SARS-CoV-2 Vaccination Safety in Guillain-Barré Syndrome, Chronic Inflammatory Demyelinating Polyneuropathy, and Multifocal Motor Neuropathy.

Author(s):
Adája E. Baars, MD 1; Krista Kuitwaard, MD PhD 1, 2; Laura C. de Koning, BSc 1; Linda W G Luijten, MD 1, 3; W. Maaike Kok, BSc 1; Filip Eftimov, MD, PhD 4; Luuk Wieske, MD PhD 4; H. Stephan Goedee, MD PhD 5; Ludo van der Pol 5; Patricia H. Blomkwist - Markens 6; Anja M.C. Horemans, MD PhD 4; Bart C Jacobs, MD, PhD 1, 7; Pieter A van Doorn, MD PhD 1

Corresponding Author:
Pieter A van Doorn, p.a.vandoorn@erasmusmc.nl

Affiliation Information for All Authors:
1. Department of Neurology, Erasmus MC University Medical Center, Rotterdam, The Netherlands; 2. Department of Neurology, Albert Schweitzer Hospital, Dordrecht, The Netherlands; 3. St Elisabeth-TweeSteden Hospital, Tilburg, The Netherlands; 4. Department of Neurology, Amsterdam University Medical Center, University of Amsterdam, The Netherlands; 5. Department of Neurology and Neurosurgery, Brain Center University Medical Center Utrecht, Utrecht, The Netherlands; 6. Dutch Patient Organization for Neuromuscular Diseases, Baarn, The Netherlands; 7. Department of Immunology, Erasmus MC University Medical Center, Rotterdam, The Netherlands.

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Contributions:
Adäja E. Baars: Drafting/revision of the manuscript for content, including medical writing for content; Major role in the acquisition of data; Study concept or design; Analysis or interpretation of data
Krista Kuitwaard: Drafting/revision of the manuscript for content, including medical writing for content; Major role in the acquisition of data; Study concept or design; Analysis or interpretation of data
Laura C. de Koning: Drafting/revision of the manuscript for content, including medical writing for content; Major role in the acquisition of data; Study concept or design; Analysis or interpretation of data
Linda W G Luijten: Drafting/revision of the manuscript for content, including medical writing for content; Major role in the acquisition of data; Study concept or design; Analysis or interpretation of data
W. Maaike Kok: Drafting/revision of the manuscript for content, including medical writing for content; Major role in the acquisition of data; Study concept or design; Analysis or interpretation of data
Filip Eftimov: Drafting/revision of the manuscript for content, including medical writing for content; Major role in the acquisition of data; Study concept or design; Analysis or interpretation of data
Lauk Wieske: Drafting/revision of the manuscript for content, including medical writing for content; Major role in the acquisition of data; Study concept or design; Analysis or interpretation of data
H. Stephan Goedee: Drafting/revision of the manuscript for content, including medical writing for content; Major role in the acquisition of data; Study concept or design; Analysis or interpretation of data
Ludo van der Pol: Drafting/revision of the manuscript for content, including medical writing for content; Major role in the acquisition of data; Study concept or design; Analysis or interpretation of data
Patricia H. Blomkwist - Markens: Drafting/revision of the manuscript for content, including medical writing for content; Major role in the acquisition of data; Study concept or design; Analysis or interpretation of data
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Pieter A van Doorn: Drafting/revision of the manuscript for content, including medical writing for content; Major role in the acquisition of data; Study concept or design; Analysis or interpretation of data

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Abstract

Background and Objectives. There are concerns on the safety of SARS-CoV-2 vaccination in patients with a history of Guillain-Barré syndrome (GBS), chronic inflammatory demyelinating polyneuropathy (CIDP), and multifocal motor neuropathy (MMN). The aim of this study is to determine the risk of recurrence of GBS, and exacerbations of CIDP or MMN following SARS-CoV-2 vaccination.

