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## **Supplementary Table 1. Outcome Measures**

| Outcome   | Measure   | Description   | Range   |
|---|---|---|---|
| Primary outcome   |   |   |   |
| Disability Inflammatory Rasch-<br>Overall Disability Scale<br>(iRODS) |   | <ul> <li>Patient reported linear disability scale, developed within the frame work of Item Response Theory¹</li> <li>Unit of measurement expressed in logits</li> <li>Higher scores represent lower levels of disability</li> </ul>                           | Logits: -6.95 - 8.11  |
| Secondary outcomes  |   |   |   |
| Muscle Strength Medical research council (MRC) sum score              |   | <ul> <li>6 pairs of muscles</li> <li>Shoulder abduction, elbow flexion, wrist extension, hip flexion, knee extension and foot dorsiflexion</li> <li>Higher scores represent more muscle strength</li> </ul>   | 0-60  |
| Grip Strength Martin Vigori meter                                     |   | <ul> <li>Measured in kilo Pascal (kPa)</li> <li>Higher score represents greater grip strength</li> <li>Highest value out of 3 measurements per hand</li> <li>Dominant hand in typical CIDP and most affected hand in multifocal or asymmetric CIDP</li> </ul> | 0-160   |
| Sensory impairment  | Modified INCAT sensory<br>Sum score (INCAT-SS)    | Sensory scale including vibration and pinprick sense plus a two-point discrimination value     Higher score represents more sensory impairment  | 0-20  |
| Pain  | Pain Intensity Numerical<br>Rating Scale (PI-NRS) | <ul> <li>Average pain over the past 4 weeks</li> <li>Higher score represents more pain</li> </ul>   | 0-10  |
| Fatigue   | Rasch-built fatigue severity scale (FSS)          | <ul><li>7 item scale</li><li>Higher score represents greater fatigue</li></ul>  | 0-49  |
| Disability AMC linear disability score (ALDS)                         |   | <ul> <li>A calibrated generic item bank to measure the level of physical disability in patients with chronic diseases.</li> <li>Higher scores represent lower levels of disability</li> </ul>   | 0-100   |
| Quality of life Short form 36 (SF-36)                                 |   | <ul> <li>Divided into physical and mental health components</li> <li>Higher scores represent better quality of life</li> </ul>  | Normalized to the<br>Dutch population mean<br>score of 50 and a SD of<br>10 |
| Patient's perception<br>of deterioration or<br>improvement            | Patient global impression of change scale         | 5 point Likert-scale on which patients indicate if their<br>CIDP complaints are much better, better, similar, worse or<br>much worse than before start of the study   | NA  |

## Supplementary Table 2. Protocol violations

| Patient | Protocol violation   | Study action   |
|---------|--|--|
| 1       | Patient in the withdrawal group refused to stay blinded at 12 weeks due to anxiety of not knowing what the treatment allocation was. This patient agreed to proceed with follow-up assessments and remained stable until last follow-up visit. | - Included in intention-to-treat analysis<br>- Excluded in per-protocol analysis |
| 2       | Patient in the IVIg continuation group was unblinded at 3 weeks of follow-up due to an invoice from the insurance company for IVIg treatment; this patient remained stable until last follow-up visit.   | - Included in intention-to-treat analysis<br>- Excluded in per-protocol analysis |
| 3       | Patient was wrongly allocated during the minimization procedure in terms of duration of treatment. The duration was corrected in the data-analysis.  | - Included in intention-to-treat analysis<br>- Included in per-protocol analysis |
| 4       | Study treatment was delayed because of one extra regular infusion after randomization.   | - Included in intention-to-treat analysis<br>- Included in per-protocol analysis |

