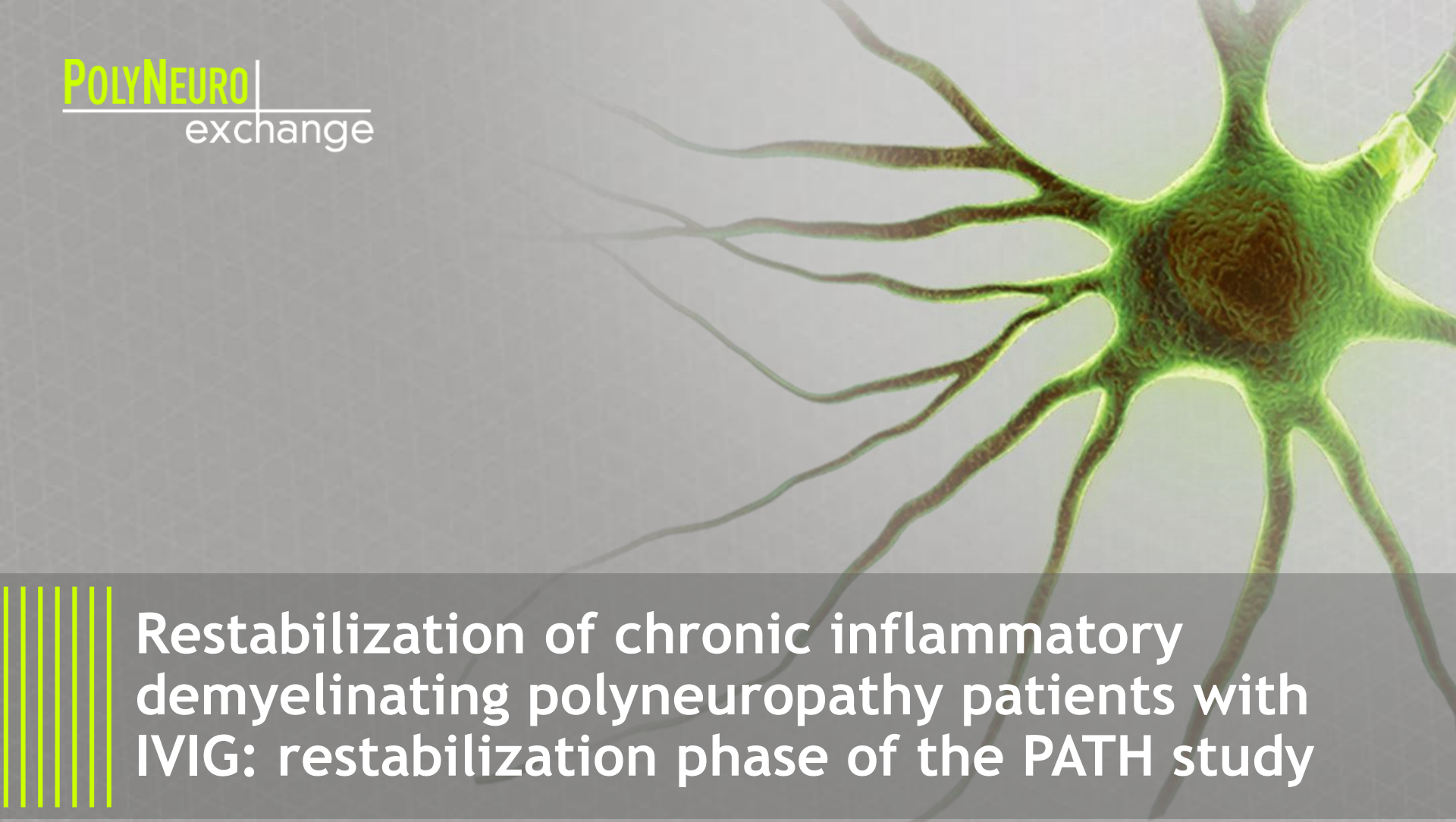
PolyNeuro exchange



Restabilization of chronic inflammatory demyelinating polyneuropathy patients with IVIG: restabilization phase of the PATH study

Chronic Inflammatory Demyelinating Polyneuropathy (CIDP)

- **Symmetric (motor and sensory) proximal and distal neuropathy**
- Follows a monophasic, progressive or relapsing course
- Developing over 2 months or more[1,2]

- **1.6–8.9 cases per 100,000 adults**
- Can occur in children and adults at any age, with a peak prevalence in adults aged 50 to 60[1]

First-line treatments include[5]

