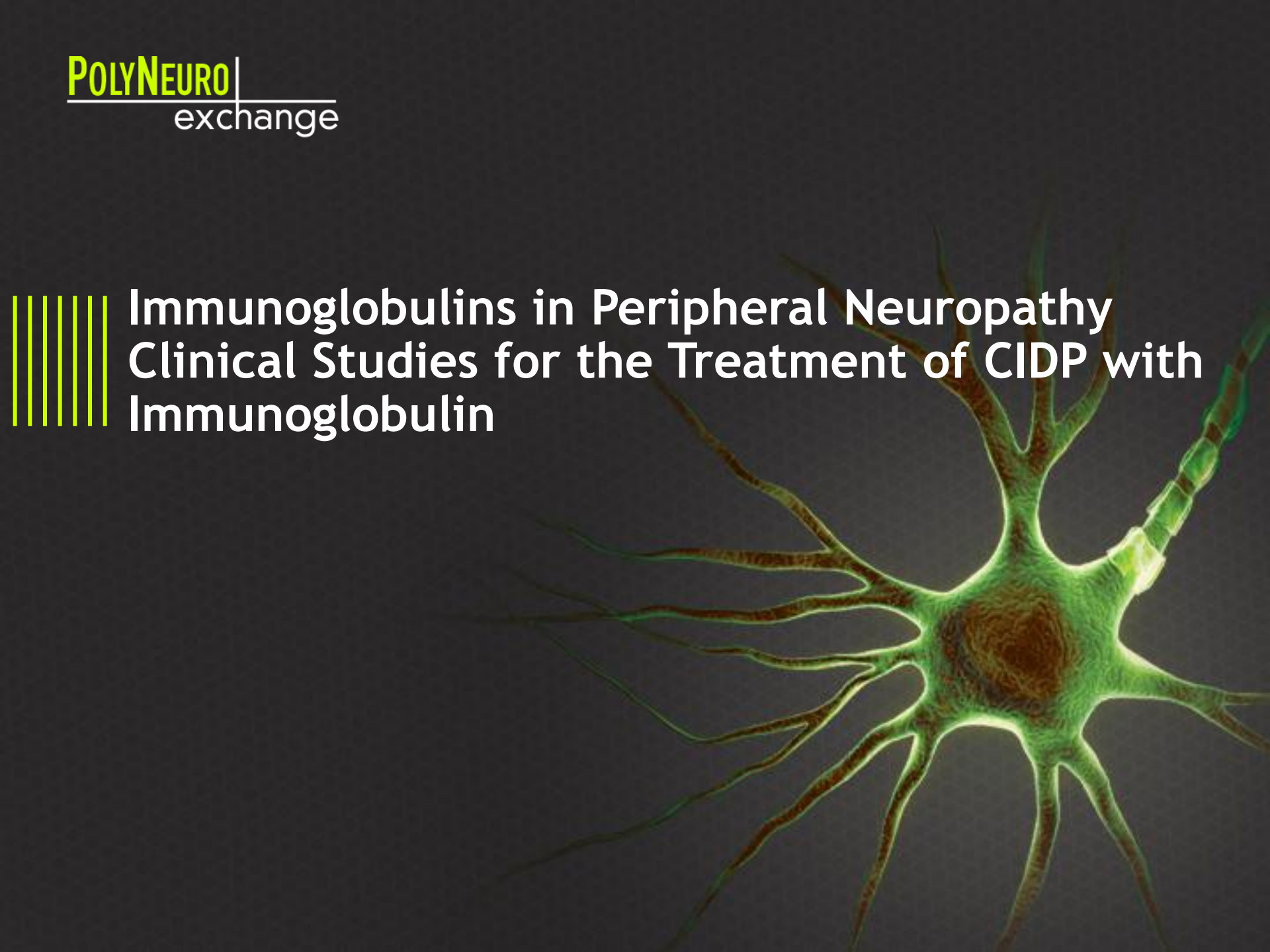
POLYNEURO exchange

Immunoglobulins in Peripheral Neuropathy Clinical Studies for the Treatment of CIDP with Immunoglobulin



Introduction

- Chronic inflammatory demyelinating polyneuropathy, Guillain-Barré syndrome and multifocal motor neuropathy are all forms of peripheral neuropathy.
- If treated early, disease progression may be slowed; however, if treatment is not started until late in the course of the disease, permanent damage may have already occurred.
- The following slides discuss two clinical trials that showed efficacy of intravenous immunoglobulins in chronic inflammatory demyelinating polyneuropathy (CIDP).

