**Table e-1: Inclusion and Exclusion Criteria**

Inclusion criteria:

1. Age ≥18 years.
2. Diabetes, as per American Diabetes Association Criteria.
3. Clinical evidence of polyneuropathy and NCS shows 2 separate motor nerves (median, ulnar, tibial, or peroneal) which meet criteria for demyelination, defined as follows:
	1. Conduction velocity <90% LLN, distal latency >110% upper limit of normal (ULN), or minimal F-wave latency >110% ULN
	2. The changes are not exclusively due to median neuropathy at the wrist, ulnar neuropathy at the elbow, or peroneal neuropathy at the fibular head.
4. Clinical suspicion of possible demyelinating polyneuropathy (CIDP).

Exclusion Criteria:

1. Pregnant patients, or those of childbearing potential not using contraception.
2. Patients <18 years of age.
3. Presence of an alternative etiology of peripheral neuropathy, such as: hereditary neuropathies (Charcot Marie-Tooth disease); B-vitamin deficiency- or excess- related neuropathy; uremic neuropathy; neuropathy secondary to monoclonal gammopathy; history of cancer- or chemotherapy-related neuropathy; other toxin exposures; and alcoholic neuropathy.
4. Contraindication to IVIg, including: history of recurrent thrombosis, IgA deficiency, or severe hypersensitivity reaction to IVIg in past, renal failure, recurrent deep venous thrombosis, pulmonary embolus, stroke, or myocardial infarction.
5. Presence of serious or unstable medical condition, which may preclude study completion or lead to inability to tolerate IVIg. This may include active heart failure, uncontrolled hypertension, or severe anemia, among other conditions.
6. Presence of concomitant neurological illness, which may confound evaluation.
7. Fails or unable to provide informed consent.

**Table e-2**. Outcomes according to sequence**.**

|  |  |  |  |
| --- | --- | --- | --- |
|  | **Sequence A** Randomized to Placebo First (n=11) | **Sequence B**Randomized to IVIG First (n=14) | P-value for Sequence effect† |
| Outcome | Baseline | Δ (95% CI)\* | Baseline | Δ (95% CI)\* | Unadjusted P-value | AdjustedP-value |
| ***Primary*** |  |  |  |  |  |  |
| ONLS | 4.5±1.6 | +0.3 (-0.5 to 1.1) | 4.4±1.9 | -1.0 (-1.6 to -0.3) | **0.018** | **0.020** |
| RODS | 28.3±9.5 | -0.4 (-7.4 to 6.6) | 31.6±5.6 | +1.8 (-4.3 to 7.8) | 0.67 | 0.63 |
| ***Secondary*** |  |  |  |  |  |  |
| Grip Strength | 53.5±19.8 | -7.1 (-14.3 to 0.1) | 62.2±14.9 | -4.0 (-10.2 to 2.2) | 0.79 | 0.50 |
| SF36 | 36.1±21.1 | +3.0 (-7.7 to 13.6) | 37.3±19.3 | +13.2 (4.0 to 22.4) | 0.15 | 0.15 |
| MRC Grade | 69.8±8.0 | -0.6 (-2.8 to 1.6) | 72.9±4.7 | -0.5 (-2.4 to 1.4) | 0.97 | 0.93 |

\*Intention-to-treat analysis.Final numbers are 9 in Sequence A and 12 in Sequence B

†Unadjusted p-value from paired Student’s t-test; adjusted p-value from ANCOVA adjusted for sequence order and baseline value.

**Table e-3.** Baseline characteristics of 25 randomized patients, according to randomization sequence.

|  |  |  |
| --- | --- | --- |
|  | Mean ± SD, Median [IQR], or Frequency (%) |  |
| Characteristic | Whole Cohort(n=25) | Sequence ARandomized to Placebo First(n=11) | Sequence BRandomized to IVIG First(n=14) | P-value |
| Age (years) | 57.5±9.2 | 57.0±8.4 | 57.9±10.1 | 0.82 |
| Height (m) | 1.73±0.11 | 1.75±0.11 | 1.72±0.10 | 0.50 |
| Weight (kg) | 91.5±23.9 | 98.4±24.2 | 86.2±23.1 | 0.21 |
| BMI (kg/m2) | 30.3±6.2 | 31.9±4.7 | 29.1±7.1 | 0.28 |
| Female Sex / Male sex | 8 (32%) / 17 (68%) | 4(36%) / 7(64%) | 4(29%) / 10(71%) | 0.68 |
| Smoking History |  |  |  |  |
| Yes | 2 (8%) | 0 (0%) | 2 (15%) | 0.27 |
| Quit | 8 (33%) | 3 (27%) | 5 (38%) |
| Never | 14 (58%) | 8 (73%) | 6 (46%) |
| Diabetes Duration (years) | 11 [4,25] | 15 [7,17] | 10 [2,26] | 0.73 |
| Polyneuropathy Duration (years) | 5.5 [2, 10] | 10 [6, 10] | 3 [2, 6] | **0.033** |
|  |  |  |  |  |
| Clinical Symptoms |  |  |  |  |
| Numbness lower limbs | 19 (76%) | 9 (82%) | 10 (71%) | 0.55 |
| Numbness upper limbs | 15 (60%) | 7 (64%) | 8 (57%) | 0.74 |
| Paraesthesias lower limbs | 16 (64%) | 7 (64%) | 9 (64%) | 0.97 |
| Paraesthesias upper limbs | 12 (48%) | 6 (55%) | 6 (57%) | 0.56 |
| Weakness lower limbs | 21 (84%) | 10 (91%) | 11 (79%) | 0.40 |
| Weakness upper limbs | 17 (68%) | 8 (73%) | 9 (64%) | 0.65 |
| Neuropathic pain lower limbs | 21 (84%) | 9 (82%) | 12 (86%) | 0.79 |
| Neuropathic pain upper limbs | 15 (60%) | 7 (64%) | 8 (57%) | 0.74 |
| Imbalance | 19 (79%) | 8 (80%) | 11 (79%) | 0.93 |
| Falls | 11 (46%) | 4 (40%) | 7 (50%) | 0.63 |
|  |  |  |  |  |
|  |  |  |  |  |