- **IVIG (intravenous immunoglobulin)**
- **Corticosteroids**
- **Plasma exchange**

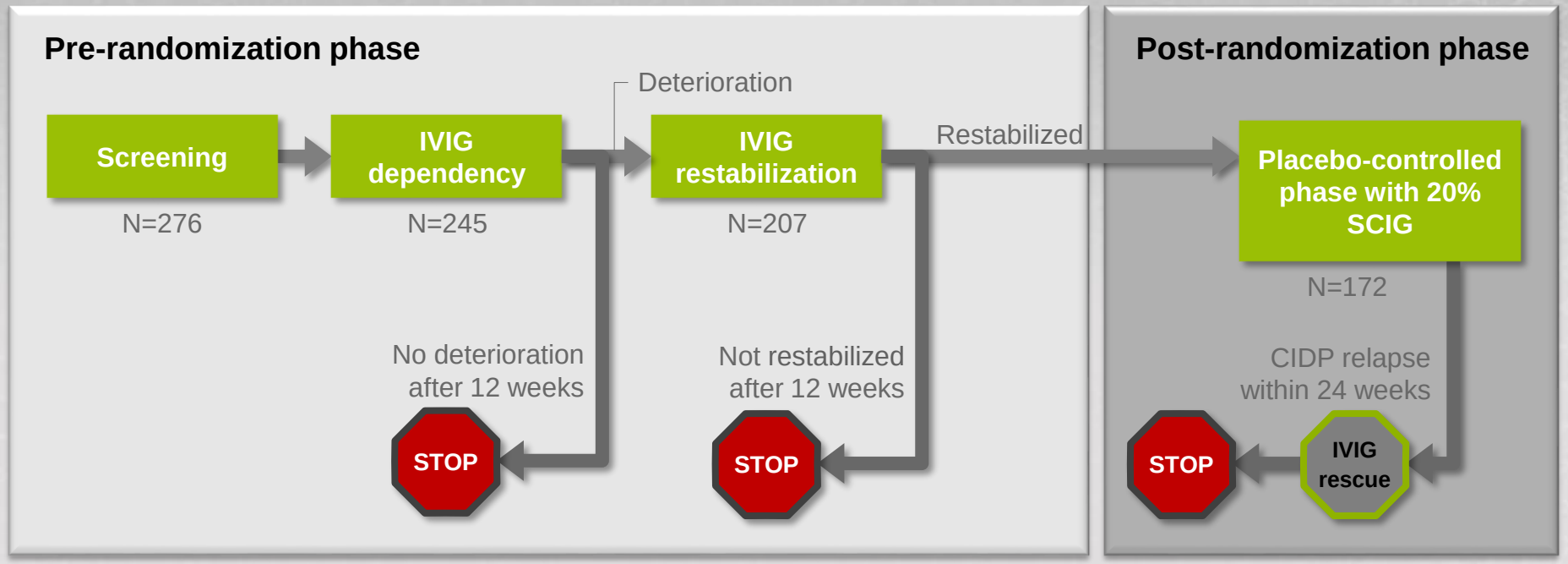
CIDP: chronic inflammatory demyelinating polyneuropathy; IVIG: intravenous immunoglobulin

1. Steinberg JS *et al*. A publication of the GBS/CIDP Foundation International 10th Edition, 2010. http://30g7el1b4b1n28kgpr414nuu-wpengine.netdna-ssl.com/wp-content/uploads/2012/01/OverviewENG.pdf. Accessed Sept 2017; 2. Vallat JM *et al*. Lancet Neurol. 2010;9(4):402–412; 3. Iijima M *et al*. J Neurol Neurosurg Psychiatry. 2008;79(9):1040–1043; 4. Laughlin RS *et al*. Neurology. 2009;73(1):39–45; 5. Oaklander AI *et al*. Cochrane Database Syst Rev. 2017, Issue 1. Art. No.: CD010369.

