# SUPPLEMENT

Effects of the COVID-19 pandemic on patients with NMO spectrum disorders and MOG-antibody associated diseases (COPANMO(G)-Study)

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## eTables:

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| **eTable 1: Spectrum of comorbidities reported by COPANMO(G)-Study participants** |
| **Comorbidity** | **n** | **%a** |
| HypertensionRheumatic disease Chronic respiratory diseaseMalignant neoplasm, CancerDiabetes mellitusPsoriasisCoronary heart diseaseChronic liver diseaseStrokeChronic kidney diseasePeripheral artery diseaseInflammatory bowel diseaseOther comorbidities | 252320149766541142 | 1413118543332<1<123 |
| aPercentages in this column refer to the number of patients who provided information on comorbidities (n=180) and may not add exactly to 100% due to rounding. |

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| **eTable 2: Spectrum of immunotherapies used by the COPANMO(G)-Study participants** |
| **Immunotherapy, one substance** | **n**  | **%** |
| RituximabAzathioprineEculizumabTocilizumabPrednisolone or other oral corticosteroidsMethotrexateSatralizumabMycophenolate mofetilIVIGGlatiramer acetateRuxolitinibOcrelizumabAll | 842611762222111145 | 58188541111<1<1<178a |
| **Immunotherapy, combinations of two substances**Rituximab, OCSAzathioprine, OCSRituximab, methotrexateEculizumab, OCSTocilizumab, OCSSatralizumab, OCSMethotrexate, satralizumabMethotrexate, tocilizumabRituximab, azathioprineMycophenolate mofetil, OCSAll | **n**533222111121 | **%**241414101010555511a |
| aPercentage refers to the number of patients who provided information on immunotherapies (n=187); 21 patients (11%) were not receiving immunotherapy. Percentages may not add exactly to 100% due to rounding.*Note:* IVIG: intravenous immunoglobulin; OCS: oral corticosteroids |

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| **eTable 3: Changes of immunotherapy due to the pandemic** |
|  | **n**  | **%** |
| Totala | 181 | 100 |
| No change of immunotherapy  | 160 | 88 |
| Change of immunotherapy Dose interval changePaused Dosing change Stopped Medication change Paused + dose interval changed | 21665211 | 1229b29241055 |
| Change carried out bycNeurologistPatient aloneNEMOS centerOther | 9542 | 43241910 |
| aSix values for ‘*changes of immunotherapy due to the pandemic’* were missing.bThe percentage refers to the cases in which changes of immunotherapy were reported.cOne value for ‘*change carried out by’* was missing. Percentages refer to the total number of cases with reported changes (n=21).Percentages may not add exactly to 100% due to rounding. |
| **eTable 4: Level of satisfaction with medical care during the pandemic** |
|  | **n** | **%** |
| Totala | 182 | 100 |
| Very satisfied | 91 | 50 |
| Rather satisfied | 74 | 41 |
| Rather dissatisfied | 11 | 6 |
| Very dissatisfied | 6 | 3 |
| aFive values for *‘Level of satisfaction with medical care during the pandemic’* were missing.Percentages may not add exactly to 100% due to rounding. |

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| **eTable 5: Suggested improvements**  |  |
|  | **n (%)** |
| Total | 36 (100) |
| More information onImplications of immunosuppressive medications for SARS-CoV-2 vaccinationPrevention measuresProcedure in case of SARS-CoV-2 infectionDisease severity in case of SARS-CoV-2 infection | 10 (28) |
| Better accessibility of doctors' offices (via telephone)/shorter waiting times | 6 (17) |
| Higher prioritization in the vaccination process  | 3 (8) |
| Improved working conditions in the medical fieldMore staffMore test and vaccination centers | 3 (8) |
| Serologic control of SARS-Cov-2 vaccination efficiency | 2 (6) |
| More telemedicine options | 2 (6) |
| Mandatory SARS-Cov-2 vaccination for caregivers | 2 (6) |
| Better coordination of immunotherapy doses and SARS-CoV-2 vaccination | 1 (3) |
| Secured supply of medication | 1 (3) |
| Psychological support | 1 (3) |
| Uniform regulations | 1 (3) |
| Certain checkups should be kept up despite the pandemic | 1 (3) |
| General suggestions for improvement without specific connection to the pandemicIf problems occur, it should be easier to get a complete diagnostic workup in the hospitalImprovement of daily life (fatigue, weakness, nausea)Improvement of spastic | 3 (8) |
| *Note:* SARS-CoV-2: severe acute respiratory syndrome coronavirus type 2Percentages may not add exactly to 100% due to rounding. |  |

