-	-	-	-	-	-	-	0/86 (0)	-	0/28 (0)
Yoshimura 2013 (160)	2005/1999	Hu,M1,GFP	65/77 (84.4)	-	-	-	-	-	-	-	-	-	-
Katsumata 2012 (76)	2006/n.a.	Hu,M23	1/3 (33.3)	0/1 (0)	1/2 (50)	-	-	-	-	-	-	-	-
Yang 2013 (159)	2006/2005	Hu,n.d.	39/53 (73.6)	-	-	-	12/42 (28.6)	-	4/86 (4.65)	-	0/29 (0)	-	-
Chan 2010 (12)	2006/2005	Hu,M1,GFP	14/18 (77.8)	10/14 (71.4)	5/23 (21.7)	-	-	0/26 (0)	0/40 (0)	-	0/42 (0)		0/10 (0)
Sum			*195/280 (69.6)*	*20/68 (29.4)*	*15/61 (24.6)*	*1/1 (100)*	*28/81 (34.6)*	*0/27 (0)*	*61/503 (12.13)*	*50/138 (36.23)*	*0/313 (0)*	*0/0 (n.a.)*	*0/118 (0)*
Children													
Rostasy 2012 (132)	2006/2005 +Krupp 2007	Hu,M23, EmGFP	2/8 (25)	0/6 (0)	0/17 (0)	-	-	-	0/43 (0)	-	0/52 (0)		
Total, in-house			*294/411 (71.5)*	*63/148 (42.6)*	*22/89 (24.7)*	*1/1 (100)*	*31/84 (36.9)*	*0/29 (0)*	*63/879 (7.17)*	*50/138 (36.23)*	*0/459 (0)*	*1/75 (1.33)*	*0/248 (0)*
b. Commercial (Euroimmun)													
Jarius 2010 (59)	2006/2001	Hu,M1	25/32 (78.1)	8/12 (66.7)	1/5 (20)	2/2 (100)	-	-	0/66 (0)	-	0/23 (0)	-	0/11 (0)
Marnetto 2009 (104)	2006/2005	Hu,M1	16/16 (100)	-	-	-	-	-	0/36 (0)	-	-	-	0/30 (0)
Granieri 2012 (31)	2006/2005	Hu,M1	19/20 (95)	-	-	-	-	-	0/41 (0)	-	-	-	0/30 (0)
Závada 2011 (161)	N.a./n.a.	Hu,M1	-	-	-	-	-	1/1 (100)	-	-	0/75 (0)	-	
Waters 2012 (152)	1999 or 2006/ n.d.	Hu,M1	21/35 (60)	11/15 (73.3)	6/8 (75)	-	3/3 (100)	0/2 (0)	0/39 (0)	-	0/7 (0)	0/15 (0)	0/22 (0)
Sum			*81/103 (78.6)*	*19/27 (70.4)*	*7/13 (53.8)*	*2/2 (100)*	*3/3 (100)*	*1/3 (33.33)*	*0/182 (0)*	*0/0 (n.a.)*	*0/105 (0)*	*0/15 (0)*	*0/93 (0)*
Asian patients													
Kim 2012 (82)	2006/2005+ not NMOSD 2006/2007	Hu,M1	50/64 (78.1)	-	-	-	-	-	-	-	-	-	-
Kim 2012 (83)	2006/2005	Hu,M1	5/9 (55.6)	-	0/32 (0)	-	-	-	1/10 (10)	0/2 (0)	-	-	-
Zhong 2012 (163)	2006/n.d.	Hu,M1	42/52 (80.8)	-	-	-	-	-	-	-	-	-	-
Kang 2012 (75)	2006/n.d.	Hu,M1	6/6 (100)	7/24 (29.2)	1/11 (9.1)	-	-	-	2/38 (5.26)	-	0/20 (0)	1/2 (50)	-
Long 2012 (95)	2006/2005	Hu,M1	30/39 (76.9)	13/22 (59.1)	1/6 (16.7)	-	-	0/9 (0)	0/42 (0)	0/8 (0)	0/12 (0)	-	-
Long 2012 (94)	N.d./2005	Hu,M1	39/44 (88.6)	15/29 (51.7)	4/13 (30.8)	-	-	0/15 (0)	2/46 (4.35)	-	0/53 (0)	-	-
Apiwattanakul 2012 (4)	2006/2005	Hu,M1	6/10 (60)	6/7 (85.7)	2/3 (66.7)	2/3 (66.7)	2/2 (100)	1/1 (100)	0/5 (0)	-	-	-	-
Long 2012 (93)	2006/n.a.	Hu,M1	30/39 (76.9)	-	-	-	-	-	-	-	-	-	-

Etemadifar 2012 (24)	2006/2005	Hu,M1	2/2 (100)	-	2/33 (6.1)	-	-	-	0/6 (0)	-	-	-	-
Etemadifar 2012 (25)	2006/Kira 2003+not NMO2006	Hu,M1	16/32 (50)	-	-	0/32 (0)	-	-	-	-	-	-	-
Sum			*226/297 (76.1)*	*41/82 (50)*	*10/98 (10.2)*	*2/35 (5.7)*	*2/2 (100)*	*1/25 (4)*	*5/147 (3.4)*	*0/10 (0)*	*0/85 (0)*	*1/2 (50)*	*0/0 (n.a.)*
Total, commercial assay			*307/400 (76.8)*	*60/109 (55)*	*17/111 (15.3)*	*4/37 (10.8)*	*5/5 (100)*	*2/28 (7.14)*	*5/329 (1.52)*	*0/10 (0)*	*0/190 (0)*	*1/17 (5.88)*	*0/93 (0)*
Total, ICC-F			*601/811 (74.1)*	*123/257 (47.9)*	*40/201 (19.9)*	*5/38 (13.2)*	*36/89 (40.4)*	*2/57 (3.51)*	*68/1208 (5.63)*	*50/148 (33.78)*	*0/649 (0)*	*2/92 (2.17)*	*0/341 (0)*