PATH Study: Restabilization Phase

PATH Study Design

A randomized, multicenter, double-blind, placebo-controlled, parallel-group, phase III study



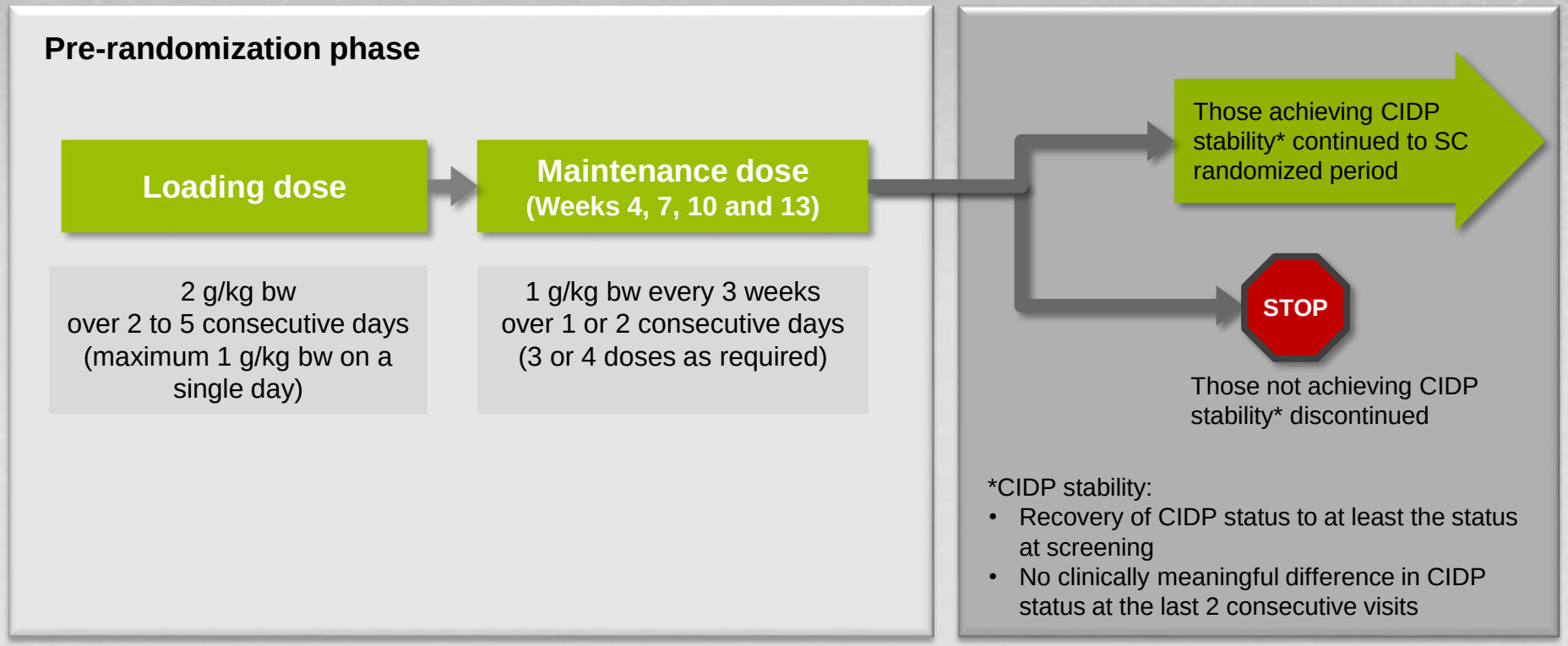
Inclusion criteria

- Definite or probable CIDP according to the EFNS/PNS criteria 2010[1]
- An IVIG treatment during the last 8 weeks prior to enrollment
- Age ≥18 years

CIDP: chronic inflammatory demyelinating polyneuropathy; EFNS: European Federation of Neurological Societies; IVIG: intravenous immunoglobulin; SCIG: subcutaneous immunoglobulin; PNS: Peripheral Nerve Society

1. Joint Task Force of the EFNS and the PNS. J Peripher Nerv Syst. 2010;15:185–195.

PATH IVIG Restabilization Phase[1,2]



bw: body weight; CIDP: chronic inflammatory demyelinating polyneuropathy; SC: subcutaneous

1. van Schaik IN *et al*. Lancet Neurol. 2017; In Press.

PATH Restabilization Phase Objectives[1]*

Primary Objective

- To investigate the efficacy of IVIG for restabilization of patients with CIDP

Secondary Objective

- To investigate the safety of IVIG for restabilization of patients with CIDP

Exploratory Objective

- To investigate serum IgG levels within the IVIG restabilization period

CIDP: chronic inflammatory demyelinating polyneuropathy; IgG: immunoglobulin G; IVIG: intravenous immunoglobulin
*All Data on file references will be updated upon publication of the PATH manuscript

1. CSL Behring Data on file.

Secondary Endpoint Efficacy Assessments[1]