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| **eTable 6: Assessment of personal risk of contracting SARS-CoV-2** |
|  | **n** | **%** |
| Totala | 184 | 100 |
| Low | 47 | 26 |
| Moderate | 70 | 38 |
| High | 54 | 29 |
| Very high | 13 | 7 |
| aThree values for *‘Assessment of personal risk of contracting SARS-CoV-2’* were missing.*Note:* SARS-CoV-2: severe acute respiratory syndrome coronavirus type 2Percentages may not add exactly to 100% due to rounding. |

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| **eTable 7: COVID-19 cohort characteristics** |
|  | **COVID-19** **cohort****n=23** | **Not knowingly infected****n=164** | **Difference in proportion** |
| **Demographic characteristics** |  |  |  |
| Age, median (IQR), yearsRange of age, years | 45 (36-52)21-62 | 49 (36-59)21-86 | ns, 0.114 |
| Female sex, n (%) | 19 (83) | 121 (74) | ns, p=0.361 |
| BMI, median (IQR), kg/m2BMI ≥30 kg/m2, n (%) | 25 (22-27)3 (13) | 25 (22-28)29 (18) | ns; p= 0.607ns; p= 0.651 |
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| **Clinical characteristics** |  |  |  |
| Antibody status, n (%)AQP-IgG+double-seronegativeMOG-IgG+ | 15 (65)3 (13)5 (22) | 80 (49)22 (13)62 (38) | ns; p=0.270 |
| Disease duration, median (IQR), yearsaRange of disease duration, years | 9 (3-10)1-30 | 5.5 (3-11)0-67 | ns; p= 0.850 |
| EDSS, median (IQR)bRange of EDSS | 2 (1-3)0-6 | 2 (1-5)0-8 | ns; p=0.143 |
| Comorbidity, n (%)cNo comorbidity1 comorbidity≥ 2 comorbidities |

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| 12 (55) |
| 6 (27) |
| 4 (18) |

 | 68 (43)54 (34)36 (23) | ns; p=0.751 |
| Spectrum of comorbidities, n (%)dChronic respiratory disease Malignant neoplasm, CancerHypertensionRheumatic diseaseDiabetes mellitusStrokePsoriasisOther comorbidities(COVID-19 group: e. g. Hypothyroidism, HIV, Myasthenia, recurrent herpes zoster, Raynaud, psychiatric disorders) | 3 (13)2 (9)1 (4)1 (4)1 (4)1 (4)1 (4)6 (26) | 17 (10)12 (7)24 (15)22 (13)8 (5)4 (2)6 (4)36 (22) | ns, p=0.718ns, p=0.684ns, p=0.322ns, p=0.318ns, p=1.000ns, p=0.485ns, p=1.000ns, p=0.790 |
| Immunotherapy, n (%)No immunotherapyOne substanceTwo substances | 3 (13)19 (83)1 (4) | 18 (11)126 (77)20 (12) | ns, p=0.727 |
| Spectrum of immunotherapies, n (%)eRituximabAzathioprineSatralizumabOCSEculizumabTocilizumab | 13 (57)3 (13)2 (9)1 (4)1 (4)1 (4) | 80 (49)27 (17)3 (2)20 (12)12 (7)9 (6) | ns, p=0.513ns, p=1.000ns, p= 0.115ns; p=0.479ns, p=1.000ns, p=1.000 |
| aData on disease duration were missing for one case in the *‘not knowingly infected’* cohort.bFour values for EDSS were missing in the *‘not knowingly infected’* cohort.cData on comorbidities were missing for one case in the *COVID-19* cohort and six cases in the *‘not knowingly infected’* cohort.dOnly comorbidities present in the *COVID-19* cohort are shown.eOnly immunotherapies present in the *COVID-19* cohort are shown. One patient received a combination of Satralizumab and OCS.*Note:* COVID-19: coronavirus disease 2019; NMOSD: neuromyelitis optica spectrum disorders; MOGAD: MOG-antibody associated disease; AQP4-IgG: aquaporin-4 immunoglobulin G antibodies; MOG-IgG: myelin oligodendrocyte immunoglobulin G antibodies; EDSS: Expanded Disability Status Scale; HIV: human immunodeficiency virus OCS: oral corticosteroidsPercentages may not add exactly to 100% due to rounding. |

