CSL Behring

Immunoglobulin Therapy for Chronic Inflammatory Demyelinating Polyneuropathy: Synopsis of PRIMA, PATH, and PATH-OLE Studies

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HIGHLIGHTS

- PRIMA study showed that immunoglobulin therapy is effective and well tolerated up to 24 weeks as CIDP maintenance treatment
- PATH and PATH-OLE studies validate these outcomes with 48-week data
- Maintenance immunoglobulin **doses should be individualized based on the patient's situation and need for treatment continuity**

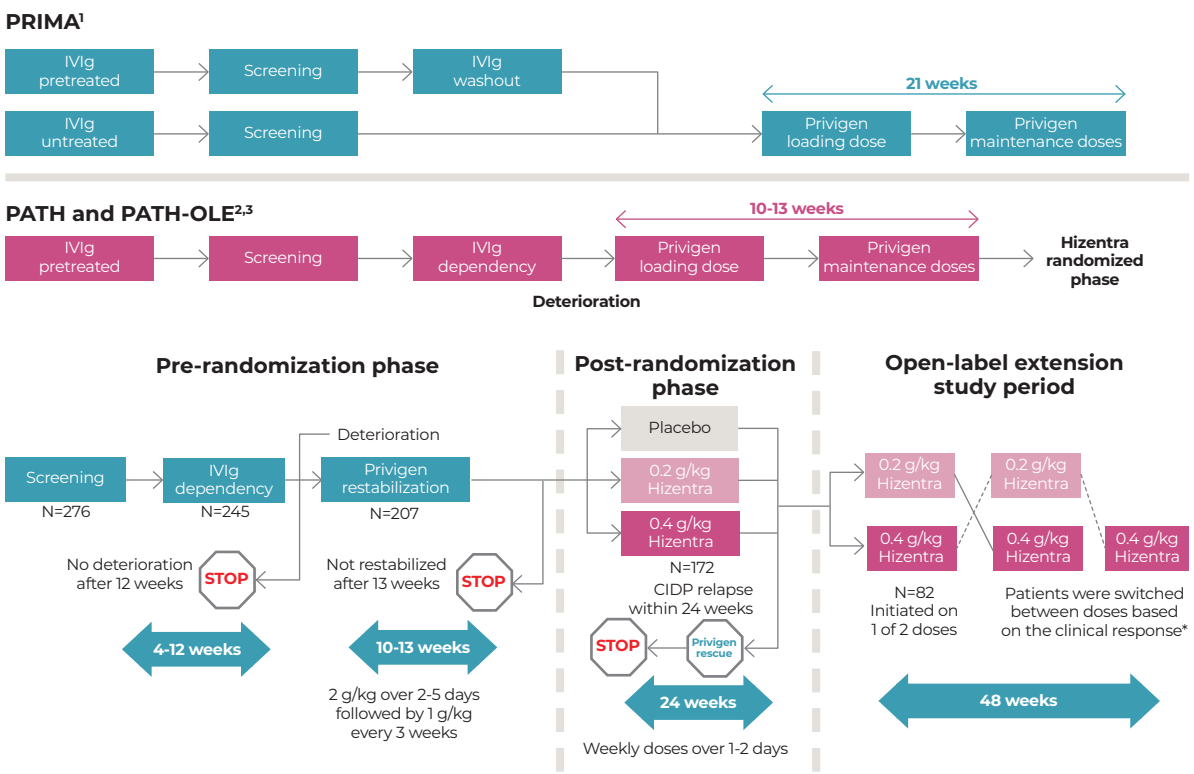
INTRODUCTION

Chronic inflammatory demyelinating polyneuropathy (CIDP) is an acquired neurological disorder **characterized by symmetric, progressive weakness, impaired limb function, and a reduced QoL**

PRIMA and PATH studies were conducted to **confirm the efficacy and safety of immunoglobulin therapy for the treatment of adult CIDP patients**

STUDY CHARACTERISTICS

Figure 1. Study overview (PRIMA, PATH, and PATH-OLE)[1-3]



