PolyNeuro exchange

IgG Levels and Wear Off Reflect Administration and Outcome

‘Wear-off’ of treatment effect towards the end of the dosing cycle

- Patients with primary immunodeficiencies have been treated with IVIG since the early 1980s
- Mechanisms of IVIG action reflect competition between therapeutic IgG and pathologic autoantibodies[1]
- Towards the end of the dosing cycle, patients with primary immunodeficiency are more susceptible to infection and their quality of life decreases[2]
- IVIG trough levels may be associated with wear-off effects

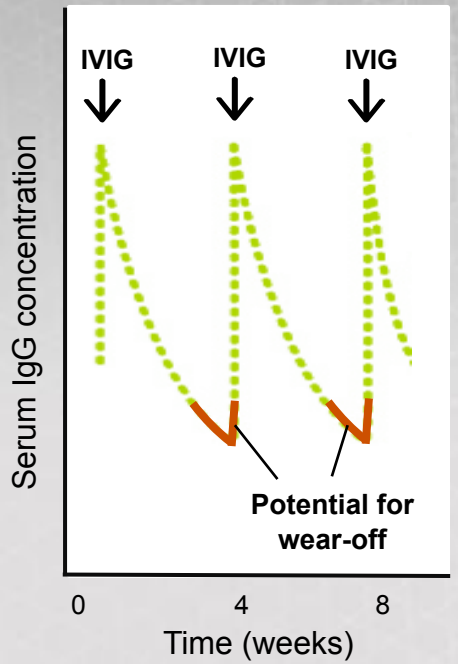


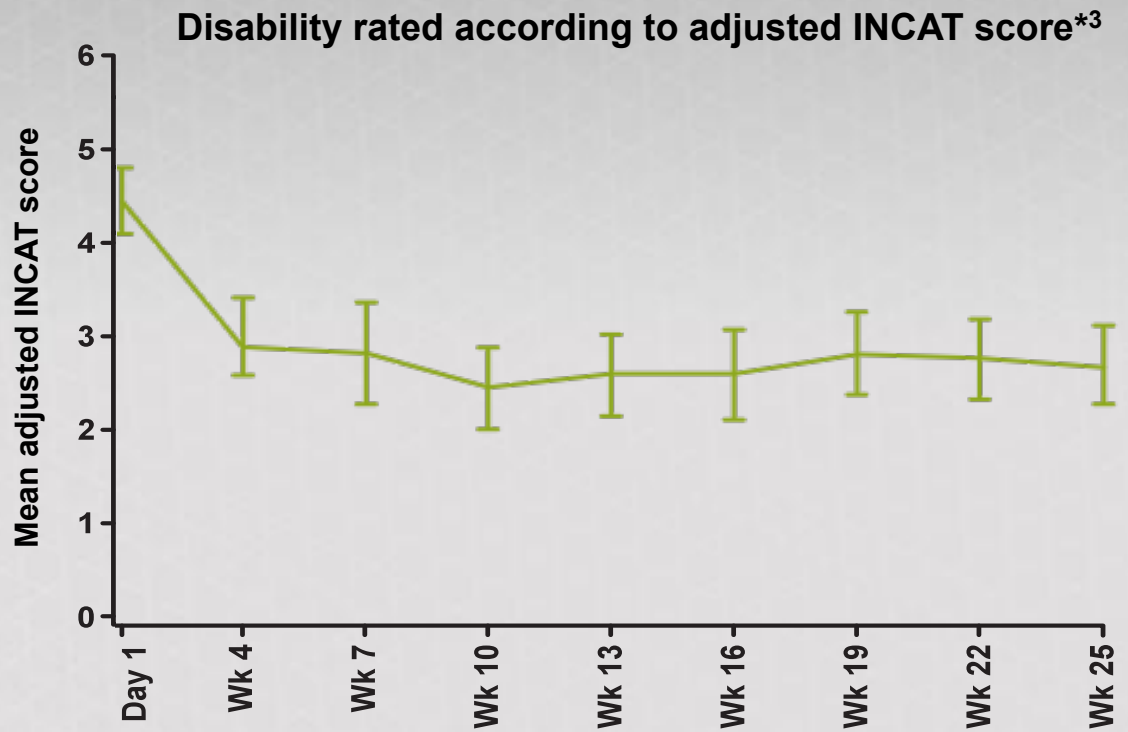
Illustration of potential wear-off occurrence in relation to IVIG dosing and IgG levels

Wear-off: “cyclic or periodic occurrence of clinical deterioration at an interval following an IVIG infusion”[3]

CIDP: chronic inflammatory demyelinating polyneuropathy,, IgG: immunoglobulin G, IVIG: intravenous immunoglobulin, MMN: multifocal motor neuropathy

1. Berger *et al.* J Peripher Nerv Syst. 2013:18;275–96.
2. Rojavin M, *et al.* J Clin Immunol. 2016;36:210–19.
3. Allen J *et al.* J Peripher Nerv Syst. 2018;[Epub ahead of print].