Flow cytometry (FACS)													
a. HEK293 cells													
Fazio 2009 (26)	2006/2001	Hu,M1, EGFP	10/33 (30.3)	-	-	-	-	0/6 (0)	1/20 (5)	-	-	-	2/67 (2.99)
De Vidi 2010 (19)	2006/2001	Hu,M1, EGFP	18/48 (37.5)	3/4 (75)	0/3 (0)	-	-	-	0/28 (0)	-	-	-	0/8 (0)
Ketelslegers 2011 (78)	2006/2005	Hu,M1+M23 EGFP	20/36 (55.6)	-	-	4/40 (17.4)			2/158 (1.27)	-	0/61 (0)	-	-
Waters 2012 (152)	1999 or 2006/n.d.	Hu,M23, DSRED	25/35 (71.4)	12/15 (80)	6/8 (75)	-	3/3 (100)	0/2 (0)	0/39 (0)	-	0/7 (0)	0/15 (0)	0/22 (0)
Asian patients													
Isobe 2012 (38)	1999/2005	Hu,M1	15/29 (51.7)	-	-	-	-	-	-	-	0/86 (0)	-	0/28 (0)
Sum, HEK293			*88/181 (48.6)*	*15/19 (78.9)*	*6/11 (54.5)*	*4/23 (17.4)*	*3/3 (100)*	*0/8 (0)*	*3/245 (1.22)*	*0/0 (n.a.)*	*0/154 (0)*	*0/15 (0)*	*2/125 (1.6)*
b. LN18 cells													
Kalluri 2010 (72)	2006/2005	Hu,M1	9/11 (81.8)	-	-	-	-	-	1/3 (33.33)	1/3 (33.33)	-	-	-
Kalluri 2010 (72)	2006/2005	Hu,M1	11/18 (61.1)	10/27 (37)	5/12 (41.7)	-	-	-	0/38 (0)	-	-	-	-
Total, FACS			*108/210 (51.4)*	*25/46 (54.3)*	*11/23 (47.8)*	*4/23 (17.4)*	*3/3 (100)*	*0/8 (0)*	*4/286 (1.4)*	*1/3 (33.33)*	*0/154 (0)*	*0/15 (0)*	*2/125 (1.6)*
C. Protein based assays	**Criteria (NMO/MS)**	**AQP4 (species, isoform, fluorophor)**	**NMO (N, %)**	**LETM (N, %)**	**ON (N, %)**	**ON+NETM (N, %)**	**Other HRS (N, %)**	**NETM (N, %)**	**MS* (N, %)**	**OSMS (N, %)**	**OND (N, %)**	**ONND (N, %)**	**HC (N, %)**
Radioimmunoprecipitation assays (RIPA)													
Paul, Jarius, Aktas 2007 (123)	1999 or 2006/2001	Hu,M1,35S-methionine-labelled	21/37 (56.8)	6/6 (100)	0/11 (0)	-	-	0/15 (0)	4/144 (2.78)	-	1/47 (2.13)	0/45 (0)	0/29 (0)
Fazio 2009 (26)	2006/2001	Hu,M1,35S-methionine-labelled	11/33 (33.3)	-	-	-	-	1/6 (16.67)	0/20 (0)	-	-	-	2/67 (2.99)
Total, RIPA			*32/70 (45.7)*	*6/6 (100)*	*0/11 (0)*	*0/0 (n.a.)*	*0/0 (n.a.)*	*1/21 (4.76)*	*4/164 (2.44)*	*0/0 (n.a.)*	*1/47 (2.13)*	*0/45 (0)*	*2/96 (2.08)*

Fluoroimmunoprecipitation assays (FIPA)													
a. M1/M23-EGFP, protein A													
Waters 2008 (151)	2006/2001	Hu,M1+M23 EGFP	19/25 (76)	6/11 (54.5)	-	-	-	-	0/38 (0)	-	0/26 (0)	-	0/14 (0)
Waters 2012 (152)	1999 or 2006/ n.d.	Hu,M23, EGFP	16/35 (45.7)	8/14 (57.1)	5/8 (62.5)	-	3/3 (100)	0/2 (0)	0/39 (0)	-	0/7 (0)	0/15 (0)	0/22 (0)
Jarius 2011 (49)	2006/2001	Hu,M1+M23 EGFP	10/17 (58.8)	-	8/139 (5.8)	-	-	-	-	-	-	-	-
Sum			*45/77 (58.4)*	*14/25 (56)*	*13/147 (8.8)*	*0/0 (n.a.)*	*3/3 (100)*	*0/2 (0)*	*0/77 (0)*	*0/0 (n.a.)*	*0/33 (0)*	*0/15 (0)*	*0/36 (0)*
b. M1-EGFP, protein G													
McKeon 2009 (110)	2006/n.d.	Hu,M1, EGFP	13/40 (32.5)	1/43 (2.3)	2/57 (3.5)	-	-	0/64 (0)	1/249 (0.4)	-	4/382 (1.05)	-	-
Kalluri 2010 (72)	N.d./n.d.	Hu,M1, EGFP	8/11 (72.7)	-	-	-	-	-	1/3 (33.33)	1/3 (33.33)	-	-	-
Waters 2012 (152)	1999 or 2006/ n.d.	Hu,M1, EGFP	16/35 (45.7)	8/15 (53.3)	5/8 (62.5)	-	3/3 (100)	0/2 (0)	1/39 (2.56)	-	0/7 (0)	0/15 (0)	1/22 (4.55)