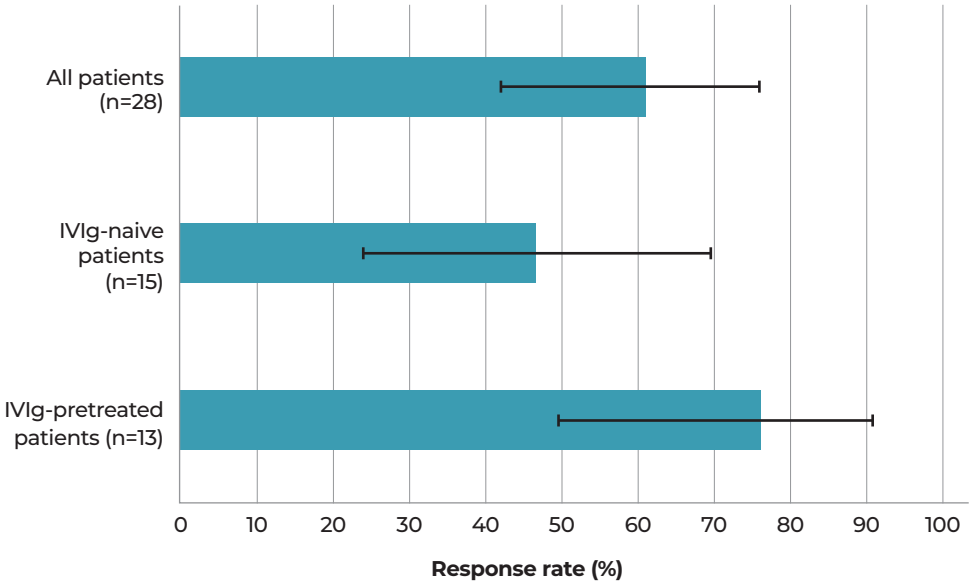
	PRIMA[1]	PATH[2]	PATH-OLE[3]
Objective	Efficacy and safety of IVIg for induction and maintenance	Efficacy and safety of SCIg for maintenance treatment	
Phase 3 study design	Multicenter, single-arm, open-label	Multicenter, randomized, double-blind, placebo-controlled	Open-label extension (OLE) study
Patient population	≥18 years of age with CIDP†		
Dosing	Induction: IVIg 2 g/kg bw over 2-5 consecutive days Maintenance: 1 g/kg bw at 3-week intervals (~7 doses)	Weekly SCIg (0.2 g/kg or 0.4 g/kg) or placebo	Weekly SCIg (0.2 g/kg or 0.4 g/kg)
Primary endpoint	Responder‡ rate based on the adjusted INCAT score	Proportion of patients who had a CIDP relapse§ or were withdrawn for any reason during SCIg treatment	Long-term safety of SCIg in CIDP patients
Key secondary endpoints‖	Mean grip strength (dominant hand), MRC sum score		

*Patients who relapsed on 0.2 g/kg (low-dose) SCIg were given the option to switch to 0.4 g/kg (high-dose) SCIg or discontinue. Patients who relapsed on 0.4 g/kg SCIg were given the option to remain on the same or be discontinued depending on the patient and investigator's judgment.
†Patients with definite or probable CIDP diagnosis according to EFNS/PNS 2010 criteria.
‡Responders were defined as patients with a clinically meaningful improvement (decrease of ≥1 point in the adjusted INCAT score) between baseline and completion at Week 25 or the last study visit in case of premature discontinuation.
§Relapse was defined as a deterioration (ie, increase) by at least 1 point in the total adjusted INCAT score (range 0 [healthy] to 10 [unable to make any purposeful movements with arms or legs]) at any subcutaneous treatment period visit compared with baseline. Baseline scores were defined as the scores assessed at the end of the IVIg restabilization period.
‖Other secondary endpoints were assessed during the studies.
¶MRC sum score: range 0-80; including shoulder abduction, elbow flexion, wrist extension, index finger abduction, hip flexion, knee extension, foot dorsiflexion, and great toe dorsiflexion.