IVIG improves and maintains functionality in patients with CIDP[1,2]



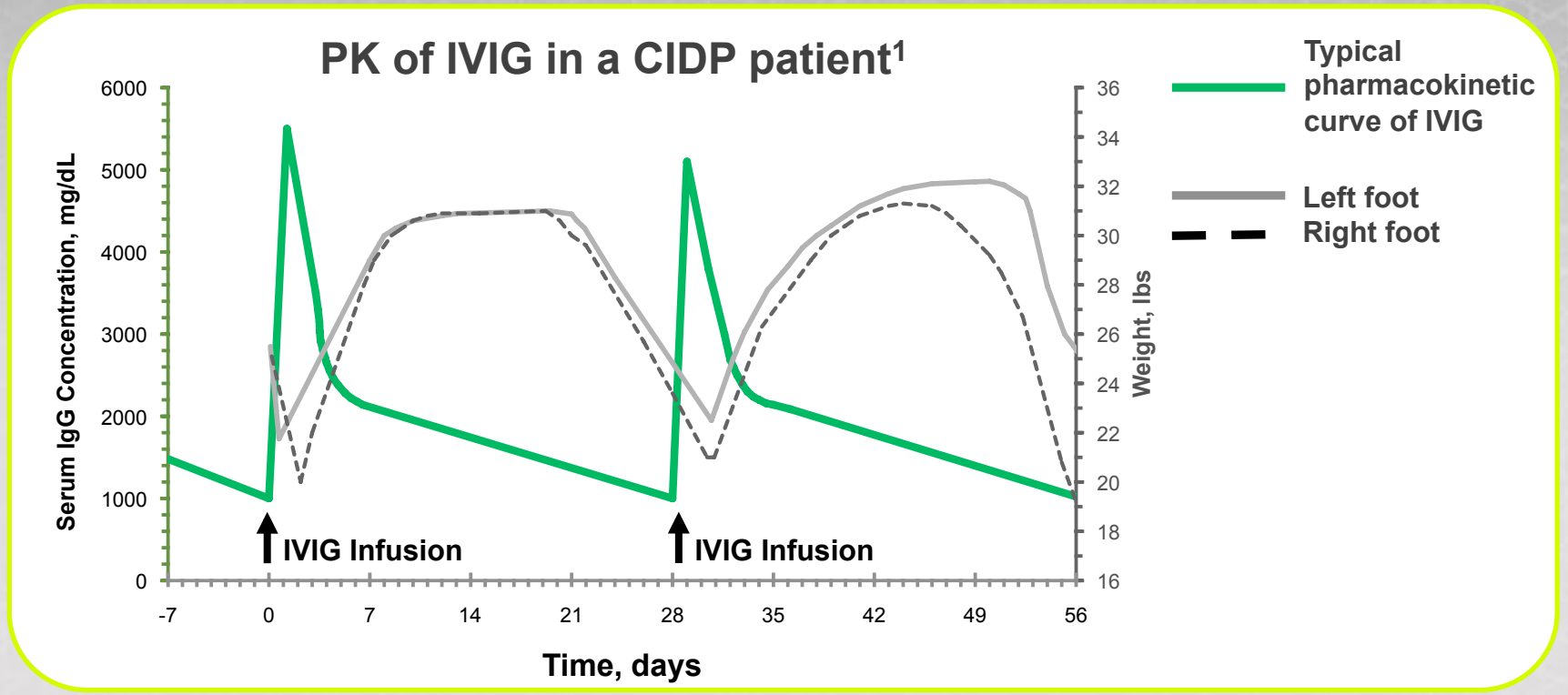
- IVIG is FDA approved for CIDP and MMN†[4]
- IVIG is effective in improving and maintaining functionality in these patients[3,5]

*Patients had previously received IVIG. Error bars represent the standard error of the mean
†Privigen, Gamunex and Gammaked are approved for CIDP, Gammagard Liquid is approved for MMN