Sum			*37/86 (43)*	*9/58 (15.5)*	*7/65 (10.8)*	*0/0 (n.a.)*	*3/3 (100)*	*0/66 (0)*	*3/291 (1.03)*	*1/3 (33.33)*	*4/389 (1.03)*	*0/15 (0)*	*1/22 (4.55)*
Total, FIPA			*82/163 (50.3)*	*23/83 (27.7)*	*20/212 (9.4)*	*0/0 (n.a.)*	*6/6 (100)*	*0/68 (0)*	*3/368 (0.82)*	*1/3 (33.33)*	*4/422 (0.95)*	*0/30 (0)*	*1/58 (1.72)*
Western blot assays (WB)													
Marnetto 2009 (104)	2006/2005	Mo,M1, denatured	13/16 (81.3)	-	-	-	-	-	2/36 (5.56)	-	-	-	0/30 (0)
Marnetto 2009 (104)	2006/2005	Mo,M21, denatured	2/16 (12.5)	-	-	-	-	-	1/36 (2.78)	-	-	-	5/30 (16.67)
Enzyme linked immunosorbent assays (ELISA)													
a. In-house assays													
Asian patients													
Hayakawa 2008 (32)	2006/2001 or 2005	Rat,M23, HIS-tagged	15/21 (71.4)	-	-	-	-	-	2/46 (4.35)	-	3/115 (2.61)	-	0/51 (0)
Kim 2012 (82)	2006/2005	Hu,M23, HIS-tagged	46/64 (71.9)	-	-	-	-	-	4/105 (3.81)	-	0/57 (0)	-	0/47 (0)
b. Commercial, RSR													
Jarius 2012 (47)	2006/2001	Hu,M1, biotin	50/66 (75.8)	17/25 (68)	3/14 (21.4)	2/3 (66.7)	-	-	1/109 (0.92)	-	1/39 (2.56)	-	0/5 (0)
Waters 2012 (152)	1999 or 2006/ n.d.	Hu,M1, biotin	18/35 (51.4)	10/15 (66.7)	5/8 (62.5)	-	3/3 (100)	0/2 (0)	0/39 (0)	-	0/7 (0)	0/15 (0)	0/22 (0)
Asian patients													
Isobe 2012 (38)	2006/n.d.	Hu,M1, biotin	14/29 (48.3)	-	-	-	-	-	-	-	0/86 (0)	-	0/28 (0)
Isobe 2012 (38)	2006/n.d.	Hu,M1, biotin	-	-	-	-	-	-	-	-	0/40 (0)	-	0/138 (0)
Apiwattanakul 2012 (4)	2006/2005	Hu,n.d.	5/10 (50)	6/7 (85.7)	2/3 (66.7)	1/3 (33.3)	1/2 (50)	1/1 (100)	0/5 (0)	-	-	-	-
Kim 2012 (83)	2006/2005	Hu,n.d.	5/9 (55.6)	-	4/32 (12.5)	-	-	-	3/10 (30)	2/2 (100)	0/60 (0)	-	-
Total, RSR ELISA			*37/74 (50)*	*16/22 (72.7)*	*7/11 (63.6)*	*1/3 (33.3)*	*4/5 (80)*	*1/3 (33.33)*	*0/44 (0)*	*0/0 (n.a.)*	*0/133 (0)*	*0/15 (0)*	*0/188 (0)*
Total, ELISA			*153/234 (65.4)*	*33/47 (70.2)*	*14/57 (24.6)*	*3/6 (50)*	*4/5 (80)*	*1/3 (33.33)*	*10/314 (3.18)*	*2/2 (100)*	*4/404 (0.99)*	*0/15 (0)*	*0/291 (0)*

NMO = neuromyelitis optica; LETM = longitudinally extensive transverse myelitis (>=3 vertebral segments); NETM = non-longitudinally extensive transverse myelitis; ON = optic neuritis; HRS = high-risk syndromes; MS = multiple sclerosis; OSMS = opticospinal multiple sclerosis; OND = other neurological diseases; ONND = other non-neurological diseases; HC = healthy controls; Hu = human; GFP = green fluorescent protein; EGFP = enhanced GFP; M1 = M1 (full length) isoform of AQP4; M23 = M23 isoform of AQP4; n.d. = no data; n.a. = not applicable. * Including OSMS. ** Wingerchuk 2006 (158): "A diagnosis of NMO or MS based on the final clinical diagnosis rendered by the study neurologist based on his or her integration of all available clinical, imaging, and laboratory data and the period of follow-up after disease onset." Remarks: Ketelslegers 2011 (78), positive patients in the MS group: "Both patients presented with