RESULTS – PRIMA

Response rate

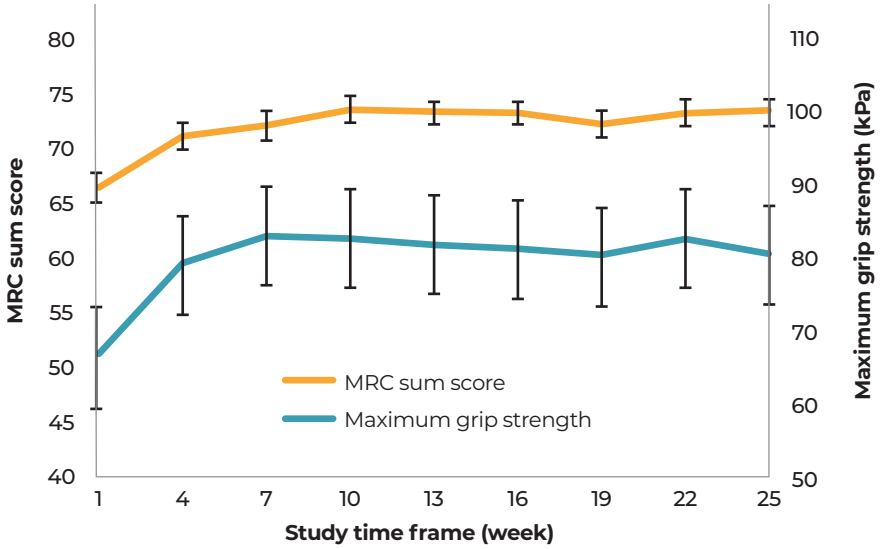
Figure 2. Response rate (%) based on the adjusted INCAT score at study completion[1,*]



*The proportion of responders at completion are shown from the intention-to-treat analysis. Last observation carried forward was used to replace missing values.

