# 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** |
| Hypertension  Rheumatic disease  Chronic respiratory disease  Malignant neoplasm, Cancer  Diabetes mellitus  Psoriasis  Coronary heart disease  Chronic liver disease  Stroke  Chronic kidney disease  Peripheral artery disease  Inflammatory bowel disease  Other comorbidities | 25  23  20  14  9  7  6  6  5  4  1  1  42 | 14  13  11  8  5  4  3  3  3  2  <1  <1  23 |
| 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** | **%** |
| Rituximab  Azathioprine  Eculizumab  Tocilizumab  Prednisolone or other oral corticosteroids  Methotrexate  Satralizumab  Mycophenolate mofetil  IVIG  Glatiramer acetate  Ruxolitinib  Ocrelizumab  All | 84  26  11  7  6  2  2  2  2  1  1  1  145 | 58  18  8  5  4  1  1  1  1  <1  <1  <1  78a |
| **Immunotherapy, combinations of two substances**  Rituximab, OCS  Azathioprine, OCS  Rituximab, methotrexate  Eculizumab, OCS  Tocilizumab, OCS  Satralizumab, OCS  Methotrexate, satralizumab  Methotrexate, tocilizumab  Rituximab, azathioprine  Mycophenolate mofetil, OCS  All | **n**  5  3  3  2  2  2  1  1  1  1  21 | **%**  24  14  14  10  10  10  5  5  5  5  11a |
| 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 change  Paused  Dosing change  Stopped  Medication change  Paused + dose interval changed | | 21  6  6  5  2  1  1 | | 12  29b  29  24  10  5  5 |
| Change carried out byc  Neurologist  Patient alone  NEMOS center  Other | | 9  5  4  2 | | 43  24  19  10 |
| 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 on  Implications of immunosuppressive medications for SARS-CoV-2 vaccination  Prevention measures  Procedure in case of SARS-CoV-2 infection  Disease 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 field  More staff  More 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 pandemic  If problems occur, it should be easier to get a complete diagnostic workup in the hospital  Improvement of daily life (fatigue, weakness, nausea)  Improvement of spastic | 3 (8) |
| *Note:* SARS-CoV-2: severe acute respiratory syndrome coronavirus type 2  Percentages 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 2  Percentages 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), years  Range 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/m2  BMI ≥30 kg/m2, n (%) | 25 (22-27)  3 (13) | 25 (22-28)  29 (18) | ns; p= 0.607  ns; p= 0.651 |
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| **Clinical characteristics** |  |  |  |
| Antibody status, n (%)  AQP-IgG+  double-seronegative  MOG-IgG+ | 15 (65)  3 (13)  5 (22) | 80 (49)  22 (13)  62 (38) | ns; p=0.270 |
| Disease duration, median (IQR), yearsa  Range of disease duration, years | 9 (3-10)  1-30 | 5.5 (3-11)  0-67 | ns; p= 0.850 |
| EDSS, median (IQR)b  Range of EDSS | 2 (1-3)  0-6 | 2 (1-5)  0-8 | ns; p=0.143 |
| Comorbidity, n (%)c  No comorbidity  1 comorbidity  ≥ 2 comorbidities | |  | | --- | | 12 (55) | | 6 (27) | | 4 (18) | | 68 (43)  54 (34)  36 (23) | ns; p=0.751 |
| Spectrum of comorbidities, n (%)d  Chronic respiratory disease  Malignant neoplasm, Cancer  Hypertension  Rheumatic disease  Diabetes mellitus  Stroke  Psoriasis  Other 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=0.718  ns, p=0.684  ns, p=0.322  ns, p=0.318  ns, p=1.000  ns, p=0.485  ns, p=1.000  ns, p=0.790 |
| Immunotherapy, n (%)  No immunotherapy  One substance  Two substances | 3 (13)  19 (83)  1 (4) | 18 (11)  126 (77)  20 (12) | ns, p=0.727 |
| Spectrum of immunotherapies, n (%)e  Rituximab  Azathioprine  Satralizumab  OCS  Eculizumab  Tocilizumab | 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=0.513  ns, p=1.000  ns, p= 0.115  ns; p=0.479  ns, p=1.000  ns, 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 corticosteroids  Percentages 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 diagnosis  SARS-CoV-2 rtPCR  SARS-CoV-2 rAgT  SARS-CoV-2 serology | 18 (78)  12 (52)  3 (13) |
| Symptoms  Fatigue  Headache  Cough  Rhinitis  Sore throat  Myalgia  Arthralgia  Fever  Ageusia  Anosmia  Dyspnea  Other 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) |
| Severity  At home treatment  Hospitalization  Hospitalization, 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/l  CSF glucose: 65 mg/dl  No bacterial or viral infection  MRZ reaction negative  OCBs negative (type 4) | AQP4-IgG: negative  MOG-IgG: 1:100 | DBC (leukocytes ↑, haematocrit ↓, MCHC ↓)  Protein in serum, total ↓  CRP  Electrolytes (potassium ↓)  Liver function parameters (ALT ↑)  Renal function parameters  Glucose  ANA-Abs: borderline positive, titre 1:160  ENA-Abs  Anti-ds-DNA-Abs  p/c ANCAs  RF  Antiphospholipid Antibodies  - anticardiolipin antibodies  - anti-beta 2 glycoprotein 1  Lupus-sensitive and -insensitive PTT  S-ACE  IL-2-receptor  Vitamin B12  Folic acid ↓  Vitamin D (25-OH-Vitamin D3) ↓  TSH  fT3  fT4  TPO-Abs  HIV serology  Borrelia serology  Treponemal test  SARS-COV-2 rtPCR: negative  Neuronal 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/l  CSF glucose: 59.6 mg/dl  No bacterial or viral infection  OCBs negative (type 1) | AQP4-IgG: negative  MOG-IgG: 1:1000 | DBC (leukocytes ↑, haematocrit ↓, RDW ↓, neutrophils ↑, lymphocytes ↓)  CRP ↑  Electrolytes  Liver function parameters  Renal function parameters  Glucose  ANA-Abs  ENA-Abs  Anti-ds-DNA-Abs  p/c ANCAs  RF  Antiphospholipid Antibodies   * anticardiolipin antibodies * anti-beta 2 glycoprotein 1 * anti-phosphatidyl serine   TSH ↓  fT3  fT4  Borrelia serology  Treponemal test  SARS-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 infection  MRZ reaction negative  OCBs negative (type 4) | AQP4-IgG: negative  MOG-IgG: 1:200 | BC  Protein in serum, total↓  CRP  Electrolytes  Liver function parameters  Renal function parameters (eGFR ↓)  Glucose  ANA-Abs  ENA-Abs  Anti-ds-DNA-Abs  p/c ANCAs  RF  Antiphospholipid Antibodies  - anticardiolipin antibodies  S-ACE  Vitamin B12  Folic acid  Vitamin D (25-OH-Vitamin D3)  TSH  fT3  fT4  TPO-Abs  SARS-COV-2 rtPCR: negative |
| 36-year-old female, NMOSD relapse, disease duration 4 years | Not done | AQP4-IgG: negative  MOG-IgG: negative | DBC (thrombocytes ↑, neutrophils ↑, lymphocytes ↓)  CRP  Electrolytes  Liver function parameters  Renal function parameters  TSH  SARS-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 | | | |