Summary of evidence for CIDP

- Intravenous Immune Globulin CIDP Efficacy (ICE) trial[1]
  - n = 117
  - Primary endpoint met
    - 54%* IVIG treated patients improved ≥1 point on the INCAT scale
  - Secondary endpoints met
    - MRC sum score = +4.7
    - Grip strength (dominant hand) = +16.1
- Privigen Impact on Mobility and Autonomy (PRIMA) trial[2]
  - n = 28
  - Primary endpoint met
    - 60.7% patients showed an improvement in INCAT score
  - Secondary endpoints met
    - MRC sum score = +6.9
    - Grip strength (dominant hand) = +14.1

*This value for Gamunex decreases to 47.5% if 4 patients with stable, adjusted INCAT score at Week 6 are excluded from the analysis.

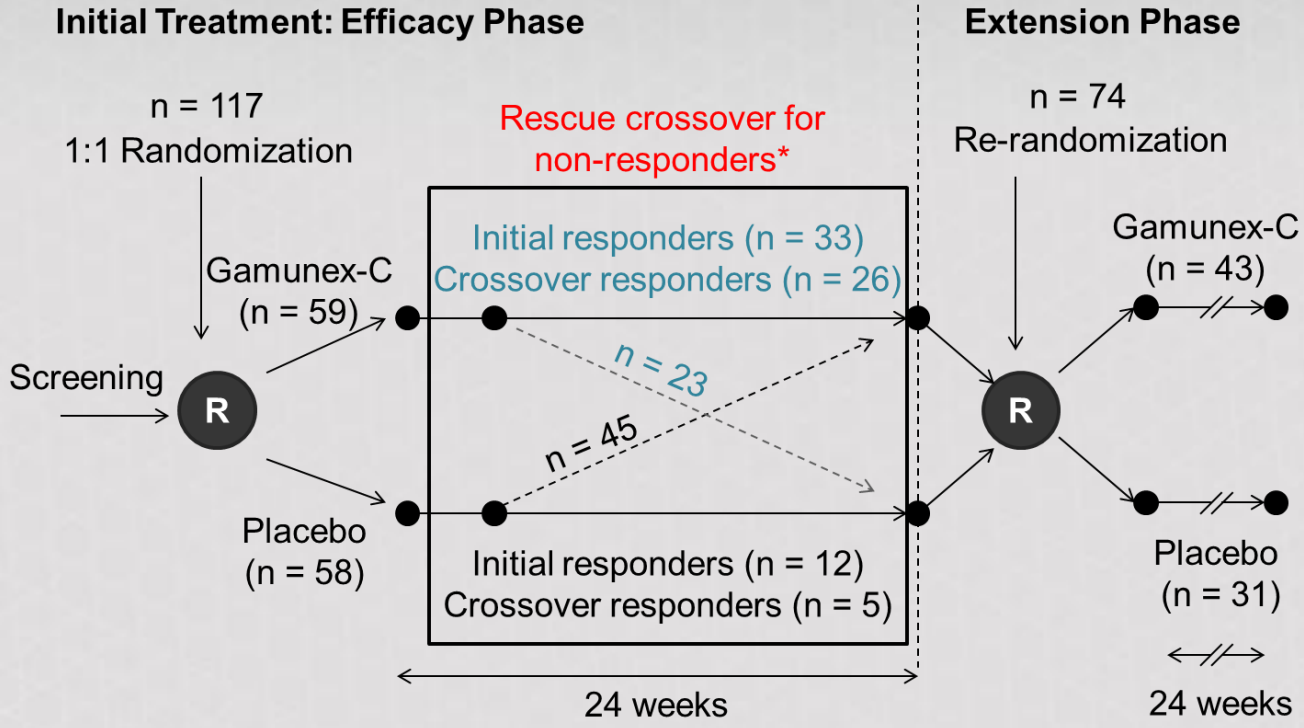
CIDP: chronic inflammatory demyelinating polyneuropathy, INCAT: inflammatory neuropathy cause and treatment, IVIG: intravenous immunoglobulin, MRC: Medical Research Council