CIDP: chronic inflammatory demyelinating polyneuropathy, FDA: US Food and Drug Administration, INCAT: inflammatory neuropathy cause and treatment, IVIG: intravenous immunoglobulin, MMN: multifocal motor neuropathy

1. Hughes RAC *et al*. Lancet Neurol. 2008;7(2):136–44.
2. Leger J-M *et al*. J Peripher Nerv Syst. 2013;18(2):130–40.
3. This work is a derivative of "Mean adjusted INCAT score over time by IVIG-pretreatment" by Léger J-M *et al*. J Peripher Nerv Syst. 2013; 18(2):130–140. This figure is licensed under CC BY 3.0 by CSL Behring.
4. FDA Immune Globulin Intravenous Indications. Available at: http://www.fda.gov/BiologicsBloodVaccines/BloodBloodProducts/ApprovedProducts/ LicensedProductsBLAs/FractionatedPlasmaProducts/ucm133691.htm. Accessed Jun 2018.
5. van Schaik IN *et al*. Lancet Neurol. 2018;17(1):35–46.

Close relationship between IgG dosing and patient response



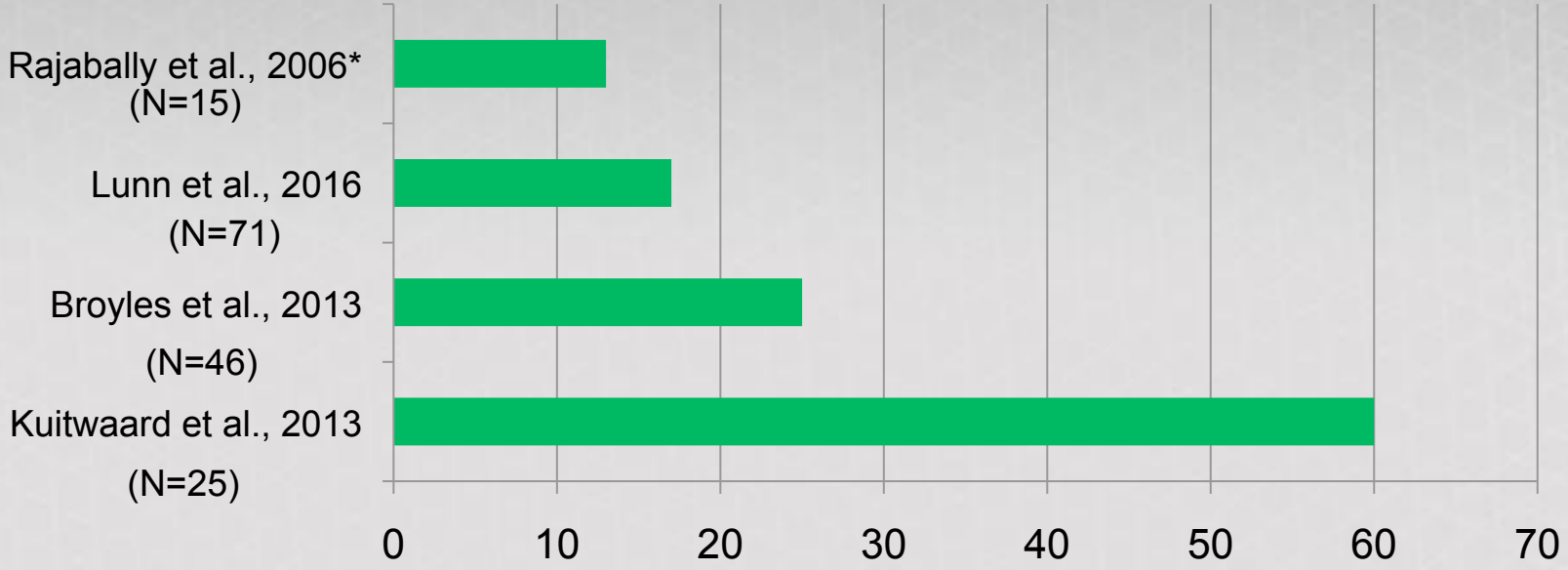
A close relationship exists between the frequency of dosing and functional capability in some patients[2]

IgG: immunoglobulin G, IVIG: intravenous immunoglobulin, PK: Pharmacokinetics

1. Berger M and Allen JA. Muscle Nerve. 2015;51(3): 315–26.
2. Berger M, *et al.* Immunotherapy. 2018;[Epub ahead of print].