Methods. We conducted a prospective, multicenter cohort study from January 2021 to August 2021. Patients known in one of three Dutch University Medical Centers with research focus on immune-mediated neuropathy, and members of the Dutch Patient Association for Neuromuscular Diseases were invited to participate if they were 18 years or older, and diagnosed with GBS, CIDP or MMN.

Participants completed a series of questionnaires at four different time points: study baseline (1), within 48 hours before any SARS-CoV-2 vaccination (2 and 3, if applicable), and six weeks after their last vaccination (4). Participants unwilling to get vaccinated completed the last questionnaire (4) four months after study baseline. We assessed recurrences of GBS, any worsening of CIDP or MMN related symptoms, treatment alterations, and hospitalization.

Results. Of 1152 individuals to whom we sent the questionnaires, 674 (59%) signed informed consent. We excluded 153 individuals, most often because they had already received a SARS-CoV-2 vaccination or had had the infection (84%) prior to study baseline. Of 521 participants included in analyses, 403 (81%) completed the last questionnaire (time point 4). None of 162 participants with a history of GBS had a recurrence after vaccination. Of 188 participants with CIDP, ten participants (5%) reported a worsening of symptoms within six weeks following vaccination. In five (3%) of these patients, maintenance treatment
was modified. Two out of 53 participants with MMN (4%) reported a worsening of symptoms, and treatment modification was reported by one participant.

Discussion. We found no increased risk of GBS recurrence, and a low to negligible risk of worsening of CIDP or MMN related symptoms following SARS-CoV-2 vaccination. Based on our data, SARS-CoV-2 vaccination in patients with these immune-mediated neuropathies appears to be safe.

Introduction
The introduction of SARS-CoV-2 vaccinations is an important milestone in the COVID-19 pandemic. However, patients with a history of an immune-mediated neuropathy are often concerned about the safety of vaccinations, because of a possible recurrence of Guillain-Barré syndrome (GBS) or exacerbations of chronic inflammatory demyelinating polyneuropathy (CIDP) or multifocal motor neuropathy (MMN).1,2

GBS usually is a monophasic disease with severe muscle weakness, which is followed by recovery to a variable extent and duration.3 CIDP and MMN are chronic polyneuropathies requiring long-term treatment, usually with intravenous immunoglobulins (IVIg) or corticosteroids. In SARS-CoV-2 vaccination phase III trials, individuals with a prior diagnosis of GBS, or receiving IVIg or systemic corticosteroids within months prior to study vaccine administration were excluded from participation.4-7 Therefore, data from these trials with regard to safety of SARS-CoV-2 vaccinations cannot instantaneously be extrapolated to most of the patients with these immune-mediated neuropathies.

Concerns regarding safety of vaccination and immune-mediated neuropathies stem from an described eightfold increased incidence rate of GBS post-vaccination during the H1N1 influenza vaccination campaign in 1976.8,9 Similar correlations have not been observed since, although temporal associations between vaccination and GBS have been reported.10-13 GBS has an estimated life-time recurrence risk between 3.5% and 6.6%.12,14-17 No GBS recurrences were reported within six weeks after seasonal flu vaccination or after various
other vaccines, such as pneumovax and Hepatitis A and B.\textsuperscript{17-18} The pathophysiological mechanisms between vaccinations and the occurrence of GBS after vaccinations however remains unclear.\textsuperscript{19} Despite these more recent studies, GBS is still listed as an adverse event of special interest in pharmacovigilance studies to ensure early detection of a potential association with any new vaccine.\textsuperscript{20}

For CIDP and MMN, no increased incidence has been reported after any vaccination, such as seasonal flu vaccination. In a retrospective study, three out of 65 patients with CIDP reported that they had experienced symptoms similar to a typical relapse of CIDP after receiving a vaccination.\textsuperscript{12}

In the general population, an increased incidence of GBS in the 28 days following vaccination with ChAdOx1nCoV-19 (AstraZeneca) has been observed.\textsuperscript{21} Following increased signals of GBS incidence in passive reporting systems, safety warnings were issued for both ChAdOx1nCoV-19 (AstraZeneca) and Ad26.COV2.S (Janssen/Johnson & Johnson).\textsuperscript{22, 23} However, an association between SARS-CoV-2 infection and an increased incidence of GBS has also been described, and this association was much stronger than for SARS-CoV-2 vaccinations.\textsuperscript{21, 24} This highlights the value of preventing SARS-CoV-2 infections, especially in patients with immune-mediated neuropathies, if SARS-CoV-2 vaccines can be safely administered in patients who have had GBS.