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| **eTable 8: Clinical features and outcome of patients with COVID-19** |
|  | **n (%)a** |
| COVID-19 laboratory diagnosisSARS-CoV-2 rtPCRSARS-CoV-2 rAgTSARS-CoV-2 serology | 18 (78)12 (52)3 (13) |
| SymptomsFatigueHeadacheCoughRhinitisSore throatMyalgiaArthralgiaFeverAgeusiaAnosmiaDyspneaOther symptoms | 18 (78)16 (70)15 (65)14 (61)14 (61)10 (44)10 (44)8 (35)7 (30)5 (22)4 (17)6 (26) |
| SeverityAt home treatmentHospitalizationHospitalization, supportive oxygen required  | 19 (83)3 (13)1 (4) |
| aPercentages in this column refer to the total number of patients with confirmed COVID-19 (n=23)*Note:* COVID-19: coronavirus disease 2019; SARS-CoV-2 rtPCR: real-time reverse transcription polymerase chain reaction for severe acute respiratory syndrome-CoV2; SARS-CoV-2 rAgT: rapid antigen test for severe acute respiratory syndrome-CoV2; SARS-CoV-2 serology: serologic confirmation of severe acute respiratory syndrome-CoV2 infection |

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| **eTable 9: Details on laboratory testing in cases presenting with first-time onset or relapse of MOGAD / NMOSD in temporal association to vaccination against SARS-CoV-2** |
| **Patient** | **CSF** | **Antibody diagnosis** | **Further Laboratory Diagnosis** |
| 34-year-old male, MOGAD first-time onset | WBC count: 13/μl ↑CSF Proteins* Total: 73.1 mg/dl ↑
* L-Albumin: 431 mg/dl ↑
* L-IgG: 61.1 mg/dl ↑
* L-IgA: 5.89 mg/dl ↑
* L-IgM: 1.41 mg/dl ↑
* Q-Albumin: 9.39 x10-3 ↑
* Q-IgG: 5.5 x10-3
* Q-IgA: 2.98 x10-3
* Q-IgM: 2.01 x10-3
* IgG-index: 0.59
* local synthesis of IgA: 0%
* local synthesis of IgG 0%
* local synthesis of IgM 0%

CSF lactate: 2,1 mmol/lCSF glucose: 65 mg/dl No bacterial or viral infectionMRZ reaction negativeOCBs negative (type 4) | AQP4-IgG: negative MOG-IgG: 1:100 | DBC (leukocytes ↑, haematocrit ↓, MCHC ↓)Protein in serum, total ↓CRPElectrolytes (potassium ↓)Liver function parameters (ALT ↑)Renal function parametersGlucoseANA-Abs: borderline positive, titre 1:160ENA-AbsAnti-ds-DNA-Absp/c ANCAsRFAntiphospholipid Antibodies- anticardiolipin antibodies- anti-beta 2 glycoprotein 1Lupus-sensitive and -insensitive PTTS-ACEIL-2-receptorVitamin B12Folic acid ↓Vitamin D (25-OH-Vitamin D3) ↓TSHfT3fT4TPO-AbsHIV serologyBorrelia serologyTreponemal testSARS-COV-2 rtPCR: negativeNeuronal antibodies (Yo, Hu, Ri, Amphiphysin, CV2/CRMP-5, Ma1, Ma2, GAD, SOX1, Tr, Zic4, Titin, Recoverin, PKCgamma)Autoimmune encephalitis antibodies (NMDA, AMPAR1/2, DPPX, CASPR2, LGI1, GABARb1/b2) |
| 35-year-old male, MOGAD first-time onset | WBC count: 142/μl ↑CSF Proteins* Total: 51.4 mg/dl ↑
* L-Albumin: 36.9 mg/dl ↑
* L-IgG: 5.01 mg/dl ↑
* L-IgA: 1.03 mg/dl ↑
* L-IgM: 0.29 mg/dl ↑
* Q-Albumin: 9.0 x10-3 ↑
* Q-IgG: 4.39 x10-3
* Q-IgA: 3.24 x10-3
* Q-IgM: 1.69 x10-3
* IgG-index: 0.49
* local synthesis of IgA: 0%
* local synthesis of IgG 0%
* local synthesis of IgM 0%

