A Comparison of the Effect of Subcutaneous Versus Intravenous Immunoglobulin Therapy on Quality of Life in Patients with Chronic Inflammatory Demyelinating Polyneuropathy

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Background

- Chronic inflammatory demyelinating polyneuropathy (CIDP) is an autoimmune neurological disorder that causes limb weakness and numbness
- The American Academy of Neurology (AAN) guidelines recommend immunoglobulin (IgG) therapy, administered as intravenous immunoglobulin (IVIG), for the long-term treatment of CIDP[1]
  - However, IVIG can result in systemic side effects in approximately 5% of patients
  - Many patients who are treated with long-term IVIG find that regular venous access can become a problem over time
  - An alternative administration route for IgG is as subcutaneous immunoglobulin (SCIG), which has been in use since the 1980s for primary immunodeficiency disorders

SCIG versus IVIG

- Compared with the intravenous route, SCIG offers a number of advantages including:[2]
  - Maintains higher trough levels of IgG
  - Reduced systemic side effects
  - Increased patient independence
  - No requirement for venous access
  - Better tolerated by those who are pregnant or sensitized to IgA
- SCIG can also be self-administered which may reduce overall treatment costs
- Disadvantages of SCIG include more frequent infusions and an increase in local reactions at the site of infusion in some patients
- Within the last decade, there have been several small studies in patients with CIDP being treated with SCIG[3-7]
  - Generally, SCIG was reported as well tolerated with a similar efficacy to IVIG and demonstrated an overall increase in patient satisfaction and quality of life (QOL)
- More recently, the PATH study demonstrated that SCIG was an effective alternative option for patients with CIDP requiring maintenance IgG therapy[8]
- Here, we present a study of patients with CIDP transitioning from IVIG to SCIG and monitored over 6 months with a focus on QOL and the barriers experienced as they transitioned

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Objectives

- To test the hypothesis that patients with CIDP experience higher QOL following transition from IVIG to SCIG
- To demonstrate that SCIG is safe and well tolerated in patients with CIDP with a comparable efficacy to IVIG

Methods

- This was a prospective, open-label, crossover study of SCIG in the treatment of subjects with CIDP dependent on IVIG for control of symptoms
- SCIG was initiated within 2 weeks of the last IVIG infusion and was administered weekly for 24 weeks using a 20% immunoglobulin solution (Hizentra®, CSL Behring AG)
  - A 1:1 conversion ratio for IV to SC was used to calculate the SCIG weekly dose
  - SCIG was infused simultaneously at multiple sites in the abdomen, flanks, arms, or thighs
  - The volume per infusion site was 35 mL (7 g) at a rate of 20–25 mL/hr/site or as tolerated
  - Subjects were trained to perform their own infusions

Surveys and Assessments

- QOL was assessed using the Medical Outcome Study 36-item short form (SF-36), and the Rasch-built Overall Disability Scale (R-ODS)
- The Treatment Satisfaction Questionnaire for Medication (TSQM) and the Chronic Immune-mediated Polyneuropathy – Patient Reported Outcome (CIP-PRO 20) scale were used to assess side effects and treatment satisfaction
- To assess safety and tolerability, subjects received regular neurological and physical examinations and were monitored by laboratory studies, electrocardiogram (ECG), and side effect questionnaires
- To monitor efficacy of SCIG, hand-held dynamometry (HHD) measures and 20-ft timed walks were captured pre- and post- each SCIG infusion
  - HHD measured the force generated by a variety of muscle groups including shoulder flexion, elbow flexion, wrist extension and first dorsal interosseous (hand)
- Baseline values (final IVIG infusion) were compared with monthly measures (during the SCIG treatment period) to determine the impact of SCIG on QOL
- An IVIG rescue protocol was in place to treat relapses (defined as a 20% decrease in force by HHD in more than 50% of the muscles tested compared with baseline)