The scale of the SARS-CoV-2 vaccination campaigns created a unique opportunity to investigate the possible relationship between SARS-CoV-2 vaccination and the course of disease in immune-mediated neuropathies. The objective of this study is to explore the risk of recurrence of GBS or worsening of disease related symptoms in CIDP and MMN following SARS-CoV-2 vaccination.
Methods

Setting and Participants

This study is a collaboration between three University Medical Centers with a research focus on immune-mediated neuropathies (Erasmus University Medical Center Rotterdam, Amsterdam University Medical Centers, and University Medical Center Utrecht) and the Dutch Patient Association for neuromuscular diseases (Spierziekten Nederland). Patients known with a prior diagnosis of GBS, CIDP, or MMN, aged 18 years or older, were considered eligible to participate. After written informed consent was obtained, we evaluated medical records to confirm the diagnosis in participants who participated via the Dutch Patient Association, to confirm any prior recurrences of GBS, and to gain insight in the course of disease of CIDP and MMN. We excluded individuals who had already received a SARS-CoV-2 vaccination or had tested positive for SARS-CoV-2 before study entry from analyses to prevent recall bias. This study follows the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) reporting guideline.

Standard Protocol Approvals, Registrations and Patient Consents

Approval of the Medical Ethics Committee of Erasmus Medical Center in Rotterdam (MEC-2021-0103) was obtained for Erasmus University Medical Center Rotterdam and Amsterdam University Medical Centers, and separately, upon request, for the Medical Ethics Committee of University Medical Center Utrecht (METC-21/253). Written informed consent was obtained from all participants in the study.

Study Design

We conducted a prospective, multicenter cohort study, using disease specific questionnaires consisting of different subsets corresponding to predefined time points. These time points are: study baseline (1), within 48 hours prior of (each) SARS-CoV-2 vaccination (2 and 3, if
applicable), and either six weeks after the last SARS-CoV-2 vaccination or four months after baseline assessment (4), see Figure 1.

Participants who chose not to be vaccinated were asked to fill out the last subset of the questionnaire (time point 4) four months after completing the baseline subset (time point 1), as we estimated that the period of time between these two time points would then be comparable for both vaccinated and unvaccinated participants.

At baseline, participants completed items on disease history, current treatment status, and the presence of potential disease triggers, such as infections and vaccinations, within 6 weeks prior to the onset of the first symptoms of GBS, CIDP or MMN. Self-reported data on demographics, current comorbidities and use of medication were collected as well. Within 48 hours prior to receiving a SARS-CoV-2 vaccination (time points 2 and 3), participants completed items on current disease related symptoms and treatment. This included items with regard to disease related symptoms such as weakness in arms or legs, sensory symptoms, fatigue, and muscle aches. In the last subset (time point 4) of the questionnaire, participants reported current disease related symptoms, experienced changes in their disease course, and treatment alterations, as well as any SARS-CoV-2 infection since baseline (time point 1).

At time points 2 and 4, standardized questionnaires regarding disability and quality of life were included to objectively assess any changes, namely the Inflammatory Rasch-built Overall Disability Scale (I-RODS) and the EuroQol-5D-5L(EQ-5D-5L).25, 26

The outcome of interest in this study is any self-reported deterioration in disease related complaints. For GBS, deterioration was defined as any reported recurrence of GBS, initiation of immunomodulatory treatment or hospitalization. In CIDP and MMN, disease related complaints were defined as any reported worsening of disease related symptoms, alteration in maintenance therapy, or hospitalization. If the reported change in disease related symptoms consisted exclusively of fatigue and/or muscle aches, these were regarded as nonspecific. A decrease of four or more centile points on the I-RODS between time points 2
and 4 was considered a minimal clinical important difference.\textsuperscript{27} The Paretian Classification of Health Change (PCHC) was used to summarize changes in the reported EQ-5D health status at time points 2 and 4.\textsuperscript{28}