Adjusted INCAT Score*	10-point score assessing functionality of legs and arms Arm disability: 0 “no upper limb problems’ to 5 ‘inability to use either arm for any purposeful movement” Leg disability: 0 “walking not affected’ to 5 ‘restricted to wheelchair, unable to stand and walk a few steps with help”’
MRC Sum Score	Sum of 8 muscle group scores Grades muscle movement from 0 ‘no visible contraction’ to 5 ‘normal’
Mean Grip Strength	Grip strength measured by Martin Vigorimeter
R-ODS Centile Score	24-item questionnaire capturing activity and social participation

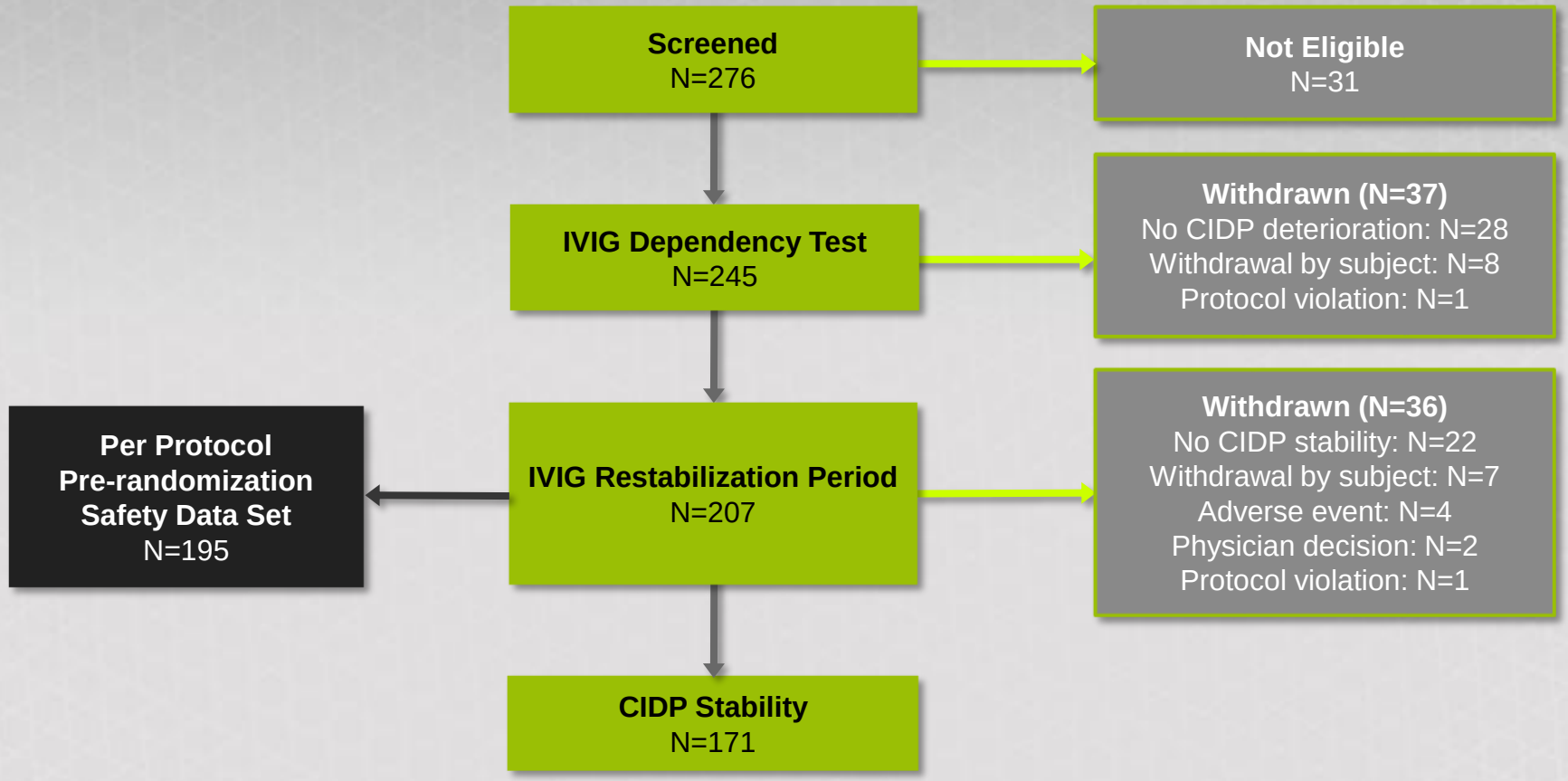
- Improvement: ≥1 point decrease in adjusted INCAT score*, ≥3 point increase in MRC sum score, ≥8 kPa increase in mean grip strength, or ≥4 point increase in R-ODS centile score

*Adjusted INCAT score: changes in upper limb function from 0 to 1 or 1 to 0 were not recorded as deterioration or improvement

INCAT: Inflammatory Neuropathy Cause and Treatment; MRC: Medical Research Council; R-ODS: Rasch-built Overall Disability Scale

1. van Schaik IN *et al*. Lancet Neurol. 2017; In Press.