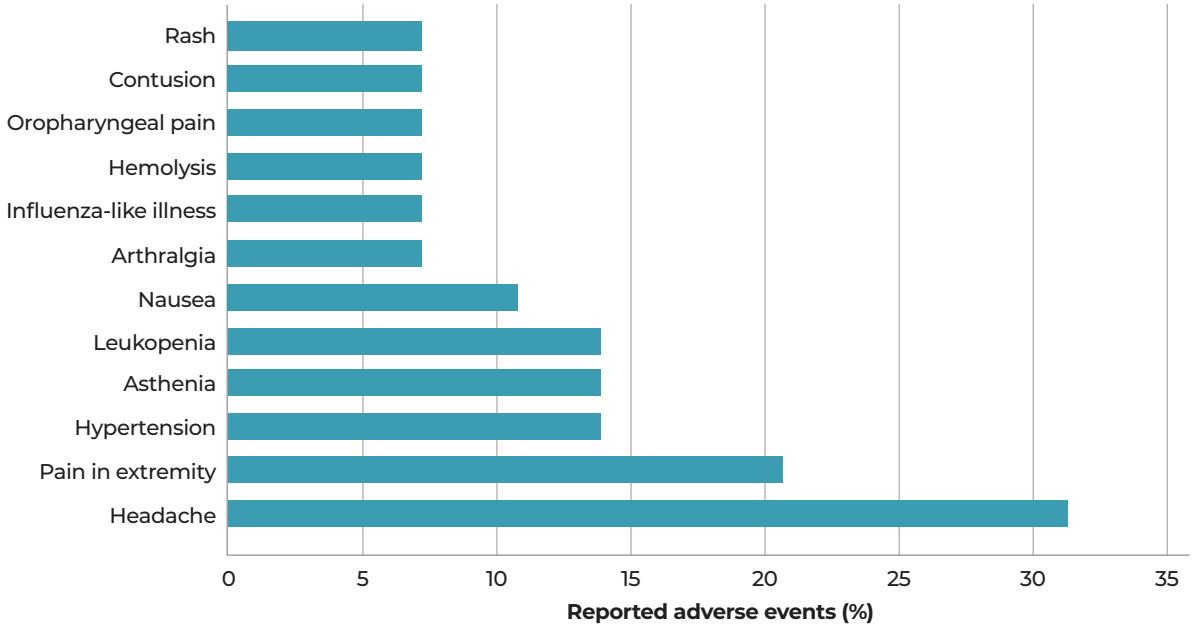
Key secondary endpoints

Figure 3. Maximum grip strength (dominant hand) and MRC sum score over time (intention-to-treat analysis)[1,*]



*Values for both are provided as means. Error bars represent the standard error of the mean.

Figure 4. Adverse events reported in ≥3.5% of PRIMA-enrolled patients (N=28, %)[1]

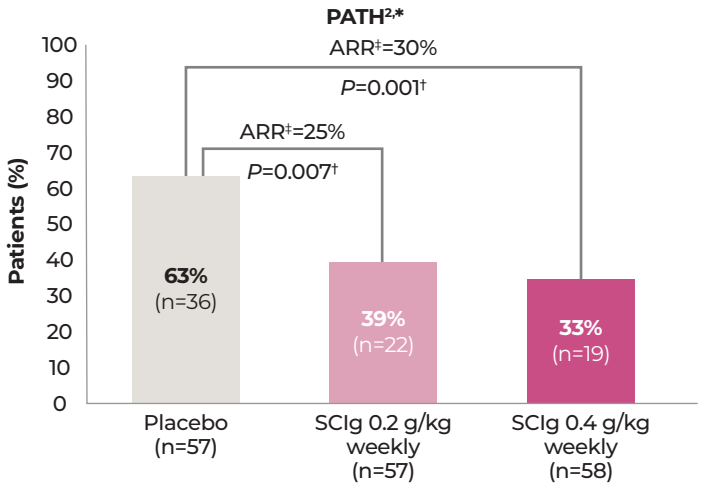


Two patients experienced treatment-related serious adverse events (SAEs): hemolysis at induction phase, which resolved with treatment discontinuation

RESULTS – PATH AND PATH-OLE

Relapse and relapse rate

Figure 5.

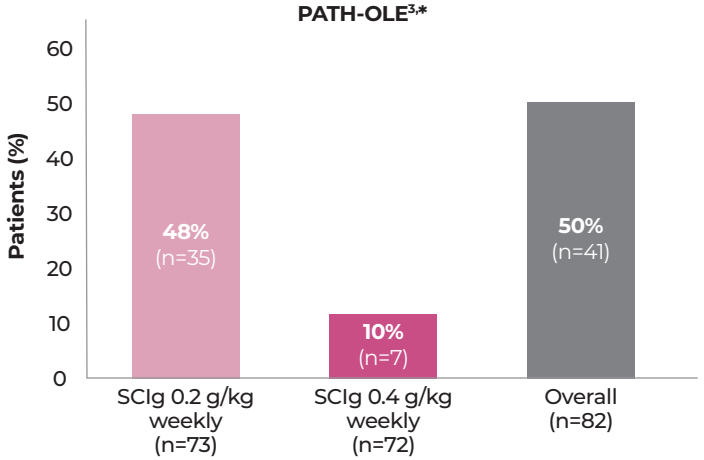


81% (47/58) and **67%** (38/57) of patients in the high-dose and low-dose groups, respectively, **remained relapse-free**

*Percentage (95% Wilson score CI) of patients who had a CIDP relapse during SCIg treatment or were withdrawn from the study during SCIg treatment for any reason.

†P-values determined by Fisher's exact test.

‡ARR=absolute risk reduction compared to placebo.



68% (19/28) who completed the PATH study without relapse **remained relapse-free** on the 0.2 g/kg dose after dose reduction in PATH-OLE

*These relapse rates refer to all subjects in the extension study, irrespective of treatment and status at the end of the PATH study. Status at the end of the PATH study (nonrelapser/relapser) was as defined by the primary endpoint. Due to the study design, the same subject could have received both doses during the study. ARR values are not provided in the PATH-OLE study.