Recurrences or worsening in disease related symptoms within six weeks after immunization were considered as possibly causally related to SARS-CoV-2 vaccination. The time period of six weeks between the last vaccination (either time point 2 or 3) and the completion of the last subset (time point 4) was chosen as the increased incidence of GBS after swine flu vaccination in 1976 was described within this same time period.\textsuperscript{9}

We considered any new symptoms or worsening of existing symptoms occurring 48 hours post-vaccination most likely to be a side-effect of the vaccination itself and not caused by a reactivation of patients’ immune-mediated neuropathy.\textsuperscript{29}

We contacted participants reporting a recurrence or deterioration during the course of the study for a structured phone interview, and requested additional information from their treating physicians. Participants were asked about any recent infections, surgery or new concomitant diagnoses, contact with their neurologist, the rationale for any changes in therapy during follow-up, and other potentially relevant events that might have contributed to a change in experienced disease activity. In addition, patients were asked whether their symptoms had resolved, and whether they would be willing to get a subsequent SARS-CoV-2 vaccine in the future. If participants stated that disease progression was present before vaccination and they did not experience sudden further deterioration after receiving a SARS-CoV-2 vaccine, we considered the worsening of symptoms unrelated.

\textit{Statistical analysis}

Statistical analyses were conducted with SPSS Statistics, version 27. Numerical variables were described using median (interquartile range), and categorical variables as absolute number (percentage). Missing values were not imputed.
Data availability

The data supporting the findings of this study are available upon reasonable request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

Results

Participants

A total of 1152 individuals were invited to participate. The three University Medical Centers invited 348 eligible patients with a history of GBS, 458 with CIDP, and 103 with MMN to participate. Members of the Dutch patient association for neuromuscular diseases with GBS, CIDP or MMN were asked to contact the investigators to participate if they were eligible and interested in participating, which 243 of the 500 invited members did. Participants were included between February 20th, 2021, and August 27th, 2021. Informed consent was signed by 245 participants with a prior diagnosis of GBS, 325 participants with a prior or current diagnosis of CIDP, and 104 participants with a prior or current diagnosis of MMN, which corresponds to a response rate of 59% according to the AAPOR guideline. A total of 478 (41%) individuals did not participate (Figure 2). We excluded 153 participants for not having an immune-mediated neuropathy at baseline, a significant lack of data, or reporting a SARS-CoV-2 vaccination or –infection prior to study entry. This resulted in a study cohort of 521 participants (Figure 2). We were able to verify 81% of GBS, CIDP, and MMN diagnoses by screening requested medical records for 155 participants that were included via the Dutch patient association. Of the 521 participants, 403 (77%) completed and returned the last subset after vaccination (time point 4): 162 of 195 (83%) individuals with a prior diagnosis of GBS, 188 of 248 (76%) individuals with CIDP, and 53 of 78 (68%) individuals with MMN.

Baseline characteristics
The majority of the participants were male (59%), the median age was 64 years (interquartile range, 55-72 years), and the median time since diagnosis was 9 years (interquartile range 5-18 years) (Table 1). Of the 215 participants with CIDP completing the item, 156 (73%) reported that they received maintenance treatment for their diagnosis, as did 73 of 75 (97%) participants with MMN. Maintenance treatment for CIDP consisted of immunoglobulins in 119 participants (76%; 109 intravenous, 7 subcutaneous), corticosteroids in 26 (17%), and plasmapheresis in 11 participants (7%). A recurrence of GBS prior to study entry was reported by 15 participants. Ten recurrences could be confirmed and the other five were not considered recurrences after critically reviewing the medical records.