1. Hughes RA, *et al.* Lancet Neurol 2008;7:136-144
2. Léger J-M, *et al.* J Peripher Nerv Syst 2013;18(2):130-140

Evidence for IVIG in CIDP: ICE trial

Intravenous Immune Globulin CIDP Efficacy trial[1]

- Designed to assess long-term efficacy of IVIG in CIDP
- Study design:



CIDP: chronic inflammatory demyelinating polyneuropathy
IVIG: intravenous immunoglobulin

1. Hughes RA, *et al.* Lancet Neurol 2008;7:136-144

Evidence for IVIg in CIDP: ICE trial

ICE trial results[1]

Efficacy measurement / endpoint	Result
INCAT	54%* (32/59) subjects who were IVIG treated and 21% (12/58) subjects placebo treated improved, p = 0.0002
MRC sum score	+4.7 (p = 0.004)
Grip strength (kPa)	Dominant hand = +16.1 (p = 0.007) Non-dominant hand = +17.6 (p = 0.001)
Safety	AEs related to study drug: 55% (62 IVIG subjects) SAEs: 9/1096 infusions IVIG group (0.8% per infusion) 11/575 infusions placebo group (1.9% per infusion) Most common AEs: headache, pyrexia and hypertension

*This value for Gamunex decreases to 47.5% if 4 patients with stable, adjusted INCAT score at Week 6 are excluded from the analysis.

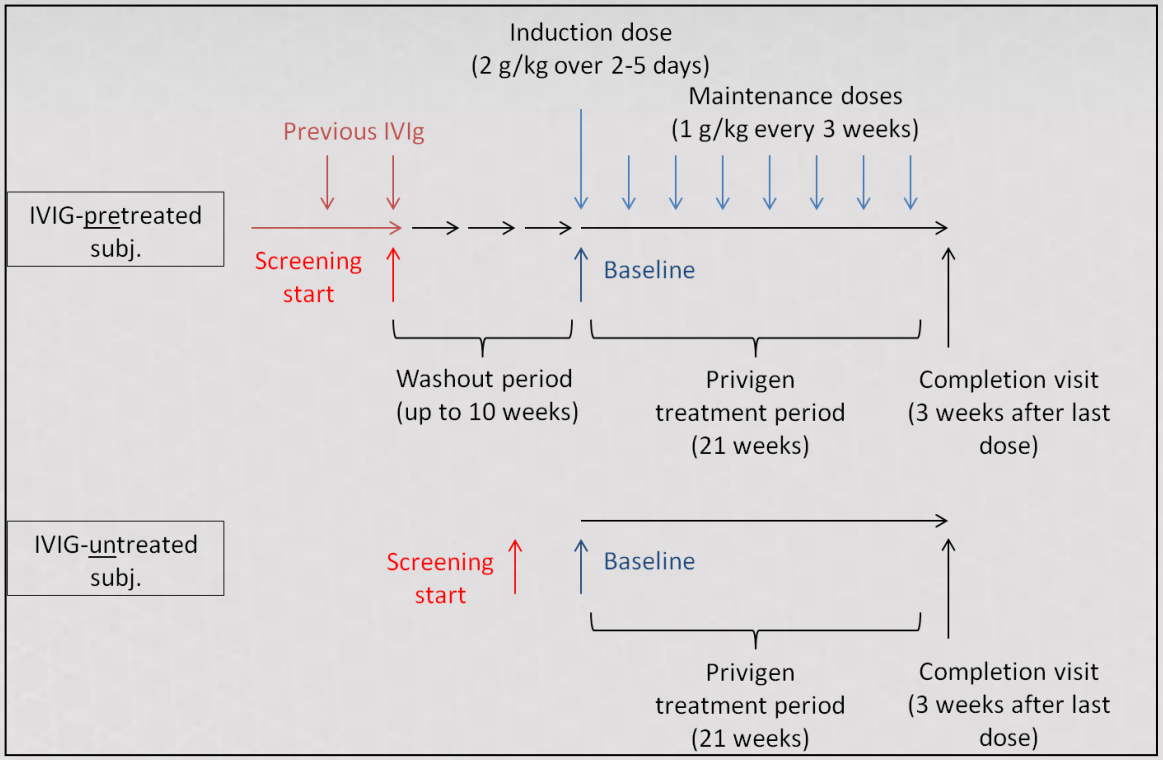
AE: adverse events, CIDP: chronic inflammatory demyelinating polyneuropathy, INCAT: inflammatory neuropathy cause and treatment scale, IVIG: intravenous immunoglobulin, MRC: Medical Research Council, SAE: serious adverse event