Additional endpoints

Table. Change from baseline in grip strength (dominant hand) and MRC sum score[2,3]

PATH[2,*]

	Placebo (n=57)	SCIg 0.2 g/kg (n=57)	SCIg 0.4 g/kg (n=58)
Grip strength (dominant hand [kPa])	–6.6 (–21.6 to 0.3)	–0.6 (–8.9 to 7.0)	–2.7 (–6.6 to 2.0)
MRC sum score	–2.0 (–6.0 to 0.0)	0 (–2.0 to 2.0)	0 (–2.0 to 1.0)

*Other secondary endpoints were assessed during the PATH study. Data are median (IQR) or median (95% Moses CI).

In the PATH study, median changes in grip strength and MRC sum score in both groups were significantly **improved compared with placebo**

PATH-OLE[3,*]

	SCIg 0.2 g/kg (n=70)	SCIg 0.4 g/kg (n=70)	Overall (n=79)
Grip strength (dominant hand [kPa])	–3.7 (–71 to 21)	0.7 (–80 to 27)	0.7 (–80 to 27)
	SCIg 0.2 g/kg (n=70)	**SCIg 0.4 g/kg (n=69)**	**Overall (n=78)**
MRC sum score	-1.0 (–20 to 18)	0.0 (–23 to 19)	0.0 (–23 to 18)

*Other secondary endpoints were assessed during the PATH-OLE study. Data are median (IQR) or median (95% Moses CI) and based on overall numbers at the last post-dose observation.

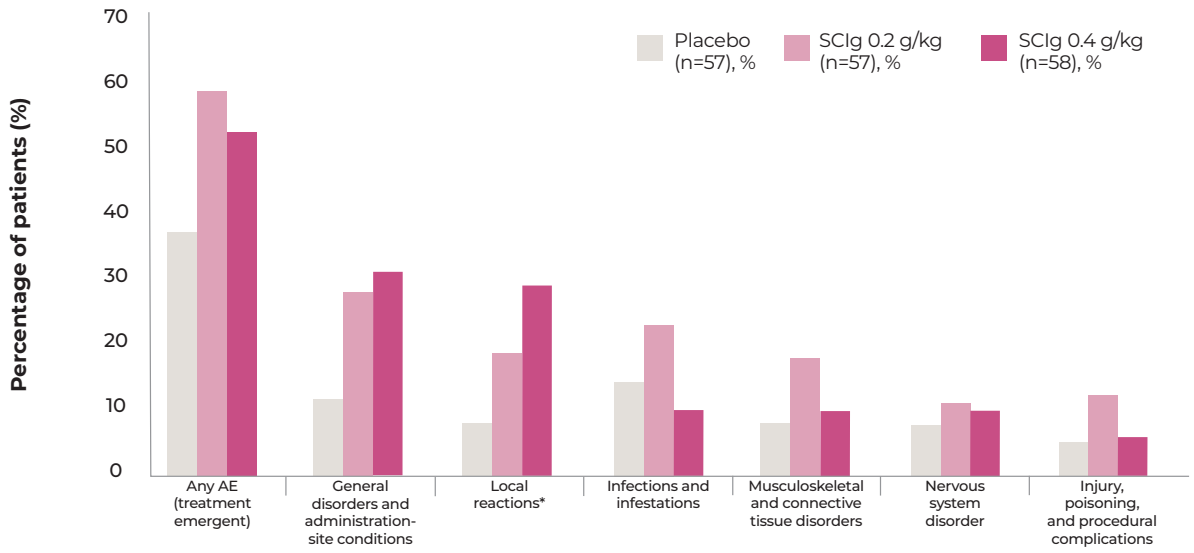
In the PATH-OLE study, median baseline scores were similiar, with significant deterioration observed for grip strength and MRC score in both groups during relapse