Symptoms of infection in the six weeks prior to the onset of neurological symptoms were reported by 125 of 194 (64%) participants with GBS, most often gastro-intestinal symptoms. For CIDP, 54 of 177 participants (31%) reported preceding infectious symptoms, most often flu.

Nine participants with GBS and ten with CIDP reported a vaccination in the six weeks prior to the onset of their neurological symptoms. More specifically, five of the participants with GBS and five with CIDP reported a flu vaccination. Two participants with CIDP and one with GBS reported a hepatitis vaccination. Other vaccinations reported prior to GBS were pneumococcal, meningococcal, and typhoid vaccination. One CIDP participant reported a combined pneumococcal and flu vaccination prior to onset of neurological symptoms. Of all participants, 37 (7%) reported that they had been advised against any particular vaccination in the past by their physician, and 81 (16%) were either uncertain or unwilling to get a SARS-CoV-2 vaccination. Most often, participants reported uncertainty on the safety of the vaccine with regard to their diagnosis of immune-mediated neuropathy as the reason for their hesitancy.

Course of disease following SARS-CoV-2 vaccination

In total, 465 participants received 844 vaccinations during the course of this study. Most participants, 302 (65%), received at least one BNT162b2 (Pfizer/BioNTech) vaccine, 69
(15%) a ChadOx-1nCoV-19 (AstraZeneca), 36 (8%) mRNA-1273 (Moderna), and 12 (3%) Ad26.COV2.S (Jansen/Johnson&Johnson). Nineteen (4%) participants did not obtain a SARS-CoV-2 vaccination during study follow-up. One of these participants with CIDP reported worsening of weakness, sensory symptoms and fatigue, resulting in a change in maintenance treatment. At time point 4, six participants reported that they had received a positive SARS-CoV-2 PCR test result since study commencement.

There were no recurrences of GBS following SARS-CoV-2 vaccination. One of 162 participants with a prior diagnosis of GBS did report a recurrence of symptoms after SARS-CoV-2 vaccination, which resulted in hospital admission. However, after critically reviewing the medical records, it appeared that the symptoms and signs were due to lumbar spinal stenosis, for which the patient underwent decompressive surgery, resulting in resolution of symptoms. Therefore, this case was not considered as a recurrence of GBS. Of the 27 participants contacted for having not completed the final questionnaire, 17 confirmed that they had not experienced a recurrence of GBS and were included in the analysis; ten participants did not reply.

Ten of 188 (5%) participants with CIDP reported a worsening in disease related symptoms following SARS-CoV-2 vaccination, such as weakness and/or sensory disturbances (Table 2). However, none contacted their neurologist for an unscheduled evaluation for these symptoms (Table 2). Five of these ten participants did report an alteration in their treatment regimen. In all except one of the patients who were able to estimate the time to normalization of symptoms, the symptoms resolved within 4 weeks. In one patient it took 8 weeks. Three of the ten participants had a deterioration corresponding to minimal clinical important difference on the I-RODS at time point 4. All of the ten participants stated they would obtain a booster vaccination when available.

For MMN, a worsening of disease related symptoms was reported by two of 53 (4%) participants (time point 4). One patient received additional treatment with IVIg six weeks after vaccination, where after the symptoms resolved.

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Discussion

Key results

No increased risk of recurrence of GBS following SARS-CoV-2 vaccination was found in this study. A small number of participants with CIDP and MMN reported that they had experienced a worsening of disease related symptoms during the study period. The majority of these participants reported having a fluctuating course of disease prior to SARS-CoV-2 vaccination. Other possible explanations for disease fluctuations, such as concurrent infections or a recent tapering attempt of maintenance treatment, were reported as well. Although changes to maintenance treatment regimens were made in six participants, the worsening of symptoms was self-limited in most participants. None required a restart of treatment.

Interpretation

One retrospective cohort study evaluated the risk of recurrence of GBS following vaccination with BNT162b2 (Pfizer/BioNTech) using the registrations of all hospital visits of 702 patients previously diagnosed with GBS. A recurrence of GBS following the second dose of BNT162b2 (Pfizer/BioNTech) vaccine was found in only one patient. In contrast, we conducted a prospective population based cohort study. The study design allowed for comparison before and after exposure to any SARS-CoV-2 vaccine. We were able to further estimate the impact on the course of disease in all participants independent of whether or not they sought help from a hospital based physician.