1. Hughes RA, *et al.* Lancet Neurol 2008;7:136-144

Evidence for IVIg in CIDP: PRIMA trial

Privigen Impact on Mobility and Autonomy[1]

- Primary endpoint:
  - The percentage of responders (responder rate) at completion visit (Week 25), assessed by adjusted INCAT score



CIDP: chronic inflammatory demyelinating polyneuropathy, INCAT: inflammatory neuropathy cause and treatment scale, IVIG: intravenous immunoglobulin

1. Léger J-M, *et al.* J Peripher Nerv Syst 2013;18(2):130-140

Evidence for IVIg in CIDP: PRIMA trial

PRIMA trial results[1]

Efficacy measurement / endpoint	Result
INCAT	Total responder rate = 60.7% (76.9% IVIG pre-treated, 46.7% IVIg untreated)
MRC sum score (change vs. baseline)	+ 6.9
Grip strength (change vs. baseline)	Dominant hand = +14.1 Non-dominant hand = +10.4
Safety	AEs: 108/259 infusions (rate per infusion 0.417) AEs possibly related to study drug: 60.7% (17 subjects) SAEs: 4 in 4 subjects Most common AE: headache

MRC sum score and grip strength increased from baseline
AE: adverse events, CIDP: chronic inflammatory demyelinating polyneuropathy, INCAT: inflammatory neuropathy cause and treatment scale, IVIG: intravenous immunoglobulin, MRC: Medical Research Council, SAE: serious adverse event

1. Léger J-M, *et al.* J Peripher Nerv Syst 2013;18(2):130-140

Responsiveness to IVIg therapy

- Not all patients with CIDP respond to IVIG.
- Factors contributing to lack of responsiveness include:
  - Delay in CIDP diagnosis and treatment:
    - Increases the extent of axonal damage[1]
    - Decreased time between symptom onset and treatment has been shown to correlate with decreased disease activity, disease progression and disability[2]
  - Increase in axonal damage leads to:
    - Decreased compound muscle action potential (CMAP)[1]
    - Muscle atrophy[3]
  - TAG-1 polymorphisms
    - Link found in Japanese population[4]

CIDP: chronic inflammatory demyelinating polyneuropathy, CMAP: compound muscle action potential, IVIG: intravenous immunoglobulin, TAG: transient axonal glycoprotein

1. Robertson EE, Donofrio PD. Curr Treat Options Neurol 2010;12:84-94
2. Koski CL, *et al.* 2010. 2010 survey of patients with chronic inflammatory demyelinating polyneuropathy in the USA: Poster presented at AAN 2011
3. Swedish National Board of Health. http://www.socialstyrelsen.se/rarediseases/cidp Accessed January 2013
4. Iijima M, *et al.* Neurol 2009;73:1348-1352