PATH Patient Disposition[1]



CIDP: chronic inflammatory demyelinating polyneuropathy; IVIG: intravenous immunoglobulin

1. Mielke O *et al*. Poster and abstract presented at Annual Meeting of the Peripheral Nerve Society (PNS); July 8-12, 2017; Sitges, Spain.

Patient Demographics: IVIG Restabilization Period[1]

	Overall N=207
Age, years	56.5 (12.8)
Sex, N (%)	
Male / Female	131 (63.3) / 76 (36.7)
Race, N (%)	
White	186 (89.9)
Asian	17 (8.2)
Other	4 (1.9)
Weight (at screening), kg	82.2 (18.3)
BMI, kg/m^2	27.3 (5.0)
Time since initial CIDP diagnosis, years	4.66 (5.2)
EFNS/PNS CIDP diagnostic criteria, N (%)	
Definite	185 (89.4)
Probable	22 (10.6)
Screening INCAT total score	2.7 (1.67)

Values are mean (standard deviation) unless otherwise stated

BMI: body mass index; CIDP: chronic inflammatory demyelinating polyneuropathy;
EFNS: European Federation of Neurological Societies;
INCAT: Inflammatory Neuropathy Cause and Treatment; IVIG: intravenous immunoglobulin;
PNS: Peripheral Nerve Society

1. CSL Behring Data on file.

Efficacy: IVIG Restabilization Period

- 91% of patients with improvement in ≥1 outcome measure[1]
- 83% of patients achieved CIDP stability[1]
- 73% of patients achieved CIDP improvement by adjusted INCAT score[1]
  - 21% of patients improved beyond their CIDP status at study entry[2]

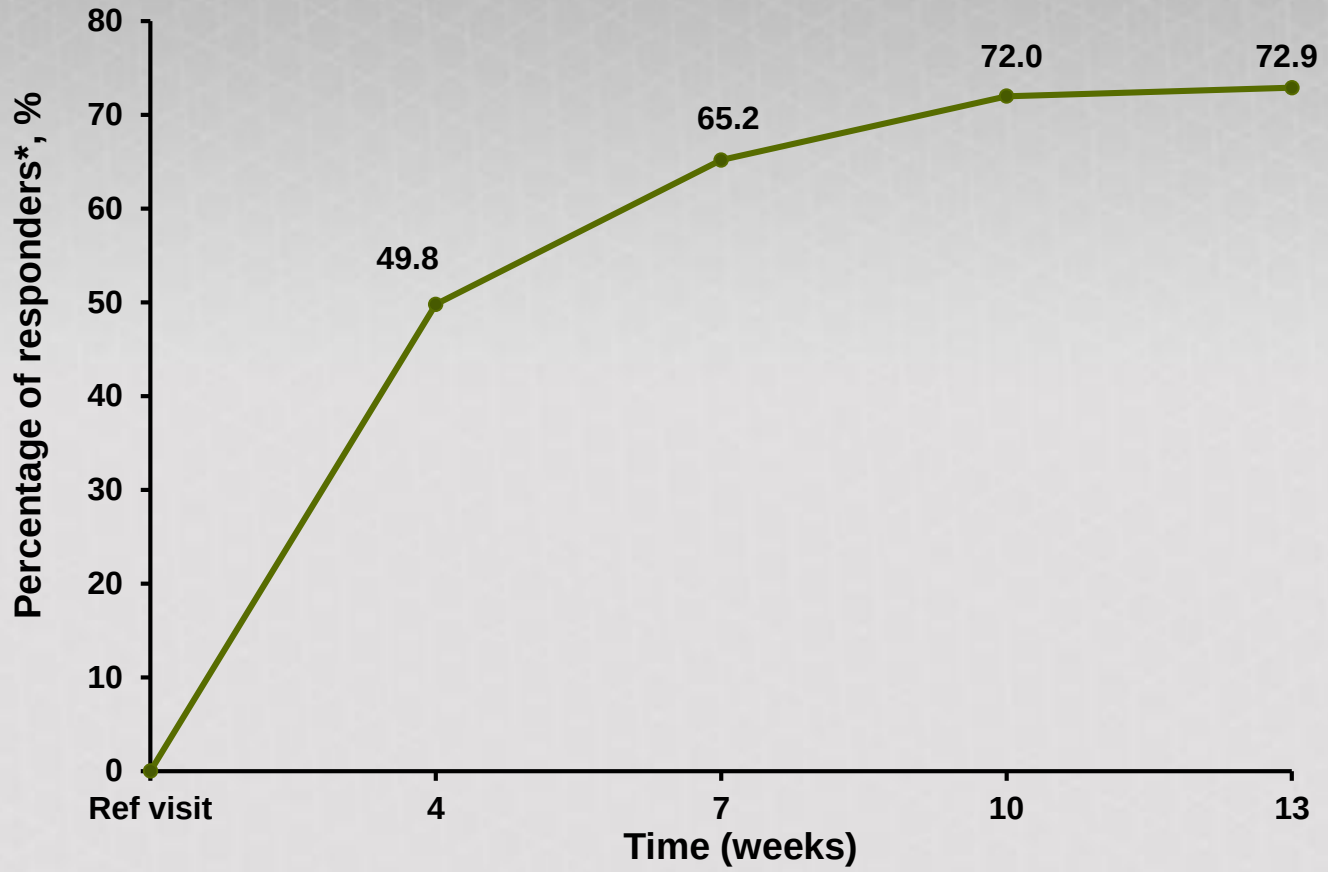
	Overall N=207				
	Adjusted INCAT Score*	**R-ODS Centile Score**	**Mean Grip Strength, Dominant Hand**	**MRC Sum Score**	**First Improvement in Any Criteria**
Number of events (improvements), N (%)	151 (72.9)	84 (40.6)	123 (59.4)	117 (56.5)	188 (90.8)
Time to first improvement, days					
Median	26.0	71.0	65.0	65.0	23.0
95% CI	24.0–41.0	66.0–86.0	64.0–66.0	64.0–67.0	22.0–23.0