Various case reports on the temporal association between incident cases of GBS and SARS-CoV-2 vaccination have been published since the commencement of national vaccination programs. However, a study describing an incident case of GBS in both the intervention and placebo arm in the phase II trial for the Ad26.COV2.S (Janssen/Johnson & Johnson) vaccine illustrates that a temporal association is not necessarily indicative of a
causal association. A recent study showed an increased incidence rate ratio for GBS after vaccination with the ChAdOx-1nCoV-19 (AstraZeneca) vaccine, although the incidence rate ratio following a positive SARS-CoV-2 PCR test was larger. An excess GBS risk of 0.576 per 100,000 administered doses of ChAdOx-1nCoV-19 (AstraZeneca) was also found in a nationwide observational study. Another study found no association between the administration of 11,845,128 doses of BNT162b2 (Pfizer/BioNTech) vaccinations and incident cases GBS in the following six weeks.

To our knowledge, there are no studies describing the safety of SARS-CoV-2 vaccinations in patients with either CIDP or MMN. However, our results are similar to studies on the safety of the BNT162b2 (Pfizer/BioNTech) vaccine in patients with multiple sclerosis. Asking patients about experienced adverse effects after exposure to vaccinations might induce a nocebo effect. A negative attitude towards vaccination might lead participants to overreport a change in disease related symptoms. Therefore, detailed data on the severity of symptoms, whether symptoms had resolved, and their attitude towards subsequent SARS-CoV-2 vaccinations were obtained by contacting participants. We also contacted their treating neurologist, with permission of the participants, to verify the severity of the change in symptoms. Our study indicated that, despite several reports of a change in disease related symptoms, most participants concluded that these changes were temporary, and still had a positive attitude towards SARS-CoV-2 vaccinations. Spontaneous disease fluctuations cannot be excluded as these are frequently seen in CIDP, with one study reporting disease fluctuations in 52% of CIDP patients.

Limitations

Our study has several limitations. First, patients with either residual symptoms or active disease may have been more inclined to participate, introducing selection bias. In contrast, individuals without any current disease related symptoms might have been less inclined to participate, while also being potentially at risk for disease recurrence or exacerbation.
Overrepresentation of more severely affected patients might have resulted in an overestimation of the impact of SARS-CoV-2 vaccination on the course of disease. The majority of the participants with CIDP or MMN reporting a worsening of their disease related symptoms also reported having a fluctuating course of disease prior to SARS-CoV-2 vaccination. This might have resulted in an overestimation of the effect of SARS-CoV-2 vaccination on the course of disease. Second, participants may have underreported disease related symptoms that had already resolved or which they considered unrelated. Third, the majority of the participants received a vaccination with BNT162b2 (Pfizer/BioNTech). Only 23 participants with a history of GBS received a ChAdOx1nCoV-19 (AstraZeneca), and twelve participants in total received Ad26.COV2.S (Janssen/Johnson&Johnson). These subgroups are too small to draw any conclusions. Lastly, this study is mainly based on patient reported data. Medical records to verify the diagnosis could not be obtained for all participants. However, we verified patient reports by additional phone interviews, and by evaluating data supplied by treating physicians. An important limitation in the reported worsening in disease course is the lack of objective confirmation, either by using grip strength measurement tools or by treating neurologists, which might have resulted in an overestimation. Not all participants completed the last subset of the questionnaire (time point 4), and not all of these participants responded to attempts to seek contact. Therefore, we cannot rule out that these participants had a recurrence of GBS.