Supplementary table 3. Different outcome measures in patients with a relapse endpoint at different time points

| N (%)                        |                    | Week 6    |               | Week 12   |             | Week 18   |             | Week 24   |             |
|------------------------------|--------------------|-----------|---------------|-----------|-------------|-----------|-------------|-----------|-------------|
|                              |                    | Freq.     | Cum.<br>Freq. | Freq.     | Cum. Freq.  | Freq.     | Cum. Freq.  | Freq.     | Cum. Freq.  |
| All relapse endpoints (N=30) |                    |           |               |           |             |           |             |           |             |
| IVIg withdrawal              | Total              | 7 (42)    | 7 (42)        | 6 (20)    | 13 (65)     | 2 (12)    | 15 (88)     | 2 (12)    | 17 (100)    |
| (N=17)                       |                    |           |               |           |             |           |             |           |             |
|                              | iRODS <sup>a</sup> | 5/7 (71)  | 5/7 (71)      | 2/6 (33)  | 7/13(54)    | 1/2 (50)  | 8/15 (53)   | 2/2 (100) | 10/17 (59)  |
|                              | GS <sup>b</sup>    | 5/7 (71)  | 5/7 (71)      | 3/6 (50)  | 8/13(62)    | 2/2 (100) | 10/15 (67)  | 2/2 (100) | 12/17 (71)  |
|                              | MRC <sup>c</sup>   | 4/7 (57)  | 4/7 (57)      | 1/6 (17)  | 5/13 (38)   | 1/2 (50)  | 6/15 (37)   | 1/2 (50)  | 7/17 (41)   |
|                              | PGIC <sup>d</sup>  | 7/7 (100) | 7/7 (100)     | 5/5 (100) | 12/12 (100) | 2/2 (100) | 14/14 (100) | 2/2 (100) | 16/16 (100) |
| IVIg continuation (N=13)     | Total              | 2 (15)    | 2 (15)        | 8 (62)    | 10 (77)     | 3 (23)    | 13 (100)    | 0         | 13 (100)    |
| <u>`</u>                     | iRODS              | 1/2 (50)  | 1/2 (50)      | 4/8 (50)  | 5/10 (50)   | 0/3       | 5/13 (38)   |           | 5/13 (38)   |
|                              | GS                 | 2/2 (100) | 2/2 (100)     | 2/8 (25)  | 4/10 (40)   | 2/3 (67)  | 6/13 (46)   |           | 6/13 (46)   |
|                              | MRC                | 1/2 (50)  | 1/2 (50)      | 4/8 (50)  | 5/10 (50)   | 1/3 (33)  | 6/13 (46)   |           | 6/13 (46)   |
|                              | PGIC               | 1/2 (50)  | 1/2 (50)      | 6/6 (100) | 7/8 (88)    | 3/3 (100) | 10/11 (91)  |           | 10/11 (91)  |
| Relapse according to M       | CID iRODS          |           |               |           |             |           |             |           |             |
| IVIg withdrawal (N= 10)      | Total              | 5 (50)    | 5 (50)        | 2 (20)    | 7 (70)      | 1 (10)    | 8 (80)      | 2 (20)    | 10 (100)    |
|                              | GS                 | 5/5 (100) | 5/5 (100)     | 1/2 (50)  | 6/7 (86)    | 1/1 (100) | 7/8 (88)    | 2/2 (100) | 9/10 (90)   |
|                              | MRC                | 4/5 (80)  | 4/5 (80)      | 1/2 (50)  | 5/7 (71)    | 0/1 (0)   | 5/8 (63)    | 1/2 (50)  | 6/10 (60)   |
|                              | PGIC               | 5/5 (100) | 5/5 (100)     | 1/1 (100) | 6/6 (100)   | 1/1 (100) | 7/7 (100)   | 2/2 (100) | 9/9 (100)   |
| IVIg continuation N=5        | Total              | 1 (20)    | 1 (20)        | 4 (80)    | 5 (100)     | 0 (0)     | 5 (100)     | 0         | 5 (100)     |
|                              | GS                 | 1/1 (100) | 1/1 (100)     | 2/4 (50)  | 3/5 (60)    |           | 3/5 (60)    |           | 3/5 (60)    |
|                              | MRC                | 1/1 (100) | 1/1 (100)     | 3/4 (75)  | 4/5 (80)    |           | 4/5 (80)    |           | 4/5 (80)    |
|                              | PGIC               | 1/1 (100) | 1/1 (100)     | 3/3 (100) | 4/4 (100)   |           | 4/4 (100)   |           | 4/4 (100)   |
| Other relapse                |                    |           | 1             |           |             |           |             |           |             |
| IVIg withdrawal (N=7)        | Total              | 2 (29)    | 2 (29)        | 4 (57)    | 6 (86)      | 1 (14)    | 7 (100)     | 0 (0)     | 7 (100)     |
| <u> </u>                     | GS                 | 2/2 (100) | 2/2 (100)     | 2/4 (50)  | 4/6 (67)    | 1/1 (100) | 5/7 (71)    |           | 5/7 (71)    |
|                              | MRC                | 0/2 (0)   | 0/2 (0)       | 0/4 (0)   | 0/6 (0)     | 1/1( 100) | 1/7 (14)    |           | 1/7 (14)    |
|                              | PGIC               | 2/2 (100) | 2/2 (100)     | 4/4 (100) | 6/6 (100)   | 1/1 (100) | 7/7 (100)   |           | 7/7 (100)   |
| IVIg continuation (N=8)      | Total              | 1 (13)    | 1 (13)        | 4 (50)    | 5 (63)      | 3 (38)    | 8 (100)     | 0 (0)     | 8 (100)     |
|                              | GS                 | 1/1 (100) | 1/1 (100)     | 0/4 (0)   | 1/5 (20)    | 1/3 (33)  | 2/8 (25)    |           | 2/8 (25)    |
|                              | MRC                | 1/1 (100) | 1/1 (100)     | 1/4 (25)  | 1/5 (20)    | 1/3 (33)  | 2/8 (25)    |           | 2/8 (25)    |
|                              | MIKC               | 1/1 (100) | 1/1 (100)     | 1/ (23)   | 1/3 (20)    | 1/3 (33)  | 2/0 (23)    |           | 2/0 (23)    |