*Adjusted INCAT score: changes in upper limb function from 0 to 1 or 1 to 0 were not recorded as deterioration or improvement

CIDP: chronic inflammatory demyelinating polyneuropathy; INCAT: Inflammatory Neuropathy Cause and Treatment; IVIG: intravenous immunoglobulin; MRC: Medical Research Council; R-ODS: Rasch-built Overall Disability Scale

1. Mielke O *et al*. Poster and abstract presented at Annual Meeting of the Peripheral Nerve Society (PNS); July 8-12, 2017; Sitges, Spain.
2. CSL Behring Data on file.

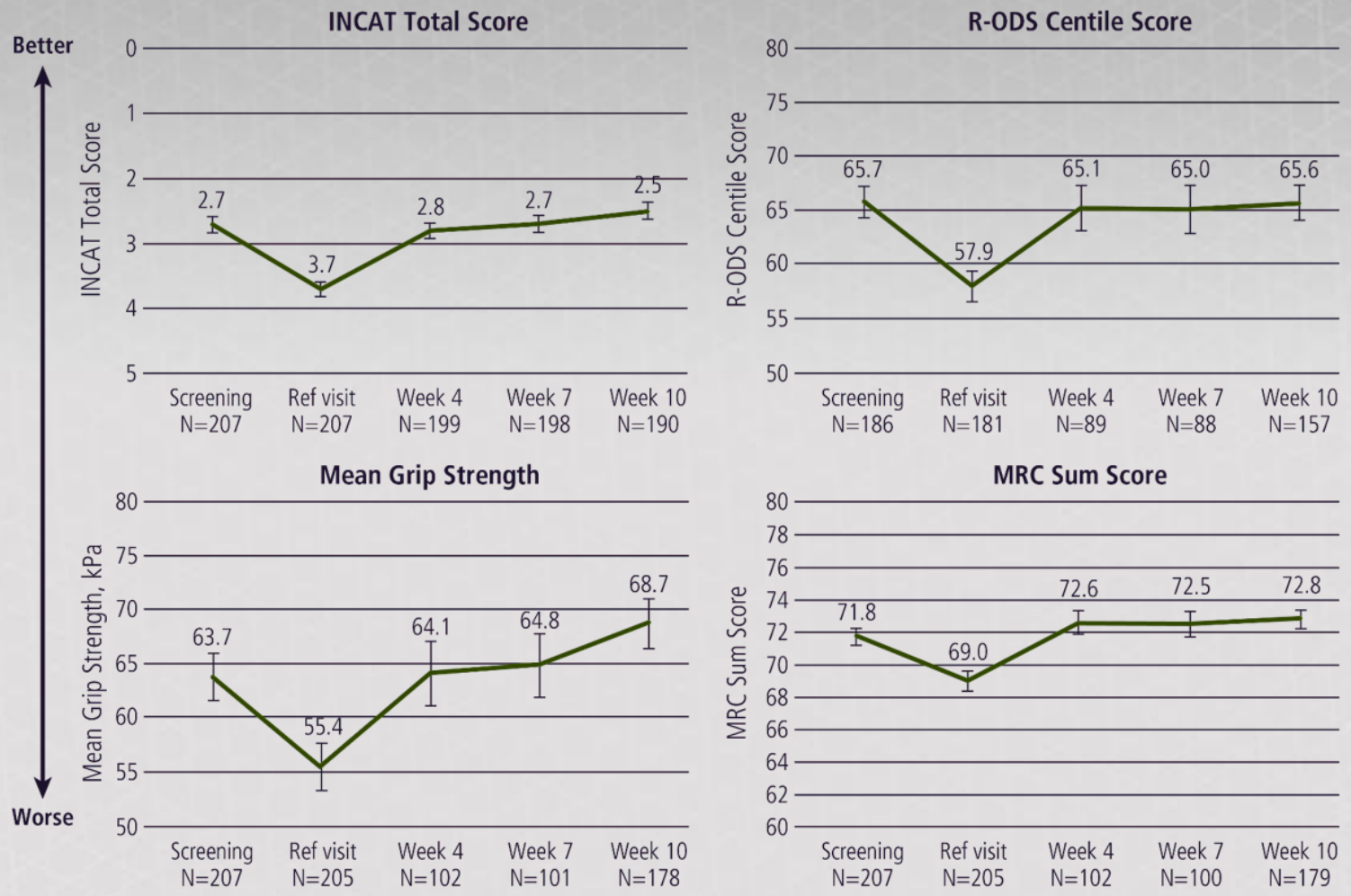
Percentage of Responders in IVIG Restabilization Period[1]



*Responders = improvement in terms of ≥ 1 point in adjusted INCAT score
Changes in upper limb function from 1 to 0 were not recorded as improvement. Mean baseline adjusted INCAT score: 2.7
INCAT: Inflammatory Neuropathy Cause and Treatment; IVIG: intravenous immunoglobulin

1. CSL Behring Data on file.

PATH Study: Restabilization with IVIG[1]



INCAT: Inflammatory Neuropathy Cause and Treatment; MRC: Medical Research Council; IVIG: intravenous immunoglobulin; R-ODS: Rasch-built Overall Disability Scale

1. Mielke O *et al*. Poster and abstract presented at Annual Meeting of the Peripheral Nerve Society (PNS); July 8-12, 2017; Sitges, Spain.

PATH Study: IVIG Efficacy Overview

- 91% of patients improved in ≥1 predefined outcome measure[1]
- 21% of patients improved CIDP status beyond that at study entry[2]