Conclusion

This study indicates no increased risk for recurrence of GBS or severe disease exacerbations in CIDP and MMN post-SARS-CoV-2 vaccination. The reported worsening of disease related symptoms post-SARS-CoV-2 vaccination was mild, and did not require treatment alteration in most participants. Symptoms resolved within several weeks in most participants, and none required hospitalization.
References


Table 1 Characteristics of all participants with Guillain-Barré syndrome (GBS), CIDP and MMN

<table>
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<tr>
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<th>GBS</th>
<th>CIDP</th>
<th>MMN</th>
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<tr>
<td></td>
<td>n = 195 (37)</td>
<td>n = 248 (48)</td>
<td>n = 78 (15)</td>
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<tr>
<td>Male</td>
<td>98 (50)</td>
<td>150 (60)</td>
<td>58 (74)</td>
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<tr>
<td>Age at diagnosis</td>
<td>48 (34 - 57)</td>
<td>55 (47 - 64)</td>
<td>47 (40 - 52)</td>
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<tr>
<td>Study baseline (time point 1)</td>
<td></td>
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<tr>
<td>Age</td>
<td>66 (54 - 72)</td>
<td>66 (57 - 72)</td>
<td>59 (52 - 65)</td>
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<tr>
<td>Years since diagnosis</td>
<td>15 (7 - 23)</td>
<td>6 (3 - 13)</td>
<td>10 (5 - 17)</td>
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<td>Number of participants receiving maintenance treatment*</td>
<td>156/215 (73)</td>
<td>73/75 (97)</td>
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<tr>
<td>IVIg</td>
<td>119 (76)</td>
<td>72 (99)</td>
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<td>CS</td>
<td>26 (17)</td>
<td>1 (1)</td>
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<tr>
<td>Plasmapheresis</td>
<td>11 (7)</td>
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<td>Number of participants willing to vaccinate (%)</td>
<td>145/187 (78)</td>
<td>211/237 (89)</td>
<td>65/78 (83)</td>
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<tr>
<td>Uncertain</td>
<td>31 (17)</td>
<td>22 (9)</td>
<td>12 (15)</td>
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<tr>
<td>Unwilling</td>
<td>11 (6)</td>
<td>4 (2)</td>
<td>1 (1)</td>
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Data are formatted as absolute number (%) or median (interquartile range).
Abbreviations: GBS = Guillain-Barré syndrome, CIDP = chronic inflammatory demyelinating polyneuropathy, MMN = multifocal motor neuropathy, IVIg = intravenous immunoglobulins, CS = corticosteroids.

* Not including participants in whom treatment was discontinued prior to study baseline
Table 2 Patient reported worsening of disease related symptoms in CIDP and MMN patients ≤6 weeks after SARS-CoV-2 vaccination

