研究用

IIFT: NMOSD Screen 1

ORDER NO.	ANTIBODIES AGAINST	SUBSTRATE	SPECIES	FORMAT SLIDES x FIELDS
FA 1128-1005-1 FA 1128-1010-1	aquaporin-4 (AQP-4) myelin-oligodendrocyte glycoprotein (MOG)	transfected cells transfected cells control transfection	EU 90	10 x 05 (050) 10 x 10 (100)

Indication: This test kit provides qualitative or semiquantitative in vitro determination of human antibodies of immunoglobulin class IgG against aquaporin-4 (AQP-4) and myelin-oligodendrocyte glycoprotein (MOG) in patient samples to support the diagnosis of demyelinating diseases of the central nervous system. The fluorescence is either evaluated using the fluorescence microscope (specifications see chapter “Incubation”, section “Evaluation”) or, following automated image recording by the EUROPattern microscope at the computer screen, optionally supported by the EUROPattern Classifier software. The product is designed for use as IVD.

Anti-Aquaporin-4 (AQP-4) IIFT:

Clinical sensitivity and specificity:

Panels for serum/plasma samples	n	Ig class	Anti-AQP-4 IIFT
Patients with neuromyelitis optica (NMO) - n = 32 (origin: Germany) - n = 20 (origin: Italy, Czech Republic) * - n = 103 (origin: Spain, France, Austria) **	155	IgG	**120 (77%)** 25/32 (78%) 19/20 (95%)* 76/103 (74%)**
Patients with NMO spectrum diseases (NMOSD) - longitudinal transverse myelitis (n = 12, origin: Germany) - recurrent optic neuritis (n = 5, origin: Germany) - recurrent optic neuritis and non-extensive transverse myelitis (n = 2, origin: Germany)	19	IgG	**11 (58%)** 8/12 (67%) 1/5 (20%) 2/2 (100%)
Clinical sensitivity	**174**	**IgG**	**131/174 (75%)**
Control samples:			
Patients with multiple sclerosis - n = 66 (origin: Germany) - n = 1038 (origin: USA) *** - n = 101 (origin: Spain, France, Austria) ** - n = 41 (origin: Italy, Czech Republic) *	1246	IgG	**1/1246 (99.9%)** 0/66 (100%) 1/1038 (99.9%)*** 0/101 (100%)** 0/41 (100%)*
Patients with other neurological diseases or non-extensive transverse myelitis (origin: Germany)	23	IgG	0/23 (100%)
Healthy controls (origin: Italy, Czech Republic) *	30	IgG	0/30 (100%)*
Patients with anti-neural antibody-associated neurological syndrome (origin: Spain, France, Austria) **	21	IgG	0/21 (100%)**
Blood donors (origin: Germany)	100	IgG	0/100 (100%)
Clinical specificity	**1420**	**IgG**	**1/1420 (99.9%)**

* The data was taken from the following literature: **Granieri L et al. Evaluation of a Multiparametric Immunofluorescence Assay for Standardization of Neuromyelitis Optica Serology. PLoS ONE 7(6): e38896.**

** The data was taken from the following literature: **Höftberger R et al. An Optimized Immunohistochemistry Technique Improves NMO-IgG Detection: Study Comparison with Cell-Based Assays. PLoS ONE 8(11): e79083.**

*** The data was taken from the following literature: **Pittock SJ et al. Seroprevalence of Aquaporin-4-IgG in a Northern California Population Representative Cohort of Multiple Sclerosis. JAMA Neurol. 2014;71(11):1433-1436.** A total of n = 1040 samples from patients with multiple sclerosis were analysed. 3 out of these samples were found positive by the EUROIMMUN IIFT. 2/3 of the samples were confirmed using another test and therefore excluded from the study. Consequently, there is only one unconfirmed sample of a total of 1038.

Panels for cerebrospinal fluid (CSF)	n	Ig class	Anti-AQP-4 IIFT
Neuromyelitis optica (NMO) [#] (n = 26, origin: Germany). 16/26 of the corresponding serum samples were anti-AQP-4 positive.	26	IgG	11/26 (42%)
Patients with NMO spectrum diseases (NMOSD) [#] - Longitudinal transverse myelitis (n = 8, LETM, origin: Germany). 7/8 of the corresponding serum samples were anti-AQP-4 positive. - Recurrent optic neuritis (rON, n = 11, origin: Germany). 8/11 of the corresponding serum samples were anti-AQP-4 positive	19	IgG	10/19 (53%) 5/8 (63%) 5/11 (45%)
Clinical sensitivity	**45**	**IgG**	**21 (47%)**
Control samples:			
Patients with multiple sclerosis (origin: Germany) [#]	28	IgG	0 (100%)
Patients with different neurological diseases (origin: Germany) [#]	14	IgG	0 (100%)
Clinical specificity	**42**	**IgG**	**0 (100%)**

[#] Jarius et al. Cerebrospinal fluid antibodies to aquaporin-4 in neuromyelitis optica and related disorders: frequency, origin, and diagnostic relevance. Journal of Neuroinflammation 2010;7:52.