<sup>&</sup>quot;Minimal clinically important difference on the iRODS;, b Relapse on grip strength: deterioration of at least 8kPa; 3Relapse on MRC: deterioration of at least 2 points on MRC sum score; dRelapse on PGIC scale (1-5) was defined as a score of: a little worse or a lot worse than before the study.

Abbreviations: freq: frequency, cum: cumulative, IVIg: intravenous immunoglobulins, GS: grip strength, MRC: MRC sum score, PGIC: patient global impression of change scale.

## Appendix 1. Linear regression in the context of non-inferiority

We used multivariable linear regression on the iRODS follow-up scores in the context of non-inferiority by comparing the lower bound of the 95% confidence interval of the between group-difference with -0.65 as the margin of non-inferiority, adjusting for both the iRODS baseline scores and duration of prior IVIg. The following results were obtained:

Model Coefficients

|                               | 95% confidence interval |       |                |             |  |  |
|-------------------------------|-------------------------|-------|----------------|-------------|--|--|
| Predictor                     | Estimate                | SE    | lower<br>bound | upper bound |  |  |
| Intercept                     | -0.319                  | 0.459 | -0.1238        | 0.600       |  |  |
| iRODS baseline                | 0.921                   | 0.077 | 0.766          | 1.076       |  |  |
| Duration prior IVIg treatment | 0.370                   | 0.395 | -0.422         | 1.163       |  |  |
| Withdrawal treatment          | -0.558                  | 0.395 | -1.348         | 0.233       |  |  |

After adjustment, the coefficient for withdrawal treatment was -0.558 with a lower bound of -1.348. With the lower bound well below the non-inferiority margin of -0.65, the multivariable approach fails to demonstrate non-inferiority of withdrawal treatment.

I. van Nes SI, Vanhoutte EK, van Doorn PA, et al. Rasch-built Overall Disability Scale (R-ODS) for immune-mediated peripheral neuropathies. *Neurology* 2011; **76**(4): 337-45.