RESULTS – PATH AND PATH-OLE

Figure 6. Adverse events (AEs) (PATH and PATH-OLE)[2,3]

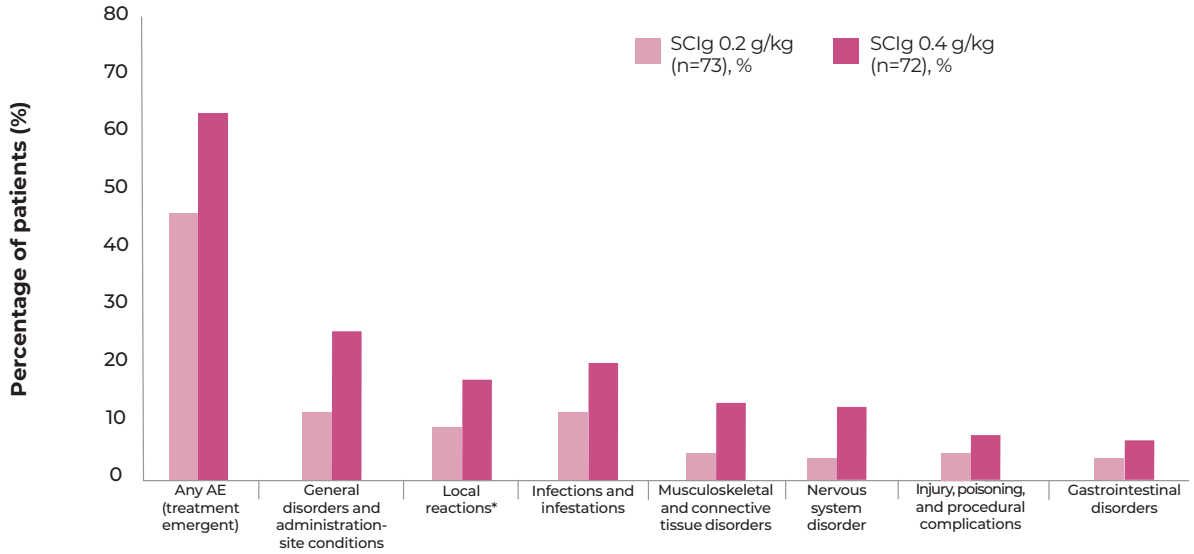
PATH

AEs in ≥5% of PATH subjects



PATH-OLE

AEs in ≥2% of PATH-OLE subjects



*This system organ class of local reactions included all AEs reported within the MedDRA high-level terms "Administration Site Reactions Not Elsewhere Classified," "Infusion Site Reactions," and "Injection Site Reactions."

Of the 11 SAEs reported in 3% of PATH-enrolled patients, **1 treatment-related allergic skin reaction occurred** in the low-dose group and led to treatment discontinuation

Majority of the AEs reported in the PATH-OLE study were **mild or moderate, with no related SAEs**

Abbreviations
AE: adverse event; ARR: absolute risk reduction; bw: body weight; CIDP: chronic inflammatory demyelinating polyneuropathy; EFNS/PNS: European Federation of Neurological Societies/Peripheral Nerve Society; INCAT: Inflammatory Neuropathy Cause and Treatment; IVIg: intravenous immunoglobulin; MedDRA: Medical Dictionary for Regulatory Activities; MRC: Medical Research Council; OLE: open-label extension; PATH: Polyneuropathy And Treatment with Hizentra; PRIMA: Privigen Impact on Mobility and Autonomy; QoL: quality of life; SAE: serious adverse event; SCIg: subcutaneous immunoglobulin.

References
1. Léger JM, De Bleecker JL, Sommer C, et al. *J Peripher Nerv Syst.* 2013;18(2):130-140.
2. van Schaik IN, Bril V, van Geloven N, et al. *Lancet Neurol.* 2018;17(1):35-46.
3. van Schaik IN, Mielke O, Bril V, et al. *Neurol Neuroimmunol Neuroinflamm.* 2019;6(5):e590.

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