Individually optimized therapy may include more frequent dosing

Percentage of patients receiving IgG at intervals ≤14 days[1]

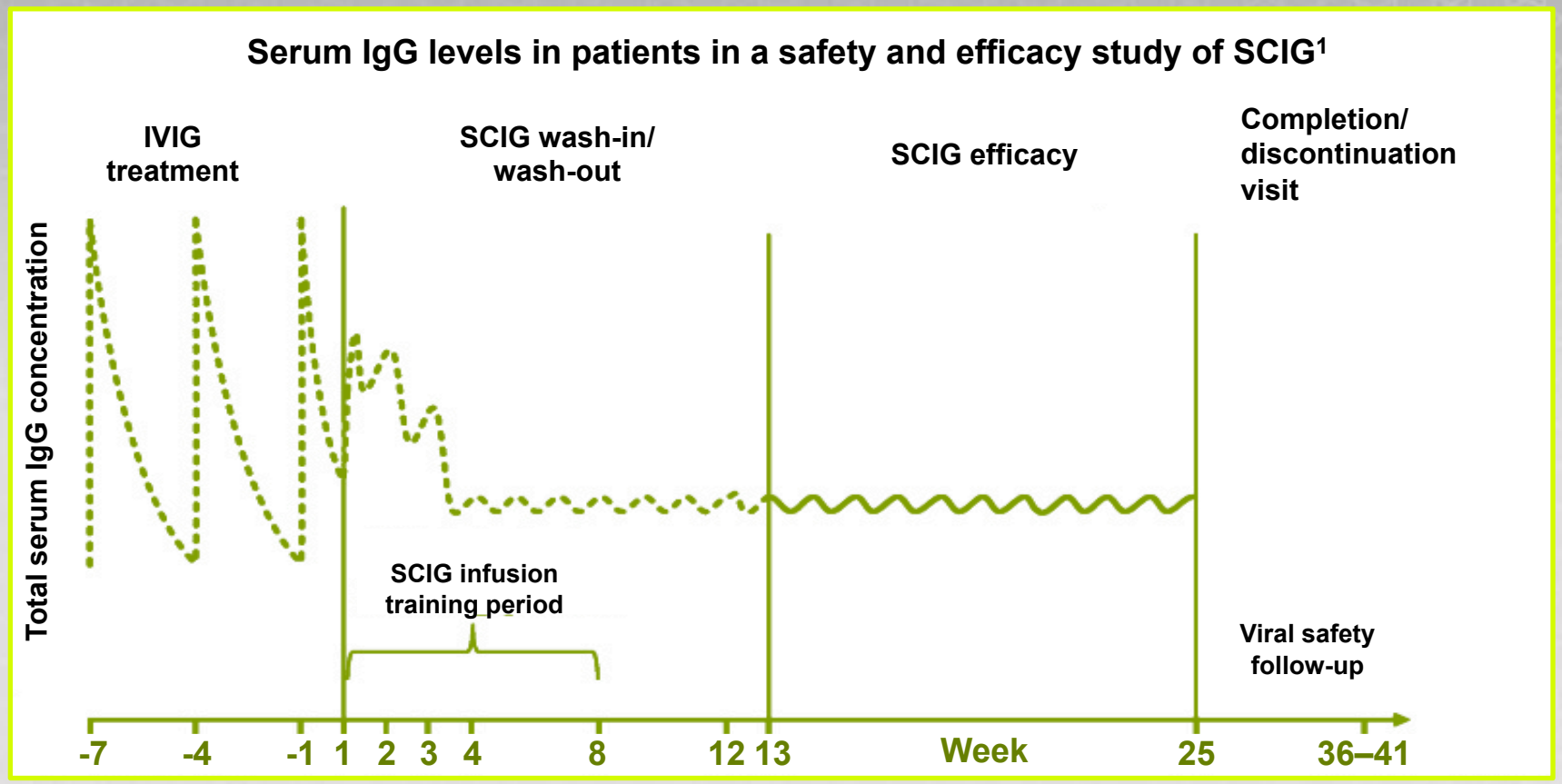


Patients who experience wear-off may do better when the IVIG dosing interval is less than the expected half-life of IgG[1]

*Final or lowest dose per course
IgG, immunoglobulin G

1. Allen J *et al.* J Peripher Nerv Syst. 2018;[Epub ahead of print].
2. Rajabally YA, *et al.* J Peripher Nerv Syst. 2006;11:325–29.
3. Lunn MP, *et al.* J Peripher Nerv Syst. 2016;21:33–7.
4. Broyles R, *et al.* Postgrad Med. 2013;125:65–72.
5. Kuitwaard K, *et al.* J Neurol Neurosurg Psychiatry. 2013;84:859–61.