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<td><strong>BASELINE (TIME POINT 1)</strong></td>
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<td>74</td>
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<tr>
<td>Maintenance treatment</td>
<td>IVIg</td>
<td>IVIg</td>
<td>None</td>
<td>CS</td>
<td>IVIg</td>
<td>Trial</td>
<td>IVIg</td>
<td>IVIg</td>
<td>IVIg</td>
<td>IVIg</td>
<td>IVIg</td>
<td>IVIg</td>
</tr>
<tr>
<td>Fluctuating course of disease, ongoing from before vaccination*</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>-</td>
<td>+</td>
<td>+</td>
<td>-</td>
<td>+</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td><strong>FOLLOWING VACCINATION (TIME POINT 4)</strong></td>
<td></td>
<td></td>
<td></td>
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<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Vaccine Brand</td>
<td>P</td>
<td>P</td>
<td>M</td>
<td>AZ</td>
<td>P</td>
<td>P</td>
<td>P</td>
<td>P</td>
<td>P</td>
<td>AZ</td>
<td>P</td>
<td>n/a</td>
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<tr>
<td>Temporal association to first or second vaccination</td>
<td>1</td>
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<td>2</td>
<td>1</td>
<td>1</td>
<td>2</td>
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<td>2</td>
<td>2</td>
<td>2</td>
<td>1</td>
<td>n/a</td>
</tr>
<tr>
<td>Time to onset of symptoms</td>
<td>&gt;14 days</td>
<td>8 - 14 days</td>
<td>3 - 7 days</td>
<td>8 - 14 days</td>
<td>&gt; 14 days</td>
<td>8 - 14 days</td>
<td>&gt;14 days</td>
<td>8 - 14 days</td>
<td>n/a</td>
<td>&gt; 14 days</td>
<td>n/a</td>
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<tr>
<td>Participant actively contacted neurologist (requested an unscheduled visit)</td>
<td>-</td>
<td>-</td>
<td>-</td>
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<td>-</td>
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<td>-</td>
<td>+</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Other concurrent event/relevant diagnosis</td>
<td>-</td>
<td>-</td>
<td>Recurring pneumonia</td>
<td>Tapering treatment</td>
<td>Viral infection, hypokalemia (medication induced)</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>n/a</td>
<td>-</td>
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<td>-</td>
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<tr>
<td>Treatment alteration at next visit</td>
<td>Increase dose, interval shortened</td>
<td>-</td>
<td>-</td>
<td>Scheduled tapering postponed</td>
<td>Double dose of IVIg, once</td>
<td>-</td>
<td>Increase dose, shorter interval</td>
<td>-</td>
<td>-</td>
<td>Increase dose IVIg / start CS</td>
<td>Extra course of IVIg</td>
<td>-</td>
</tr>
<tr>
<td>Worsening of symptoms resolved?</td>
<td>+</td>
<td>n/a</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>-</td>
<td>+</td>
<td>-</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>I-RODS: MCID deterioration**</td>
<td>n/a</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>n/a</td>
<td>n/a</td>
<td>n/a</td>
<td>n/a</td>
<td>n/a</td>
</tr>
<tr>
<td>Change EQ-5D-5L***</td>
<td>unknown</td>
<td>mixed</td>
<td>improved</td>
<td>mixed</td>
<td>worse</td>
<td>no change</td>
<td>worse</td>
<td>unknown</td>
<td>no change</td>
<td>no change</td>
<td>worse</td>
<td>improved</td>
</tr>
<tr>
<td>Interpretation</td>
<td>EOD, progressive from before vaccination</td>
<td>Fluctuating course of disease, ongoing from before vaccination</td>
<td>Fluctuating course of disease, other possible cause</td>
<td>Other possible cause</td>
<td>Other possible cause</td>
<td>No other explanation found</td>
<td>Progressive from before vaccination</td>
<td>Possible EOD effect</td>
<td>No other explanation found</td>
<td>Fluctuating course of disease ongoing from before vaccination</td>
<td>Increasing IVIg requirement, ongoing from before vaccination</td>
<td>Slow disease progression (MMN)</td>
</tr>
</tbody>
</table>
Abbreviations: CIDP = chronic inflammatory demyelinating polyneuropathy, MMN = multifocal motor neuropathy. M = Male, F = Female. IVIg = intravenous immunoglobulins, CS = corticosteroids. P = Pfizer/BioNTech, AZ = AstraZeneca, M = Moderna. n/a = not available. WA = weakness arms, WL = weakness legs, SS = sensory symptoms, F = fatigue, MA = muscle aches, NOS = not otherwise specified. MCID = minimal clinical important difference. EOD = End-of-dose

* These participants reported the presence of end of dose symptoms, or changing presence and severity of disease related symptoms prior to SARS-CoV-2 vaccination

** A minimal clinical important difference (MCID) on the I-RODS scale is defined as a deterioration of at least four points on the centile scale

*** Change EQ-5D-5L: worsening = deterioration on at least one of five items, improvement = improvement on at least one of five items, mixed = both deterioration and improvement on at least one of five items
**Figure 1** Study design

Abbreviations: GBS = Guillain-Barré Syndrome, MMN = multifocal motor neuropathy, CIDP = chronic inflammatory demyelinating polyneuropathy

**Figure 2** Flowchart of the study population and response rate

Abbreviations: GBS = Guillain-Barré Syndrome, MMN = multifocal motor neuropathy, CIDP = chronic inflammatory demyelinating polyneuropathy

*These participants completed the last questionnaire, at time point 4