- CIDP status improved rapidly after treatment with IVIG[1]
  - Median 23 days to improvement in ≥1 outcome measure
- 83% of patients achieved CIDP stability with IVIG[1]
- All efficacy outcome measures showed clinically relevant improvements during the Restabilization Period[1]
  - 1.2 points in INCAT score
  - 5.7 points in R-ODS
  - 12.15 kPa in mean grip strength (dominant hand)
  - 3.6 points in MRC sum score

CIDP: chronic inflammatory demyelinating polyneuropathy; INCAT: Inflammatory Neuropathy Cause and Treatment; IVIG: intravenous immunoglobulin; MRC: Medical Research Council; R-ODS: Rasch-built Overall Disability Score

1. Mielke O et al. Poster and abstract presented at Annual Meeting of the Peripheral Nerve Society (PNS); July 8-12, 2017; Sitges, Spain.
2. CSL Behring Data on file.

PATH Study: Adverse Events in IVIG Restabilization Period[1,2]

Preferred term	Patients, N (%)	Number of AEs	Rate per Infusion
TOTAL	**100 (48.3)**	**284**	**0.175**
Headache	34 (16.4)	53	0.033
Nasopharyngitis	12 (5.8)	12	0.007

AEs reported in ≥5% of subjects are listed

- 57 (27.5%) patients experienced an AE considered related to IVIG
- 11 (5.3%) patients experienced a serious AE[1]
- 4 (1.9%) patients withdrew as a result of an AE[1]

AE: adverse event; IVIG: intravenous immunoglobulin

1. CSL Behring Data on file.
2. Mielke O et al. Poster and abstract presented at Annual Meeting of the Peripheral Nerve Society (PNS); July 8-12, 2017; Sitges, Spain.