bilateral ON and symptoms related to the spinal cord and cerebral MRI showed lesions typical of MS. During follow-up these patients developed a recurrent disease that is more suspected of an NMOSD.". Ketelslegers 2011 (78), other HRS: includes 23 patients with ON+NETM (4 x pos) and 17 with either isolated LETM or isolated ON (numbers not given separately; all NMO-IgG/AQP4-Ab-negative). Paul 2007 (123), seropositive MS samples: Patients had clinical syndromes related to spinal cord lesions but did not meet Wingerchuk's 1999 criteria for NMO. Kim 2012 (82): M1 was used in parallel, but "positivity rate (...) did not differ significantly". Hayakawa 2008 (32), seropositive MS samples: Patients had "some of the clinical and laboratory features of NMO". Lennon 2005 (90): The authors reported on the first ICC for the detection of AQP4-Ab. However, the assay was not intended for routine testing but to demonstrate that NMO-IgG targets AQP4. Therefore, only three NMO-IgG-positive samples from patients with NMO and three NMO-IgG-negative samples from control patients were tested. Apiwattanakul 2012 (4): Patients with other HRS had LETM + ON + brain lesion meeting Barkhof criteria. Kalluri 2010 (72), second cohort: Samples from 64 OND controls were used to generate the cut-off and were therefore negative *per definitionem*; accordingly, these samples were not taken into account in the table. McKeon 2009 (110): Two seropositive patients in the OND group had intractable vomiting and hiccups, symptoms typically found in NMO-IgG/AQP4-Ab positive NMO; results may thus be truly positive; two additional seropositive OND patients had myelopathy of unknown cause and paraesthesia. Lennon 2004 (91), other HRS: LETM and delayed visual evoked potentials. Lennon 2004 (91): The two NMO-IgG positive patients with MS had "optico-spinal symptoms". McKeon 2009 (110), ON group: For the sake of inter-study consistency – most studies did not distinguish monophasic and relapsing ON – the 40 patients with ON were moved from the OND to the ON group in this table. Nakashima 2006 (116), 'false-positive' patients: One patient developed severe myelitis and optic neuritis, but the brain MRI showed extensive brain lesions; the other patient had two episodes of LETM and two succeeding episodes of cerebellar ataxia and hemiparesis due to the brain lesions; her brain MRI was normal until her third exacerbation. Kim 2012 (83) and Isobe 2012 (38): Transverse myelitis group not included since data on the proportion of LETM and NETM patients was missing. Isobe 2012 (38): The MS group comprised patients with LETM, a HRS, and patients who met NMO criteria; this group was therefore excluded from the analysis. Yoshimura 2013 (160), NMOSD group: Exact clinical data were missing; therefore this study was excluded from the analysis (however, 12/39 [30%] patients were positive, in line with the mean