Serum IgG levels vary with administration route



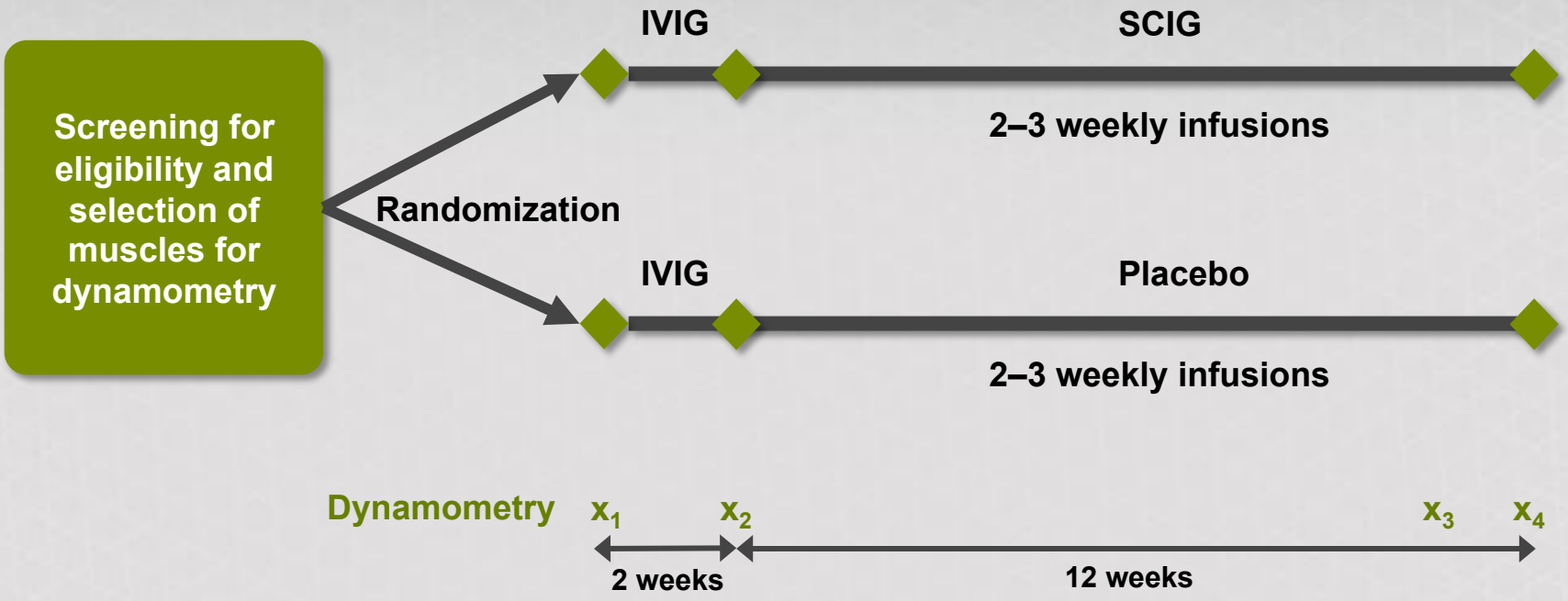
It is possible to achieve near constant steady-state serum IgG levels with frequent SCIG administration[2]

IgG: immunoglobulin G, IVIG: intravenous immunoglobulin, SCIG: subcutaneous immunoglobulin

1. Kanegane H, *et al.* J Clin Immunol 2014; 34(2):204–11.
2. Berger M, *et al.* Immunotherapy. 2018;[Epub ahead of print].

SCIG in patients with CIDP

- Randomized, double-blinded, placebo-controlled trial of the effect of SCIG on muscular performance in 30 patients with CIDP[1,2]