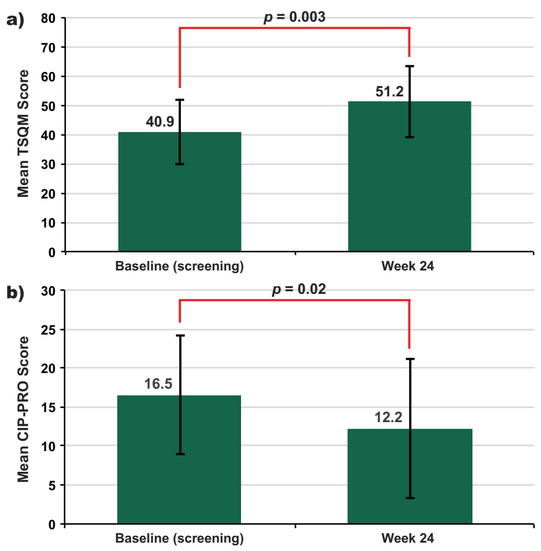
Results

- Of 23 screened subjects with CIDP, 15 were enrolled to receive weekly SCIG
- 12 subjects completed the study and 3 withdrew (1 did not perceive benefit, 1 discontinued the study early due to neutropenia and 1 was lost to follow up)
- Of the 12 subjects who completed the study:
  - 8 chose to stay on SCIG
  - 2 returned to IVIG (due to insurance coverage issues)
  - 2 chose to stop IgG treatment to review their IgG dependency (these subjects were doing well at the time of IgG withdrawal)

QOL Outcome Measures

- There were statistically significant changes between baseline and Week 24 for both the TSQM **(Figure 1)** and CIP-PRO 20 **(Figure 2)**
  - There were no statistically significant changes in R-ODS scores (p = 0.32)

Figure 1: TSQM (a) and CIP-PRO 20 Score (b)



Error bars represent standard deviation. TSQM, Treatment Satisfaction Questionnaire for Medication; CIP-PRO, Chronic Immune-mediated Polyneuropathy – Patient Reported Outcome

- The increase in TSQM score indicates improved satisfaction with treatment, which takes into account ease of use, planning, side effects, infusion frequency, and mental/physical function
- The decrease in CIP-PRO 20 score indicates improved patient-reported functionality, activity, and mental state

Efficacy Outcome Measures

- There were no statistically significant changes over time for the 20-ft walk test or any of the HHD parameters (p-value range = 0.10–0.99) **(Table 1)**
  - This reflects the comparable efficacy of IVIG and SCIG in CIDP maintenance

Table 1: Efficacy Outcome Measures

	N	Screening Mean ± SD	Week 24* Mean ± SD	Change Mean (95% CI)	P-value
HHD Measures (lbs)					
Shoulder Flexion L	14	35.4 ± 12.6	36.7 ± 10.9	1.3 (-4.1, 6.8)	0.60
Shoulder Flexion R	14	37.2 ± 15.0	37.2 ± 14.0	0.0 (-5.2, 5.1)	0.99
Elbow Flexion L	14	43.4 ± 15.3	39.2 ± 11.9	-4.1 (-10.1, 1.8)	0.16
Elbow Flexion R	14	42.1 ± 12.5	39.8 ± 11.6	-2.4 (-6.9, 2.1)	0.27
Wrist Extension L	13	23.0 ± 12.3	23.8 ± 10.4	0.8 (-4.1, 5.6)	0.73
Wrist Extension R	14	24.2 ± 11.5	28.3 ± 12.6	4.1 (-1.4, 9.5)	0.13
FDI L(*)	13	6.6 [4.5, 10.3]	7.7 [4.1, 10.0]	0.5 [-2.2, 1.6]	0.92
FDI R(*)	14	9.2 [5.1, 11.4]	8.5 [5.7, 10.0]	-0.1 [-1.6, 0.6]	0.40
20-ft walk test (sec)	15	9.2 ± 6.0	8.1 ± 8.3	-1.0 (-2.9, 0.8)	0.24

HHD, hand-held dynamometry; N, number of subjects; SD, standard deviation; CI, confidence interval; R-ODS, Rasch-built Overall Disability Scale; L, left; R, right; FDI, first dorsal interosseous.
(*) Observed value at 24 weeks, or last observation carried forward if no observed value
(*) Median [inter-quartile range] reported, along with median difference [95% CI]. Analysis using Wilcoxon matched-pairs test

Conclusions

- SCIG was associated with improved QOL; changes in the TSQM and CIP-PRO 20 reflected improved functionality, activity and mental state
- SCIG appeared as efficacious as IVIG in this study
- SCIG was well tolerated and the majority of subjects opted to remain on SCIG at the conclusion of the study

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