Anti-Myelin-oligodendrocyte glycoprotein (MOG) IIFT:

Specificity and sensitivity: Specificity and sensitivity of the Anti-MOG IIFT were investigated in an internal study with a total of 167 patient samples, serologically pre-characterised externally using in-house assays (60 samples with positive pre-characterisation, 107 samples with negative pre-characterisation; origin: Germany, Norway, Austria, Luxembourg).

Reference test system: In-house Anti-MOG Assay of the Neurological Research Laboratory, University Clinic for Neurology, Medical University Innsbruck, Austria.

Overview on the investigated samples:	**n = 167**
1a. Samples with information on the clinical picture of the patients (origin: Norway)	14
1b. Samples without information on the clinical picture (origin: Germany, Luxembourg)	44
1c. Samples without information on the clinical picture (origin: Austria)	50
2a. Control panel: anti-aquaporin-4 positive samples (origin: Germany)	9
2b. Samples from apparently healthy blood donors (origin: Germany)	50

n = 167		**In-house anti-MOG assay Innsbruck**	
		positive	negative
EUROIMMUN	positive	57	17
Anti-Myelin-oligodendrocyte glycoprotein (MOG) IIFT	negative	3	90

Specificity (%)	**84.1%**
Sensitivity (%)	**95.0%**
Positive predictive value (%)	**77.0%**
Kappa value	**0.75**

Clinical sensitivity: One panel (origin: Germany, China, Norway) consisting of n = 72 clinically characterised patients with different diseases from the group of neuromyelitis optica spectrum disorders (NMOSD) and individual clinical symptoms was investigated for antibodies against MOG.

Panels	**n**	**Ig class**	**Anti-MOG IIFT**	
			positive	**prevalence**
Optic neuritis (ON), different forms (thereof n = 22 with negative AQP-4 antibody finding)	23	IgG	17	74%
Neuromyelitis optica (NMO) with negative AQP-4 antibody finding	1	IgG	0	0%
NMOSD with accompanying collagenosis	45	IgG	0	0%
Neuropathy/paralysis/spinal canal inflammation	3	IgG	0	0%

EUROPattern (software evaluation) from classifier version 2.3.21

The fluorescence is either evaluated using the fluorescence microscope (specifications see chapter “Incubation”, Section “Evaluation”) or, following automated image recording by the EUROPattern microscope at the computer screen, optionally supported by the EUROPattern Classifier software. The performance data are stored in the EUROPattern software.

Literature

1. Wingerchuk DM, Banwell B, Bennett JL, Cabre P, Carroll W, International Panel for NMO Diagnosis. **International consensus diagnostic criteria for neuromyelitis optica spectrum disorders.** Neurology. 2015; 85(2): 177-89
2. Bruscolini A, Sacchetti M, La Cava M, Gharbiya M, Ralli M, Lambiase A, et al. **Diagnosis and management of neuromyelitis optica spectrum disorders – An update.** Autoimmun Rev. 2018; 17(3): 195-200
3. Pittock SJ, Lucchinetti CF. **Neuromyelitis optica and the evolving spectrum of autoimmune aquaporin-4 channelopathies: a decade later.** Ann N Y Acad Sci. 2016; 1366(1): 20-39
4. Borisow N, Mori M, Kuwabara S, Scheel M, Paul F. **Diagnosis and Treatment of NMO Spectrum Disorder and MOG-Encephalomyelitis.** Front Neurol. 2018; 9: 888
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6. Reindl M, Waters P. **Myelin oligodendrocyte glycoprotein antibodies in neurological disease.** Nat Rev Neurol. 2019; 15(2): 89-102
7. Narayan R, Simpson A, Fritsche K, Salama S, Pardo S, Mealy M, et al. **MOG antibody disease: A review of MOG antibody seropositive neuromyelitis optica spectrum disorder.** Mult Scler Relat Disord. 2018; 25: 66-72
8. Di Pauli F, Berger T. **Myelin Oligodendrocyte Glycoprotein Antibody-Associated Disorders: Toward a New Spectrum of Inflammatory Demyelinating CNS Disorders?** Front Immunol. 2018; 9: 2753
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