frequency of NMO-IgG/AQP4-Ab [27.6%] of all other studies). Wingerchuk 2006 (158), MS group: See online supplement to reference (158). Petzold 2010 (124): All MS patients had a history of ON. Rostasy 2012 (132), number of LETM and ON patients and AQP4 isoform: Personal communication. Bizzoco 2009 (10), MS group: Included 51 with "probable MS". Bizzoco 2009 (10), other HRS: Optic neuritis and non-extensive transverse myelitis. Bizzoco 2009 (10): The NMO-IgG-positive "MS" patient had a recurrent brainstem syndrome. Lennon 2004 (91), Asian patients: The six positive "(OS)MS" patients were retrospectively found to meet NMO criteria. Jarius 2007 (46) and Jarius 2010 (59): The IHC-positive patient with MS had no features suggestive of NMO. Kim 2013 (81): The four patients with 'other HRS' had myelitis with brain lesions typical of NMO. Waters 2012 (152): The OND group included one patient with LETM; for the sake of inter-study consistency, this sample was included in the LETM group for analysis. Waters 2012 (152), AQP4 isoform CBA Oxford: Personal communication. Matsushita 2009 (107), IHC-F (not CBA): The MS group included patients with OSMS; however, the number of OSMS patients among the seropositives was not specified. Marignier 2008 (102): MS group included nine patients with ""probable MS"". Hayakawa 2008 (32), IHC and ELISA: The seropositive patients with diagnoses other than NMO had "some of the clinical and laboratory features of NMO". Kang 2012 (75): The two OND patients had "autoimmune neurological disorders"; one of them was positive. Takahashi 2007 (142), IHC (not CBA): The two patients with "other HRS" had NETM und brain lesions typical of NMO. Kalluri (72), first and second cohort (FACS): "Similar results" were obtained with the LN18 cell line transfected with the M23 variant of AQP4. Takahashi 2007 (142), other HRS: Included ON, LETM, and cases of ON and/or NETM plus brain lesions compatible with NMO according to Pittock et al.(127-128) Banwell 2008 (6): Patients with other HRS had LETM + ADEM. Takahashi 2007 (142): IHC-F results not considered, since only CBA-positive samples (i.e. highly selected samples) were tested. Nakashima 2006 (116): All OSMS patients met the 2006 NMO criteria. Matsuoka 2007 (106): Patients with 'other' HRS had LETM and brain lesions. Matsuoka 2007 (106), OSMS: Thirty-one of the OSMS patients had LETM. Matsuoka 2007 (106), CBA: Twenty-six additional OND patients had parasitic, atopic or HTLV-associated myelitis (all AQP4-Ab-negative); however, these patients were not stratified according to lesion length by the authors and are therefore not considered here. Kim 2012 (82), ELISA: The 'other HRS' group comprises patients with recurrent LETM and patients with recurrent ON (proportions not specified). Tanaka 2007 (144): Twenty of 26 OSMS patients had LETM+ON; all NMO-IgG/AQP4-Ab-positive OSMS patients had LETM+ON.