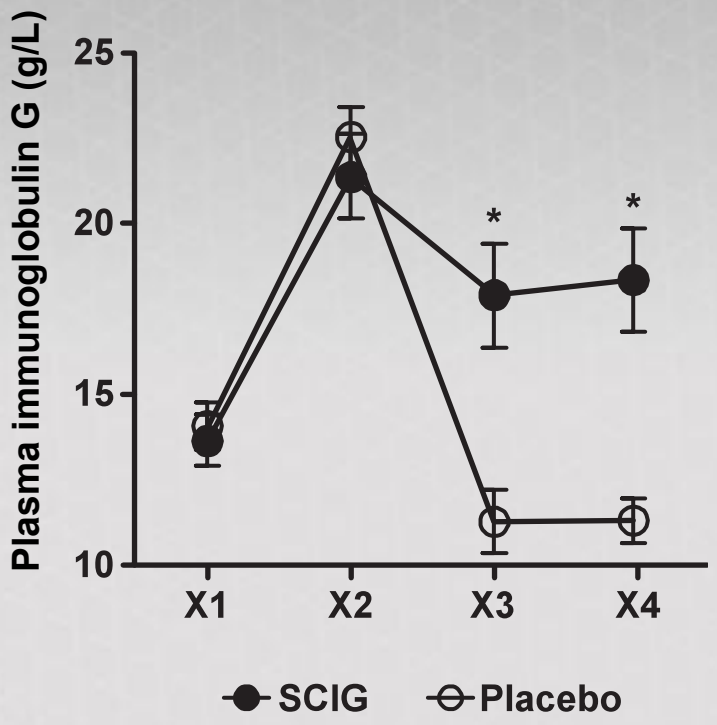


CIDP: chronic inflammatory demyelinating polyneuropathy, IVIG: intravenous immunoglobulin

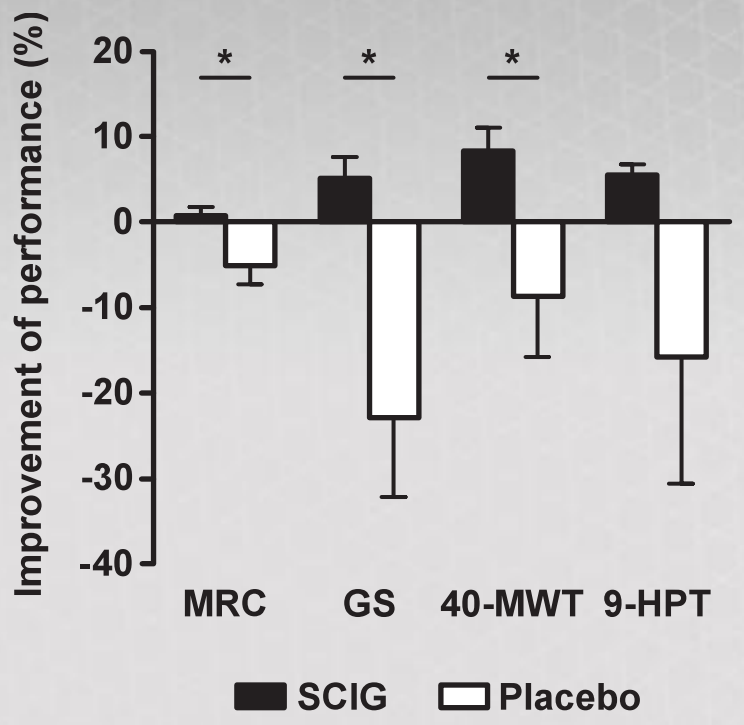
1. Markvardsen LH, *et al*. Eur J Neurol. 2013;20:836–42.

SCIG in patients with CIDP

Mean (±SD) change in IgG levels[1]



Mean (SD) change in functionality[1]



SCIG significantly increases plasma IgG levels and improves muscle strength, walking performance and disability score as compared with treatment with placebo[1]

40-MWT: 40-mwalking test, 9-HPT, nine-hole-peg test, CIDP: chronic inflammatory demyelinating polyneuropathy, GS: grip strength, IVIG: intravenous immunoglobulin, MRC: Medical Research Council score, SCIG: subcutaneous immunoglobulin

1. Markvardsen LH, *et al*. Eur J Neurol. 2013;20:836–42.

Summary

Mechanisms of IVIG action reflect competition between therapeutic IgG and pathologic autoantibodies[1,2]

Insufficient levels of therapeutic IgG just prior to repeat IVIG treatments may lead to wear-off and loss of peripheral nerve function[1,2]

Wear-off may be avoided by shortening the dosing interval or by switching from IVIG to SCIG[1,2]

EFNS: European Federation of Neurological Societies, IVIG: intravenous immunoglobulin, PNS: Peripheral Nerve Society

1. Allen J *et al*. J Peripher Nerv Syst. 2018;[Epub ahead of print].
2. Berger M and Allen JA. Muscle Nerve. 2015;51(3): 315–26.