CSF lactate: 2,4 mmol/lCSF glucose: 59.6 mg/dl No bacterial or viral infectionOCBs negative (type 1) | AQP4-IgG: negative MOG-IgG: 1:1000 | DBC (leukocytes ↑, haematocrit ↓, RDW ↓, neutrophils ↑, lymphocytes ↓)CRP ↑ElectrolytesLiver function parametersRenal function parametersGlucoseANA-AbsENA-AbsAnti-ds-DNA-Absp/c ANCAsRFAntiphospholipid Antibodies* anticardiolipin antibodies
* anti-beta 2 glycoprotein 1
* anti-phosphatidyl serine

TSH ↓fT3fT4Borrelia serologyTreponemal testSARS-COV-2 rtPCR: negative |
| 64-year-old male, MOGAD first-time onset | WBC count: 5,7/μl ↑CSF Proteins* Total: 47.3 mg/dl
* L-Albumin: 26.4 mg/dl ↑
* L-IgG: 2.58 mg/dl ↑
* L-IgA: 0.69 mg/dl ↑
* L-IgM: 0.02 mg/dl ↑
* Q-Albumin: 6.2 x10-3
* Q-IgG: 3.33 x10-3
* Q-IgA: 1.87 x10-3
* Q-IgM: 0.29 x10-3
* IgG-index: 0.54

CSF lactate: 2,67 mmol/l ↑No bacterial or viral infectionMRZ reaction negativeOCBs negative (type 4) | AQP4-IgG: negativeMOG-IgG: 1:200 | BCProtein in serum, total↓CRPElectrolytes Liver function parameters Renal function parameters (eGFR ↓)GlucoseANA-AbsENA-AbsAnti-ds-DNA-Absp/c ANCAsRFAntiphospholipid Antibodies- anticardiolipin antibodiesS-ACEVitamin B12Folic acidVitamin D (25-OH-Vitamin D3)TSHfT3fT4TPO-AbsSARS-COV-2 rtPCR: negative |
| 36-year-old female, NMOSD relapse, disease duration 4 years | Not done | AQP4-IgG: negativeMOG-IgG: negative | DBC (thrombocytes ↑, neutrophils ↑, lymphocytes ↓)CRPElectrolytes Liver function parameters Renal function parameters TSHSARS-COV-2 rtPCR: negative |
| **Values outside the standard range are marked (↑: increased; ↓: decreased) and, if indicated, specified in brackets.***Note:* MOGAD: MOG-antibody associated disease; NMOSD: neuromyelitis optica spectrum disorders; CSF: cerebrospinal fluid; WBC: white blood cell count; IgG: immunoglobulin G; IgA: immunoglobulin A; IgM: immunoglobulin M; MRZ reaction: intrathecal humoral immune response against-Measles (M), Rubella (R) and Varicella Zoster (Z) viruses; OCBs: oligoclonal bands; AQP4-IgG: aquaporin-4 immunoglobulin G antibodies; MOG-IgG: myelin oligodendrocyte glycoprotein immunoglobulin G antibodies; analysed by cell-based assay; DBC: differential blood count; MCHC: mean corpuscular hemoglobin concentration; CRP: C-reactive protein; ALT: Alanine transaminase; ANA-Abs: antinuclear antibodies; ENA-Abs: extractable nuclear antigen antibodies; Anti-ds-DNA-Abs: anti-double stranded DNA antibodies; p/c ANCAs: Anti-neutrophil cytoplasmic antibodies; RF: Rheumatoid factor; PTT: partial thromboplastin time; S-ACE: Serum Angiotensin Converting Enzyme; IL-2-receptor: Interleukin-2 receptor; TSH: thyroid stimulating hormone; fT3: free triiodothyronine; fT4: free thyroxine; TPO-Abs: thyroid peroxidase antibodies; SARS-CoV-2 rtPCR: real-time reverse transcription polymerase chain reaction for severe acute respiratory syndrome-CoV2; RDW: Red Cell Distribution Width; eGFR: estimated glomerular filtration rate |