PATH Study: IVIG Safety Overview[1]

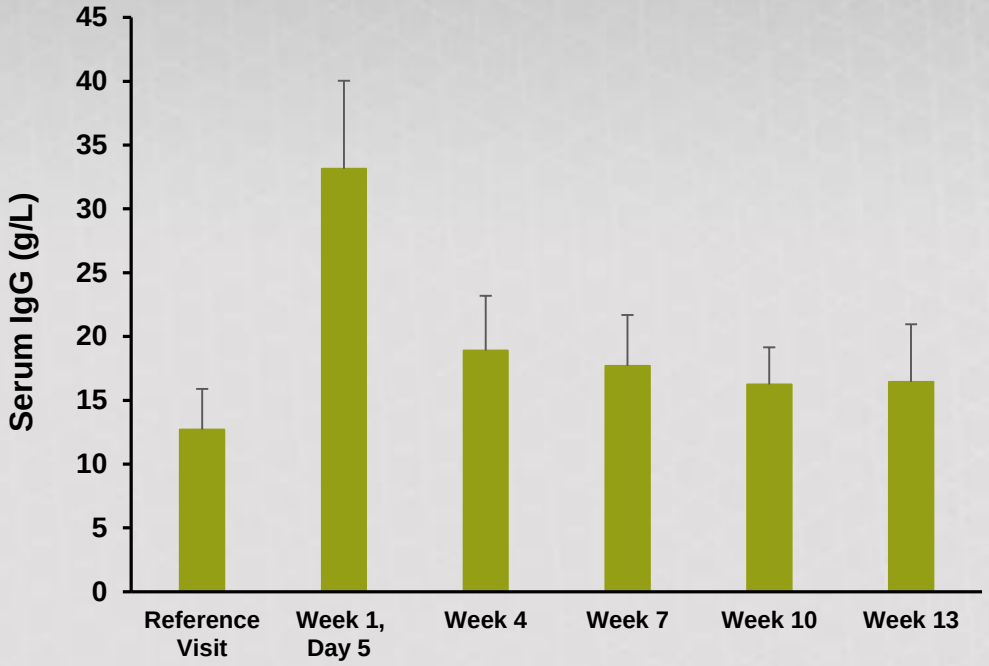
- Mean (range) duration of exposure: 65.9 (2–100) days[1]
- Mean (range) number of infusions: 7.8 (2–13)[1]
- 100 (48.3%) patients experienced an AE, 27.5% experienced an AE considered related to IVIG[2]
  - The majority were mild or moderate
- 11 (5.3%) patients experienced a serious AE[1]
  - 7 serious AEs were considered related to IVIG: hypersensitivity; pulmonary embolism; increased blood pressure; exacerbation of CIDP; respiratory failure; rash; migraine
  - All serious AEs resolved without sequelae
- 4 patients withdrew as a result of an AE[2]
- Hemolysis was seen in 3.4% of patients, most did not present with clinical symptoms and no subjects required clinical intervention (no serious AEs)[1]

AE: adverse event; CIDP: chronic inflammatory demyelinating polyneuropathy; IVIG: intravenous immunoglobulin

1. CSL Behring Data on file.
2. Mielke O et al. Poster and abstract presented at Annual Meeting of the Peripheral Nerve Society (PNS); July 8-12, 2017; Sitges, Spain.

PATH Study: Pre-infusion IgG Levels During the Restabilization Period[1]

- Following the IVIG loading dose, the mean increase in serum IgG levels was 19.3 g/L
- At Week 4, before the first maintenance dose, IgG levels had decreased to a level above that at the Reference Visit



IgG: immunoglobulin G; IVIG: intravenous immunoglobulin

1. CSL Behring Data on file.

PATH Study: IVIG Conclusions

IVIG reduces disability in patients with CIDP by improving neuromuscular disability after previous clinical deterioration

IVIG demonstrated clinically relevant improvements in a variety of clinical outcome measures: a rapid response to therapy, CIDP stability, and improvement even beyond the CIDP status at study entry

IVIG was well tolerated when administered as loading and maintenance intravenous infusions

CIDP: chronic inflammatory demyelinating polyneuropathy; IVIG: intravenous immunoglobulin